Critical Care Volume 7 Suppl 2, 2003

23rd International Symposium on Intensive Care and Emergency Medicine

Brussels, Belgium, 18–21 March 2003

Published online: 3 March 2003
This article is online at http://ccforum.com/supplements/7/S2

P1 Endocrine dysfunction in the immediate period following traumatic brain injury

I Dimopoulou, S Tsagarakis, G Assithianakis, M Christoforaki, M Theodorakopoulou, A Kouyialis, S Korfias, N Thalassinos, C Roussos
Department of Critical Care Medicine and Department of Endocrinology, Evangelismos Hospital, Athens, Greece
Critical Care 2003, **7(Suppl 2)**:P001 (DOI 10.1186/cc1890)

Studies on head injury-induced pituitary dysfunction are limited in number and conflicting results have been reported. To further clarify this issue, 29 consecutive patients (24 males), with severe ($n=21$) or moderate ($n=8$) head trauma, having a mean age of 37 ± 17 years were investigated in the immediate post-trauma period. All patients required mechanical ventilatory support for 8–55 days and were enrolled in the study within a few days before ICU discharge. Basal hormonal assessment included measurement of cortisol, corticotropin, free thyroxine (fT4), thyrotropin (TSH), testosterone (T) in men, estradiol (E2) in women, prolactin (PRL), and growth hormone (GH). Cortisol and GH levels were measured also after stimulation with 100 μg human corticotropin releasing hormone (hCRH) and 100 μg growth hormone releasing hormone (GHRH), respectively. Cortisol hyporesponsiveness was considered when peak cortisol concentration was less than 20 μg/dl following hCRH. TSH deficiency was diagnosed when a subnormal serum fT4 level was associated with a normal or low TSH. Hypogonadism was considered when T (males) or E2 (women) were below the local reference ranges, in the presence of normal PRL levels. Severe or partial GH deficiencies were defined as a peak GH below 3 μg/l or between 3 and 5 μg/l, respectively, after stimulation with GHRH. Twenty-one subnormal responses were found in 15 of the 29 patients (52%) tested; seven (24%) had hypogonadism, seven (24%) had cortisol hyporesponsiveness, five (17%) had hypothyroidism, and two patients (7%) had partial GH deficiency.

These preliminary results suggest that a certain degree of hypopituitarism occurs in more than 50% of patients with moderate or severe head injury in the immediate post-trauma period, with cortisol hyporesponsiveness and hypogonadism being most common. Further studies are required to elucidate the pathogenesis of these abnormalities and to investigate whether they affect long-term morbidity.

P2 Cortisol reserve in head trauma victims: evaluation with the low-dose (1 μg) corticotropin (ACTH) stimulation test

I Dimopoulou, A Kouyialis, S Tsagarakis, M Theodorakopoulou, G Assithianakis, M Christoforaki, N Thalassinos, C Roussos
Department of Critical Care Medicine and Department of Endocrinology, Evangelismos Hospital, Athens, Greece
Critical Care 2003, **7(Suppl 2)**:P002 (DOI 10.1186/cc1891)

To investigate cortisol reserve in head trauma, 35 consecutive patients (30 men) with a mean age of 36 ± 16 years were studied 5–60 days after physical injury. Patients were enrolled in the study within a few days before ICU discharge. First, a morning blood sample was obtained to measure baseline cortisol, and ACTH plasma levels. Subsequently, 1 μg synthetic ACTH was injected intravenously and, 30 min later, a second blood sample was drawn to determine stimulated plasma cortisol. Patients having stimulated cortisol levels below 18 μg/dl were defined as nonresponders to the low-dose stimulation test (LDST). Mean (± SD) values for ACTH, baseline, and stimulated cortisol concentrations were 49 ± 27 pg/ml, 19.7 ± 5.5 μg/dl and 23.6 ± 6.7 μg/dl, respectively. Six of the 35 patients (17%) failed the LDST. Nonresponders were similar to responders with regard to age, gender, and severity of head injury. However, nonresponders more frequently required vasopressors (6/6 vs 14/29, $P=0.02$) and for a longer time interval (median, 293 hours vs 24 hours, $P=0.01$) to maintain haemodynamic stability compared with responders to the LDST.

In conclusion, adrenal cortisol secretion following dynamic stimulation is deficient in a subset of head injury patients; this condition is associated with vasopressor dependency.

P3 Steroid hormone synthesis is impaired in patients with severe sepsis

M Angstwurm, A Rashidi Kia, J Schopohl, R Gaertner
Medical Intensive Care Unit, Medizinische Klinik, Ziemssenstraße 1, 80336 Munich, Germany
Critical Care 2003, **7(Suppl 2)**:P003 (DOI 10.1186/cc1892)

In patients with severe illness, adrenal insufficiency is often suspected and treatment with hydrocortisone has been shown to decrease mortality. However, the pathophysiology of an adrenal failure is only partially understood.

We analyzed the synthesis of different steroid hormones within the adrenal in severely ill patients in a prospective study using the established high dose stimulation test with synthetic cosyntropin.

Using commercially available essays, the steroid hormones progesterone, cortisole, testosterone, dehydroepiandrostenedione (DHEAS) and 17β-estradiol were determined before, and 30 and 60 min after stimulation with cosyntropin. Patients were characterized by scoring systems (APACHE II, SAPS II, MOD score). The underlying admission diagnosis grouped patients in septic, cardiogenic shock or control.

Sixty-five patients (22 in cardiogenic and 43 in septic shock, five and nine women, mean age 58 years, APACHE score of 20) were compared with 34 control patients (17 cancer patients, 10 healthy, four pulmonary emphysema and three other).

At baseline, septic and cardiogenic patients showed similar cortisol levels (21 and 21 μg/dl), higher than control (15 μg/dl, $P<0.05$). Progesterone was increased fourfold ($P<0.001$) in septic (1.2 ng/ml) and cardiogenic shock (1.1 ng/ml) compared with control (0.3 ng/ml). Men with sepsis had the highest β-estradiol levels. Baseline cortisol levels were only slightly higher in intensive care patients compared with control. There were no clear correlations between steroid hormones and scoring systems or laboratory signs of infections like CRP, PCT, leukocyte or platelet counts.

After stimulation with cosyntropin, testosterone, 17β-estradiol and DHEAS remained constant, whereas progesterone increased ($P<0.001$) in all groups of patients without significant difference between groups. In control or cardiogenic patients cosyntropin stimulation leads to significantly increasing values of cortisol ($P=2.15\times10^{-12}$ and $P=0.04$); in patients with sepsis the increase of cortisol ($P>0.1$) was blunted, however. This decrease in cortisol stimulation was independent of the use of sedatives or mechanical ventilation. In cardiogenic patients the increase in cortisol levels after stimulation was similar to control patients (7 μg/dl) and was not influenced by increasing dosage of catecholamines; in septic patients the cortisol increase was significantly lower ($P<0.01$) with high catecholamines (2 μg/dl) than with low catecholamines (7 μg/dl).

At baseline, patients at the intensive care unit had higher progesterone levels than normal. Septic patients showed diminished response to cosyntropin stimulation regarding cortisol levels despite a normal increase of progesterone. This points to an impairment of cortisol synthesis.

P4 Determination of functional states during sepsis-induced activation of the hypothalamic–pituitary–adrenal (HPA) axis using measurement of ACTH, cortisol, dehydroepiandrosterone-sulfate (DHEAS) and dehydroepiandrosterone (DHEA)

C Marx[1,2], M Wendt[1], S Petros[3], L Engelmann[1], M Weise[2], G Höffken[1]
[1]Internal Medicine II/[2]Medical ICU, University Hospital Carl Gustav Carus, Fetscherstraße 74, 01307 Dresden; [3]Medical ICU, University of Leipzig, Germany
Critical Care 2003, **7(Suppl 2)**:P004 (DOI 10.1186/cc1893)

Introduction Activation of the HPA axis occurs in order to control potentially deleterious effects of systemic inflammation during sepsis. Practically, it is difficult to determine different states of HPA activation since a differing dynamics and individual risk have to be considered.

Methods Recently, we examined levels of cortisol, DHEAS, DHEA as well as ACTH in 30 patients with severe sepsis (15 survivors, 15 nonsurvivors) and correlated the time course during early and late sepsis to the clinical course and inflammatory markers [1]. Here, we demonstrate and describe different states of HPA activation in characteristic surviving ($n=3$) and nonsurviving ($n=3$) septic patients of this study by use of hormone and inflammatory profiles.

Results Four functional states of HPA response with prognostic relevance could be differentiated. I) Activation: infection, systemic inflammation and activation of the HPA axis; high cytokine levels lead to release of ACTH and cortisol. II) Immunogenic stimulation: high cytokine levels maintain cortisol release whereas ACTH is suppressed by high glucocorticoid levels. III) Suppression of inflammation or exhaustion and hyperinflammation, respectively: suppression of inflammation by glucocorticoids or development of relative adrenal insufficiency by adrenal exhaustion resulting in relative hyperinflammation. IV) Recovery or insufficiency, respectively: normalisation of cytokine levels and regeneration of the adrenal driven by normalisation of ACTH. Reconstitution of physiologic ACTH-driven regulation or relative adrenal insufficiency with poor prognosis, respectively.

Discussion The HPA axis reflects the individual prognostic risk of the patient. The clinical course rarely enables the detection of all time-dependent states of HPA response. For individual diagnostic benefit of hormone measurements in septic patients, rapid availability of hormone levels is necessary.

Reference

1. Marx C, *et al.*: **Adrenocortical hormones in survivors and nonsurvivors of severe sepsis: diverse time course of dehydroepiandrosterone, dehydroepiandrosterone-sulfate, and cortisol.** *Crit Care Med* 2003, in press.

P5 Does transient hyperglycaemia affect cerebral energy metabolism in patients with severe brain trauma?

C-H Nordström, P Diaz-Parejo, N Ståhl, W Xu, P Reinstrup, U Ungerstedt
Department of Clinical Neuroscience, Lund University Hospital, S-22185 Lund, Sweden
Critical Care 2003, **7(Suppl 2)**:P005 (DOI 10.1186/cc1894)

Objective To study whether transient hyperglycaemia adversely affects cerebral energy metabolism in patients with severe traumatic brain lesions.

Design Prospective, nonrandomised study.

Interventions All patients were treated according to neurosurgical intensive care routine including monitoring of intracranial pressure. One microdialysis catheter was inserted via a burr hole frontally to that used for the intraventricular catheter ('better' position). In patients with focal lesions one or more catheters were inserted into

the cerebral cortex surrounding an evacuated focal contusion or underlying an evacuated haematoma ('worse' position). The perfusion rate was 0.3 µl/min and samples were taken every 30 or 60 min. The levels of glucose, pyruvate, lactate, glutamate, and glycerol were analysed and displayed bedside.

Measurements and main results In 108 patients, 18 episodes of moderate (12–15 mmol/l) and six episodes of pronounced (>15 mmol/l) hyperglycaemia occurred. Moderate hyperglycaemia did not change intracerebral levels of lactate, pyruvate, glutamate, glycerol or lactate/pyruvate ratio. During pronounced hyperglycaemia lactate concentration increased. A pronounced cerebral lactic acidosis and a moderate increase in interstitial glycerol concentration indicating cell membrane degradation was observed in a single patient with pronounced, long-lasting hyperglycaemia.

Conclusions Cerebral energy metabolism was affected by transient hyperglycaemia only at blood glucose concentration above 15 mmol/l as shown by a moderate increase in interstitial lactate level.

P6 Hyperglycemia at admission to ICU is independently associated with increased serum levels of IL-6 and reduced *ex vivo* TNF-alpha production

HE Wasmuth[1], F Lammert[1], J Graf[2], EA Purucker[1], A Koch[1], C Gartung[1], D Kunz[3], AM Gressner[3], S Matern[1]
[1]Department of Medicine III and [2]Department of Medicine I, and [3]Institute of Clinical Chemistry and Pathobiochemistry, University Hospital Aachen, Aachen University, Pauwelsstraße 30, 52074 Aachen, Germany
Critical Care 2003, **7(Suppl 2)**:P006 (DOI 10.1186/cc1895)

Background Hyperglycemia has been shown to be an independent risk factor of mortality in patients with stroke and myocardial infarction. Furthermore, strict control of hyperglycemia reduces mortality and rates of infectious complications in surgical ICU patients. The aim of the present study was to investigate immunological changes in medical patients in relation to blood glucose at admission to ICU.

Patients and methods Overall, 189 consecutive medical ICU patients were enrolled. At admission, blood glucose and serum levels of IL-6, IL-8, IL-10, and TNF-alpha were measured. Furthermore, monocyte HLA-DR expression and *ex vivo* TNF-alpha production in whole blood after stimulation with LPS were determined. In all patients, SAPS II score was calculated for day of admission to ICU. Hyperglycemia was defined as a venous blood glucose >126 mg/dl in fasting and >200 mg/dl in nonfasting individuals. Frequencies in contingency tables were calculated with Fisher's exact test. Logistic regression was used with hyperglycemia as the dependent variable and immune parameters, SAPS II score, and history of diabetes as covariates.

Results Overall mortality within the study period was 20.1%. Patients with hyperglycemia had an increased risk of mortality in the ICU compared with patients with normoglycemia at admission (29.3% vs 15.2%; OR=2.3, $P=0.03$). Sepsis according to Bone criteria was equally distributed between groups (14.3% vs 10.7%; $P>0.05$). At logistic regression analysis, higher serum levels of IL-6, a reduced *ex vivo* production of TNF-alpha, and a history of diabetes were independently associated with hyperglycemia at admission to ICU ($P=0.007$, $P<0.001$, $P=0.002$, respectively), while IL-8, IL-10, TNF-alpha, monocyte HLA-DR expression and the SAPS II score were not associated with increased blood glucose levels (all $P>0.05$).

Conclusions Independent of SAPS II score and underlying disease, hyperglycemia at admission to ICU is associated with immunological changes that are frequently observed in critically ill patients ('immunoparalysis'). Particularly, a reduced *ex vivo* production of TNF-alpha might contribute to the increased risk for infectious complications and death in patients with acute and chronic hyperglycemia.

P7 Influence of insulin clearance to glucose tolerance in acutely ill severe patients: analysis with glucose clamp method by means of artificial pancreas

M Hoshino[1], Y Haraguchi[2], M Sakai[1], I Mizushima[1], Y Morita[1], M Kobayashi[1]
[1]Department of Intensive and Critical Care Medicine, Tokyo Police Hospital, Fujimi 2-10-41, Chiyoda-ku, 102-8161 Tokyo, Japan; [2]Tokyo Disaster Medical Center, Tokyo, Japan
Critical Care 2003, **7(Suppl 2)**:P007 (DOI 10.1186/cc1896)

Purpose Acutely ill patients often have glucose intolerance (GI), which is one of the factors preventing appropriate nutritional support. However, mechanisms of GI are not clearly understood. Among the factors that influence GI, insulin sensitivity (IS) and insulin clearance (IC) are considered to be the important factors, because insulin is one of the most important factors which control glucose metabolism and insulin therapy is usually performed for patients with GI. We investigated glucose tolerance in terms of IS and IC in acutely ill severe patients by the glucose clamp method (GC) by means of a bedside-type artificial pancreas (STG-22: NIKKISO Corporation, Tokyo, Japan).

Method Thirty-one patients (27 patients had sepsis) in whom blood glucose levels were controlled by means of the artificial pancreas were investigated. First measurement of GC was performed in acute condition or within 3 days after admission for all the patients, and second measurement was done 1 week after the first measurement for 13 patients. GC was performed with clamped blood glucose level of 80 mg/dl and Insulin Infusion Rate (IIR) of 1.12 and 3.36 mU/kg per min. I1/I3 and M1/M3 indicate the blood insulin level (µU/ml) and glucose disposal rate : M value (mg/kg per min), when IIR is 1.12/3.36 mU/kg per min, respectively (normal value of M1: 5–10 mg/kg per min). M1/I1: (M1/I1 × 1000) was calculated as the parameter of IS (normal value of M1/I1: more than 50 mg/l per kg per min per µU). IC was calculated from the following formula: IC=(3.36–1.12) × 1000/(I3–I1) (normal value of IC: 10–15 ml/kg per min). Glucose tolerance was analyzed in terms of M1, IS (M1/I1), and IC.

Results 1) The proportion of the patients who had M1 levels less than 5 mg/kg per min (GI), IS (M1/I1) less than 50 mg/l per kg per min per µU (insulin resistance), and IC more than 15 ml/kg per min (increased IC) were 66% (29/44), 27% (12/44), and 61% (27/44), respectively. 2) Among the patients with GI ($n=29$), only 38% (11/29) of the patients had insulin resistance. Sixty-two percent (18/29) of the patients with GI had normal IS, and 83% of

them (15/18) had increased IC (mean ± SD of IC, I1: 22 ± 3.8 ml/kg per min, 38.3 ± 9.5 μU/ml, $n = 15$). 3) Among the patients with normal glucose tolerance ($n = 15$), 93% (14/15) of them had normal IS. However, one patient had both insulin resistance (M1/I1 = 43.5 mg/l per kg per min per μU) and decreased IC (IC = 3.9 ml/kg per min, I1 = 131 μU/ml).

Interpretation and conclusions 1) IC was the important factor that influenced the glucose tolerance in acutely ill severe patients, although the mechanisms of the change of IC was unclear. 2) Sufficient insulin administration was considered to be necessary from the aspect of metabolic and nutritional control for those patients with increased IC.

P8 Bone turnover in prolonged critical illness: effect of vitamin D

P Vanhove, D Van Roosbroeck, P Wouters, L De Pourcq, R Bouillon, G Van den Berghe
Department of Intensive Care & LEGENDO, Leuven University Hospital, Herestraat 49, 3000 Leuven, Belgium
Critical Care 2003, **7(Suppl 2)**:P008 (DOI 10.1186/cc1897)

Introduction In prolonged critical illness, substantially increased bone resorption and osteoblast dysfunction have been reported in the face of low 25-hydroxy vitamin D [25(OH)D] concentrations. The current prospective, randomized, controlled study investigates the impact of increased daily vitamin D supplement during intensive care on the time course of bone turnover and its major regulators such as cytokines and calciotropic hormones.

Methods Critically ill patients, assumed to require >10 days of intensive care, were compared with healthy matched controls and randomly allocated to a daily vitamin D supplement of either ± 200 IU (low dose) or ± 500 IU (high dose). Of the 33 patients included, 22 remained in ICU for >10 days and were analyzed. Urine from 24 hour collections and blood was sampled daily for characterization of vitamin D status, bone turnover and inflammation.

Results The 12 patients who received the high dose vitamin D and 10 patients who received the low dose were comparable at baseline. At intensive care admission, serum concentrations of 25(OH)D, $1,25(OH)_2D$, DBP, ionized calcium, osteocalcin, IL-1 and sIL-6-R were lower than in controls; PTH and bone-specific alkaline phosphatase levels were normal; serum carboxy and amino terminal of propeptide type-I collagen, serum and urinary collagen cross-links (βCTX, PYD and DPD) as well as IL-6, TNF-α and OPG were several fold elevated. sRANKL was undetectable.

The high dose increased circulating 25(OH)D ($P < 0.05$) but normal levels were not reached and low $1,25(OH)_2D$ levels not altered. High dose vitamin D slightly increased osteocalcin and decreased carboxy terminal propeptide type-I collagen ($P < 0.05$). Bone-specific alkaline phosphatase and collagen cross-links markedly increased with time in both groups ($P < 0.01$). Elevated CRP and IL-6 decreased significantly with time and more so in the high dose group ($P < 0.05$). TNF-α and IL-1 remained unaltered. Except for a mirroring of βCTX rise by a decrease in OPG, circulating cytokines were unrelated to the progressively aggravating bone resorption.

Conclusions Prolonged critically ill patients were vitamin D deficient. Increasing vitamin D supplement to the currently recommended dose did not normalize circulating 25(OH)D or $1,25(OH)_2D$. Furthermore, severe bone hyperresorption was associated with osteoblast dysfunction and aggravated with time in intensive care, independent of vitamin D supplementation.

P9 Assessment of energy expenditure and CO_2 production with different enteral feeds

Z Rusavy, M Zourek, Z Jankovec, D Cechurova, S Lacigova
Department of Medicine I, University Hospital, Plzen Alej Svobody 80, Plzen 300 00, Czech Republic
Critical Care 2003, **7(Suppl 2)**:P009 (DOI 10.1186/cc1898)

The aim of the study is to consider to which extent the production of CO_2 (V_{CO2}) and the resting energy expenditure (REE) are influenced by overfeeding and to which extent by the composition of enteral nutrition.

Five male and four female patients with Crohn's disease in remission were enrolled. REE and V_{CO2} were measured using the method of indirect calorimetry. The measurements were performed under hospitalization in the morning after 10 hours fasting in four modifications: I. high sugar (60%) in dose 1.2 × REE; II. high sugar (60%) and high-energy supply (2.4 × REE); III. high fat (60%) in dose 1.2 × REE; IV. high fat (60%), high energy (2.4 × REE). Between measurements there was a time interval of 7–10 days, when patients were only on home enteral nutrition.

Results did not differ depending on the different composition of nutrition in the case of adequate energy supply I. (REE = 1438 ± 264.1 kcal/24 hours, V_{CO2} = 179.1 ± 31.6 ml/min) × III. (REE = 1431 ± 342.7, V_{CO2} = 190 ± 54.2), likewise upon overfeeding II. (REE = 1674 ± 389.6, V_{CO2} = 218 ± 52.0) × IV. (REE = 1661 ± 378.7, V_{CO2} = 202 ± 42.3). In the high-sugar (60%) diet the overfeeding increased REE ($P < 0.05$) and V_{CO2} ($P < 0.01$) (I. × II.). In the high-lipid (60%) diet the overfeeding increased REE ($P < 0.01$) but not V_{CO2} (III. × IV.)

Conclusion Excessive energy supply results in higher V_{CO2} and in higher REE in comparison with adequate food intake. However, the nutrition with high content of fat does not lead upon overfeeding to significant increase of CO_2 production. The composition of the nutrition with appropriate energy amount does not significantly influence V_{CO2} and the REE.

P10 The metabolic effect of induced mild hypothermia in critically ill patients

M Bitzani, G Vassiliadou, C Iasonidou, S Tsaggalof, T Kontakiotis, D Riggos
ICU, 'G. PAPANIKOLAOU' Hospital, Thessaloniki, Greece
Critical Care 2003, **7(Suppl 2)**:P010 (DOI 10.1186/cc1899)

Introduction The aim of our study was to evaluate the metabolic effect of induced mild hypothermia in critically ill patients and to assess if rewarming reverses these effects.

Methods During a 2 year period, 12 consecutive critically ill patients under continuous veno-venous hemofiltration (CVVH), due to acute renal failure, were studied prospectively. All patients were mechanically ventilated, nine of them were sedated but none was paralyzed. Core temperature (*T*) was continuously monitored through a nasopharyngeal sensor, while resting energy expenditure (REE), V_{O2} and V_{CO2} were evaluated by means of indirect calorimetry. Baseline measurements were recorded before the onset of CVVH. Serial measurements were performed each time *T* was decreased by 1°C. After the interruption of CVVH, measurements were also repeated serially with the increase of core temperature of 1°C.

Results Decrease of temperature from 37°C to 35°C has no statistically significant influence on metabolic demands. During the reduction of temperature from 38°C to 35°C a statistically significant decrease in REE (2593 ± 228 kcal vs 2095 ± 618 kcal, $P=0.041$), as well as in V_{CO2} ($P=0.051$) was observed. A difference at the limits of significance was also observed in REE from 38°C to 36°C (2593 ± 228 kcal vs 2292 ± 434 kcal, $P=0.056$). Rewarming was followed by a gradual reverse of these effects.

Statistics were calculated with SPSS version 10, using nonparametric tests. Correlation between T, REE, V_{O2} and V_{CO2} was tested by Pearson's correlation coefficient. Comparison between REE, V_{O2} and V_{CO2} at different temperatures was performed using Student's paired *t* test.

Conclusion Mild hypothermia does not affect the metabolic rate in critically ill patients. Cooling in the febrile critically ill patient is followed by a significant decrease in energy expenditure. This may prove beneficial, minimizing the potential for tissue hypoxia, in situations of limited oxygen delivery.

References

1. Faenza S: **Hypothermia: an adverse effect or a missing partner?** *Intensive Care Med* 1997, **23**:1015-1017.
2. Frank SM, *et al.*: **Adrenergic respiratory and cardiovascular effects of core cooling in humans.** *Am J Physiol* 1997, **272**:557-562.
3. Sessler DI: **Deliberate mild hypothermia.** *J Neurosurg Anesthesiol* 1995, **7**:38-46.
4. Prakash O, *et al.*: **Cardiorespiratory and metabolic effects of profound hypothermia.** *Crit Care Med* 1978, **6**:340-346.

P11 Changes in lymphocyte subpopulations during enrichment of early enteral nutrition with lactic acid bacterium after major abdominal surgery

S Lüdemann[1], O Ahlers[1], A Möller[1], D Keh[1], I Kürer[1], N Rayes[2], P Neuhaus, H Gerlach[3]
[1]Department of Anesthesiology and Intensive Care, and [2]Department of Surgery, Charité-Virchow-Klinikum, 13344 Berlin, Germany; [3]Department of Anesthesiology, Vivantes-Klinikum Neuköln, 12313 Berlin, Germany
Critical Care 2003, **7(Suppl 2)**:P011 (DOI 10.1186/cc1900)

Background/aims Major abdominal surgery causes changes in lymphocyte subpopulations and impairs the immune response. Early enteral nutrition (EEN) enriched with probiotic bacteria may reduce this phenomenon and may improve the clinical course of this patients. The aim of this randomised, double-blind trial was to investigate changes of lymphocyte subpopulations of patients receiving EEN either enriched with lactic acid bacterium (LAB) or placebo before and after major abdominal surgery.

Patients and methods Thirty-three patients undergoing either pylorus-preserving pancreaticoduode-nectomy or Whipple's operation were enrolled. EEN enriched with either LAB ($n=17$) or placebo ($n=16$) was supplied for a period of 5 days beginning on the day before surgery. Blood samples were taken before surgery as well as postperatively on day 1, 4 and 8. Flow cytometry analysis was performed immediately.

Results Numbers of total lymphocytes as well as T-helper (T4)-, T-suppressor (T8)- and natural-killer-lymphocytes decreased significantly in both groups. No significant differences in this parameters could be found between the groups. However, the T4/T8 ratio showed a higher increase from day 1 until day 8 in the verum-group. Simultaneously, mean expression of CD45RA on T4 cells was significantly lower in the verum-group while mean expression of CD45RO on T8 cells was significantly higher in this group.

Summary/conclusion Enrichment of EEN with LAB seems to have no significant influence on the well known postoperative decrease of total lymphocytes and natural-killer cells. In contrast, LAB supply seems to improve the T4/T8 ratio by mobilisation of mature T4 and T8 cells. Further investigations are necessary to evaluate the underlying mechanisms and clinical consequences.

P12 Enrichment of early enteral nutrition with lactic acid bacterium influences the innate immune system after major abdominal surgery

A Möller[1], O Ahlers[1], S Lüdemann[1], I Kürer[1], N Rayes[2], D Keh[1], P Neuhaus[3], H Gerlach[3]
[1]Department of Anesthesiology and Intensive Care, and [2]Department of Surgery, Charité-Virchow-Klinikum, 13344 Berlin, Germany; [3]Department of Anesthesiology, Vivantes-Klinikum Neuköln, 12313 Berlin, Germany
Critical Care 2003, **7(Suppl 2)**:P012 (DOI 10.1186/cc1901)

Background/aims There is strong evidence that early enteral nutrition (EEN) enriched with probiotic bacteria may improve the clinical course of patients undergoing major abdominal surgery. Reduced bacterial translocation in the gut and resulting changes in innate immune response may be responsible for this phenomenon. The aim of this randomised, double-blind trial was to investigate

changes of innate immunity of patients receiving EEN either enriched with lactic acid bacterium (LAB) or placebo before and after major abdominal surgery.

Patients and methods Thirty-three patients undergoing either pylorus-preserving pancreaticoduode-nectomy or Whipple's operation were enrolled. EEN enriched with either LAB ($n=17$) or placebo ($n=16$) was supplied for a period of 5 days beginning on the day before surgery. Blood samples were taken before surgery as well as postperatively on day 1, 4 and 8. Flow cytometry analysis was performed immediately.

Results Number of neutrophil granulocytes (PMNs), monocytes and total leukocytes increased significantly in both groups during the observation period. CD62L-positive PMNs decreased while CD62L-positive monocytes increased in both groups with significantly lower values in the verum-group. HLA-DR-positive monocytes decreased in both groups until day 1 but showed a significantly lower increase until day 8 in patients receiving LAB. Number of PMNs, monocytes, total leukocytes and CD62L-positive PMNs showed no significant differences between both groups.

Summary/conclusion Numbers of PMNs, monocytes and total leukocytes as well as CD62L-positive PMNs showed well known changes after major surgery regardless of enrichement of EEN with LAB. In contrast, LAB supply seems to impair the expression of HLA-DR and CD62L on monocytes. Further investigations are necessary to evaluate the underlying mechanisms.

P13 High correlation between increased negative calorie balance and morbidity in critically ill patients

D Dvir, L Gibstein, E Grozovski, I Alterman, M Shapiro, J Cohen, P Singer
General Intensive Care Department, Rabin Medical Center, Beilinson Campus, petah Tikva 49100, Israel; Sackler School of Medicine, Tel Aviv University, Israel
Critical Care 2003, **7(Suppl 2)**:P013 (DOI 10.1186/cc1902)

Accurate energy balance is difficult to assess since prescribed energy intake is not always actual energy intake administered, intravenous dextrose given as part of a fluid program is not always taken into account and resting energy expenditure (REE) is not usually measured on a daily basis. We used a bedside computerized information system to measure daily and cumulative energy balance in critically ill ventilated patients to assess its impact on patient outcome.

Methods and patients Twenty-five ventilated patients (mean age 54.7 ± 18.4 years, 19 males, six females) were prospectively followed during their ICU stay. Energy balance (REE) was measured daily using both indirect calorimetry (Deltatrac II, Datex-Ohmeda, Finland) and a bedside computerized information system (iMDsoft, Israel) which was able to collect data from all sources (enteral, parenteral nutrition and and IV fluids containing calories). Daily and total energy balance were calculated on a continuous basis. Morbidity (acquired organ dysfunction, pressure sores, need for surgery) and mortality were noted.

Results Mean body mass index was 26.9 ± 5.0 kg/m^2 and mean APACHE II was 22.7 ± 7.2. The bedside information system revealed a mean IV calorie intake of 154 kcal/day and reaching 370 kcal/day in some patients. Mean cumulative balance for an overall ICU stay of 395 days was −4261 kcal (range 172 to −17,274 kcal). Six of 25 patients had a negative calorie balance >−10,000 kcal. A strong correlation ($r=-0.75$) was found between negative energy balance and complication rate, but not with length of ventilation, length of ICU stay or length of hospitalization. Six patients died (three had a negative energy balance >−10,000 kcal).

Conclusion We conclude that a bedside information system provides online and accurate information regarding energy balance in critically ill patients and may allow for the early detection and prevention of severe negative energy balance, which is correlated with the occurrence of significant complications (organ dysfunction and pressure sores).

P14 Use of anabolic steroid therapy in critically ill ICU patients

J Pikul[1], MD Sharpe[2]
[1]Department of Clinical Nutritional Services and [2]Department of Anesthesia, University of Western Ontario, London, Canada N6A5A5
Critical Care 2003, **7(Suppl 2)**:P014 (DOI 10.1186/cc1903)

Critical illness leads to a loss of lean body mass (LBM) and is associated with impaired immune function and wound healing, increased infection, and poorer outcomes [1,2]. Aggressive nutritional support can decrease net catabolic losses by only ~50%, therefore other methods need to be examined. We initiated anabolic steroid therapy (AS) (nandrolone intramuscular injection, once weekly × three doses) on 10 critically ill patients. Criteria for AS: moderate to severe malnutrition, ICU stay >14 days, tolerating enteral feeds, and exhibiting poor response to nutritional support. Feeds were 130–150% of measured energy expenditure and protein at 2.0–2.5 g/kg per day. Response was monitored by nitrogen balance and LBM.

Table 1

	2 weeks prior to AS			After 3 doses		
Patient	Pre-ALB	N balance (g/day)	LBM (kg)	Pre-ALB	N balance (g/day)	LBM (kg)
1. F	0.09	+2.3	22.3	0.09	+3.2	22.8
2. F	0.08	−3.4	18.4	0.21	+4.8	19.2
3. M	0.11	−5.8	36.3	0.32	+7.2	38.1
4. M	<0.07	−6.7	27.2	0.19	+1.8	27.9
5. M	0.18	−14.2	39.4	0.28	+6.9	40.8
6. F	0.07	−5.2	12.8	0.16*	+5.3*	15.3*
7. M	0.14	−6.8	N/A	0.35	+3.8	N/A
8. M	<0.07	−10.2	29.1	0.16	+5.4	29.9
9. M	0.15	−17.6	20.5	0.14	−10.0	22.1
10. M	0.10	−19.6	26.8	0.14	+4.6	25.8

*Data collected 6 weeks post steroid.

Eight of 10 patients exhibited a good response to AS, with attainment of positive nitrogen balance and improvement in skeletal and visceral protein levels. AS may be useful as adjunctive therapy for malnourished, critically ill patients for protein repletion.

References
1. Chang DW, DeSanti L, Demling RH: *Shock* 1998, **10**:155-160.
2. Ferrando AA, Sheffield-Moore M, Wolf SE *et al.*: *Crit Care Med* 2001, **29**:1936-1942.

P15 Hypercapnia attenuates the endotoxin-induced tissue metabolic acidosis in esophageal mucosa

M Ponichter[1], H Billert[2], J Jastrzebski[1]
[1]Clinic of Anesthesiology and Intensive Care, Center of Medical Postgraduate Education, Warsaw, Poland; [2]Clinic of Anesthesiology and Intensive Care, Medical Academy of Poznan, Poland
Critical Care 2003, **7(Suppl 2)**:P015 (DOI 10.1186/cc1904)

Objective To assess the effects of hypercapnia on the tissue metabolic response to *Escherichia coli* endotoxemia in rabbits.

Design Prospective, controlled experimental study.

Setting University laboratory.

Subjects Thirty-six rabbits of both sexes, anesthetized with pentobarbital and ventilated mechanically (normoventilation).

Interventions Animals were assigned to one of four groups: a) endotoxemic control group ($n=9$), receiving intravenous *Escherichia coli* endotoxin (20 mg/kg bolus) via a peripheral vein; b) hypercapnia control group ($n=9$), receiving exogenous carbon dioxide to achieve mild hypercapnia 60–90 mmHg; c) hypercapnia treated group ($n=9$), treated identically to endotoxemic controls, and additionally receiving exogenous carbon dioxide to achieve mild hypercapnia 60–90 mmHg; d) control group ($n=9$), receiving neither endotoxin nor carbon dioxide.

Measurements We compared hemodynamics, blood gases, WBC, rectal temperature and tonometric findings in esophageal mucosa obtained in each group. Endotoxin injection decreased mean arterial pressure from 79 ± 9 to 54 ± 17.5 mmHg, decreased bicarbonate level from 21.6 ± 3 to 17.6 ± 4 mmHg, decreased WBC from 7.9 ± 2 to 1.9 ± 0.7 G/l, increased rectal temperature from 37.7 ± 1 to 39.9 ± 1.5°C, and caused a marked, continuous decrease in regional pH (pHi) from 7.40 ± 0.08 to 7.12 ± 0.11 at the end of the experiment. Hypercapnia alone had a minimal effect on the parameters and findings. Both hypercapnia and endotoxemia had no significant effect on regional CO_2 ($PrCO_2$) compared with controls, indicating lack of significant mucosal blood flow abnormalities throughout the experiment. In the hypercapnia treated group we observed an initial decrease in regional pH (pHi) from 7.42 ± 0.13 to 7.13 ± 0.08, but the value of this parameter remained stable (7.07 ± 0.05 at the end of the experiment) and the statistical difference compared with hypercapnia controls was nonsignificant ($P>0.05$).

Conclusions 1. Endotoxin injection caused marked tissue acidosis without disturbing esophageal mucosal blood flow, which indicates a metabolic character of acidosis and underlines the significance of intracellular abnormalities during endotoxemia. 2. We hypothesize that hypercapnia attenuates the endotoxin-induced tissue metabolic acidosis and may exert a cytoprotective effect.

P16 Blood gases: a dreadful combination of metabolic, respiratory and lactic acidosis

A Aaron[1], AS Bachwani[2]
[1]Intensive Care Unit, Parsee General Hospital, Cumballa Hill, Mumbai 400026, India; [2]BARC Hospital, Mumbai 400094, India
Critical Care 2003, **7(Suppl 2)**:P016 (DOI 10.1186/cc1905)

Introduction Arterial blood gases (ABGs) are the immediate, easiest, most reliable and cost effective bedside method of assessing an unstable patient. It portrays an array of functional reserves from the lungs to the kidneys and the blood cells in between. It also hints at the causes of hypoxia and hypercarbia. We applied the Henderson Hasselbalch Equation ($PCO_2=HCO_3\times1.5+8$) to interpret the blood gas and used it effectively to prognosticate the patient's outcome.

Methods All patients with acidosis on blood gas were included. In addition, PCO_2 was calculated independently using the Henderson Hasselbalch Equation. Patients are divided into three groups as shown in Table 1. Prototype ABGs of each group as shown in Table 2.

Explanation *Group 1.* Patients in blood gas group 1 did not have any problem, responded very well to the treatment and were stable. The PCO_2 matches with the HCO_3 according to the Henderson Hasselbalch Equation. In dehydrated patients, sodabicarb was given to replace the loss of carbonates.

Group 2. These patients came to the ICU deteriorated with multiorgan involvement, in an unstable condition needing mechanical support beside all medical strategies. The outcome was not that good in this group.

Group 3. Very poor outcome from this group. Patients did not survive after this combination of metabolic, respiratory and lactic acidosis occurred. This was much in evidence in a patient who had multiorgan failure and septic shock. The PCO_2 in this group was always on the higher side then the calculated value as is in evidence in sample number 3.

Conclusion 1. The Henderson Hasselbalch Equation is very useful in the interpretation of blood gases and guides us about the severity of illness and prognosis of the patient.

2. If soda-bicarbonate has to be used, the equation can be used to guide us of its effect on the patient.

3. The combination of metabolic, lactic and respiratory acidosis is a dreadful combination usually culminating in death. Commonly patients had multiorgan dysfunction and irreversible shock.

Table 1

Group (%)	Features	Calculated PCO_2	Typical case scenario	Treatment	Mortality
1	Metabolic acidosis without lactic acidosis (*n*=200)	Matches with blood gas	Infections, dehydration	Antibiotics, fluids	5
2	Metabolic acidosis with lactic acidosis (*n*=151)	Matches with blood gas	Sepsis, cardiogenic shock	Ventilator, inotropes	20
3	Metabolic acidosis with lactic acidosis (*n*=119)	Higher than blood gas by +4–5	Septic shock, MOF	Ventilator, iInotropes	99

Table 2

Group	pH	PCO_2	PO_2	HCO_3	TCO_2	BE	SO_2	Interpretation
1	7.25	25	120	11.2	12.2	–5	98.1	Dehydration, pulmonary edema, infection
2	7.27	29.1	135.6	13.6	14.5	–11.4	98.4	MODS, septic shock
3	6.96	59.4	142.3	13.4	15.2	–20.1	97.1	MODS, septic shock

4. It is imperative that we adopt an aggressive approach early on in treatment of metabolic and lactic acidosis combination and should not allow patients to go in to Group 3.

5. To begin with, patients presenting in group 3 were more severely ill and warranted an aggressive approach irrespective of the blood gas.

P17 Lactic versus nonlactic metabolic acidosis: outcomes in critically ill patients

KJ Gunnerson, M Saul, JA Kellum
CRISMA Laboratory, Department of Critical Care Medicine, University of Pittsburgh School of Medicine, 200 Lothrop Street, Pittsburgh, PA 15261, USA
Critical Care 2003, **7(Suppl 2)**:P017 (DOI 10.1186/cc1906)

Introduction Critical care physicians associate lactic acidosis (LA) with higher morbidity and mortality. Other forms of metabolic acidosis are generally regarded as less dangerous and any association with adverse outcomes in critically ill patients is poorly understood. We sought to compare differences in mortality and length of stay (LOS) between LA and other forms of metabolic acidoses.

Methods In this observational pilot study, we reviewed records of 9799 patients admitted to the ICUs at our institution between 1 January 2001 and 30 June 2002. This cohort of patients had an inpatient mortality of 14%, a hospital LOS of 12 days and an ICU LOS of 5.8 days. We selected cases on the following criteria: 1) clinicians caring for each patient suspected the presence of LA; 2) arterial blood gas (ABG) and lactate were measured; 3) Na^+, K^+, Cl^-, and CO_2^- were drawn within 4 hours of the referenced ABG, Ca, Mg, Phos within 24 hours, and albumin any time during the hospitalization. When multiple data sets were available, the set with the highest lactate was used. We classified patients into four groups: A) *no metabolic acidosis*, standard base excess (SBE) ≥–2; B) *lactic acidosis*, lactate accounted for >50% of SBE; C) *strong ion gap (SIG) acidosis*, SIG accounted for >50% of SBE (and not LA); D) *hyperchloremic acidosis*, absence of A, B, or C.

Results We identified 862 patients (8.9% of ICU admissions). Of these, 546 patients (63.3%) had a metabolic acidosis. LA occurred in 43% of acidemic patients and was associated with a 57% mortality. Table 1 presents the unadjusted relative mortality and LOS. Other forms of acidosis were collectively associated with a 37% mortality. There was no difference in ICU or hospital LOS between all groups.

Table 1

	All cases SBE<–2	Lactic acidosis	SIG acidosis	Hyperchloremic
n	546	237	205	104
% of acidosis	100	43	38	19
ICU LOS days (survivors)	18.02	19.38	21.41	14.42
LOS days (survivors)	31.2	33.2	33.6	29.3
Mortality (%)	46	57	40	30

Conclusions In patients suspected of having LA, LA was more commonly associated with hospital mortality than non-LA. However, all forms of metabolic acidosis, even hyperchloremic, appear to be associated with high mortality and increased ICU and hospital LOS.

P18 Relationship between platelet counts, C-reactive protein and plasma fibrinolytic capacity in critically ill patients

K Zouaoui Boudjeltia[1], M Piagnerelli[1], E Carlier[2], S Jamart[2], Ph Cauchie[1], M Vanhaeverbeek[1]
[1]Experimental Medicine Laboratory, ULB 222 Unit, and [2]Department of Intensive Care, A. Vésale Hospital, 6110 Montigny-le-Tilleul, Belgium
Critical Care 2003, **7(Suppl 2)**:P018 (DOI 10.1186/cc1907)

Background Multiple Organ Failure (MOF) complicating the sepsis remains the first cause of death in the ICU. A recent study showed that vascular endothelial damage was the primary cause of MOF in patients with thrombopenia and that humoral mediators played a major role in the development of this process [1]. Other parameters like C-protein reactive were also probably important via a direct effect on endothelial cells and increasing the secretion of IL-6. In this study, we aimed to evaluate the relation between the platelet counts (PC), the C-reactive protein and plasma fibrinolytic capacity (as a marker of endothelium dysfunction) in ICU patients.

Methods We studied blood samples of ICU patients with ($n=11$) and without ($n=21$) sepsis at the first day of admission. Fibrinolytic capacity was evaluated by the Euglobulin Clot Lysis Time (ECLT) determined by a new method [2]. We also collected biological data and the SAPS II score for each patients. The correlations were depicted by Spearman's test.

Results The ECLT was significantly correlated with CRP ($R=0.64$; $P<0.001$) and PC ($R=-0.4$; $P=0.02$). The two-way ANOVA showed that the sepsis status increased significantly the ECLT ($P=0.023$) and that platelets under 208,500 cells/µl (median of the histogram of PC was used as the cut-off) also increased the ECLT ($P=0.023$). However, there was no interaction ($P=0.184$).

Conclusion Platelets can protect the endothelium against several forms of oxidative injuries [3]. With this study we showed that the decrease of the platelets count could favor the endothelium dysfunction and impaired fibrinolytic capacity, and this independently of sepsis. In addition, C-reactive protein is not only an inflammatory marker, but it might be involved in the endothelium damage.

References
1. Hirokazu U, *et al.*: *Crit Care Med* 2002, **30**:2242-2248.
2. Zouaoui Boudjeltia K, *et al.*: *BMC Biotechnology* 2002, **2**:8.
3. Vincent JL, *et al.*: *Crit Care Med* 2002, **30**:S313-S317.

Table 1

	Sepsis ($n=11$)	Nonsepsis ($n=21$)	*P* value
CRP (mg%)	25 (17–30)	6.9 (2.1–11.6)	<0.001
WBC (x 10^3 cells/µl)	10.5 (7.7–12.9)	9.8 (8–12)	0.69
Fibrinogen (mg%)	662 (597–686)	455 (333–542)	<0.001
SAPS	48 (39–56)	23 (15–35)	0.003
Platelets (x 10^3 cells/µl)	186 (123–227)	229 (179–296)	0.17
ECLT (min)	987 (845–1375)	599 (477–950)	0.01

Data presented as median (25–75%).

P19 Drotregocin alfa (activated) inhibits degradation of cytokine-mRNA in an endothelial model of inflammation

M Brueckmann, HM Weiler, V Liebe, A Marx, U Hoffmann, S Lang, C Liebetrau, M Borggrefe, KK Haase, G Huhle
Department of Medicine I, Faculty of Clinical Medicine Mannheim, University of Heidelberg, 68167 Mannheim, Germany
Critical Care 2003, **7(Suppl 2)**:P019 (DOI 10.1186/cc1908)

Background The activated protein C (APC) pathway has been suggested to be a common link between coagulation and inflammation. APC may function to restore hemostasis via modulation of cytokine expression. We investigated the effect of Drotrecogin alfa (activated) (recombinant human activated protein C [rhAPC]) on the expression of monocyte chemoattractant protein-1 (MCP-1), interleukin-6 (IL-6) and IL-8 in human umbilical vein endothelial cells (HUVEC) in the presence and absence of tumor necrosis factor-alpha (TNF-alpha). MCP-1, IL-6 and IL-8 are mediators of inflammation and their gene expression is controlled by the activation of the transcription factor nuclear factor-kappa B (NF-κB).

Results rhAPC (2.5–20 µg/ml) upregulated the amount of MCP-1-mRNA and IL-8-mRNA and caused a time-dependent and dose-dependent increase in MCP-1-, IL-6- and IL-8-protein production ($P<0.001$ for rhAPC 5 µg/ml at 4–24 hours) in HUVEC. Experiments were conducted to evaluate the effect of rhAPC on mRNA degradation and mRNA stability independently of its possible effects on gene transcription. After stimulation of mRNA transcription by TNF-alpha (0.1–1 ng/ml) for 3 hours, HUVEC were treated with actinomycin D (1 µg/ml), preventing new synthesis of transcript, in the presence or absence of rhAPC. HUVEC receiving rhAPC contained more MCP-1-mRNA and IL-8-mRNA after 1 hour and up to 8 hours than controls, suggesting an inhibitory effect of rhAPC on mRNA degradation. Electrophoretic mobility shift assays (EMSA) revealed that APC attenuated NF-κB activity implying that NF-κB may not be involved in the upregulatory effect of rhAPC on MCP-1, IL-6 and IL-8 production.

Conclusions The ability of APC to upregulate the production of MCP-1, IL-6 and IL-8, most likely by increasing the stability of MCP-1-mRNA rather than by transcriptional activation via NF-κB, identifies a novel post-transcriptional pathway, by which APC may control the local inflammatory reaction, thereby modulating the extent of endothelial injury.

P20 Gene array transcript profiling of human endothelial cells identifies pathways regulated by Drotrecogin alfa (activated)

M Brueckmann, S Lang, HM Weiler, V Liebe, U Hoffmann, M Borggrefe, KK Haase, G Huhle
Department of Medicine I, Faculty of Clinical Medicine Mannheim, University of Heidelberg, 68167 Mannheim, Germany
Critical Care 2003, **7(Suppl 2)**:P020 (DOI 10.1186/cc1909)

Background Although the role of Drotrecogin alfa (activated) (recombinant human activated protein C [rhAPC]) in modulating microvascular coagulation through the inhibition of thrombin generation has been well studied in experimental and clinical settings of severe sepsis, little is known about its direct anti-inflammatory effects on vascular endothelial cells. To better understand the molecular mechanisms of action of rhAPC on endothelial cell function during sepsis we used gene array transcript profiling of messenger RNA (mRNA) from primary cultured human umbilical vein endothelial cells (HUVEC) exposed to Drotregocin alfa (activated) in the presence of the central proinflammatory mediator tumor-necrosis factor-alpha (TNF-alpha).

Methods and results The effect of rhAPC on TNF-alpha-activated HUVEC was assessed using Affymetrix microarrays. Briefly, mRNA from treated cells was isolated and converted to double-stranded copy (c)DNA, which was then used to generate biotinylated cRNA. Biotinylated cRNA was hybridized to Affymetrix oligonucleotide arrays, containing approximately 33,000 human genes. Data analysis was performed using GeneChip 3.1 software. We found that rhAPC reproducibly upregulated TNF-alpha-induced gene expression of the following genes: monocyte chemoattractant protein-1 (MCP-1), platelet-derived growth factor-alpha-chain (PDGF-A), interleukin-6 (IL-6), transforming growth factor-beta receptor II, insulin-like growth factor-binding protein (IGF-BP) and interleukin-8 (IL-8). rhAPC downregulated the following genes induced by TNF-alpha stimulation: the secreted apoptosis related protein-1 (SARP-1), basic fibroblast growth factor (bFGF), lymphotoxin-β, the adhesion molecules vascular cell adhesion molecule-1 (VCAM-1) and intercellular adhesion molecule-1 and -2 (ICAM-1 and ICAM-2). Results for IL-6, IL-8 and MCP-1 were confirmed by protein measurements in cell culture supernatants by ELISA as well as by a colorimetric assay for mRNA quantitation (Quantikine assay).

Conclusions The ability of rhAPC to modulate gene expression of a cluster of proinflammatory genes, genes responsible for cell adhesion and leukocyte trafficking as well as genes involved in endothelial apoptosis, provides insight into the molecular mechanisms contributing to the efficacy of rhAPC in systemic inflammation and sepsis.

P21 Treatment of adults with sepsis-induced coagulopathy and purpura fulminans with a plasma-derived protein C concentrate (Ceprotin®)

P Schellongowski[1], E Bauer[2], G Locker[1], M Frass[1], T Staudinger[1], P Knöbl[1]
[1]Department of Internal Medicine I and [2]Department of Internal Medicine IV, University of Vienna, Währinger Gürtel 18-20, A-1090 Wien, Austria
Critical Care 2003, **7(Suppl 2)**:P021 (DOI 10.1186/cc1910)

Disseminated intravascular coagulation (DIC) is a severe complication of sepsis, especially when associated with skin or organ necrosis appearing as purpura fulminans. Several reports described beneficial effects of protein C replacement in preterm neonates, infants, and adults with purpura fulminans. We treated seven adult patients (six female, one male), median age 35 years (range 19–48 years), with DIC and purpura fulminans with a plasma-derived human protein C concentrate (Ceprotin®; Baxter, Vienna, Austria). Three patients had meningococcal, three had pneumococcal, and one had pseudomonas and cytomegaly-virus infections. At admission, all patients had signs of skin necrosis, severe infection and acute illness. Coagulation assays suggested DIC in five patients (median [range]): platelet count 19 (17–23) G/l, fibrinogen 60 (44–103) mg/dl, antithrombin activity 0.47 (0.25–0.76) U/ml, normotest 32 (14–39)%, APTT 88 (42–160) s, D-dimer 66 (3.3–140) ng/ml; the remaining two patients were treated because of typical skin necrosis and meningococcemia alone. Initial protein C activity was reduced to 0.35 (0.2–0.5) U/ml. Five patients had neurologic alterations, five renal failure, three respiratory failure, one a large intrahepatic necrosis. In five patients Ceprotin® was given as a level-adjusted continuous infusion (starting with 10 U/kg per hour) after an initial bolus of 100 U/kg, two patients were treated with bolus infusions (100 U/kg every 8 hours). Additionally, heparin infusions (seven patients), fresh-frozen plasma (five patients), antithrombin concentrates (three patients), fibrinogen concentrates (two patients), low-dose rtPA (two patients), platelet and erythrocyte transfusions, antibiotics, and hydrocortisone (four patients) were given. Protein C activity increased to 1.34–2.0 U/ml in all patients, coagulation abnormalities resolved within 1–6 days. A total of 8000–77,000 U Ceprotin® were given during 1–7 days. One patient died the same day from multiorgan failure, one died 14 days after the end of Ceprotin® infusion from candida sepsis. All other patients survived, three needed amputations of toes, two had no sequels. Our data suggest that Ceprotin® can be a useful hemostatic support in the treatment of adults with severe, life-threatening purpura fulminans, which would have a high mortality with conventional therapy alone. Controlled studies are needed to establish the value of this drug in the treatment of sepsis.

P22 Treating medical and surgical patients with activated protein C: a preliminary comparison

HL Evans, ML Milburn, T Calloway, DF Volles, SM Lowson, RG Sawyer
Surgical Infectious Disease Research Laboratory, UVA Health System, Box 801380, Charlottesville, VA 22908-1380, USA
Critical Care 2003, **7(Suppl 2)**:P022 (DOI 10.1186/cc1911)

Sepsis is a significant cause of morbidity and mortality in the critically ill patient. Drotrecogin alfa (activated) (APC) has been shown to significantly decrease mortality in patients with severe sepsis, although surgical patients constituted the minority in the initial multicenter trial. In our initial experience with APC, we sought to determine whether surgical intensive care unit (ICU) patients have the same rate of bleeding complications as medical ICU patients. We hypothesized that surgical patients are more apt to bleed following APC administration, but have higher survival rates than medical patients.

Methods We performed a retrospective analysis of all medical and surgical patients in a single academic medical center who received APC for the treatment of sepsis between January 2002 and November 2002. Primary outcome variables included incidence of clinically significant bleeding, defined as blood loss requiring transfusion of at least 4 units of packed red cells (PRBC) during APC treatment, and 28-day mortality. Secondary outcomes included ICU length of stay (ILOS), hospital length of stay (LOS), completion of treatment course, and units of blood products transfused. Demographic data such as sex, age, severity of illness at the time of APC administration (APACHE II score), and primary site of infection at the time of sepsis diagnosis were obtained. Coagulation parameters were compared at three time points: within 24 hours of APC administration, during APC infusion, and within 24 hours of stopping APC. Hospital mortality following APC treatment was compared with baseline mortality for historically similar patients in our ICU matched 2:1 by age within 12 years, APACHE II score within 10 points and same site of infection.

Results A total of 29 patients were treated with APC, 59% in the surgical ICU. Demographics and severity of illness were similar (Table 1). Prior to APC infusion, surgical patients were more coagulopathic and anemic, and had already received on average four times as many PRBC units than medical patients. Surgical patients also received more PRBC after APC infusion was started. All bleeding events occurred in surgical patients at surgical sites and two of the bleeds occurred in patients who received therapeutic heparin infusions as well as APC. However, no difference was demonstrated in the number of patients who completed APC therapy, LOS or mortality. For all patients, the mean partial thromboplastin time during APC infusion was higher than has been previously reported (99.4 medical vs 94.3 surgical, $P=0.7408$), and there was an 84% increase in the mean PTT (52.4 ± 4.9 before vs 96.4 ± 7.5 during, $P<0.0001$), as well as a 32% decrease in the mean platelet count during the APC administration (189.9 ± 24 vs 130.0 ± 16, $P=0.008$), both of which normalized in the 24 hour period following cessation of APC. Mean maximum INR during APC infusion was 1.9 ± 0.2; after treatment, there was a 21% decrease to 1.5 ± 0.1 ($P=0.0025$). In the case–control analysis, APC recipients had a similar age (61 ± 3.1 vs 60 ± 1.9, $P=0.83$) and APACHE II score (31 ± 1.4 vs 29 ± 0.9, $P=0.37$), but significantly lower mortality than matched controls (35% vs 66%, $P=0.0119$).

Table 1

	Medical	Surgical	*P*
n	12 (41%)	17 (59%)	–
Age	60.2 ± 5.3	61.3 ± 3.8	0.86
Sex = female	5 (42%)	8 (47%)	0.77
APACHE II score	31.1 ± 0.7	31.0 ± 1.9	0.97
PTT before APC	39.6 ± 2.7	61.5 ± 7.5	0.03
HCT before APC	30.7 ± 1.8	26.1 ± 1.4	0.0561
# PRBC units transfused	0.58 ± 0.3	2.5 ± 0.7	0.03
Bleeding (≥ 4 U)	0 (0%)	5 (29%)	0.0588
Completed APC course	6 (50%)	10 (59%)	0.64
Hospital LOS	23.4 ± 7.7	41.3 ± 7.9	0.13
28-day mortality	4 (33%)	3 (18%)	0.40

Conclusions In this preliminary comparison of the open-label use of activated protein C in patients with severe sepsis, we witnessed a 30% reduction in overall hospital mortality compared with historical controls, and a substantial, but reversible, coagulopathy during APC infusion. Although the severity of illness and degree of coagulopathy were similar between medical and surgical patients, the only clinically significant bleeding complications were observed in the surgical cohort. This may be due to the unique features of surgical sepsis, with increased incidence of tissue barrier violation and blood loss anemia, or perhaps a reflection of the burden of blood product transfusion and greater tendency towards coagulopathy than thrombosis. Further studies should endeavor to define risk factors for bleeding among surgical patients and to determine whether interventions such as repletion of other coagulation factors, intermittent infusion of APC, or restriction of other anticoagulant therapies may be beneficial.

P23 Quality of life in ICU survivors with severe sepsis who received activated protein C

WT Cook, JM Eddleston, D Conway, J Streets
Critical Care Directorate, Manchester Royal Infirmary, Oxford Road, Manchester M13 9WL, UK
Critical Care 2003, **7(Suppl 2)**:P023 (DOI 10.1186/cc1912)

Appropriate treatment of severe sepsis with activated protein C (rhAPC) has been associated with an absolute reduction in mortality of 6.1% [1]. The aim of this study was to followup patients who received rhAPC and to evaluate their quality of life postdischarge from the intensive care unit (ICU).

Method Twenty-three patients in our unit were recruited into the ENHANCE study and received rhAPC. The 28 and 90 day mortality was calculated and quality of life was assessed at 90 days using the Short Form-36 (SF-36) [2]. Psychological distress and depression was measured at the same time using the Hospital Anxiety and Depression score (HAD) [3].

Table 1

SF-36 scores for patients who received rhAPC, published figures for a general ICU population [4] and those of the UK population [2]

	Physical function	Role Lim physical	Role Lim emotion	Social function	Mental health	Energy vitality	Pain	Health perception
rhAPC	69.4	46.9	54.3	91.8	76.0	61.9	84.9	72.3
General ICU [4]	58.9	46.1	56.4	70.9	68.9	44.2	77.6	57.6
UK population [2]	92.5	91.4	85.6	91.3	75.4	64	86.3	78.8

Results Twenty-three subjects had at least three or more acute organ dysfunction associated with severe sepsis, with a range of APACHE II scores of 8–33. The median length of stay in ICU for survivors was 16.4 days, and hospital stay post-ICU was 19.5 days. The 28 and 90 day all-cause mortality was 21.7% (five patients) and 26.1% (six patients), respectively. Eight of the 17 survivors completed the SF-36 (Table 1) and HAD forms. HAD scores indicated heightened anxiety in two patients and none were clinically depressed.

Conclusion Mortality is similar to that already published [1]. Encouraging, the quality of life for these patients is comparable at 90 days with a general ICU population. A limitation is the number of patients.

References

1. Bernard GR, *et al.*: **Efficacy and safety of recombinant human activated protein C for severe sepsis.** *N Engl J Med* 2001, **344**:699-709.
2. Jenkinson C, *et al.*: **SF-36 Health survey questionnaire: normative data for adults of working age.** *BMJ* 1993, **306**:1437-1440.
3. Zigmond A, *et al.*: **The Hospital Anxiety and Depression Scale.** *Acta Psychiatr Scand* 1983, **67**:361-370.
4. Eddleston JM, *et al.*: **Survival, morbidity and quality of life after discharge from intensive care.** *Crit Care Med* 2000, **28**:2293-2299.

Correction (12 March 2003)

The original published version of the abstract (as shown above) included incorrect data in the first sentence of the Results section. The sentence should read as follows:

Results Twenty-three patients had at least one or more acute organ dysfunction associated with severe sepsis, with a range of APACHE II scores of 8–33.

P24 Spanish project on benchmarks related to recombinant human activated protein C use: best clinical practices identification

MC Martín[1], J Ruiz[2], C León[3], JA Lorente[4], A López[5], A Artigas[6], F Castillo[7], JC Ruiz[8]

[1]Hospital General de Cataluña, General Morato s/n, 08221-Sant Cugat del Vallés, Barcelona, Spain; [2]Hospital Sagrat Cor, 08029 Barcelona, Spain; [3]Hospital de Valme, Sevilla, Spain; [4]Hospital Universitario de Getafe, Madrid, Spain; [5]Hospital Infanta Cristina, Badajoz, Spain; [6]Hospital de Sabadell, CSPT, 08208 Sabadell, Barcelona, Spain; [7]Hospital Duque del Infantado, Sevilla, Spain; [8]Hospital General del Valle, Hebrón, 08035 Barcelona, Spain

Critical Care 2003, **7(Suppl 2)**:P024 (DOI 10.1186/cc1913)

Background Recombinant human activated protein C (rhAPC) has been shown to significantly reduce mortality in severe sepsis (SS) patients.

Purpose To identify best clinical practices (BCPs) using several benchmarks (BMs) related to rhAPC administration as the starting point.

Methods Five Spanish experts on SS and main investigators involved in the PROWESS trial were interviewed in order to identify BCPs for rhAPC administration with regard to the following BMs also obtained from the same experts: BM1) SS identification; BM2) clinical or microbiologically documented infection; BM3) standardized criteria for infection focus identification; BM4) SS considered as the main diagnosis; BM5) length of SS induced organ dysfunctions (OD) $<$48 hours; BM6) no limitation of life support measures; BM7) adequate standard therapy; BM8) rhAPC administration. Interviews were oriented to identify BCPs to succeed in reaching the BMs when considering rhAPC administration in clinical practice. Each BCP implied key factors and an objective.

Results The following BCPs were identified for each BM: BM1) SS patient considered a critically ill patient, consensus criteria for SS definition, early identification of SS. BM2–BM3) Complete medical history; radiological and macroscopic examinations, basic microbiological study, other medical specialties' involvement. BM4) SS documented as main reason for patient admission. BM5) Use of validated score systems, unified required OD degree (SOFA score $>$2), undocumented OD does not imply normality; no consideration of chronic ODs. BM6) Evaluation of previous health status and concomitant medical history, involvement of patient's family and other health professionals, no scale score considered as criterion for rhAPC indication. BM7) Protocol-driven antibiotic therapy, antibiogram, control of infection focus, sequential order in shock therapy, early mechanical ventilation. BM8) Lack of rhAPC contraindications, drug prescribed by a critical care physician

Conclusions The use of BMs related to the clinical use of rhAPC allows the identification of BCPs for BMs compliance, which my lead to an optimization of the drug cost-effectiveness

P25 Thrombolysis in fulminant menigococcemia (FM) with myocardial infarction (MI) and shock

M Simon[1], L Mertens[1], F Meurant[1], DR Wagner[2]
[1]Department of Critical Care Medicine and [2]Department of Cardiology, Centre Hospitalier Luxembourg, 4 rue Barblé, Luxembourg City 1210, Luxembourg
Critical Care 2003, **7(Suppl 2)**:P025 (DOI 10.1186/cc1914)

A 15-year-old boy presented with fever, confusion, headache and nausea. On examination, he had purpuric lesions, meningeal irritation and signs of systemic inflammatory response to sepsis. Cultures were obtained and ceftriaxone was administered. Laboratory findings were consistent with impending disseminated intravascular coagulation (DIC) and the patient was given fresh frozen plasma (FFP), antithrombin III (AT III) and low dose enoxaprin. Hemodynamics improved with fluid challenge. However, 12 hours later, he became agitated and developed shock. The patient was intubated and given high doses of catecholamines. The ECG and the echocardiogram showed extensive acute anterior wall MI. We decided to perform thrombolysis with recombinant tissue plasminogen activator (t-PA) given over 4 hours (total dose 1.25 mg/kg) [1]. Shortly after thrombolysis, hemodynamics improved and the ECG normalized. Peak CPK levels were 5200 IU/ml. The patient developed multiple organ failure (MOF) with adult respiratory distress syndrome and renal failure. Neisseria meningitidis group C was found in the cerebrospinal fluid. The patient recovered completely afterwards. The followup echocardiogram showed normal left ventricular function and mild anterior hypokinesis.

FM, or Waterhouse Friderichsen syndrome, is characterized by the abrupt development of shock, DIC and MOF. Impaired myocardial contractility is commonly seen in FM and contributing to shock. It is well established that endotoxin causes myocardial dysfunction [1] and plays a key role in septic myocardial dysfunction. The exact mechanisms of endotoxine-induced myocardial dysfunction are complex and probably involve cytokines such as tumor necrosis factor-α [2,3] and perhaps also myocardial apoptosis [4]. MI during FM is exceedingly rare, and to our knowledge only one case hase been reported in the pediatric literature [5]. Our patient developed MI, presumably on the basis of DIC, despite aggressive treatment. Although levels of plasminogen activator antigen are increased in septic shock, its activity is almost completely inhibited by plasminogen activator inhibitor type 1 (PAI-1). Theoretically, treatment with t-PA may help reverse the procoagulant state. Zenz *et al*. [1] and others [6–8] observed significant clinical improvement after a 4-hour infusion of t-PA in a few pediatric patients with FM. This is the first report of successful thrombolysis with t-PA in a patient with FM complicated by MI and shock.

References

1. Zenz W, Muntean W, Gallistl S, Zobel G, Grugbbauer HM: **Recombinant tissue plasminogen activator treatment in two infants with fulminant meningococcemia.** *Pediatrics* 1995, **96**: 144-148.
2. Parker JL, Adams HR: **Development of myocardial dysfunction in endotoxin shock.** *Am J Physiol* 1985, **248**:H818-H826.
3. Meng X, Ao L, Meldrum DR, Cain BS, Shames BD, Selzman CH, Banerjee A, Harken AH: **TNF-alpha and myocardial depression in endotoxemic rats: temporal discordance of an obligatory relationship.** *Am J Physiol* 1998, **275**:R502-R508.
4. Feldman AM, Combes A, Wagner DR, Kadakomi T, Kubota T, Li YY, McTiernan C: **The role of tumor necrosis factor in the physiopathology of heart failure.** *J Am Coll Cardiol* 200, **35**: 537-544.
5. Fauvel H, Marchetti P, Chopin C, Formstecher P, Neviere R: **Differential effects of caspase inhibitors on endotoxin-induced myocardial dysfunction and heart apoptosis.** *Am J Physiol* 2001, **280**:H1608-H1614.
6. Briassoullis G, Kalabakis P, Thanopoulos V, Hatzis T: **Non-Q wave acute myocardial infarction in acute meningococcemia in a 10-year old girl.** *Pediatr Emerg Care* 2000, **16**:33-38.
7. Aiuto LT, Barone SR, Cohen PS, Boxer RA: **Recombinant tissue plasminogen activator restores perfusion in meningococcal purpura fulminans.** *Crit Care Med* 1997, **25**:1079-1082.
8. Gessler P, Bachmann DCG, Pfenninger P: **Meningokokkensepsis und purpura fulminans.** *Monatsschr Kinderheilkd* 1999, **147**: 1010-1013.

P26 Asymmetrical dimethylarginine (ADMA) in critically ill patients: high plasma ADMA concentration is an independent risk factor of ICU mortality

RJ Nijveldt, T Teerlink, B van der Hoven, MPC Siroen, DJ Kuik, JA Rauwerda, PAM van Leeuwen
VU University Medical Center, Department of Surgery, De Boelelaan 1117, 1081 HV Amsterdam, The Netherlands
Critical Care 2003, **7(Suppl 2)**:P026 (DOI 10.1186/cc1915)

Background and aims Accumulation of ADMA has been linked to endothelial dysfunction, and is an important risk factor for cardiovascular disease. Its elimination from the body is dependent on urinary excretion and degradation by the enzyme dimethylarginine dimethylaminohydrolase. This enzyme is highly expressed in the liver, and in rat studies a high net hepatic uptake of asymmetrical dimethylarginine was found. In critically ill patients, we investigated the relation between indicators of renal and hepatic dysfunction and plasma ADMA concentration, and tested the association between ADMA concentration and outcome.

Methods We prospectively collected blood samples from a cross-section of critically ill patients ($n=52$) with clinical evidence of dysfunction of more than two organs. We identified correlates of plasma ADMA concentration with laboratory values, organ failures score and outcome by univariate and multiple regression analyses.

Results In critically ill patients, plasma ADMA concentration was independently related to the presence of hepatic failure ($b=0.334$, 95% CI=0.207–0.461; $P<0.001$), and to lactic acid ($b=0.395$, 95% CI=0.230–0.560; $P<0.001$) and bilirubin ($b=0.121$, 95% CI=0.031–0.212; $P=0.009$) concentration as markers of hepatic function. Twenty-one (40%) patients deceased during their ICU stay. In a logistic regression model, plasma ADMA ranked as the first and strongest predictor for outcome, with a 17-fold (95% CI=3–100) increased risk for ICU death in patients who were in the highest quartile for ADMA.

Conclusions In critically ill patients, plasma ADMA concentration is a strong and independent risk factor for ICU mortality, and hepatic dysfunction is the most prominent determinant of ADMA concentration in this population.

P27 The epidemiology of sepsis in Scottish intensive care units

F MacKirdy, G Harris, SJ Mackenzie
Scottish Intensive Care Society Audit Group, Victoria Infirmary, Langside Road, Glasgow G42 9TY, UK
Critical Care 2003, **7(Suppl 2)**:P027 (DOI 10.1186/cc1916)

Introduction Recent developments [1] have increased the requirement for good clinical data on the aetiology, incidence and outcome from sepsis in the intensive care unit (ICU). Assessment of sepsis in the Scottish ICU database has previously been limited. Our aim was to conduct a prospective audit of sepsis, severe sepsis and septic shock following ICU admission in Scotland using predetermined sepsis criteria.

Methods Between January 2002 and 31 May 2002, 25 of the 26 adult, general ICUs in Scotland participated in a prospective audit of sepsis. Daily data were recorded on Ward Watcher software (Critical Care Audit Ltd) enabling identification of the first episode of sepsis: fulfilment of the systemic inflammatory response syndrome (SIRS) [2] criteria in response to infection. First 24-hour APACHE II scores are generated routinely in Scottish ICUs; however, source and type of infection and a sepsis-related organ failure assessment (SOFA) [3] were also mandatory in patients identified as septic.

Results In this 5 month study, 46% ($n=1618$) of ICU admissions developed sepsis, equating to 0.77 cases per 1000 population, per annum, in Scotland. Sepsis was present at, or shortly after, admission (median of 1 day). ICU length of stay (LOS) was double that of the Scottish ICU population (mean=9.02 days, median=5.1 days). Of all admissions, 38% ($n=1341$) had severe sepsis or septic shock. Two-thirds of this group had more than one organ failure, of which 290 also had an APACHE II score of 25 or more. Both mortality and APACHE score rose with the number of organs failing. In those with severe sepsis or septic shock, the major source of sepsis (bronchopulmonary=56.5%) and the ICU mortality (33%) were similar to those of the placebo group in the PROWESS study [1]. The septic shock group had a significantly higher ICU mortality than those with severe sepsis (61.5% vs 31.8%, $P<0.0001$). Mean SOFA (10.9 vs 5.1, $P<0.0001$) and APACHE II scores (24.1 vs 20, $P<0.0001$) were also significantly higher in this group.

Conclusion Almost one-half of the admissions to Scottish ICUs have sepsis, which presents on or shortly after admission. Mortality increases with APACHE score and the number of organs failing. Septic shock appears to be significantly associated with poor outcome.

References
1. Bernard GR, Vincent J-L, Laterre PF, *et al.*: *N Engl J Med* 2001, **344**:699-709.
2. American College of Chest Physicians/Society of Critical Care Medicine Consensus Conference: *Crit Care Med* 1992, **20**:864-874.
3. Vincent JL, Moreno R, Takala J, *et al.*: *Intensive Care Med* 1996, **22**:707-710.

Acknowledgement Supported with a grant from Eli Lilly.

P28 Correlation between changes in mediators and number of dysfunctional organs in sepsis-associated multiple organ dysfunction syndrome (MODS)

H Taniuchi, T Ikeda, K Ikeda, H Suzuki, M Nagura, K Ooshima, Y Kuroki
Division of Critical Care and Emergency Medicine, Hachioji Medical Center, Tokyo Medical University, 1163 Tatemachi, Hachioji, Tokyo 193-0998, Japan
Critical Care 2003, **7(Suppl 2)**:P028 (DOI 10.1186/cc1917)

Introduction Changes in hemodynamics and a variety of mediators such as cytokines were compared with respect to the number of dysfunctional organs in MODS cases treated with blood purification.

Subjects and methods This study included 113 cases of MODS that were treated with endotoxin-absorption therapy (PMX-DHP). Background factors, respiration, circulatory parameters and inflammatory mediators (IL-6, IL-1ra, ELAM-1, PAI-1, MIP-1α and BNP) were measured before the start of PMX-DHP. Organ dysfunction was evaluated using the MOF score according to Goris, where organ dysfunction was judged positive when the score was more than one point for each organ.

Results The rate of survival for more than 28 days from the start of blood purification clearly decreased as the number of dysfunctional organs increased. The APACHE II score, the Septic Severity Score (SSS), and the SOFA score significantly increased with an increase in dysfunctional organs, with a significant positive correlation ($P<0.0001$) between the scores ($r=0.59$ between APACHE II and SOFA, $r=0.60$ between APACHE II and SSS, and $r=0.76$ between SSS and SOFA). In comparison, by prognosis, the number of dysfunctional organs was 3.1 ± 1.2 in survival cases and 4.3 ± 1.0 in the nonsurvival cases before the start of blood purification. The mean IL-6 level was highest in cases with dysfunction of four organs. The BNP level appeared to increase as the number of organs with dysfunction increased. In particular, the difference between the two-organ dysfunction group and the three-organ dysfunction group was statistically significant ($P<0.05$).

Conclusion A variety of humoral mediators, including cytokines, increased as the number of dysfunctional organs increased, while the level of the increase differed for each mediator. Hemodynamics and PaO_2/FiO_2 ratio prior to the start of PMX-DHP appeared to influence the prognosis. Possible involvement of BNP was suggested in development of sepsis-associated MODS and will be further studied in the future.

P29 Safe and effective mediastinal drainage along the carotid sheath for septic mediastinitis

Y Moriwaki, M Sugiyama, K Yoshida, S Yamagishi, K Kanaya, G Matsuda, S Hasegawa, H Toyoda, T Kosuge, T Kosuge, K Uchida, T Yamamoto, N Suzuki
Yokohama City University Medical Center, Department of Critical Care and Emergency Center, 4-57 Urafune-cho, Minami-ku, Yokohama 232-0024, Japan
Critical Care 2003, **7(Suppl 2)**:P029 (DOI 10.1186/cc1918)

Summary Mediastinitis is still a challenging condition, which can easily result in lethal sepsis. We previously reported parasternal anterior mediastinal drainage. In this congress, we will present another method of mediastinal drainage along the carotid sheath around the aortic arch approach without thoracotomy (oblique cervical incision, exposed carotid sheath, and bluntly dissected and inserted drainage tube along the carotid sheath reaching to the aortic arch). Three patients were treated by this procedure.

Introduction Mediastinitis is still a challenging condition, which can easily result in severe lethal sepsis. It is important for management of mediastinitis to perform an effective and noninvasive drainage. We reported the 'parasternal anterior approach' as a method of mediastinal drainage for mediastinitis around the superior caval vein. In this congress we will present another method of mediastinal drainage for the septic mediastinitis around the aortic arch by the 'along carotid-sheath approach' without thoracotomy. The aim of this presentation is to clarify the usefulness and safety of this method.

Patients and surgical procedure Three patients with septic mediastinitis were treated by this procedure. We drained the upper mediastinum from the supraclavicular pouch along the neck vessels, or the carotid sheath, by blunt dissection. We performed at first an oblique cervical incision, exposed the carotid sheath, and bluntly dissected and inserted a drainage tube along the carotid sheath reaching to the aortic arch. The neck and chest CT revealed that the drainage tube reached the aortic arch in two cases. The inflammatory signs of these two patients were improved after this procedure and repeated neck and chest CT revealed improvement of mediastinitis. No complications such as vascular injury related with this procedure was seen. The other case underwent this procedure when sepsis was already uncontrollable and died due to uncontrollable sepsis. The report of her autopsy showed the position of drain in the level of the aortic arch in front of the esophagus without any vascular injury and mediastinitis localized within the upper mediastinum.

Conclusion Our method of mediastinal drainage, the 'along carotid-sheath approach', is useful, safe, and a minimal invasive procedure for septic patients with mediastinitis.

P30 Critical role of pulmonary endothelial production of prostacyclin in the endotoxin-resistant mechanism in mice

K Okajima, P Enkhbaatar, H Isobe, M Uchiba
Department of Laboratory Medicine, Kumamoto University School of Medicine, Honjo 1-1-1, Kumamoto 860-0811, Japan
Critical Care 2003, **7(Suppl 2)**:P030 (DOI 10.1186/cc1919)

Tumor necrosis factor-α (TNF-α) plays an important role in the induction of the pulmonary endothelial cell injury by activating neutrophils in sepsis. The resultant pulmonary endothelial cell injury leads to a decrease in the production of PGI_2, which might be an important etiology for the development of acute respiratory distress syndrome, a critical complication of sepsis. Endotoxin (ET)-resistant mechanisms in C3H/HeJ mice involve the mutation of Toll-like receptor-4 (TLR-4) by which ET signals to increase TNF-α production in monocytes. Thus, it is possible that the pulmonary endothelial cell injury leading to the impairment of the production of PGI_2 could be attenuated in C3H/HeJ mice, contributing to the ET-resistant mechanism. The present study was conducted to examine this possibility.

Plasma levels of 6-keto-PGF1a were significantly higher in C3H/HeJ mice than those in C3H/HeN mice, the ET-sensitive strain, 90 min after intravenous injection (IV) of ET. Survival rates on the 6th day of IV of ET were 100.0% and 0% in C3H/HeJ mice and C3H/HeN mice, respectively, while it was 50.0% in C3H/HeJ mice when they were pretreated with indomethacin (IM), which inhibits PGI_2 production. Plasma levels of 6-keto-PGF1a in C3H/HeJ mice 90 min after intra-arterial injection (IA) were significantly lower than those in C3H/HeJ mice 90 min after IV of ET. Although the survival rate of C3H/HeJ mice on the 6th day of IV of ET was 81.2%, it was only 27.7% in these mice on the 6th day of IA of ET. These observations suggested that the major part of 6-keto-PGF1a in the plasma of C3H/HeJ mice after IV of ET could be derived from PGI_2 released from the lung vasculature, and the PGI_2 release might be critical for the ET-resistance in C3H/HeJ mice. Plasma levels of 6-keto-PGF1a 90 min after IV of ET were significantly higher in C3H/HeN mice pretreated with ONO-5046, an inhibitor of neutrophil elastase, than those in these mice without ONO-5046 pretreatment. The survival rate of C3H/HeN mice pretreated with ONO-5046 on the 6th day of IV of ET was 80.0%, while that of these mice without ONO-5046 pretreatment was 10.0%.

Taken together, these observations raise a possibility that the activated neutrophil-induced pulmonary endothelial cell injury could be attenuated in C3H/HeJ mice, leading to maintaining higher production of PGI_2 than that in C3H/HeN mice, which could at least partly explain the ET-resistant mechanism in C3H/HeJ mice.

P31 Circulating complement proteins for differentiation of SIRS and sepsis

H Sungurtekin, C Balcı, U Sungurtekin
Department of Anesthesiology and Reanimation, Pamukkale Unv. School of Medicine, Tokat Cad No 41-8 Özkan Apt. Denizli, Turkey
Critical Care 2003, **7(Suppl 2)**:P031 (DOI 10.1186/cc1920)

Introduction The systemic inflammatory response of the body to invading microorganisms, termed sepsis, leads to profound activation of the complement (C) system. The main proinflammatory properties of the complement system can be attributed to the ana-

Table 1

Best cutoff values, area under the curve (AUC) (mean ± SE), sensitivity and specificity of all variables to differentiate patients with sepsis from patients with SIRS

	C3 (mg/dl)	C4 (mg/dl)	CRP (mg/dl)	Thrombocyte	Leukocyte
Best cutoff value	55.0	20.5	14.5	164000	14800
AUC	0.560 ± 0.06	0.544 ± 0.06	0.522 ± 0.05	0.640 ± 0.06	0.507 ± 0.06
Sensitivity	0.61	0.56	0.58	0.66	0.41
Specificity	0.62	0.53	0.50	0.69	0.66

phylatoxins C3a, C4a, C5a. These polypeptides are generated after proteolytic cleavage of the α-chain of C3, C4 or C5. The present study was conducted to determine serum complement 3 and 4 levels for differentiation in patients with SIRS and sepsis, in comparison with C-reactive protein (CRP), thrombocyte and leukocyte counts.

Method Fifty-eight patients with SIRS and 41 patients with sepsis were admitted to the study. Blood samples were taken at the first day of intensive care unit for analysis of C3, C4, CRP, thrombocyte and leukocyte counts.

Results Thrombocyte count was significantly lower in septic patients (mean ± SE: 179,975 ± 14,932, $P=0.005$) compared with SIRS patients (243,165 ± 16,243). The plasma concentrations of CRP, C3 and C4 level were not different between groups. The power of parameters to discriminate between septic and SIRS patients was determined in a receiver operating characteristic analysis. Thrombocyte was the best analysis to differentiate between both populations with a maximal sensitivity and specificity (Table 1).

Discussion In this study, C3, C4 and CRP had poor sensitivity and specificity for the differentiation of SIRS and sepsis. Because of the complex pathophysiology involved, it is likely that not a single mediator but a panel of different inflammatory mediators will ultimately predict the outcomes of individual patients.

Reference

1. Selberg O, Hecker H, Martin M, *et al.*: *Crit Care Med* 200, **28**:2793-2798.

P32 Initial plasma levels of lipopolysaccharide binding protein are associated with severe sepsis in patients with community-acquired pneumonia

ML Martino[1,2,3], A Krichevsky[2], S He[4], J Fine[5], DC Angus[1,2], for the GenIMS Investigators
[1]CRISMA Laboratory, [2]University of Pittsburgh School of Medicine, and [4]University of Pittsburgh School of Public Health, Pittsburgh, PA 15261, USA; [3]Saint Clair Memorial Hospital, Pittsburgh, PA, USA; [5]Norwalk Hospital, CT, USA
Critical Care 2003, **7(Suppl 2)**:P032 (DOI 10.1186/cc1921)

Background Many researchers are investigating the expression of inflammatory proteins as contributors to the variable onset and progression of infection, sepsis, and organ dysfunction. We explored the relationship between plasma lipopolysaccharide binding protein (LBP) levels and the development of severe sepsis in community-acquired pneumonia (CAP).

Hypothesis Plasma LBP levels are higher in CAP patients who develop severe sepsis.

Methods We are conducting a large multicenter inception cohort study of patients arriving in the Emergency Department (ED) with CAP. We conducted a planned interim analysis on the first 385 enrolled patients. Plasma LBP was assayed using a commercially available immunoassay system (Diagnostic Products Corp., Los Angeles, CA, USA). Severe sepsis was defined as a Sequential Organ Failure Assessment Score increase of 2 for any one nonrespiratory organ, or an increase of 1 for any two nonrespiratory organs, or an absolute score of 3 or 4 for the respiratory component.

Results Plasma LBP levels were available for 379/385 (98.4%) patients. Of the 379 patients, 26.1% had severe sepsis at initial presentation; 29.8% were PSI class I or II, 27.2% class III, 33.0% class IV, and 10.0% class V; 29.6% had chronic lung disease; 50.9% were female; 12.9% were black and 85.0% white; average age was 65.5 ± 17.2 years. Day 1 serum LBP levels distinguished between ED presentation of CAP with severe sepsis ($n=87$) and without ($n=236$): 40.4 ± 31.9 μg/ml vs 27.9 ± 19.3 μg/ml, respectively; $P=0.0005$ by Wilcoxon. Over the course of hospitalization, mean LBP levels for each patient correlated with worst diagnosis: 26.8 ± 17.2 μg/ml for CAP patients who at any time met criteria for severe sepsis ($n=158$), compared with 20.8 ± 13.9 μg/ml for patients who did not ($n=221$); $P<0.0001$ by Wilcoxon. Mortality analysis was not possible in this preliminary interim analysis.

Conclusions In our CAP cohort, patients who developed severe sepsis had significantly higher plasma LBP levels.

Acknowledgement Supported by NIH grant R01 GM61992-01.

P33 TIMP-1, TIMP-2 and MMP-9 as prognostic markers for clinical outcome in sepsis

U Hoffmann, M Brückmann, E Dvorsak, V Liebe, M Borggrefe, KK Haase, G Huhle
1st Department of Clinical Medicine, University Hospital Mannheim, University of Heidelberg, Germany
Critical Care 2003, **7(Suppl 2)**:P033 (DOI 10.1186/cc1922)

Background Acute inflammatory diseases such as sepsis are characterized by activation of leukocytes, which contain MMP-9 (Gelatinase B) in tertiary granules. Matrix metalloproteinases play an important role in the degradation of extracellular matrix and basement membranes by destroying the elastic lamina. These main enzymes of tissue turnover are controlled by their inhibitors such as TIMP-1 (tissue inhibitor 1 of metalloproteinase). To assess the importance of clinical outcome of septic patients we measured TIMP-1, TIMP-2, MMP-2, MMP-3 and MMP-9 in septic patients.

Patients and methods Serum was collected from 37 septic patients admitted to the ICU with APACHE score 14.5 on day 1 (SD 7.6). Blood was collected from the 37 septic patients and from 14 healthy controls on day 1. Twelve of the 37 critically ill patients died within 28 days. We measured MMP-9, MMP-2, MMP-3, TIMP-2 and TIMP-1 serum levels from all healthy controls, from the 25 survivors and the 12 nonsurvivors with ELISA methods. We compared the serum levels of MMP-9, TIMP-2 and TIMP-1 between the three groups.

Results MMP-9 and TIMP-1 levels (MMP-9 mean ± SD = 80 ± 86, TIMP-1 = 3216 ± 1222) in the severely ill patients were significantly higher ($P < 0.001$) than in controls (MMP-9 = 6 ± 7, TIMP-1 = 953 ± 184). MMP-2 showed no difference between septic patients (948 ± 287) and control group (928 ± 165). We noted a significantly ($P = 0.003$) increased concentration of TIMP-1 in the nonsurvivors (953 ± 184) compared with the survivors (4675 ± 1507). TIMP-2 was significantly higher ($P < 0.001$) in nonsurvivors than in the control group. Statistic analysis shows a correlation (Spearman Rank correlation, $r = 0.7958$) between serum levels of TIMP-1 and the severity of sepsis and the probability to die, but there was no correlation shown between the serum levels of MMP-3 and MMP-2.

Conclusion Our results indicate that MMP-9, TIMP-2 and TIMP-1 may serve as sensitive and early markers for cell activation during the course of sepsis. Furthermore, TIMP-1 may be related to the prognosis and clinical outcome of septic patients.

P34 Peripheral blood lymphocytes of critically ill patients show signs of late stage apoptosis

SU Weber, J-C Schewe, S Schroeder, A Hoeft, F Stueber
Department of Anaesthesiology and Intensive Care Medicine, University Bonn Medical Center, Germany
Critical Care 2003, **7(Suppl 2)**:P034 (DOI 10.1186/cc1923)

Among the immunological events, apoptosis plays an important role in sepsis. Inhibition of apoptosis in mouse models of sepsis improved survival [1]. Phosphatidyl serin externalisation has been detected in peripheral blood leukocytes of patients suffering from sepsis as an early stage of apoptosis [2,3]. It has not been shown if they undergo complete apoptosis. Therefore, the aim of the current study was to examine if circulating lymphocytes of septic patients display DNA degradation as a sign of late apoptosis.

Isolated mononuclear cells of 11 critically ill patients (three with severe sepsis) were compared with eight healthy controls. Phosphatydil serin externalisation was evaluated by annexin V binding. Necrotic cells were excluded by propidium iodine stain. DNA fragmentation was detected by TUNEL staining using flow cytometry.

In critically ill patients annexin binding was increased to 12.1 ± 7.5% compared with a basal population of 3.8 ± 0.9% in healthy controls ($P < 0.05$). The TUNEL-positive population increased from 0.5 ± 0.1% to 2.3 ± 1.5% in critically ill patients ($P < 0.05$).

The study demonstrates that mononuclear cells of critically ill patients show signs of early apoptosis and to a lesser degree also signs of DNA fragmentation. This may be explained by rapid clearing of phosphatydil serin expressing cells from the circulation by phagocytosis.

References
1. Hotchkiss, *et al.*: *Nat Immunol* 2000, **1**:496-501.
2. Schroeder, *et al.*: *Langenbeck's Arch Surg* 2001, **386**:42-46.
3. Adrie C, *et al.*: *Am J Respir Crit Care Med* 2001, **164**:389-395.

Acknowledgement This study was supported by a grant from BONFOR.

P35 The effects of salbutamol on neutrophil function

GD Perkins[1], S Quinton[1], DR Thickett[2], F Gao[1]
[1]Birmingham Heartlands Hospital, Bordesley Green East, Birmingham B9 5SS, UK; [2]University of Birmingham, Birmingham B15 2TT, UK
Critical Care 2003, **7(Suppl 2)**:P035 (DOI 10.1186/cc1924)

Background Polymorphonuclear cell (PMN) activation, adhesion and transpulmonary emigration to the alveolar space are important steps in the pathogenesis of the acute respiratory distress syndrome (ARDS). β_2 agonists accelerate alveolar fluid clearance and have been suggested as a potential treatment for patients with ARDS. In addition, these agents have a variety of effects on polymorphonuclear cells (PMN). In animal models of sepsis, treatment with β_2 agonists has been shown to reduce pulmonary neutrophil sequestration and ameliorate the development of lung injury. The aim of this study was to investigate the effect of the β_2 agonist salbutamol on three aspects of PMN function: PMN activation (CD 64 expression), chemotaxis, and adhesion molecule expression (VLA-4).

Methods PMNs from 10 healthy volunteers were separated using Ficoll-histopaque gradients and incubated with RPMI or salbutamol (10^{-4} to 10^{-10} M). PMN chemotaxis to FMLP (10^{-6}) was determined using the under agarose method. The effects of salbutamol

Table 1

Salbutamol	0	10^{-9} M	10^{-7} M	10^{-5} M
Chemotaxis (mm) [mean (SD)]	9.3 (1.8)	8.7 (2.3)	8.4 (2.3)	6.7 (1.6)*
VLA-4 (MFI) [median (IQR)]	10 (1.5–16)	9 (2–20)	X	11 (5.5–25)
CD 64 (MFI) [median (IQR)]	12 (6–18.5)	13.5 (1.7–20.8)	X	10.5 (5.3–26.8)

* $P < 0.05$ compared with control. IQR, interquartile range.

(10^{-5} M and 10^{-9} M) on unstimulated PMN VLA-4 and CD 64 expression were determined using flow cytometry on whole blood.

Results There was no effect on VLA-4 or CD 64 expression. However, salbutamol did reduce PMN chemotaxis (see Table 1).

Conclusion Salbutamol reduced PMN chemotaxis but had no effect on VLA-4 adhesion molecule expression or CD 64 expression (PMN activation). β_2 agonists may have beneficial effects beyond simply enhancing alveolar fluid clearance in patients with ARDS.

P36 Lymphopenia, hypoprolactinemia and lymphocyte depletion in pediatric multiple organ failure

K Felmet[1], M Hall[1], R Jaffe[2], R Clark[1], J Carcillo[1]
[1]Department of Critical Care Medicine and [2]Department of Pathology, Children's Hospital of Pittsburgh, 3705 Fifth Avenue, Pittsburgh, PA 15217, USA
Critical Care 2003, **7(Suppl 2)**:P036 (DOI 10.1186/cc1925)

Introduction Lymphopenia is associated with secondary infection, multiple organ failure (MOF) and death in adults. Lymphocyte apoptosis has been described in autopsies of adults dying of MOF. In experimental models, prolactin protects against lymphocyte apoptosis.

Hypothesis Lymphocyte apoptosis occurs in pediatric patients with MOF and is associated with prolonged hypoprolactinemia and lymphopenia.

Methods Blood was collected on days 1, 3, 7, and 14 from 55 critically ill children without MOF and 58 with MOF (organ failure index ≥2 for ≥3 days.) Lymphopenia was defined as lymphocyte count $< 1000 \times 10^6$/l. Hypoprolactinemia was defined as <2.5 ng/ml in patients >6 months and <20 ng/ml in patients >6 months (chemiluminescent assay; DPC, Los Angeles, CA, USA). Both were considered prolonged when lasting ≥1 week. Severe lymphocyte depletion (SLD) was determined by a pathologist's histologic evaluation of lymph nodes and spleen at autopsy. Linear and logistic regression models were used to control for immune suppression, steroid use, and severity of illness (PRISM score).

Results Lymphocyte counts were lower in children with MOF than in those without (median [range]: 864 [0–5525], $n=58$ vs 1787 [0–16,250], $n=55$; $P=0.001$, rank sum) even when controlling for immune suppression and steroid use ($P=0.001$). Prolonged lymphopenia was only seen in children with MOF (17/58 vs 0/55) and was independently associated with secondary infection (OR=5.5, 95% CI=1.7–17, $P=0.004$) and death (OR=6.8, 95% CI=1.3–34, $P=0.02$). Sixteen patients died; 11 underwent autopsy. SLD was seen in 89% of those dying of MOF. Two patients died without MOF; neither had autopsy evidence of SLD. In patients with MOF, prolonged hypoprolactinemia (OR=12.2, 95% CI=2.2–65, $P=0.01$) and prolonged (OR=42.2, 95% CI=3.7–473, $P=0.001$) were independently associated with SLD.

Conclusions Prolonged lymphopenia and SLD occur in pediatric MOF. Prolonged lymphopenia predicts death independent of severity of illness. Unrecognized hypoprolactinemia may contribute to SLD.

P37 Impaired blood PMN migration as an indicator of increased susceptibility for bacterial infections in critically ill patients

KH Smolle[1], H Mitterhammer[1], P Kaufmann[1], W Wonisch[1], R Aigner[2], G Egger[3]
[1]Department of Internal Medicine and [2]Department of Nuclear Medicine, University Hospital, Graz, Austria; [3]Department of Pathophysiology, Karl-Franzens University, Graz, Austria
Critical Care 2003, **7(Suppl 2)**:P037 (DOI 10.1186/cc1926)

Objective Directed migration is a crucial element of PMN's defence capacity against microorganisms in a septic state.

The aim of our study was to look at the course and the significance of PMN migration capacity in surviving and nonsurviving critically ill patients.

Method Intensive care patients with the diagnosis of SIRS or sepsis according to the SCCM/ACCP criteria were enrolled in this prospective study. The APACHE III score for each patient was calculated within 24 hours of admission.

PMN migration capacity was measured in 30 µl fresh whole blood in a membrane filter assay. Measurements were made daily from admission until discharge from the ICU or until death.

Numbers and distribution of the PMNs immigrant into the filters were evaluated in an automated image analyser. The relevant parameter was the percentage of PMNs migrating from the blood samples into the filters upon FMLP stimulation.

In parallel, the PMN blood count, reactive oxygen species production, blood levels of C-reactive protein, PMN elastase, procalcitonin, neopterin and sL-selectin were determined.

Results Sixteen patients (10 men/six women), mean age 48.8 ± 16.43 and mean APACHE III score 94.37 ± 23.71, were investigated. During the major part of the observation time, all patients had migration values below the critical minimum of 6%. The nonsurvivers kept this low reactivity until death, while survivors regained normal PMN migration during the period of clinical recovery. No such discriminative power could be attributed to the other inflammation parameters.

Conclusion PMN migration was impaired both in sepsis and SIRS. An improvement of PMN migration capacity signals the restoration of PMN-based immunity and may be a useful aid in deciding how long to maintain and when to discontinue antimicrobial therapies in intensive care patients.

P38 Impaired PMN migratory capacity: a risk marker for impending infections in severe trauma patients

H Mitterhammer[1], KH Smolle[1], P Kaufmann[1], W Wonisch[1], R Aigner[2], G Egger[3]
[1]Department of Internal Medicine and [2]Department of Nuclear Medicine, University Hospital, Graz, Austria; [3]Department of Pathophysiology, Karl-Franzens University, Graz, Austria
Critical Care 2003, **7(Suppl 2)**:P038 (DOI 10.1186/cc1927)

Objective PMNs represent the foremost line of host defence against bacterial and fungal infections. We investigated the association between impaired PMN migratory capacity and subsequent infections in critically ill trauma patients.

Method Twenty-six patients with different ISSs were included in a prospective study. PMN migration was measured daily in fresh whole blood in a membrane filter assay. Migration was evaluated in an automated image analyser. The relevant parameter was the percentage of PMNs migrating from the blood samples into filters upon FMLP stimulation. Migration values below the critical minimum of 6% on three consecutive days predict high infection risk, as we have repeatedly found in our numerous studies on this subject.

Results Nine patients developed microbiologically verified infections. In comparison with the 17 noninfected patients, these patients showed reduced PMN migratory capacity 1–19 days before infection occured.

The group with infections developed a significantly lower total PMN migration ($P = 0.0018$); they more frequently had values below the critical limit of 6% ($P = 0.0005$) and low values over longer periods ($P = 0.0008$). When these parameters were combined, infections could be predicted with a specifity/sensivity of 82.3/88.8%. Trauma severity had no influence on PMN migration. An increase of PMN migration signalled the restoration of immunity.

Conclusion Trauma patients with impaired PMN migratory capacity are at increased risk for infections. PMN migration tests can define the risk and may be useful for deciding when to initiate, maintain and discontinue antimicrobial treatment.

P39 Role of chemokine receptor 5 during respiratory syncytial virus infection

HA Haeberle[1,2], WA Kuziel[3], H-J Dieterich[2], Z Gatalica[4], RP Garofalo[1,5]
[1]Department of Pediatrics, [4]Department of Pathology and [5]Department of Microbiology and Immunology, The University of Texas Medical Branch, Galveston, TX, USA; [2]Department of Anesthesiology, Eberhard Karls Universitaet, Tuebingen, Germany; [3]Department of Genetics and Microbiology, University of Texas, Austin, TX, USA
Critical Care 2003, **7(Suppl 2)**:P039 (DOI 10.1186/cc1928)

Lower respiratory tract disease caused by respiratory syncytial virus (RSV) is characterized by profound airway mucosa inflammation, both in infants with naturally acquired infection and in experimentally inoculated animal models. Chemokines are central regulatory molecules in inflammatory, immune and infectious processes of the lung. Previously we have shown that the depletion of MIP-1α/CCL3 reduces lung inflammation and chemokine expression in RSV-infected lung tissue. In this study, we demonstrate that depletion of CCR5 as a receptor for MIP-1α results in upregulation of chemokines and cytokines in RSV-infected lung tissue but had no influence on viral clearance or histopathology compared with the wild type animals. Genetically altered mice with additional deletion of the MIP-1α/CCL3 gene demonstrated an upregulation in the chemokine mRNA expression paralleled by comparable cytokine expression following RSV infection, compared with wild type mice. There was no difference in lung inflammation or viral clearance. Pathology scores were only reduced in mice depleted for MIP-1α/CCL3. These results provide some evidence that the pattern of chemokine expressed in lung tissue determines the severity of lung inflammation during RSV infection.

P40 Measurement of endotoxin, IL-6, IL-8 and blood lactate after cardiac surgery: re-evaluation of the systemic inflammatory response induced by cardiopulmonary bypass

K Masayuki[1], T Kikuchi[1], J Sunanaga[1], K Kitahara[1], N Okayama[1], T Moriyama[1], T Omae[1], Y Kakihana[1], Y Kanmura[1], T Arimura[2]
[1]Division of Intensive Care Medicine, Kagoshima University Hospital, 23-1-1401 Tenpozan, 890-0061 Kagoshima, Japan; [2]Department of Anesthesiology, Kagoshima Medical Association Hospital, Kagoshima, Japan
Critical Care 2003, **7(Suppl 2)**:P040 (DOI 10.1186/cc1929)

Introduction Cardiopulmonary bypass (CPB) has been thought to induce endotoxemia and/or ischemia-reperfusion injury. These factors are believed to play an important role in the systemic inflammatory response following cardiac surgery with CPB. However, recent surgical advances made coronary artery bypass grafting (CABG) without CPB possible. In our study, we re-evaluate the relative contributions of CPB on the production of various mediators in patients who received cardiac surgery with CPB by comparing them with patients who received the off-pump coronary artery bypass grafting (OPCAB) procedure.

Methods With institutional approval and informed consent, we studied: (1) the changes of endotoxin (ET) and beta-glucan (BG) during the perioperative period of cardiac operations performed with CPB ($n=15$) or without CPB ($n=5$) by using the kinetic turbidmetric assay (KTA) with ET-specific and BG-specific LAL reagents that allows separate determinations of ET and BG; and (2) the changes of interleukin-6 (IL-6), interleukin-8 (IL-8), and blood lactate during the perioperative period of CABG with CPB ($n=5$) or without CPB ($n=5$). Those were compared within the group and between the groups by ANOVA and other methods.

Results (1) ET was not detectable at any time-point in any patients. In patients with CPB, BG rose in a time-dependent fashion, reaching a maximum (130.2 ± 93.1 pg/ml) at 2 hours after the initiation of CPB, then gradually decreased. No BG elevations were observed in patients without CPB. (2) IL-6 and IL-8 were elevated on ICU admission in both groups, but no significant differences were observed between the groups. In patients with CABG with CPB, blood lactate increased from ICU admission to 12 ICU hours compared with OPCAB patients, and decreased to the same level as those in OPCAB patients on 24 ICU hours.

Discussion These results indicate that CPB does not affect the production of endotoxin, IL-6 and IL-8. Other factors may contribute to the rise in blood lactate. Further studies are needed to clarify the relationship between CPB and the postsurgical inflammatory response.

P41 Enterococcal aggregation substance as target for opsonic antibodies *in vitro* and in murine sepsis

WA Krueger[1,2], M Escher[1], A Woll[1], M Gross[3], AB Muscholl-Silberhorn[4], I Vollmer[1], S Krueger-Rameck[2], KE Unertl[1], F Götz[3], GB Pier[2]
[1]Department of Anesthesiology and [3]Institute for Microbial Genetics, Tuebingen University, Germany; [2]Channing Laboratory, Harvard Medical School, Boston, MA, USA; [4]Department of Microbiology, Regensburg University, Germany
Critical Care 2003, **7(Suppl 2)**:P041 (DOI 10.1186/cc1930)

Introduction In ICU patients, the mortality of enterococcal sepsis is high, and treatment is often difficult due to multiple antibiotic resistance. Aggregation substance (AS) is a surface protein of *E. faecalis*, which mediates transfer of (resistance) plasmids and was also identified as a virulence factor. We investigated whether AS may serve as target for antibodies in phagocytosis assays and in a murine sepsis model.

Methods Using the Qiagen pQE vector system, AS was expressed in *E. coli* and a histidine-tag served for purification by Ni-NTA chromatography. After purity was verified by western blot, AS was used to immunize rabbits. In phagocytosis assays, the immune rabbit sera (IRS) were compared with pre-immune sera for their opsonic activity, using human leukocytes, complement, and mutants of *E. faecalis* OG1. In order to show the specificity of the antibodies, the sera were absorbed with mutants of *E. faecalis* OG1 constitutively expressing (AS+), or not expressing AS (AS–). In the sepsis model, aliquots of IRS or normal rabbit sera (NRS) were used for IV passive immunization of Balb/c mice 24 hours before bacterial challenge, and 4 hours and 24 hours thereafter. IV bacterial challenge was performed via tail vein injection of AS+ *E. faecalis*. The mice were sacrificed 5 days thereafter for examination of bacterial levels in internal organs.

Results When incubated with IRS, the number of AS+ *E. faecalis* recovered at the end of the phagocytosis assay was reduced by more than 50% compared with incubation with pre-immune sera ($P<0.01$), whereas there was no difference against AS– strains. IRS was still opsonic after absorption with AS– *E. faecalis* but the activity was lost after absorption with AS+ mutants. In the mouse sepsis model, weight loss was significantly less in the IRS group (mean ± SD, 97.9 ± 3.6% of baseline weight) versus the NRS group (95.3 ± 2.9%, $P=0.04$). The highest organ load with enterococci were found in the kidneys and the log cfu/g were significantly lower in the IRS group ($P=0.03$).

Conclusion In our mouse sepsis model, antisera against AS significantly reduced weight loss and also the number of enterococci recovered from kidneys. The usefulness of AS as a target for antibodies is further confirmed by enhanced killing of AS+ enterococci by IRS. Our results are encouraging and point to the possibility of adjunctive immunotherapeutic approaches in enterococcal sepsis.

P42 Identification of diagnostic criteria of septic complications in children with neutropenia

DA Furmanchuk[1], VV Kurek[1], VV Dmitriev[2], OV Aleinikova[2]
[1]Byelorussian Academy of Postgraduate Education, Department of Pediatric Anesthesia and Intensive Care, Scoriny ave 64, Minsk 220013, Belarus; [2]Byelorussian Center for Pediatric Oncology and Hematology, Lesnoy-2, Minsk 223052, Belarus
Critical Care 2003, **7(Suppl 2)**:P042 (DOI 10.1186/cc1931)

Introduction Septic complications in neutropenic patients after chemotherapy lead to high morbidity and mortality in the pediatric oncology ward. There are no clear criteria of systemic inflammatory response syndrome (SIRS) and sepsis for neutropenic patients. It is usual that patients after chemotherapy have altered WBC, and the majority of them demonstrate tachycardia and mild to moderate fever (signs of SIRS) without infection. There is no clear differentiation between definitions of febrile neutropenia and sepsis for this group of patients.

Objective To define additional diagnostic criteria of SIRS in children with febrile neutropenia after chemotherapy.

Study design Monocentric, retrospective, case–control (equilibration of age, sex, diagnose) study, cases of severe sepsis and septic shock compared with control patients with febrile neutropenia.

Methods Ninety-two patients were investigated (48 cases and 44 controls), aged 12 ± 4.5, and included 52 males and 40 females. The majority of patients had lymphoproliferative and myeloproliferative disorders, acute lymphoblastic leukemia 27%, acute myeloblastic leukemia 26%, non-Hodgkin lymphoma 13%, CNS tumors 17%, solid tumors (oseosarcoma, Ewing sarcoma, neuroblastoma, rhabdomyosarcoma) 14%. All patients had fever and neutropenia. We compared data of vital signs, levels of C-reactive protein, fibrinogen, urea and creatinin during 72 hours before a febrile episode or ICU admission. For the statistical analysis the Mann–Whitney U test was used; $P<0.05$ was considered significant.

Results Forty-eight patients (case group) (52%) developed severe sepsis or septic shock and required ICU admission (27 and 21 patients, respectively); all of these patients had clinical signs of sepsis, but only 76% had positive blood cultures. The mortality rate in the case group was 65%. In the control group only eight patients out of 44 had ICU admission, and in the control group we observed recovering in 24–32 hours after start of treatment with antibiotics in all patients. There was no mortality in the control group. Heart rate higher than 140% to normal, fever higher than 38 more than three times daily, and CRP level higher than 7.5 mg/dl was found in 92% patients of the case group 48 hours before ICU admissions. In the control group the level of CRP was significantly lower (2.6 ± 1.1 mg/dl), the heart rate was in a range between 110 and 122% to normal, fever higher than 38 was observed one or two times daily and discontinued in 24–48 hours. There were no significant difference in levels of fibrinogen, urea, and creatinin in the two groups as well as the presence of tachypnea, blood pressure and other signs during the period of observation.

Conclusion The presence of high levels of CRP, tachycardia, and severe fever in children with neutropenia are predictors of transformation febrile neutropenia to sepsis, severe sepsis and septic shock. The use of these factors as diagnostic criteria should allow preventing severe complication in patients after chemotherapy.

P43 The IL-10 –819T polymorphism is associated with increased susceptibility to severe sepsis

KA Wood[1], JA Kellum[1], R Ferrell[2], VC Arena[3], RL Delude[1], DC Angus[1], for the GenIMS Investigators
[1]CRISMA Laboratory, Department of Critical Care Medicine, [2]Department of Human Genetics and [3]Department of Biostatistics, University of Pittsburgh School of Medicine, 200 Lothrop Street, Room 606D, Pittsburgh, PA 15261, USA
Critical Care 2003, **7(Suppl 2)**:P043 (DOI 10.1186/cc1932)

Introduction Severe sepsis is characterized by an aggressive inflammatory response, and is more common in patients with genetic polymorphisms that promote *greater* production of *pro*-inflammatory cytokines (e.g. –308A on the TNF gene). Thus, we hypothesized that the genetic predisposition to *lesser anti*-inflammatory response (–819T on the IL-10 gene) would also increase the risk of severe sepsis.

Methods As part of a first interim analysis of an ongoing NIH-sponsored multicenter study of Genetic and Inflammatory Markers of Sepsis (GenIMS), we analyzed 284 adult patients presenting to the Emergency Department (ED) with community-acquired pneumonia (CAP). We drew blood from patients presenting to EDs in southwest Pennsylvania with CAP for genotyping and plasma IL-10 levels. We defined severe sepsis as a Sequential Organ Failure Assessment Score increase of 2 for any one nonrespiratory organ, or an increase of 1 for any two nonrespiratory organs, or an absolute score of 3 or 4 for respiratory organs.

Results The cohort had a mean age of 66.9 ± 17.1 years; 49.6% were female; 87.7% were Caucasian; 30.3% had underlying respiratory disease; and 39.4% developed severe sepsis. Subjects with either genotype C/T or T/T at IL-10 –819 were associated with a greater risk of progression to severe sepsis compared with the common homozygote C/C (odds ratio = 1.71, $P = 0.03$). We did not find a consistent difference in plasma IL-10 levels in subjects with different genotypes.

Table 1

IL-10 –819 polymorphisms

	All	C/C	C/T	T/T
n	284	151	114	19
% severe sepsis	39.4	33.8	43.9	57.9

Conclusion: In this preliminary analysis of subjects with CAP, those with the IL-10 –819 C/T or T/T genotypes are more likely to develop severe sepsis compared with those with the usual homozygous C/C phenotype.

Acknowledgement Supported by NIH grant R01 GM61992-01.

P44 Modulation of NF-κB signaling in macrophages under long-term and second-hit stimulation

HV Groesdonk, A Baur, E Reithmeier, B Stahl, U Senftleben
Department of Anesthesiology and Intensive Care, University Hospital of Ulm, Steinhövelstraße 9, D-89075 Ulm, Germany
Critical Care 2003, **7(Suppl 2)**:P044 (DOI 10.1186/cc1933)

Introduction Sepsis often leads to deterioration of organ function, so-called multiple organ dysfunction syndrome (MODS). Pathophysiologically, impaired control mechanisms of NF-κB activation result in a dysbalance between proinflammatory and anti-inflammatory gene transcription. In regard to hyperinflammation, NF-κB activation is thought to play a central role [1], while being inalienable for the inflammation process [2]. Therefore it is conceivable that both proinflammatory and anti-inflammatory cell functions are mediated by NF-κB in the same cell system. The aim of this study is to elucidate the activation kinetics of NF-κB under long-term stimulation (LTS) and two-time stimulation (TTS), simulating conditions in critical diseases.

Methods Murine macrophages (cell line RAW 264.7) were cultured in standard medium (DMEM + 10% FCS) and incubated in 0.1 μg/ml, 1.0 μg/ml and 10 μg/ml lipopolysaccharide (LPS). After 5, 10, 20, 30, 60 min, and again after 2, 4, 8, 12, 16, and 24 hours, we analyzed the activity of NF-κB in cellular and nuclear protein extracts using the methods of Electrophoretic Mobility Shift Assay (EMSA) and western blots (p65, IκBα). After 4 hours preincubation with 0.1 μg/ml, 1.0 μg/ml and 10 μg/ml LPS, we stimulated again a second time with 1 μg/ml LPS (TTS). The analysis mentioned above was done after 5, 10, 20, 30, 60, and 120 min.

Results Cells incubated with high concentrations of LPS (10 μg/ml) showed a biphasic activation pattern of NF-κB after 5–10 min and 12–16 hours. Cells incubated with lower LPS concentrations showed no further activation after the early activation peak. After preincubation with 0.1 μg/ml LPS and TTS an *unaltered timely* activation of NF-κB with delayed IκBα degradation was observed.

Conclusion The LPS tolerance [3] often described in the literature does not exist in macrophages preincubated with low concentrations of LPS. The biphasic activation pattern of the NF-κB signaling pathway induced by high LPS concentrations occurs possibly within the scope of an anti-inflammatory regulation mechanisms. These results clarify the varying activation kinetic of the NF-κB signaling pathway.

References
1. Senftleben U, Karin M: **The IKK/NF-kappa B pathway.** *Crit Care Med* 2002, **30**:S18-S26.
2. Lawrence T, Gilroy DW, Colville-Nash PR, Willoughby DA: **Possible new role for NF-kappaB in the resolution of inflammation.** *Nat Med* 2001, **7**:1291-1297.
3. Bohuslav J, Kravchenko VV, Parry GC, Erlich JH, Gerondakis S, Mackman N, Ulevitch RJ: **Regulation of an essential innate immune response by the p50 subunit of NF-kappaB.** *J Clin Invest* 1998, **102**:1645-1652.

P45 Adenosine enhanced preconditioning prevents apoptosis in the small intestine and inhibits bacterial translocation

S Unal, I Cinel, F Demirkan, L Cinel, C Oztürk, N Doruk, U Oral
Adnan Menderes Bulvarý, Marina Sitesi C Blok No 4, 90033 Mersin, Turkey
Critical Care 2003, **7(Suppl 2)**:P045 (DOI 10.1186/cc1934)

Introduction Previously it has been shown that ischemic preconditioning could increase the tolerance of intestinal tissue to ischemia [1]. In this study we investigated the effects of pharmacological preconditioning with adenosine infusion on intestinal ischemia/reperfusion (I/R) injury and bacterial translocation. We also evaluated the presence of any additive effects of adenosine administration when used together with ischemic preconditioning.

Materials and methods Forty-six Sprague–Dawley rats were used, and rats were randomly divided into five groups: Group I, sham operated controls: only laparotomy was performed; Group II, ischemia-reperfusion (I/R): superior mesenteric artery was clamped for 40 min to induce ischemia in the small bowel that was followed by 24 hours of reperfusion; Group III, ischemic preconditioning (IPC): two cycles of 5 min of ischemia–5 min of reperfusion were performed prior to the I/R schedule given in Group II; Group IV, pharmacologic preconditioning (Ado): adenosine at a dose of 1000 μg/kg was infused from the internal jugular vein prior to the I/R schedule given in Group II; Group V, adenosine enhanced IPC: adenosine was infused as in Group IV prior to ischemic preconditioning that was followed by a 40 min ischemia–24 hours reperfusion schedule. Twenty-four hours later, to evaluate whether the I/R induced intestinal injury and bacterial translocation, blood, liver, spleen, and mesenteric lymph node (MLN) specimens were obtained under sterile conditions for microbiological analysis. Samples of jejunum were removed for histopathological evaluation by Chiu scoring and determination of apoptotic cell number is achieved by the staining of M30 monoclonal antibody.

Results In the I/R group, the incidence of bacteria-isolated MLNs, spleen, and liver was significantly higher than other groups ($P < 0.05$). IPC, Ado and Ado + IPC prevented I/R-induced bacterial translocation and they significantly reduced the I/R-induced intestinal injury and intestinal epithelial apoptosis.

Conclusions This is the first study showing that adenosine administration was as effective as ischemic preconditioning in inducing ischemic tolerance and in preventing bacterial translocation in the rat intestine. However, there was no enhancement of IPC with prior adenosine infusion.

Reference
1. Aksöyek S, Cinel I, Avlan D, Cinel L, Oztürk C, Polat G, Nayci A, Oral U: **Intestinal ischemic preconditioning protects the intestine and reduces bacterial translocation.** *Shock* 2002, **18**:476-480.

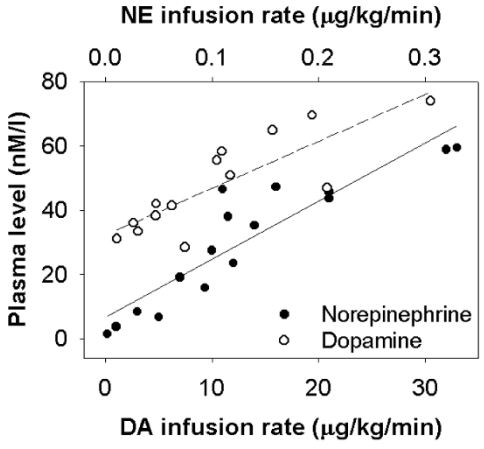
P46 Catecholamine pharmacokinetics and pharmacodynamics in critical illness

AJ Johnston[1], LA Steiner[1,2], M O'Connell[2], DA Chatfield[1], AK Gupta[1], DK Menon[1]
[1]Department of Anaesthesia and [2]Academic Neurosurgery, Addenbrooke's Hospital, Cambridge, CB2 2QQ, UK
Critical Care 2003, **7(Suppl 2)**:P046 (DOI 10.1186/cc1935)

Objective Despite their widespread use, there are limited data on the pharmacokinetics and pharmacodynamics of dopamine (DA) and norepinephrine (NE) in critically ill patients. We have addressed these issues in a randomised cross-over study in a group of head-injured patients.

Methods Eight patients with a head injury, requiring DA or NE infusions to support cerebral perfusion pressure (CPP), were recruited following informed assent from patients' next of kin. Patients received in randomised order either DA or NE to achieve and maintain a CPP of 70 mmHg and then, following a 30 min period of stable haemodynamics, a CPP of 90 mmHg. Data were then acquired using the second agent. Haemodynamic measurements were made during each period and a blood sample was obtained at the end of each study period; plasma was stored for later analysis of catecholamine levels by high performance liquid chromatography. Data were analysed with paired *t* tests and regression analysis using Statview 4 (SAS), with $P < 0.05$ treated as significant.

Figure 1



Results Plasma levels of NE and DA were significantly related to infusion rates (Fig. 1), but neither predicted haemodynamic parameters. However, there was a significant quadratic relationship between the infusion rate of DA and CI ($r^2 = 0.431$), and SVRI ($r^2 = 0.605$), with a breakpoint (at which the CI reduced and the SVRI increased) at a DA plasma level of ~ 50 nM/l (corresponding to an infusion rate of ~ 15 µg/kg per min).

Conclusions NE and DA have predictable pharmacokinetics; however, those of DA do not fit a simple first-order kinetic model. The pharmacodynamic effects of DA and NE show much inter-individual variability and unpredictability. DA plasma levels appear to relate to variations in adrenergic receptor effects with break points that reflect expectations from infusion rate related pharmacodynamics.

P47 The effect of vasopressin on gastric perfusion in catecholamine-dependent septic shock patients

FMP van Haren, FW Rozendaal, JG van der Hoeven
Department of Intensive Care Medicine, Jeroen Bosch Hospital, PO Box 90153, 5200 ME Hertogenbosch, The Netherlands
Critical Care 2003, **7(Suppl 2)**:P047 (DOI 10.1186/cc1936)

Introduction Vasopressin increases blood pressure and decreases catecholamine requirements in septic shock patients [1–3]. Few clinically relevant data are available on the effect of vasopressin on the splanchnic circulation.

Objective To study the effect of continuous infusion of vasopressin on the splanchnic circulation in septic shock patients.

Design Prospective clinical study.

Setting Intensive care unit in a teaching hospital.

Patients Eleven consecutive patients with documented septic shock who remained hypotensive despite norepinephrine infusion at a rate of ≥ 0.2 µg/kg per min.

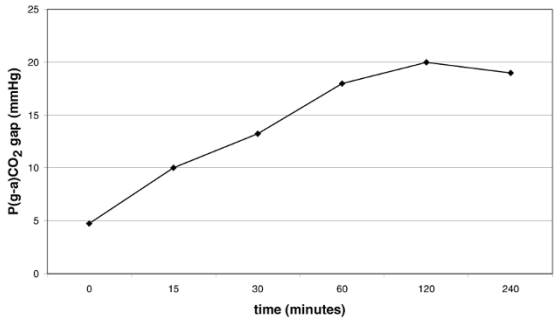
Interventions Insertion of a gastric tonometry catheter; continuous infusion of vasopressin 0.04 U/min during 4 hours.

Measurements and main results P(g–a)CO_2 gap, blood pressure and cardiac index were recorded at baseline and after 15, 30, 60, 120 and 240 min.

The median P(g–a)CO_2 gap increased from 5 mmHg at baseline to 19 mmHg after 4 hours ($P = 0.022$; Fig. 1). Blood pressure (mean ± SD) increased from 61 ± 13 mmHg at baseline to 68 ± 9 mmHg after 4 hours ($P = 0.055$). No significant changes in cardiac index were noted ($P = 0.978$). There was a strong correlation between median plasma levels of vasopressin and the median P(g–a)CO_2 gap ($r^2 = 0.98$) as is shown in Fig. 2.

Conclusions In norepinephrine-dependent septic shock patients, continuous infusion of low-dose vasopressin results in a significant and dose-dependent increase of the P(g–a)CO_2 gap compatible with gastrointestinal hypoperfusion.

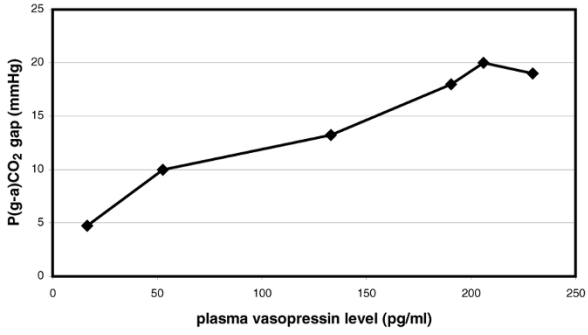
Figure 1



25th percentile	1.9	4.8	9.3	10.6	12.8	13.3
75th percentile	10.9	19.4	20.5	23.9	29.1	26.8

Median P(g–a)CO_2 gap (mmHg) with 25th and 75th percentiles.

Figure 2



Relationship between median plasma levels of vasopressin and median P(g–a)CO_2 gap.

References

1. Patel BM, Chittock DR, Russell JA, Walley KR: **Beneficial effects of short-term vasopressin infusion during severe septic shock.** *Anesthesiology* 2002, **96**:576-582.
2. Holmes CL, Walley KR, Chittock DR, Lehman T, Russell JA: **The effects of vasopressin on hemodynamics and renal function in severe septic shock: a case series.** *Intensive Care Med* 2001, **27**:1416-1421.
3. Tsuneyoshi I, Yamada H, Kakihana Y, Nakamura M, Nakano Y, Boyle WA III: **Hemodynamic and metabolic effects of low-dose vasopressin infusions in vasodilatory septic shock.** *Crit Care Med* 2001, **29**:487-493.

P48 Hepato-splanchnic and pancreatic blood flow during administration of vasopressin in septic shock

V Krejci[1], L Hiltebrand[1], M Ten Hoevel[1], GH Sigurdsson[2]
[1]Department of Anaesthesiology and Intensive Care, University Hospital, Inselspital, 3010 Bern, Switzerland; [2]Department of Anesthesia & Intensive Care Medicine, Landspitali University Hospital, Reykjavik, Iceland
Critical Care 2003, **7(Suppl 2)**:P048 (DOI 10.1186/cc1937)

Background and goal of study The use of vasopressin for treatment of hypotension in sepsis might deteriorate splanchnic regional and microcirculatory blood flow. The aim of this study was to measure regional blood flow and microcirculatory blood flow (MBF) continuously and simultaneously in multiple abdominal organs during administration of Ornithin-8-Vasopressin in peritonitis-induced sepsis.

Materials and methods Pigs (20–25 kg, $n=32$) were anaesthetised and ventilated. Cardiac index was measured with thermodilution. Blood flow was measured in the superior mesenteric and hepatic artery as well as in the portal vein using transit time flowmetry. MBF was measured on the surface of the liver and pancreas, using a multichannel Laser Doppler flowmeter. Peritonitis was induced by instillation of autologous faeces in the peritoneal cavity. After 240 min of peritonitis, intravenous colloids were given to transform hypodynamic shock into hyperdynamic septic shock. After 300 min of peritonitis, 0.06 IU/kg per hour of Ornithin-8-Vasopressin was administered continuously as an intravenous infusion. Four groups of animals were investigated: Group C ($n=8$) served as control; Group V ($n=8$) received only ornithin-vasopressin; Group S ($n=8$) was exposed to peritonitis and fluid resuscitation; Group SV ($n=8$) received ornithin-vasopressin after peritonitis and fluid resuscitation.

Results and discussion Baseline measurements were taken at $T=300$ min (before ornithin-vasopressin). Results are presented as percent of baseline. $P<0.05$ was considered significant. Mean arterial blood pressure increased during infusion of vasopressin by 25% ($P<0.05$) in the groups V and SV ($P>0.05$), while it remained constant in the other two groups. Cardiac output decreased by 30% in the groups V and SV ($P<0.05$) and remained constant in groups C and V. Blood flow in the superior mesenteric artery and in the portal vein decreased by 25% in group V ($P<0.05$) while there was no change in group C, and by 50% in group SV ($P<0.05$), which was significantly more compared with a decrease of 25% in group S. Blood flow in the hepatic artery increased by 120% ($P<0.05$) in group V and by 50% ($P<0.05$) in group SV, while there was an increase by 25% in group C and a 20% decrease in group S. MBF of the liver decreased gradually in groups S and SV to 15% ($P<0.05$) below baseline after 180 min in both groups. MBF of the liver decreased during infusion of vasopressin in nonseptic animals (Group V) by 30% ($P<0.05$) while it remained constant in nonseptic controls (Group C). MBF of the pancreas decreased by 20% ($P<0.05$) in groups C and S, while it decreased 35–40% ($P<0.05$) in groups S and SV.

Discussion and conclusions 1) During the infusion of ornithin-vasopressin, blood flow in the superior mesenteric artery and the portal vein decreased. 2) Increased blood flow in the hepatic artery during administration of ornithin-vasopressin suggests that the hepatic arterial buffer response was involved. 3) MBF in the liver decreased during administration of ornithin-vasopressin in nonseptic animals in contrast to the septic group. 3) Ornithin-vasopressin appeared to decrease significantly MBF in the pancreas in both septic and nonseptic animals. 4) In this model, increasing arterial blood pressure with ornithin-vasopressin did not result in an increase of microcirculatory blood flow in any of the organs studied.

P49 Renal arterial and microcirculatory blood flow during administration of Ornithin-8-Vasopressin in septic shock

L Hiltebrand[1], V Krejci[1], M Ten Hoevel[1], GH Sigurdsson[2]
[1]Department of Anaesthesiology and Intensive Care, University Hospital, Inselspital, 3010 Bern, Switzerland; [2]Department of Anesthesia & Intensive Care Medicine, Landspitali University Hospital, Reykjavik, Iceland
Critical Care 2003, **7(Suppl 2)**:P049 (DOI 10.1186/cc1938)

Background and goal of study The use of vasopressin for treatment of hypotension in sepsis might deteriorate splanchnic regional and microcirculatory blood flow. The aim of this study was to measure renal artery blood flow and microcirculatory blood flow (MBF) of the kidney continuously and simultaneously during administration of Ornithin-8-Vasopressin in peritonitis-induced sepsis.

Materials and methods Pigs (20–25 kg, $n=32$) were anaesthetised and ventilated. Cardiac index was measured with thermodilution. Blood flow was measured in the renal artery using transit time flowmetry. MBF was measured on the surface of the kidney using a multichannel Laser Doppler flowmeter. Peritonitis was induced by instillation of autologous faeces in the peritoneal cavity. After 240 min of peritonitis, intravenous colloids were given to transform hypodynamic shock into hyperdynamic septic shock. After 300 min of peritonitis, 0.06 IU/kg per hour of Ornithin-8-Vasopressin was administered continuously as an intravenous infusion. Four groups of animals were investigated: Group C ($n=8$) served as control; Group V ($n=8$) received only vasopressin; Group S ($n=8$) was exposed to peritonitis and fluid resuscitation; Group SV ($n=8$) received vasopressin after peritonitis and fluid resuscitation.

Results and discussion Baseline measurements were taken at $T=300$ min (before ornithin-vasopressin). Results are presented as percent of baseline. $P<0.05$ was considered significant. Mean arterial blood pressure increased during infusion of vasopressin by 25% ($P<0.05$) in groups V and SV ($P>0.05$), while it remained constant in the other two groups. Cardiac output decreased by 30% in groups V and SV ($P<0.05$) and remained constant in groups C and V. Renal artery blood flow decreased after 60 min of vasopressin by 15% ($P<0.05$) in group V and returned to baseline after 180 min. In group SV, renal blood flow decreased by about 10% ($P>0.05$) after 30 min and returned to baseline after 90 min. MBF of the kidney remained constant in groups C and S. In group V, MBF of the kidney decreased by 25% ($P<0.05$) after 60 min of ornithin-vasopressin but returned to baseline after 180 min. In group SV, MBF of the kidney decreased by 15% ($P<0.05$) and remained decreased. Urine output increased signifi-

cantly in both septic and nonseptic groups receiving ornithin-vasopressin.

Discussion and conclusions 1) In nonseptic animals, blood flow in the renal artery and microcirculatory blood flow of the renal cortex decreased only initially and recovered after 180 min during infusion of vasopressin. This finding suggests the presence of an autoregulatory mechanism. 2) Although vasopressin decreased renal artery blood flow to a lesser extent in the septic group, microcirculatory blood flow decreased. This finding suggests that autoregulation at the microcirculatory level of the renal cortex might be impaired in sepsis. 3) In this model, increased urine output was not due to increased blood flow but rather the result of pressure diuresis.

P50 Effects of corlopam infusion on pHi and ΔO_2: a randomized controlled clinical trial. Preliminary data

A Donati, S Loggi, S Falcetta, E Bruni, V Zompanti, F Alò, G Ioannidis, P Pelaia
Institute of Medical Surgical Emergencies, University of Ancona, Ospedale Regionale Torrette, Via Conca 1, 60020 Torrette, Ancona, Italy
Critical Care 2003, **7(Suppl 2)**:P050 (DOI 10.1186/cc1939)

Introduction The hepatosplanchnic region is quite important in the physiopathology of shock, trauma, SIRS and sepsis [1]. The intestinal mucosa is one of the first parenchimis that are influenced by the alterations of the perfusion and/or splanchnic oxygenation [2]. Particularly, a pHi <7.1 for a period greater than 2 hours, defined as sigmoid ischemia of low degree, is predictive for major complications and death [3].

Fenoldopam has been demonstrated to improve glomerular perfusion through D_1 receptors, which are present also in the mesenteric region.

The purpose of our study is to verify whether fenoldopam infusion during abdominal aortic surgery can prevent gut ischemia.

Materials and methods It is a prospective, controlled, randomized clinical trial on a preliminary series of 14 patients operated for abdominal aortic aneurysm. These patients were monitored with a sigmoid tonometer and with a NiCO system to measure cardiac index (CI). Patients just after anesthesia induction were randomized, allocated in two groups: one receiving corlopam at the dosage of 0.05 μg/kg per min (Group A) and the other receiving placebo (Group B). ΔO_2, pHi and CO were detected at the following times: just after the anesthesia inducion (t0), before aortic clamping (t1), 30 min after aortic clamping (t2), and just after the operation (t3). At these times an arterial sample was taken to detect arterial blood lactate, tumor necrosis factor alpha (TNF-α), and interleukin-1B, interleukin-6 and interleukin-8 (IL-1β, IL-6, IL-8). At T1 and T2 a portal blood sample was taken to detect portal blood lactate, TNF-α, IL-1β, IL-6, IL-8. At each time point medians of pHi, ΔO_2, systemic and portal lactate, and hemoglobin (Hb) were calculated for both groups of patients. The trend of pHi was determined with the Friedman test and Dunn's post-test. Median comparison was performed using the two-tailed non-parametric Mann–Whitney test. The Fischer exact test was used to compare a possible abnormal distribution of pHi and/or ΔO_2 within groups of patients.

Results Phi decreased significantly at T2 in both groups ($P<0.01$), but at T3 was significantly higher, compared with T0, only in Group B ($P<0.05$). ΔO_2 did not increase significantly during aortic clamping in Group A, while in Group B at T2 it increased significantly ($P<0.01$). CI decreased significantly in both groups at T2 ($P<0.05$). Portal lactates were significantly higher in group B at T1 ($P<0.05$), but at T2 there was not any significant difference. The arterial lactates trend was similar in the two groups. Any significant difference could be found for cytokines between the two groups.

Conclusions From these preliminary data it seems that corlopam can ameliorate gut perfusion, as suggested by the increase of pHi and ΔO_2, even if these data have to be confirmed on a larger number of patients. After that other work must be done to investigate whether corlopam infusion can increase the outcome, that is morbidity and mortality, of patients undergoing abdominal aorta aneurysm.

References

1. Marshall JC, Christou NU, Meakins JL: **The gastrointestinal tract. The 'undrained abscess' of multiple organ failure.** *Ann Surg* 1993, **218**:111-119.
2. Dantzker DR: **The gastrointestinal tract — the canary of the body?** *JAMA* 1993, **270**:1247-1248.
3. Heino A, Hartikainen J, Merasto ME, *et al.*: **Systemic and regional effects of experimental gradual splanchnic ischemia.** *J Crit Care* 1997, **12**:92-98.

P51 Capillary ischemia and abnormal capillary O_2 flux during sepsis is not prevented by nitric oxide inhibition

RM Bateman[1], MD Sharpe[2], CG Ellis[1]
[1]Department of Medical Biophysics and [2]Department of Anesthesia, University of Western Ontario, London, Ontario, Canada N6A5C1
Critical Care 2003, **7(Suppl 2)**:P051 (DOI 10.1186/cc1940)

Sepsis causes increased capillary stopped-flow, loss of capillary density, maldistribution of blood flow and increased oxygen extraction from 'normal' capillaries [1] in skeletal muscle. Since nitric oxide overproduction has been associated with refractory hypotension, capillary stopped-flow and decreased RBC deformability [2], we hypothesized that NO inhibition would prevent microvascular dysfunction. In a rat cecal ligation and perforation sepsis model, plasma NOx^- level (NO chemiluminescence) was maintained at baseline by NO inhibition (L-NIL) and skeletal muscle capillary geometry, hemodynamics and RBC O_2 saturation (SO_2) were quantified (spectrophotometric functional imaging). O_2 flux, amount of O_2 leaving the capillary per unit surface area, was calculated from capillary dimensions and O_2 flow rates. Sepsis increased plasma NOx^- (145%), capillary stopped-flow (140%) and O_2 flux (70%) and decreased MAP (30%) and RBC supply rate (SR) (25%) ($P<0.05$). NO inhibition maintained RBC SR and partially maintained MAP (90% of baseline), but had no effect on capillary stopped-flow or O_2 flux. We conclude that NO-independent capillary ischemia caused functional capillaries to off-load greater amounts of O_2 to supply larger tissue volumes. Capillary $SO_2<8\%$ indicated microvascular dysregulation and inefficient matching of local O_2 delivery to local O_2 demand. Improving capillary flow may benefit the septic patient.

References

1. Ellis CG, Bateman RM, Sharpe MD, Sibbald WJ, Gill R: **Effect of a maldistribution of microvascular blood flow on capillary O_2 extraction in sepsis.** *Am J Physiol Heart Circ Physiol* 2002, **282**:H156-H164.
2. Bateman RM, Jagger JE, Sharpe MD, Ellsworth, M, Mehta S, Ellis CG: **Erythrocyte deformability is a nitric oxide mediated factor in decreased capillary density during sepsis.** *Am J Physiol Heart Circ Physiol* 2001, **280**:H2848-H2856.

P52 Does generalized edema in sepsis increase muscular tissue pressure?

J Maňák[1], M Schreiber[2], H Matulová[2], M Šlemrová[1], J Cerman[1], M Šitina[1], S Špelda[3], L Sobotka[1], Z Zadák[1]
[1]Department of Metabolism and Gerontology, and [2]Department of Neurology, Charles University Teaching Hospital, Hradec Králové, Czech Republic; [3]Animal Research Laboratory, Military Medical Academy JE Purkyně, Hradec Králové, Czech Republic
Critical Care 2003, **7(Suppl 2)**:P052 (DOI 10.1186/cc1941)

Objective In sepsis, generalized tissue edema develops as a rule due to fluid management under conditions of systemic capillary leak. Edema formation in a closed and noncompliant anatomic compartment can lead to increased intracompartmental pressure and subsequent tissue damage as seen, for example, in post-ischemic compartment syndrome. We hypothesized that increased intramuscular tissue pressure caused by muscle swelling in a closed fascial space can contribute to skeletal muscle damage in sepsis. The aim of this study was to describe intramuscular pressure changes during massive fluid resuscitation in experimental porcine sepsis.

Material and methods Seven anesthetised, artificially ventilated and multicatheterized domestic pigs (body weight 29.7 ± 3.9 kg) were randomly subjected to either live *E. coli* IV infusion to induce sepsis ($n=4$) or to a sham procedure ($n=3$). Animals were fluid resuscitated with 20 ml/kg per hour Ringer's lactated solution and followed for 24 hours after start of the microbial infusion. Hourly fluid balance and cumulative fluid balance were recorded. Intramuscular pressure was measured every hour using an electronic transducer-tipped catheter system placed into the m. tibialis longus of the right pelvic extremity. For statistical analysis, ANOVA for repeated measures, the Dunnett test and the Mann–Whitney U test were used.

Results In both groups, positive fluid balance was observed. In septic animals, final cummulative fluid retention was 345 ± 121 ml/kg per 24 hours compared with 149 ± 25 ml/kg per 24 hours in controls ($P<0.00001$). Intramuscular pressure increased from initial values (median 10 mmHg, range 6–11 mmHg) gradually in both groups during the experiment to 13 (11–20) mmHg in septic and 16 (15–17) mmHg in controls. Despite lower fluid retention, the intramuscular pressure increased to significantly higher values in the control group ($P<0.01$) compared with septic animals. The increase reached statistical significance compared with baseline in hour 5 in controls, and in hour 13 in the septic group. In both groups, the intramuscular pressure never exceeded 20 mmHg, which is clearly below the pressure that is proven to cause skeletal muscle damage in compartment syndrome.

Conclusions Increased skeletal muscle tissue pressure during fluid retention following crystaloid infusion was observed in both septic and control animals. Tissue pressures did not reach levels proven to promote direct damage to skeletal muscle in any group.

The increase was delayed and significantly lower in septic animals compared with controls despite higher fluid retention in the septic group.

P53 Myocardial cell injury in septic shock

MG Rodrigues, PRC Junior, WH Junior, AC Camarozano, JCR Verdeal
Vila Isabel, Rio de Janeiro, Brasil
Critical Care 2003, **7(Suppl 2)**:P053 (DOI 10.1186/cc1942)

Objective To determine the presence of otherwise undetected myocardial cell injury in patients with septic shock using daily eletrocardiographics, and bidimensional echocardiography, serum troponin I (cTN I) and serum C-reactive protein (when electrocardiographic evidence of acute myocardial infarction).

Design Prospective observational study.

Setting Intensive care unit (ICU) of a tertiary institution.

Patients Twenty-eight consecutive patients with sepsis or septic shock.

Interventions Daily collection of blood for the measurement of cTN I serum levels. Cineangiography when necessary. Illness severity assessment and collection of demographic data.

Measurements and main results Twenty-eight patients were studied for a mean period in the ICU of 17.2 days (range, 3–37 days). All 10 patients who died in the intensive care unit had elevated levels of cTN I, mean 21.9 ng/ml (range, 2.9–94.1). Survivors tended to lower levels of cTN I than nonsurvivors in septic shock, mean 12.4 ng/ml (range 0.5–57.0). All five patients who had abnormal cineangiography had elevated levels of cTN I, mean 38.4 ng/ml (range, 5.4–94.1), while normal cineangiography had cTN I mean 9.1 ng/ml (range, 0.5–27.8). The difference between serum C-reactive protein and cTN I or mortality failed to reach statistical significance. No patient had electrocardiographic evidence of acute myocardial infarction, although, on admission, five patients had left bundle branch patterns, two patients had right bundle branch patterns and two had evidence of an atrial fibrillation. Seventeen cardiac catheterizations were done and five were abnormal correlating to abnormalities of the ecochardiogram. Three patients used intraaortic baloon pumping in a period of time up to 6 days (mean 3 days).

Conclusion Myocardial cell injury (cardiac dysfunction) appears to be common in patients with septic shock but does not correlate with coronary artery disease. It seems to be an imbalance between oxygen delivery and consumption.

P54 Severe acute mitral regurgitation complicating acute myocardial infarction: case for aggressive therapy

J Belohlavek, R Skulec, T Kovarnik, A Linhart, M Psenicka, M Aschermann
Department of Internal Medicine II, Faculty General Hospital, Charles University, Prague, Czech Republic
Critical Care 2003, **7(Suppl 2)**:P054 (DOI 10.1186/cc1943)

Introduction The mortality of patients with cardiogenic shock (CS) following acute myocardial infarction (AMI) remains high, despite modern reperfusion strategies. The progressive hemodynamic deterioration in patients with AMI is usually caused by left ventricular systolic dysfunction as a consequence of necrosis or ischaemia. The special subset of CS patients comprises patients with mechanical complications, mainly the severe acute mitral regurgitation (SAMR), ventricular septal and free wall rupture (8%, 6% and 2.7%, respectively, of all CS patients).

Methods Prospective observation of six consecutive patients with SAMR September 2001–October 2002.

Results See Table 1.

Conclusion Initial aggressive organ support and stabilization followed by mitral valve replacement can offer the patients with SAMR good long-term prognosis.

References
1. Qiang C, *et al.*: **Mitral valve surgery for acute papillary muscle rupture following myocardial infarction.** *J Heart Valve Dis* 2002, **11**:27-31 [33 patients/22 years, 21 long-term survivors].
2. Yehezkiel K, *et al.*: **Mitral valve operation in postinfarction rupture of a papillary muscle: immediate results and long-term follow up of 22 patients.** *Mayo Clin Proc* 1992, **67**:1023-1030 [22 patients/9 years, 14 long-term survivors].
3. Tavakoli R, *et al.*: **Surgical management of acute mitral valve regurgitation due to post-infarction papillary muscle rupture.** *J Heart Valve Dis* 2002, **11**:22-26 [21 patients/10 years, 14 long-term survivors].

Table 1

Patient (9/2001–10/2002)	AMI	IRA	MI to shock	Shock/MODS	Outcome	Valve replacement
50-year-old male	Anterior	LAD	< 1 day	+/+	Survived	+
57-year-old male	Posterior	LCx	3 days	+/+	Survived	+
70-year-old female	Inferior	LCx	3 weeks	+/–	Survived	+
38-year-old male	Lateral	LCx	Immediately	+/+	Died	–
60-year-old male	Anterior	LAD	Immediately	–	Died	–
54-year-old female	Lateral	LCx	3 weeks	+/–	Survived	+

LCx, left circumflex (coronary) artery.

P55 Hemodynamic effects of levosimendan after surgery in LPS pretreated rabbits

V Faivre, D Payen, A Mebazaa
Anesthesia and Intensive Care Department, Lariboisiere University Hospital, 2 rue Ambroise Pare, 75475 Paris cedex 10, France
Critical Care 2003, **7(Suppl 2)**:P055 (DOI 10.1186/cc1944)

Introduction Sepsis induces myocardial dysfunction and vascular hypocontractility. Recent data suggest that phosphorylation of myocardial contractile proteins decreases myofilament sensitivity to calcium and may contribute to myocardial depression [1]. Levosimendan (LS), a new calcium sensitizing drug and K_{ATP} channel opener, is used in human heart failure [2].

Aim To evaluate the LS effect on heart function, vascular tone and renal microcirculation in rabbit without LPS (LPS–) and 36 hours after LPS administration (LPS+).

Methods $n=8$ LPS+ and $n=4$ LPS– rabbits were analyzed. No animal died following LPS or saline injection, nor during the experiment. Heart rate (HR), systolic (sAP) and diastolic (dAP) arterial pressure (mmHg), systolic (sAoV), and mean aortic (mAoV) blood flow velocities (20 MHz pulsed Doppler [cm/s]), systolic (sRen) and diastolic (dRen) renal artery blood flow (transonic Doppler [ml/min]) and renal cortical (Cort) and medullary (Med) flows (laser Doppler [tissue perfusion units, TPU]) were measured in anesthetized and ventilated rabbits. Heart inotropic quality was estimated by maximal acceleration (γmax [cm/s]) and sAoV. In the LPS+ group, LPS (600 µg/kg) was injected 36 hours before the experiment. Data were collected in both groups before and at the end of a fluid loading test (20 ml in 5 min), 10 min after, and then every 15 min during a 4 hour LS infusion (200 µg/kg per hour).

Statistical analysis was performed using one-way and two-way ANOVA.

Results (Mean ± SD, all parameters were gaussian.) Myocardial failure in LPS+ animals was confirmed by fluid loading effect on γmax and sAoV (+8% vs +14% and +8% vs +20%, respectively, in LPS+ and LPS–; $P<0.05$, two-way ANOVA).

Despite its effects on macrocirculation, LS only slightly decreased Cort in LPS– animals, whereas no effect was observed on Med (Table 1).

Conclusion In this model of endotoxin-induced myocardial dysfunction, LS improved cardiac systolic parameters. Hypotension could be related to LS interaction with K_{ATP} channels. The effects on renal macro and microcirculation need further investigation.

Table 1

Effects of LS

	10 min after fluid		LS 30 min		LS 4 hours	
	LPS+	LPS–	LPS+	LPS–	LPS+	LPS–
HR	276 ± 40	319 ± 10	309 ± 36	336 ± 8	318 ± 35*†	328 ± 19
γmax	6898 ± 1955	6576 ± 1372	8177 ± 2151	7821 ± 1541	7812 ± 2069†	7205 ± 1150†
sAoV	91 ± 27	86 ± 9	102 ± 27	101 ± 15	102 ± 27†	97 ± 12†
sAP	99 ± 23	111 ± 8	88 ± 22	93 ± 9	76 ± 15†	88 ± 7†
dAP	61 ± 22	85 ± 6	44 ± 20	66 ± 8	35 ± 16*†	52 ± 5†
sRen	36 ± 10	28 ± 5	51 ± 16	44 ± 10	52 ± 17†	40 ± 7†
dRen	17 ± 7	16 ± 3	17 ± 9	19 ± 2	12 ± 6†	7 ± 6†

* $P < 0.05$, two-way ANOVA and † $P < 0.05$, one-way ANOVA.

References

1. Tavernier B, *et al.*: *Am J Respir Crit Care Med* 2001, **163**:362-367.
2. Harjola VP, *et al.*: *Am J Cardiol* 1999, **83**:4-8.

P56 Levosimendan benefits critically ill patients with decompensated heart failure assessed with plasma B-type natriuretic peptide (BNP) and LVEF

AS McLean, SJ Huang, B Tang, M Nalos
Intensive Care Unit, Nepean Hospital, University of Sydney, Penrith NSW 2750, Australia
Critical Care 2003, **7(Suppl 2)**:P056 (DOI 10.1186/cc1945)

Background Levosimendan enhances cardiac contractility and ventricular diastolic function [1], acting as a calcium sensitiser, and producing vasodilation via vascular smooth muscle relaxation by ATP-dependent K^+-channel activation. Although hemodynamic variables are often used to assess patients, less invasive measures are often preferred. Plasma levels of BNP correlate well with cardiac wall stress and changes in plasma BNP are associated with changes in morbidity and outcomes [2]. We investigated using echocardiographic-determined left ventricular ejection fraction (LVEF) and plasma BNP concentrations as surrogate endpoints to assess the efficacy of levosimendan in decompensated heart failure patients.

Methods Informed consent was obtained to treat 14 critically ill patients, five with unstable hemodynamic conditions admitted to the ICU and nine with left ventricular ejection fraction (LVEF) < 25%; five with ischemic cardiomyopathy and four with dilated idiopathic cardiomyopathy (all NYHA class IV) were recruited. Levosimendan was infused as a 10-min bolus of 12 μg/kg, followed by 0.1 μg/kg per min for 24 hours. The left ventricular ejection fraction was determined echocardiographically by Simpson's method, before and after (< 1 hour) the infusion. Blood (4 ml) was collected before and immediately after infusion for plasma BNP measurements (Biosite®, San Diego, CA, USA). $P < 0.05$ was regarded as significant.

Results See Table 1.

Table 1

$n = 14$	Pre-infusion	Post-infusion	% Change	P*
LVEF (%)	25 ± 3	31 ± 3	+31 ± 10	0.006
BNP (pg/ml)	859 ± 140	475 ± 111	–35 ± 11%	0.004

Data presented as mean ± SE. * Wilcoxon Rank Sum.

Conclusion In this initial study, we have confirmed the improvement in cardiac function after levosimendan infusion in patients with decompensated heart failure. We have demonstrated that levosimendan produces significant improvements in cardiac function as demonstrated by plasma BNP and echocardiographic LVEF measures. Changes in BNP level were more easily obtained and prone to less technical error than LVEF by echocardiography, which requires an experienced operator.

References

1. Janssen PM, *et al.*: **Levosimendan improves diastolic and systolic function in failing human myocardium.** *Eur J Pharmacol* 2000, **404**:191-199.
2. Cheng V, Kazanagra R, Garcia A, *et al.*: **A rapid bedside test for BNP predicts treatment outcomes in patients admitted for decompensated heart failure.** *J Am Coll Cardiol* 2001, **37**:386-391.

P57 Interaction between renal function and the effect of levosimendan on long-term mortality of patients with low-output heart failure

J Cleland[1], M Nieminen[2], M Kivikko[3]
[1]University of Hull, Castle Road, Cottingham, Kingston-upon-Hull, HU16 5JQ, UK; [2]Cardiology Division, Helsinki University Central Hospital, Helsinki, Finland; [3]Orion Pharma, Clinical Research, Cardiovascular Projects, PO Box 65, FIN-02101, Espoo, Finland
Critical Care 2003, **7(Suppl 2)**:P057 (DOI 10.1186/cc1946)

Renal dysfunction is an adverse prognostic sign in patients with chronic stable heart failure. We used pooled data from the LIDO ($n=203$) and RUSSLAN ($n=498$) trials to explore the influence of renal function on outcome in severe, unstable heart failure, and to evaluate the effects of the novel calcium sensitising agent, levosimendan, in those patients with severe heart failure with different levels of renal impairment. Patients in the LIDO study with low-output heart failure received infusions of either levosimendan, loading dose 24 μg/kg over 10 min, followed by a continuous infusion of 0.1 μg/kg per min, or dobutamine, 5 μg/kg per min with no loading dose, for 24 hours. In patients with <30% increase in cardiac output after 2 hours the infusion rate of both drugs was doubled for the rest of the treatment period. Patients in the RUSSLAN study with heart failure following an acute ischaemic event were given either levosimendan, loading dose 6–24 μg/kg over 10 min, then 0.1–0.4 μg/kg, or placebo, for 6 hours. Six patients were excluded as baseline serum creatinine values were unavailable. Patients were classified according to their baseline renal function by calculating creatinine clearance (CLcr) values from baseline serum creatinine by the formula of Cockroft and Gault. The groups were, normal renal function (CLcr >80 ml/min; $n=236$); mild impairment (CLcr 50–80 ml/min; $n=274$); moderate impairment (CLcr 30–49 ml/min; $n=151$); and severe impairment (CLcr <30 ml/min; $n=40$). The overall 180-day mortality rate in the total study population increased significantly in relation to the severity of renal impairment (overall hazard ratio [HR] for each incremental increase in renal impairment, 1.5 [1.2, 1.9]; $P=0.001$). Mortality was 18% for patients with normal renal function, 23% for mild impairment, 43% for moderate impairment and 45% for severe impairment. However, the 180-day mortality rate was significantly lower in patients treated with levosimendan compared with patients treated with dobutamine or placebo in LIDO and RUSSLAN, respectively (HR 0.64 [0.47, 0.88]; $P=0.006$). The HRs for the reduction in mortality within each class of renal impairment were similar. These results suggest that levosimendan has a long-term beneficial effect on patient survival, independent of the degree of observed renal impairment.

P58 Outcome of pharmacological treatment of patients with atrial fibrillation in the emergency room

H Ivekovic, V Gasparovic
Division of Emergency and Intensive Care Medicine, Clinical Hospital Centre Zagreb, Kispaticeva 12, 10000 Zagreb, Croatia
Critical Care 2003, **7(Suppl 2)**:P058 (DOI 10.1186/cc1947)

Two pharmacological approaches are established in the treatment of atrial fibrillation (AF): 'rhythm control' – usage of antiarrhythmic agents, in order to restore and maintain normal sinus rhythm (NSR); and 'rate control' – usage of agents that prolong cardiac atrioventricular conduction, in order to alleviate clinical symptoms. A retrospective study was conducted, aiming to determine outcome of pharmacological treatment of patients with AF in the emergency room (ER). Discharge Letters of all patients admitted to the ER and subsequently diagnosed with AF over a 1-year period were reviewed (May 2001–May 2002). Data on symptoms duration, drugs administered and outcome of treatment were analysed.

In a 1-year period, AF was registered in 242 patients, which represented 4% of total medical emergency admissions ($n=6142$). In patients with AF, 64% ($n=152$) had paroxysmal AF, 12% ($n=29$) had persistent AF, and 24% ($n=58$) had permanent AF. In a group of patients with paroxysmal AF, pharmacological conversion into NSR was attempted in 74% of patients ($n=113$). 'Rhythm control' was achieved in 50% ($n=56$) of patients, 'rate control' in 12% ($n=14$) and 38% ($n=43$) of patients required prolonged hospital treatment. The anti-arrhythmic drug of choice was propafenon, with conversion attempted in 62% of patients ($n=71$) and control achieved in 61% ($n=43$), and amiodarone, with conversion attempted in 7% of patients ($n=8$), and rhythm control achieved in 50% patients ($n=4$).

In a group of patients with permanent AF ($n=58$), pharmacological treatment was attempted in 69% of patients ($n=40$). 'Rate control' was achieved in 50% ($n=20$) patients, whereas the others required prolonged hospital treatment. The pharmacological drug of choice was a combination of verapamil and digoxine, with 81% success rate.

AF is the most common cardiac arrthymia presented in the emergency room. The 'rhythm control' approach still represents the main target in the treatment of patients with AF presented in the emergency room, whereas 'rate control' is attempted in patients with persistent and permanent AF. In the study, the drug of choice for pharmacological conversion of AF into NSR is propafenon, and for 'rate control' the best results are obtained by administering the combination of verapamil and digoxine.

P59 The Resuscitation Council UK Immediate Life Support Course

GD Perkins, J Soar, S Harris, J Nolan, on behalf of the Immediate Life Support Working Group
Resuscitation Council UK, 5th Floor, Tavistock House North, Tavistock Square, London WC1H 9HR, UK
Critical Care 2003, **7(Suppl 2)**:P059 (DOI 10.1186/cc1948)

Recognising and intervening in the early stages of critical illness, basic life support and defibrillation are essential for improving outcome from inhospital cardiac arrest [1,2]. The Resuscitation Council (UK) (www.resus.org.uk) launched the Immediate Life Support Course (ILS) in January 2002. This multiprofessional 1-day resuscitation course provides tuition on the knowledge and

Table 1

	Doctors	Nurses	Professions allied to medicine	Pre-hospital staff	Dental staff	Medical/nursing students	Other
Number	964	11,179	786	94	192	878	316
%	6.7	77.6	5.5	0.6	1.3	6.1	2.2

skills required by a first responder to manage a patient in cardiac arrest for the short time before the arrival of a cardiac arrest team. ILS also introduces healthcare professionals to the role of a cardiac arrest team member. Recognition and intervention in the acutely unwell patient prior to cardiac arrest, basic airway skills and rapid safe defibrillation using either manual or automated external defibrillators (AEDs) are the prime objectives of the course. The course includes lectures, skill stations and cardiac arrest scenarios. ILS has standardised much of the life support training that already takes place in hospitals in the UK.

In the first year, 14,409 candidates attended ILS courses in 122 course centres. The backgrounds of the participants are summarised in Table 1. Participants are continually assessed during the course and those that demonstrate satisfactory performance are awarded a certificate valid for 12 months. During the first year the majority (99%) of participants successfully achieved the course objectives. The preliminary results presented here show a promising start for the new ILS course. The challenge now is opening up the course in more centres while maintaining the quality of teaching.

References

1. Soar J, *et al*.: *Resuscitation* 1998, **38**:145-149.
2. Buist MD, *et al*.: *BMJ* 2002, **324**:387-390.

P60 Medicine college curriculum and problem based learning: a training program guided with Basic Life Support course

M Canesin[1], S Timerman[2], C Grion[1], L Cardoso[1], S Silva[1], P Gordan[1]
[1]Skills Laboratory/C.C.S., Londrina University Medical School, Parana, Brasil; [2]Heart Institute University of São Paulo, School of Medicine, São Paulo, Brasil
Critical Care 2003, **7(Suppl 2)**:P060 (DOI 10.1186/cc1949)

Introduction The medical college curriculum at the University of Londrina uses the PBL (problem based learning) method of teaching. This method is based on adult education and it is focused in learning to learn and doing to learn. One of the worries of this teaching method is the development of practical skills and the practicing of these skills before the application in patient care. The objective of this paper is to describe the experience of the Basic Life Support training in the curriculum of a medicine college that uses the PBL method.

Materials and methods The Basic Life Support training uses a skills laboratory of the University Hospital. This laboratory has five skills classrooms equipped with video monitoring, training manikins with monitoring system, automatic external defibrillator simulator and other materials for technical support. The Basic Life Support training is divided in two parts of growing complexity and has the main objective of training the adult in prehospital cardio respiratory arrest. In the first year of the medicine college the students are divided into groups of 20 for the cognitive classes and groups of 10 for the skills or psychomotor classes of cardiopulmonary resuscitation (CPR) with one or two rescuers. In the third year of the college the students are divided in the same way for the reinforcement of the cognitive and the skills classes, now including the use of the automatic external defibrillator. The knowledge and skills performance evaluation is realized in the second year so the retention is well documented.

Results Since the institution of this method of teaching 240 students were trained in Basic Life Support. A first evaluation has been performed after 1 year of training in the first group of 80 students. The percentage of the students that performed right skills in this first evaluation was 84.9%. The initial results showed excellent performance of the students in the first evaluation and a good retention after 1 year of training. The students showed high interest for the subject with a frequency to the classes superior of 95%.

Conclusion The institution of basic life support guided courses in the PBL curriculum of the medicine college is very important. The student that already has trained in CPR in the laboratories starts the patient care very well prepared and with a padronized view. This recommendation follows the International and American Heart Association recommendation for the padronization of CPR. This new recommendation says that the training of CPR may be started in the medical college and then reinforced later with other specific courses.

P61 Seasonal variation in the incidence of inhospital cardiac arrest: analysis of three groups of cardiac arrest

N Parenti, G de Rose, G Valtancoli, S Sau, A Fanciulli
Department of Emergency, M. Bufalini Hospital of Cesena, Italy
Critical Care 2003, **7(Suppl 2)**:P061 (DOI 10.1186/cc1950)

Introduction Many studies have analysed circadian variation in the onset of cardiovascular disorders. Only a few studies have examined the occurrence of cardiac arrest by month of year. To our knowledge none has studied seasonal variation in the incidence of three kinds of inhospital cardiac arrest: nontraumatic with presumed noncardiac etiology cardiac arrest (NTNCA), traumatic cardiac arrest (TCA), and cardiac arrest (CA).

Methods We performed a retrospective analysis of computerized records of all patients discharged from our hospital from September

1998 to September 2002. We examined 101,390 clinical computerized records. One thousand two hundred and ninety-three consecutive patients were included with the diagnosis of cardiac arrest using codes according to the International Classification of Diseases, Ninth Revision (ICD-9). We divided (using the ICD-9 codes) all cases found in the three groups: NTNCA, TCA, CA. Data were aggregated using the medical program Oracle and MS Access 2000 software. With the chi-square test we examined whether cardiac arrests uniformly occurred during seasons and months.

Results There were 1293 cardiac arrests with 956 NTNCA, 143 TCA, 194 CA. For our analysis we divided the year into four seasons: winter (December–February), autumn (September–November), spring (March–May), summer (June–August).

Our data shows a seasonal variation in all cases, with a greater number of cardiac arrests in winter (26.8%) and fewer in autumn (24.2%) and summer (24%). This variation is different among three groups: in the group of NTNCA there are more cases in spring (26%) and winter (25.8%) and fewer in autumn (23.7%), in the CA group the cases are more in winter (33.5%) and fewer in spring (20.6%) and summer (21.2%), and in the TCA there are more in autumn (25.8%) and fewer in spring (24.5%) and summer (24.5%). Unluckily the chi-square test did not reject uniformity over the whole year for all groups examined.

Discussion Our data show a seasonal variation in all cardiac arrests with a greater number of cases in the cold months. This trend is similar to that found in other studies. In particular we found a similar trend in the group of CA and of TCA: more cases in autumn and winter. The seasonal hormonal variation and stresses caused by shorter hours of daylight could explain this distribution. On the contrary the NTNCA group showed a different trend: more cardiac arrests in spring and winter. We suppose that the NTNCA cardiac arrests are not linked to the same seasonal hormonal variation of CA and TCA.

Conclusion There are several limitations to our findings, one of the major is the use of a database using ICD-9 codes. Moreover our results were not confirmed by statistic test. Nevertheless we believe that our findings are reliable, because they were confirmed by several studies. In any case we suggest further research: large studies on the link between environmental factors and the NTNCA cardiac arrests.

P62 Serum cardiac markers response to biphasic compared with monophasic electrical cardioversion

R Skulec, J Belohlavek, T Kovarnik, A Linhart, M Psenicka, M Aschermann
2nd Department of Internal Medicine, 1st School of Medicine, Charles University, Prague, Czech Republic
Critical Care 2003, **7(Suppl 2)**:P062 (DOI 10.1186/cc1951)

Introduction Defibrilation or cardioversion in critically ill cardiac patients may be followed by serum cardiac marker elevation. However, only few studies with limited patient samples assessing electrical myocardial injury have been published [1,2]. The aim of our study was to evaluate the response of serum cardiac markers following elective cardioversion for supraventricular tachyarrhythmias (SVT) and to analyze the impact of type of shock waveform.

Methods Eighty-three patients with various SVTs indicated for elective cardioversion were randomized to monophasic or biphasic electrical cardioversion (CV). Serum levels of creatine kinase (CK), MB fraction of CK (CK-MB), myoglobin (Mg) and troponin I (TnI) were analyzed before CV and 262 ± 69 min after the procedure.

Results Average age was 66.3 ± 11.2 years, 43 patients underwent biphasic and 40 monophasic CV. The most frequent type of arrhythmia was atrial fibrilation (63%). Mean cumulative energy (CE) was 301 ± 260 J. Delivered CE > 150 J was associated with significant elevation of CK and Mg levels after CV (0.96 μmol/l and 166 μg/l, respectively), while CE < 150 was not ($P < 0.01$). Baseline values of TnI were negative in all patients. No significant changes in CK-MB and TnI levels after CV were identified. Strong correlation between increase of CK and Mg levels and CE was observed. Multivariate logistic regression analysis identified only cumulative energy > 150 J as an independent positive predictor for CK and Mg elevation. Randomization to the biphasic or monophasic waveform group was not associated with significant differences in serum cardiac marker elevation and with the success rate in sinus rhythm restoration (88.37% vs 87.18%, respectively; $P = 0.8692$). However, a trend to lower CE necessary for sinus rhythm restoration was detected for biphasic wave shock (259 vs 347, $P = 0.1237$).

Conclusion According to our study, elective electrical cardioversion for SVTs is not associated with biochemical signs of myocardial injury. Application of cumulative energy > 150 J can be followed by CK and Mg elevation most likely due to skeletal muscle damage. This pattern is not dependent on the type of the shock waveform.

References
1. Vikenes K, Omvik P, Farstad M, *et al.*: *Am Heart J* 2000, **140**:690-696.
2. Bonnefoy E, Chevalier P, Kirkorian G, *et al.*: *Chest* 1997, **111**:15-18.

P63 Difference in end-tidal carbon dioxide changes during cardiopulmonary resuscitation between cardiac arrest due to asphyxia and VF/VT cardiac arrest

Š Grmec, K Lah
Center for Emergency Medicine – Prehospital Unit Maribor, Ulica talcev 9, Maribor 2000, Slovenia
Critical Care 2003, **7(Suppl 2)**:P063 (DOI 10.1186/cc1952)

Introduction In recent years there has been an increased interest in the use of capnometry, the noninvasive continuous measurement of partial pressure of end-tidal carbon dioxide ($petCO_2$) in expired air. $petCO_2$ monitoring has been useful in determining the effectiveness of cardiopulmonary resuscitation. During cardiopulmonary reanimation (CPR) the $petCO_2$ correlates with cardiac output and efficacy of cardiac compressions and as such has been shown to have prognostic value in CPR. This study was undertaken to compare initial $petCO_2$ and $petCO_2$ after 1 min during CPR in cardiac arrest due to asphyxia versus cardiac arrest due to ventricular fibrillation (VF).

Table 1

The value of initial, average, final and $petCO_2$ after 1 min of CPR for arrest due to asphyxia and VT/VF cardiac arrest

	Initial $petCO_2$ (mean)	$petCO_2$ after 1 min of CPR (mean)	Average $petCO_2$ (mean)	Final $petCO_2$ (mean)
Asphyxial arrest	64.2 ± 15.2	28.4 ± 5.3	43.2 ± 10.2	28.4 ± 10.6
VF/VT cardiac arrest	12.5 ± 5.1	23.6 ± 4.3	16.4 ± 6.3	22.4 ± 8.3
P	< 0.05	0.71	< 0.05	0.65

Methods This prospective study was conducted at the Center of Emergency Medicine – Pre-hospital Unit Maribor, Slovenia. The study included two groups of patients. The first group represented patients who suffered from heart arrest due to asphyxia. The causes of asphyxia included foreign body in the airway, aspiration, suicide with hanging, drowning, edema or tumor of airway and acute asthma attack. The initial rhythm was either asystole or pulseless electrical activity. We compared this group of patients with those whose cause of heart arrest was AMI or malignant arrhythmias (VF or pulseless VT). $petCO_2$ measurements were made by infrared side stream capnometer (BCI Capnocheck Model 20600A1; BCI international, Waukesha, WI, USA). $petCO_2$ was measured for both groups immediately after intubation (first measurement) and then repeatedly every minute. Thus the initial, average and end $petCO_2$ was detected for both groups. We performed the same procedure for the patients with return of spontaneous circulation (ROSC) and for those without ROSC. Statistics used: Student's *t* test, χ^2 test, $P < 0.05$ was considered significant.

Results From February 1998 to February 2002 we analyzed 126 patients with cardiac arrest (initial rhythm VF/pulseless VT) and 36 patients with cardiac arrest due to asphyxia (initial rhythm asystolia or PEA). Patients with cardiac arrest caused by asphyxia were younger than patients whose cardiac arrest was provoked by VF (50.7 ± 21.4 vs 64.5 ± 15.4; $P < 0{,}05$). Time spent from beginning of the arrest to start of CPR was not significantly different (patients with ROSC: 8.2 ± 5.2 min vs 9.1 ± 4.6 min, $P = 0{,}79$; patients without ROSC: 14.1 ± 4.6 min vs 13.6 ± 5.2 min, $P = 0.83$). The mean value of $EtCO_2$ for all patients (with and without ROSC) is presented in Table 1. In the group of patients who presented with arrest due to asphyxia there was no significant difference in initial values of $petCO_2$, even when compared with those with and without ROSC (72.4 ± 13.4 mmHg vs 67.4 ± 14.6 mmHg). However, there was a significant difference in $petCO_2$ after 1 min of CPR between those patients with ROSC and those without ROSC (34.5 ± 9.7 mmHg vs 18.1 ± 8.3 mmHg).

Conclusions In cardiac arrest caused by asphyxia, the initial $petCO_2$ is much higher than in cardiac arrest due to VF and does not correlate with ROSC.

After 1 min of CPR, $petCO_2$ correlates with ROSC and it is an important method for noninvasive monitoring of the effectiveness of CPR.

P64 Improved hemodynamics with a novel chest compression device during treatment of inhospital cardiac arrest

S Timerman[1], LF Cardoso[1], JAF Ramires[1], HR Halperin[2]
[1]University São Paulo Medical School, São Paulo, Brasil; [2]The Johns Hopkins Hospital, Baltimore, MD, USA
Critical Care 2003, **7(Suppl 2)**:P064 (DOI 10.1186/cc1953)

Introduction Previous research has shown that increased coronary perfusion pressure (CPP) during cardiopulmonary resuscitation (CPR) correlates with increased coronary blood flow and improved survival from sudden cardiac arrest. The purpose of this clinical study was to determine whether a novel chest compression device (AutoPulse; Revivant Corp, Orange County, CA, USA) improves hemodynamics during CPR when compared with manual chest compressions. The AutoPulse is an automated, electromechanical chest compression device that utilizes a load-distributing band to compress the anterior chest. AutoPulse automatically adjusts to the size and shape of each patient.

Methods With institutional review board approval, 16 terminally ill subjects (68 ± 6 years) who suffered inhospital sudden cardiac arrest were studied. All subjects were endotracheally intubated. Following a minimum of 10 min of failed advanced life support, fluid-filled catheters were advanced into the thoracic aorta and the right atrium, with placement confirmed by pressure waveforms and chest radiograph. Subjects then received alternating periods of manual and AutoPulse chest compressions for 90 s each. Chest compressions were administered at 100/min for manual, and 60/min for AutoPulse. Subjects received bag-valve ventilation (12/min) between compressions. Epinephrine (1 mg IV bolus) was given at the request of the attending physician at 3–5 min intervals. CPP was measured as the difference between the aortic and right atrial pressures during chest decompression.

Results Peak aortic pressures were higher with AutoPulse chest compressions when compared with manual chest compressions (150 ± 8 vs 122 ± 11 mmHg, $P < 0.05$; mean ± SEM), as was CPP (20 ± 3 vs 15 ± 3 mmHg, $P < 0.02$). The AutoPulse improved peak aortic pressure and CPP despite the use of high-quality manual compressions (47 ± 3 kg).

Conclusion Hemodynamics with the AutoPulse were improved over those of standard manual CPR in this terminally ill patient population. CPP was raised above the level generally associated with improved survival, and strongly suggests that survival may be improved with the use of AutoPulse in viable patients.

P65 Performance of an automated external cardioverter defibrillator for inhospital ventricular malignant arrhythmia

S Timerman, A Bento, LF Cardoso, MA Moretti, NE Sanadi, JAF Ramires
Heart Institute (InCor), University of São Paulo Medical School, São Paulo, Brasil
Critical Care 2003, **7(Suppl 2)**:P065 (DOI 10.1186/cc1954)

Purpose Ventricular fibrillation (VF) and ventricular tachycardia (VT) are the major underlying rhythm during inhospital cardiac arrest. For a patient in VF/VT the probability of successful defibrillation and subsequent survival to hospital discharge is directly and negatively related to the time interval between onset of the arrhythmia and delivery of the first shock. The data about this interval in clinical practice is heterogeneous and inconclusive, however the literature estimates it to be about 60 s in monitored units. Continuous ECG monitoring allows identification of such arrhythmias and alert nursing and medical staff. The time delay between the arrhythmic event and human intervention is still a challenge for clinical practice.

Methods We reported the use of an automated external cardioverter defibrillator (AECD) in 45 patients considered to be at higher risk for malignant arrhythmia for 24–48 hours. The inclusion criteria was acute coronary syndrome, cardiogenic shock and previous episode of sudden death or malignant ventricular arrhythmia. The exclusion criteria was the use of pacemaker or an implantable cardioverter defibrillator and an R-wave amplitude less than 0.7 mV peak to peak at the monitor.

Results We recorded 17 episodes of VT/VF in three patients. The median time between the beginning of the arrhythmia and the first defibrillation was 33.37 s (range 21–65 s). The sensibility and specificity were 100%. The success of the defibrillation was 94.11% (16/17) for the first shock and 100% (1/1) for the second shock. There was no adverse event during the study period and no episodes of inappropriate therapy delivery (the detection was accurate in all episodes – sensitivity 100%).

Conclusion AECD was safe and effective. It presents the possibility of providing consistently rapid identification and response to ventricular malignant arrhythmia.

P66 Comparison of exponential truncated biphasic versus damped sine wave monophasic shocks in transthoracic cardioversion of atrial fibrillation

VS Kawabata, LF Cardoso, S Timerman, LAM Cesar, JAF Ramires
Heart Institute (InCor), University of São Paulo Medical School, São Paulo, Brasil
Critical Care 2003, **7(Suppl 2)**:P066 (DOI 10.1186/cc1955)

Background Clinical studies have shown the efficacy of the biphasic waveform (BW) in reversion of ventricular fibrillation using lower energies. However, the effects of the BW in the treatment of other arrhythmias is unclear. The amount of energy of each shock and the sequency of shocks are to be determined. The purpose of this study is to compare the efficacy and side effects of the BW and the monophasic waveform (MW) in reversion of atrial fibrillation (AF).

Methods In this prospective, randomized and unicenter trial we submitted 158 patients with AF to transthoracic cardioversion (CV). They were randomized in two groups. Group I, 80 patients underwent BW shocks (average age 55.9 ± 12.6 years old); and Group II, 78 patients underwent MW shocks (average age 59.8 ± 13.0 years old). Group I received sequential shocks of 50, 100, 150, and 175 J (half the energy used in Group II). Group II received sequential shocks of 100, 200, 300 and 360 J. We analyzed the clinical characteristics of both groups before CV (weight, height, AP thoracic diameter, body surface, oxymetry, body temperature, noninvasive blood pressure, duration of AF, ventricular response). Blood samples of cardiac and muscle markers of injury (CK, MB-CK, AST, ALT, DHL) were obtained before, 1 hour and 24 hours after CV.

Results The first-shock efficacy was similar in both groups (56.3% vs 53.9%, Group I and Group II, respectively) as well the cumulative efficacy of sequential shocks rate (88.0% vs 92.3%, $P=0.415$). Baseline characteristics were similar in both groups. Age and baseline cardiac frequency were independent predictors of CV success. Patients in Group II had higher elevations on serum CK (83.0 ± 106.3 vs 178.9 ± 306.9, $P=0.0087$). There was a clear relation between CK elevation and cumulated energy used in CV ($P=0.0001$). No other injury marker was elevated after CV in both groups.

Conclusions Biphasic shock with a truncated exponential waveform was equally effective as monophasic damped sine waveform, causing less muscular injury, using only half the energy of the monophasic defibrillator.

P67 Ventricular fibrillatory frequency and its correlation with transthoracic defibrillation current requirement

VA Vostrikov, KV Razumov
Moscow Medical Academy, 2/6 Bolshaya Pirogovskaya str, Moscow, Russia 119881
Critical Care 2003, **7(Suppl 2)**:P067 (DOI 10.1186/cc1956)

Correlation between ventricular fibrillatory frequency (VFF) in patients with ventricular fibrillation (VF) and transthoracic defibrillation current was studied. Strong positive correlation between VFF and optimal defibrillation current was revealed in patients with primary VF. There was a significant negative correlation between TTI and defibrillation current, that ceased secondary VF, and there was no significant correlation between TTI and current in patients with primary VF.

Introduction The efficacy of external defibrillation depends on various both cardial and noncardial factors. Heart function status, waveform shock (monophasic and biphasic) and chest impedance play important roles among them. The aim of this study was the research of the correlation between VFF in patients with primary (1-ry) and secondary (2-ry) VF and the value of defibrillation current.

Methods Twenty patients with 1-ry VF and 28 patients with 2-ry VF were studied. VF mostly occurs during the acute phase of myocardial infarction. The efficacy of external defibrillation depends on various both cardial and noncardial factors. Heart function status, waveform shock (monophasic and biphasic) and chest impedance play important roles among them. The duration of VF was from 1 to 8 min (definition: 2-ry VF, fibrillation that occurs in patients with clinical signs of acute or chronic heart failure; 1-ry VF, in patients with the absence of these signs). Defibrillation was done with a biphasic quasi-sinusoidal shock through hand-held electrode paddles (12/12 cm diameter); the peak current (I [A]), delivered energy (DE [J]) and transchest impedance (TTI [Ohm]) were registered during the shock. VFF was estimated 5–7 s before the successful shock from surface ECG lead I or II.

Results A strong positive correlation between VFF (range 310–435 per min) and the value of the optimal defibrillation current (range 8–21 A) ($r=0.81$; $P<0.001$) was revealed in patients with 1-ry VF. The correlation coefficient between VFF and defibrillation energy (range 16–85 J) was less to some extent ($r=0.69$; $P<0.01$). There was no correlation in patients with 2-ry VF (range of VFF 200–410 per min; range of I (A) 9–40 A). Meanwhile, there was a significant negative correlation between TTI (range 22–117 Ohms) and the value of the defibrillation current, that ceased 2-ry VF ($r=-0.69$; $P<0.01$), and there was no significant correlation between TTI and I (A) in patients with 1-ry VF ($r=-0.32$, $P=0.11$).

Conclusions The obtained data suggest that the strong positive correlation between ventricular fibrillation frequency and defibrillation current value in patients with 1-ry VF is mainly related to electrophysiologycal heterogeneity of the myocardium. At the same time the influence of chest impedance on the value of the current depolarising critical amount of myocardium was, probably, insignificant. Fibrillation frequency obtained from the surface ECG predicts current and energy requirements in patients with primary VF undergoing external defibrillation.

P68 Post-resuscitation myocardial dysfunction: correlated clinical factors and prognostic implications

WT Chang, MHM Ma, Ch Hwang, WJ Chen, FY Lin, YT Lee
Department of Emergency Medicine, National Taiwan University Hospital, Taipei, Taiwan
Critical Care 2003, **7(Suppl 2)**:P068 (DOI 10.1186/cc1957)

Purpose To evaluate the clinical course of post-resuscitation LV dysfunction, clinical factors correlated with its severity, and the prognostic value in the survival outcome.

Methods Forty-two patients (26 men and 16 women) resuscitated from out-of-hospital cardiac arrest underwent echocardiographic evaluation of the LV systolic and diastolic functions 6 hours, 24 hours, 3 days, and 7 days after return of spontaneous circulation. The serial LV functions were analyzed in correlation to the event characteristics, resuscitation factors, and the patients' survival outcomes.

Results The LV fraction shortening and ejection fraction were impaired on the first day and improved gradually on serial followup. Isovolumic relaxation time (IVRT) lengthened gradually. Patients with cardiac etiologies had worse LV systolic function on the first and third post-resuscitation days. Defibrillation and use of high doses of epinephrine during resuscitation were associated with poorer LV systolic function on day 1, while the effect of amiodarone persisted up to 3 days. In terms of the prognostic implications, initial rhythm of VT/VF, lower doses of epinephrine during resuscitation, and shorter IVRT at the 6th hour were correlated with better survival outcomes.

Conclusion LV function is impaired early in the post-resuscitation phase, and would recover gradually within the first 3 days. Several event and resuscitation factors are associated with this dysfunction. Once the patient survives the initial stage, the prognostic value of this transient phenomenon seems limited.

P69 The gamma isoform of enolase (NSE) is predictive of mortality after cardiopulmonary resuscitation (CPR): comparison with clinical neurologic examination and CT scan of the brain

K Magnusson[1], M Stemberg[1], T Othman[2], NA Cicco[1], EG Vester[1]
[1]Department of Cardiology and [2]Department of Internal Medicine, Evangelisches Krankenhaus, Duesseldorf, Germany
Critical Care 2003, **7(Suppl 2)**:P069 (DOI 10.1186/cc1958)

Introduction NSE (the gamma isoform of enolase) is released into the cerebrospinal fluid and blood after the occurrence of stroke and anoxia; and correlates with the extent and duration of ischemia in animal models of stroke and the outcome in humans, including neonates, with hypoxic ischemic encephalopathies.

Accordingly, the objective of the current study was: 1) To assess the prognostic significance of plasma concentrations of NSE for early prediction of outcome in patients at risk for anoxic encephalopathy after CPR. 2) To compare the prognostic information provided by NSE measurements with that provided by conventional risk indicators (clinical neurological examination and CT scan of the brain).

Results Ten patients (age 60.5 years [mean] ± 20.8 [SD]) were enrolled up to now. In two patients CPR was performed due to ventricular fibrillation, in one due to low blood pressure during hemodialysis, in three due to acute myocardial infarction, in three due to cardiac arrest for unknown reason and in one patient due to ketoacidotic coma. Clinical neurological examination, computed tomogram of the brain, and plasma concentration of NSE on the third day after CPR were compared. The clinical neurological examination was differentiated in standardized three levels of midbrain syndrome (MBS) and three levels of bulbar brain syndrome (BBS). Four of the patients had a MBS I, one had a MHS II, two had a MBS III, and three had a BHS III at the third day after CPR. In three patients neurological examination was not reliable due to given anticonvulsive therapy because of early onset of myoclonias. The CT scan of the brain showed only in six patients cerebral edema; in two patients there was no CT scan available because of the deleterious hemodynamic situation; and in two patients ischemic lesions were found, but no edema. The NSE level was elevated in seven of 10 patients (61.0 ± 65.1 ng/ml [range 7.2–194.6]). In three patients the level was normal. Surprisingly the low NSE level found in this patient was associated with a significant swelling due to cerebral edema documented by the neu-

roimaging study. This patient had the highest neurological score (BBS III). All patients with elevated NSE levels died, one patient of those with normal NSE level died, and the others with normal levels survived. The mean survival time after admission was 12.8 ± 5.0 days. CT scan of the brain and neurologic examination, especially in patients with early onset of myoclonias, were less sensitive than NSE in predicting a poor outcome.

Conclusion In patients who have been resuscitated after cardiac arrest or other conditions associated with hypotension, increased plasma levels of NSE predict an increased risk of death. NSE measurements appear to provide prognostic information complementary to and possibly superior to that obtained from the neurological examination and CT scan of the brain.

P70 Clinical and electrophysiologic associations with outcome in initially comatose survivors of cardiac arrest

GB Young[1], G Doig[2], A Ragazzoni[3]
[1]Department of Medicine, University of Toronto, Ontario, Canada; [2]Northern Clinical School, University of Sydney and Intensive Therapy Unit, Royal North Shore Hospital, Sydney, Australia; [3]Ospedake S Maria Nuova, Firenze, Florence, Italy
Critical Care 2003, **7(Suppl 2)**:P070 (DOI 10.1186/cc1959)

Background Prognostic assessment of the comatose survivor of cardiac arrest with intact brain stem reflexes is still problematic and requires further study to determine those factors correlate with an outcome no better than vegetative state (VS).

Methods *Inclusion criteria*: Comatose survivors of cardiac arrest with GCS ≤8 on day 1 before sedation; first EEG and SSEP between 24 and 36 hours from cardiac arrest; survival for at least 4 days. *Exclusion criteria*: patients with brain death, sedation immediately after resuscitation, additional cause for coma, preceding peripheral neuropathy or cervical myelopathy. Standardized EEG classification system and SSEPs were applied. Followup at 3 months with phone call to determine the Glasgow Outcome Scale score (GOS) and whether or not awareness had been recovered.

Results Forty-six men and 29 women with mean age of 74 (range 21–84) years. Fifty-seven (76%) of the arrests were out-of-hospital and were due to primary cardiac causes in 70 (93%). Significant differences in clinical features between those who died and those who survived were oculovestibular and pharyngeal reflexes (no survivors in those who lost these) and motor response. There were no survivors with better than VS in those with generalized epileptiform discharges or suppression of <20 μV on EEG and absent N20 on SSEPs. EEG and EP responses correlating with recovery of awareness included those with intermittent EEG slowing and those with preserved N70 responses.

Conclusions In this preliminary study, the only variables that were consistently associated with an outcome no better than VS were: absence of oculovestibular and pharyngeal reflexes, generalized epileptiform discharges or suppression of <20 μV on EEG and absent N20 on SSEPs.

P71 Continuous EEG recording in the intensive care unit: epileptiform activity

GB Young
Department of Medicine, University of Toronto, Ontario, Canada
Critical Care 2003, **7(Suppl 2)**:P071 (DOI 10.1186/cc1960)

Background Digital EEG technology has recently become available for long-term ICU recordings. Epileptiform activity, as seizures or spikes, is worthy of detection, as this often indicates structural brain lesions, and seizures may contribute to further damage.

Methods Adult patients in our general ICU were randomized into two groups: those who received continuous digital EEG (CEEG) and those who had standard, 20-min recordings. We excluded those in coma after cardiac arrest and others for whom the prognosis was deemed to be hopeless for significant recovery.

Results Of patients with acute structural brain lesions (ASBLs), 31 had CEEG and 21 had standard care; each group was similar for age, sex ratio and initial Glasgow Coma Scale scores. Of these, 10 of the 32 (32%) CEEG patients and only two of the 21 (9.5%) of the standard group had showed epileptiform activity ($P<0.05$). In two separate, comparable groups of patients with metabolic encephalopathies, two of 24 (8%) patients with CEEG and zero of 13 (0%) with standard care showed epileptiform activity ($P=0.04$).

Conclusions CEEG monitoring of patients with ASBLs gives a considerably higher yield of epileptiform activity than standard EEG in these patients or CEEG or standard EEG in patients with metabolic disorders. This has implications for further study and resource utilization.

P72 The role of EEG and brain stem auditory evoked potentials (BAEPS) as predictors of outcome in severe brain injury

A Donati, AM Mauro, G Bini, M Bonifazi, P Carletti, M Ruzzi, E Papadopoulou, P Pelaia
Department of Neurology and Intensive Care Unit, Torrette Regional Hospital, University of Ancona, via Conca 1, 60020 Torrette di Ancona, Italy
Critical Care 2003, **7(Suppl 2)**:P072 (DOI 10.1186/cc1961)

Objective To determine the role of EEG and BAEPs to predict the outcome and to build a predictive model in patients suffering from severe head injury (SHJ).

Materials and methods The prospective cohort study includes 102 patients admitted to a university ICU. The first EEG and BAEPs recordings were obtained within 48 hours of the trauma, followed by recordings after 2 days and later on the basis of the clinical evolution. For every patient the first Glasgow Coma Scale (GCS) and the worst CT scan during the first week were evaluated following Marshall classification. The patient's outcome was classified on the basis of the Glasgow Outcome Scale (GOS): 1) death

or vegetative state, and 2) recovery (with different degrees of impairment). The EEG was classified on the basis of reactivity in three categories: 1) flat, 2) reactivity, and 3) no reactivity [1]. The BAEPs were classified on the basis of the Greenberg classification criteria and subsequently for statistical evaluation compacted on two classes: 1) present, and 2) absent [2]. First, each clinical and instrumental parameter was tested for discrimination, calculating the area under the receiving operator curve (ROC). Then, a predictive model was made using Stepwise Logistic Regression (SPSS 10.1). EEG, BAEPs, GCS, CT scan and age were the parameters tested to enter the model. Calibration was evaluated with the Goodness-of-Fit Hosmer–Lemeshow test and discrimination with the ROC curve.

Results The mean age of the patients was 40.5 ± 20.3 and GCS was 7.4 ± 2.7. Seventy-eight of the 102 patients had a GOS = 2 (recovery). Parameters with good discrimination were: EEG (area = 0.888; ES = 0.051; $P < 0.0001$); GCS (area = 0.828; ES = 0.052; $P < 0.0001$); BAEPs (area = 0.765; ES = 0.065; $P < 0.0001$). Parameters that entered the model were: GCS ($\beta_G = -0.404$); EEG ($\beta_{El} = 6.83004$; $\beta_{E2} = -1.426608$; $\beta_{E3} = -5.386608$); BAEPs ($\beta_{Bl} = 0.827$; $\beta_{B2} = -0.827$); constant = 5.640. This model was well calibrated (Hosmer–Lemeshow test = 8.91; $P = 0.350$) and had a good discrimination (area under the ROC = 0.981; $P < 0.0001$).

Conclusions The different parameters considered have good discrimination ability to predict the outcome of the patients. The EEG seems to be the best parameter to predict the patient's outcome, even if all the patients were sedated. In our case studies, this did not seem to significantly influence the parameter of reactivity to sensory stimulus. Age seems not to be a reliable parameter to predict outcome.

Reference

1. Gutling E, *et al.*: *Neuurology* 1995, **45**:915-918.
2. Greenberg RP, *et al.*: *J Neurosurg* 1981, **55**:227.

P73 The relationship of electroencephalograph fluctuations to intracranial pressure B waves

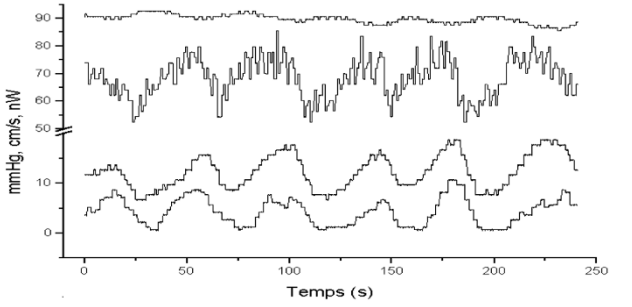
T Lescot, L Abdennour, J-C Muller, P Coriat, L Puybasset
Department of Anesthesiology, Pitié-Salpêtrière hospital, Boulevard de l'hôpital, 75013 Paris, France
Critical Care 2003, **7(Suppl 2)**:P073 (DOI 10.1186/cc1962)

Introduction Lundberg B waves, characterized as repetitive changes in intracranial pressure occurring at frequencies of 8–33 mHz, have been attributed to cerebral blood flow fluctuations induced by central nervous system pacemakers and cerebral pressure autoregulation.

Methods Simultaneous measurements of mean arterial pressure (MAP), intracranial pressure (ICP), mean flow velocity (MFV) of the middle cerebral artery (transcranial Doppler WAKI™) and left and right spectral edge frequency (SEFl, SEFr) of continuous EEG recording (Philips™ technologies) obtained 10 ± 4 days after injury in six patients with a closed head injury were recorded and digitalized at a frequency rate of 50 Hz (Acq*Knowledge*™ software). All patients were mechanically ventilated and sedated using a combination of sufentanil and midazolam.

Results Cerebral electric activity (oscillations at a mean frequency of 26 ± 9 mHz) and MFV fluctuations were synchronous and in phase with the B waves (mean frequency 23 ± 7 mHz). Figure 1 illustrates simultaneous recording of (from the top to the bottom) MAP, MFV, ICP and SEFr on one characteristic patient.

Figure 1



Discussion The change in cerebral electrical activity observed by the use of continuous EEG recording resulting from cerebral pacemakers could increase $CMRO_2$, leading to an increase in cerebral blood flow and secondarily of ICP through a change in cerebral blood volume.

P74 Hyperventilation-induced reductions in cerebral blood flow velocity outlive the reduction in intracranial pressure in head-injured patients

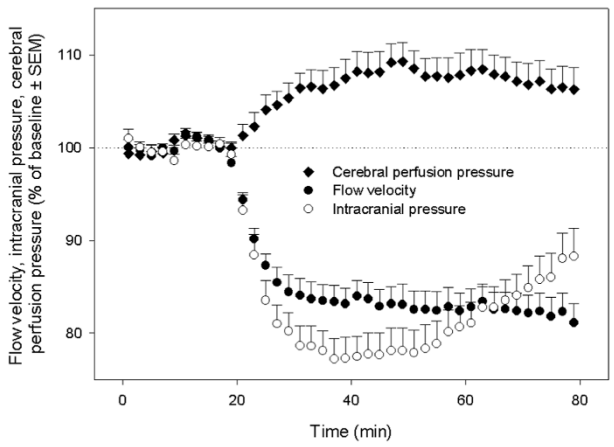
LA Steiner[1,2], M Balestreri[1], AJ Johnston[2], M Czosnyka[1], JP Coles[2], JD Pickard[1], DK Menon[2]
[1]Academic Neurosurgery and [2]Department of Anaesthesia, Addenbrooke's Hospital, Cambridge, UK
Critical Care 2003, **7(Suppl 2)**:P074 (DOI 10.1186/cc1963)

Objective In healthy volunteers, cerebral blood flow (CBF) recovers to baseline within a few hours of continued hyperventilation due to normalization of perivascular pH. The same mechanism is thought to be responsible for the brevity of intracranial pressure (ICP) control in head-injured patients. We measured recovery of middle cerebral artery mean flow velocity (FVm) in head-injured patients during continued hyperventilation and investigated the relationship between the time-course of changes in FVm and ICP.

Methods Twenty-eight head-injured patients were investigated. After recording baseline data (cerebral perfusion pressure, ICP, averaged bilateral FVm, $PaCO_2$) for 20 min, the respirator settings were changed to achieve an acute 20–25% increase in minute volume. This was followed by a 10-min stabilization period and 50 min of continued hyperventilation at constant arterial CO_2 levels.

Results: In 64% of the patients FVm did not recover during hyperventilation. The time-course of ICP changes was significantly different from that of FVm, with ICP reaching its lowest value earlier (23 ± 12 vs 37 ± 20 min; $P = 0.001$) and returning more rapidly towards baseline than FVm (0.23 ± 0.22 vs −0.04 ± 0.14%/min; $P = 0.00001$) (Fig. 1).

Figure 1



Conclusions The impaired FVm recovery and the discordance between ICP and FVm recovery patterns suggest that cerebrovascular responses to hyperventilation are altered after head injury. Reductions in ICP and reductions in FVm may involve different microvascular compartments. Potentially harmful reductions in CBF persist beyond the duration of useful ICP reduction.

P75 Decompressive craniectomy in severe traumatic brain injury

CA Castioni[1], C Olivieri[1], R Potenza[1], E Magli[2], S Livigni[1]
[1]Department of Anesthesia and Intensive Care Unit, and [2]Department of Neurosurgery, G Bosco Hospital, Torino, Italy
Critical Care 2003, **7(Suppl 2)**:P075 (DOI 10.1186/cc1964)

Introduction The management of refractory post-traumatic cerebral oedema remains a frustrating endeavour for the neurosurgeon and the intensivist. Mortality and morbility rates remain high, despite refinements in medical and pharmacological means of controlling intracranial hypertension.

Materials and methods In this retrospective study we have evaluated the efficacy of therapeutic decompressive craniectomy with uncontrollable intracranial pressure as a last resort therapy in 16 patients, from March 2000 to October 2002. The patients were treated according to a local protocol that assigned them to barbiturate coma or decompressive craniectomy. The following parameters were considered: age, GCS after stabilization, intracranial pressure, GOS at ICU discharge and at 6 months, neuropsychological evaluation for patients with GOS 4 and 5 after 6 months.

The mean age of the patients was 28 ± 11.5 years and the GCSm after stabilization varied from 1 to 5.

Results All the 16 patients have been operated on by a FTP craniectomy when ICP was higher than 30 mmHg for more than 15 min. At 6 months three of them were dead (19%), one was in PSV (6%), one was severely disabled (6%), four were moderately disabled (25%) and seven had a good recovery (44%). All the patients with GOS of 5 had normal neuropsychological tests, and all the patients with GOS of 4 had at least one pathological neuropsychological test.

Discussion We evaluated our ability to be accurate to the local protocol for decompressive craniectomy. We found that when we did not respect the inclusion criteria according to the patient's age (< 50 years old) we still had good results, but when we did not respect the inclusion criteria for GCSm after stabilization (≥ 3) we obtained poor outcome. In our opinion patients with STBI, developing delayed intracranial hypertension caused by diffuse cerebral oedema, definitely benefit from craniectomy when ICP is out of control. Nevertheless, of extreme importance is our ability to identify those patients who could really benefit by this therapy in terms of GOS. In our experience, age < 50 years old could be a too restrictive criteria, but all the patients with GCSm ≤ 3 had a poor outcome irrespective of age.

P76 Sequential organ failure assessment in neurocritical care

D Zygun, C Doig, A Gupta, G Whiting, C Nicholas, E Shepherd, C Conway-Smith, D Menon
Neuroscience Critical Care Unit, Box 1, Addenbrooke's Hospital, Hills Road, Cambridge CB2 2QQ, UK
Critical Care 2003, **7(Suppl 2)**:P076 (DOI 10.1186/cc1965)

Purpose To determine the incidence of non-neurological organ dysfunction in the neurologically injured patient and to determine its association with outcome.

Methods We calculated daily modified SOFA (mSOFA) scores for patients with TBI or SAH admitted to the Neuroscience Critical Care Unit at Addenbrooke's Hospital. The mSOFA score was defined as the sum of the five non-neurological component SOFA scores (range 0–20). Maximum mSOFA was defined as the sum of the most abnormal non-neurological SOFA component scores during the patient's stay. ΔmSOFA was defined as the difference between the maximum SOFA and the admission mSOFA. An organ system failure was defined as a SOFA component score ≥ 3.

Results Thirty-two patients with severe TBI and 23 patients with SAH were included in the study. Sixty-seven per cent of patients were male. Mean age was 41 ± 18. The mean APACHE II score was 13.6 ± 6.8. Hospital mortality was 29%. Median ICU LOS was 11 days. Mean admission, maximum and ΔmSOFA scores were 4.4 ± 2.5, 7.2 ± 2.7, and 2.8 ± 2.1, respectively. Eighty per cent of

patients developed respiratory failure and 82% of patients developed cardiovascular failure. No patient developed renal or hepatic failure. Three patients (5.5%) developed haematological failure. Those patients with a maximum mSOFA score ≥8 had significantly longer ICU and hospital LOS. There was no significant difference between survivors and nonsurvivors with respect to admission mSOFA (P=0.45), maximum mSOFA (P=0.54), or ΔmSOFA (P=0.19). Neurological outcome was available for 45 patients (82%). There was no significant difference between those patients with good or poor neurological outcome with respect to admission mSOFA (P=0.24), maximum mSOFA (P=0.84), or ΔmSOFA (P=0.20). The development of multiple organ dysfunction (≥2 organ dysfunctions) was not associated with mortality or neurological outcome.

Conclusions We found no association between non-neurological organ dysfunction as measured by the modified SOFA score and mortality or neurological outcome. The use of sequential organ dysfunction scores as surrogate outcomes in this population must be questioned.

P77 Osmolality changes during mannitol therapy in cerebral oedema

V Špatenková[1], A Kazda[2]
[1]Neurocentre, Liberec Hospital, Czech Republic; [2]Postgraduate Medical School, Prague, Czech Republic
Critical Care 2003, **7(Suppl 2)**:P077 (DOI 10.1186/cc1966)

Introduction Mannitol is still used for reduction of intracranial pressure (ICP) in cerebral oedema. Its therapeutic effect might be caused by different mechanisms. One of them is an increase in blood–brain osmotic gradient, which is followed by a reduction of the brain water.

Method Our investigation was prospectively carried out on 60 ICU patients. Fifty-eight patients had acute brain disease with Glasgow Coma Scale (GCS) in the range 11–14 (tumour, 23 patients; trauma, four patients; subarachnoid hemorrhage, eight patients; intracerebral haemorrhage, 21 patients; infection, one patient; epilepsy, one patient) and two patients had spine trauma.

The investigation started at least 24 hours from the beginning of therapy with 20% mannitol. Serum sodium and osmolality were measured before and after the mannitol infusion and before the next dose. Patients were divided into three groups, which differed in doses of mannitol and intervals between infusions (each infusion lasted 20 min): I, 40 g/day (10 g/6 hours); II, 60 g/day (10 g/4 hours); III, 80 g/day (20 g/6 hours).

No other hypertonic agents were used. All samples were taken from the same vein on an extremity where neither mannitol nor any other infuse were applied.

Results There were no significant changes in blood sodium concentration or osmolality in any of the groups. For parameters, reference ranges, mean values ± standard deviations in samples 1, 2 and 3, see Table 1.

Conclusion This prospective study does not show any evidence that 20% mannitol significantly altered blood sodium or osmolality values in CNS diseases, although the osmolality was around the upper reference range. Therefore, there still remains a question, whether this significant elevation of serum osmolality is sufficient for a reduction of the brain volume or whether the reduction is caused by a different mechanism.

References

1. Albanese J, Léone M, Martin C: **Severe head injury in patients with multiple trauma.** In *Yearbook of Intensive Care and Emergency Medicine*. Edited by Vincent JL. Springer; 2001:353-375.

Table 1

Parameter	Reference range (mmol/l)	Mannitol (g)	Sample 1	Sample 2	Sample 3
S_Na^+	132–146	40	142 ± 3.52	141 ± 3.35	143 ± 3.73
		60	142 ± 3.93	141 ± 3.86	142 ± 4.08
		80	143 ± 3.48	141 ± 3.73	143 ± 3.93
S_osm	275–295	40	296 ± 9.86	297 ± 8.76	297 ± 7.31
		60	293 ± 7.93	294 ± 7.16	294 ± 7.88
		80	298 ± 10.2	298 ± 8.72	299 ± 8.82
S_osmC	275–300	40	298 ± 7.51	297 ± 6.88	299 ± 7.97
		60	296 ± 8.20	295 ± 7.90	297 ± 8.32
		80	299 ± 7.34	296 ± 7.45	300 ± 8.26
S_osmE	272–290	40	291 ± 7.47	290 ± 6.8	292 ± 7.75
		60	290 ± 7.69	289 ± 7.53	291 ± 7.97
		80	293 ± 6.83	290 ± 7.22	293 ± 7.77

S_osmC, calculated osmolality; S_osmE, calculated effective osmolality.

2. Bereczki D, Liu M, do Prado GF, Fekete I: **Mannitol for acute stroke (Cochrane Review).** In *The Cochrane Library*, Issue 4. Oxford: Update Software; 2002.
3. Cooper DJ, Murray L: **Hypertonic saline resuscitation for traumatic brain injury?** In *Yearbook of Intensive Care and Emergency Medicine*. Edited by Vincent JL. Springer; 2001: 342-349.
4. Schierhout G, Roberts I: **Mannitol for acute traumatic brain injury (Cochrane Review).** In *The Cochrane Library*, Issue 4. Oxford: Update Software; 2002.

P78 Effects of citicoline treatment in patients with isolated head trauma: a randomized trial

T Lazowski[1], K Kierul[1], M Bartnicki[1], E Mayzner-Zawadzka[2], B Toczylowska[3], M Ryba[4], Z Lewandowski[5]
[1]II Department of Anaesthesiology and Intensive Care, [2]I Department of Anaesthesiology and Intensive Care, and [5]Department of Epidemiology, Warsaw Medical School, Poland; [3]Institute of Biocybernetics and Biomedical Engineering of the Polish Academy of Sciences, Poland; [4]Laboratory of Experimental Pharmacology, Medical Research Centre of the Polish Academy of Sciences, Poland
Critical Care 2003, **7(Suppl 2)**:P078 (DOI 10.1186/cc1967)

Background and goal of study CDP Choline (CDPC, citicoline) is one of the neuroprotectants used for the clinical and experimental treatment of stroke [1] and brain injury [2]. In the present study the authors examined the effect of citicholine treatment on survival and neurological outcome in patients with brain injury caused by isolated head trauma.

Materials and methods The study was approved by the institution ethical comity. Twenty-eight patients after head trauma (23 men) were randomly enrolled to typical treatment + citicholine (1 g IV for 14 days) group or typical treatment + placebo group. Glasgow Coma and Glasgow Outcome Scale (GCS, GOS) were used to monitor patients up to 30 days.

Results and discussions Our preliminary report of the citicoline-treated group shows no correlation between GCS in day 7 (GCS 7) and day 14 (GCS 14). This lack of correlation is interpreted as a result of treatment, and significant correlation between GCS 14 and GCS 21 ($r=0.82$; $P<0.007$) is interpreted as an expanded effect of treatment to 21 days. In the citicoline group, GCS 21 is significantly correlated with GOS 30 ($r=0.68$; $P<0.01$) showing the protective effect of the used drug.

Conclusions Our preliminary results suggest that CDPC can be an effective neuroprotective agent in patients with brain injuries following head trauma. Our study has to and will be continued to confirm our data.

References
1. Sandage BW: **Citicoline: neural protection and repair.** *Ischemic Stroke II*. Edited by LM Savage. Southborough, MA: International Business Communications, Inc; 1996:210-224.
2. Baskaya MK, Dogan A, Rao AM: *J Neurosurg* 2000, **92**:448-452.

Table 1

Variable	*n*	Mean	Standard deviation	Median	Minimum	Maximum
GCS 0	14	6.00000	1.10940	6.00000	4.00000	8.00000
GCS 1	13	6.03846	1.19829	6.00000	4.00000	8.00000
GCS 7	11	7.13636	2.12239	6.00000	4.00000	10.00000
GCS 14	10	9.35000	2.62520	9.50000	4.00000	13.00000
GCS 21	9	11.33333	3.67423	13.00000	4.00000	15.00000
GCS 30	8	12.50000	2.77746	13.50000	8.00000	15.00000
GOS 30	14	2.42857	1.55486	2.00000	1.00000	5.00000

P79 Delayed paraplegia after thoracoabdominal aortic aneurysm repair announced by changes in CSF

R Imberti[1], V Rizzo[2], I Blangetti[1], G Bellinzona[1], R Moratti[2], M Langer[1]
[1]Department of Anesthesiology and Critical Care Medicine, IRCCS S. Matteo, Pavia, Italy; [2]Department of Biochemestry, University of Pavia, Italy
Critical Care 2003, **7(Suppl 2)**:P079 (DOI 10.1186/cc1968)

Delayed paraplegia is an unpredictible, albeit devastating complication of thoracoabdominal aortic aneurysm (TAAA) repair [1]. We report on a patient who, 24 hours after TAAA repair, developed paraplegia that was announced by biochemical changes in cerebrospinal fluid (CSF).

A 57-year-old man was submitted to TAAA repair. A lumbar spinal drain was placed after induction of anesthesia and left in place in order to reduce CSF pressure and sample collection. Samples were collected immediately after catheter placement and at time intervals during aortic cross-clamping, after cross-clamp release and postoperatively in the ICU, and stored at –80°C. Excitatory and inhibitory amino acids (glutamate, aspartate, glycine, GABA), non-transmitter amino acids (taurine, alanine), energetic metabolism parameters (lactate, adenosine) were analyzed by HPLC altogether 5 days later. The surgical procedure was performed with the aid of a left-side bypass.

Fifteen minutes after proximal aortic cross-clamping, excitatory, inhibitory and nontransmitter amino acids in the CSF increased

several times with respect to baseline and stayed high throughout reperfusion. Proximal aortic cross-clamping resulted also in an increase of lactate that stayed high also during reperfusion, while adenosine, a product of purine metabolism, increased during cross-clamping and normalized at reperfusion. Four hours after the end of surgery, while the patient was in the ICU, all parameters returned to baseline. The following day, a new sample of CSF was collected. At that time the patient was awake, hemodynamically stable, CSF pressure was 10 mmHg, and his lower extremities motility was preserved. Three hours later he developed paraplegia. Emergency CT scan excluded epidural hematoma. The analysis of the CSF sample collected 3 hours prior to the onset of paraplegia showed an increase of excitatory, inhibitory and nontransmitter amino acids, as well of lactate and adenosine.

Altogether our findings indicate that the biochemical changes that occurred in the CSF of our patient announced the impending spinal cord ischemia. Bedside, real-time evaluation of the biochemical changes in CSF, which has been recently made possible by new apparatus, could be useful to evaluate spinal cord perfusion and, hopefully, to contrast the onset of paraplegia associated with TAAA repair.

Reference

1. Crawford ES, *et al.*: *J Thorac Cardiovasc Surg* 1988, **95**:357-367.

P80 Brain natriuretic peptide in acute brain diseases

V Špatenková[1], A Kazda[2], P Škrabálek[3]

[1]Neurocentre and [3]Clinical Biochemistry Department, Liberec Hospital, Czech Republic; [2]Postgraduate Medical School, Prague, Czech Republic

Critical Care 2003, **7(Suppl 2)**:P080 (DOI 10.1186/cc1969)

Introduction Brain natriuretic peptide (BNP) is a member of the family of natriuretic peptide hormones, which are involved in regulation of sodium and water homeostasis. It has been proven that natriuretic peptide plays a role in sodium dysbalance in acute brain diseases, especially in Cerebral Salt Wasting Syndrome (CSWS). It is also elevated in intracranial hypertension. Now there is a method available that can assay an N terminal fragment pro brain natriuretic peptide (NT-proBNP).

Method We retrospectively analysed 77 blood samples for NT-proBNP from 18 patients hospitalised at our ICU from February until May 2002. Seventeen patients had acute brain disease (subarachnoid hemorrhage [SAH], eight cases; intracerebral hemorrhage, one case; tumor, five cases; and others, five cases) and one patient had spine disease.

All patients were classified as NYHA I, and their age was between 23 and 73 years (mean age 53 years).

We investigated NT-proBNP, serum osmolality (S_osm) and sodium (S_Na^+) on day 1. S_osm, S_Na^+, daily urinary loss of sodium (dU_Na^+), creatinine clearance (C_krea), diuresis, income of fluids and sodium in 24 hours on day 2. Moreover, we assessed NT-proBNP changes in time. Upper reference range for NT-proBNP is 150 pg/l.

Results Parameters ± standard deviation (SD) and correlation coefficients (*r*) are presented in Table 1.

NT-proBNP was significantly elevated in all the patients ($P=0.007$) and the value did not significantly change in time (difference between two samples in 13 patients; $P=0.3$), and in tree samples in eight patients ($P=0.28$, $P=0.37$). NT-proBNP had no correlation with other parameters measured.

Conclusion In our retrospective study we found significant elevation of NT-proBNP in patients with acute brain disease and without sodium dysbalance. Values of NT-proBNP did not significantly change in time and did not correlate with any biochemical parameters measured.

References

1. Berendes E, Walter M, Cullen P: **Secretion of brain natriuretic peptide in patients with aneurysmal subarachnoid haemorrhage.** *Lancet* 1997, **349**:245-249.
2. Betjes MGH: **Hyponatremia in acute brain disease: cerebral salt wasting syndrome.** *Eur J Internal Med* 2002, **13**:9-14.
3. Ruskoaho H, Leskinen H, Taskinen JMP, Mäntymaa P, Leppäluoto OVJ: **Mechanisms of mechanical load-induced atrial natriuretic peptide secretion: role of endothelin, nitric oxide, and angiotensin II.** *J Mol Med* 1997; **75**:876-885.

Table 1

Parameter	NT-proBNP (pg/l)	S_Na^+ (mmol/l)	S_Na^+ (mmol/l)	S_osm (mmol/l)	S_osm (mmol/l)	dU_Na^+ (mmol)	C_krea (ml/s)	Diuresis (ml)	Income of fluids (ml)	Income of Na^+ (mmol)
Day	1	1	2	1	2	2	2	2	2	2
Minimum	31	132	135	278	284	207	1.2	2150	3000	254
Median	227	142	143	290	294	459	1.8	3700	4000	400
Maximum	834	149	151	314	305	735	3.1	7000	7680	590
Mean value ± SD	321 ± 244	141 ± 5	142 ± 5	292 ± 11	293 ± 6	449 ± 160	2.1 ± 0.6	3756 ± 1302	4192 ± 1095	427 ± 91
Correlation coefficient		0.13	0.0006	0.34	0.003	0.10	0.12	0.2	0.20	0.17

P81 Transcranial cerebral oximetry (TCCO) monitoring in neurosurgical critically ill patients

G Toma[1], V Amcheslavski[2], V Lukianov[2], A Ostrovski[2], D DeWitt[1]
[1]Department of Anesthesiology, The University of Texas Medical Branch at Galveston, USA; [2]Department of Neuroscience ICU, Burdenko Neurosurgical Institute, Moscow, Russia
Critical Care 2003, **7(Suppl 2)**:P081 (DOI 10.1186/cc1970)

Introduction Near-infrared spectroscopy (NIRS) has been used to monitor cerebral oxygenation in various clinical fields. However, its utility has not been demonstrated in more complex situations, such as neurosurgical critically ill patients. The objective of this study was to examine the ability of TCCO to detect cerebrovascular events, such as oligemic hypoxia, relative cerebral hyperemia and vasospasm in neurosurgical critically ill patients with different outcome.

Methods This study involved a retrospective analysis of regional cerebral saturation (rSO_2) data collected in 64 neurosurgical patients in critical states using the INVOS 4100 cerebral oximeter as a part of multimodal neuromonitoring. Patients were divided into three groups: group I, good outcome/moderate disability (GOS 5–4, 14 male/four female, 38.9 years old); group II, severe disability/vegetative state (GOS 3–2, 12 male/four female, 37.6 years old); and group III, dead (20 male/10 female, 39.2 years old). The outcome was assessed at discharge of the patients from the hospital.

Results TCCO monitoring detected a pathological pattern of regional cerebral oxygenation in 83% of patients. In patients with vasospasm, early appearance and increasing rSO_2 fluctuations more than 10% were correlated with poor outcome. 74.3% of patients where we monitored both rSO_2 and $SjbO_2$ have had the same pattern of increased or decreased parameters (Table 1).

Discussion As a noninvasive, bedside, nonoperator-dependent tool TCCO is effective in identifying such cerebrovascular events as oligemic cerebral hypoxia, relative cerebral hyperemia and vasospasm, which were more pronounced in neurosurgical patients with unfavorable outcome.

Table 1

	Group I ($n = 18$)	Group II ($n = 16$)	Group III ($n = 30$)
Patients with normal rSO_2 pattern (%), mean rSO_2 (%)	22%, 71.5 ± 2.8	25%, 69 ± 1.7	10%, 67 ± 2.4*
Patients with decreased rSO_2 pattern (%), mean rSO_2 (%)	17%, 55.6 ± 3.3	37.5%, 51 ± 2*	40%, 50.4 ± 4.4*
Patients with erradic rSO_2 pattern (vasospasm) (%), mean rSO_2 (%)	72%, 67 ± 10	25%, 63.8 ± 13.5	40%, 58.1 ± 16.5*
Patients with increased rSO_2 pattern (%), mean rSO_2 (%)	5.5%, 78.4 ± 1.7	18.7%, 78 ± 3	33%, 83 ± 4

Parameters of NIRS are mean ± SD. * $P < 0.05$ in comparison with group I.

P82 Transcranial Doppler ultrasonography at the admission of trauma head-injured patients and their neurological outcome at 3 months

J Brun, P Declety, D Anglade, C Jacquot, JF Payen
Department of Anesthesia and Intensive Care, Michallon's Hospital, 38043 Grenoble, France
Critical Care 2003, **7(Suppl 2)**:P082 (DOI 10.1186/cc1971)

Introduction Early cerebral ischemia after brain trauma is predictive of poor outcome [1]. Since brain hemodynamics can be noninvasively assessed using transcranial Doppler ultrasonography (TCD), we prospectively investigated the relation between TCD measurements at the admission of head-injured patients and their neurological outcome at 3 months.

Methods Twenty-nine head-injured patients (35 ± 16 years, Glasgow Coma Scale [GCS] 10 ± 4, Apache II score 35 ± 15) were included in the study, in the absence of systemic hypotension (systolic blood pressure > 90 mmHg), hypoxemia (SpO_2 > 92%) and $PaCO_2$ alterations ($PaCO_2$ 4–4.5 kPa) at the admission. TCD right and left middle cerebral artery systolic (SV), diastolic (DV) and mean (MV) flow velocities and pulsatility index (PI) were measured within the first 6 hours after the brain trauma (Waki 1-TC; ATYS Medical, Lyon, France). Neurological evaluation was performed at 3 months following the brain trauma, using the Glasgow Outcome Scale (GOS). A GOS score of 4 and 5 (moderate disability to total recovery) was considered as a good outcome (group 1), and a GOS score of 1–3 (death to severe disability) as a bad outcome (group 2). The Student *t* test was used to compare the data (mean ± SD), and $P < 0.05$ was considered significant.

Results Nine patients had bad outcome at 3 months (five deaths, four GOS score of 3), and 20 had good outcome (five GOS score of 4, 15 GOS score of 5). At admission, there was no significative difference between the two groups in their age, the systemic blood

Table 1

		Group 1	Group 2	*P* values
Right MCA	SV	92 ± 22	85 ± 16	0.46
	MV	51 ± 14	36 ± 6	0.006
	DV	39 ± 12	23 ± 6	0.01
	IP	1.23 ± 0.52	1.88 ± 0.67	0.01
Left MCA	SV	97 ± 24	82 ± 15	0.11
	MV	53 ± 17	43 ± 18	0.10
	DV	41 ± 13	23 ± 10	0.003
	IP	1.23 ± 0.53	1.89 ± 0.67	0.01

pressure, the ventilatory parameters, and the GCS. Group 2 exhibited lower DV and higher PI values than did group 1 (Table 1).

Conclusions Noninvasive estimation of brain hemodynamics by TCD at the admission of head-injured patients could be related to neurological status at 3 months. Further studies are needed to determine TCD threshold values of outcome.

Reference

1. Marion DW, Darby J, Yonas H: **Acute regional cerebral blood flow changes caused by severe head injuries.** *J Neurosurg* 1991, **74**:407-414.

P83 Complications of monitoring of jugular bulb venous saturation

MG Rodrigues, DR Salgado, VM Resende, MVP Negri, RAN Paiva, JCR Verdeal
Vila Isabel, Rio de Janeiro, Brasil
Critical Care 2003, **7(Suppl 2)**:P083 (DOI 10.1186/cc1972)

Introduction Neurological monitoring is very important to change the prognosis of a critical neurological patient. The jugular venous bulb saturation is extremely important to evaluate the consumption and delivery of oxygen.

Objective To describe complications during insertion and the permanence period of a jugular venous bulb catheter.

Materials and methods Prospective, observational study of 21 patients from June 2000 to September 2002 in an intensive care unit. All patients were monitored with an intracranial pressure device (ICP – CAMINO). The jugular venous line was cannulated independent of which side. The catheter flow was sustained by continuous saline infusion (rate, 3 ml/hour). The monitor used was VIGILANCE (Baxter). Complications were observed during insertion such as arterial puncture, bleeding, and misplacement; during catheter permanence, obstruction and infection (daily examination); after decanulation, thrombosis detected through Doppler, which was performed after 24 hours. All the catheter tips were sent to bacteriological examination.

Results The meaning time of canulation was 5 days. The thrombosis rate detected by Doppler was 31.6% (without clinical compromise). The catheter obstruction rate was 15.8% and the infection rate 10.5%.

Conclusion Strict control with Doppler examination is very important to warrant optimal flow. The catheter must be changed every 5 days in order to avoid infection.

P84 The incidence of sinusitis and the use of ultrasound in early diagnosis of sinusitis in patients with head injury

G Celikbilek, L Dosemeci, M Yilmaz, M Cengiz, A Ramazanoglu
Department of Anaesthesiology and ICU, University of Akdeniz, Faculty of Medicine, Antalya, Turkey
Critical Care 2003, **7(Suppl 2)**:P084 (DOI 10.1186/cc1973)

Introduction Sinusitis, complication of the head injury in critically ill patients, is an important cause of sepsis and may well be difficult to be diagnosed. In this study, we assayed the sensitivity and specificity of ultrasonography (USG) by comparing it with the computerized tomography (CT) and we determined the incidence of maxillary sinusitis with existing fluid in the maxillary sinuses.

Materials and methods In an 8 month period, 41 patients with head injury that requires CT for diagnosis and control were admitted to the ICU. The paranasal CT was performed along with the routine cranial control CT in these patients. After paranasal CT scanning, a B-mode USG was performed blindly. Radiological maxillary sinusitis (RMS) is defined by an air-fluid level or a complete opacification of the maxillary sinus area in the CT. Absence of RMS was defined as a normal sinus. Total opacity or air-fluid level, larger than half of the sinus area, defined important RMS. Air-fluid levels inferior to the half of the sinus area defined moderate RMS. In an ultrasonographic procedure, if the acoustic shadow rises from the front wall, the image is defined normal. Moderate form was defined as the hyperechogenic visualization of the whole posterior wall. Severe form was defined as the hyperechogenic visualization of both the posterior and internal wall of the sinus as a border of hypoechogenic sinus cavity. The indication of the punction includes moderate and/or severe RMS, fever (temperature $\geq 38°C$), leukocytosis (white blood cell $>12{,}000/mm^3$) and an increase in CRP values. When the maxillary sinusitis developed we performed a punction of the maxillary sinus using a sinoject. All aspirated material was cultured for aerobic and anaerobic agents. Antibiotics were modified according to the sensitivity of the cultures.

Results In an 8 month period we performed 100 CT and USG examinations at the same time. Sensitivity and specificity of USG compared with CT were, respectively, 92.15% and 81.63%. We performed a punction in 35 of 47 sinuses, which show medium and/or severe fluid existence in both CT and USG. Using appropriate microbiological techniques 22 bacterial strains were isolated in 19/35 aspirates (40.42%). The most frequently isolated species were *Pseudomonas* sp. ($n=8$, 36.36%) and *E. coli* ($n=5$, 22.72%).

Conclusions The incidence of sinusitis is indicated high in patients with head injury. USG may be proposed in first-line diagnosis of radiological maxillary sinusitis.

P85 Risk factors related to death in patients with ischemic stroke

M Palacios[1], E Morales[1], V Segura[2], F Delgado[3]
[1]Departamento de Medicina Interna, [2]Unidad de Medicina Critica and [3]Departamento de Neurología y Electrofisiología, Hospital Médico Quirurgico del Instituto Salvadoreño del Seguro Social (ISSS), San Salvador, El Salvador
Critical Care 2003, **7(Suppl 2)**:P085 (DOI 10.1186/cc1974)

Background Ischemic stroke is a disease with high mortality and morbidity because of the limited advance in therapeutics and lack of adequate technology for its treatment in some hospitals. The objective of our study is to demonstrate which factors are related to higher mortality, so they can be taken into account in selecting high risk groups at the time of treatment.

Methods A retrospective study was made in patients who were admitted with diagnosis of ischemic stroke at the Hospital Médico Quirurgico del ISSS in a period of 18 months, from July 2000 to December 2001. Twenty-eight variables were analyzed, including clinical criteria, laboratory and imagining. A total of 106 patients were studied, excluding 14 patients who did not fulfill inclusion criteria. The statistical analysis was realized by chi-square test and Student *t* test and we took $P<0.05$ to consider a significant difference. The odds ratio (OR) was determined for each variable.

Results Ninety-two patients were studied, of which 36 (39.1%) were female with average age of 71 years, and 56 (60.9%) were male with average age of 69 years. Twenty-four (26.1%) died and 68 (73.9%) were discharged. We found only 10 variables to be statistically significant: mean arterial pressure (MAP) at admittance, seizures, temperature >37.5°C, hyperglycemia, sepsis, age, arrhythmia, cardiovascular complications, computerized tomography (CT) results at admittance, and leucocytosis (Table 1). The average MAP in deceased patients was 91 mmHg, and pressures below this value were related to death with an OR=5.92 (range: 1.93–18.59) and $P=0.0003$. Patients who were given hospital discharge had an average MAP of 107 mmHg, and pressures=107 mmHg had an OR=0.24 (range: 0.06–0.85) and $P=0.012$, which shows it is beneficial to maintain a relatively high MAP to ensure adequate cerebral perfusion. Other significant variables related to death were: temperature >37.5°C at admittance, with OR=13, and $P=0.000038$; seizures with OR=17.63, and $P=0.011$; hyperglycemia (>200 mg/dl) with OR=6.27, and $P=0.00031$; leucocytosis (WBC>12,000) with OR=13.11, and $P=0.0000005$. In patients with a negative CT at admittance, an OR=0.04 was found, with $P=0.000076$. All patients with ischemic stroke and sepsis died.

Conclusions There are risk factors closely related to mortality in patients with ischemic stroke, some of which may be modified at admittance, such as temperature >37.5°C, MAP<91 mmHg, and hyperglycemia. Some require early detection to avoid further complications, such as seizures, arrhythmias and leucocytosis. Certain factors are related to lower mortality rate: age ≤69 years, negative CT at admittance and MAP ≥107 mmHg.

Table 1

Variable	Survivals ($n=68$)	Deaths ($n=24$)	OR	*P*
Seizure	1.5% (1)	20.8 % (5)	17.63	0.001
Temperature > 37.5°C	4.4% (3)	37.5% (9)	13.0	0.00038
Arrhythmias	10.3% (7)	54.2% (13)	10.3	0.0000084
MAP ≤91 mmHg	19.1% (13)	58.3% (14)	5.92	0.0003
Hyperglycemia (>200 mg/dl)	32.3% (22)	75% (18)	6.27	0.00031
Cardiovascular complications	1.5% (1)	12.5% (3)	9.57	0.023
Sepsis	4.4% (3)	79.2% (19)	125.4	0.0000000
CT (–) at admittance	50% (34)	95.8 % (23)	0.04	0.000076
Leucocytosis	13.2% (9)	66.7% (16)	13.11	0.0000005
Age ≤69 years	54.4% (37)	29.2% (7)	0.34	0.034

P86 Early signs of critical illness polyneuropathy in porcine sepsis

J Maňák[1], M Schreiber[2], H Matulová[2], M Šlemrová[1], J Cerman[1], M Šitina[1], S Špelda[3], L Sobotka[1], Z Zadák[1]
[1]Department of Metabolism and Gerontology, and [2]Department of Neurology, Charles University Teaching Hospital, Hradec Králové, Czech Republic; [3]Animal Research Laboratory, Military Medical Academy JE Purkyne, Hradec Králové, Czech Republic
Critical Care 2003, **7(Suppl 2)**:P086 (DOI 10.1186/cc1975)

Background Critical illness polyneuropathy is a well known complication of critical illness causing prolonged artificial ventilation, increased ICU and inhospital length of stay and higher mortality in critically ill patients. Although two studies reported early signs of polyneuropathy on day 2–5 after ICU admission, the exact time of onset of this complication is still unknown.

Aim To investigate the electrophysiologic manifestations of critical illness polyneuropathy in a porcine model of sepsis during the first 24 hours after the septic insult.

Materials and methods Seven anaesthetised, artificially ventilated and multicatheterized domestic pigs (body weight 29.7±3.9 kg)

were randomly subjected to either live *E. coli* IV infusion to induce sepsis ($n=4$) or to a sham procedure ($n=3$). Animals were fluid resuscitated with 20 ml/kg per hour of Ringer's lactated solution. Conduction studies (compound muscle action potential after supramaximal stimulation, latency and duration of the potential) of a motoric peripheral nerve (n. peronaeus) and needle electromyography (insertion activity, presence of positive sharp waves or fibrillations) of one of the corresponding muscles (m. tibialis longus) on the left pelvic extremity were recorded before, and 6, 18 and 24 hours after *E. coli* infusion. For statistical analysis, ANOVA for repeated measures and Fisher's LSD test were used.

Results No differences were present in latency and duration of the compound action muscle potential between septic and control animals. No changes in insertion activity and no signs of spontaneous muscle activity (presence of positive sharp waves or fibrillations) were found in either groups. Compound muscle action potentials (CMAP) were significantly reduced compared with baseline in septic animals starting from 6 hours ($P<0.01$) after microbial infusion and further decreasing at 18 ($P<0.0001$) and 24 hours ($P<0.00001$). In control animals, there was significant decrease in CMAP at 24 hours ($P<0.05$). The time course of CMAPs was significantly different between the groups ($P<0.04$). Positive fluid balance was significantly higher in the septic group ($P<0.00001$).

Conclusions We detected a very early and significant decrease of compound muscle action potential in septic animals. This result may be caused by the changes in peripheral nerve or in the correspondent skeletal muscle analogic to either critical illness polyneuropathy or myopathy, although changes due to tissue edema can not be excluded. To our best knowledge, this is the first animal model of critical illness neuromuscular abnormalities.

P87 Serial S-100 levels before, during and after cerebral herniation: a case report

J Undén[1], J Bellner[1], P Reinstrup[2], C Alling[3], B Romner[1]
[1]Department of Neurosurgery, [2]Department of Anaesthesiology and [3]Department of Clinical Neurochemistry, Lund University Hospital, Lund, Sweden
Critical Care 2003, **7(Suppl 2)**:P087 (DOI 10.1186/cc1976)

S-100B is a small dimeric calcium-binding protein that is abundant in astroglial cells within the central nervous system (CNS). It has been shown to increase in cerebrospinal fluid (CSF) and serum after various neurological diseases, including minor head injury, severe head injury, subarachnoid haemorrhage and cerebral infarcts as well as after cardiopulmonary bypass surgery.

We report on a patient with severe head injury after a traffic accident who was followed with routine neuromonitoring techniques (intracranial pressure [ICP], microdialysis, clinical examination and neuroimaging) with the addition of serial serum S-100B measurements (a total of 41 S-100B measurements during admission of almost 3 days). Results of S-100B analysis were available within 2 hours of sampling allowing us to increase the sampling rate at physician discretion. Cerebral herniation, confirmed by cerebral angiography, occurred 1 day after admission. After brain death was established we continued to monitor S-100B levels in conjunction with an organ harvesting procedure for transplantation.

We found that S-100B levels seemed to peak immediately prior to cerebral herniation and then decreased shortly thereafter. In conjunction with the organ harvesting procedure S-100B levels increased, indicating a clear extracerebral source of the protein.

P88 Motor neuron disease caused prolonged mechanical ventilation after high-voltage electrical injury

M Yilmaz, L Dosemeci, E Kaplan, R Yagmur, A Ramazanoglu
Burhanettin Onat cad 1425 sok, 8/22, 07070 Antalya, Turkey
Critical Care 2003, **7(Suppl 2)**:P088 (DOI 10.1186/cc1977)

Objective In the literature, 65 cases with diagnoses of ALS/motor neuron disease after electrical injuries have been reported. However, in almost all of these cases the onset of the neurological findings was delayed and the evidence of the damage of spinal cord could not be shown. We describe a case, requiring prolonged mechanical ventilation, with the early onset neurological injury after high voltage electrical injury and showed evidence of the damage of the spinal cord on MR.

Case report A 29-year old man was admitted into our ICU as a result of being exposed to high voltage (31,500 V) current and then falling down from 10 meters. He was unconscious and had second to third degrees of burned areas on the right side of his face (exit) and right lower limb (entry). There was no abnormality on his cervical CT and X-rays. After 1 week of his admission and mechanical ventilation, when he became conscious and cooperated, we noticed that there was no motor response on his four limbs with normal touch and pain sensation. DTR were not taken on the upper limbs.

Results Needle EMG revealed diffuse, acute denervation potentials on all studied muscles. Cervical magnetic resonance imaging (MRI) indicated myelomalasic changes (transverse myelitis) on the C_{2-5} segments of the spinal cord. The first motor response was noticed on the 55th day of his admission and he could be liberated from mechanical ventilation on the 70th day.

Conclusion Electrical shocks commonly cause immediate damage to the heart and musculoskeletal system. However, a few cases with neurological complications secondary to electrical injury have been reported in the literature. In the reported cases, the onset of motor neuron disorder usually occurred in the limb through which the shock entered and none of them required prolonged mechanical ventilation due to respiratory muscle weakness. The pathogenesis of most acquired motor neuron disease is poorly understood, and treatment is mainly supportive.

We showed in this case the pathologic change of the spinal cord on MRI, which may lead to the motor weakness.

P89 Diffusion weighted magnetic resonance imaging in early moderate and severe head injury

PB Bradley[1], SG Harding[2], A Pena[2], DA Chatfield[1], JD Pickard[2], TA Carpenter[2], DK Menon
[1]Department of Anaesthesia and [2]Wolfson Brain Imaging Centre, Addenbrooke's Hospital, Cambridge CB2 2QQ, UK
Critical Care 2003, **7(Suppl 2)**:P089 (DOI 10.1186/cc1978)

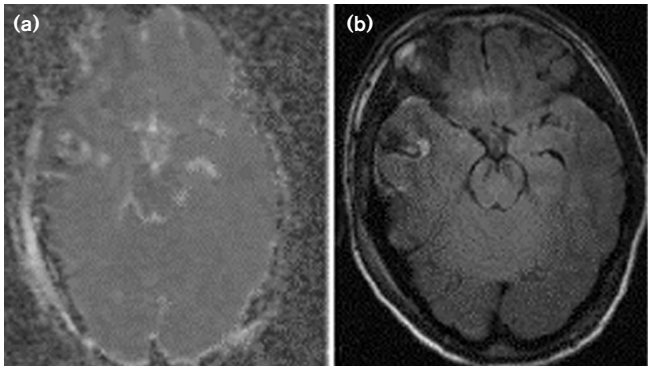
Introduction Magnetic resonance imaging (MRI) has been widely used in brain imaging, and diffusion weighted imaging (DWI) with MR has been used to image early ischaemia in stroke. We have used early DWI following head injury to map cerebral ischaemia.

Patients and methods We studied six patients with severe head injury, with a median (range) initial Glasgow Coma Score 3.5 (3–8), and X-ray computed tomography (CT) demonstrated contusions in all subjects. All patients were managed using protocol-driven therapy including sedation, neuromuscular blockade and mechanical ventilation, and were imaged at a mean of 63 hours (range 15–90 hours) post injury. MRI examination included DWI and fluid attenuation inversion recovery (FLAIR) sequences, the latter showing vasogenic oedema as high signal intensity on CSF nulled images.

Results All patients showed substantial but variable perilesional oedema, best demonstrated on FLAIR images. Perilesional oedema was well seen as early as 15 hours post injury, suggesting that some previous estimates of temporal evolution of this process may have been incorrect [1]. In addition many images show regions of restricted diffusion in the brain adjacent to the perilesional oedema, suggesting evolving pathophysiology with cytotoxic oedema.

Discussion These results underline the superiority of MRI in imaging the pathophysiological processes in acute head injury. The diffusion weighted abnormalities that we observe are intriguing, but their mechanism remains uncertain. The confounding effects of microhaemorrhage and high oxygen extraction may need to be considered in the interpretation of such images.

Figure 1



(a) Diffusion image. **(b)** FLAIR image.

Reference
1. Bullock R, Statham P, Patterson J, Wyper D, Hadley D, Teasdale E: **The time course of vasogenic oedema after focal human head injury — evidence from SPECT mapping of blood brain barrier defects.** *Acta Neurochir Suppl (Wien)* 1990, **51**:286-288.

P90 BrainView: a software designed for quantifying brain volume, weight and density

T Lescot[1], C Fetita[2], A Zouaoui[3], J-C Muller[1], P Coriat[1], F Préteux[2], L Puybasset[1]
[1]Anesthesiology Department and [3]Neuroradiology Department, La Pitié-Salpêtrière Hospital, 47–83 boulevard de l'hôpital, 75013 Paris, France; [2]ARTEMIS Project Unit, Institut National des Télécommunications, Evry, France
Critical Care 2003, **7(Suppl 2)**:P090 (DOI 10.1186/cc1979)

Introduction Because radiological densities are linearly correlated with the physical densities in human tissue, the use of CT gives the opportunity to measure *in vivo* the volume, weight and density of the brain. BrainView is a software specially designed to compute these parameters.

Methods DICOM images obtained from the cerebral CT (high-speed advantage CT scan; GE medical system, USA) performed for headache assessment in 10 patients (43 ± 18 years, mean ± SD) were analyzed. Each exam, acquired as 5-mm-thick-ness contiguous slices, was considered as normal by the neuro-radiologist (AZ). As a first step, BrainView automatically excluded extracranial compartments on each CT section by means of a mathematical morphology-based algorithm. One single physician (TL) then delineated on each section the two hemispheres, the cerebellum, the brainstem and the intraventricular and subarachnoid cerebrospinal fluid (CSF) according to anatomical landmarks. The volume of each anatomical compartment was computed as the number of voxels included in this compartment times the volume of the voxel. The weight of each voxel was computed as its volume

Table 1

Volume, weight and physical density of each compartment (mean ± SD)

	Right hemisphere	Left hemisphere	CSF	Cerebellum	Brainstem	Total intracranial
Volume (ml)	517 ± 64	517 ± 61	130 ± 60	143 ± 19	25 ± 5	1348 ± 150
Weight (g)	534 ± 66	534 ± 64	132 ± 61	149 ± 20	26 ± 6	1392 ± 155
Density (g/ml)	1.0334 ± 0.0012	1.0332 ± 0.0011	1.0209 ± 0.0012	1.0377 ± 0.0014	1.0278 ± 0.0016	1.0325 ± 0.0014

times its density knowing that the physical density of a voxel having a radiological density of 0 HU (i.e. water) is 1 g/ml. The weight of each compartment was computed by summing the weights of all voxels composing it.

Results See Table 1.

Discussion BrainView is a tool providing the measurements *in vivo* of volume, weight and density of the human brain. It gives new opportunities to assess the global and regional effects of anti-edematous treatment as well as the permeability of the brain–blood barrier in patients with intracranial hypertension.

P91 Brain temperature changes during selective brain cooling

H Trübel[1,2], P Herman[1], CH Kampmann[3], R Huth[3], PK Maciejewski[4], F Hyder[1], EJ Novotny[2,5]
[1]Department of Diagnostic Radiology, [2]Department of Pediatrics, [4]Department of Psychiatry and [5]Department of Neurology, Yale University, 333 Cedar Street, New Haven, CT, USA; [3]Department of Pediatrics, Joh. Gutenberg University, 55101 Mainz, Germany
Critical Care 2003, **7(Suppl 2)**:P091 (DOI 10.1186/cc1980)

Introduction Induced hypothermia is used in patients with brain injury [1,2]. During selective brain cooling (SBC), only the brain temperature (T_B) is reduced while the core temperature (T_C) remains unchanged [3]. Under normal conditions $T_B \leq T_C$; however, in some diseased states $T_B > T_C$ is found [4]. Since SBC renders $T_B << T_C$, heat deposition from incoming blood to brain tissue can occur. The purpose of our animal study was 1) to investigate the temperature changes that can arise during SBC and 2) relate them to commonly encountered clinical situations (i.e. seizure activity, hypercapnia) with respect to brain temperature.

Methods Experiments were conducted in artificially ventilated rats under sedation with α-chloralose (40 mg/kg per hour IP) and *d*-tubocurarine (0.05 mg/kg per hour). Bicuculline (1 mg/kg; Sigma-Aldrich, St Louis, MO, USA) was infused for generalized seizure induction. The animal was placed on a heating blanket with its head in a stereotaxic holder. Through a small burr hole a thermocouple wire (Oxylite™; Oxford Optronix, Oxford, UK) was inserted to measure the brain temperature in the cortex ($n=18$). The head was covered with cotton balls to minimize heat loss to the environment. SBC was achieved by a new approach: Tygon™ Ultra-Soft tubing (R-1000, ID 3.2 mm; SGPP Corp, Akron, OH, USA) was perfused with water at +4°C. A V-shaped part of the tubing with inflow and outflow was placed into the pharynx of the animal ($n=8$). The temperature in the mouth during SBC was measured ($n=2$). To raise pCO_2 to ca 80 mmHg, the ventilatory rate was halved.

Results With SBC T_B could be lowered to 33.1 ± 1.23°C (mean ± SD) from 36.9 ± 0.67°C ($P<0.001$). There was a trend towards a lower T_C during SBC (from 36.90 to 36.44, $P=0.22$). The temperature in the pharynx during SBC was 29.1 ± 2.19°C. From the lowest achieved SBC temperature T_B rose during CO_2 challenge by 1.22 ± 0.67°C which is significantly higher than the increase of T_B seen without SBC (0.85 ± 0.34°C, $P<0.05$). The increase in T_B from the lowest SBC level during seizure was 2.08 ± 0.35°C (1.15 ± 0.55°C in non-SBC animals [$P=0.001$]).

Conclusion Significant cooling of the cortex could be achieved by SBC from the pharynx in a rat model. Marked changes during hypercapnia and with seizure activity were seen that partially reversed the cooling effect of SBC. It therefore seems advisable to avoid, for example, permissive hypercapnia in patients where SBC is to be achieved. Whether the proposed approach to cool the brain from the pharynx can be applied in a clinical setting needs to be tested in larger animal species because of different anatomical compositions.

References

1. Biagas KV, Gaeta ML: **Treatment of traumatic brain injury with hypothermia.** *Curr Opin Pediatr* 1998, **10**:271-277.
2. Bernard SA, *et al.*: **Treatment of comatose survivors of out-of-hospital cardiac arrest with induced hypothermia.** *N Engl J Med* 2002, **346**:557-563.
3. Gunn AJ, Gluckman PD, Gunn TR: **Selective head cooling in new born infants after perinatal asphyxia: a safety study.** *Pediatrics* 1998, **102**:885-892.
4. Rumana CS, Gospinath SP: **Brain temperature exceeds systemic temperature in head-injured patients.** *Crit Care Med* 1998, **26**:562-567.

P92 A comparison of effects of propofol or remifentanil bolus on BIS variations during tracheal suction in mechanically ventilated critically ill patients

T Gaszyński, A Wieczorek, W Gaszyński
Department of Anaesthesiology and Intensive Therapy, Medical University of Lodz, Barlicki Hospital, ul.Kopcinskiego 22, 90-153 Lodz, Poland
Critical Care 2003, **7(Suppl 2)**:P092 (DOI 10.1186/cc1981)

Background and objective of study The tracheal suction – a part of routine care in ICU – is a nociceptive stimuli. We evaluated the impact of remifentanil or propofol bolus on Bispectral index variations and cardiovascular response to tracheal suction in ICU sedated patients.

Patients and methods Nineteen ICU sedated (midazolam), mechanically ventilated patients were enrolled into a prospective pilot study.

Observation Continuous monitoring BIS, cardiovascular parameters measured before and after administration of drug (propofol 100 mg or remifentanil 1 μg/kg), and after suctioning. All patients received propofol, and for next routine suctioning remifentanil.

Results The steady-state BIS value was 52.21 ± 9.9. After administration of propofol and remifentanil, BIS decreased significantly: 31.5 ± 15.9 vs 37.64 ± 9.1, respectively. During the first minute after suctioning, a higher increase in BIS level was observed for remifentanil (72 ± 16.28) than for propofol (63.14 ± 30). The mean duration of returning the BIS value to baseline was for propofol 23.5 ± 7 min and for remifentanil 14.2 ± 9 min ($P<0.05$). Systolic arterial pressure was initially 125 ± 12.97 mmHg and decreased significantly after administration of propofol and remifentanil: 107.35 ± 22.12 mmHg vs 107.5 ± 20.53 mmHg, respectively. After suctioning SAP increased more for propofol (120 ± 20.45 mmHg) than for remifentanil (113.21 ± 24.33 mmHg). The HR initially was 95.78 ± 14.84 bpm, and changed after administration of drugs: 94.85 ± 17.61 bpm vs 95.78 ± 20.26 bpm for propofol and

remifentanil, respectively, and after suctioning: 100.64 ± 16.45 vs 97.43 ± 20.62 bpm, respectively.

Conclusion Propofol and remifentanil altered the BIS variation and cardiovascular response to tracheal suctioning in similar way. However, remifentanil seemed to be more effective in providing the required level of sedation. We found BIS monitoring helpful during routine care in the ICU.

P93 The COX-2-specific inhibitor parecoxib sodium is opioid-sparing and improves pain relief as part of a multimodal treatment strategy

F Camu[1], TP Malan[2], RH Wender[3], MC Snabes[4], RC Hubbard[4]
[1]University of Brussels, Belgium; [2]University of Arizona Health Sciences Center, AZ, USA; [3]Cedars-Sinai Medical Center, CA, USA; [4]Pharmacia Corporation, Skokie, IL, USA
Critical Care 2003, **7(Suppl 2)**:P093 (DOI 10.1186/cc1982)

Background Opioid analgesics, although effective in managing acute postoperative pain, are associated with side effects, which can limit pain control and can delay recovery. Thus, multimodal (combination) analgesia is often utilized to reduce opioid use and improve pain relief. The opioid-sparing effects and analgesic efficacy of parecoxib sodium (parecoxib), a novel injectable COX-2-specific inhibitor, were evaluated in two postsurgical pain models.

Methods In two multicenter, double-blind, randomized, placebo-controlled studies, patients who had undergone either hip or knee replacement received morphine by patient-controlled analgesia (PCA) plus either parecoxib 20 mg IV every 12 hours, parecoxib 40 mg IV every 12 hours, or placebo. The total cumulative amount of morphine used, pain intensity difference, pain relief, and Patient's Global Evaluation of Study Medication were assessed.

Results Parecoxib demonstrated significant opioid-sparing effects in both surgical models. In the first 24 hours following surgery, patients receiving parecoxib 20 mg and 40 mg used 16–22% and 28–39% less morphine, respectively, than patients receiving placebo. The effects of parecoxib on morphine consumption were dose dependent and statistically significant. Despite this reduction in morphine use, parecoxib-treated patients experienced significantly improved pain relief and significant reductions in pain intensity compared with patients receiving morphine alone. For example, in the hip replacement model, 85.2% and 81.8% of patients in the parecoxib 20 mg and 40 mg treatment groups were categorized as having 'a lot' or 'complete' pain relief compared with 61.9% of patients receiving morphine alone ($P < 0.05$). Consistent with these findings, in both studies parecoxib-treated patients reported a significantly better level of satisfaction with their medication than those receiving morphine plus placebo. Parecoxib also demonstrated significant reductions in some adverse events (fever and vomiting) in the hip replacement model.

Conclusions Parecoxib in combination with morphine provides significant opioid-sparing effects, and improved pain management and patient satisfaction, in two major surgical pain models, compared with morphine alone.

P94 Efficacy and safety of a single dose of IV parecoxib sodium followed by up to 7 days of oral valdecoxib for pain following laparoscopic cholecystectomy

H Minkowitz[1], G Joshi[2], TJ Gan[3], R Cheung[4], RC Hubbard[5], C Chen[5], J Fort[4]
[1]Memorial Hermann – Memorial City Hospital, Houston, TX, USA; [2]University of Texas, Southwestern Medical Center, Dallas, TX, USA; [3]Duke University Medical Center, Durham, NC, USA; [4]Pharmacia Corporation, Peapack, NJ, USA; [5]Pharmacia Corporation, Skokie, IL, USA
Critical Care 2003, **7(Suppl 2)**:P094 (DOI 10.1186/cc1983)

Objectives To assess the efficacy and safety of a single dose of parecoxib sodium 40 mg IV given 30–45 min preoperatively, followed by oral valdecoxib 40 mg every day for pain given for up to 7 days postsurgery.

Methods This was a multicenter, randomized, double-blind, parallel-group trial. All patients received standard of care (SOC) fentanyl on demand for pain during the immediate postoperative period and acetaminophen 500 mg/hydrocodone 5 mg PO every 4–6 hours as required (for pain) following discharge for up to day 7 postsurgery. The active arm received, in addition, parecoxib sodium 40 mg IV administered 30–45 min preoperatively and valdecoxib 40 mg every day initiated 6–12 hours after surgery and continued up to day 7 postsurgery. The comparator arm received placebo (SOC) matched for the parecoxib sodium and valdecoxib. Pain was evaluated daily using the modified Brief Pain Inventory (mBPI) with 'Worst Pain' assessed using a 0–10 numerical rating scale (NRS) where 10 = worst pain imaginable.

Results In the cohort ($n = 223$) during the immediate postoperative period (4 hours), the parecoxib sodium group ($n = 119$) required significantly lower amounts of fentanyl (152.8 µg vs 192.9 µg: $P = 0.011$) than the comparator group ($n = 104$). Significantly fewer patients in the valdecoxib group required supplemental analgesia over days 1–5 postsurgery ($P < 0.02$). 'Worst Pain' scores were also statistically significantly improved in the valdecoxib-treated group compared with placebo (SOC). Percent of patients reporting worst pain as none or mild (NRS ≤ 4) in the valdecoxib and placebo (SOC) group on day 1 was 63.1% vs 29.2% ($P < 0.001$); day 2 69.2% vs 56.0%. The most common adverse events were nausea, headache, constipation, pain, fatigue and diarrhea, which were comparable between groups.

Conclusions Preoperative administration of parecoxib sodium 40 mg IV resulted in significant opioid sparing immediately following laparoscopic cholecystectomy surgery. Valdecoxib 40 mg every day provided significant opioid-sparing effects and reduced 'Worst Pain' levels in these patients following discharge. Both parecoxib sodium and valdecoxib were well tolerated.

P95 Use of Dexemedetomidine beyond 24 hours in the intensive care unit

MG Rodrigues, DR Salgado, RNA Paiva, G Chindamo, LC Martins, JCR Verdeal
Vila Isabel, Rio de Janeiro, Brasil
Critical Care 2003, **7(Suppl 2)**:P095 (DOI 10.1186/cc1984)

Introduction Adequate sedation of critically ill patients is essential to ensure maximal quality of care in the high-stress enviroment of the intensive care unit. The main goals of sedation include augmentation of pain control, management of agitation and psychological distress, and improvement of patient tolerance and acceptance of the endotracheal tube and ventilatory support.

Dexemedetomidine (DEX) is a potent α_2-adrenoceptor agonist with an α_2: α_1 ratio of 1300:1 that produces stable tranquility with rousability. DEX permits haemodynamic stability by effectively blunting both cathecolamine and haemodynamic responses to endotracheal intubations, surgical stress, and arousal from anesthesia.

Materials and methods A retrospective analysis of the data of 240 patients admitted to a 27-bed general intensive care unit (ICU) from 0ctober 2000 to May 2002 was performed

We evaluated duration of DEX usage, posology – average and maximum doses, length of stay in ICU, and patient average age.

Results Patient age average was 65.3 years and APACHE II score was 13.4. The average dose used was 0.3 μg/kg per hour (0.2–0.6). Time of usage was 3.24 days (1–19 days). The length of hospitalization was 8.9 days.

Conclusions The use of Dexmedetomidine beyond 24 hours appears to be safe and effective for the sedation of ICU patients. The need for other sedating/analgesic drugs occurred in less than one-quarter of the patients and was well tolerated with no extra pyramidal signs seen with antipsychotic drugs or respiratory depression with opiates

P96 Effects of intravenous loxapine on systemic and brain hemodynamics

T Lescot, J-C Muller, L Abdennour, P Coriat, L Puybasset
Department of Anesthesiology, La Pitié-Salpêtrière hospital, 47–83 boulevard de l'hôpital, 75013 Paris, France
Critical Care 2003, **7(Suppl 2)**:P096 (DOI 10.1186/cc1985)

Introduction Intravenous loxapine is an injectable neuroleptic that can be used as a sedative drug in intensive care. Its effects in patients with severe head trauma are still unknown. The effects of intravenous loxapine on intracranial pressure, cerebral hemodynamics and EEG were studied 11 ± 5 days after trauma (mean ± SD) in seven severe brain-injured patients sedated with continuous infusions of sufentanil and midazolam and mechanically ventilated (age = 37 ± 11 years, initial Glasgow coma scale = 7 ± 3, mortality = 0%).

Methods Loxapine (10 mg) was injected IV at a constant flow during a period of 10 min; mean arterial pressure (MAP), end tidal CO_2 ($ETCO_2$), intracranial pressure (ICP), heart rate (HR), mean flow velocity (MFV) and pulsatility index (IP) of the middle cerebral artery (transcranial Doppler WAKI™), left and right spectral edge frequency (SEFl, SEFr) of continuous EEG recording (Philips© technologies) were simultaneously recorded and digitalized at a frequency rate of 50 Hz (Acq*Knowledge*™ software) before, during and after loxapine. Statistical analysis was performed by Student *t* test. $P < 0.05$ was considered significant.

Results Before loxapine injection: MAP = 99 ± 11 mmHg, ICP = 14 ± 5 mmHg, MFV = 53 ± 16 cm/s, IP = 0.96 ± 0.26 mmHg, SEFl = 3.1 ± 1.4 Hz, SEFr = 2.5 ± 1.2 Hz. Loxapine did not induce any significant change on these parameters: MAP = 98 ± 12 mmHg ($P = 0.7$), ICP = 13 ± 4 mmHg ($P = 0.1$), MFV = 53 ± 16 cm/s ($P = 0.9$), IP = 1.00 ± 0.20 ($P = 0.5$), SEFl = 2.4 ± 0.9 Hz ($P = 0.06$), SEFr = 2.2 ± 0.7 Hz ($P = 0.56$). $ETCO_2$ and the dose of vasopressors did not change during the recording.

Discussion Deep sedation is necessary to control ICP but should not induce a decrease in cerebral perfusion pressure or a direct vasoconstrictor effect. The use of loxapine is safe in terms of cerebral mechanics and hemodynamics and might permit a reduction of benzodiazepine's consumption.

Conclusion A 10 mg IV injection of loxapine does not induce any change in intracranial pressure, cerebral blood flow or brain electrical activity in patients with severe head trauma.

P97 Morphine and remifentanil and their effects on dreams, nightmares and hallucinations in critically ill patients

M Lane, A Serrano, S Walters, GR Park
The John Farman Intensive Care Unit, Addenbrooke's Hospital, Cambridge CB2 5EG, UK
Critical Care 2003, **7(Suppl 2)**:P097 (DOI 10.1186/cc1986)

Background Dreaming, nightmares and hallucinations are common in the critically ill and have many causes. These may lead to serious adverse psychological sequelae such as post-traumatic stress disorder. The type of sedation and analgesia used to make patients comfortable may influence this. Morphine causes dreams because of its μ-agonist effects. It is unknown if the new highly lipophilic and potent opioid remifentanil is different.

Method We studied the influence of sedative practice on many variables over an 8 month period in 2002. During the first period of 12 weeks, 'conventional' sedative and analgesic techniques were used where midazolam and propofol were titrated to make the patient comfortable and analgesics added. Over the next 2 months we developed guidelines for the use of remifentanil relieving pain first and adding hypnotics only if needed. The final 12 weeks

involved using remifentanil as the major sedative agent in the ICU, as part of an analgesia-based regimen. As part of the followup in the first 4 days after discharge all patients are asked whether they had any dreams, nightmares or hallucinations and, if so, were they distressing?

Results In the first 12 weeks, 47 patients were followed up and 20 (42%) of them experienced dreams or hallucinations, 13 (65%) did find the experience distressing. These patients all received morphine in combination with midazolam and propofol. In the final 12 weeks, 57 patients were seen and 28 (49%) of them experienced dreams or hallucinations and 16 patients (57%) found them unpleasant or distressing. Morphine (12), remifentanil (12), propofol (9) and midazolam (2) were given to 26/28. Two patients received no sedative or analgesic drugs.

Comment This study shows that the use of potent opioids, such as remifentanil, does not increase the risk of dreaming. Some patients have distressing dreams despite having had no hypnotic or analgesic drugs.

Conflict of interest statement This study was sponsored by Elan Pharma Ltd and GSK Ltd.

Acknowledgement We thank the medical and nursing staff of the ICU for their invaluable contribution to this study.

P98 Additive effects of propofol and midazolam on dopamine vasodilatation of isolated rabbit renal arteries

C Eyigör[1], L Ýyilikçi[1], N Murat[2], H Akdað[2], S Gidener[2], A Günerli[1]
[1]Department of Anaesthesiology and [2]Department of Pharmacology, Dokuz Eylül University, School of Medicine, Turkey
Critical Care 2003, **7(Suppl 2)**:P098 (DOI 10.1186/cc1987)

Background and objective This study evaluated the effects of varying doses of propofol and midazolam on the vasodilatation due to low-dose dopamine in an isolated rabbit artery model.

Methods Twenty-four New Zealand rabbits (2–2.5 kg) were used in the study. All of their left renal arteries were extracted. Renal artery strips 2–3 mm in length were mounted in 20 ml organ baths containing Krebs–Henseleit solution. In order to determine the maximal concentration for dilating the artery tissue, dopamine was added in cumulative log concentrations (10^{-9}–10^{-5} M) to the bath after the tissue had been contracted with the KCl solution. The concentration that had the maximal relaxation effect was the one used in the subsequent trials of propofol and midazolam. After contraction with KCl solution and then relaxation with low-dose dopamine, tissue preparations were exposed to either cumulative log concentrations (10^{-9}–10^{-5} M) of propofol ($n=8$) or midazolam ($n=10$). The force on the transducer was then recorded, and these measurements were translated into percentages of the initial contraction force.

Results Dopamine-induced relaxation (3×10^{-7} M) of the renal artery preparation was increased to a similar extent with the addition of midazolam at all concentrations (10^{-9}–10^{-5} M). Propofol caused a concentration-dependent increase in relaxation ($P<0.05$). Midazolam concentrations greater than 10^{-9} M (10^{-8}–10^{-5} M) resulted in a significant increase in relaxation of the artery tissues ($P<0.05$). The amount of relaxation in the propofol and midazolam groups was not significantly different ($P>0.05$).

Conclusions In this rabbit renal artery dilatation model using dopamine, the addition of either propofol or midazolam results in a statistically significant increase in the vasodilatatory effect of dopamine.

References

1. Hall RI, Sandham D, Cardinal P, *et al.*: **Propofol vs midazolam for ICU sedation.** *Chest* 2001, **119**:1151-1159.
2. Nakamura K, Hatano Y, Hirakata H, *et al.*: **Direct vasoconstrictor and vasodilator effects of propofol in isolated dog arteries.** *Br J Anaesth* 1992, **68**:193-197.

P99 Effects of protracted administration of FNT on immune function of surgical cancer patients

M Bitzani, G Vassiliadou, O Hatzizisi, Ch Iasonidou, G Kyriazis, D Riggos
ICU, Immunology Laboratory, 'G. Papanikolaou' Hospital, Thessaloniki, Greece
Critical Care 2003, **7(Suppl 2)**:P099 (DOI 10.1186/cc1988)

The opioid agonist fentanyl is widespread used for acute pain management and sedation in the ICU. The aim of this study was to investigate the effects of fentanyl on both innative and adapted immune function in surgical cancer patients recovered in the ICU.

Materials and methods This study was prospectively performed in 10 cancer patients (mean age 66 ± 5, APACHE II 9 ± 3) who underwent elective surgery and who recovered in the ICU for 2 days. Fentanyl was administered for analgesia during surgery and postoperatively as the only analgesic and sedative for a total of 12 hours. The dose of FNT was regulated according to the demands of the patients in order to obtain optimal analgesia and sedation. Respiratory burst activity and phagocytosis of both polymorphonuclear cells (PMNC) and monocytes (MNC), as well as NKc percentage and phenotypes of peripheral blood lymphocytes were determined from blood samples drawn before induction of anesthesia and at 24 and 48 hours after surgery. Sample testing was performed utilizing the flow cytometric technique. Statistical analysis was computed with the paired *t* test. $P<0.05$ was considered significant.

Results The cumulative dose of fentanyl was 2.58 ± 1.03 mg. MNCs presented a statistically significant ($P<0.05$) increase in their phagocytic function at 48 hours while their respiratory burst activity increased significantly at 24 hours and returned to baseline values at 48 hours. Phagocytic function of PMNCs was significantly ($P<0.05$) depressed at 24 hours but recovered at 48 hours while their respiratory burst activity remained unchanged. The percentage of NK cells decreased significantly ($P<0.05$) at 48 hours.

Overall, T lymphocytes as well as the subsets of T-helper and T-cytotoxic cells decreased significantly ($P<0.05$) at 24 hours but returned to baseline values at 48 hours. There was no effect on B lymphocytes.

Conclusion Protracted administration of recommended doses of fentanyl affects both innative and adapted immune function in sur-

gical cancer patients. It exerts a suppressive effect on PMNCs, NKc and T lymphocytes while it is enhancing in MNCs. This effect is generally transient, reversing 36 hours after the interruption of the administration with the exception of NKc and the phagocytic function of MNCs, the changes of which are significantly persistent The different response between MNCs and PMNCs might be attributed to different opioid receptors.

P100 Effect of high dose remifentanil or sufentanil on postoperative pulmonary function in patients undergoing coronary surgery

HK Eltzschig, TH Schroeder, G Kadner, H Guggenberger
Department of Anaesthesiology and Critical Care Medicine, University of Tuebingen, Hoppe-Seyler-Straße 3, 72070 Tuebingen, Germany
Critical Care 2003, **7(Suppl 2)**:P100 (DOI 10.1186/cc1989)

Introduction Intraoperative use of high dose opioid anesthesia is common practice for hemodynamic control in patients undergoing coronary artery bypass grafting (CABG). It is unclear whether postoperative pulmonary function is affected by this practice. Remifentanil is an ultra-short acting μ-agonistic opioid [1]. We hypothesized that remifentanil is associated with improved pulmonary function, compared with longer acting opioids. Therefore, we performed a controlled randomized trial to evaluate pulmonary function in patients undergoing CABG with high dose remifentanil versus sufentanil.

Methods Fifty patients undergoing CABG were randomized to receive intraoperative remifentanil or sufentanil via continuous infusion. Demographic data, surgery, and anaesthesia times, ICU and hospital LOS, Parsonett, and Tumanscore were recorded. Pulmonary function was evaluated by measuring functional residual capacity (FRC), CO_2-rebreathing method, spirometry, and chest radiography before surgery, and up to the third postoperative day.

Results Demographic data, risk scores, weaning time, and surgery characteristics did not differ between groups. Lung volumes decreased to 21% vs 26% compared with preoperative values, and reached 48% vs 76% on the third postoperative day. Postoperative CO_2 sensivity was significantly decreased in both groups. Partial lung collapse on postoperative chest X-ray was present in half of the patients. No differences between groups could be detected for any measurement.

Conclusion Pulmonary function is impaired after CABG. Despite its short half-life, intraoperative use of high dose remifentanil was not associated with an improvement of pulmonary function, compared with sufentanil.

Reference

1. Babenco HD, Conard PF, Gross JB: **The pharmacodynamic effect of remifentanil bolus on ventilatory control.** *Anesthesiology* 2000, **92**:393-398.

P101 Combination of mild hypothermia and delayed fluid resuscitation improved the survival rate after uncontrolled hemorrhagic shock in rat

X Yang, S Hachimi-Idrissi, R Lauwers, M Zizi, L Huyghens
Laarbeeklaan 101, Department of Critical Care Medicine and Cerebral Resuscitation Group, 1090 Brussels, Belgium
Critical Care 2003, **7(Suppl 2)**:P101 (DOI 10.1186/cc1990)

Objective To evaluate the effect of mild hypothermia combined with delayed fluid resuscitation on the survival rate in mechanically ventilated rats.

Methods An initial blood withdrawal of 3 ml/100 g over 15 min of time followed by 75% tail amputation of its length and observed during an additional 45 min to induce phase I. Homeostasis of the tail wound and maintaining the mean arterial pressure (MAP) of 100 mmHg during resuscitation phase II from 60 to 120 min. Phase III is an observational phase up to 72 hours. Forty-eight male rats were anaesthetised, mechanically ventilated and were randomised into four groups (12 in each group). Group 1 received immediate fluid resuscitation and normothermia; group 2 received immediate fluid resuscitation and mild hypothermia. Both these groups were allowed to normalize the MAP by giving Ringer's solution. Group 3 received limited Ringer's solutions to maintain a MAP of 40 mmHg and normothermia. In group 4, the rats also received limited Ringer's solution to maintain a MAP of 40 mmHg but were subjected to mild hypothermia. During phase II, all rats were allowed to normalize the MAP by giving shed blood. At the end of the observational phase III, the rats were killed, and the brain was fixed and histologically analysed.

Results The blood loss from the tail during phase I was significantly higher in groups where immediate fluid resuscitation was performed (groups 1 and 2). Group 4 required the lowest fluid resuscitation. The survival rate was 33.3%, 83.3%, 58.3% and 91.7%, respectively, in group 1, group 2, group 3 and group 4. In all surviving rats no brain histological damage was observed.

Conclusions Mild hypothermia or limited (hypotensive) fluid resuscitation increases the survival rate. However, when mild hypothermia and limited fluid resuscitation were combined during phase I, the survival rate was the highest.

P102 The effect of resuscitative mild hypothermia and oxygen concentration on the survival time during lethal uncontrolled hemorrhagic shock in mechanically ventilated rats

X Yang, S Hachimi-Idrissi, M Zizi, L Huyghens
Laarbeeklaan 101, Department of Critical Care Medicine and Cerebral Resuscitation Group, 1090 Brussels, Belgium
Critical Care 2003, **7(Suppl 2)**:P102 (DOI 10.1186/cc1991)

Objective To test the hypothesis that resuscitative mild hypothermia (MH) (34°C) or breathing FiO_2 of 1.0 would prolong survival time during lethal uncontrolled hemorrhagic shock (UHS) in mechanically ventilated rats.

Methods Forty Wistar rats were anaesthetised with halothane, N_2O and O_2 (70/30%), intubated and mechanically ventilated. UHS was induced by volume-controlled blood withdraw of 3 ml/100 g over 15 min, followed by 75% tail amputation of its length. The animals were randomised into four UHS treatment groups (10 rats in each group): group 1 was maintained on FiO_2 of 0.21 and rectal temperature of 37.5°C. Group 2 was maintained on FiO_2 of 0.21 and induced MH. Group 3 was maintained on FiO_2 of 1.0 and 37.5°C. Group 4 was maintained on FiO_2 of 1.0 and MH. Rats were observed otherwise untreated until death (pulseless and mean arterial blood pressure [MAP] less than 10 mmHg, and without fluctuation).

Results During the initial blood withdraw, MAP decreased to an average of 40 mmHg, and the heart rate (HR) increased to an average of 400 beats/min. Induction of MH increased the MAP to 60 mmHg, and the survival time moreover, it reduced the HR to 300 beats/min but did not increase bleeding. Ventilation with FiO_2 of 1.0 did not influence the MAP, the blood loss or the survival time, but increased the PaO_2. The mean survival time was 62 min, 202 min, 68 min and 209 min in group 1, group 2, group 3 and group 4, respectively. Blood loss from the tail was 1.0 ml, 1.2 ml, 0.9 ml and 0.7 ml, respectively, in group 1, group 2, group 3 and group 4 (not significant).

Conclusion MH prolonged the survival time during UHS in mechanically ventilated rats. However, a FiO_2 of 1.0 did not influence the survival time or the blood loss from the tail.

P103 Usefulness of transarterial embolization in patients with blunt splenic injury showing transient response

A Hagiwara, H Fukushima, A Murata, H Matsuda, S Shimazaki
Department of Traumatology and Critical Care Medicine, Kyorin University School of Medicine, Japan
Critical Care 2003, **7(Suppl 2)**:P103 (DOI 10.1186/cc1992)

Purpose The usefulness of transarterial embolization (TAE) in patients with blunt splenic injury has been recently reported. However, TAE can be performed only in patients who are hemodynamically stable on admission or who rapidly respond to fluid resuscitation (rapid response) according to the Advanced Trauma Life Support. The present study was performed in order to clarify whether nonsurgical management using TAE could be performed even in patients who transiently respond to fluid resuscitation (transient response).

Methods Contrast CT was performed in the patients with blunt abdominal injuries except those who did not respond to fluid resuscitation. Angiography was performed in patients who had contrast extravasation and/or had splenic injury of AAST grade ≥3 on CT. TAE was performed when angiography showed disruption of the terminal arteries or arterial extravasation. When the patients had complicated injuries, TAE of these complicated lesions was simultaneously performed.

Results Of 104 patients with splenic injury who were admitted to our hospital between January 1999 and August 2002, 73 received contrast CT. Forty of these 73 patients were in shock status on admission (SBP ≤90 mmHg, shock index ≥1). Twenty-two of the 40 patients showed rapid response. Among them, 16 received TAE and nonsurgical managements were successfully performed in all these patients. The remaining 18 patients showed transient response. The one patient went into no response after CT and received emergent laparotomy. Therefore, 17 patients were subjects of the present study. The subjects were 11 males and six females at the mean age of 37.1 ± 19.7 years with a mean ISS score of 34.6 ± 19.7. Two patients had AAST Grade III, 13 Grade IV, and two Grade V. TAE for splenic injury was performed for all the 17 patients. Seven patients had complicated injuries that required TAE (one had renal injury of AIS 4 and pelvic fracture of AIS 4; one hepatic injury of AIS 4 and pelvic fracture of AIS 4; two pelvic fracture of AIS 4; two hepatic injury of AIS 4; and one facial injury of AIS 4 and hepatic injury of AIS 4). TAE of spleen and complicated lesions was successfully performed on all the patients. Systolic blood pressure before and after TAE was 79.3 ± 16.9 and 128.3 ± 20.5 mmHg, respectively ($P < 0.001$). Shock index before and after TAE was 1.6 ± 0.6 and 0.8 ± 0.2, respectively ($P < 0.001$). Fluid resuscitation required after TAE (196.2 ± 194.7 ml/hour) significantly decreased compared with that required before TAE (1169.5 ± 287.4 ml/hour) ($P < 0.01$). Two patients died of cerebral hernia after head injuries.

Conclusion TAE for blunt spleen injury could be successfully performed in patients showing transient response. TAE could be the first-choice treatment for splenic injury in patients other than those showing no response.

P104 Recombinant activated coagulation factor VII (rFVIIa) as an adjunctive hemostatic therapy in patients with multiple system organ failure and acute upper gastrointestinal bleeding

S Milanov, M Milanov, E Gyurov, Z Shterev
Emergency institute 'Pirogov', General ICU, Totleben 21, Sofia, Bulgaria
Critical Care 2003, **7(Suppl 2)**:P104 (DOI 10.1186/cc1993)

Major upper gastrointestinal bleeding leads to increased length of stay and increased risk of death among critically ill patients [1]. Despite recent developments in prophylaxis, large randomized trials have not shown a decrease in mortality. Patients with multiple system organ failure (MSOF) accompanied by coagulopathy are among those with high risk for clinically important major gastrointestinal bleeding. The combination of increased risk of gastrointestinal lesions and coagulopathy makes this population of critically ill extremely vulnerable once the bleeding begins. Recombinant activated factor VII (NovoSeven®; Novo Nordisk, Denmark) has recently been used to reduce bleeding complications and to control bleeding in hemophilic patients [2], and also in cases of intractable postsurgical intra-abdominal hemorrhage and traumatic bleeding. Fifteen surgical and nonsurgical patients with clinically significant gastrointestinal bleeding and MSOF (Simplified Acute Physiology Score II between 53 and 69 points) were enrolled in this study. All patients had different types and degrees of coagulation abnormalities before the bleeding episode as a part of their MSOF. After the onset of bleeding all patients required fluid resuscitation, red blood cell transfusion, fresh frozen plasma and platelet concentrates, and in 73% we used inotropes and pressors to support the failing circulation. The initial bleeding rate among

patients was between 14 and 22 ml/min. After the bleeding was considered clinically significant we used a single standard intravenous dose of rFVIIa along with other standard accepted therapeutic measures, including endoscopy. Bleeding decreased after this first dose of rFVIIa and ceased within a period of 18–110 min, with progressive return of coagulation parameters to near pre-bleeding values. Four patients required a second dose of rFVIIa. There were no thromboembolic adverse effects and recurrent episodes of bleeding within the first 5 days after the bleeding episode. We concluded the successful use of rFVIIa in patients with MSOF and acute upper gastrointestinal bleeding, when this hemostatic agent could compensate for MSOF-related coagulation abnormalities. Further large studies are needed to assess the efficacy of rFVIIa use and its relationship with possible decreased transfusion requirements in such patients.

References

1. Cook, *et al.*: **The attributable mortality and length of intensive care unit stay of clinically important gastrointestinal bleeding in critically ill patients.** *Crit Care* 2001, **5**:368-375.
2. Hedner U: **Recombinant activated factor VII as a universal haemostatic agent.** *Blood Coagul Fibrinolysis* 1998, **9(suppl 1)**: S147-S152.

P105 Efficacy of recombinant activated factor VII (rFVIIa; NovoSeven®) in obstetrical haemorrhagic shock

S Sobieszczyk[1], GH Bręborowicz[2], B Kubiaczyk[2], T Opala[3]
[1]Laboratory of Cardiovascular and Haemostasis Disorders, Department of Mother and Child Health, [2]Department of Perinatology and Gynaecology, and [3]Department of Mother and Child Health, University of Medical Sciences, Poznań, Poland
Critical Care 2003, **7(Suppl 2)**:P105 (DOI 10.1186/cc1994)

Background Recombinant factor VII (rFVIIa) (NovoSeven®; Novo Nordisk, Denmark) is mainly indicated for treatment of the patients with haemophilia and inhibitors in the control of perioperative and spontaneous bleeding. However, no information is available on the use of rFVIIa in the treatment of severe and recurrent bleeding and its complications in the obstetrical patients. Treatment difficulties of hemorrhagic shock arise from coagulopathy coexistence. Therefore, the use of rFVIIa in patients suffering from uncontrolled haemorrhage appears to be rational.

Methods We report 15 cases of obstetrical hypovolaemic shock (after massive bleeding) in ATLS classification between II and IV category (class) with coagulopathy coexistence. After the failure of conventional methods of therapy, they were treated with small doses of rFVIIa (median, 18 µg/kg; range, 16.7–48 µg/kg) to achieve haemostasis.

Results The rapid response after administration of rFVIIa resulted in cessation of the diffuse bleeding (in 78.6% bleeding was completely stopped, in the remaining 21.4% it weakened relevantly) with significant limitation of supplemented blood products; red cell concentrate from 2100 ml to 1236 ml ($P<0.05$); fresh frozen plasma from 1000 ml to 490 ml ($P<0.05$) and good coagulologic control; shortening of prothrombin time and activated partial thromboplastin time from 16.5 s (range, 9.3–25.2 s) to 11.1 s (range, 9.1–20.2 s) ($P<0.001$) and 52.5 s (range, 26.1–80.2 s) to 32.75 s (range, 25.9–75.8 s) ($P<0.001$), respectively. In four cases of uterine atony, the hysterectomy was not necessary after rFVIIa applications. No side effects related to use of rFVIIa were noted.

Conclusion The results of our study suggest that, in obstetrical hypovolaemic shock after massive bleeding and coagulopathy, rFVIIa may play a role as an adjunctive haemostatic agent in these cases where the surgical haemostasis was adequate.

P106 Life-threatening hemorrhage in neonates and children: treatment with activated recombinant factor VII

D Fischer, A Veldman, RL Schloesser, HJ Boehles
Vlijmener straße 6, 65510 Idstein, Germany
Critical Care 2003, **7(Suppl 2)**:P106 (DOI 10.1186/cc1995)

According to the small circulating blood volume, acute hemorrhage in children, especially in preterms and newborns, leads rapidly into a life-threatening event. The successful use of activated recombinant factor VII (rFVIIa) in life-threatening hemorrhage has been reported in adult critical care patients. Except for one case report, the application of rFVIIa in children has not yet been described.

We report on our experience with five preterms and neonates and two children (mean age 4 weeks, range 2 days–7 years) with acute hemorrhage, who were treated with rFVIIa (Novo Seven®; Novo Nordisk, Denmark). Prior to the acute blood loss they had no hereditary coagulation disorder nor disseminated intravascular coagulopathy. One preterm showed bleeding from an intecostal artery, whereas the manifestation in the other cases was of pulmonal (diffuse pulmonary bleeding) or abdominal origin (isolated liver bleeding, traumatic mucosal bleeding of the distal esophagus, gastrointestinal bleeding according to viscerocutaneous hemangiomatosis). All patients received rFVIIa after other attempts (treatment with fresh frozen plasma, platelet concentrate and packed red cells; surgical interventions) failed and hemorrhagic shock persisted. Except in one 7-year-old girl, within 15 min after the application or rFVIIa bleeding stopped and all patients recovered. No acute adverse event nor thromboembolic complications over a long observation period could be observed.

Conclusion Application of rFVIIa in hemostasiologic healthy newborns or children with acute hemorrhage seems to be a promising therapeutical approach after other pharmacological or surgical attempts have failed.

P107 Hydroxyethyl starch HES 130/0.4 in paediatric surgery: results of an explorative, controlled, multicentre safety study

H Lochbühler[1], Ch Galli[2], H Hagemann[2]
[1]Paediatric Surgical Intensive Care Unit, Dr v Haunersches Kinderspital, Ludwig-Maximilians University, Munich, Germany; [2]Department of Anaesthesia, University Hospital Hannover, Carl-Neuberg-Straße 1, D-30625 Hannover, Germany
Critical Care 2003, **7(Suppl 2)**:P107 (DOI 10.1186/cc1996)

Background Human albumin (HA) has been the gold standard for plasma volume replacement in paediatric anaesthesia in the past while clinical experiences with artificial colloids such as hydroxyethyl starch (HES) are limited.

Patients and methods After local EC approval and parents' signed consent, 2 × 41 patients (aged < 24 months) scheduled for major abdominal, cranial, thoracic, or urologic surgery were randomised to receive either 6% HES 130/0.4 (Voluven®) or 5% HA for intra-operative volume replacement. Study parameters were haemodynamics, coagulation, laboratory parameters, and adverse events from induction of anaesthesia until day 3 postoperative. The treatment groups were compared descriptively by ANOVA or ANCOVA. Subgroup analyses were performed for age and dose of colloid. Predefined covariates were surgical procedure and duration, body weight, baseline value, and centre.

Results Treatment groups were well balanced with respect to demographics, age groups, and surgical procedures. The mean dose of colloid infused (HES vs HA) until 6 hours postoperative was 16 ml/kg versus 17 ml/kg. No major differences were observed for infused crystalloids (67 ml/kg [HES] versus 65 ml/kg [HA]), changes of haemodynamics (blood pressure, heart rate) and also of laboratory parameters. In both groups, platelets and Quick decreased and aPTT increased postoperative; however, they were not clinically relevant. Adverse events were reported in 80% (HES) and 78% (HA) of patients, respectively. None of the adverse events were considered as probably drug related to HES or HA.

Conclusion For the first time the novel HES 130/0.4 was clinically evaluated in newborns and infants. We conclude that HES 130/0.4 was well tolerated and as safe as human albumin in paediatric surgery.

P108 The effect of different chloride concentrations in intravenous fluids on patient outcomes

ME Hartman, G Clermont, RS Watson, JA Kellum, DC Angus
The CRISMA Laboratory, Department of Critical Care Medicine, University of Pittsburgh, Pittsburgh, PA, USA
Critical Care 2003, **7(Suppl 2)**:P108 (DOI 10.1186/cc1997)

Objective A controversial, but poorly studied aspect of fluid resuscitation is whether the chloride (Cl) concentration of the fluid is important. We performed a systematic review of the literature to determine the effect of different Cl concentrations in intravenous (IV) fluids on the outcome of critically ill patients.

Data sources Studies were identified by MEDLINE search combining the medical subject heading 'Fluid Therapy' with the index terms: saline, lactate, Ringer's, and Hartmann's. Bibliographies were hand-searched for additional references.

Study selection We selected studies based on the following inclusion criteria: randomized, controlled trials comparing IV fluids of different Cl concentration in patients requiring volume resuscitation. We classified the fluids as 'standard Cl' (154 mEq/l) or 'low Cl' (< 154 mEq/l). Studies comparing: fluids of different tonicities; crystalloids with colloids; or IV with oral therapy were excluded.

Data extraction We extracted quantitative information regarding the type of crystalloid used, mortality, hemodynamic changes, acid–base balance, coagulation, and any other studied endpoint.

Results Of 451 articles identified, seven met inclusion criteria (489 patients, 24–230 patients/study). Five compared normal saline (NS) (Na 154 mEq/l, Cl 154 mEq/l) with lactated Ringer's (Na 131 mEq/l, Cl 111 mEq/l), one compared NS with Plasmalyte 148 (Na 140 mEq/l, Cl 98 mEq/l), and one compared Hespan (Na 154 mEq/l, Cl 154 mEq/l) with Hextend (Na 143 mEq/l, Cl 124 mEq/l). In the four studies that reported mortality, only three deaths occurred. Two studies evaluated hemodynamics (changes in pulse pressure, pulse rate, duration of shock) and found no difference between crystalloids. All five studies that evaluated metabolic changes found statistically significant increases in serum Cl, decreases in pH, and larger base deficits with standard Cl versus low Cl solutions.

Conclusions Limited data from randomized clinical trials consistently suggest that resuscitation with standard concentrations of chloride results in metabolic acidosis, but there is insufficient evidence to draw conclusions about the effect on mortality.

P109 Blood substitutes consumption and coagulation changes: 200/0.5 vs 130/0.4 hydroxyethyl starch administration

MG Costa, L Pompei, C Coccia, G Della Rocca
Clinica di Anestesia, University of Udine, P le SM della Misericordia 15, 33100 Udine, Italy
Critical Care 2003, **7(Suppl 2)**:P109 (DOI 10.1186/cc1998)

Introduction The aim of the study was to evaluate blood substitutes consumption and coagulation profile differences in patients undergoing liver transplantation (LT) receiving volume replacement with 6% hydroxyethyl starch (HES 200/0.5) or with a low-molecular weight (LMW) HES (130/0.4) [1].

Methods Thirty-five consecutive patients scheduled for LT were prospectively randomized to receive either 6% HES (group HES; $n = 20$) or LMW (group LMW; $n = 15$) for additional volume replacement. Normal saline at 10 ml/kg per hour was continuously infused in all patients. Conventional global coagulation tests,

Table 1

Fluid	Group HES ($n = 20$)	Group LMW ($n = 15$)
Cystalloids (ml/kg per hour)	6804 (2000), 3700–12350	8114 (2696), 3720–12015
HES 6% (ml)	897 (443), 500–2000	
LMW Voluven (ml)		750 (250), 500–1000
FFP (U)	9.3 (3.2), 3–15	7.6 (2.1), 3–10
RBC (U)	3.4 (2.9), 1–12	3.8 (2.9), 1–7
HA (U) [1 U = 50 ml]	6.5 (3.1), 0–12	5.7 (3.2), 0–12
PLT (U)	–	–
Intraop cell saver (ml)	500(179), 130–890	777 (303), 500–1200
Urine output (ml/kg per hour)	6.1 (2.9), 2.0–9.5	5.0 (2.7), 1.6–8.6

Data presented as mean (SD), range.

hemoglobin, hematocrit and platelet values were monitored at the start of surgery (T0), during the anhepatic phase (T1), and at the end of surgery (T2). All data yielded were compared and analyzed with the paired Student *t* test: $P<0.05$ was considered significant (SPSS, PC plus).

Results No differences in coagulation profile was observed between groups. Fluid and blood substitutes consumption are reported in Table 1.

Conclusion We observed the same coagulation profile and minor blood components consumption using either HES or LMW, and they can be both safely used in liver transplant patients.

Reference

1. Bennett-Guerrero E, *et al.*: *Arch Surg* 2001, **136**:1177-1183.

P110 The prevalence of deep venous thrombosis in Chinese medical ICU patients

GM Joynt, J Kew, CD Gomersall, FHY Yap, D Lam
Department of Anaesthesia and Intensive Care, The Chinese University of Hong Kong, Sha Tin, Hong Kong, People's Republic of China
Critical Care 2003, **7(Suppl 2)**:P110 (DOI 10.1186/cc1999)

Introduction and aim The incidence of deep venous thrombosis (DVT) in critically ill medical patients is approximately 30% [1,2]. The proportion of proximal lower limb thrombi (above the knee) is reported to be approximately 50% [1]. However, several studies in Chinese patients have shown a markedly lower rate of DVT than reported in Caucasian populations [3]. The aim of this study was to determine the frequency of DVT in Chinese medical ICU patients not receiving prophylaxis.

Methods We studied a prospective cohort of adult Chinese medical patients admitted to the ICU and expected to stay longer than 48 hours. Existing policy was to not routinely prescribe DVT prophylaxis in Chinese patients. Patients with previously diagnosed DVT, or already receiving anticoagulant therapy, were excluded. Screening for lower limb DVT was performed twice weekly in the ICU and repeated 1 week after discharge. DVT was detected by compression and duplex Doppler ultrasound.

Results Seventy-eight patients were entered. One patient died within 48 hours and was excluded. Fourteen patients (18%) died in the ICU after 48 hours and at least one ultrasound examination. Of the 77 patients evaluated, 14 (18%) demonstrated DVT. On five of 14 occasions (36%), thrombus was present in both limbs. Proximal (above knee) DVT was present in three of 14 patients (20%).

Discussion and conclusion The prevalence of DVT in Chinese medical ICU patients is lower, by approximately 50%, than that reported for Caucasian medical ICU patients. The proportion of proximal lower limb thrombi is also lower. We believe the prevalence is sufficient, however, to justify the use of DVT prophylaxis. The data support the need further studies to quantify the possible benefit of DVT prophylaxis in this group.

References

1. Hirsch DR, *et al.*: **Prevalence of deep venous thrombosis among patients in medical intensive care.** *JAMA* 1995, **274**:335-337.
2. Attia J, *et al.*: **Deep vein thrombosis and its prevention in critically ill adults.** *Arch Intern Med* 2001, **161**:1268-1279.
3. Liu HSY, *et al.*: **Venous thromboembolism in the Chinese population — experience in a regional hospital in Hong Kong.** *Hong Kong Med J* 2002, **8**:400-405.

P111 Deep venous thrombosis in medical–surgical ICU patients: prevalence, incidence and risk factors

D Cook, M Crowther, M Meade, C Rabbat, D Schiff, W Geerts, L Griffith, G Guyatt
McMaster University, Hamilton, Canada & University of Toronto, Toronto, Canada
Critical Care 2003, **7(Suppl 2)**:P111 (DOI 10.1186/cc2000)

Objective To estimate the prevalence, the incidence, and the baseline and time-dependent risk factors for lower limb deep vein thrombosis (DVT).

Design Longitudinal cohort study conducted from January 2001 to January 2002.

Setting Fifteen-bed medical–surgical closed multidisciplinary ICU in Hamilton, Canada.

Methods We enrolled consecutive consenting patients age ≥18 years if they were expected to be in ICU for ≥72 hours. Patients were excluded if they had an admitting diagnosis of trauma, orthopedic surgery, cardiac surgery, pregnancy, or if they were undergoing withdrawal of life support. All patients underwent lower limb compression ultrasonography on admission, twice weekly, and with any clinical suspicion of VTE. Investigations for upper limb DVT were performed only if signs or symptoms of DVT were present. We recorded risk factors for DVT on ICU admission and daily thereafter. All patients received VTE prophylaxis. We present prevalence and incidence data as proportions and 95% confidence intervals (CIs). To identify baseline and time-dependent independent risk factors for lower limb DVT, we used backwards stepwise elimination Cox regression analysis.

Results Of 261 patients, we identified lower limb DVT in seven (2.7%, 95% CI=1.1–5.5) patients on admission to the ICU, in 25 (9.6%, 6.3–13.8) patients over the course of the ICU stay, and in four (1.5%, 0.4–3.9) following ICU discharge. Upper limb DVTs were found in three patients (1.1%, 0.2–3.3) all related to central venous catheterization. We found two independent baseline risk factors for DVT: personal or family history of DVT (hazard ratio [HR] 3.95 [1.53–10.15]), and dialysis dependent renal failure (HR 3.71, 1.24–11.08). The two time-dependent risk factors were vasopressor use (HR 2.70, 1.03–7.07) and platelet administration (HR 3.08, 1.15–8.20).

Conclusions In medical–surgical critically ill patients, the prevalence of lower limb DVT at ICU admission was 3%, and the incidence of ICU-acquired DVT was 11%. Patients with an increased risk of ICU-acquired DVT are those with a personal or family history of DVT, pre-ICU dialysis dependence, vasopressor use and platelet administration.

P112 Relationship between peak anti-Xa levels and calculated creatinine clearance in ICU patients receiving low molecular weight heparin

E McDonald, F Landry, C Rabbat, C Boudreau, M Crowther, M Meade, W Geerts, D Cook
McMaster University, Hamilton & University of Toronto, Toronto, Canada
Critical Care 2003, **7(Suppl 2)**:P112 (DOI 10.1186/cc2001)

Objective To evaluate serial anti-Xa 'peak' levels drawn 2 or 4 hours post LMWH prophylaxis in 13 consecutive ICU patients with a range of renal function.

Setting Multidisciplinary, closed, university-affiliated 15-bed medical–surgical ICU.

Method We measured anti-Xa blood levels either 2 or 4 hours post dalteparin administration each day until death or discharge. We calculated creatinine clearance daily using the Cockroft–Gault formula. We graphed these peak anti-Xa levels against calculated creatinine clearance values, and examined their relation to bleeding events.

Results We performed 287 anti-Xa levels on these ICU patients, and found that peak anti-Xa levels were consistently less than 0.5 U/ml. We did not demonstrate a relationship between the timing of the peak anti-Xa levels, and a) the value of the peak anti-Xa levels, b) the patients' calculated creatinine clearance, or c) bleeding events.

Conclusions Anti-Xa levels drawn 2 or 4 hours post subcutaneous injection of 5000 U dalteparin in this sample of patients were consistently less than 0.5 U/ml, but did not vary significantly with renal function.

P113 Dalteparin reduces ischemia/reperfusion-induced liver injury in rats by increasing the hepatic tissue level of prostacyclin

M Uchiba, N Harada, K Okajima
Department of Laboratory Medicine, Kumamoto University School of Medicine, Kumamoto 860-0811, Japan
Critical Care 2003, **7(Suppl 2)**:P113 (DOI 10.1186/cc2002)

Dalteparin, a low molecular weight heparin, is an anticoagulant that shows less frequency of bleeding than regular heparin. Ischemia/reperfusion (I/R)-induced organ injury is a pathologic condition associated with shock or hepatic transplantation. Since intravascular coagulation is frequently associated with these pathologic conditions, dalteparin is used to treat such disease states. However, whether dalteparin reduces the I/R-induced organ injury is not known. We examined this possibility using a rat model of I/R-induced liver injury. Male Wistar rats were subjected to 60-min ischemia and the subsequent reperfusion. Pretreatment with dalteparin (300 anti-FXa IU/kg) reduced I/R-induced liver injury. The I/R-induced decrease in the hepatic tissue blood flow was inhibited by dalteparin. Hepatic tissue levels of tumor necrosis factor (TNF)-α and neutrophil accumulation were increased after I/R. Dalteparin significantly attenuated these increases. Neither regular heparin nor DX-9065a, a selective inhibitor of FXa, showed any protective effects. Dalteparin inhibited neither monocytic TNF-α production nor neutrophil activation *in vitro*. Dalteparin increased the hepatic levels of prostacyclin, which reduces the liver injury by inhibiting neutrophil activation. Pretreatment of animals with indomethacin completely abrogated the protective effects of dalteparin. However, dalteparin did not increase the endothelial production of prostacyclin *in vitro*. The dalteparin-induced increases in hepatic tissue levels of prostacyclin were not observed when animals were pretreated with capsazepine, an inhibitor of vanilloid receptor-1 of the capsaicin-sensitive sensory neurons (CSSN) that increase the tissue level of prostacyclin upon being stimulated. Hepatic tissue levels of calcitonin gene-related peptide (CGRP), which is released from CSSN, were significantly increased by dalteparin. The protective effects induced by dalteparin were not observed in animals pretreated with CGRP 8-37, an antagonist of CGRP, as well as capsazepine. Administration of CGRP produced effects similar to those of dalteparin. These results strongly suggest that dalteparin might reduce the I/R-induced liver injury by increasing the hepatic tissue level of prostacyclin through the stimulation of CSSN. The dalteparin-induced effects could not be explained by its anticoagulant effects.

P114 Arterial to end-tidal CO_2 ($PaCO_2$–$EtCO_2$) gradient as a monitoring parameter of efficacy during thrombolytic therapy for massive pulmonary embolism (PE) in spontaneously breathing patients

D Clause[1], G Liistro[1], F Thys[1], J Col[2], MS Reynaert[3], F Verschuren[3]
[1]Pneumology Intensive Care Unit, [2]Coronary Intensive Care Unit and [3]Emergency Intensive Care Unit, Cliniques universitaires Saint-Luc, Belgium
Critical Care 2003, **7(Suppl 2)**:P114 (DOI 10.1186/cc2003)

Introduction Alveolar dead space is increased in PE and can be evaluated by measuring the $PaCO_2$–$EtCO_2$ gradient during time-based capnography. The evolution of this gradient during thrombolysis in six spontaneously breathing patients with massive PE follows.

Methods Six patients with massive PE were assigned to thrombolysis. Diagnosis was comfirmed by V/Q lung scanning and/or CT angiography. The 'massive' feature was attributed to the presence of acute right ventricular pressure overload or pulmonary hypertension signs on the twodimensional and Doppler transthoracic echocardiography: pulmonary hypertension with a trans-tricuspid gradient (RA/RV gradient) >30 mmHg, paradoxic septal wall motion, right to left ventricle size ratio >0.6 and loss of inspiratory collapse of the inferior vena cava. The $PaCO_2$–$EtCO_2$ gradient was monitored during and several hours after the treatment. Echocardiography was repeated about 12–24 hours after thrombolysis to assess the treatment's efficacy.

Results Two patients showed a large decrease in the $PaCO_2$–$EtCO_2$ gradient (mean gradient from 17 mmHg before treatment to 7 and 1.5 mmHg, respectively, at 2–4 hours and at 12–24 hours) and a nearly complete disappearance of right cardiac signs with, in particular, a normalization of RA/RV gradient for one patient and a 62% reduction for the other one. Three patients had no significant change in the $PaCO_2$–$EtCO_2$ gradient (from 11.5 mmHg to 12 mmHg at 2–4 hours and 12–24 hours) and showed partial improvement of echocardiographic findings (mean RA/RV gradient from 61 to 44 mmHg). One patient had a stable $PaCO_2$–$EtCO_2$ gradient in contrast with echocardiographic improvement (RA/RV gradient from 56 to 28 mmHg) but the echocardiographic control was performed 10 days after thrombolysis.

Conclusions To our knowledge, this small series is the first to investigate the interest of capnography as monitoring for thrombolysis in spontaneously breathing patients with massive pulmonary embolism. The decrease of $PaCO_2$–$EtCO_2$ gradient suggests the efficacy of thrombolysis, and an elevated persistent $PaCO_2$–$EtCO_2$ gradient may question the efficacy of the treatment. Capnography could be a promising noninvasive and bedside application in the monitoring of thrombolysis for massive pulmonary embolism.

P115 Usefulness of double luminal drain with continuous high-pressure aspiration for draining mucinous discharge in abdominal sepsis: prevention of worsening of local inflammation until definitive surgery

M Yoshihiro, M Sugiyama, K Uchida, H Toyoda, H Tomita, K Yoshida, S Yamagishi, K Kanaya, T Kosuge, T Yamamoto, N Suzuki
Critical Care and Emergency Centre, Yokohama City University Medical Centre, Yokohama, Japan
Critical Care 2003, **7(Suppl 2)**:P115 (DOI 10.1186/cc2004)

Objective In intra-abdominal abscesses and leakage of intestinal contents, adequate and effective drainage is essential for prevention of MODS and abdominal sepsis. In the management of these conditions, we have preferred a double luminal drain with continuous high-pressure aspiration method (DLD-CHPA) with good outcome. The aim of this procedure is rapid and continuous removing of discharge and pus, maintaining a dry condition of the abscess and fistula, and stimulating granulation; which leads (a) to quickening the closure of the abscess and fistula, and (b) to prevention of worsening of the local condition of the localized abscess and the leaking point of injured intestine until definitive surgery. We presented the preliminary report concerning the former (a) effect of this procedure in the 21st International Symposium. The purpose of this presentation is to clarify both effects of DLD-CHPA by clinical experience.

Materials and methods DLD-CHPA was performed in 25 patients (with leakage of intestinal juice, duodenal juice, pancreatic juice, or bile, or with continuous production of pus) from April 1999 to March 2002. The volume of discharge soaking in gauze, the character of a wash recovered in intermittent lavage, the grade of local inflammation of skin surrounding the drain (DLD), the volume of aspirated material by DLD-CHPA, the volume of discharge from the wound and drain other than DLD, and the frequency of dressing changes per day were examined before and after CHPA. The fundamental structure of a DLD is same as that of aspiration device used during surgery, which consists of an outer tube with multiple pores (or basket) and an inner tube directly connected with a high-pressure central aspirating system. We use a Duple Drain or 20~26 Fr size of Nelaton Catheter as an outer tube. Some additional side pores are punched out in this outer tube according to the condition of the abscess cavity or fistula, and the velocity and character of the discharge. As an inner tube, we prefer an 8~12 Fr size of aspiration catheter, which is fixed in the position of the tip situated 5 mm behind of the tip of the outer tube by sticking-tape for easy and quick change of the inner tube. The inner tube is frequently changed as soon as it is obstructed due to adhesion of dry material of the discharge. The inner tube is aspirated with a high pressure of central vacuum system (valve of the vacuum system is fully open).

Results 1. Discharge soaking in gauze, a wash recovered in intermittent lavage, local inflammation of the skin surrounding the drain (DLD): the mean grade of all these factors improved with statistical difference after DLD-CHPA ($P<0.001$).

2. Volume of aspirated material by DLD-CHPA, volume of discharge from the wound and drain other than DLD, and the frequency of dressing change: the mean volume of discharge from the wound and drain other than DLD was depressed from 880 ± 630 g/day before DLD-CHPA to 270 ± 330 g/day after DLD-CHPA ($P<0.001$). The mean volume of aspirated discharge by DLD-CHPA for 3 days was 440 ± 480 g/day. The sum of the volume of discharge and aspirated material after DLD-CHPA is smaller than the volume of discharge before DLD-CHPA, with a statistical difference ($P=0.005$). The frequency of dressing change including daily routine procedure was significantly decreased from 7 ± 3/day to 3 ± 1/day ($P<0.001$).

3. Prevention of worsening of the local condition of the abscess and leaking point until definitive surgery: in all cases, we were able to perform definitive surgery without worsening of local inflammation, especially inflammation of skin around the drain, even with continuous leakage of intestinal juice or bile.

4. Complications due to DLD-CHPA: there was no complication with DLD-CHPA.

Conclusion DLD-CHPA is thought to be useful for managing abdominal sepsis by draining mucinous purulent fluid effectively. This procedure can prevent worsening of the local condition of a localized abscess and the leaking point of injured intestine until definitive surgery with continuous leakage of the intestinal juice.

P116 Complications of arterial lines in an intensive care unit

MG Rodrigues, DR Salgado, RAN Paiva, VM Resende, A Chindamo, JCR Verdeal
Vila Isabel, Rio de Janeiro, Brasil
Critical Care 2003, **7(Suppl 2)**:P116 (DOI 10.1186/cc2005)

Introduction Arterial cannulation is a very useful tool in the management of patients in mechanical ventilation or hemodynamic instability. However, local complications are always a concern.

Objective To describe complications of different arterial cannulation sites, correlating them with line obstruction, local and distal ischemia, infection and thrombosis.

Materials and methods A prospective, observational study of the arterial cannulations performed in a clinical and surgical intensive care unit from October 2001 to November 2002. Daily evaluations for catheter obstruction (dumping of waves, difficulty in draining blood) or local and distal ischemia (*livedo reticularis*, pale or cyanotic extremity) were carried out. Arterial Doppler scans were obtained 24 hours after catheter removal, searching for partial or total obstructive thrombosis.

Results Five hundred and sixty-five arterial cannulations were analyzed (Table 1).

Conclusion Despite the lower utilization of the axillary artery, the number of complications favored this site for monitoring over the mostly used radial artery.

Table 1

	Radial	Axillary	D. pedis	Femoral
n (%)	272	162	89	42
Obstruction	15 (5.51%)	4 (2.46%)	6 (6.74%)	1 (2.38%)
Ischemia	45 (16.54%)	0	7 (7.86%)	0
Pseudo-aneurisma		0		1
Thrombosis	74 (27.2%)	0	16 (17.97%)	0
Dumping wave	19 (6.98%)	10 (6.17%)	14 (15.73%)	2 (4.76%)
Total	153 (56.25%)	14 (8.64%)	43 (48.31%)	4 (9.52%)

Chi square = 20.26, degrees of freedom = 5, $P = 0.00111922$.

P117 Arterial catheter-related infections in the intensive care unit: prospective study during 1 year

S Abdellatif[1], H Ksouri[1], R Nasri[1], S Abdedayem[2], B Zouari[3], S Alaya[1], S Ben Lakhal[1], A Masmoudi[2], Ch Fendri[2]
[1]Intensive Care Unit and [2]Laboratory of Microbiology, Rabta Hospital, 1007 Jabbari, Tunis, Tunisia; [3]Department of Epidemiology, University of Medicine, 1007 Jabbari, Tunis, Tunisia
Critical Care 2003, **7(Suppl 2)**:P117 (DOI 10.1186/cc2006)

Introduction Peripheral arterial catheters (PAC) are usually inserted into the radial or femoral artery and permit continuous blood pressure monitoring and blood gas measurements. There are no recommendations concerning change for arterial catheters.

Aim To estimate the incidence of the arterial catheter-related infections (ACRI) and to identify the associated risk factors.

Materials and methods It is a prospective study, performed between December 2001 and November 2002. We realize a culture of the hub of stopcock. After removal, the tip of the catheter was systematically cultured using a quantitative culture technique and we realize a simultaneous bloodstream by venipuncture.

Results One hundred successive PAC are studied (77 radial and 23 femoral) in 70 patients with mean age 48 ± 18 years, sex ratio = 1.5, SAPS II = 42 ± 17, APACHE II = 20 ± 10, McCabe = 0.95 ± 0.9, OSF = 2.7 ± 1. The mean duration of cannulation was 7.3 days. Twelve are contaminated ($< 10^3$ CFU/ml), two colonized ($> 10^3$ CFU/ml). The rate of catheter-related sepsis is three of 100, and that of catheter-related bacteraemia is two of 100. Risk factors retained are: duration of catheterization (additional risk is multiplied by 4.33 in passing from 1–5 days to 6–10 days), length of stay in ICU (> 28 days), and positive culture of the hub of stopcock (sensibility = 100%, specificity = 82%, positive predictive value = 22% and negative predictive value = 100%).

Discussion Peripheral arterial catheters can be accessed several times per day for haemodynamic measurement or to obtain samples for laboratory analysis, increasing the potential for contamination and subsequent clinical infection. The following three risk factors for catheter-related infections were identified: duration of catheterization, length of stay in ICU and manipulation of the stopcock.

Conclusion The ACRI are not frequent. Their arising is bound to the duration of catheterization with an increase of the risk of colonization after 5 days. A positive culture of stopcock may indicate the removal or the change of APC.

P118 Femoral central lines and clinical sepsis

V Poulose, J Tan, A Tee
Department of Medicine, Changi General Hospital, 2, Simei Street 3, Singapore 529889, Singapore
Critical Care 2003, **7(Suppl 2)**:P118 (DOI 10.1186/cc2007)

Objective Femoral central lines are traditionally believed to have a higher risk of septic complications when compared with neck lines. Our study looked at the incidence of catheter-related blood stream infections and local sepsis from femoral central lines placed in the medical intensive care unit (MICU).

Methods A prospective observational study of central venous catheters placed in the femoral veins over a 4 month period. The patients were assessed daily for evidence of local infection (erythema, purulent discharge) or catheter-related blood stream infections (CRBSI). CRBSI was defined by a) clinical evidence of new sepsis (fever or leukocytosis) plus b) isolation of the same bacteria from the culture of the catheter tip and a peripheral blood culture.

Results Sixty catheters were placed in 53 patients with a total of 367 catheter days. The mean duration of catheter placement was 6.1 days. There was one case of CRBSI (1.66% or 2.7 per 1000 catheter days) and no incidence of local infection.

Conclusion Femoral central venous lines, when placed over an average duration of 1 week, have a low incidence of septic complications. The rate compares favourably with the data from neck catheterization.

P119 The efficacy of an antiseptic-impregnated catheter on catheter-related bloodstream infection in the ICU

S Osma[1], SF Kahveci[1], H Akalin[2], C Ozakin[2], FN Kaya[1], E Yilmaz[2], O Kutlay[1]
[1]Department of Anaesthesiology and Intensive Care, and [2]Department of Clinical Microbiology and Infectious Disease, Uludag University School of Medicine, Bursa, Turkey
Critical Care 2003, **7(Suppl 2)**:P119 (DOI 10.1186/cc2008)

Aim Despite improvement in central venous catheter (CVC) design and insertion techniques, catheter-related bloodstream infection (CRBI) continues to be a significant problem in the intensive care unit (ICU) [1]. Recently, CVCs impregnated with chlorhexidine and silver sulfadiazine (CCS) have been introduced for the prevention of CRBI [2,3]. The objective of this study is to compare between the efficacy of CCS-impregnated CVC and a standard catheter during the CRBI incidences in the ICU.

Method In this prospective study, we observed that 108 patients who needed a CVC were randomized to receive either a triple-lumen catheter impregnated with CCS (ARROWgard Blue, PA, USA; $n = 54$) or a standard triple-lumen catheter (Certofix®; B/Braun, Melsungen, Germany; $n = 54$). We observed each patient from catheter insertion to removal, and collected data on patient-related factors. Catheters were removed when no longer needed or suspected as a cause of infection. The tip and a 5 cm segment of the intradermal portion of the catheter were cultured using the semiquantitative technique developed by Maki *et al.* [4]. If sepsis was suspected, peripheral venous blood samples, blood aspirated from the distal lumen and also approximately 20 cm^2 of the skin at the insertion site were cultured. Catheter colonization (CC) was defined as the presence of ≥15 CFUs. CRBI was defined as isolation of the same organism from a catheter segment semiquantitative culture and from a peripheral blood culture.

Results Data are mean ± standard error of mean or the number of patients (Table 1).

Table 1

Group	APACHE II	Duration of catheterization (days)	CC/CRBI (*n*)
CCS CVC ($n = 54$)	18.3 ± 0.7	11.8 ± 0.8*	12/4
Standard CVC ($n = 54$)	19.3 ± 0.7	8.6 ± 0.6	13/1

* $P < 0.01$.

Conclusion These findings suggest that a CVC impregnated with CCS does not affect the incidence and magnitude of CC and CRBI in long-term catheterization but it could be beneficial for short-term catheterization in critically ill patients.

References
1. Gosbell IB: **Central venous catheter-related sepsis: epidemiology, pathogenesis, diagnosis, treatment and prevention.** *Intensive Care World* 1994, **11**:54-58.
2. Heard SO, Wagle M, Vijayakumar E, McLean S, Brueggemann A, Napolitano LM, Edwars P, O'Connell FM, Puyana JC, Doern GV: **Influence of triple-lumen central venous catheters coated with chlorhexidine and silver sulfadiazine on the incidence of catheter-related bacteremia.** *Arch Intern Med* 1998, **158**:81-87.
3. Yorganci K, Krepel C, Weigelt JA, Edmiston CE: **Activity of antibacterial impregnated central venous catheters against *Klebsiella pneumoniae*.** *Int Care Med* 2002, **28**:438-442.
4. Maki DG, Weise CE, Sarafin HW: **A semi-quantitive culture method for identifying intravenous catheter-related infection.** *N Engl J Med* 1977, **296**:1305-1309.

P120 The relationship between catheter indwelling time and catheter-related infections

F Akin, M Yilmaz, L Dosemeci, M Cengiz, A Ramazanoglu
Department of Anaesthesiology and ICU, University of Akdeniz, Faculty of Medicine, Antalya, Turkey
Critical Care 2003, **7(Suppl 2)**:P120 (DOI 10.1186/cc2009)

Introduction Catheter infection, the most frequent complication of the central venous catheter (CVC), is associated with increased morbidity, mortality and duration of hospital stay. In this study we evaluated the relationship between catheter indwelling time and catheter-related infections. Besides, we searched for the incidence of mechanical complications due to placement of the CVC, the microorganisms responsible for catheter infections and risk factors associated with the catheter infection.

Materials and methods During the study period (January–October 2002), 140 nontunneled CVCs having been replaced in 100 patients in our 25-bed ICU were collected. They were replaced when there was a suspicion of catheter-related infection or when there was no more need for a CVC. When a CVC was removed, the distal and the subsegmental part were cut off aseptically, and sent to the microbiology laboratory at our hospital where they were cultured by a semiquantitative method and two sets of blood samples were drawn for culture, with at least one set drawn percutaneously. Cultures yielding 15 or more colonies were recorded.

Results Forty-eight mechanical complications occurred in total, including arterial puncture in 30 procedures (21%), cardiac arrhythmias in 14 procedures (10%), pneumothorax in three procedures (2%) and catheter malposition in one procedure (0.7%). The incidence of catheter-related sepsis (CRS), catheter colonization, secondary bacteremia, catheter-related bacteremia (CRB) and exit site infection were 8% ($n=11$), 13% ($n=19$), 11% ($n=16$), 4% ($n=5$) and 2% ($n=2$), respectively. In 87 (62%) catheters, no clues for infection were found. The patients were respectively assigned to two groups according to the indwelling time of catheters (group I, less than 12 days; group II, more than 12 days). In groups I and II, CRS was observed in eight (73%) and in three (27%) patients, respectively. The mortality rates in the patients with CRS or bacteremia were 73% and 60%, while the mortality rate was 31% in patients without infection. *S. aureus* (18%), *Klebsiella* (18%) and *C. albicans* (18%) were found as the most frequent microorganism causing CRS. Coagulase-negative staphylococcus was the first bacteria causing colonization (63%) and bacteremia (60%).

Conclusion Although the group with indwelling time more than 12 days was associated with increased mortality and the incidence of CRS and CRB were higher in group II, these evaluations were not verified according to the statistics. Even though we have completed an extensive study on 140 catheters, we believe the study should be improved with participation of a large series.

P121 Intravascular catheter infection during 10,000 days of risk

L Lorente, C García, MM Martín, R Galván, J Málaga, ML Mora
Department of Intensive Care, Hospital Universitario de Canarias, Tenerife, Spain
Critical Care 2003, **7(Suppl 2)**:P121 (DOI 10.1186/cc2010)

Objective To analyze central venous and artery catheterization-related infections in critical care.

Methods It is a prospective study in a 20-bed medical surgical ICU. We included 500 patients, who had some catheter during 24 hours or more, admitted from 1 May 2000.

Results The study finised on 26 February 2001. Included were 500 patients (58.20%). Mean age was 56.48 ± 17.60 years, APACHE II was 13.30 ± 5.24. Mortality was 15.80%. Patient distribution was: 47.4% cardiac surgery, 8% cardiologic, 6% respiratory, 4.6% digestive, 12% neurologic, 11% traumathology, 3.4% intoxication, 7.2% sepsis and 0.4% others. The number of central venous catheters and the length of stay (days) were: global 882 and 6226, peripheral access 182 and 1186, jugular 382 and 2258, subclavian 237 and 2118, femoral 81 and 664. Central venous catheter-related infections and bloodstream infections secondary to central venous catheter per 1000 days of catheterization were: general 4.81 and 1.44, peripheral access 2.52 and 0.84, jugular 6.20 and 0.88, subclavia 1.88 and 1.41, femoral 13.55 and 4.51. The number of artery catheters and the length of stay (days) were: global 675 and 3925, radial 578 and 3149, femoral 69 and 595, pedia 17 and 128, humeral 11 and 53. Artery catheter-related infections and bloodstream infections secondary to artery catheter per 1000 days of catheterization were: general 1.01 and 0.25, radial 0.95 and 0.31, femoral 1.68 and 0, pedia 0, humeral 0.

Conclusions There were more intravascular catheter infections in central venous catheters and in femoral localization.

P122 Bacterial colonisation of midline and central venous catheters

J Wale, M Oleolo, P Stewart, M Tivey
Department of Intensive Care, Queens Hospital, Burton on Trent, UK
Critical Care 2003, **7(Suppl 2)**:P122 (DOI 10.1186/cc2011)

The provision of parenteral nutrition conventionally requires the insertion of a central venous catheter (CVC) with the attendant risks of pneumothorax, vascular damage and line sepsis [1]. In addition, CVC insertion requires appropriately trained medical staff. It is possible to provide central venous access with peripherally inserted central catheters (PICC) but these are associated with malposition, catheter fracture, leakage and occlusion [2]. An alternative to these is the use of 20 cm single lumen 22 G venous catheters inserted in the antecubital fossa (midlines). This unit provides a 'midline' service for parental nutrition or long-term venous access, and this audit describes the experience of this service to date. All lines were inserted on a general ward by a trained theatre technician using standard sterile techniques including chlorhexidine or iodine (in 70% methylated spirit) skin preparation and a

semipermeable film dressing (tegaderm™). At removal, midline tips were sent for microbiological analysis using a Maki roll technique.

There were 160 midlines inserted over an 18 month period, 139 catheters were inserted for parental nutrition and 21 for other reasons. Catheters remained *in situ* for median of 6 days with a range of 1–60 days. Reasons for catheter removal included blockage (13%), concerns over arm swelling (17.5%) and completion of therapy (39%). Of the 160 midlines inserted, microbiological data were available on 120. There was an overall bacterial colonisation rate of 20.8%. By comparison the colonisation rate for CVC in this unit is 49%. The colonisation rates for midlines and CVCs become significantly different by day 7 ($P=0.03$, χ^2) and remain so thereafter. For midlines, the majority of catheters that eventually become colonised do so by day 8. In contrast, for CVCs the colonisation rate continues to rise until day 15. The majority of organisms isolated from midline catheters were staphylococcus epidermidis (19/27). Other organisms included β-haemolytic streptococcus (two cases), enterobacter aerogenese (two cases), MRSA (one case), coliform (one case), staphylococcus aureus (one case) and candida (one case).

Midline catheters represent a simple technique that can be performed by nonmedical staff. They can be used for long-term intravenous access with a lower risk of colonisation than central venous catheters.

References

1. Tivey M, West M, Carr J, Coates S, Cunningham M, Allsop P: **Time course for internal jugular and subclavian central venous catheter tip colonization.** *B Anaesth* 2001, **87**:336P.
2. Cowl CT, Wienstock JV, Al-Jurf A, Ephgrave K, Murphy JA, Dillon K: **Complications and cost associated with parenteral nutrition delivered to hospitalized patients through subclavian or peripherally inserted cantral catheters.** *Clin Nutr* 2000, **19:**237-243.

P123 Effects of an education: prevention strategy on decreasing catheter-related infections in intensive care

V Karali, P Stefanopoulou, M Bitzani, F Ambatzidou, G Vassiliadou, D Riggos
ICU, 'G. Papanikolaou' Hospital, Exohi, Thessaloniki, Greece
Critical Care 2003, **7(Suppl 2)**:P123 (DOI 10.1186/cc2012)

Background Primary bloodstream infections resulting from central venous catheterization are a leading source of nosocomial infection. The purpose of this study was to investigate whether the implementation of a prevention program aimed at improving central venous catheter (CVC) insertion and care, directed towards ICU doctors and nursing stuff, could decrease the occurrence of catheter-related infections and the frequency of catheter removal and exchange.

Methods This prospective cohort study was performed in 80 critically ill patients admitted in a 19-bed general intensive care unit at a tertiary center between August 2002 and October 2002. Patients were divided into two groups: Group A, 40 patients (APACHE II 17 ± 4, mean age 49 ± 15 years) were studied in the preintervention period; Group B, 40 patients (APACHE II 17 ± 5, mean age 50 ± 18 years) were studied in the postintervention time. The incidence of catheter-related infections classified as catheter-related bloodstream infection (CRBSI) (definite or probable), exit-site catheter-related infection (CRI) and no CRI (colonized, contaminated, sterile) was measured. The frequency of catheter removal and exchange was also measured in the two groups.

Statistical analysis was computed by paired *t* test. $P<0.005$ was considered significant. The relative risk (RR) was also determined.

Results The median duration of CVC use was 7.6 ± 1.8 days in Group A and 8 ± 1.9 days in Group B.

We investigated 314 catheter days in Group A and 323 in Group B. Twenty CRI occurred in 80 patients (25 CRI/100 admissions). The incidence rate of CRBSI was 31.8 episodes/1000 catheter days in Group A and 9.3 episodes/1000 catheter days in Group B (RR 0.3). Corresponding rates of exit-site infections were 16 episodes/1000 catheter days and 6 episodes/1000 catheter days, respectively (RR 0.4). The incidence density of catheter colonization was 28.6 episodes/1000 catheter days in Group A and 12.3 episodes/1000 catheter days in Group B, while catheter contamination was 25 episodes/1000 catheter days and 12 episodes/1000 catheter days, respectively. After the intervention, the incidence density of exit-site catheter infection decreased by 61% ($P<0.005$) and that of bloodstream infection decreased by 71% ($P< 0.005$)

Fofty-seven catheter exchanges were measured in Group A versus 44 catheter exchanges in Group B, leading to a decrease of 25% ($P<0.005$) in the frequency of catheter removal and exchange. The mean length of catheter stay before a new site replacement was 6.9 ± 2.6 days in Group A versus 7.9 ± 2 days in Group B.

Discussion Our results demonstrate that a focused and multidimensional invention directed at the ICU physicians and nursing staff can lead to a dramatic decrease in the incidence of catheter-related infections.

P124 Risk factors and molecular typing associated with colonization or infection by a multidrug-resistant (MDR) *Pseudomonas aeruginosa* in intensive care unit (ICU) patients

S Milas[1], M Piagnerelli[1], M Vanhaeverbeek[1], E Carlier[1], A Deplano[2], D Govaerts[1]
[1]Department of Internal Medicine, Intensive Care and Microbiology, ISPPC Andre Vesale Hospital, 6110 Montigny le Tilleul, Belgium; [2]Department of Molecular Biology, Erasme University Hospital, 1070 Brussels, Belgium
Critical Care 2003, **7(Suppl 2)**:P124 (DOI 10.1186/cc2013)

Background *Pseudomonas aeruginosa* infections are associated with high mortality. *Ps. aeruginosa* has developed, after many years, multidrug resistance. We conducted a retrospective study to identify risks factors associated with acquisition of MDR *Ps. aeruginosa* in ICU patients.

Methods A retrospective study was performed in the 12-bed medico-surgical ICU from January to December 2000. All charts corresponding to acquisition of *Ps. aeruginosa* were reviewed; among them, we compare patients with or without a MDR strain. The MDR strains were genotyped by pulsed-field gel electrophoresis

(PFGE) and were defined as resistance to at least three drugs among ciprofloxacin (CIP), amikacin, ceftazidim and imipenem.

Results Six hundred and ninety-nine patients were admitted to the ICU during the study period. Fifty-two (7.5%) had a colonization or an infection with *Ps. aeruginosa* during their ICU stay. Forty (77%) had a susceptible strain and 12 (23%) had a MDR strain. Alcoholism was more frequent in the MDR group ($P=0.047$). The previous use of CIP, cefuroxime (CEF) and bitherapy with cefepime (CEP) plus amikacin were identified as a risk factor associated with acquisition of a MDR *Ps. aeruginosa* (for CIP, $P=0.0012$; for CEF, $P=0.03$; and for bitherapy, $P=0.026$). No clonal strain was identified by PFGE.

Conclusions The previous use of some broad-spectrum antibiotics was associated with development of MDR *Ps. aeruginosa*. Control prescriptions and optimizing use of broad-spectrum antibiotics is now established in our hospital to reduce the risk of emergence of MDR strains.

P125 Endotoxin-neutralising effect and anti-inflammatory properites of tobramycin and ceftazidime in porcine endotoxic shock

G Goscinski[1], M Lipcsey[2], M Eriksson[3], A Larsson[4], J Sjölin[1]
[1]Section of Infectious Diseases and [4]Section of Clinical Chemistry, Department of Medical Sciences, and [3]Section of Anesthesiology and Intensive Care, Department of Surgical Sciences, Uppsala University Hospital, SE 751 85 Uppsala, Sweden; [2]Department of Anesthesiology and Intensive Care, Gävle-Sandviken County Hospital, SE 80187 Gävle, Sweden
Critical Care 2003, **7(Suppl 2)**:P125 (DOI 10.1186/cc2014)

Introduction Administration of antibiotics represents a cornerstone in the treatment of severe bacterial infections. In addition to their antibacterial effect, antibiotics have been shown to cause other effects on the inflammatory response. Aminoglycosides have been considered to neutralise endotoxin and ceftazidime to modulate the inflammatory response by an antioxidative effect.

The primary aim of this study was to investigate whether endotoxin given as an infusion in a porcine model could be neutralised by the addition of tobramycin. The secondary endpoint was to study whether ceftazidime could affect the inflammatory response by modifying the cytokine release during the end of the study period.

Methods Fourteen pigs were exposed to an endotoxin infusion of 4 μg/kg during 30 min followed by 1 μg/kg during the rest of the 6 hour experiment. Five of the animals were randomised to receive tobramycin 6 mg/kg, five were given ceftazidime 40 mg/kg, and four received saline solution.

Results The endotoxin levels remained stable after 1 hour of the experiment and there was no difference between the treatment groups, thus indicating that there were no neutralising effects by any of the antibiotics. The plasma TNF-α levels reached peak values 1 hour after starting the endotoxin infusion, median value 7265 ng/l (2492–10,625 ng/l), and there were no significant differences in peak TNF-α or elimination rate between the treatment groups. Plasma IL-6 levels peaked after 2–3 hours with a median maximum IL-6 value of 2509 ng/l (1544–7854 ng/l). A significantly greater reduction of IL-6 was seen in the animals treated with ceftazidime or tobramycin compared with those receiving saline ($P<0.05$). In the ceftazidime group also, absolute values obtained at 6 hours were significantly lower than the corresponding values in the saline group ($P<0.05$).

Conclusion Endotoxin was not neutralised by tobramycin or ceftazidime in this porcine model. However, data indicate a slight anti-inflammatory effect of ceftazidime and perhaps also of tobramycin as measured by the reduction in IL-6.

P126 *In vitro* activity of imipenem ± aminoglycosides against *Pseudomonas aeruginosa* and *Acinetobacter calcoaceticus/baumanii* isolated from patients in ICUs in German hospitals (1999–2002)

EE Mueller[1], M Stek Jr[2], DC Draghi[3], JA Karlowsky[3], C Thornsberry[3], DF Sahm[3], ME Jones[4]
[1]Department of Anesthesiology, Heinrich-Heine University, Düsseldorf, Germany; [2]Merck & Co, Whitehouse Station, NJ, USA; [3]Focus Technologies Inc, Herndon, VA, USA; [4]Focus Technologies Inc, Hilversum, The Netherlands
Critical Care 2003, **7(Suppl 2)**:P126 (DOI 10.1186/cc2015)

Objectives Carbapenems such as imipenem (IM) provide important antimicrobial activities against *Pseudomonas aeruginosa* (*PA*) and *Acinetobacter calcoaceticus/baumanii* (*ACB*). Additionally coadministration with an aminoglycoside provides broad-spectrum coverage. The current activity of IM, and the activity of IM and gentamicin (GN) or amikacin (AK), considered together, was reviewed by analysis of cross-susceptibility to this combination, as reported to physicians, by clinical microbiology laboratories in Germany.

Methods Data were analyzed (January 1999–October 2002) from The Surveillance Network® (TSN) Database Germany, an electronic surveillance system that collects routine susceptibility test results from 169 hospital laboratories distributed throughout the country. Only data from nonrepeat isolates from patients >17 years of age, located on ICUs, and derived from antibiotics concomitantly tested were included in the analysis. NCCLS (2002) breakpoints were used to interpret the data.

Results For all *PA* ($n=1316$) isolated from lower respiratory tract infection (LRTI) specimens during 1999–2000, 65.3% were reported susceptible (S) and 20.9% resistant (R) to IM. The following susceptibility and resistance frequencies were found for *PA* from LRTI, reported by year: 1999 ($n=127$; 65.4% S; 31.5% R), 2000 ($n=346$; 66.5% S; 28.9% R), 2001 ($n=539$; 63.5% S; 15.4% R), and 2002 ($n=304$; 67.1% S; 17.1% R). Among *PA* from blood reported by year: 1999 ($n=7$; 85.7% S; 14.3% R), 2000 ($n=20$; 80.0% S; 15.0% R), 2001 ($n=31$; 74.2% S; 16.1% R), and 2002 ($n=39$; 84.6% S; 12.8% R). Considering data of IM combined with an aminoglycoside, for *PA* from LRTI isolated during 2000–2002, 86.3% of isolates were S ($n=1634$; 5.8% R) to both IM and gentamicin (GT), and 93.8% of isolates were S ($n=1171$; 2.8% R) to IM and AK. *PA* isolates from blood were 89.1% S ($n=64$; 3.1% R) to the combination of IM and GT, and 100% S ($n=45$) to the combination of IM and AK. Overall (2000–2002) for *ACB* isolated from LRTI, 98.2% were S ($n=225$;

0% R) compared with 100% S ($n=25$) for blood isolates. For *ACB* by year, the following IM susceptibility percentages were detected: 90.5% S in 2000 ($n=21$; 9.5% R), 99.3% S in 2001 ($n=143$; 0.7% R), and 97.5% S in 2002 ($n=163$; 0% R).

Conclusions: In Germany, IM susceptibility has remained consistent for *PA* since 1999 and *ACB* since 2000, and no increase in resistant phenotypes was detected. Combinations of IM with an aminoglycoside still approach 100% coverage against *PA*.

P127 Activity of ceftriaxone and comparator agents against bacterial pathogens isolated from central nervous system (CNS) (meningeal) specimens: TSN Database USA 2000–2002

ME Jones[1], DD Draghi[2], JA Karlowsky[2], C Thornsberry[2], DF Sahm[2]
[1]Focus Technologies Inc, Hilversum, The Netherlands; [2]Focus Technologies Inc, Herndon, VA, USA
Critical Care 2003, **7(Suppl 2)**:P127 (DOI 10.1186/cc2016)

Objectives Meningeal infections are life-threatening and require immediate, parenteral treatment, often with β-lactams such as ceftriaxone (CTX). Using The Surveillance Database (TSN®) USA, we analyzed the susceptibility of pathogens frequently causing meningitis isolated from CNS specimens (including cerebral fluids and shunts).

Methods We analyzed data (January 2000–October 2002) from The Surveillance Network (TSN®) Database USA, an electronic surveillance system that collects routine susceptibility test results from 326 hospital laboratories distributed throughout the USA. Data is the same data reported to physicians. Only data from non-repeat isolates from patients' CNS specimen sources were included in the analysis. NCCLS (2002) breakpoints (BPs) were used to interpret as susceptible (S) or resistant (R) (included CTX BPs for meningeal isolates of *Streptococcus pneumoniae* [*SP*]). The number of organism susceptibilities tested by drug varied.

Results A total of 10,436 organisms were isolated and the susceptibility tested. The relative incidence of key pathogens known to be frequently involved in meningitis was coagulase-negative Staphylococci (CoNS) (44.9%, $n=4688$) (1.5%, $n=155$ isolated from shunt infections), *Staphylococcus aureus* (*SA*) (10.7%, $n=1114$), *SP* (5.6%, $n=580$), *Escherichia coli* (*EC*) (2.5%, $n=266$) ($n=11$ isolated from shunt infections), *S. agalactiae* (*SAG*) (1.1%, $n=114$), *Haemophilus influenzae* (*HF*) (0.7%, $n=71$), and *Neisseria meningitidis* (*NM*) (0.3%, $n=26$). 72.2% ($n=1046$) of *SA* from all CNS sources and 33.8% ($n=145$) of CoNS were involved in shunt infections, and were oxacillin-susceptible. Among oxacillin S *SA*, 99.4% of isolates tested were S to CTX ($n=179$). Against all CNS sources, 85.3% (2.9% R) of *SP* and 100% of *SAG* were S to CTX. *SP* and *SAG* were 55.7% S (17.9% R) and 100% S to penicillin, respectively. All Gram-positive isolates tested were vancomycin S. Erythromycin R was detected in all streptococcal species. *EC* isolated from shunts were 100% ($n=6$) S to CTX and 100% ($n=7$) were S to imipenem. For *HF* from all CNS sources, 29.1% ($n=55$) were ampicillin R but 100% ($n=45$) CTX S. No interpretive criteria are defined for *NM*, although 39 isolates were identified during this time period.

Conclusions Although oxacillin-resistant Staphylococci would require glycopeptide therapy, after 18 years of clinical use CTX retains very high efficacy against most isolates likely to cause meningeal infections, including *SP* and *HF*.

P128 Continuous infusion versus intermittent bolus of ceftazidime for the treatment of nosocomial pneumonia

L Lorente, C García, MM Martín, R Galvan, J Villegas, ML Mora
Department of Intensive Care, Hospital Universitario de Canarias, Tenerife, Spain
Critical Care 2003, **7(Suppl 2)**:P128 (DOI 10.1186/cc2017)

Objective Betalactamics antibiotics exhibit concentration-independent bactericidal activity. The primary determinant of betalactamics efficacy is the duration of time that concentrations remain above the minimum inhibitory concentration (MIC). Several studies have found that ceftazidime by continuous infusion appears to optimize the pharmacodynamic profile by constantly providing concentrations in excess of the MIC of susceptible organisms over the course of therapy. Limit data exist on clinical efficacy by continuous infusion of ceftazidime. The purpose of this study was to evaluate the clinical efficacy associated with the administration of continuous infusion of ceftazidime (CI) and intermittent bolus of ceftazidime (IB) for the treatment of nosocomial pneumonia (NP) in critically ill patients.

Methods Prospective and randomized study of patients admitted in the ICU from 1 July 2002 to 31 October 2002 and who developed late-onset NP. Pneumonias were diagnosed according to CDC criteria. NP were treated during 14 days with two antibiotics: ceftazidime plus another (aminoglycoside or quinolone). Patients were randomized in two groups: one group received CI of ceftazidime (4 g/day IV), and another group IB of ceftazidime (2 g/8 hours IV). The statistical analysis was realized by chi-square, Student *t*, and values $P<0.05$.

Results Twenty-seven patients were included. Both groups of patients (13 with CI and 14 with IB) were similar in age, sex, APACHE II, failure rate of different system organs (cardiovascular, respiratory, renal, hematologic, hepatic), number of organ failures, microorganisms responsible for NP, NP with bacteremia. Clinical cure in the patient group treated with ceftazidime administration by CI was higher, but not statistically significant (92% vs 60%, $P=0.08$), with one-third of total doses of ceftazidime.

Conclusions These data suggest that continuous infusion ceftazidime therapy may have more clinical efficacy and may be cheaper than intermittent bolus administration for the treatment of nosocomial pneumonia, but further larger studies are required to confirm it.

P129 Use of 'Synercid'™ (Aventis) in 132 polytrauma patients with Gram-positive nosocomial infection

E Gyurov, S Milanov, M Milanov, J Shterev
General ICU, University Hospital 'N.I. Pirogov', 21 'Totleben' 1606 Sofia, Bulgaria
Critical Care 2003, **7(Suppl 2)**:P129 (DOI 10.1186/cc2018)

The purpose of this study was to evaluate the effectiveness of a new powerful antibiotic 'Synercid'™ (Aventis) in the treatment of ICU patients with nosocomial infection. During 2002 (January–September) we prospectively followed 132 patients with polytrauma (two body cavities and/or pelvic bones and/or extremities injured) requiring mechanical ventilation for more than 72 hours. These patients suffered Gram-positive nosocomial infection and were treated with new for Bulgaria antibiotic agent 'Synercid'™ (Aventis) after microbiological confirmation. Eighty-two patients (62%) were treated for nosocomial pneumonia, which was diagnosed clinically (fever, leucosytosis, purulent tracheal secretions and new infiltrate on chest X-ray) and by positive culture (transtracheal aspirate). Forty-three patients (32.6%) were treated for bacteriaemias (fever, leucosytosis, positive blood culture). The rest of the patients were with surgical wound infections (local signs of infection and systemic inflammatory response syndrome). The main causative pathogen was methicillin-resistant *S.* α-haemolyticus (59 patients with pneumonia [72%]; 34 patients with bacteriaemias [79%]). In patients with surgical wound infections (17 patients), the leading role belonged to methicillin-resistant *S. epidermidis* (11 patients, or 64.7%) and to MRSA (four patients, or 23.5%). The treatment lasted between 8 and 16 days (mean 11 ± 2 days). The rate of success for pneumonia was 96.3% (79 patients). Three patients developed Gram-negative infection. The rate of success for bacteriaemias was 100%. The rate of success for surgical infection was 82% (14 patients) and the reason was some delayed surgical debridement of the wound. In conclusion, we appreciate the power of this new, for our country, antibiotic agent and added it to group 3 (Hospital Antibiotic Management Policy Protocol) for use only after microbiological confirmation.

P130 Fungal infections in patients with severe acute pancreatitis and the use of prophylactic therapy

JJ De Waele, S Blot, E Hoste, J Decruyenaere, F Colardyn
Intensive Care Unit, Ghent University Hospital, Ghent, Belgium
Critical Care 2003, **7(Suppl 2)**:P130 (DOI 10.1186/cc2019)

Introduction Infection of pancreatic necrosis is associated with an increased mortality rate in patients with severe acute pancreatitis. It is not clear whether fungal involvement in pancreatic infection further increases the odds for mortality.

Objective To analyze the incidence of fungal infection in patients with infected pancreatic necrosis, to identify risk factors for development of fungal infection and to assess the use of early fluconazole treatment.

Patients and methods We retrospectively (1995–2002) analyzed 46 consecutive patients with infected pancreatic necrosis from a total of 106 patients that were admitted to the ICU because of severe acute pancreatitis. We recorded demographic characteristics, incidence of organ failure, data on antimicrobial and antifungal treatment, and disease severity.

Results Intra-abdominal fungal infection was found in 17 of 46 patients (37%). Primary infection was present in eight patients, in nine others fungal infection occurred later in the course of the disease. *Candida albicans* was isolated most frequently (15/17); *C. tropicalis* and *C. Krusei* were found in one patient each. Characteristics (age, gender, APACHE II score, Ranson score, the use and duration of prophylactic antibiotics) of patients with fungal infections were not different from patients without fungal infection. Mortality was statistically not significantly different in patients with fungal infections (35% vs 27% in the other patients, $P = 0.58$). Antifungal prophylaxis or pre-emptive antifungal therapy was used in 19 patients, and only three of them developed fungal infection: there was one breakthrough infection with *C. Krusei*, and two patients developed *C. albicans* infections later in the course of the disease, after antifungal treatment had been stopped for 3 and 4 weeks, respectively.

Conclusion The incidence of fungal infections in patients with infected pancreatic necrosis is high. In this cohort of critically ill patients, no risk factors for fungal infection could be demonstrated, and mortality was not different. Early treatment with fluconazole seems to prevent fungal infections in these high-risk patients.

P131 Itraconazole IV solution in the treatment of candidemia in non-neutropenic patients

O Tuil, Y Cohen
Hospital Avicenne, Bobigny, France
Critical Care 2003, **7(Suppl 2)**:P131 (DOI 10.1186/cc2020)

Aim To investigate the efficacy and safety of the itraconazole intravenous (IV) formulation followed by oral solution in the treatment of candidemia in non-neutropenics versus fluconazole.

Methods This was an international multicenter, randomized, open-label study, sponsored by Johnson & Johnson Pharmaceutical Research and Development (Beerse, Belgium). The study involved patients with candidemia documented by at least one positive blood culture with isolation of yeast (presumed *Candida* spp.) within 4 days of study entry, and clinical evidence of infection. Patients were randomized to receive either itraconazole or fluconazole. Intravenous itraconazole 200 mg was given twice daily on days 1 and 2, and then once daily for 5 days (and for a further 7 days if the patient could not take or tolerate oral medication); subsequently, itraconazole oral solution 200 mg twice daily was given until 14 days after resolution of symptoms and signs of fungal infection and cultures. Intravenous fluconazole 400 mg was given once daily for 7 days (extended for a further 7 days if required); then oral fluconazole 400 mg once daily was given until 14 days after resolution of infection and cultures. The intention-to-treat (ITT) population included all

randomized patients who had candidemia documented by at least one positive blood culture of *Candida* spp. The primary efficacy measure was the investigators' global assessment of successful response to treatment at followup week 12.

Results The study was terminated early because of the very slow enrollment rate after 197 patients had been randomized ($n=99$ itraconazole and $n=98$ fluconazole). The ITT population consisted of 193 patients ($n=96$ itraconazole and $n=97$ fluconazole); however, only 37 patients receiving itraconazole and 44 patients receiving fluconazole could be evaluated for the primary efficacy measure. At week 12 of followup, itraconazole had a success rate of 92% (34 of 37 patients) compared with a 91% success rate for fluconazole (40 of 44 patients). The overall safety profiles of the itraconazole and fluconazole groups were similar.

Conclusion Results from this study do not indicate any clinically meaningful differences in efficacy or safety outcomes in patients with candidemia treated with itraconazole compared with those treated with fluconazole.

P132 Treatment of invasive candidiasis with caspofungin in the intensive care unit

MJ DiNubile, RJ Lupinacci, CA Sable, NA Kartsonis
Merck Research Laboratories, West Point, PA, USA
Critical Care 2003, **7(Suppl 2)**:P132 (DOI 10.1186/cc2021)

Background Invasive candidiasis (IC) is increasingly recognized as an important complication of intensive care, and yet remains difficult to diagnose. Standard therapies have included amphotericin B (AmB), despite concerns about its toxicity, or fluconazole, even though some non-*albicans Candida* species may be azole-resistant. Caspofungin (CAS) is a novel, generally well-tolerated antifungal drug with fungicidal activity against both *C. albicans* and non-*albicans Candida* species. We retrospectively examined the demographics, risk factors, baseline characteristics, and outcomes of patients initially treated in an intensive care unit (ICU) enrolled in a randomized study of CAS vs AmB for IC.

Methods Adults with symptoms or signs of IC and positive cultures for *Candida* from blood and/or another normally sterile site were eligible for participation in a double-blind, randomized trial comparing CAS (50 mg/day after a 70 mg/day loading dose) with AmB (0.6–1.0 mg/kg per day). Antifungal therapy was to be continued for 14 days after the last positive *Candida* culture, but could be completed with oral fluconazole after 10 days of intravenous (IV) study drug. A favorable outcome required complete resolution of symptoms and eradication of *Candida* pathogen(s). We have retrospectively analyzed results from all patients who received their first dose of study drug while in the ICU. All treated patients with a confirmed diagnosis were included in the modified intention-to-treat (MITT) analysis at the completion of IV study therapy; missing assessments were counted as unfavorable. Mortality rates include death due to any cause from the initiation of the study through the 6–8 weeks following completion of IV therapy. Relapse rates represent documented relapses in the 6–8 weeks after completion of IV therapy in those patients who achieved a favorable response at the completion of IV study therapy.

Results Ninety-seven (43%) of the 224 MITT patients received their first dose of study drug in an ICU, including 40/109 (37%) of the CAS-treated patients and 57/115 (50%) of the AmB-treated patients ($P=0.06$). Medians (range) for age and APACHE II score were 59 (17–84) and 17 (6–36). Investigator-specified risk factors present in >20% of patients were: broad-spectrum antibiotics (92%), central venous catheters (84%), recent surgery (70%), hyperalimentation (47%), and underlying cancer (22%). Eighty-one percent of the ICU patients were candidemic, including three who also had pleural or peritoneal candidiasis. Among the ICU patients, there were no differences between the two treatment arms with regard to age, APACHE II scores, risk factors, or site of *Candida* infection. ICU and non-ICU patients had comparable baseline characteristics, except for lower APACHE scores (13; 0–28) and less frequent surgery (35%) in the non-ICU group. Favorable response, relapse, and mortality rates were as presented in Table 1.

Conclusions In this *post hoc* subgroup analysis, the efficacy of CAS was similar to AmB for IC in patients whose treatment was initiated in the ICU. CAS provides another therapeutic option for seriously ill patients with documented IC.

Table 1

	End of IV study therapy	Confirmed relapse at 6–8 weeks post-therapy	All-cause mortality at 6–8 weeks post-therapy
ICU patients	59/97 (61%) [51%, 71%]	10/59 (17%) [7%, 27%]	41/97 (42%) [32%, 52%]
CAS	27/40 (68%) [53%, 82%]	5/27 (19%) [4%, 33%]	18/40 (45%) [29%, 61%]
AmB	32/57 (56%) [43%, 69%]	5/32 (16%) [3%, 28%]	23/57 (40%) [28%, 53%]
Non-ICU patients	92/127 (72%) [65%, 80%]	5/92 (5%) [1%, 10%]	30/127 (24%) [16%, 31%]

Data presented as m/*n* (%) [95% confidence intervals].

P133 Nosocomial infection incidence in patients after hepatic transplantation

MM Martin, C Colmenero, L Lorente, I Molina, A Trujillo, A Chopitea
Department of Intensive Care, Hospital Universitario Nuestra Señora de Candelaria, Santa Cruz de Tenerife, Canary Islands, Spain
Critical Care 2003, **7(Suppl 2)**:P133 (DOI 10.1186/cc2022)

Objective To determine nosocomial infection incidence of patients undergoing liver transplantation.

Methods It is a descriptive study in a tertiary hospital. Included were all patients admitted to the ICU after liver transplant during

5 years (from 16 April 1996 to 16 April 2001). Infections were diagnosed according to the criteria of the Centers for Disease Control and Prevention (CDC). We analyzed the percentage of patients who developed device-associated infection and the number who developed device-associated infection per 1000 days of device-days.

Results Included were 96 patients (68.25% male). Mean age was 50.87 ± 9.86 years. Mean ICU stay was 7.35 ± 7.54 days. ICU mortality was 13.54%. Etiology of liver failure was: alcoholic cirrhosis 44.06%, virus hepatitis 28.81%, autoinmmune disease 12.70%, metabolic 5.92%, cancer 1.69%, cirrhosis crytogenic 4.30%, genetic disease 0.84%, vascular disease 2.54%. Patients developed further infections: 10 ventilation-associated pneumonias, six central venous catheter-related infections, four abdominal infections, two urinary tract infections, four surgical wound infections. The percentage of patients who developed pneumonia, venous central-related infections and urinary tract infection were, respectively, 10.41%, 2.08% and 6.25%. The number of ventilation-associated pneumonia, central venous catheter-related infections and urinary tract infections per 1000 device-days were, respectively, 28.57, 5.67 and 2.83.

Conclusions The most frequent infection in patients undergoing liver transplantation was respiratory. Our infection incidence is similar to other seria.

P134 A decade with Falciparum Malaria in the ICU

A Aaron[1], AS Bachwani[2], SU Madkaiker[1], R Singh[3]
[1]Intensive Care Unit, Parsee General Hospital, Cumballa Hill, Mumbai 400026, India; [2]BARC Hospital, Mumbai 400094, India; [3]Breach Candy Hospital, Mumbai 400026, India
Critical Care 2003, **7(Suppl 2)**:P134 (DOI 10.1186/cc2023)

Aims and introduction To study and compare the various treatment modalities and the attendant complications of Falciparum Malaria with or without concomitant Vivax in the intensive care unit.

Method Retrospective study between 1993 and 1995 and prospective study from 1996 to 2002 of patients having severe malaria warranting intensive care management.

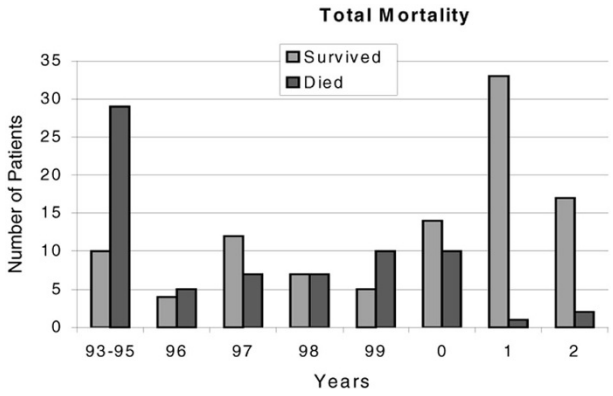
Table 1

Drug(s) used	Year	Complication	Comments
Mefloquine	1993–1997	Prolonged parasitemia	High incidence of drug resistance and side effects
Mefloquine + others	1993–1997	Nausea, vomiting	High incidence of gastro side effects
Mefloquine + others + Quinine and outcome	1993–1997	Vomiting, intolerance	Neither cost nor time effective, unpredictable response
Quinine	1993–1999	Mainly GI in PO administration	Better results in all types except MOF/shock
Artesunate	2000–2002	Virtually nil	Drastic reduction of parasite index
Artemether	2000–2002		
Quinine + Artesunate	1999–2002	Virtually nil; noteworthy is no prolongation of QT interval	Best combination to date; reserved for P.I. > 4%, failure to reduce P.I. by 25% in 48 hours and shock

Table 2

Year	Total	Died	%	Complications, survivor group	Complications, mortality group
1993–1995	39	29	75	30 uncomplicated; given Quinine	86% had ARDS, of which 50% were directly admitted to the ICU
1996	09	05	55	8 CNS, ARF, ARDS; excellent response to early Quinine	45% of the remainder developed ARDS on the 4th day of admission
1997	19	07	36	6 MOF; excellent response to Quinine + Artesunate	ARDS was the single most common dreaded complication during the course of management
1998	14	07	50	20 treated with multidrug regime had delayed recovery and unacceptable rates of side effects and complications	
1999	15	05	33		
2000	24	10	55		
2001	34	01	2.5		
2002	19	02	03		

Figure 1



Results A total of 173 patients; 107 survived and 66 died (61% survival, 38% mortality) (Fig. 1).

Conclusions Quinine has given good and consistent results (10 mg/kg up to 600 mg, thrice daily for 5–10 days) and can cure all stages of Falciparum and other plasmodia. The treatment must be initiated with Quinine only in patients sick enough to need the ICU.

Parasites may have developed resistance to a multidrug regimen. It is also very much in evidence in the study that if the Quinine is given after Mefloquine the results are not really encouraging, besides having an unacceptable rate of side effects due to its long half-life.

Artisunate 120 mg bolus followed by 60 mg daily IV × 5 days given with Quinine yielded good results. This is perhaps the best that can presently be offered to patients with shock/MOF.

Artesunate or Arthemether alone although effective are probably insufficient to treat severely complicated patients.

Cinchonism and hypoglycemia were easily manageable. Most importantly, prolonged QTc was not encountered in any patient.

Patients who came to the ICU in multiorgan failure did not do well with whatever interventions. We must do a planned study on these patients and the blood exchange transfusion therapy must be tried to salvage these patients.

P135 No significant excess mortality in ICU patients with nosocomial *Escherichia coli* bacteremia

S Blot, K Vandewoude, F Colardyn
Intensive Care Unit, Ghent University Hospital, Ghent, Belgium
Critical Care 2003, **7(Suppl 2)**:P135 (DOI 10.1186/cc2024)

Purpose and methods The objective of this retrospective matched cohort study was to evaluate the excess mortality in critically ill patients with *E. coli* bacteremia after accurate adjustment for severity of illness. ICU patients with nosocomial *E. coli* bacteremia were matched (1:2 ratio) on the basis of the APACHE II system: equal APACHE II score (± 2 points) and diagnostic category. Since expected mortality can be calculated from this severity of disease scoring system, this matching procedure results in an equal expected inhospital mortality rate for patients with (cases: $n=64$) and without *E. coli* bacteremia (controls: $n=128$).

Results The average APACHE II score (± SD) for cases and controls was 25 ± 9.2 (median: 23). This represented an expected inhospital mortality rate of approximately 47 ± 27.4% (median 44%) in both groups. ICU patients with *E. coli* bacteremia had more hemodynamic instability (75% vs 56%; $P=0.009$), they were mechanically ventilated for a more extended period (median 14 days vs 3 days; $P=0.001$), and had a longer ICU stay (median 17 days vs 5 days; $P<0.001$). No statistically significant differences between cases and controls were noted in incidence of acute respiratory failure (respectively 81% vs 77%; $P=0.534$), acute renal replacement therapy (respectively 27% vs 18%; $P=0.167$) and age (respectively median 57 years vs 58 years; $P=0.260$). Inhospital mortality rates for cases and controls were not different, respectively 43.8% and 43.0% ($P=0.918$). Thus, the excess mortality was 0.8% (95% CI: −14.1 to 15.7%). The absence of a significant excess mortality in the cases might be due to the high rate of appropriate antibiotic therapy (93%) and the overall short delay in the start of treatment (0.6 ± 1.0 days).

Conclusion After careful adjustment for severity of underlying disease and acute illness, no significant excess mortality was found between ICU patients with and without *E. coli* bacteremia. These results must be seen in the light of fast initiation of appropriate therapy.

P136 Nosocomial bloodstream infection from abdominal origin in a general ICU: microbiological factors influencing outcome

S Blot, J De Waele, F Colardyn
ICU, Ghent University Hospital, De Pintelaan 185, B-9000 Gent, Belgium
Critical Care 2003, **7(Suppl 2)**:P136 (DOI 10.1186/cc2025)

Purpose and methods A retrospective (January 1992–December 2000) cohort study was performed in order to identify microbiological factors associated with bad outcome in ICU patients with nosocomial bloodstream infection (BSI) from abdominal infection ($n=96$).

Results During the study period, 1071 episodes of nosocomial BSI were found in 29,727 patients admitted to the ICU. In 91 patients, 143 BSI were found originating from an abdominal source. In patients with multiple episodes only the first was considered for the outcome analysis. Mean (± SD) age of the patients was 54 (± 16.1).

Table 1

	Survivors ($n = 39$)	Nonsurvivors ($n = 52$)	P value
Antibiotic-resistant microorganism	17 (43.6%)	19 (36.5%)	0.523
Colonization prior to onset BSI	23 (59.0%)	24 (46.2%)	0.290
Polymicrobial BSI	9 (23.1%)	16 (30.8%)	0.482
> 1 presumed source of BSI	6 (15.4%)	4 (7.7%)	0.312

APACHE II scores averaged 24 (±9.5). The median length of ICU stay prior to the BSI was 6 days and the total ICU stay 20 days. The inhospital mortality was 57.2%. In 25 patients the BSI was polymicrobial (27.5%). The causative microorganisms and respectively associated mortality rates were: Gram-negative bacteria (n=64; 59.4%), *E. coli* (n=20; 60.0%), *Enterobacter* spp. (n=11; 63.6%), *P. aeruginosa* (n=9; 66.7%), *Klebsiella* spp. (n=9; 44.4%), *Acinetobacter* spp. (n=8; 37.5%), other Gram-negatives (n=12; 75.0%), Gram-positives (n=30; 50.0%), coagulase-negative Staphylococci (n=11; 45.5%), Enterococci and Streptococci (n=16; 50.0%), *S. aureus* (n=6; 50.0%), Candida spp. (n=9; 77.8%) and anaerobe bacteria (n=6; 50.0%). No type of microorganism was associated with a statistically significant higher mortality (P>0.05). In 39.6% of BSI the microorganism involved was antibiotic resistant. In Table 1, microbiological factors are compared for hospital survivors and nonsurvivors. Also in a multivariate analysis no microbiological factor could be recognised as independently associated with mortality (P>0.05).

Conclusion In our cohort of ICU patients with nosocomial BSI from abdominal origin, microbiological characteristics of the infection seem not to affect the outcome.

P137 Transfer in ICU of febrile neutropenic patients: prospective validation of a prognostic score identifying 'high-risk' patients

J Larché[1], F Alla[2], P Maurer[1], O Kunzberger[1], A Gérard[1]
[1]Service de Réanimation Médicale, CHU Nancy Brabois, 54500 Vandoeuvre les Nancy, France; [2]Service d'Epidémiologie et d'Evaluation Cliniques, CHU Nancy Hôpital Marin, 54000 Nancy, France
Critical Care 2003, **7(Suppl 2)**:P137 (DOI 10.1186/cc2026)

Objective Infectious complications in neutropenic febrile patients are associated with a high mortality rate. A previous case–control study in postchemotherapy neutropenic patients identified three early risk factors for ICU transfer (abnormal chest X-ray, positive blood cultures, and C-reactive protein ≥120 mg/l), and a prognostic score based for ICU transfer on the presence or not of at least one of these variables was then performed. Our objective was to validate accuracy, adequacy and reliability of this score with another cohort of febrile neutropenic patients.

Design A prospective consecutive cohort study over 18 months in a tertiary care hospital.

Results and measurements Ninety patients have been included; 57.7% were men, and mean age was 50±19 years. The majority of them were hospitalized for acute myeloblastic leukaemia (AML) (78 patients), the others for acute lymphoblastic leukaemia (ALL) (12 patients). Twenty-four (26.7%) patients were referred in the ICU and nine (37.5%) of them died in the ICU. The following data were associated with an increased risk of transfer in the ICU during their stay in the hematology ward: ALL, more than three previous episodes of febrile neutropenia, microbiological documentation, clinical pulmonary location, and abnormal chest X-ray. When applied to this prospective cohort, sensitivity, specificity, negative and positive predictive values of our prognostic score were, respectively, 100%, 56.1%, 100% and 45.3%.

Conclusion No prognostic score focused on identification of 'high-risk' neutropenic patients has yet been validated. Moreover, different severity-of-illness scores used in the ICU and recently tested in hematology wards have failed to predict accurately patients at 'high risk'. These results confirmed the validity of this score for eliminating patients without risk of transfer in the ICU, but also for identifying a 'sensitive' population at higher risk of complication and transfer in the ICU. The use in haematology wards of such a prognostic score, associated with an optimization strategy, should be prospectively tested on febrile neutropenic patients in a randomized controlled trial, with outcome as the primary objective.

P138 Bacteremia mortality according to microorganism responsible and origin source of bacteremia in critically ill patients

L Lorente, R Galvan, MM Martín, C García, S Huidobro, ML Mora
Department of Intensive Care, Hospital Universitario de Canarias, Tenerife, Spain
Critical Care 2003, **7(Suppl 2)**:P138 (DOI 10.1186/cc2027)

Objective To determine the incidence, microorganism responsible and mortality of bacteremias in critically ill patients. To analyze bacteremia mortality according to microorganisms responsible and origin sources in critically ill patients.

Methods It is a prospective study of bacteremias in patients admitted in a medical–surgical ICU, from 1 May 2000 to 31 August 2002. We analyzed mortality bacteremia according to the microorganism responsible and bacteremia mortality according to origin sources. The statistical analysis was realized by chi-square test and we took values P<0.05 to consider a significant difference.

Results Included were 1389 patients. Diagnosed were 116 bacteremias, due to 116 microorganisms, in 106 patients (a total of

7.63% patients developed bacteremia). The mortality of patients who developed bacteremia was 19.81% (21/106). Bacteremia mortality for each microorganism responsible was: MRSA 1/9, MSSA 3/5, CNS 6/44, *Streptococcus faecalis* 2/13, *Streptococcus pneumoniae* 1/4, *Escherichia coli* 3/8, *Proteus mirabilis* 0/2, *klebsiella* 2/4, *Morganella morgani* 0/2, acinetobacter 0/1, enterobacter 1/7, *Pseudomonas aeruginosa* 1/7, *Candida albicans* 1/4, others 0/6. Bacteremia mortality for each origin source was: primary 9/55, respiratory 6/25, central venous catheter 5/22, wound surgical 1/4, others 0/10. No significant differences were found in bacteremia mortality according to the microorganism responsible and according to origin source of bacteremia.

Conclusions In our series, bacteremia mortality was not different according to origin source nor according to the microorganism responsible.

P139 Severe community acquired pneumonia and ARDS: prognostic factors in infants

G Chidini, U Casella, L Napolitano, G Ardissino, E Calderini
Istituti Clinici di Perfezionamento Terapia Intensiva Pediatrica, via della Commenda 9, 20122 Milano, Italy
Critical Care 2003, **7(Suppl 2)**:P139 (DOI 10.1186/cc2028)

Objective Severe CAP is a common reason for emergency paediatric intensive care (mortality rate: 40–70%). In this population, refractory hypoxemia is frequently associated with poor outcome. Our hypothesis is that the mortality rate in infants with severe CAP and ARDS correlates not only with respiratory impairment, but also with associated organ failure. The purpose of this study is to evaluate organ failures quantified with paediatric modified SOFA (mSOFA) score and to correlate it with mortality.

Design A retrospective observational study. Period of the study: January 2000–January 2002.

Setting PICU in a national children's hospital.

Methods Twenty-two infants with severe CAP meeting ACCP/SCCM criteria for ARDS, age between 6–24 months admitted in the hospital less than 2 days before. Excluded were infants with ARDS from RSV, prematurity and bronchodysplasia, neuromuscular diseases, immunodepression or immunosuppression, congenital cardiopathy. The ventilatory strategy employed was permissive hypercapnia (target pO2 $\geq$60 mmHg, pH $>$7.25) with limitation of peak inspiratory pressure (Pplat $<$35 cm H_2O) while employng elevated mean airway pressure to ensure maximum lung volume recruitment (PEEP above the lower inflection point on PV curve). Sedation and paralysis were performed according to

Table 1

Population on admission

	Dead (D)	Survivors (S)	*P* (*)
Age (months)	13 ± 6	16 ± 6	NS
Weight (kg)	7.3 ± 6	9.1 ± 1	NS
Prism	17 ± 11	11 ± 6	NS
Lung injury score	3	2	NS

Table 2

Results

	D1		D2		D3		D7		D0	
	D	S	D	S	D	S	D	S	D	S
Lactate (*)	4.0 ± 2.4	0.5 ± 0.5	2.6 ± 1.2	0.5 ± 0.9	3.0 ± 1.2	0.3 ± 0.5	2.8 ± 1	0.9 ± 0.3	5.8 ± 1.2	1 ± 0.2
P	$<$0.001		$<$0.001		$<$0.001		$<$0.001		$<$0.001	
LDH (**)	1693 ± 1124	847± 251	1575 ± 775	824 ± 211	1466 ± 405	672 ± 500	2700 ± 2300	760 ± 168	2700 ± 2000	680 ± 170
P	$<$0.05		$<$0.05		$<$0.05		$<$0.01		$<$0.01	
SOFA TOT (*)	8.0 ± 1.3	3.2 ± 1.2	8.0 ± 2.9	3.1 ± 1	8.3 ± 2.4	3 ± 0.9	7.7 ± 2	2 ± 0.9	9.7 ± 1.8	1.8 ± 0.2
P	$<$0.01		$<$0.01		$<$0.01		$<$0.01		$<$0.01	
SOFA EMO (*)	1.5 ± 1.9	0.8 ± 1.5	1.7 ± 1.8	0.5 ± 0.6	1.5 ± 1	0.2 ± 0.6	3.5 ± 0.5	0	3.5 ± 0.5	0.2 ± 0.1
P	NS		NS		NS		$<$0.01		$<$0.01	
SOFA RES (*)	3.3 ± 0.5	3 ± 0.4	3.3 ± 0.4	2.5 ± 0.3	3.4 ± 0.3	2.6 ± 0.5	4.0 ± 0	1.4 ± 0.5	4 ± 0	2 ± 0.3
P	NS		NS		NS		$<$0.05		$<$0.01	
SOFA PLT (*)	2.2 ± 1.2	0.2 ± 0.4	2.3 ± 1.3	0.1 ± 0.3	2.5 ± 0.8	0.1 ± 0.2	2.3 ± 0.7	1.0 ± 0.3	2.0 ± 0.9	0
P	$<$0.01		$<$0.01		$<$0.01		$<$0.01		$<$0.01	

clinical protocols. At different times, day 1 (D1), day 2 (D2), day 3 (D3), day 7 (D7), day 0 (D0: exitus vs dimission), were collected the mSOFA score, HR, mean arterial pressure, lactate, pH, BE, WBC, PCR, LDH. The end point was mortality in PICU, outcome 2 and 6 months after dimission. The data were analysed with Microsoft Excel 7.0 and Statview McIntosh statistical software: Student's *t* test ($P<0.05$) (*), Mann–Whitney test ($P<0.05$) (**), Fisher's exact *t* test ($P<0.05$) (***).

Results: Enrolled patients were divided into two subgroups: deaths ($n=10$ [D]) and survivors ($n=12$ [S]). Mortality in the PICU was 45%. Eighty per cent of survivors were still alive 6 months later.

The following parameters are statistically different in the studied subgroups: lactate, LDH, mSOFA total, mSOFA coagulation. Lactate (cutoff 3 mmol/l), and mSOFA total (cutoff ≥5) were correlated with mortality on admission and in all observations ($P<0.001$ Fisher's exact test). There were no other differences between the two subgroups.

Conclusion The study suggest that the early evaluation of total mSOFA, lactates and LDH can be used to identify infants with severe CAP at elevated risk of death.

References

1. Bernard GR, Artigas A, Brigham K, *et al.*: **The American European Consensus Conference on ARDS: definitions, mechanism, relevant outcome and clinical trial coordination.** *Am J Respir Crit Care Med* 1994, **149**:818-824.
2. Shime N, Kageyama K, *et al.*: **Application of modified sequential organ failure assessement score in children after cardiac surgery.** *J Cardiothorac Vasc Anaesth* 2001, **15**:463-468.

P140 Glucose in airway secretions and an association with the presence of *Staphylococcus aureus* in the respiratory tract

J Redman[1], G Maloney[1], E Baker[2], BJ Philips[3]
[1]Department of Intensive Care, St George's Hospital, Blackshaw Road, London SW17 0QT, UK; [2]Department of Physiological Medicine and [3]Department of Anaesthesia and Intensive Care Medicine, St George's Hospital Medical School, Jenner Wing, Cranmer Terrace, London SW17 0RE, UK
Critical Care 2003, **7(Suppl 2)**:P140 (DOI 10.1186/cc2029)

Good glycemic control has been shown to decrease mortality in critically ill patients [1], the predominant effect being a decrease in the incidence of serious infection. Glucose is normally absent from airway surface liquid [2], which may be important to host defenses against infection. Glucose in endotracheal secretions has been attributed to the aspiration of enteral feed [3]. Previously we have found this to be false and that glucose appears in the airway secondary to hyperglycemia. We hypothesize that glucose in airway secretions increases the risk of bacterial airway infections. Our objectives were to observe for relationships between hyperglycemia and the presence of glucose and bacteria in airway secretions.

Methods and results One hundred critically ill, ventilated patients admitted to a general (medical and surgical) adult intensive care were recruited. Glucose concentrations were measured simultaneously in arterial blood (ABL2000; Radiometer, Copenhagen, Denmark) and endotracheal (ET) secretions (glucose oxidase sticks and GM9D Analyzer; Analox, London, UK). Sputum samples were sent for qualitative microscopy and culture. All patients were enterally fed, unless clinically contraindicated.

Of 100 patients, 89 had microbiology results returned. Fifty-four of 100 had glucose detected in their ET secretions (>0.5 mmol/l). Patients with ET glucose had a significantly higher blood glucose (8.82 ± 0.31) than those without (6.69 ± 0.23, $P=0.004$); this was unrelated to enteral feeding. Significantly more patients with ET glucose had *Staphylococcus aureus* detected in their sputum (33/49 vs 10/40, $P=0.007$). Table 1 presents the results for sensitive *S. aureus* and methicillin-resistant *S. aureus* (MRSA).

Table 1

Microbiology results

	Positive for ET glucose	Negative for ET glucose	Significance *P* (χ^2 test)
Total number of patients	49	40	
Sensitive *S. aureus*	8	0	0.007
MRSA	25	10	0.017
Total	33	10	< 0.0001

Comment Glucose appears in airway secretions and is associated with hyperglycemia. It is not related to enteral feeding. Possible mechanisms include saturation of airway epithelial sodium glucose cotransporters, or increased epithelial permeability. Glucose in airway secretions is strongly associated with *S. aureus* infection (Table 1). This may be one mechanism by which control of glucose decreases infectious complications.

References

1. van den Berghe G, Wouters P, Weekers F, Verwaest C, Bruyninckx F, Schetz M, Vlasselaers D, Ferdinande P, Lauwers P, Bouillon R: **Intensive insulin therapy in the surgical intensive care unit.** *N Engl J Med* 2001, **345**:1359-1367.
2. Barker PM, Boyd CA, Ramsden CA, Strang LB, Walters DV: **Pulmonary glucose transport in the fetal sheep.** *J Physiol* 1989, **409**:15-27.
3. Winterbauer RH, Durning RB Jr, Barron E, McFadden MC: **Aspirated nasogastric feeding solution detected by glucose strips.** *Ann Intern Med* 1981, **95**:67-68.

P141 Pulmonary infection in brain-injured patients

P Pelosi[1], G Apostolou[1], B Gomiero[1], S Cominotti[1], P Severgnini[1], E Lucchini[1], R Colombo[1], G LiBassi[2], M Chiaranda[1]
[1]Department of Clinical and Biological Sciences, University of Insubria, Varese-Circolo and Fondazione Macchi Hospital, Varese, Italy; [2]Institute of Anesthesia and Intensive Care, Policlinico Hospital – IRCCS, Milan, Italy
Critical Care 2003, **7(Suppl 2)**:P141 (DOI 10.1186/cc2030)

Background and goal of study Brain-injured patients are characterized by an increased risk to develop respiratory failure due to pneumonia, incidence of which is estimated at around 30–50% [1]. The aim of this study was to analyze in brain-injured patients during mechanical ventilation: 1) the incidence of pulmonary infection (P.I.), diagnosed by cultural data of bronchoalveolar lavage ($>10^4$ cfu/ml); 2) predisponent factors of P.I.; 3) the prevalence of sepsis and severe sepsis criteria [2]; 4) the association with morphological alterations of chest X-ray, respiratory failure (PaO_2/FiO_2 <200 mmHg), presence of tracheobronchial secretions; 5) the association with leucocyte count and core temperature; 6) peripheral organ failure, evaluated by SOFA score.

Material and methods In this study we prospectively analyzed 60 brain-injured patients (sex M/F, 40/20; age, 43 ± 20 years; BMI, 24.5 ± 2.7 kg/m^2; trauma/not trauma, 23/37; GCS, 9 ± 3) during mechanical ventilation.

Results and discussion Results are specified in Tables 1 and 2.

Conclusions In brain-injured patients, during mechanical ventilation: 1) 48% of patients developed P.I.; 2) GCS at entry seems to be the principal risk factor of P.I.; 3) 48.4% of patients without P.I. developed signs of SIRS + cathecolamines need; 4) the chest X-ray of 96.5% of patients with P.I. was modified, associated with severe hypoxiemia in the 58% of cases; 5) 40–50% of patients without P.I. showed alterations of the leukocyte count and of the secretions; 6) peripheral organ failures (renal, cardiac, hepatic) are infrequent.

References
1. Ewig S, *et al.*: *Am J Respir Crit Care Med* 1999, **159**:188-198.
2. American College of Chest Physicians/Society of Critical Care Medicine Consensus Conference: *Crit Care Med* 1992, **20**:864-874.

Table 1

	Number of patients	GCS at entry	SIRS	Sepsis	Septic shock	SIRS + cathecol
BAL+	29	7.8 ± 3.7	0%	44.8%	55.1%	0%
BAL–	31	10.5 ± 3.8	48.4%	0%	0%	25.8%
P		<0.05	<0.01	<0.01	<0.01	<0.01

Table 2

	Altered chest X-ray	$PaO_2/FiO_2<200$	Secretions	Leucocyte count $>12{,}000$ or <4000	Temperature >38°C or <36°C
BAL+	96.5%	58.6%	89.6%	79.3%	86.2%
BAL–	3.2%	9.6%	51.6%	54.8%	25.8%
P	<0.01	<0.01	<0.01	<0.05	<0.01

P142 Nosocomial pneumonia mortality according to antibiotic sensibility of the microorganism responsible

L Lorente, R Galvan, MM Martín, J Málaga, C García, ML Mora
Department of Intensive Care, Hospital Universitario de Canarias, Tenerife, Spain
Critical Care 2003, **7(Suppl 2)**:P142 (DOI 10.1186/cc2031)

Objective To analyze the mortality of ventilator-asociated pneumonia (VAP) produced for a potential multiresistant microorganism (PMRM) according to antibiotic sensibility of the microorganisms responsible.

Methods It is a prospective study of patients admitted in the ICU from 1 May 2000 until 31 August 2002 and who developed VAP produced for a PMRM (*Staphylococcus aureus*, *Pseudomonas aeruginosa*, *Stenotrophomona maltofilia*, Acinetobacter). The statistical analysis was realized by chi-square test and Student *t* test, and we took values $P<0.05$ to consider a significant difference.

Results In the study period, 1389 patients were admitted. We documented 66 VAP for a PMRM. VAP mortality for MSSA versus MRSA was 27.77% (5/18) and 14.28% (2/14) ($P=0.35$). VAP mortality for a Gram-negative bacilli PMRP was analyzed according to the sensitivity to four antibiotics (piperacillin–tazobactam, ceftazidime, imipenem and ciprofloxacin). VAP mortality for *P. aeruginosa* with 0–1 antibiotic resistances versus 2–4 antibiotic resistances was 2/22 (9.09%) and 2/4 (50%) ($P=0.03$). VAP mortality for *S. maltofilia* with 0–2 antibiotic resistances versus 3–4 antibiotic resistances was 0/2 (0%) and 2/2 (100%) ($P=0.04$). VAP mortality for Acinetobacter with 0 antibiotic resistances

versus 1–4 antibiotic resistances was 0/2 (0%) and 1/2 (50%) ($P=0.24$).

Conclusions In our series, the VAP mortality for *P. aeruginosa* and *S. maltofilia* was different according to antibiotic sensibility, but not when it was due to *S. aureus* and Acinetobacter.

P143 Empiric antibiotic therapy for ventilator-associated pneumonia: a systematic review of the evidence

MW Aarts[1], JN Hancock[2], DK Heyland[2], JC Marshall[1]
[1]Toronto University, Toronto, Canada; [2]Queen's University, Kingston, Canada
Critical Care 2003, **7(Suppl 2)**:P143 (DOI 10.1186/cc2032)

Introduction Ventilator-associated pneumonia (VAP) is associated with significant morbidity and mortality. Several published guidelines recommend early and broad-spectrum empiric therapy for patients with a suspicion of VAP; however, uncertainty exists regarding the indications for and selection of appropriate agents.

Methods To determine whether evidence exists to support the use of a particular parenteral regimen in the empiric treatment of VAP, we conducted a systematic review of the literature for all randomized controlled trials (RCTs) from 1966 to November 2002. Two authors (MWA and JNH) independently searched MEDLINE, EMBASE, the Cochrane Controlled Trials Register library, and the bibliographies of all reviews, for RCTs. Experts in the field and all authors of trials included in this review were contacted to identify unpublished trials. Data were abstracted and trial quality was assessed independently by the two review groups. Additional information was sought when necessary from the corresponding authors of the retrieved trials. Trials comparing similar antibiotic strategies were pooled, and the risk difference and relative risk were reported for the outcomes of mortality, clinical response, superinfections and adverse events.

Results In the 33 trials identified, a total of 5049 patients were enrolled; 73.0% were ventilated, 65.1% had microbiological evidence of infection, 17.7% had *P. aeruginosa* isolated from one or more cultures; and the overall mortality rate was 20.5% (922/4492). No trials with a placebo arm were identified; however, 24 different comparisons were evaluated involving 27 unique antibiotic regimens (13 monotherapies, 14 combination therapies). The sample size of trials ranged from 32 to 400 patients. In every trial the primary objective was to evaluate equivalence as opposed to superiority, and no trials were sufficiently powered to determine a difference of 10% or less between groups. The overall quality of the 33 trials was very low; randomization was concealed in only 10, followup was complete in only eight, an intention-to-treat (ITT) analysis was completed in 18, detection of the outcome was blinded in 10, and a double-blinded strategy was employed in only three. All-cause mortality did not significantly differ between treatment groups for any individual trials or when data was pooled. When evaluating clinical response, a significant benefit was demonstrated with amikacin/ceftazidime versus pefloxacin/ceftazidime, risk difference (RD) = 20% (95% CI, 4–36%), in a single low-quality trial. With pooling of trials a significant benefit was also demonstrated with meropenem versus the combination ceftazidime/amikacin, RD = 13% (4–22%); and aztreonam versus an aminoglycoside, RD = 25% (4–45%).

Conclusions There is some evidence to suggest that choice of parenteral empiric antibiotic therapy for VAP may influence outcome, although study design limitations preclude strong recommendations regarding the optimal choice of therapy. There is no proven beneficial empiric therapy for which to compare alternate regimens; and no trials have ever evaluated the utility of empiric therapy versus a strategy of delayed directed therapy based on culture results.

P144 Impact of ventilator-associated tracheobronchitis on outcome in patients with chronic obstructive pulmonary disease

S Nseir[1], C Di Pompeo[2], S Soubrier[1], P Pronnier[1], T Onimus[1], F Saulnier[1,2], A Durocher[1,2]
[1]ICU, Calmette Hospital, CHRU, bd du Pr Leclercq, 59037 Lille cedex, France; [2]Medical Assessment Laboratory, Lille II University, Lille, France
Critical Care 2003, **7(Suppl 2)**:P144 (DOI 10.1186/cc2033)

Background In the absence of nosocomial pneumonia (NP), ventilator-associated tracheobronchitis (VAT) may generate weaning difficulties in patients with chronic obstructive pulmonary disease (COPD), resulting in longer duration of mechanical ventilation (MV) and intensive care unit (ICU) stay. The aim of our study is to test this hypothesis.

Methods A prospective matched risk-adjusted cohort study, in a 30-bed ICU, over a period of 6.5 years. Immunocompetent medical COPD patients who were intubated and ventilated for >48 hours were eligible. All patients with NP were excluded. Tracheobronchitis was defined as follows: fever (>38°C) with no other recognizable cause; new or increased sputum production, and a positive ($\geq 10^6$ cfu/ml) endotracheal aspirate culture, yielding a new bacterial strain; without radiographic evidence of pneumonia. Only first episodes of VAT occurring after >48 hours of MV were included. A matching process was conducted according to the following criteria: MV duration before the occurrence of VAT, primary diagnosis for admission, indication for MV, SAPS II on admission ±5, age ±5, and date of admission. McNemar's test and the Wilcoxon log-rank test were used to compare cases with controls. Univariate and multivariate analyses were performed in order to determine variables associated with longer than median MV duration among case and control patients.

Results A total of 1259 patients were eligible; 128 (10%) of them were excluded for NP. VAT was diagnosed in 103 (8%) patients; 11 (10.6%) of them were excluded for subsequent NP. Matching was successful for 88% of the cohort; 81 matched case–control pairs were studied. Acute exacerbation of COPD was the main cause for admission (64%). *P. aeruginosa* was the most common causing bacteria (27%). Although the mortality rate was similar (40% vs 34%; P = NS), the median duration of MV (20 days vs 12 days; $P=0.015$) and ICU stay (25 days vs 18 days; $P=0.022$) were higher in cases than in controls. VAT was the only variable independently associated with longer than median duration of MV (OR = 4.7 [95% CI = 2–10.9]; $P<0.001$). In patients with VAT, antibiotics were associated with shorter median duration of MV (15 days vs 23 days; $P=0.043$), and ICU stay (23 days vs 29 days; $P=0.007$) and similar mortality rate (40% vs 41%,

P=NS). Appropriate antimicrobial treatment was associated with a tendency towards a better outcome.

Conclusion VAT is associated with increased duration of MV and ICU stay in COPD patients. Antibiotics are associated with shorter length of MV and ICU stay in patients with VAT. Further studies are required to confirm our results.

P145 Ventilator-associated pneumonia in intubated children: comparison of different diagnostic methods

F Gauvin, C Dassa, M Chaïbou, F Proulx, CA Farrell, J Lacroix
Division of Pediatric Intensive Care, Department of Pediatrics, Sainte-Justine Hospital, 3175 Côte Ste-Catherine, Montréal, Canada, H3T 1C5
Critical Care 2003, **7(Suppl 2)**:P145 (DOI 10.1186/cc2034)

Introduction The best method for diagnosis of ventilator-associated pneumonia (VAP) in children is much debated. Clinical criteria alone may not be sufficiently reliable. Bronchoscopic techniques are not routinely used. Blind (nonbronchoscopic) protected bronchoalveolar lavage (BAL) has been studied in pediatrics but has never been validated according to the gold standard (autopsy).

Objective To compare different diagnostic methods of VAP in children, using clinical judgment of an adjudicating committee of experts as the reference standard.

Methods *Setting* Prospective study of all consecutive PICU patients <18 years with suspected VAP.

Diagnostic methods compared 1) clinical data using Centers for Disease Control (CDC) criteria; 2) blind protected BAL, evaluating quantitative cultures, bacterial index, Gram stain and presence of intracellular bacteria; 3) nonquantitative cultures of endotracheal secretions.

Reference standard Consensus of three independent experts (Delphi method) who retrospectively established the presence of VAP based on clinical, microbiological and radiological data.

Analysis Concordance between each diagnostic method and the reference standard was evaluated by concordance percentage and kappa score. Validity was evaluated using sensitivity, specificity and global value.

Results Thirty patients were included in the study. According to the reference standard, VAP occured in 10/30 patients (33%). Concordance and validity of the different methods are presented in Table 1.

Conclusion Our data show that the most reliable diagnostic method for VAP is a bacterial index >5. Further studies should evaluate the validity of all these methods according to the gold standard (autopsy).

Table 1

Diagnostic method	Number of patients with positive results (*n*/30)	Concordance with reference standard (%)	Kappa score	Sensitivity (%)	Specificity (%)	Global value (%)
Clinical criteria (CDC)	28	43	0.11	100	15	43
BAL						
Culture ≥ 10^2 CFU/ml	14	67	0.32	70	65	67
Culture ≥ 10^3 CFU/ml	11	70	0.34	60	75	70
Culture ≥ 10^4 CFU/ml	9	70	0.31	50	80	70
Culture ≥ 10^5 CFU/ml	6	67	0.17	30	85	67
Intracellular bacteria	4	73	0.29	30	95	73
Gram stain	9	70	0.31	50	81	73
Bacterial index > 5	9	83	0.61	78	86	90
Endotracheal culture	21	57	0.24	90	40	57

P146 The complications associated with mechanical ventilation

L Dosemeci, M Yilmaz, G Celikbilek, R Yagmur, A Ramazanoglu
Burhanettin Onat Cad., 1425 sok. 8/19, 07070 Antalya, Turkey
Critical Care 2003, **7(Suppl 2)**:P146 (DOI 10.1186/cc2035)

Objective Although mechanical ventilation (MV) of critically ill patients may be life saving, complications associated with MV occur commonly. In this prospective study, we investigated the complications of the MV including injuries to the airway due to intubations and/or tracheostomy, self-extubation, nosocomial pneumonia (NP), and barotrauma. Furthermore, we noted the duration of MV and prognosis of the patients with and without NP.

Materials and methods Fifty-five patients who required MV for more than 48 hours in our ICU during a 6 month period were included in the study. Patients who had pneumonic infiltration at admission and/or underwent ventilatory therapy in other hospitals were excluded from the study. The patients were daily evaluated in terms of the complications of MV. Age, Glasgow Coma Scala (GCS) score, APACHE II score, risk factors, duration of MV and

prognosis of the patients were recorded daily. The nurse-to-patient ratio was 1:4 in our ICU.

Results The average age, GCS score, APACHE II score, and MV duration were 47.2 ± 20.9 years, 8.2 ± 4.1, 17.8 ± 5.7 and 15.0 ± 11.2 days, respectively. In 23 patients (41.8%) NP was diagnosed, and the NP/ventilation day ratio was 23/836 (27.5/1000). The mean MV duration in patients with or without NP was 20.4 ± 12.8 and 11.2 ± 8.1 days, respectively ($P < 0.05$). The mortality rate was 34.8% in the pneumonia group and 18.8% in the nonpneumonia group ($P > 0.05$). Barotrauma related to MV (pneumomediastinum and subcutaneus amphisema) was observed in two patients, and the other complications including larengeal edema, cuff leak, self-extubation and right main bronchial intubation were seen in 13 patients.

Conclusions The incidence of NP and other complications determined in this study was comparable with previous studies reported in the literature [1]. The mortality rate of the patients with NP was found to be higher than the patients without NP, but the difference was not statistically significant. The duration of MV in the pneumonia group was significantly higher than the nonpneumonia group.

Reference

1. Torres a, *et al.: Am Rev Respir Dis* 1990, **142**:523-528.

P147 A comparison of the frequency of aspiration pneumonia in three groups, receiving sucralfate, receiving ranitidine and control group, in Khatam-Ol-Anbia hospital ICU

M Nekooee, SK Nezam, O Rahati
Zahedan University of Medical Science, Zahedan, Iran
Critical Care 2003, **7(Suppl 2)**:P147 (DOI 10.1186/cc2036)

Summary Stress ulcer is one of the most common complications in ICU patients. Usually an H_2-blocker or sucralfate is used for prophylaxis. In the past decade, some investigators showed a decreased number of aspiration pneumonia in patients receiving sucralfate compared with receiving ranitidine or a control group.

Method During a 7 month course (October 2001–April 2002), 150 patients in the ICU were randomized to two 50 patients groups receiving sucalfate (1 g every 6 hours PO) and ranitidine (50 mg every 8 hours IV) and a control group. All patients were examined daily and, if needed, laboratory examinations or radiographs were requested for the diagnosis of aspiration pneumonia.

Results Aspiration pneumonia was observed in 13 patients in the sucralfate group, 15 patients in the ranitidine group and 10 patients in the control group. There was no significant difference between suralfate and ranitidine ($P = 0.65$), sucralfate and control ($P = 0.48$) or ranitidine and control ($P = 0.25$).

Also, the difference between three groups was not significant ($P = 0.51$).

Conclusion In this study no significant difference in the frequency of aspiration pneumonia was observed between sucralfate, ranitidine and control groups.

P148 Periodic change of ventilator circuits: an unnecessary cost

L Lorente[1], M Lecuona[2], C García[1], R Galvan[1], ML Mora[1], A Sierra[2]
[1]Department of Intensive Care and [2]Department of Microbiology, Hospital Universitario de Canarias, Tenerife, Spain
Critical Care 2003, **7(Suppl 2)**:P148 (DOI 10.1186/cc2037)

Objective To analyze the utility of periodic change of ventilator circuits (PCVC) to prevent the incidence of ventilator-associated pneumonia (VAP).

Methods It is a prospective study. Included were all patients admitted in the ICU from 1 April 2001 until 30 September 2002 and who required mechanical ventilation for 72 hours or more. At admission to the ICU patients were randomized in two groups: one group ventilated with PCVC each 48 hours, and another one without PCVC. A throat swab on admission and afterwards twice weekly were taken. Infections were diagnosed according to CDC criteria and classified bassed on throat flora in endogenous and exogenous. The statistical analysis was realized by chi-square test and Student *t* test, and we took values $P < 0.05$ to consider a significant difference.

Results Included were 304 patients (62.82% male). Mean age was 58.86 ± 18.24 years. APACHE II was 16.01 ± 7.26. Mortality was 32.23%. Both groups of patients (143 with PCVC and 161 without PCVC) were similar in age, sex, mortality and APACHE II. No significant differences were found in the percentage of patients who developed VAP (23.07% vs 22.98%), nor in the number of VAP per 1000 mechanical ventilation-days (20.27 vs 27.81). Neither in the percentage of patients who developed VAP and in the number of VAP per 1000 mechanical ventilation-days in each group of mechanical ventilation-days. Neither in the percentage of patients who developed exogenous VAP (2.79% vs 2.48%), neither in the number of exogenous VAP per 1000 mechanical ventilation-days (1.71 vs 1.09).

Conclusions In our series, the periodic change of ventilator circuits did not reduce the incidence of VAP nor was VAP exogenous.

P149 Ventilator-associated pneumonia with a closed versus an open endotracheal suction system

L Lorente[1], M Lecuona[2], MJ Palomo[1], D Delgado[1], T Mohr[1], ML Mora[1]
[1]Department of Intensive Care and [2]Department of Microbiology, Hospital Universitario de Canarias, Tenerife, Spain
Critical Care 2003, **7(Suppl 2)**:P149 (DOI 10.1186/cc2038)

Objective To analyze the incidence of ventilator-associated pneumonia with a closed endotracheal suction system (CESS) versus an open system (OESS).

Methods It is a prospective study during 3 months. Included were all patients who required mechanical ventilation for 12 hours or more. At admission to the ICU patients were randomized in two groups: one

group was suctioned with CESS, and another group with OESS. Infections were diagnosed according to CDC criteria. The statistical analysis was realized by chi-square test and Student *t* test, and we took values $P<0.05$ to consider a significant difference.

Results Included were 121 patients (64% male). Mean age was 57.68 ± 16.90 years, APACHE II was 14.40 ± 6.25. Mortality was 14.85%. Patient distribution was: 50% cardiac surgery, 9% cardiologic, 7% respiratory, 4% digestive, 10% neurologic, 11% traumathology, 3% intoxication, 6% abdominal sepsis. Both groups of patients (58 with CESS and 63 with OESS) were similar in age, sex, diagnosis groups, mortality and APACHE II. No significant differences were found in the percentage of patients who developed ventilator-associated pneumonia (13.79% vs 14.28%), nor in the number of ventilator-associated pneumonia per 1000 mechanical ventilation-days (15.85 vs 16.12).

Conclusions In our series, a closed endotracheal suction system did not reduce significantly the ventilator-associated pneumonia incidence.

P150 Comperative clinical trial of translaryngeal tracheostomy and forceps dilatational tracheostomy

K Kokkinis, T Vrettos, P Manolopoulou, A Lefkaditi, A Tragou, A Zbouki
Anesthesiology/General Hospital of Aigio – ICU/University Hospital of Patras, Greece
Critical Care 2003, **7(Suppl 2)**:P150 (DOI 10.1186/cc2039)

Introduction Percutaneous tracheostomy is a well-established technique in the ICU setting. The methods described by Ciaglia *et al*. and by Griggs *et al*. are the most popular and have been advocated by many authors. Translaryngeal tracheostomy (TLT) according to Fantoni and Ripamonti was initially introduced in 1997. The aim of the present study was to assess the difficulties and complications of TLT and forceps dilatational tracheostomy (FDT) in critically ill patients.

Methods Sixty patients were randomized to undergo TLT or FDT. The techniques as described by Griggs and Fantoni were followed with the use of commercially available kits. Statistical analysis was performed using the Student *t* test. At the end, tracheal injury was assessed by endoscopy.

Results There were no significant statistical differences regarding the age, sex, Apache II score or the endotracheal intubation between the two groups. Table 1 summarizes the perioperative complications and duration of TLT and FDT.

Table 1

	TLT	FDT	*P* value
Hemorrhage minor	0	1	NS
Difficult cannula insertion	1	0	NS
Cuff damage	0	2	NS
Duration of procedure (min)	17 ± 2.5	6 ± 2	< 0.0001
Posterior tracheal wall injury	0	1	NS
Paramedical tube insertion	0	1	NS
Total	1	5	

NS, nonsignificant.

Conclusion Based on our data we conclude that TLT represents an equally safe percutaneous technique as FDT and is also an attractive alternative in long-term airway access in critically ill patients.

P151 Dilatation tracheostomy under visual control

D Nalos, R Splechtna, L Pokorny, E Huskova
Critical Care Unit, Masaryk Hospital, Ustí nad Labem, Czech Republic
Critical Care 2003, **7(Suppl 2)**:P151 (DOI 10.1186/cc2040)

Introduction In our ICU we use modified bedside operative tracheostomy. The operation consists of consecutive blunt dilatation of all tissular structures above the trachea with the aim of denudating it. After that we execute a small incision of the trachea between the second and the third annulus, dilatation of trachea and insertion of a tracheostomy cannula with the possibility of an adjustment tracheal aperture. There is no need for ligation of the thyroideal isthmus or resection of the tracheal cartilage.

The aim of this study was to compare our method with surgical tracheostomy (ST) and percutaneous dilation tracheostomy (PDT-Ciaglia) for early and long-term complications.

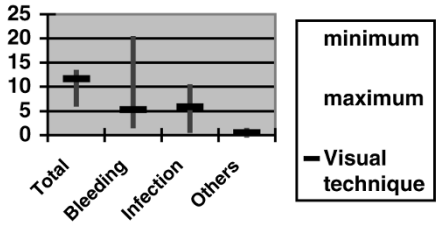
Method The group of 205 patients with tracheostomy was included in our observation (hospitalized 1997–2001 in our ICU) without exceptions (basic diagnosis, indication of tracheostomy, anatomical conditions and other risk factors to the results of the operation). Data of long-term complications were gained from a questionnaire. Data of ST and PDT were taken from medical literature. Descriptive statistical methods and the Student *t* test were used to analyze the data.

Results Results in percent of complications are graphically demonstrated in Figs 1–3.

The total complication rate for our method was found to be 11.7%. Incidence of bleeding (perioperative and postoperative) was 5.3%. There was no need for use of transfusions. Infectious complications were 5.9%. Other complications including pneumothorax, pneumomediastinum, subcutaneus emphysema and other minor complications were 0.5%.

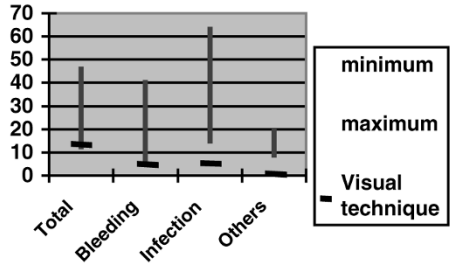
The total number of patients who were discharged from our hospital was 67. Rate of return of the questionnaire was 46%. Long-term complications were: none of the patients developed laryngotracheal stenosis, cosmetic difficulties with cicatrice (23%), voice changes (15%), and dysphagia (8%).

Figure 1



Comparison of early complications of the visual technique with PDT.

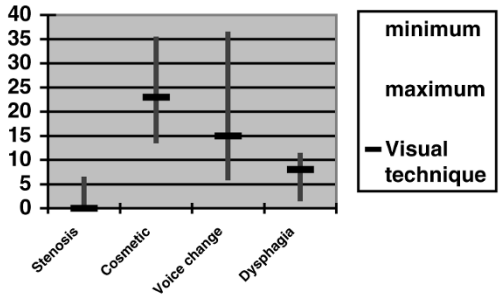
Figure 2



Comparison of early complications of the visual technique with ST.

Conclusions Our method of tracheostomy can be an accepted procedure for airway access. The rate of complications is comparable with other methods (PDT, ST). There are also important differences in costs. The cost of the described method is one-third of the cost of PDT in Czech conditions. Prospective randomized studies are necessary to compare the late complications of these reported techniques.

Figure 3



Comparison of long-term complications of the visual technique with PDT.

P152 Complication rates of percutaneous tracheostomy in the intensive care unit

M Kuper, C Theaker, N Soni
Chelsea and Westminster Hospital, 369 Fulham Road, London SW10 9NH, UK
Critical Care 2003, **7(Suppl 2)**:P152 (DOI 10.1186/cc2041)

Since complication rates from clinical trials may not reflect those obtained in practice we report the prospectively audited complication rates from the 201 percutaneous tracheostomies performed on the intensive care unit at the Chelsea and Westminster Hospital, London between 6 March 1997 and 3 December 2002. All were performed under anaesthetic consultant supervision, and bronchoscopic confirmation of tracheostomy position and complications was utilised.

Of the 201 tracheostomy patients, 28 patients had complications; an incidence of 13.9%. Comparing the patients who suffered complications with those who did not, their median admission APACHE was worse (25 vs 21) and more died in intensive care (40% vs 19%) although length of stay was similar (26 days vs 25 days). There was a highly significant sex difference in the incidence of complications; for males the complication incidence was 6.3% (seven of 111 patients), whereas for females the complication incidence was 23.3% (21 of 90 patients), $P=0.0005$.

Serious complications occurred in 15 patients, an incidence of 7.4%. Surgical intervention was required in four patients, two for major early bleeding and two for major late bleeding. There was one arrest secondary to respiratory obstruction by blood clot but no tracheostomy-associated mortality.

Three different insertion methods were used, without randomisation; Griggs' forceps (Portex, NH, USA) in 65 patients, Ciaglia sequential dilators (Cook, IN, USA) in 87 patients, and single tapered dilators in 49 patients (from Cook in 31 patients and from Portex in 18 patients). Comparing the different insertion methods, the incidence of complications was 11 of 65 patients or 17% with Griggs' forceps, 14 of 87 patients or 16% with sequential dilators, and three of 49 patients or 6% with a single tapered dilator, although differences were not significant.

In summary, we report a serious complication rate of 7.4% in 201 percutaneous tracheostomies performed on the Chelsea and Westminster intensive care unit, with no mortality. We found a lower incidence of complications using the single tapered dilator methods for tracheostomy insertion, as opposed to Griggs' forceps or sequential dilators, although differences did not reach statistical significance. We also found a highly significant association of complications with female sex.

P153 Complications during tracheal intubation and percutaneus dilatational tracheostomy in the ICU

St Aloizos, P Aravosita, M Eforakopoulou, P Tzavaras, H Loannidou, S Karatzas, G Baltopoulos
Athens University School of Nursing ICU and A ICU Department, KAT Hospital, Athens, Greece
Critical Care 2003, **7(Suppl 2)**:P153 (DOI 10.1186/cc2042)

Objective This study investigates the immediate complications and adverse consequences of endotracheal intubation (ETI) and bedside percutaneus dilatational tracheostomy (PDT) performed in ICU patients.

Design Prospective observational study.

Setting Two 15-bed general ICU units in a 600-bed general hospital.

Subjects All ETI and PDT that were carried out in our ICUs, over a period of 6 months, were studied prospectively. The procedures were performed by skilled ICU attending physicians or by supervised residents. Complications and adverse consequences, which occurred during the procedures, were recorded, as well as sedatives, muscle relaxants and any other drug used, according to a previously approved protocol.

Results One hundred and forty-two ETI and 54 PDT were carried out successfully. Complications occurred in 41% of ETI and 33% of PDT cases. Major ETI complications including difficult or esophageal intubation, aspiration, desaturation of hemoglobin and severe hypotention, were recorded in 34.5% of cases. Local injury and transient hypotention occurred in 9% of cases. Severe complications (bleeding, false passage of tracheostomy tube, desaturation of hemoglobin, severe hypotention) occurred in 15% of PDT cases. Minor complications that are false or difficult passage of the guide wire and puncture of the ET tube were noted in 19% of cases. No difference was recorded in the incidence of complications regardless of whether the procedure was performed by the attending physicians or the supervised residents.The only incidence that was statistically higher in the ETI group ($P<0.01329$, χ^2 test) was desaturation. Also no significant differences were recorded between the groups treated with different sedatives and analgesics.

Conclusions 1) Adverse consequences and complications commonly happen in the ICU during ETI and PDT. 2) ETI and PDT can be safely performed by supervised residents.

P154 Survey of airway management in intensive care units in the UK

R Raobaikady[1], G McAnulty[2]
[1]St Heleir Hospital, Carshaltan, London SM5 1AA, UK; [2]St George's Hospital, Tooting, London SW17 0QT, UK
Critical Care 2003, **7(Suppl 2)**:P154 (DOI 10.1186/cc2043)

Background Guidelines for minimum standards of monitoring in the anaesthetic room and operating theatres are now part of standard anaesthetic practice throughout the UK. Manipulation of the airway, including tracheal intubation and percutaneous tracheostomies, is a common undertaking in the intensive care unit (ICU). Critically ill patients can pose specific technical difficulties during tracheal intubation. There is no accepted minimum standard of monitoring for procedures involving manipulation of the airway in UK ICUs. We surveyed monitoring practices used for the confirmation of tracheal tube placement during tracheal intubation and percutaneous tracheostomy.

Methods Anonymous questionnaires were sent to the clinical directors of randomly selected general adult ICUs across the UK.

Results One hundred and thirty-six replies were received out of 200 questionnaires sent (response rate 68%). The majority (73%) of tracheal intubations were performed by trainee anaesthetists. Only 14% of the ICUs always used end-tidal carbon dioxide ($F_{\acute{E}}CO_2$) monitoring during tracheal intubation. Twenty-five per cent of the ICUs did not have a $F_{\acute{E}}CO_2$ monitor. Eighty-nine per cent of the ICUs routinely performed percutaneous tracheostomy. Sixty-seven per cent of the ICUs used fibreoptic bronchoscopy to confirm tracheostomy tube position, 7% used $F_{\acute{E}}CO_2$ monitoring alone. Seventeen per cent of the ICUs used both. Nine per cent of ICUs relied on clinical signs alone to confirm tracheostomy tube placement. Nearly one-half of the respondents from ICUs without a $F_{\acute{E}}CO_2$ monitor cited lack of resources as one of the reasons for not routinely using this monitoring parameter.

Conclusions Most tracheal intubations in ICUs are performed by trainee anaesthetists, and percutaneous tracheostomy is a widely accepted practice in the UK. Although 75% of units had a $F_{\acute{E}}CO_2$ monitor, only a small proportion of intensivists used it to confirm correct placement of the tracheal tube after intubation and percutaneous tracheostomy.

P155 Relationship between absolute humidity of inspired and expired gases with an active humidifier

P Pelosi[1], P Severgnini[1], E Bianchi[1], R Terzi[1], C Lanza[1], G Minoja[1], D Chiumello[2], E Storelli[2], M Chiaranda[1]
[1]Department of Clinical and Biological Sciences, University of Insubria, Varese-Circolo and Fondazione Macchi Hospital, Varese, Italy; [2]Institute of Anesthesia and Intensive Care, Policlinico Hospital – IRCCS, Milan, Italy
Critical Care 2003, **7(Suppl 2)**:P155 (DOI 10.1186/cc2044)

Background and goals To evaluate the relationship between absolute humidity of inspired (AHi) and expired gases (AHe) during mechanical ventilation using a hot water humidifier (ConchathermIII®).

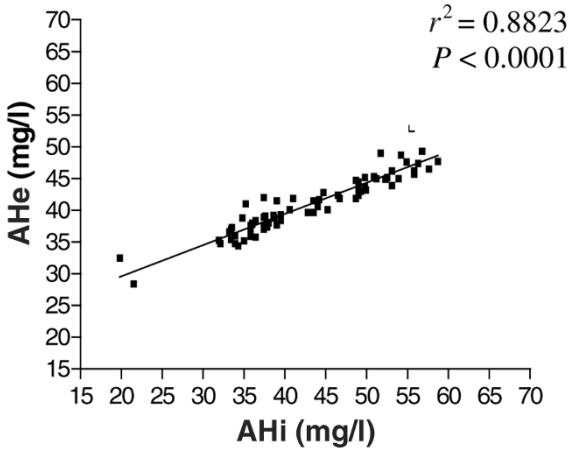
Materials and methods We measured the absolute humidity (AHi) and relative humidity (RHi) of inspired and expired gases in 40 sedated and paralyzed patients (mean age 60.7 ± 16.9 years). The AHi and AHe was measured using a psycrometer (Yoko-

gawa®). The airflow was separated by a flow separator placed between the Y piece of the ventilator circuit and the catheter mouth. The psycrometer is made of four thermic probes, two of them measure the dry temperature and two of them, covered with a cotton gauze (wet with physiological solution 15 min before every measurement), measure the wet temperature. Dry and wet temperatures were measured on the inspiratory and expiratory lines at the flows separator. We set the active humidifier at 31, 34, 36 and 38°C, and the measurements were made after 30 min for each temperature.

Results The relationship between AHi and AHe are shown in Fig. 1.

Conclusions 1) AHi is related to AHe (AHi > 38.8 mg/l, positive airway fluid balance; AHi < 38.8 mg/l, negative airway fluid balance). 2) We suggest an AHi of 38.8 mg/l (RHi 100%) with a temperature of 34°C during mechanical ventilation to maintain adequate airway conditioning.

Figure 1



P156 Use of the ProSeal Laryngeal Mask to protect the airway from methylene blue dye

J Miller, M Mercer
Department of Anaesthesia, Torbay District General Hospital, Lawes Bridge, Torquay TQ2 7AA, UK
Critical Care 2003, **7(Suppl 2)**:P156 (DOI 10.1186/cc2045)

Introduction In the trauma patient tracheal soiling is usually from the upper airway [1]. Although the ProSeal Laryngeal Mask Airway (LMA) gives a better seal pressure than the standard LMA [2] and is designed to prevent inadvertent gastric insufflation, and thus should reduce aspiration of gastric contents, its ability to protect the airway from material already in the mouth has not been formally assessed.

Method After local ethics committee approval, 13 ASA 1 and 2, starved patients undergoing elective general anaesthesia gave informed consent. Only patients with grade 1 or 2 direct laryngoscopic views were included. At induction of anaesthesia, an appropriately sized ProSeal LMA was placed into the larynx and the cuff inflated. Ten millilitres of 0.1% methylene blue dye was instilled in the mouth. Full monitoring was used and adequate ventilation ensured throughout. At the end of surgery, or after a minimum of 10 min, all dye was suctioned away and the oral cavity dried with swabs. The ProSeal LMA was removed and the airway examined by direct laryngoscopy for dye staining. Other adverse events were also noted.

Results No dye was detected in the trachea of 10/13 (77%) patients. Two of 13 (15%) of the patients had significant blue staining of the vocal cords. One patient developed stridor following dye removal, prior to the ProSeal LMA removal, and the trachea was intubated for the remainder of the duration of surgery. There were no problems at extubation, and the trachea was free from dye.

Conclusions The ProSeal LMA failed to protect 2/13 (15%) of patients from aspiration of dye from the oral cavity. In the trauma setting blood and oral debris may therefore not be prevented from entering the airways. One of these failures may have occurred after patient movement; however, patient movement would be expected in the trauma situation.

References

1. Lockey DJ, Coats T, Parr MJA: **Aspiration in severe trauma: a prospective study.** *Anaesthesia* 1999, **54**:1097-1098.
2. Brain AIJ, Verghese C, Strube PJ: **The LMA ProSeal — a laryngeal mask with an oesophageal vent.** *Br J Anaesth* 2000, **84**:650-654.

P157 Heliox improves aerosol deposition and tidal volume in a model of acute airway obstruction

JB Fink[1], MZ Heramia[1], D Bathe[2], A Watson[2]
[1]Aerogen, Inc, 2071 Stierlin Ct, Mountain View, CA 94043, USA; [2]Datex-Ohmeda, Inc, Madison, WI, USA
Critical Care 2003, **7(Suppl 2)**:P157 (DOI 10.1186/cc2046)

Heliox has been reported to reduce work of breathing and to improve aerosol deposition in patients with acutely obstructed airways. We wanted to evaluate the effects of an aerosol delivery system (Aerogen, Inc, Mountain View, CA, USA) with a prototype heliox delivery system (Datex-Ohmeda, Inc, Madison, WI, USA) incorporating an electronic demand valve with an active exhalation valve, and its impact on aerosol deposition and tidal volume (V_t).

Methods Air and heliox (70% He, 30% O_2) were administered through a 60 inch coaxial circuit to an absolute filter and active servo test lung (IngMar) set to simulate spontaneous tidal ventilation (rate 20, V_t 500 ml). To simulate airway obstruction, fixed orifice resistors producing resistive pressures of 20 cmH_2O/l per s (Rp20) and 50 cmH_2O/l per s (Rp50) were placed between the distal end of the coaxial circuit and the filter. Three milliliters of 0.083% albuterol (Dey Labs) was aerosolized in an Aeroneb® Professional Nebulizer placed in the inspiratory limb of the circuit, at the outlet of the prototype heliox delivery device, with both gases and both resistors ($n = 3$ for each test). Drug was eluted from the filter and assayed to quantify deposition as a percent of the total dose. The delivered tidal volume was measured at the test lung.

Results Presented in Table 1.

Table 1

	Rp 20		Rp 50	
	Deposition (mean ± SD) (%)	Tidal volume (ml)	Deposition (mean ± SD) (%)	Tidal volume (ml)
Air	36.8 ± 1.9	410	32.2 ± 1.8	330
Heliox 70:30	47.8 ± 2.5*	535	44.3 ± 1.1*	430

* $P < 0.05$.

Both aerosol deposition and tidal volume were lower with the greater resistance of the Rp50 than with the Rp20. Compared with air, heliox increased tidal volume 30% with both resistors, while deposition increased 30% and 38% (with Rp20 and Rp50, respectively). We conclude that heliox administration improved both tidal volume and aerosol deposition in this *in vitro* model of airway obstruction.

P158 Inspiratory gas temperature in the endotracheal tube when ventilated with a heated humidifier

Y Fujino, A Uchiyama, E Miyoshi, T Mashimo, M Nishimura
Intensive Care Unit, Osaka University Hospital 2-15, Yamadaoka, Suita, Osaka 565-0871, Japan
Critical Care 2003, **7(Suppl 2)**:P158 (DOI 10.1186/cc2047)

International Organization of Standardization recommends that inspiratory gas should possess absolute humidity of more than 33 mg/l. In this study we measured the temperature in the endotracheal tube (ETT) with a hypothesis that actual temperature of inspiratory gas is lower than that set by heated humidifier resulting in an inadequate humidification.

Methods A lung model (TTL, Michigan Instruments) was ventilated using a PB840 ventilator (Puritan-Bennett) via an 8 mm ETT. A heated humidifier (MR290, Fisher & Paykel) was set in the inspiratory limb of a standard ventilator circuit with a target temperature of 37°C. The ventilator settings were: volume control mode, rate 10/min, PEEP 0 cmH_2O with various tidal volumes (V_T). The temperature of inspiratory gas was measured at 22 cm, 27 cm and 32 cm from the distal end of the ETT using a thin wire thermocouple thermometer.

Results Mean inspiratory temperatures (°C) are shown in Table 1.

Conclusion The actual mean inspiratory gas temperature was lower than the target temperature set by the humidifier, especially with low V_T, which may result in an inadequate humidification.

Table 1

V_T (ml)	300 ml	400 ml	500 ml	600 ml	700 ml
22 cm	28.9 ± 0.1	29.9 ± 0.1	31.8 ± 0.1	32.6 ± 0.0	32.5 ± 0.0
27 cm	30.6 ± 0.1	31.2 ± 0.1	31.8 ± 0.1	32.3 ± 0.2	32.2 ± 0.1
32 cm	32.5 ± 0.1	33.2 ± 0.2	33.7 ± 0.1	33.7 ± 0.0	34.2 ± 0.1

V_T, tidal volume (ml). Values expressed as mean ± standard deviation calculated from three breaths.

P159 Carbon dioxide monitoring during high-frequency jet ventilation for rigid bronchoscopy

T Principi[1], S Pantanetti[1], D Elisei[1], D Strovegli[1], S Gasparini[2], P Pelaia[1]
[1]Department of Anaesthesiology and Intensive Care, and [2]Department of Pneumology, University Hospital, via Conca 60100 Ancona, Italy
Critical Care 2003, **7(Suppl 2)**:P159 (DOI 10.1186/cc2048)

At present, high-frequency jet ventilation (HFJV) is a common and well-accepted method of ventilation during laser therapy performed using a rigid bronchoscope [1]. The ability of jet ventilation to maintain an adequate oxygenation and to provide an effective CO_2 elimination during operative procedures, allowing the bronchoscopist satisfactory operating conditions, is well known [2]. Oxygenation of the patient can be monitored in an easy way by means of a pulse oximetry (measurement of SpO_2); carbon dioxide monitoring is more difficult to evaluate and requires adequate equipment [3].

The aim of this study was to assess the reduction of transcutaneous CO_2 partial pressure, as an approximation for $PaCO_2$, measured by a new noninvasive technique at the ear lobe during progressive changes of the driving pressure (DP).

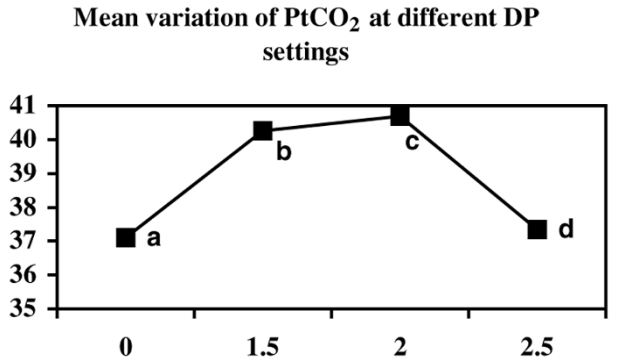
Methods After informed consent, 20 adult patients, scheduled for elective interventional rigid bronchoscopy, were enrolled. Patients undergoing broncoscopy for bronchial cancers involving the carena, post-intubation or post-tracheostomy malacia, and tracheobronchial stenoses were treated with laser therapy and/or tracheobronchial stent implantation. Total intravenous anaesthesia (TIVA) was conducted with propofol and fentanyl for induction and maintenance, and with rocuronium for muscle relaxation. HFJV was performed with a jet ventilator (Acutronic Medical Systems, Hiezel, Switzerland) via the rigid bronchoscope. A respiratory frequency of 120 cycles/min, an inspiratory duration of 40% and a fraction of inspired oxygen of 50% were set. During the procedure, DP was set at different levels (1.5, 2, 2.5 atm), on the basis of clinical evaluations and of intraoperative CO_2 monitoring. In addition to the

usual monitoring, all patients had a transcutaneous sensor in the ear lobe for the noninvasive measurement of arterial oxygen saturation and CO_2 partial pressure (TOSCA System; Linde Medical Instruments, Basel, Switzerland). $PtCO_2$ values were documented at various DP settings.

Results The results obtained (Fig. 1) show how the progressive increase of jet DP may avoid the rise of $PtCO_2$ during bronchoscopy. In particular, a DP of 2.5 atm ($P < 0.01$) seems to be the best ventilatory setting to assure an adequate PCO_2 elimination (with a CO2 reduction of 8.3% in comparison with a DP of 2 atm).

Conclusion In conclusion, our study confirms that HFJV may assure an effective CO_2 elimination during rigid bronchoscopy and suggests that the TOSCA system allows a reliable estimation of ventilation efficiency, with increased sensitivity during PCO_2 changes and the benefit of avoiding hypercapnia.

Figure 1



a, basal; b, 1.5 atm; c, 2 atm; d, 2.5 atm. Wilcoxon test, d significantly different vs b and c ($P < 0.01$), d vs a not significantly different.

References
1. Hautmann H, Gamarra F, *et al.*: **High frequency jet ventilation in interventional fiberoptic bronchoscopy.** *Anaesth Analg* 2000, **90**:1436-1440.
2. Biro P, Layer M, *et al.*: **Carbon dioxide elimination during high-frequency jet ventilation for rigid bronchoscopy**. *Br J Anaesth* 2000, **84**:635-637.
3. Principi T, Elisei D, *et al.*: **Non invasive measurement of arterial oxygenation saturation and CO_2 partial pressure at the ear lobe: TOSCA.** *Anaesthesia, Pain, Intensive Care and Emergency Medicine (APICE) 2002; 15–19 November; Trieste.* 2002:139.

P160 Inhaled nitric oxide in postpneumonectomy pulmonary edema

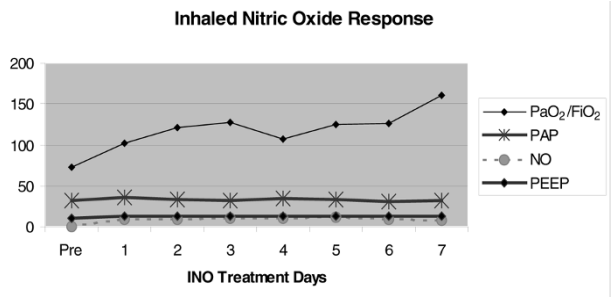
MT Keegan[1], ML De Ruyter[2], C Deschamps[1], BA Harrison[2]
[1]Mayo Clinic, 200 1st Street SW, Rochester MN 55905, USA; [2]Mayo Clinic, 4500 San Pablo Road, Jacksonville, FL 32224, USA
Critical Care 2003, **7(Suppl 2)**:P160 (DOI 10.1186/cc2049)

Introduction The one published case series detailing the use of inhaled nitric oxide (INO) in acute respiratory distress syndrome after lung resection found a 31% increase in oxygenation associated with a 70% survival [1]. The total cost of INO therapy if using commercial INO was approximately $500,000. This abstract details our experience with the use of INO in postpneumonectomy pulmonary edema (PPPE).

Methods We retrospectively reviewed the charts of all PPPE patients between 1994 and 2001 who received INO. Outcomes and physiological endpoints including P/F ratio, pulmonary artery pressures and PEEP were analyzed.

Results There were nine right-sided and one left-sided pneumonectomy patients. There were five deaths, all directly related to PPPE. There were no complications from the use of INO. The approximate total commercial cost of the INO was $108,700. Figure 1 demonstrates the change in mean PaO_2/FiO_2 ratio, pulmonary artery pressure, positive end expiratory pressure and INO concentration.

Figure 1



Discussion The increased PaO_2/FiO_2 ratio was similar to the previous report, with minimal change in mean PEEP. Mean pulmonary artery pressure did not increase during INO therapy. The mean INO concentration was 10 ppm. Although promising with respect to physiological endpoints, considering the expense of INO and equivocal outcome, a randomized control trial of the use of INO in this condition is needed.

Reference
1. Mathisen DJ, *et al.*: *Ann Thorac Surgery* 1998, **65**:1894-1902.

P161 Nitric oxide therapy in persistent pulmonary hypertension of the newborns (PPHN): predictors of survival in a single center experience

I Maruniak-Chudek, D Więcek-Włodarska, J Świetliński
Neonatal Intensive Care Department, Medical University of Silesia, ul. Medyków 16, 40-752 Katowice, Poland
Critical Care 2003, **7(Suppl 2)**:P161 (DOI 10.1186/cc2050)

Background and aim Inhaled nitric oxide therapy is an established method for management of PPHN – introduced in our unit 3 years ago. We summarized our experience with iNO treatment in search for predictors of the outcome.

Materials and methods Thirty newborns (range of gestational age, 25–39 weeks; birth weight range, 700–4500 g; CRIB range, 1–14; mean, 9 pts) admitted to neonatal intensive care unit with clinical features of PPHN and treated with inhaled nitric oxide were analysed. The mean time of NO inhalation was 83 hours (range: 4–192 hours). All infants were ventilated with a Babylog 8000 infant ventilator with NO-Domo adapter. Twenty-two survived, eight died. Arterial blood gases, hemoglobin saturation (pulsoxymetry), respiratory parameters and echocardiography were obtained at least every 12 hours up to 24 hours after discontinuation of the therapy. High pulmonary resistance was defined by tricuspid regurgitation jet $V_{max} > 3$ m/s, pulmonary artery blood flow AT/ET < 0.27 and decreased cardiac output CO < 200 ml/kg per min.

Results The group of survivors did not differ in respect to gestational age and Apgar scores from fatal cases. However, survivors had significantly higher birth weight (3094 ± 940 g vs 2075 ± 1018 g, $P < 0.05$) and lower CRIB (8 ± 3 vs 12 ± 2 pts, $P < 0.001$).

The newborns in the survival group had significantly higher hemoglobin saturation (88 ± 8% vs 74 ± 20%, $P = 0.03$) and blood hydroxycarbonate levels (21.7 ± 3.3 vs 18.7 ± 2.5 mmol/l, $P = 0.03$) and lower serum lactates values before the initiation of therapy (4.0 ± 3.7 vs 11.5 ± 2.8 mmol/l, $P < 0.001$). In ECHO evaluation all nonsurvivals presented very severe pulmonary hypertension, while in the other group nine had severe and 13 had moderately elevated resistance in pulmonary circulation. A marked decrease in mean airway pressure (MAP) and oxygenation index (OI) accompanied with an increase in pO_2 was observed since the 6th hour of treatment in the group of survivals. The decline of serum lactates was observed much later (after 24 hours). Such changes were not observed in nonsurvivors. Twelve hours after discontinuation of the therapy, transient increases in MAP and decrease in pO_2 were observed.

Conclusions Based on the results we conclude that initial values of hemoglobin saturation and blood hydroxycarbonate as well as quick improvement of OI and pO_2 and a decrease in MAP are important predictors of survival PPHN newborns designated for iNO therapy. Additionally, high serum lactate concentration at the beginning of iNO therapy, persistent through the following hours, very strongly indicates a negative outcome.

P162 Is the inhaled nitric oxide useful in pulmonary embolism? An experimental study

C Aldecoa[1], J Castañeda[2], L Vaquero[1], JI Gomez[1], J Rico[1], A Alonso[1]
[1]Department of Anaesthesia and Postoperative Critical Care, Hospital Universitario Rio Hortega, Valladolid, Spain; [2]Faculty of Medicine, Valladolid, Spain
Critical Care 2003, **7(Suppl 2)**:P162 (DOI 10.1186/cc2051)

Background In perioperative and critical patients, inhaled nitric oxide (NO) decreased pulmonary artery pressure and pulmonary vascular resistance in several diseases [1]. In the presence of pulmonary vasoconstriction, the higher pulmonary vascular resistance then the greater the inhaled NO vasodilator effect. Recently it has been demonstrated that inhaled NO could attenuate the pulmonary vasoconstriction caused by active mediators in an experimental model of massive air pulmonary embolism (PE) [2].

Objective The goal of study is to investigate the effects (hemodynamics and in gas exchange) of inhaled NO in a massive pulmonary embolism model in dogs.

Materials and methods We performed a prospective study in four groups of adult mongrel dogs in two phases. Phase 1 (normoventilated with FiO_2 0.21): Group A (control), nine dogs; Group B (NO inhaled), nine dogs. Phase 2 (normoventilated with an hypoxic mixture [FiO_2 0.16]): Group C (control), five dogs; Group D, six dogs (NO inhaled). Pulmonary embolism was induced by the modified Fisher's method [3]. Inhalation of NO was started 15 min prior to induction of PE and was kept constant throughout the experiment. Mean pulmonary artery pressure (PAPm), central venous pressure (CVP) and mean systemic arterial blood pressure (SAPm), cardiac output, arterial and mixed venous blood samples were obtained in basal conditions, hypoxic period previous embolism, after started NO inhalation and 5, 15, 30 and 45 min after embolism induction. Results as expressed as mean ± standard deviation. Nonparametric test (Mann–Whitney U test and Wilcoxon test) were used. Statistical significance was set at $P < 0.05$.

Results In phase 1 no significant differences in all variables measured at any time were found. There was an improvement in gas exchange. In phase 2 NO inhalation both improved gas exchange and reduced PAPm in the hypoxic ventilation prior to PE. After pulmonary embolism we observed a reduction in PAPm and improve arterial oxygenation but no statistical differences were found. No significant intergroup differences were found with regard to CO, PVC. A trend to lower cardiac output was observed in the group of inhaled NO.

Conclusions Our data suggest that in pulmonary embolism induced by Fisher's method, inhaled NO did not modify either pulmonary haemodynamics or oxygenation. We have shown that inhaled NO improved the hypoxic induced pulmonary hypertension without effects in systemic arterial pressure.

References

1. Haddad E, Lowson SM, Johns RA, *et al.*: *Anesthesiology* 2000, **92**:1821-1825.
2. Tanus-Santos JE, Moreno H, Zappellini A, *et al.*: *Anesth Analg* 1999, **88**:1025-1029.
3. Fisher J, Noble WH, Kay JC: *Anesthesiology* 1981, **54**:204-209.

P163 Respiratory drive at rest and during exercise in obstructive sleep apnea patients before and after CPAP treatment

A Tasiou, S Nanas, A Prekates, P Tselioti, Ch Roussos
Pulmonary and Critical Care Medicine, University of Athens, Greece
Critical Care 2003, **7(Suppl 2)**:P163 (DOI 10.1186/cc2052)

Respiratory drive at rest and during exercise has not been fully investigated in obstructive sleep patients. The aim of this study is to enlighten the response of respiratory drive to CPAP treatment in obstructive sleep apnea patients.

Methods Fifteen consecutive patients (14 males/one female, aged 53 ± 6 years) with newly diagnosed disease were enrolled in this study. Diagnosis was made by all-night polysomnography using standard criteria. Blood gases, body mass index measurement (BMI) and spirometry were performed in all patients. $P_{0.1}$ and the mean inspiratory flow (V_T/T_I) were used as indices of respiratory drive. All parameters of the respiratory cycle were measured during the $P_{0.1}$ procedure (V_T, f, V_E, T_I, T_{TOT}, T_I/T_{TOT}). We measured the parameters at rest and during two stages of submaximal exercise. We evaluated all the parameters before and 6 months after CPAP treatment.

Results Our patients seem to have moderate to severe disease as indicated by polysomnographic data (apnea hypopnea index 34–120). There was no significant difference in BMI, FEV_1 and FVC before and after treatment. PO_2 was significantly increased (76 ± 11 mmHg vs 82 ± 9 mmHg, $P<0.01$) and PCO_2 was significantly reduced (45 ± 6 mmHg vs 41 ± 2 mmHg, $P<0.01$). At rest there was no difference in respiratory drive and respiratory cycle parameters. At the first stage of submaximal exercise $P_{0.1}$ was significantly reduced (6.7 ± 2.7 cmH_2O vs 5.0 ± 2.2 cmH_2O, $P<0.05$) and V_T/T_I was reduced (75 ± 29 l/min vs 61 ± 12 l/min, $P<0.05$). At the second stage of submaximal exercise $P_{0.1}$ was unchanged, V_T/T_I was significantly reduced (99 ± 33 l/min vs 85 ± 17 l/min, $P<0.05$) and T_I was significantly increased (0.9 ± 0.3 min vs 1.3 ± 0.2 min, $P<0.05$).

Conclusion Respiratory drive indices and respiratory cycle parameters at rest did not change in our population, although mild hypoxemia and hypercapnia significantly improved. Changes in respiratory drive during submaximal exercise could possibly explain changes of ventilatory control after CPAP treatment, which may not be detected at rest.

P164 Effects of a low tidal volume ventilation strategy on the pressure/volume curve in ALI/ARDS patients

D Chiumello, E Carlesso, E Storelli, G Li Bassi, F Vagginelli, N Bottino, L Gattinoni
Institute of Anesthesia and Intensive Care, Policlinico Hospital – IRCCS, Milan, Italy
Critical Care 2003, **7(Suppl 2)**:P164 (DOI 10.1186/cc2053)

To evaluate, in ARDS/ALI patients ventilated with a low tidal volume and PEEP, according to the NIH network trial [1], the effects on the parameters of the pressure/volume (PV) curve of the respiratory system.

Four ARDS/ALI sedated and paralyzed patients (age 62 ± 24 years, weight 66 ± 10 kg, PaO_2/FiO_2 216 ± 70 mmHg, PEEP 12.7 ± 2.2 cmH_2O) were studied. P/V curves were performed at the beginning and after 120 min with the supersyringe technique. A recruitment maneuver was performed at the beginning of the study. Chest wall volume was measured by the optoelectronic plethysmography technique. Lower and upper inflection points (Pcl, Pcu), maximal compliance (C_{max}) and vital capacity (VC) on the inflation limb were computed according to Venegas' analysis [2]. Compliance at 100 ml ($C_{0.1}$), inflation compliance (C_{inf}), percentage hysteresis (Hyst%) and unrecovered volume (UV) were calculated using standard formulas [3]. In Table 1, the results are expressed as mean ± SD.

These data suggest that after 2 hour ventilation with a low tidal volume strategy there are no major modifications in the P/V curve parameters.

Table 1

	Time 0	Time 120 min
Pcl (cmH_2O)	7.4 ± 3.4	4.9 ± 2.2
Pcu (cmH_2O)	33.1 ± 5.1	33.2 ± 6.6
C_{max} (ml/cmH_2O)	46.2 ± 19.3	41.0 ± 16.6
VC (l)	1.1 ± 0.4	1.1 ± 0.4
$C_{0,1}$ (ml/cmH_2O)	14.5 ± 2.9	13.1 ± ±2.7
C_{inf} (ml/cmH_2O)	40.0 ± 14.7	33.9 ± 12.1
Hyst%	15.7 ± 5.3	15.6 ± 4.0
UV (ml)	142.5 ± 43.5	185.0 ± 78.5

References
1. The Acute Respiratory Distress Syndrome Network: **Ventilation.** *N Engl J Med* 2000, **342**:1301-1308.
2. Venegas JG, *et al.*: *J Appl Physiol* 1998, **84**:389-395.
3. Gattinoni L, *et al.*: *Intensive Care Med* 1987, **13**:19-25.

P165 Histopathological effects of lidocain and methylprednisolone in experimental acute lung injury

N Doğan, ZU Sevıımlıı, H Kürşad, M Kizilkaya
Universty of Atatürk, Departments of Anaesthesia and Intensive Care Medicine, Erzurum, Turkey
Critical Care 2003, **7(Suppl 2)**:P165 (DOI 10.1186/cc2054)

Introduction and purpose Acute lung injury (ALI) resulted from acid aspiration is an important problem for anaesthesia and intensive care. In our study, we aimed to compare the histopathological effects of lidocain and methylprednisolone used in the treatment of ALI developed by acid aspiration.

Materials and methods With the approval of the faculty ethic board, we formed three groups randomly from 30 rabbits as a 0.9% NaCl control group (Group C, $n=10$), a lidocain group (Group L, $n=10$), and a methylprednisolone group (Group M, $n=10$). The subjects were applied tracheotomy under anaesthesia. Anaesthesia induction and maintenance, 2% isoflurane, 50% oxygen, 50% N_2O were used. Later all the subjects were given 3 ml/kg of 0.1 N HCl (pH 2) as drops intratracheally. Following this, the subjects in group C were administered 2 ml/kg per hour continious 0.9% NaCl infusion and 2 ml/kg intravenous bolus, those in Group L 2 ml/kg per hour continuous infusion and 2 mg/kg intravenous bolus lidocain, and those in Group M 30 mg/kg intravenous bolus single dose methylprednisolone. ALI development was determined by PaO_2/FiO_2. After 6 hour mechanical ventilation, the subjects were sacrificed. ALI was scored histopathologically as to alveolar congestion, hemorrhage, neutrophil infiltration or aggregation, and alveolar wall thickness–Hyalin membrane occurrence. Each item was graded as 0 = least injury, 1 = slight injury, 2 = mod-

erate injury, 3 = severe injury, 4 = maximum injury. The groups were statistically evaluated with Kruskal–Wallis variance analysis.

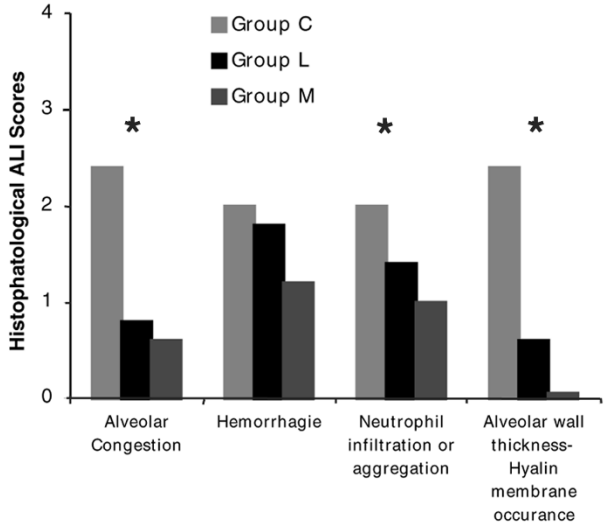
Results Average total ALI scores of the groups were 8.80 ± 1.54 for group C, 4.06 ± 1.07 for group L and 2.80 ± 1.03 for group M. ALI was found to be higher in group C than in groups L and M ($P < 0.01$). Likewise, ALI was higher in group L than in group M ($P < 0.01$) (Fig. 1).

Conclusion We have the conclusion that lidocain and methylprednisolone are the drugs to be used for reducing histophatological effects of ALI, and methylprednisolone is more effective than lidocain. However, we are of the conclusion that our findings should be supported with clinical studies.

References

1. Nishina K, *et al.*: *Anesthesiology* 1998, **88**:1300-1309.
2. Borg T, *et al.*: *Acta Anaesthesiol Scand* 1985, **29**:831-845.

Figure 1



Comparison of ALI in groups (* $P < 0.01$).

P166 Effect of perfluorocarbon emulsion on the level of nitric oxide and hydrogen peroxide in patients with acute respiratory failure

TA Shumatova, VB Shumatov, NG Prikhodchenko, UA Shastun
Medical University, Vladivostok, Russia
Critical Care 2003, **7(Suppl 2)**:P166 (DOI 10.1186/cc2055)

The purpose of our research was to evaluate the effects of the perfluorocarbon emulsion in patients with ARDS by the results of biochemical testing of expired air condensates.

We have examined expired air condensates (EAC) in patients with various stages of ARDS using spectrophotometry to study NO metabolites and fluorescence to study H_2O_2. Perfluorocarbon emulsion, perftoran, was administrated 5 ml/kg two to three times on the day. Our investigation showed the increase of NO metabolite level in EAC patients with the first and second stages of ARDS and its significant reduction in EAC patients with the third and fourth stages. The level of H_2O_2 in EAC elevated with the progression of ARDS. In the present study, it was established that the NO metabolite level and H_2O_2 level in the EAC patients with perfluorocarbon administration was not so increased as the level in the EAC patients without it. It was more expressed in the patients with the first and second stages of ARDS. All these patients had positive disease dynamics. Administration of perftoran to the patients with the third and fourth stages was not noted as a clear dynamic of inflammatory marker level.

We conclude that infusions of oxygen-carrying blood substituted by the oxidative stress, which takes place in the last ARDS stages, may increase lung injury due to the increase of the H_2O_2 level. Applications of perfluorocarbon emulsion to the ARDS patients are effective and pathogenic expedient methods in the early stages (first and second) of ARDS.

P167 Improvement of cardiac output with BiLevel ventilation in patients with high airway pressures

D Ziegler, V Burch, M Geno Tellez, D Casey, C Derbes, T Dipprey
John Peter Smith Hospital, Fort Worth, TX, USA
Critical Care 2003, **7(Suppl 2)**:P167 (DOI 10.1186/cc2056)

Hypothesis Studies have shown that airway pressure release ventilation increases cardiac output when compared with synchronized intermittent mandatory ventilation (SIMV). This occurs by allowing more spontaneous ventilation, which increases venous return. BiLevel ventilation is a form of augmented pressure ventilation that allows for spontaneous breathing at any moment of the ventilatory cycle. The purpose of this study is to determine whether BiLevel increases cardiac output when compared with SIMV.

Method Patients on a ventilator with high peak airway pressures in an intensive care unit from December 2000 to November 2002 were studied. Patients with respiratory failure were initially managed with SIMV. If the peak airway pressure persistently remained greater than 40 cmH_2O, patients were changed to BiLevel using a Puritan-Bennett 840 ventilator. Cardiac output measurements were made while on SIMV and after being converted to BiLevel. Results were compared using a paired Student *t* test.

Results Thirty-six patients met criteria for the study. Thirteen patients developed respiratory failure from sepsis, 11 from trauma, seven from pneumonia, two from congestive heart failure, one from variceal bleeding, one with renal cell cancer and one after a lung lobectomy. Twenty-five patients (69%) increased their cardiac output after being changed to BiLevel. In 11 patients with a PaO_2

Table 1

	Cardiac output (l/min)	Stroke volume (ml/beat)	Peak airway pressure (cmH_2O)	PaO_2/FiO_2	PO_2 A–a gradient
SIMV	6.8 ± 2.6	63 ± 26	40.2 ± 3.8	160 ± 81	351 ± 166
BiLevel	7.3 ± 2.8	67 ± 28	32.9 ± 4.1	176 ± 93	336 ± 157
P value	0.01	0.05	0.01	NS	NS

A–a gradient >500, five (45%) increased their cardiac output. Overall results are as presented in Table 1. There was no significant difference in the systemic vascular resistance and wedge pressure.

Conclusion: BiLevel can increase cardiac output in most patients at lower airway pressures when compared with SIMV. It is less likely to increase cardiac output in patients with severe lung injury. Further studies are needed to determine whether this improvement in cardiac output will affect outcome.

P168 Effects of PEEP on intrathoracic blood volumes and cardiac function in ARDS patients assessed by a double indicator dilution technique

N Patroniti, A Manfio, B Cortinovis, E Maggioni, G Bellani, F Sala, F Consonni, A Pesenti
Department of Anaesthesia and Intensive Care, University of Milano-Bicocca, S. Gerardo Hospital, Italy
Critical Care 2003, **7(Suppl 2)**:P168 (DOI 10.1186/cc2057)

Introduction The aim of the study was to evaluate the effects of PEEP on intrathoracic blood volumes and cardiac function measured by the COLD system in ARDS patients.

Methods We studied eight sedated and paralyzed ARDS patients (age 58 ± 13.8 years, PaO_2/FiO_2 146 ± 84 mmHg), ventilated in CPPV. All patients had a Swan–Ganz catheter and a 4 F thermistore-tipped, fiberoptic catheter inserted through a femoral artery, both connected to the COLD system. All patients randomly received, for at least 30 min, three levels of PEEP (5, 10 and 15 cmH_2O). We measured: cardiac (CI) and stroke volume (SVi) indexes; heart rate (HR), central venous pressure (CVP); wedge pressure (WP); intrathoracic (ITBVi), global-end diastolic (GEDVi), right heart end-diastolic (RHEDVi), left heart end-diastolic (LHEDVi), and pulmonary (PBVi) blood volume, all indexed for body surface area. PEEP effects were assessed by one-way analysis of variance for repeated measurements and linear trend analysis. Multiple regression analysis by a stepwise procedure was used to find major determinants of stroke volume index (SVI) and cardiac index (CI) changes induced by PEEP.

Results Increased PEEP levels resulted in a significant reduction of CI, RHEDVi, PBVi and an increase in CVP. GEDVi, ITBVi, LHEDVi, HR and WP did not change significantly with PEEP. HR changes correlated with pH and $PaCO_2$ changes. SVi changes were explained by changes of RHEDVi and LHEDVi ($\Delta SVi = 0.0365 \times \Delta LHEDVi + 0.122 \times \Delta RHEDVi$, $r^2 = 0.823$, $P < 0.01$). CI changes were positively correlated with GEDVi, ITBVi, RHEDVi, and $PaCO_2$ changes, and were negatively correlated with pH changes. CI changes were explainable by changes of RHEDVi and $PaCO_2$ ($\Delta CI = 0.007 \times \Delta RHEDVi + 0.113 \times \Delta PaCO_2$, $r^2 = 0.78$, $P < 0.001$).

Conclusions In ARDS patients, PEEP affected significantly the RHEDVi and PBVi. RHEDVi and LHEDVi changes accounted for 82% of SVi changes induced by PEEP. Changes in $PaCO_2$ and RHEDVi were the main determinant of CI changes.

P169 Relationship between intrapulmonary oxygen consumption and oxygenation index in patients with post-traumatic acute respiratory distress syndrome

S Milanov, M Milanov, E Gyurov, Z Shterev
Emergency Institute 'Pirogov', General ICU, Totleben 21, Sofia, Bulgaria
Critical Care 2003, **7(Suppl 2)**:P169 (DOI 10.1186/cc2058)

Post-traumatic acute respiratory distress syndrome (ARDS) is a stereotyped response caused by a variety of pulmonary and extrapulmonary insults following major trauma. Increased intrapulmonary oxygen consumption (VO_2ipulm) was described in different conditions with impairment of lung function, including septic patients with ARDS [1] and patients with pneumonia [2]. In this study we measured intrapulmonary oxygen consumption and oxygenation index ($OI = Paw \times FiO_2 \times 100/PaO_2$) in order to describe and compare the time course of these variables on the 1st, 3rd, 7th, 10th and 14th day after the ARDS onset. The study was performed in our level 1 trauma center ICU. We prospectively measured all hemodynamic and oxygen transport variables, including VO_2ipulm and OI in 37 adult ventilated trauma patients, who fulfil the ARDS criteria according to the North American Concensus Conference. All patient were post-traumatic, ventilated with volume-controlled mode, and were included in the study if they met the above criteria at any time during their ICU stay. We excluded those patients with history of Chronic Obstructive Lung Disease and those ventilated with $FiO_2 > 0.80$. VO_2ipulm was estimated by subtracting calculated VO_2 using the reverse Fick method from whole body VO_2 using indirect calorimetry (Datex Ohmeda M-COVX metabolic monitor). All measurements and calculations were performed simultaneously during steady-state conditions four times daily and the mean values were taken. The overall mortality in this setting was 57%. We found substantial increases in VO_2ipulm as a component of whole body VO_2 in all patients with post-traumatic ARDS

(median 31.3%; interquartile range 27.2–34.1%) and good positive correlation between VO_2ipulm and OI on the 3rd, 7th, 10th and 14th day, but not on the first day after the onset of ARDS. Our data suggest that VO_2ipulm can be used as an additional pulmonary injury severity parameter but large observational studies are needed to link this variable with mortality in post-traumatic ARDS patients.

References

1. Smithies MN, Royston B, Makita K, Konieczko K, Nunn JF: **Comparison of oxygen consumption measurements: indirect calorimetry versus reversed Fick method.** *Crit Care Med* 1991, **19**:1401-1406.
2. Henzel M, Kox WJ: **Increased intrapulmonary oxygen consumption in mechanically ventilated patients with pneumonia.** *Am J Respir Crit Care Med* 1999, **160**:137-143.

P170 Intermittent prone positioning improves oxygenation but has no influence on outcome in the treatment of post-traumatic lung injury: a prospective, randomized, controlled study

RJ Stiletto[1], MG Baacke[1], G Voggenreiter[2], M Aufmkolk[3], C Waydhas[3], C Ose[4], E Bock[4], L Gotzen[1], D Nast-Kolb[3], U Obertacke[2]
[1]Department of Trauma Surgery, Philipps-University Marburg, Marburg, Germany; [2]Department of Trauma Surgery, University Hospital Mannheim, 68135 Mannheim, Germany; [3]Department of Trauma Surgery, University Hospital Essen, 45122 Essen, Germany; [4]Institut of Medical Informatics, Biometry and Epidemiology, University Hospital Essen, 45122 Essen, Germany
Critical Care 2003, **7(Suppl 2)**:P170 (DOI 10.1186/cc2059)

In a randomized trial the effect of a predefined strategy of prone positioning on the duration of mechanical ventilation was evaluated in multiple trauma patients with acute lung injury or acute respiratory distress syndrome. Patients in the prone group ($n=21$) were continuously kept prone for at least 8 hours and a maximum of 24 hours per day. Prone positioning was continued until a PaO_2:FiO_2 ratio of more than 300 was present in the prone as well as the supine position over a period of 48 hours. Patients in the supine group ($n=19$) were positioned according to standard care guidelines. The duration of ventilatory support did not differ significantly between the two groups (20 ± 17 days in the prone group and 33 ± 23 days in the supine group). The mean duration of ventilatory support in prone position was 11 ± 5 hours a day. A mean of 7 ± 4 posture changes was applied per patient. One patient in the prone group and three patients in the supine group died due to multiorgan failure ($P=0.33$). The PaO_2:FiO_2 ratio increased significantly more in the prone group than in the supine group in the first 4 days ($P=0.03$). Thereafter no significant difference in the PaO_2:FiO_2 ratio was evident between the two groups. The number of adverse effects was not different between the groups. Therefore, despite an improvement of gas exchange, no clinical outcome benefit was detected.

P171 Kinetic therapy in Germany: results of a randomized cross-sectional survey

MG Baacke[1], M Floren[1], C Ose[2], F Pessler[3], D Mann[1], RJ Stiletto[1]
[1]Center for Trauma Surgery and Intensive Care Medicine, Philipps-University-Marburg, D-35043 Marburg, Germany; [2]Institut für Med. Informatik, Biometrie und Epidemiologie, Universitätsklinikum, Hufeland straße 55, D-45122 Essen, Germany; [3]Hospital for Joint Diseases, 301 East 17th Street, New York, NY 1003, USA
Critical Care 2003, **7(Suppl 2)**:P171 (DOI 10.1186/cc2060)

Introduction Prone positioning developed to the most hopeful therapeutical approach in the treatment of severe respiratory failure. Different types of kinetic therapy are practiced, but so far no data are available about the real number of institutions that practice kinetic therapy in the treatment of respiratory failure and which sort of therapy is practiced. For the first time we present representative data of the number of clinics that practice kinetic therapy in Germany. Eighty-six per cent of all answering clinics practice prone positioning. The mean time for positioning was 17 min, the mean duration was 4.8 hours. Mostly a usual ICU bed was used. No severe unexpected events were reported. The estimation of this sort of treatment was mostly good (62%) and very good (32%).

Methods In order to evaluate the incidence of kinetic therapy in the treatment of respiratory failure in Germany we initiated a randomized survey, including all 1589 German ICUs. Following a regional randomization, to achieve a representative distribution of the hospitals we divided into four groups of ICUs: surgical=SICU (52), anaethesiological=AICU (15), medical=MICU (52) and multidisciplinary=MdICU (124). According to statistical analysis we sent a standardized questionnaire to 201 hospitals, enough to receive representative results. For statistical analysis the Chi-Quadrat test, the exact Fischer test, and the Wilcoxon test/Kruskal–Wallis test, following the NPAR1WAY procedure, were used. We asked what sort of bed was used, how often and how long prone positioning was performed, how many nurses were involved and the time it took for positioning and the duration of prone therapy. Additionally we asked for the indications and main complications of prone/kinetic therapy. Finally we asked for the general estimations of kinetic therapy.

Results Most of the ICUs were MdICU (124), followed by SICU (52), AICU (15) and MICU (nine). One hundred and seventy-three (86%) ICUs practice kinetic therapy, only 28 ICUs (14%) did not; 79% (136 ICUs) used a normal bed for kinetic therapy, just 6% (11 ICUs) used special beds for prone positioning. Rotorest® beds (side-to-side) were used by only 2% (three ICUs). In 23% (15 ICUs), special beds like water beds, rotational beds or similar were used. Usually three persons were needed to turn a patient into prone positioning, with a mean time of 17 min (SD 9.28), Prone positioning lasted 4.8 hours (SD 2.82), with a maximum of 10.27 hours. ARDS/ALI (58%) were main indications for kinetic therapy. In 18% it was used on prophylactic purposes. Main complications were welling (35%), skin lesions (32%) and short-time hemodynamic instability (13%). The estimation of kinetic therapy and its value in the treatment of respiratory failure was good (62%) and very good (32%).

Conclusion For the first time we present representative data of the number of clinics that practice kinetic therapy in Germany. Eighty-six percent of all answering clinics practice prone positioning. The mean time for positioning was 17 min, and the mean duration was 4.8 hours. Mostly a usual ICU bed was used. No severe unexpected events were reported.

P172 The prognostic value of the change of oxygenation index after starting prone position ventilation in ARF

JC Lewejohann, E Rieh, E Muhl, HP Bruch
Department of Surgery, Universitätsklinikum Lübeck, Ratzeburger Allee 160, 23538 Lübeck, Germany
Critical Care 2003, **7(Suppl 2)**:P172 (DOI 10.1186/cc2061)

Introduction In acute respiratory failure, classified as acute lung injury (ALI) or the more severe acute respiratory distress syndrome (ARDS), prone position ventilation (PPV) can improve oxygenation by recruiting alveoli situated in dorsal-dependent regions of the lung and by alteration of the ventilation/perfusion ratio. The aim of our study is to analyze the prognostic value of the change of oxygenation after starting prone position ventilation in ARF.

Methods We studied 110 consecutive patients with an ARF, $n=18$ with ALI and $n=92$ with ARDS, at a mean age of 66 ± 13 (SE) years in a clinical followup design at a surgical ICU in a university hospital, who met the criteria of the American European consensus definition. All patients were ventilated intermittent in the SP and in the PP (135° left/right-side-position) for at least 6 hours per day for supportive treatment of ARF. Data collection included, apart from baseline characteristics, the individual oxygenation index. We compared the individual oxygenation index (PaO_2/FiO_2) before and after the start of prone position with the SPSS® Mann–Whitney test and the data set of each patient with outcome.

Results PPV was well tolerated in all $n=110$ patients and showed a significant increase of PaO_2/FiO_2 ratio in $n=106$ within the first 6 hours of PPV (SP 149 ± 0.52 vs PP 230 ± 0.73 mmHg [mean ± SEM]). In the remaining four cases there was a positive effect within the first 24 hours. The surviving patients ($n=43$) and the patients who survived 28 days, but died in further course, showed a median increase of oxygenation index of +50.00 and +65.67 mmHg, respectively, after 24 hours of ventilation in the prone position. The patients who died within the first 7 days in ICU showed a median deterioration of −11.46 mmHg. Patients who died after 8–28 days after starting PPV showed a median improvement of +29.92 mmHg after the first 24 hours of ventilation in the prone position.

Conclusion Our results show that in patients with an acute respiratory failure who are ventilated in the prone position the extent of functional recruitment as a result of the body position change is of prognostic value. Patients with an improvement of the oxygenation index of 50 mmHg and more within the first 24 hours after starting prone position ventilation have a better prognosis than patients with a slight increase or even a deterioration. A less improvement of oxygenation index seems to increase the risk to die in the course of acute respiratory failure. Thus, patients with a high risk of change for the worse can be identified in good time and lead to more interventional approaches for treatment of acute respiratory failure.

P173 A prospective randomised study on clinical and economical aspects of closed loop control and common weaning protocols after cardiac surgery

H Vogelsang[1,2], T Uhlig[3]
[1]Department of Applied Physiology, Ruhr-University Bochum, Universitätsstrasse 150, Building MA 2/59, D-44780 Bochum, Germany; [2]Department of Anaesthesiology, St Josef Hospital Bochum, Germany; [3]Department of Anaesthesiology, Friedrich-Schiller-University, Jena, Germany
Critical Care 2003, **7(Suppl 2)**:P173 (DOI 10.1186/cc2062)

Introduction Adaptive support ventilation (ASV) is a microprocessor-controlled ventilatory mode allowing automated weaning. Under controlled ventilation a preset minimum minute ventilation is guaranteed and, based on a breath-to-breath-analysis, ventilatory support is withdrawn gradually with recovering spontaneous breathing. The self-controlled weaning process includes both reduction of mandatory breaths and reduction of pressure support. Respiratory rate and tidal volume are calculated using Otis' formula for optimal breathing pattern [1].

We asked whether there are differences between weaning protocols based on ASV or on common ventilatory modes after cardiac surgery regarding clinical and economical aspects.

Methods After IRB approval and informed consent we studied 2×28 patients for hemodynamic and 2×10 patients for ventilatory parameters admitted to the ICU after aortocoronary bypass surgery. They were randomly assigned to the ASV group (GALILEO®; Hamilton Medical, Rhäzüns, Switzerland) or to the standard group (EVITA 4®; Dräger Medical, Lübeck, Germany). ICU staff was not involved in the study except in the instruction to use ASV in the ASV group until extubation, and no interventions were planned. The standard group was ventilated in the routine way using CPPV, SIMV and PS. Switches in the ventilatory mode (standard group) and ventilator adjustments according to blood gas analyses (both groups) were carried out by the nursing staff in consultation with the physician. All patients were sedated with propofol during the rewarming phase until the rectal temperature reached 36°C. Extubation was possible at normothermia, hemodynamic stability, sufficient spontaneous ventilation and without signs of imminent organ failure or major complications. We documented ventilatory and hemodynamic parameters every 60 min from admission to the ICU until transfer to the peripheral ward. For statistical analyses we built up matched pairs by age, gender and preexisting diseases. Patient groups were equal regarding anaesthesia, postoperative sedation, kind and duration of operation and body temperature.

Results There were no significant differences between both groups, neither in hemodynamic parameters nor in breathing parameters or blood gas analyses. Length of ICU stay was 1.7 ± 2.5 days (standard group) and 1.5 ± 1.4 days (ASV group), and time until extubation totalled 7.2 ± 3.4 h (standard group) and 7.8 ± 4.5 h (ASV group). Reintubation was not necessary in both groups. No patient failed ASV, so there was no need to change the ventilatory mode in this group. Using the ASV ventilator, adjustments were necessary 0.5 times at median (range 0–3), adapting the guaranteed minimal ventilation ('%MinVol') to blood gas analyses. In the standard group, the ventilatory mode was switched once at median (range 1–3), plus adaption of respiratory frequency

or pressure support until extubation. The procedures to reduce FiO_2 were equal in both groups and PEEP remained constant.

Conclusion In this study no differences in clinical parameters could be found between closed loop control and standard weaning protocol using the fast track concept after cardiac surgery. Considering economical aspects, adaptive support ventilation was superior to standard weaning since the nursing staff spent significantly less workload on ventilatory adjustments.

Reference

1. Otis, *et al.*: *J Appl Physiol* 1950, **2**:592-607.

P174 The effects of different weaning modes on stress response

O Sen, GM Koksal, C Sayilgan, H Oz

Department of Anesthesiology and Reanimation, Istanbul University, Cerrahpasa Medical Faculty, 34303 Fatih, Istanbul, Turkey

Critical Care 2003, **7(Suppl 2)**:P174 (DOI 10.1186/cc2063)

Introduction The aim of this study was to compare the effects of different weaning modes (pressure support ventilation [PSV], continuous positive airway pressure [CPAP], T-piece) on stress response in humans.

Methods The study was performed on 60 patients, which were mechanically ventilated for 2 days or more and had inclusion weaning criteria in ICU. After taking the initial blood samples for cortisol, insulin and glucose values and urine samples for vanilmandelic acid (VMA) value measurement, patients were randomly divided into three groups ($n=20$). In group 1, the patients ventilated with PSV, with $F_iO_2 < 0.4$, level of support $< 10\,cmH_2O$, PEEP $< 5\,cmH_2O$, parameters for 2 hours. In group 2, the patients received $5\,cmH_2O$ CPAP via endotracheal tube for 2 hours. In group 3, the patients received 4 l/min oxygen via T-piece for 2 hours. At the end of the 2 hours and after 48 hours of extubation, blood and urine samples were taken for aforementioned measurements. Weaning was considered successful if reintubation was not required within 48 hours of extubation.

Results Insulin, cortisol and urine VMA values of group 3 were higher than of groups 1 and 2, after 48 hours of the extubation ($P<0.01$, $P<0.05$, $P<0.05$, respectively). Blood glucose values of group 3 were lower than those of groups 2 and 1 after 48 hours of extubation ($P<0.01$, $P<0.01$, respectively).

Conclusion The T-piece device had a higher stress response than PSV and CPAP modes after weaning off mechanical ventilation.

P175 Effect of the 'upper limb trainer' on lung volume during the weaning phase with ICU patients: an exploring study

E Van den Steen[1], L DeCorte[2], R D'Haese[3], B Zwaenepoel[2], F Colardyn[1,2]

[1]Rijksuniversiteit Gent (RUG), Gent, Belgium; [2]Arteveldehogeschool Gent, Sint-Lievenspoortstraat 143, 9000 Gent, Belgium; [3]University Hospital Gent, ICU Prof.dr.Colardyn, De Pintelaan 185, 9000 Gent, Belgium

Critical Care 2003, **7(Suppl 2)**:P175 (DOI 10.1186/cc2064)

The goal of this study was to find out whether daily exercise with the upper limb trainer (ULT) has an influence on lung volumes and, by consequence, on the diaphragm. By doing so we hope to improve the process of weaning from mechanical ventilation in order to prevent weaning failure.

We tested four adult patients at our university hospital intensive care unit in Belgium. They were ventilated for at least 1 week and fell within the scope of the following weaning criteria: $PaO_2/FiO_2 > 200$, PEEP $\leq 5\,cmH_2O$, HF < 120 bpm and RR ≤ 35 breaths/min.

The patients were asked to perform 10 min of cycling with the ULT. This was done daily, up to the moment that the patients were extubated or until they no longer fell within the scope of the criteria. One patient was tested 2 days, the others only 1 day.

Respiratory rate, tidal volume and minute volume were measured before, during and after cycling. Heart rate and blood pressure were monitored continuously. Before and after the testing, arterial blood was taken and PaO_2, $PaCO_2$, pH and lactate were measured. We found a decrease in pH, but an increase in $PaCO_2$. This seems to indicate that this exercise was too demanding for our patients. The fact that the respiratory rate increased during cycling while the tidal volume stabilized proved that there was no shallow breathing.

More investigations to confirm these findings have to be performed. Moreover, a parameter immediately indicating the load of the exercise needs to be found. Our findings suggest that arm exercise with the ULT could have a positive influence on the diaphragm and, hence, can be useful for patients who fail to wean.

Acknowledgement This work was performed in association with the 'Arteveldehogeschool', Department of Health Care, Ghent.

P176 Cardiorespiratory measurements during weaning from mechanical ventilation in critical care patients: comparison of pressure support ventilation and T-piece

SRR Vieira, AD Costa, MM Rieder

Serviço de Medicina Intensiva, Hospital de Clinicas de Porto Alegre, Universidade Federal do Rio Grande do Sul, RS, Brasil – Rua São Luis 1127, 501 Porto Alegre, RS, Brasil, CEP 90620-170

Critical Care 2003, **7(Suppl 2)**:P176 (DOI 10.1186/cc2065)

Introduction Weaning from mechanical ventilation in critical care patients is responsible for alterations in cardiorespiratory function. However, it is not clear whether different methods of weaning are associated with different cardiorespiratory responses. The goal from this study was to compare cardiorespiratory measurements during pressure support ventilation (PS) and during T-piece.

Materials and methods Twenty patients in the weaning process (57 ± 15 years) were studied in this crossover randomized clinical trial comparing PS and T-piece. Variables recorded at 0, 15 and 30 min in each method included: mean arterial pressure (MAP), heart (HR) and respiratory (RR) rates, arterial oxygen saturation (SaO_2), end-tidal CO_2 ($PetCO_2$), tidal volume (V_T), minute ventilation (V_E), total work of breathing (WOB), mean airway pressure (P_{mean}), changes in ST segment in the electrocardiogram and presence of arrhythmias. The *t* test, ANOVA and χ^2 tests were used in the statistical analysis. The level of significance was $P < 0.05$.

Results The comparison between PS and T-piece showed that: no significant difference was observed in MAP and HR; values of SaO_2, $PetCO_2$, V_T, V_E, total WOB and P_{mean} were significantly higher with PS at 0, 15 and 30 min ($P < 0.05$); values of RR were lower with PS, at least at 0 and 15 min ($P < 0.05$), and they increased from 0 to 30 min ($P < 0.05$); alterations in ST segment (nine patients in each method) as well as the occurrence of arrhythmias (four in each method) and of sinus tachycardia (five in each method) were similar.

Conclusion Comparing PS with T-piece, no differences were observed concerning cardiovascular measurements or electrocardiographic evaluation, but a better response was observed in the respiratory pattern and oxygenation.

P177 Clinical features and outcome of patients with extubation failure

L Gianesello[1], V Pavoni[1], G Gritti[2], L Paparella[1], P Pavarin[1], N Todesco[1], F Badii[1]
[1]UO of Anaesthesia and Intensive Care, University-Hospital, Via Giustiniani 1, 35100 Padova, Italy; [2]Department of Critical Medical–Surgical Area, Section of Anaesthesia and Intensive Care, Firenze, Italy
Critical Care 2003, **7(Suppl 2)**:P177 (DOI 10.1186/cc2066)

Introduction The need for reintubation within 24–72 hours of planned extubation is an event occurring in 2–25% of extubated patients [1]. Developing predictive tools and optimizing extubation decisions require knowledge of the risk factors and clinical features of patients with extubation failure (EF).

Methods We studied all patients who were intubated and mechanically ventilated in a polyvalent intensive care unit (ICU) during a 12-month period. The following data were collected: age, sex, SAPS II on admission, Glasgow Coma Score (GCS) on day of extubation, length of mechanical ventilation (MV), length of ICU stay (LOS), ICU and hospital mortality. Patients who need reintubation after successful trial of weaning and planned extubation were identified (EF). We considered two parameters that assess airway patency and protection like predictors of EF: cough strength and suctioning frequency. Parameters were analysed using Student's *t* test ($P < 0.05$).

Results Six hundred and sixty-five patients were admitted to the ICU during the study period; 511 of them (76.8%) underwent intubation and MV. Twenty-three patients (4.5%) (17 men and six women) needed reintubation. EF occurred in seven elective surgery, seven emergency surgery, eight medical and one trauma patient. Causes of EF were: inability to manage respiratory secretions (9/23, 39.1%), surgical complications (9/23, 39.1%), severe alteration in consciousness (3/23, 13.2%), pulmonary embolism (1/23, 4.3%) and septic shock (1/23, 4.3%). Significant differences regarding age (72.2 ± 10.8 vs 65 ± 16, $P < 0.05$) and SAPS II (45 ± 12.7 vs 34 ± 13.1, $P < 0.05$) were found between EF patients and the others with extubation successful. The value of GCS was similar (14 ± 2.5 vs 13.8 ± 3.1, NS). EF patients have a longer period of MV (11 ± 15.8 vs 4 ± 8.9, $P < 0.05$) and LOS (23 ± 24.3 vs 6.6 ± 11, $P < 0.05$); they even have greater ICU and hospital mortality (39.1% vs 9.9% and 47.8% vs 16%). Seven EF patients (30%) needed at least one suctioning every 2 hours after extubation; moreover almost one-half of the patients (10/23, 43.3%) had a weak cough.

Conclusion Clinical features associated with EF include age, severity of illness and being a medical patient. EF increases the length of VM and LOS and is associated with a higher mortality. Most of EF is unable to protect the airway, a cause of weak cough and abundant secretions; moreover, during the trial of extubation, it is also important to consider the ability to cough and to clear respiratory secretions.

Reference

1. Epstein SK: **Decision to extubate.** *Intensive Care Med* 2002, **28**:535-546.

P178 Haemodynamic monitoring during high-frequency oscillatory ventilation in adults

A Wieczorek, T Gaszyński, M Kleszcz, P Kolasiński, W Gaszyński
Department of Anaesthesiology and Intensive Therapy, Medical University of Lodz, Barlicki Hospital, ul.Kopcinskiego 22, 90-153 Lodz, Poland
Critical Care 2003, **7(Suppl 2)**:P178 (DOI 10.1186/cc2067)

High-frequency oscillatory ventilation (HFOV) has been described as an effective therapy of RDS in prematurities and neonates. However, there are only few reports about using this technique in adults. The main goals of our study were establishing, during adult ventilation, the optimal parameters for monitoring HFOV, relative risk of hemodynamic disturbances connected with HFOV, and contraindications for HFOV. Until the present time six patients were enrolled to the study. The indications were: unsuccessful classical ventilation (CMV + PEEP + Plateau for at least 6 hours), or unsuccessful weaning (routine procedure for at least 7 days). After qualification all patients were ventilated using the SensorMedics 3100B oscillator. The following parameters were continuously measured: cardiac output using the Doppler technique (Abbott monitor), heart rate, blood pressures (systolic, diastolic, mean), EKG, SaO_2, and $ETCO_2$. Every hour CVP, arterial gases and diuresis were measured. In all patients a rapid increase in PaO_2 was observed, which enabled progressive decrease in FiO_2 (20–40%). After several hours of HFOV the condition of two patients deteriorated and it was necessary to immediately resume classical ventilation. One of these patients was morbidly obese (BMI = 43.2), whereas the other had critically low ejection fraction (14.3%) and low cardiac output (2.7–3.4 l/min). The first symptom of disturbances was a decrease of signal and amplitude of the plethysmographic curve. At that moment $PaCO_2$ was 34.2 and 47.0 mmHg, respectively, and

cardiac output was a little higher than initially. Another symptom was the disappearance of pleth signal. The next symptom was bradycardia and a sudden decrease of cardiac output (30–50%), while the stroke volume value remained unchanged. After resuming classical ventilation (CMV mode) and hemodynamic stabilization, a temporary increase of $PaCO_2$ was observed (60.1 and 65.3 mmHg). We concluded that: 1) The documented scenario of the deterioration was different from that typically observed during classical ventilation; 2) The SaO_2 and pleth curve monitoring during HFOV is essential for safety reasons; 3) The first symptom of deterioration during HFOV may be the decrease of amplitude and signal of the pleth curve; 4) The disappearance of the pleth signal is a sign of an imminent deterioration during HFOV; 5) The arterial gas analysis may not give sufficient information about the patient's condition; 6) Significant obesity and left ventricular insufficiency may be contraindications for HFOV in adults.

P179 Effects of different body positions on intra-abdominal pressure and dynamic respiratory compliance

MLNG Malbrain, N Van Mieghem, W Verbrugghe, R Daelemans, R Lins
Medical ICU, ACZA Campus Stuivenberg, 2060 Antwerpen, Belgium
Critical Care 2003, **7(Suppl 2)**:P179 (DOI 10.1186/cc2068)

Introduction Intra-abdominal pressure (IAP) is an important parameter and prognostic indicator of the patient's underlying physiologic status [1]. Measurement of IAP via the bladder has been forwarded as the gold standard. The abdomen is considered primarily fluid in character and therefore it follows the law of Pascal. If this is true IAP should be the same regardless of the body position since fluid is not compressible. Putting the patient in the upright position is a common practice in patients with acute respiratory failure (e.g. lung oedema). This study will look at the effects of different body positions on IAP and dynamic compliance (Cdyn) in mechanically ventilated patients.

Methods In total, 79 paired IAP and Cdyn measurements were performed at each body position in 10 mechanically ventilated ICU patients. The four positions studied were: supine, anti-trendelenburg, trendelenburg and the upright position. The IAP was calculated using the gold standard via an indwelling bladder catheter with a pressure transducer [1]. The Cdyn was calculated by dividing tidal volume (ml) by plateau pressure minus PEEP (cmH_2O). The male/female ratio was 3/2, BMI 26.3 ± 5.4, age 64.5 ± 15.7 years, APACHE II score 30.3 ± 10.5, SAPS II score 59.5 ± 11.1, MODS score 8.3 ± 3.8, and SOFA score 10.7 ± 3.6. The number of measurements in each patient was 7.9 ± 4. Statistical analysis was performed with SPSS 10™ software, and values are expressed as mean ± SD.

Results Table 1 presents the mean values for IAP and Cdyn in the different positions. The IAP was significantly higher in the anti-trendelenburg and upright positions versus the supine, and significantly lower in the trendelenburg position versus the supine ($P < 0.0001$, one-way ANOVA). The Cdyn was lowest in the upright position (P = NS). There was only in the upright position a poor but slightly significant correlation between IAP and Cdyn ($P = 0.047$). In five patients with a BMI > 25 (mean BMI 30.8 ± 3.2) the effect on IAP of the upright position versus the supine was significantly greater compared with patients with a BMI < 25 (mean BMI 21.8 ± 1.6): 10.1 ± 4.4 versus 6.8 ± 3.3 ($P = 0.001$), but the effect on Cdyn was the opposite: 6.8 ± 12.3 versus 21.1 ± 35.6 ($P = 0.02$).

Conclusions Putting a patient in different body positions has significant effects on IAP. This is in contradiction with the hypothesis that the abdominal compartment is primarily fluid in character, since IAP would then remain constant regardless of body position. Assessment of IAP should therefore always be done in the complete supine position. The upright position significantly increases IAP, and lowers Cdyn although not significantly. The effects on IAP are more pronounced in obese patients, and the effects on Cdyn more in the nonobese. Putting a patient with acute respiratory failure in the upright position may further deteriorate respiratory function, caused by the acute increase in IAP.

References

1. Malbrain MLNG: **Intra-abdominal pressure in the intensive care unit: clinical tool or toy?** In *Yearbook of Intensive Care and Emergency Medicine.* Edited by Vincent JL. Berlin: Springer-Verlag; 2001:547-585.

Table 1

	Supine	Anti-trendelenburg	Trendelenburg	Upright	Total	*P* value (ANOVA)
IAP (mmHg)	8.8 ± 3.9	13.3 ± 4.8	4.3 ± 3.8	17.1 ± 6.1	10.9 0 ± 6.8	< 0.0001
Cdyn (ml/cmH_2O)	40.2 ± 18.8	39.7 ± 18	38.6 ± 19.9	36.8 ± 18.6	38.8 ± 18.8	NS

P180 Pressures in the superior and inferior vena cava and intra-abdominal pressure

N Markou[1], P Myrianthefs[2], E Boutzouka[2], M Rizos[1], D Hroni[1], P Evagelopoulou[2], H Apostolakos[1], G Baltopoulos[2]
[1]ICU-B and [2]Athens University School of Nursing, ICU, Athens Trauma Hospital KAT, Athens, Greece
Critical Care 2003, **7(Suppl 2)**:P180 (DOI 10.1186/cc2069)

Purpose To investigate the relationship of pressure in the inferior vena cava (Pivc) with a) pressure in the superior vena cava (Psvc), and b) intra-abdominal pressure as measured in the urinary bladder (Pcyst).

Materials and results A prospective study of 38 mechanically ventilated patients. Simultaneous measurements of Psvc, Pivc and Pcyst (151 sets of measurements) were performed. Measurements were divided in: Group A (Pcyst < 10 mmHg), group B

(10 mmHg ≤ Pcyst < 15 mmHg), group C (Pcyst ≥ 15 mmHg). Statistical analysis was performed with the paired *t* test, Pearson correlation. Results are expressed as mean ± SEM (Table 1).

There was significant correlation of Psvc and Pivc in groups A and B (group A $r=0.93$, group B $r=0.87$). In Group C, Pivc correlated ($P<0.01$) with both Pcyst ($r=0.78$) and Psvc ($r=0.7$).

When Pcyst > Psvc, Pivc was higher than Psvc ($P<0.01$). Furthermore: a) with Pcyst < 15 mmHg, no significant difference was found between Pcyst and Pivc ($P=0.068$) and they were correlated ($r=0.766$, $P<0.05$). Pressures in the superior and inferior vena cava were also correlated ($r=0.764$, $P<0.05$). b) With Pcyst ≥ 15 mmHg, Pivc was lower than Pcyst ($P<0.01$). It highly correlated with Pcyst ($r=0.85$, $P<0.01$) and less strongly correlated with Psvc ($r=0.701$, $P<0.01$).

When Pcyst ≤ Psvc, no difference between Pivc and Psvc was observed. Furthermore: a) with Pcyst < 15 mmHg, Pivc was higher than Pcyst ($P<0.01$) and highly correlated with Psvc ($r=0.932$, $P<0.01$). Pivc also correlated with Pcyst ($r=0.69$, $P<0.01$). b) With Pcyst ≥ 15 mmHg, Pivc was higher than Pcyst ($P<0.01$) and correlated with Psvc ($r=0.74$, $P<0.01$) and Pcyst ($r=0.789$, $P<0.01$).

Table 1

	Psvc (mmHg)	Pivc (mmHg)	Pcyst (mmHg)
Group A ($n=62$)	10.8 ± 0.5	10.93 ± 0.49	6.35 ± 0.26*
Group B ($n=45$)	14.44 ± 0.71	14.67 ± 0.58	11.44 ± 0.22*
Group C ($n=43$)	16.39 ± 0.72*	18.88 ± 0.69	19.18 ± 0.63

* Difference from Pivc statistically significant (*t* test, $P<0.05$).

Conclusions Although Psvc and Pivc are interchangeable in the absence of an increased Pcyst, when Pcyst is high measurements of Pivc are misleading. A Pcyst > Psvc results to a 'waterfall' effect, and Pivc does not accurately reflect Psvc any more.

P181 Continuous negative abdominal pressure decreases intra-abdominal and central venous pressure in ICU patients

F Valenza, N Bottino, D Chiumello, G Li Bassi, E Storelli, R Russo, K Canavesi, L Gattinoni
Istituto di Anestesia e Rianimazione, Ospedale Maggiore di Milano – IRCCS, via F. Sforza n. 35, 20122 Milano, Italy
Critical Care 2003, **7(Suppl 2)**:P181 (DOI 10.1186/cc2070)

We set out to investigate whether continuous negative abdominal pressure (CNAP) might be used to decrease abdominal pressure. We investigated the effects of CNAP on both intra-abdominal pressure (IAP) and central venous pressure (CVP) on 30 consecutive patients admitted to our ICU (age 62 ± 14 years, BMI 26.3 ± 4, SAPS II 40.4 ± 18). Patients with severe hemodynamic instability and/or with recent laparotomy were not studied. Measurements included bladder pressure as an index of IAP, CVP, invasive mean arterial pressure (APm) and heart rate (HR). Following baseline measurements (Basal), CNAP (Life Care – Nev 100, Respironics) was applied on the abdomen at three levels: CNAP=, CNAP –5 and CNAP –10, corresponding to negative pressure equal to baseline IAP, 5 or 10 cmH_2O lower than CNAP=, respectively. Results are as presented in Table 1.

CVP was correlated with IAP ($R^2=0.790$, $P<0.001$, multiple linear regression).

Given these results, we conclude that CNAP decreases IAP and CVP; the higher the negative pressure applied, the greater the changes. CVP decreases possibly because of a blood shift from the intrathoracic compartment.

Table 1

	Basal	CNAP =	CNAP –5	CNAP –10	RM ANOVA
IAP (cmH_2O)	11.9 ± 5.8	8.2 ± 5.7*	5.9 ± 4.3*†	5.2 ± 4.9*†	< 0.001
CVP (mmHg)	9.2 ± 3.4	8.4 ± 3.4*	7.5 ± 3.5*†	7.5 ± 3.8*†	< 0.001
APm (mmHg)	88 ± 13	86 ± 14	86 ± 14	87 ± 15	NS
HR (bpm)	87 ± 16	89 ± 18	88 ± 17	91 ± 19*	0.03

* $P<0.05$ vs basal, † $P<0.05$ vs CNAP =. Multiple comparisons (Student–Newman–Keuls).

P182 Effects of continuous negative abdominal pressure on intrathoracic blood shift with and without increased intra-abdominal pressure: experimental study

F Valenza, M Guglielmi, S Gatti, N Bottino, S Giacomini, M Irace, C Tedesco, M Maffioletti, P Maccagni, L Gattinoni
Istituto di Anestesia e Rianimazione, Ospedale Maggiore di Milano – IRCCS, via F. Sforza n. 35, 20122, Milano, Italy
Critical Care 2003, **7(Suppl 2)**:P182 (DOI 10.1186/cc2071)

We set out to investigate whether continuous negative abdominal pressure (CNAP) may produce blood shift from the intrathoracic compartment, and whether this effect would be influenced by abdominal pressure. We investigated eight sedated, paralysed and mechanically ventilated pigs (19.4 ± 4 kg). Blood shift was assessed by measuring intrathoracic blood volume (ITBV; PiCCO Pulsion), and central venous pressure (CVP). Measurements were taken before (Pre), a few seconds and 15 min after CNAP (–20 cmH_2O; Life Care – Nev 100, Respironics) was applied on the abdomen (CNAP 1 and CNAP 2, respectively), and after CNAP was relieved (Post). The sequence of measurements was taken with and without abdominal hypertension. This was induced by means of helium (He) insufflation targeted to a value of 25 mmHg (24.7 ± 5.5 direct peritoneal measurement), corresponding to a bladder pressure of

Table 1

		Pre	CNAP 1	CNAP 2	Post	RM ANOVA
ITBV	Basal	293.2 ± 41.6	256.6 ± 43.6*	254.0 ± 37.9*	291.4 ± 31.1	< 0.001
	He	333.5 ± 44.9	331.3 ± 47.3	318.9 ± 33.9	337.1 ± 44.5	
CVP	Basal	6.36 ± 1.63	4.02 ± 1.75*	4.61 ± 1.71*†	7.03 ± 1.64	< 0.001
	He	6.67 ± 2.11‡	6.84 ± 2.06	6.81 ± 2.09	6.77 ± 2.13	

* $P < 0.05$ vs Pre, † $P < 0.05$ vs CNAP 1, ‡ $P < 0.05$ vs basal. Multiple comparisons (Student–Newman–Keuls).

29 ± 4 cmH_2O. Basal and He measurements were randomised with respect to time. Results are shown in Table 1.

CVP was correlated with ITBVI ($R^2 = 0.818$, $P < 0.001$, multiple linear regression).

We conclude that CNAP induces a blood shift from the intrathoracic compartment. Blood shift is greater without abdominal hypertension.

P183 Can abdominal perimeter be used as an accurate estimation of intra-abdominal pressure?

N Van Mieghem, W Verbrugghe, R Daelemans, R Lins, MLNG Malbrain
Medical ICU, ACZA Campus Stuivenberg, 2060 Antwerpen, Belgium
Critical Care 2003, **7(Suppl 2)**:P183 (DOI 10.1186/cc2072)

Introduction Intra-abdominal pressure (IAP) is an important parameter and prognostic indicator of the patient's underlying physiologic status [1]. Correct IAP measurement therefore is crucial. Most of the direct and indirect techniques are not free of risks and require some time and skills. This study will look at the possibility of using the abdominal perimeter (AP) as a quick estimation for IAP.

Methods In total, 132 paired measurements were performed in 12 ICU patients. The IAP was calculated using the gold standard via an indwelling bladder catheter using a pressure transducer [1]. The AP was calculated by measuring the abdominal circumference at its largest point using body marks as reference for consecutive measurements. The male/female ratio was 7/5, age 68.5 ± 17.2 years, APACHE II score 27.8 ± 6.5, SAPS II score 58.9 ± 12.5. The number of measurements in each patient was 11 ± 4.2. Calculation of correlation was done with the Prism GraphPad™ software (version 2.00, 31 October 1995), values are mean ± SD.

Results The values for IAP (mmHg) were 13.2 ± 12.6 versus 106.7 ± 15.2 for AP. There was a poor but slightly significant correlation between IAP and AP (Fig. 1): AP = 1.0357 × IAP + 94.107 ($R^2 = 0.12$, $P = 0.042$), but the bias was considerable. The correlation was better between ΔIAP (the difference between two consecutive IAP measurements) and ΔAP (the difference between two consecutive AP measurements) in 119 paired measurements (Fig. 2): ΔAP = 0.4598 × ΔIAP + 0.158 ($R^2 = 0.22$, $P < 0.0001$, two-tailed Pearson correlation). The analysis according to Bland and Altman showed that ΔIAP was almost identical to ΔAP with a mean difference or bias of 0.05 ± 3.54 (SD) mmHg (95% CI −0.6 to 0.7); the limits of agreement (LA) were −7.04 to 7.13 mmHg (95% CI −8.16 to −5.92 for the LLA and 6.01 to 8.25 for the ULA), these intervals are large and thus reflect poor agreement.

Conclusions In view of the poor correlation between IAP and AP, the latter cannot be used as a clinical estimate for IAP. The evolution of AP (ΔAP) can be used as an indicator for the evolution of IAP over time (ΔIAP); however, for making a definite diagnosis of IAH or ACS, the exact value of IAP needs to be measured.

Reference

1. Malbrain MLNG: **Intra-abdominal pressure in the intensive care unit: clinical tool or toy?** In *Yearbook of Intensive Care and Emergency Medicine.* Edited by Vincent JL. Berlin: Springer-Verlag; 2001:547-585.

Figure 1

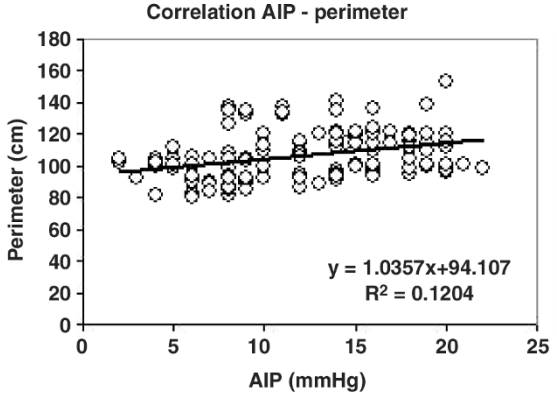
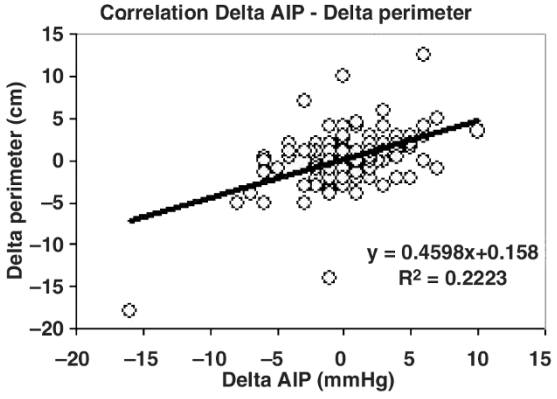


Figure 2



P184 Estimating the optimal bladder volume for intra-abdominal pressure measurement by bladder pressure–volume curves

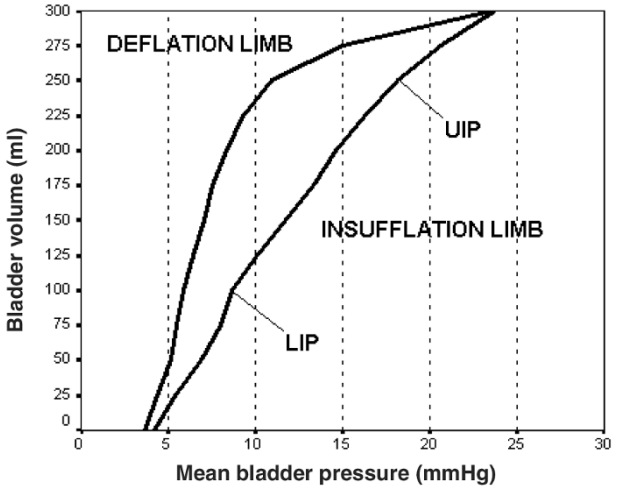
W Verbrugghe, N Van Mieghem, R Daelemans, R Lins, MLNG Malbrain
Medical ICU, ACZA Campus Stuivenberg, 2060 Antwerpen, Belgium
Critical Care 2003, **7(Suppl 2)**:P184 (DOI 10.1186/cc2073)

Introduction Intra-abdominal pressure (IAP) is an important parameter and prognostic indicator of the patient's underlying physiologic status [1]. Correct IAP measurement therefore is crucial. Because measurement of IAP by an indwelling catheter in the urinary bladder is simple, minimally invasive, and reproducible, it has been forwarded as the gold standard. It was thought that the highly compliant wall of the bladder acts as a passive diaphragm, and intrinsic bladder pressure did not rise when its volume is between 50 and 100 ml. However, considerable variability in the measurement technique has been noted, not only interindividual and intraindividual but also intercentre and intracentre. Variations in IAP from −6 to +30 mmHg have been noted. The measurement technique itself is also not uniform, some authors recommend injecting 50 ml saline, others up to 200 ml. The aim of the present study is to determine the optimal bladder volume for correct IAP transmission but without the risk of 'over inflation' of the bladder and raising intrinsic intrabladder pressure (IBP).

Methods In six sedated and mechanically ventilated patients sterile saline was injected via a Foley catheter with 25 ml increments up to 300 ml. In total 13 'insufflation' and 'deflation' pressure–volume (PV) curves were constructed in these patients. The male/female ratio was 5/1, age 63.8 ± 14, MODScore 8.6 ± 4, SOFA score 10 ± 4.5, APACHE II score 31 ± 11.4, SAPS II score 59.2 ± 13.2. The number of measurements in each patient was 2.3 ± 0.5. Construction of PV curves was done with the SPSS 10™ software, values are mean ± SD.

Results The values for IBP with regard to bladder volume are summarized in Table 1. Figure 1 plots the 'insufflation' and 'deflation' PV curve as a curve fit of the means of the 13 measurements. A lower inflection point (LIP) can be seen at a bladder volume of 100 ml and an upper inflection point (UIP) at a bladder volume of 250 ml. The difference in bladder pressure was 2.7 ± 3.3 mmHg between 0 and 50 ml volume, 1.7 ± 1.2 mmHg between 50 and 100 ml, 7.7 ± 5.7 mmHg between 50 and 200 ml, and 16.8 ± 13.4 mmHg between 50 and 300 ml.

Figure 1



Conclusions If IBP is used as an estimate for IAP the volume instilled in the bladder should be between 50 and 100 ml; however, in some patients with a low bladder compliance, intrinsic bladder pressure can be raised at low bladder volumes. Ideally a bladder PV curve should be constructed for each individual patient before using IBP as an estimation for IAP.

Reference

1. Malbrain MLNG: **Intra-abdominal pressure in the intensive care unit: clinical tool or toy?** In *Yearbook of Intensive Care and Emergency Medicine.* Edited by Vincent JL. Berlin: Springer-Verlag; 2001:547-585.

Table 1

Bladder volume (ml)	0	50	100	150	200	250	300
IBP (mmHg)	4.2 ± 3.2	6.9 ± 5	8.7 ± 5.2	11.8 ± 6.8	14.6 ± 8.9	18.2 ± 12.3	23.7 ± 16.1

P185 Bioelectrical impedance analysis as a predictor for survival in patients with systemic inflammatory response syndrome

S Swaraj[1], G Marx[1], G Masterson[2], M Leuwer[1]
[1]University Department of Anaesthesia, University of Liverpool, Liverpool L69 3GA, UK; [2]Department of Intensive Care, Royal Liverpool University Hospital, Liverpool, UK
Critical Care 2003, **7(Suppl 2)**:P185 (DOI 10.1186/cc2074)

Objectives Noninvasive bioelectrical impedance analysis (BIA) measures resistance, reactance and the derived phase angle (phi, degrees). A low phase angle has been associated with an altered cellular membrane function [1]. In septic shock patients, a phase angle of less than 4° has been reported to be associated with increased mortality [2]. Furthermore a low phase angle was highly correlated with mortality in patients with AIDS [3] and burns [4]. In our study we examined the prognostic value of the phase angle using BIA in patients with systemic inflammatory response syndrome (SIRS).

Design Prospective clinical observational study.

Measurements Thirty consecutive patients (11 female, 19 male, median age of 67 [16.5] years) were included after admission to the intensive care unit, all of whom met two or more SIRS criteria. SIRS was defined using the criteria suggested by ACCP/SCCM guidelines. Severity of illness was characterised according to the Acute Physiology and Chronic Health Evaluation (APACHE) II. Noninvasive impedance analysis was performed using a tetra polar hand-to-foot BIA measuring device (BIA 2000, Data input) as resistance (Ohms) and reactance (Ohms). The derived phase angle was calculated as arc tan(reactance/resistance). Two diagnostic electrodes were attached to the hand and two diagnostic electrodes were attached to the ipsilateral foot. All measurements were performed in supine position of the patient with special care taken that arms and legs did not touch the rest of the body or any grounding object. The joints were semiflexed. Data are presented as median and interquartile range (IQR). Fisher's exact test was performed to compare a phase angle of more than 4° at inclusion day with the 28 day mortality and APACHE II scores between survivors and nonsurvivors. $P<0.05$ was considered significant.

Results After 28 days, out of the 30 patients investigated 10 had died and 20 were survivors. The APACHE II score on inclusion day of the survivors was 11 (7.0) compared with 16 (6.8) in nonsurvivors ($P=0.87$). In seven out of the 20 survivors a phase angle of more than 4° was measured on the first study day, whereas in all patients who died the phase angle was smaller than 4° ($P=0.038$).

Conclusion These results demonstrate that, in patients developing SIRS, an initial phase angle of more than 4° may be significantly correlated with survival.

References

1. Mattar JA: *New Horiz* 1996, **4**:493-503.
2. Marx G, *et al.*: *Intensive Care Med* 2000, **26**:1252-1258.
3. Ott M, *et al.*: *J Acquir Immune Defic Syndr Hum Retrovirol* 1995, **9**:20-25.
4. Zdolsek HJ, *et al.*: *Burns* 1998, **24**:233-240.

P186 Assessment of variables affecting the accuracy of extravascular lung water (EVLW) by single versus double indicator dilution techniques in ARDS patients

E Maggioni, F Sala, A Manfio, E Saccavino, B Cortinovis, G Bellani, N Patroniti
Department of Anaesthesia and Intensive Care, University of Milano-Bicocca, S. Gerardo Hospital, Italy
Critical Care 2003, **7(Suppl 2)**:P186 (DOI 10.1186/cc2075)

Introduction Estimation of extravascular lung water (EVLW) by the single indicator dilution technique (SDT) implemented in the PICCO monitoring system relies on a relationship between intrathoracic blood volume (ITBV) and global end diastolic volume (GEDV), which has been derived from a large population of mixed critically ill patients using the double indicator dilution technique (thermal and indocyanine green dyes, DDT): $ITBV_{sdt} = 1.25 \times GEDV$ [1]. Since the difference between ITBV and GEDV corresponds to pulmonary blood volume (PBV), we can write: $PBV_{sdt} = 0.25 \times GEDV$. Any factor influencing this relationship can affect SDT accuracy. The aims of our study were: 1) to compare SDT versus DDT for EVLW measurements in ARDS patients; and 2) to explore factors influencing the PBV and GEDV relationship, and affecting SDT accuracy.

Methods We studied 21 ARDS patients ($PaO_2/FiO_2 = 165 \pm 65$), monitored with a Swan–Ganz catheter, and a 4 F thermistore-tipped, fiberoptic catheter inserted through a femoral artery, both connected to a COLD monitoring system. SDT measurements were obtained by mean transit time and down slope time of thermal indicator using standard formula. Statistical analysis was performed by single and multiple linear regression analysis; accuracy was assessed according to Bland and Altman method.

Results Agreement between $EVLW_{ddt}$ and $EVLW_{sdt}$ showed a bias of 15.3 ± 135.8, and a 95% confidence interval of −256 and 287; the correlation coefficient was $r=0.92$ ($P<0.001$). Correlations of GEDV and PBV_{sdt} with PBV_{ddt}, although significant, were poor ($r=0.394$, $P<0.01$). $EVLW_{ddt}$ indexed to body weight (EVLWi) and cardiac index (CI) explained 64% of PBV indexed to body surface area (PBVi) variance ($P<0.001$). EVLWi, CI, central venous pressure (CVP), and $PaCO_2$ explained 82% of PBVi to GEDVi ratio variance ($P<0.001$). $EVLW_{ddt}$ to $EVLW_{sdt}$ differences were highly correlated with PBV_{ddt} ($r=0.88$, $P<0.001$). EVLWi, CI and $PaCO_2$ explained 65% of the differences between $EVLW_{ddt}$ and $EVLW_{sdt}$ variance ($EVLW_{ddt} - EVLW_{sdt} = -263 + 18.64 \times EVLWi - 50.9 \times CI + 5.3 \times PaCO_2$, $r^2=0.65$, $P<0.001$).

Conclusions The SDT gives acceptable estimates of EVLW in ARDS patients. EVLWi, CI and $PaCO_2$ may influence the relationship between PBV and GEDV, and may affect accuracy of EVLW measured by SDT.

Reference

1. Sakka SG, *et al.*: **Assessment of cardiac preload and extravascular lung water by single transpulmonary thermodilution.** *Intensive Care Med* 2000, **26**:180-187.

P187 Is there a role of extravascular lung water (EVLW) in the development of atelectasis in ARDS?

T Szakmány, Z Molnár, P Heigl
Department of Intensive Care, University of Pécs, Ifjuság 13, 7643 Pécs, Hungary
Critical Care 2003, **7(Suppl 2)**:P187 (DOI 10.1186/cc2076)

Objectives To evaluate the relationship between PaO_2/FiO_2 ratio and EVLW in septic shock induced ARDS in a prospective observational clinical trial.

Materials and methods Twenty-three patients suffering from sepsis-induced ARDS were recruited. All patients were ventilated in pressure control/support mode. Haemodynamic parameters were determined by arterial thermodilution (PiCCO) 8 hourly for 72 hours. At the same time blood gas analyses were done and respiratory parameters were also recorded. Data are presented as mean ± SD. For statistical analysis, Pearson's correlation test, and analysis of variance (ANOVA) was used, respectively.

Results Significant negative correlation was found between EVLW and PaO_2/FiO_2 ($r=-0.355$, $P<0.001$), and significant positive correlation was shown between EVLW and PEEP ($r=0.557$,

$P<0.001$). A *post-hoc* analysis was also performed when 'low' PEEP ($<10\,cmH_2O$) and 'high' PEEP ($\geq 10\,cmH_2O$) were applied (Table 1).

Table 1

	'Low' PEEP ($n=49$)	'High' PEEP ($n=140$)	P
PaO_2/FiO_2 (mmHg)	175 ± 56	170 ± 73	0.730
$PaCO_2$ (mmHg)	44 ± 8	46 ± 11	0.155
ΔP(PIP – PEEP) (cmH_2O)	20 ± 4	20 ± 6	0.960
EVLWI (ml/kg)	9 ± 2	13 ± 5	0.001

Discussion Several animal trials reported contradicting results on the effect of PEEP on EVLW [1]. We found significant correlation between EVLW and PaO_2/FiO_2 and PEEP. Furthermore, patients with increase EVLW required higher PEEP, while none of the other parameters differed significantly when 'high' or 'low' PEEP were applied. Based on the current results we assume that it is the EVLW that indirectly determines the required PEEP by playing a part in the development of alveolar atelectasis. Further studies are required to evaluate the clinical significance of this finding, for example in the fine-tuning of PEEP in ARDS.

Reference

1. Ruiz-Bailen M, Fernandez-Mondejar E, Hurtado-Ruiz B, *et al.*: *Crit Care Med* 1999, **27**:380-384.

P188 Intrathoracic blood volume is not a sensitive indicator for hypervolaemia in healthy, mechanically ventilated pigs

G Marx[1], S Pedder[1], S Swaraj[1], U Pfeiffer[2], M Leuwer[1]

[1]University Department of Anaesthesia, University of Liverpool, Liverpool L69 3GA, UK; [2]Technical University of Munich, Faculty of Medicine, Germany

Critical Care 2003, **7(Suppl 2)**:P188 (DOI 10.1186/cc2077)

Objectives Intrathoracic blood volume (ITBV) measured by the transpulmonary technique has been suggested as an alternative parameter predicting cardiac preload in critically ill patients [1]. So far, it has never been shown that by measuring ITBV it is possible to detect hypervolaemia.

Design Prospective animal laboratory study.

Setting University animal laboratory.

Measurements Healthy, anaesthetized, and mechanically ventilated pigs ($n=4$) with a median weight of 24.5 kg (23.3–26.5 kg) were investigated. A pulmonary artery catheter (831HF75, 7.5 F Edwards Lifesciences Ltd) inserted via the right jugular vein and an arterial catheter for transpulmonary thermodilution (4 F PV 2014L16, Pulsion Medical Systems) was inserted into the right carotid artery. Measurements of haemodynamic parameters included heart rate (HR), mean arterial pressure (MAP), cardiac output (CO), pulmonary arterial occlusion pressure (PAOP), central venous pressure (CVP), extravascular lung water (EVLW) and ITBV. After baseline measurement, hypervolaemia was induced by stepwise (10% per step) cumulative administration of 50% of the estimated blood volume of the animals (80 ml/kg) using 6% hydroxyethylstarch 200/0.5. The interval between each of the five steps was 10 min. Haemodynamic parameters, EVLW and ITBV before and after hypervolaemia were compared by Friedman's test. Data are presented as the median and interquartile range. $P<0.05$ was considered significant.

Results After establishment of hypervolaemia the following parameters increased significantly: HR from 85 beats/min (68–103) to 130 beats/min (124–134), MAP from 98 mmHg (96–101) to 116 mmHg (107–128), CO from 120 ml/min per kg (100–138) to 190 ml/min per kg (156–233), EVLW from 3.9 ml/kg (3.5–8.5) to 19.0 ml/kg (14.8–24.2), CVP from 9 mmHg (8–9) to 27 mmHg (25–30), and PAOP from 10 mmHg (10–11) to 27 mmHg (25–27), whereas ITBV did not change significantly from 21.9 ml/kg (19.0–24.7) to 23.1 ml/kg (20.8–26.3).

Conclusion Intrathoracic blood volume is not a sensitive indicator for hypervolaemia in healthy, mechanically ventilated pigs in the presence of severely increased EVLW.

Reference

1. Sakka SG, Bredle DL, Reinhart K, *et al.*: *J Crit Care* 1999, **14**:78-83.

P189 Ultrasound diagnosis of an acute dyspnea

D Lichtenstein, G Mezière

Hôpital Ambroise Paré, Department of Intensive Care, F-92100 Boulogne (Paris), France

Critical Care 2003, **7(Suppl 2)**:P189 (DOI 10.1186/cc2078)

Introduction Acute dyspnea is a typical emergency situation. The usual tools (physical examination, radiography) can sometimes be insufficient. Although 1) ultrasound is rarely performed in emergency by the physician, and 2) lung is considered out of reach of the ultrasound field, we have studied its potential to provide an adequate diagnosis, at the bedside.

Patients This prospective study initially included 74 consecutive patients seen for acute dyspnea and referred to the intensivist by a senior (ER, prehospital setting). Fourteen patients where no definite diagnosis was made were subsequently excluded. Sixty patients were thus enrolled (27 women and 33 men, mean age 73 years, range 22–91 years). The patients had cardiogenic pulmonary edema ($n=16$), acute pneumonia ($n=16$), exacerbation of chronic obstructive pulmonary disease ($n=11$), severe asthma ($n=7$), pulmonary embolism ($n=6$), pneumothorax ($n=2$) and substantial pleural effusion ($n=2$).

Methods The 'initial diagnosis' was the diagnosis made by the senior using clinical examination and basic tools like bedside radiograph, before admission of the patient to the ICU. The 'ultrasound diagnosis' was a diagnosis made after studying six items and establishing an 'ultrasound profile'. Lung sliding, comet-tail artefacts of the type 'lung rockets' (i.e. interstitial syndrome), alveolar

consolidation, pleural effusion (with quantitative approach), left ventricle and venous status were included. 'Initial diagnosis' and 'ultrasound diagnosis' were compared together. The gold standard was the diagnosis concluding the hospitalisation report. The patients were analysed with a small ultrasound unit Hitachi-405 equipped with a 5 MHz probe without Doppler, by an intensivist trained to emergency general ultrasound. The whole examination took less than 5 min. This study did not consider the ability of decreasing delay for adequate treatment.

Results Ultrasound was possible in all patients (i.e. a feasibility of 100%). All in all, the initial diagnosis was correct in 31 cases (i.e. 51% of cases). The ultrasound diagnosis was correct (allowing appropriate management) in 51 cases (i.e. 85% of cases).

The number of cases in which ultrasound gave the correct diagnosis in a patient with a wrong initial diagnosis was 24. The number of cases in which ultrasound led to a wrong diagnosis in patients whose initial diagnosis was correct was four. In 32 cases, ultrasound was not contributive (27 cases whose initial diagnosis was correct, and five cases in whom both initial diagnosis and ultrasound diagnosis were in failure).

Conclusions Taking into account ultrasound items using simple methods provided an accurate diagnosis of acute dyspnea in 85% of cases, versus 51% with the traditional methods. The ultrasound approach checked lungs, heart and veins like a stethoscope. Obviously, the physician's accuracy will be enhanced by integrating clinical and paraclinical data. In conclusion, this method should contribute to quicker diagnosis, resulting in decreased costs, and above all quicker relief of dyspneic patients.

P190 Beat-by-beat measurement of cardiac output during aortocoronary surgery

P Giomarelli, S Scolletta, B Biagioli, SM Romano
Department of Surgery and Bioengineering, University of Siena, Italy
Critical Care 2003, **7(Suppl 2)**:P190 (DOI 10.1186/cc2079)

Introduction Unavailability of online continuous data, invasiveness, and expensiveness are the major drawbacks of the most commonly employed techniques to measure cardiac output. Cardiac output (CO) is often monitored after cardiac operations with a pulmonary artery catheter. A new method has been introduced that measures cardiac output by arterial pressure (pressure recording analytical method [PRAM]) without calibration by thermodilution (ThD). This study assessed the reliability of cardiac output determinations by PRAM before, during and after cardiac surgery.

Materials and methods In 12 patients undergoing aortocoronary bypass surgery, between September and November 2002 at the Department of Cardiothoracic Surgery of the University of Siena, CO was measured after induction of anesthesia, after closure of the sternum, and upon returning to the ICU (30 min and 3 hours) by thermodilution and PRAM. PRAM is a new method based on the objective mathematical analysis of changes of arterial pressure profile with time. PRAM allows real time beat-by-beat CO assessment from the pressure signals recorded in radial artery without calibration by ThD. Cardiac output (l/min) was measured continuously throughout the duration of the study.

Statistical analysis CO values obtained at the same time of the ThD dilution curve (240 paired data) were used for the comparison by linear correlation and Bland–Altman analyses. ThD, the established clinical method to measure CO, was taken as the independent variable.

Results The correlation between PRAM and ThD CO values was 0.83 ($R^2 = 0.69$; $P < 0.01$) with a bias of 0.05 (95% CI −0.71 to 0.81). The correlation at 3 hours from arrival at ICU (the moment of steady-state clinical condition) showed a better agreement ($R^2 = 0.82$; $P < 0.001$) with a bias of 0.02 (95% CI −0.78 to 0.86).

Conclusions In this small series of cardiac surgery patients, PRAM reflects ThD values and permits one to monitor continuously CO with reduced invasiveness and at a much lower cost with respect to ThD. In conclusion, PRAM provides reliable estimates of cardiac output in hemodynamically stable and unstable cardiac patients.

References

1. Romano SM, Pistolesi M: **Assessment of cardiac output from systemic arterial pressure in humans.** *Crit Care Med* 2002, **30**:1834-1841.
2. Jansen JR, Schreuder JJ, Mulier JP, *et al*: **A comparison of cardiac output derived from the arterial pressure wave against thermodilution in cardiac surgery patients.** *Br J Anaesth* 2001, **87**:212-222.
3. Zollner C, Haller M, Weis M, *et al*: **Beat to beat measurement of cardiac output by intravascular pulse contour analysis: a prospective criterion standard study in patients after cardiac surgery.** *J Cardiothorac Vasc Anesth* 2000, **14**:125-129.
4. Goedje O, Hoeke K, Lichtwaerck-Aschoff M, *et al*: **Continuous cardiac output by femoral arterial thermodilution calibrated pulse contour analysis: comparison with pulmonary arterial thermodilution.** *Crit Care Med* 1999, **27**:2407-2412.

191 Early detection of cardiovascular instability by monitoring oxygen uptake and carbon dioxide production

V Pilas, N Vucic, K Cala
GH Holy Ghost, Zagreb, Croatia
Critical Care 2003, **7(Suppl 2)**:P191 (DOI 10.1186/cc2080)

The oxygen uptake and carbon dioxide production were measured in 21 patients in sepsis during conventional hemodynamic resuscitation. We assumed that in the state of low oxygen delivery, carbon dioxide is increasingly eliminated from the body. We hypothesized that this condition can be recognized from the VCO_2/VO_2 relationship.

VO_2 and VCO_2 were measured by analysis of expired gas by metabolic monitor; hemodynamics was monitored by pulmonary artery catheter. Cardiac output was determined by thermodilution, oxygen transport variables were gauged according to standard formulas using samples from peripheral arterial and mixed venous blood from pulmonary artery.

The patients were monitored for 6 hours. Lower values of VO_2 were followed with higher values of VCO_2. There was a high coefficient of negative correlation between cardiac index and respiratory quotient ($r=-0.85$; $P=0.002$). The similar correlation, as expected, was found between oxygen delivery and respiratory quotient ($r=-0.75$; $P=0.01$). The positive correlation was detected between respiratory quotient and venous–arterial CO_2 difference ($v-aDCO_2$) ($r=0.79$; $P=0.016$).

Our preliminary conclusion was that cardiovascular instability in patients with sepsis can be recognized from variations in VO_2 and respiratory quotient.

P192 Transpulmonary thermodilution technique for cardiac output measurements: single versus double indicator

MG Costa, L Pompei, C Coccia, G Della Rocca
Clinica di Anestesia, University of Udine, P le S. M. della Misericordia 15, 33100 Udine, Italy
Critical Care 2003, **7(Suppl 2)**:P192 (DOI 10.1186/cc2081)

Introduction The aim of the study was to compare ITBVI and EVLWI measured by the double indicator ($ITBVI_{TD}$, $EVLWI_{TD}$) [1] with those estimated by the single indicator technique ($ITBVI_{ST}$, $EVLWI_{ST}$) [2].

Methods Thirty-five patients (24 male, 11 female), mean age 49 (10) years, body surface area 1.8 (0.2) m^2, undergoing liver transplantation (Ltx) were studied. Each patient received a pulmonary artery catheter placed via the right internal jugular vein and a 4 Fr thermistor-tipped fiberoptic catheter for thermal dye dilution inserted into the descending aorta connected to the COLD-Z021 (Pulsion Medical System, Munich, Germany). For the double indicator method, a bolus injection was made with cooled (0–4°C) indocyanine green dissolved in glucose 5% in a concentration of 2 mg/ml, and for the single indicator technique 15 ml cooled normal saline was used. Bland and Altman analysis was used for statistical evaluation.

Results The mean bias between $ITBVI_{TD}$ and $ITBVI_{ST}$ was 8.6 ml/m^2 with a standard deviation of 61.8 ml/m^2, and the mean bias between $EVLWI_{TD}$ and $EVLWI_{ST}$ was −0.2 ml/kg with a standard deviation of 2.2 ml/kg.

Conclusions The single transpulmonary thermodilution technique is as accurate as the double indicator method for ITBVI and EVLWI estimation.

References
1. Sakka SG, *et al.*: *J Crit Care* 1999, **14**:78-83.
2. Sakka SG, *et al.*: *Intensive Care Med* 2000, **26**:180-187.

Figure 1

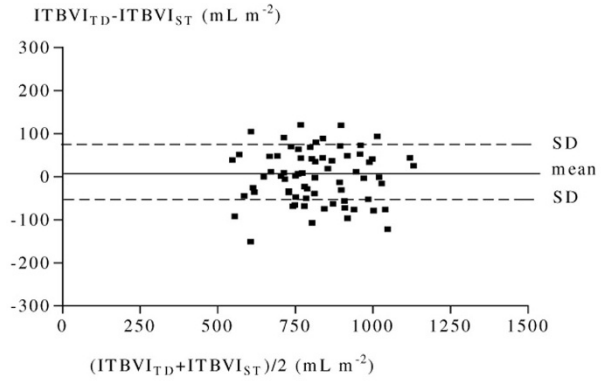
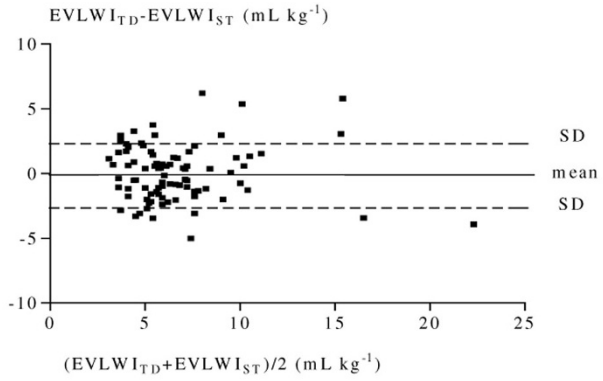


Figure 2



P193 Continuous monitoring of cardiac output during pneumoperitoneum by esophagal Doppler

F Zveibil[1], S Yvri[2], A Schlepak[2], N Makhoul[3]
[1]General Intensive Care Unit and [3]Respiratory Intensive Care Unit, and [2]Department of Anesthesia, Western Galilee Medical Center, Nahariya, Israel
Critical Care 2003, **7(Suppl 2)**:P193 (DOI 10.1186/cc2082)

Objective The recognition of hemodynamic disturbances during an apparently uneventful surgery is important. Therefore, we applied esophageal Doppler monitoring (EDM) to examine cardiovascular events caused by insufflation during laparoscopy.

Methods Twenty-three patients undergoing laparoscopic cholecystectomy were studied. EDM readings were taken, starting 10 min after induction of anesthesia, every 3 min throughout pneumoperitoneum, and 10 min after exsufflation.

Results During pneumoperitoneum, the cardiac output was significantly lower and the systemic vascular resistance significantly higher than either before or after insufflation. The semi-continuous EDM revealed that, despite the sharp decrease in cardiac output upon insufflation, during pneumoperitoneum it recovered gradually in many patients. The increase ranged from 4% to 84%. In about two-thirds of the patients the final values of cardiac output during pneumoperitoneum were within ±10% of the post-exsufflation values. In three patients (13%), however, there was a substantial

decline of cardiac output during pneumoperitoneum. Obese individuals exhibited a larger proportional recovery of the cardiac output during pneumoperitoneum ($P=0.009$). No gender or age dependence was noted, and the duration of surgery or ASA grade was not correlated with the recovery, nor was the absolute drop in cardiac output upon insufflation.

Conclusions The findings suggest that, after the initial decreases of venous and portal return, a compensating mechanism, responsible for the subsequent relief of cardiac output depression, becomes effective. The findings demonstrate the utility of EDM for continuous monitoring during laparoscopy, especially in high-risk patients.

P194 The effect of a decrease in arterial blood pressure on renal urodilatin excretion in anesthetized rats

M Heringlake[1], S Klaus[1], L Bahlmann[1], J Schumacher, P Schmucker[1], H Pagel[2]
[1]Universität zu Lübeck, Klinik für Anaesthesiologie and [2]Institut für Physiologie, 23538 Lübeck, Germany
Critical Care 2003, **7(Suppl 2)**:P194 (DOI 10.1186/cc2083)

Background We have recently shown that the renal excretion of urodilatin ($U_{URO}V$) can be modified by renal perfusion pressure *in vitro* [1]. It is not clear whether an interaction between arterial blood pressure and $U_{URO}V$ may also be observed *in vivo*.

Methods Anesthetized male Sprague–Dawley rats were studied for 180 min. Measurements were performed every 30 min. We determined mean arterial pressure (MAP), urine flow (UV), glomerular filtration rate (GFR), the renal excretion of sodium ($U_{Na}V$), and of urodilatin ($U_{URO}V$; determined by RIA). Rats were randomly assigned to a control group (CON: $n=10$) and a hypotension group (HYP: $n=10$). After 60 min stabilization (baseline [BL]), in the HYP group, blood pressure was decreased 30 mmHg below individual BL levels for 60 min by a continuous infusion of sodium nitroprusside (intervention [IV]). Thereafter, rats were allowed to recover for another 60 min (recovery [RC]). Data were averaged for the respective study periods; renal function parameters and $U_{URO}V$ are given as relative values in comparison with the BL period.

Results In the HYP group, the decrease in MAP during the IV period was accompanied by decreased UV (CON: 216.8 ± 36.9%; HYP: 89.3 ± 11.1%; $P=0.04$). $U_{Na}V$ (CON: 267.2 ± 74.9%; HYP: 70.9 ± 12.6%; $P=0.018$), and $U_{URO}V$ (CON: 178.4 ± 40.5%; HYP: 70.9 ± 12.6%; $P=0.01$). GFR during the IV period was not different between both groups.

Conclusions These data further support a role of arterial blood pressure in the regulation of the renal excretion of urodilatin.

Reference

1. Heringlake M, Wagner K, Schumacher J, Pagel H: **Urinary excretion of urodilatin is increased during pressure natriuresis in the isolated perfused rat kidney.** *Am J Physiol* 1999, **277**:F347-F351.

P195 A new device for measuring dermal blood flow in critically ill patients

J Cohen, I Skoletsky, D Geva, H Ephrath, P Singer
Department of General Intensive Care, Rabin Medical Center, Campus Beilinson, Petah Tikva and the Sackler School of Medicine, Tel Aviv University, Israel
Critical Care 2003, **7(Suppl 2)**:P195 (DOI 10.1186/cc2084)

A new monitor, the Dermal Blood Flow (DBF) meter, which noninvasively (skin probe) assesses capillary flow, has recently been developed and used in a variety of medical settings, including the assessment of wound perfusion during surgery and peripheral perfusion in patients with vascular conditions. We tested the monitor in the ICU setting, where early and objective evidence of altered skin perfusion may provide important information regarding impending impairment of organ function, and compared it with the mean arterial blood pressure (MAP).

Methods Ten critically ill patients were included in the study, which involved the continuous recording of minute-by-minute measurement of DBF and MAP (Datex- Ohmeda). The effect of specific interventions on both the measures, such as the giving of fluid boluses or vasopressors, was noted. We determined efficacy in terms of correlation between DBF and MAP (overall impression between the series graphs, and graded from rarely change together to nearly always change together), reliability (evaluated by a precision test of two randomly selected segments for each patient where the coefficient of variation is defined as the percentage of measurement error to mean results) and sensitivity analysis (any response to a specific intervention such as fluid bolus or use of vasopressor).

Results The MAP and DBF changed together mostly or nearly always throughout the recording for seven of the 10 patients. The DBF showed superior precision (1.5%, 95% CI 1.1–2.0%) when compared with MAP (2.2%, CI 1.7–3.0%). Response to 16 interventions in all the patients was detected by a change in DBF in 13 observations and by a change in MAP in only 11 observations. The response to vasopressors was always detected while the response to fluid administration was less well detected by both measures.

Conclusions This preliminary study has shown that the noninvasive DBF monitor was sensitive to therapeutic interventions in critically ill patients and was more reliable than MAP. Further studies comparing DBF with other modalities of peripheral perfusion are presently being performed.

P196 Postoperative on-line monitoring with intraperitoneal microdialysis (IPM) detects early visceral ischemia and correlates to the current intraperitoneal cytokine response

K Jansson[1], B Redler[1], L Norgren[1], U Ungerstedt[2]
[1]Department of Surgery, Örebro University Hospital, Örebro, Sweden; [2]Department of Physiology and Pharmacology, Karolinska Institute, Stockholm, Sweden
Critical Care 2003, **7(Suppl 2)**:P196 (DOI 10.1186/cc2085)

Background Visceral ischemia and macrophage activation are early signs in the development of shock and multiorgan failure. Activated macrophages produce proinflammatory cytokines (like TNF-α) that generate an inflammatory reaction. If the inhibition of this reaction (mainly by IL-10) is not strong enough, cascade systems will be activated; shock and multiorgan failure will be the result. The aim of this study was to investigate the reliability and safety of intraperitoneal microdialysis and to find out whether early visceral ischemia can be detected.

Methods Nineteen patients were operated, 14 elective patients and five patients as emergencies. These 19 patients were followed during 45 postoperative hours with IPM. A CMA 65 catheter was placed intraperitoneally before closure of the abdomen. Analysis was performed every second hour of glucose, pyruvate, lactate and glycerol, the ratio between lactate and pyruvate was calculated as a factor of peritoneal ischemia. Samples of peritoneal fluid were collected from an 18 Fr peritoneal drainage every sixth hour and TNF-α and IL-10 were analysed.

Sixteen of the patients had a normal postoperative course during the study, the lactate/pyruvate ratio started at the level of 20 immediately postoperatively, decreasing to 15 and, after 27 hours there was a short peak to 22, rapidly decreasing to a steady state around 12. This pattern was also seen regarding peritoneal TNF-α, it decreased immediately postoperatively and had a short peak after 27 hours. Peritoneal lactate/pyruvate ratio and peritoneal TNF-α correlated (Spearman nonparametric test 0.303, $P=0.001$).

Three of the patients had abnormalities in the microdialysis results.

- Patient 1 was operated due to rectal cancer. After 24 hours, his lactate/pyruvate ratio started to increase and he developed low saturation. He was treated with oxygen and the lactate/pyruvate ratio was normalized. Peritoneal TNF-α and IL-10 had high and short peaks during this time.
- Patient 2 was operated due to esophageal cancer. After 23 hours, his lactate/pyruvate ratio increased and he developed abdominal pain despite epidural anesthesia. Peritoneal TNF-α and IL-10 increased to a second peak after 80 hours.
- Patient 3 was operated due to an acute perforated gastric ulcer. Postoperatively there was a high lactate/pyruvate ratio, which increased to 60 after 15 hours; clinically the patient was in shock with decreasing blood pressure and oliguria. He developed acute renal failure and died 42 hours postoperatively. His peritoneal TNF immediately postoperatively was increased 30 times related to the patients with normal postoperative course. During the last 15 hours, his peritoneal TNF increased, while his IL-10 decreased.

Conclusions A normal postoperative course results in decreasing the lactate/pyruvate ratio, peritoneal TNF-α and IL-10. In our study we present three patients with abnormalities in IPM; these patients also had clinical and peritoneal cytokine abnormalities that support the theory that visceral ischemia is a preceeding factor in shock and multiorgan failure. IPM seems to be a safe method for the patient and we have not seen any complication due to the catheters in these 19 patients nor in the 65 patients we have studied with postoperative IPM. We believe IPM can act as an early marker of visceral ischemia even in clinical practice, but further studies to confirm this are mandatory. Our aim is to continue this investigation in ICU patients at risk of developing septicemia and multiorgan failure.

P197 Hyperhomocysteinaemia as an indicator of infection and disease severity in ICU patients

S Vassiliagou[1], E Andoniadou[1], E Kiparissi[1], V Papaioannou[1], M Stougianni, A Bekridelis[1], X Lagoudaki[2], T Varvataki[2]
[1]ICU Department and [2]Laboratory Department, General Hospital 'G. Gennimatas', 41 Ethnikis Aminis str, 54635 Thessaloniki, Greece
Critical Care 2003, **7(Suppl 2)**:P197 (DOI 10.1186/cc2086)

Objective The goal of this study was to evaluate the correlation of homocystein (HCY) with a severity score and other hematological and biochemical parameters in critically ill patients treated in a multidisciplinary ICU.

Materials and methods After ethical committee approval, 31 ICU patients were enrolled in this prospective study. They had mean age 56.33±15.8 and APACHE score 28.5±3.11 at the time of admission in the ICU. The 13/31 patients were admitted after surgical procedures while the others 18/31 on account of medical reasons. The following parameters were recorded: HCY, folic acid, WBC, PT, PTT, PLTs, fibrinogen, temperature and CRP. They were all documented in all patients at admission time and every 2 days for 2 weeks. The statistical analysis was performed with Pearson's correlation test. The level of correlating significance was assumed if $r<0.05$.

Results At admission time, we observed a significant correlation between HCY and APACHE II score ($r<0.01$). At the same time, the parameters temperature, WBC, CRP, folic acid, and PTT were significantly correlated to HCY ($r<0.01$, $r<0.01$, $r<0.01$, $r<0.01$, $r<0.05$, respectively). The next 4 days after admission the correlation between the parameters mentioned above remains strong but the correlating level of the significance was lower ($r<0.05$, for all parameters). After the 6th day until the end of the study, the correlation was changed and remained steady for folic acid, WBC and CRP ($r<0.05$ for each of them). The mean duration of ICU stay was 17.13±3.14 days.

Conclusions Hcy is an amino acid, which seems to be correlated with disease severity (APACHE score) and also strongly correlated with infections factor as temperature, WBC, CRP. This lets us accept HCY as an evaluation factor of inflammatory conditions in ICU patients.

Reference

1. Schindler K, Zauner C, *et al.*: **High prevalence of hyperhomocysteinemia in critically ill patients.** *Crit Care Med* 2000, **28**: 991-995.

P198 Is PCT a marker of infection and/or mortality?

P Marily, K Bourlidou, N Sidiropoulou, E Papazafiriou, N Gerogianni-Gritisi
ICU, General Hospital Hippokration, Konstadinoupoleos 49, 54642 Thessaloniki, Greece
Critical Care 2003, **7(Suppl 2)**:P198 (DOI 10.1186/cc2087)

Introduction There is much evidence to suggest that increased, early induction of PCT following varying incidents is suggestive of subsequent potential complications. This applies to the postoperative period and multiple trauma, as well as other diseases.

Aim of the study In our study, the purpose was to examine the PCT fluctuation in relation to the early signs of infection, to find out whether PCT indicates a significant predictive value of infection.

Materials and methods Between 1 January 2001 and 31 December 2001, 248 patients were studied (among the 347 patients who were admitted in our general ICU). Finally, 125 patients were stratified in our study. The rest of the patients were excluded because the length stay in ICU was limited (<5 days). All patients were divided into four groups according to the reason for admission. *Group A*: 56 multiple trauma (43 men, 13 women, mean age 49.2 years, mean ICU stay 13.4 days, APACHE II score 17–22). *Group B*: 19 postoperative (10 men, nine women, mean age 49.5 years, mean ICU stay 11.7 days, APACHE II score 20–24). *Group C*: 19 pathologic (12 men, seven women, mean age 50.7 years, mean ICU stay 14.8 days, APACHE II score 22–25). *Group D*: 31 cerebral stroke (18 men, 13 women, mean age 49.5 years, mean ICU stay 14.2 days, APACHE II score 18–23). Each group was divided in two subgroups: (I) patients possessing early (days 0–2) signs of infection (elevated WBC, CRP, temperature/reduced platelets, fibrinogen/positive cultures); (II) patients free of early signs of infection.

Results In group A, 32 patients had positive signs of infection, but PCT had no parallel fluctuation with the other markers of inflammation, whereas mortality (30%) was related to high PCT levels (>2 ng/ dl). In group B, seven patients had positive signs of infection, mortality was 31% and similar results with group A were noted. In group C, nine patients had positive signs of infection and mortality was 47%, while PCT levels indicated promptly the fatal outcome. Finally, in group D, only 14 patients had positive signs of infection, mortality was 32% and PCT levels were slightly higher in those who did not survive.

Conclusion Numerous triggers can induce PCT and it has no significant predictive value as the only marker of inflammation. In our study, mortality was directly related to high PCT levels (>2 ng/dl), while values more than 30 ng/dl were absolutely related to fatal outcome.

P199 Regional variation in anti-endotoxin core antibody levels in healthy and preoperative surgical populations

M Rashid[1], R Stephens[1], M Siva[1], M Grocott[1], E Burdett[1], D Turner[2], M Mythen[1]
[1]UCL Centre for Anaesthesia, Middlesex Hospital, Mortimer Street, London W1T 3AA, UK; [2]National Blood Transfusion Service, Colindale, London, UK
Critical Care 2003, **7(Suppl 2)**:P199 (DOI 10.1186/cc2088)

Introduction Endotoxin has a central role in sepsis and organ dysfunction after surgery. Levels of one of our natural defences against endotoxin, antibodies to endotoxin core (EndoCAb), are independent predictors of postoperative outcome [1]. There is a heterogeneity in EndoCAb levels between European and North American healthy donor populations that remains unexplained [2].

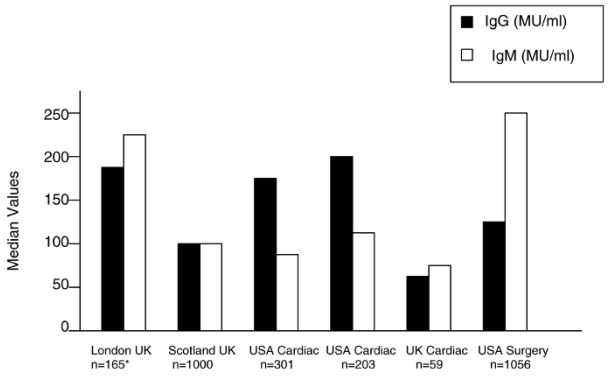
Methods Blood samples from healthy blood donors were collected in London, UK and compared with levels of baseline EndoCAb in previous studies. An ELISA assay of serum EndoCAb IgG (n=165) and IgM (n=65*) levels was performed and expressed as median units per ml (MU/ml) [3].

Results The median serum EndoCAb IgG and IgM levels in this population were 189.7 (41.8–1023) MU/ml and 222.5 (42.3–913.9) MU/ml, respectively (Fig. 1).

Conclusion EndoCAb levels are higher in London healthy donors than in the Scottish population. US cardiac patients show higher IgG levels than UK cardiac patients and Scottish healthy donors, but are similar to London healthy donors. US surgery patients show higher IgM levels than all groups but are similar to London healthy donors. Differences may be due to prior exposure to endotoxin, different disease process, differences in sampling and patient management, or genetic variation between countries. We are collecting further healthy donor samples to assess a larger cohort of EndoCAb levels in London.

References
1. Bennett-Guerrero E, Panah MH, Barclay GR, Bodian CA, Winfree WJ, Andres LA, Reich DL, Mythen MG: **Decreased endotoxin immunity is associated with greater mortality and/or prolonged hospitalization after surgery.** *Anesthesiology* 2001, **94**:992-998.
2. Grocott *et al.*: [Abstract] *Br J Anesth* 1999, **82**:170.
3. Barclay GR, Scott BB: **Serological relationship between Escherichia coli and Salmonella smooth- and rough-mutant lipopolysaccharides as revealed by enzyme-linked immunosorbent assay for human immunoglobulin G antiendotoxin antibodies.** *Infect Immun* 1987, **55**:2706-2714.

Figure 1



P200 How high risk are 'high-risk' surgical patients?

CD Gomersall, SJ Ramsay, S Lee, HS Lim, KS Tan, G Joynt
Department of Anaesthesia & Intensive Care, The Chinese University of Hong Kong, Prince of Wales Hospital, Shatin, Hong Kong
Critical Care 2003, **7(Suppl 2)**:P200 (DOI 10.1186/cc2089)

Introduction Preoperative optimization of 'high-risk' elective surgical patients has been demonstrated to result in improved outcomes. However, it has been argued that the mortality in the control groups was higher than expected, given the inclusion criteria. There have been no previous systematic studies of the outcome of patients who meet 'high-risk' criteria.

Method A retrospective cohort study involving case reviews of all adult (>18 years) patients undergoing elective major general or vascular surgery in a tertiary referral university teaching hospital during the year 2001. No patients were admitted to the ICU for preoperative optimization. Hospital mortality, age, duration of surgery and the presence or absence of the following risk factors was recorded: extensive ablative abdominal surgery for cancer, congestive cardiac failure, ischaemic heart disease, cardiac arrhythmia, hypertension, chronic obstructive pulmonary disease, pulmonary embolus, chronic renal insufficiency, diabetes mellitus with end-organ damage, long-term steroid therapy, chronic liver disease, cerebrovascular accident and peripheral vascular disease.

Results Data was available from 727 of 874 patients undergoing major general or vascular surgery. Of these, 450 underwent an operation lasting 2 hours or more. Only data from these 450 patients was analysed. The average age was 61 years and 48% of the patients were male. Overall hospital mortality was 3.8%. Hospital mortality in patients with one or more risk factors was 5.4%. The mortality associated with the presence of one or more risk factors is presented in Table 1.

Table 1

Number of risk factors	All patients		Patients aged 60 years or more	
	n	Mortality (95% CI)	*n*	Mortality (95% CI)
0	172	1.2 (0.3–5.7)	91	2.2 (0.6–7.7)
1	155	4.5 (2.2–9.0)	103	6.8 (3.3–13.4)
2	81	6.2 (2.6–13.6)	46	10.9 (4.7–23.0)
3 or more	42	7.1 (2.5–19.0)	39	7.7 (2.7–20.3)

Conclusions The hospital mortality of 'high-risk' surgical patients undergoing elective surgery may not be as high as the control group mortality (17–50%) of previous randomized controlled trials [1,2]. As a result, the reduction in mortality demonstrated in these studies may be an overestimate of the reduction that will be achieved if preoptimization is provided for all 'high-risk' surgical patients undergoing elective surgery.

References

1. Wilson J, *et al*.: **Reducing the risk of major elective surgery; randomised controlled trial of preoperative optimisation of oxygen delivery.** *Br Med J* 1999, **318**:1099-1103.
2. Lobo SM, *et al*.: **Effects of maximizing oxygen delivery on morbidity and mortality in high-risk surgical patients.** *Crit Care Med* 2000, **28**:3396-3404.

P201 Perioperative myocardial infarction can be predicted by preoperative electrocardiography

SK Appavu, TR Haley, K Mbekeani, A Khorasani, S Patel
Surgical Critical Care, Cook County Hospital, and the University of Illinois College of Medicine, Chicago, IL, USA
Critical Care 2003, **7(Suppl 2)**:P201 (DOI 10.1186/cc2090)

Preoperative identification of the predictors of perioperative myocardial infarction following noncardiac surgery (PMI) may help decrease its high mortality rate. In previous studies, atrial and ventricular rhythm abnormalities in the preoperative ECG have been identified to be risk factors for PMI. We performed this prospective study to determine whether or not other ECG findings may also predict PMI. Adults with significant comorbid conditions admitted to the SICU following high-risk noncardiac operations and who underwent workup to rule out PMI were studied. PMI workup consisted of a 12-lead ECG, CK-MB, and later troponin determination at 6–8 hour intervals for 24 hours. Data collection included patient demographics, comorbid conditions, preoperative work up including 12-lead ECG, surgical diagnoses, type and duration of anesthesia and operations, preoperative, intraoperative, and postoperative vital signs and clinical events, results of PMI workup, incidence of PMI and final outcome. The data was analyzed using SPSS statistical software.

There were 356 patients; 168 males and 188 females with the mean age of 62.9 years. The preoperative ECG was normal in 85 (23.9%) and abnormal in 271 (76.1%) patients. Normal sinus rhythm was present in 254/356 (71.3%), premature atrial complexes in 11/356 (3.1%), atrial fibrillation in 14/356 (3.9%), premature ventricular complexes (PVC) in 26/356 (7.3%), left ventricular hypertrophy (LVH) in 72/356 (20.2%), T-wave abnormality in 156/356 (46.3%), ST segment abnormality in 97/356 (27.2%), and a Q wave in 53/356 (14.9%). PMI developed in 31/356 (8.7%) patients, and three (9.7%) died as a result.

Comparison of the preoperative ECG findings of patients without and with PMI showed sinus tachycardia in 45/325 (13.8%) without PMI and in 7/31 (22.6%) with PMI, atrial fibrillation in 13/325 (4%) without PMI and in 1/31 (3.2%) with PMI, PVCs in 22/325 (6.8%) without PMI and in 4/31 (12.9%) with PMI, LVH in 61/325 (18.8%) without PMI and in 11/31 (35.5%) with PMI, and ST segment abnormality in 83/325 (25.5%) without PMI and in 14/31 (45.2%) with PMI. Logistic regression analysis showed LVH and ST segment abnormality to be significant predictors of PMI.

Conclusion LVH or ST segment abnormality on the preoperative ECG are predictors of PMI.

P202 Perioperative optimisation may be associated with different ICU outcomes in AAA and major thoracotomy

L McDonnell, M Bieker, L Lynch, F Gao
Intensive Care Unit, Birmingham Heartlands Hospital, Birmingham B9 5SS, UK
Critical Care 2003, **7(Suppl 2)**:P202 (DOI 10.1186/cc2091)

Introduction The importance of perioperative optimisation using fluid or inotropic agents has been underestimated, although it is recognised that preoperative optimisation may improve postoperative mortality after major surgery. Both abdominal aortic aneurysm (AAA) and major thoracic surgery have among the highest postoperative mortality rates. In our institute, all AAA (elective or emergency) patients receive perioperative optimisation in the ICU while all major thoracotomy (oesophagectomy or pneumonectomy) patients are cared for by the surgical team on the HDU or ward until ICU treatments are required. The aim of this study was to compare ICU overall outcomes between AAA and major thoracotomy groups.

Methods The data were collected from the ICNARC of 429 patients who underwent AAA ($n=211$) and major thoracotomy ($n=218$) between February 1996 and August 2001. The Mann–Whitney U test and chi-square test were used for statistical analysis.

Results AAA group had significant lower APACHE II score, length of ICU stay and ICU mortality despite of greater age, ASA grades and number of emergency cases compared with the major thoracotomy group.

Conclusion Perioperative optimisation may be associated with better ICU outcomes in the AAA group compared with the major thoracotomy group.

Table 1

Outcome of AAA and major thoratomy

	AAA ($n = 211$)	Major thoracotomy ($n = 218$)
Age (years)	73 (67–78)*	69 (59–74)
ASA II–III	149/211 (71%)*	212/218 (97%)
ASA IV–V	62/211 (29%)*	6/218 (3%)
Elective/emergency	62/211 (29%)*	6/218 (3%)
APACHE II	13 910–17)*	18 (12–25)
ICU stay (days)	1 (0.8–2.9)*	3 (1.3–7)
ICU mortality (elective/emergency)	11.4 (2.7/31)%*	34 (34/16)%

Data presented as median (interquartile range). * $P < 0.05$ compared with thoratomy.

Table 2

Outcome of survivals and nonsurvivals in AAA and thorocotomy

	Survival AAA ($n = 187$)	Nonsurvival AAA ($n = 24$)	Survival T ($n = 144$)	Nonsurvival T ($n = 74$)
Age (years)	73 (66–77)*‡	77 (74–83)	69 (59–74)	66 (61–74)
APACHE II	13 (10–17)*‡	20 (18–22)	15 (11–19)†	25 (19–36)
ICU stay (days)	1 (0.8–2.3)‡	1 (0.3–8.5)	2 (1.4–6)	4 (1.2–8.4)

Data presented as median (interquartile range). $P < 0.05$ compared with * nonsurvival AAA or † nonsurvival T or ‡ survival T.

P203 Plasma levels of urotensin II are increased in patients with three-vessel coronary artery disease and left ventricular dysfunction

M Heringlake[1], T Kox[2], O Uzun[2], S Klaus[1], L Bahlmann[1], N Franz[2], J Thale[2], KF Klotz[1]
[1]Klinik für Anaesthesiologie, Universität zu Lübeck, Ratzeburger Allee 160, 23538 Lübeck, Germany; [2]Klinik für Kardiologie, Schüchtermann-Klinik, Bad Rothenfelde, Germany
Critical Care 2003, **7(Suppl 2)**:P203 (DOI 10.1186/cc2092)

Background We have recently shown that the plasma levels of urotensin II (U-II), a highly potent vasoactive peptide, are increased in patients with reduced left ventricular function during coronary artery bypass grafting (CABG) surgery [1]. The present study was thus designed to confirm whether the plasma levels of this peptide are indeed related to the severity of coronary artery disease and accompanying variations in left ventricular filling pressures.

Material and methods Twenty-six consecutive patients (age: 58 ± 11 years) were examined during routine right heart catheriza-

Table 1

	CAD-1 (n = 13)	*CAD-3(n = 13)*	*P*
PAOP (mmHg)	6.77 ± 2.95	14.39 ± 7.9	0.003
PAPS (mmHg)	21.54 ± 6.62	34.15 ± 14.62	0.009
PAPD (mmHg)	8.92 ± 3.9	14.23 ± 6.66	0.021
PAPm (mmHg)	14.31 ± 4.48	22.93 ± 8.87	0.005
U-II (pg/ml)	1526.1 ± 581.22	3641 ± 3108	0.024

tion. Patients were grouped according to the angiographic coronary status at hospital admission into a one-vessel CAD group (CAD-1; $n=13$) and a three-vessel CAD group (CAD-3; $n=13$). Patients were examined after 30 min supine rest. Mixed venous plasma levels of U-II were determined by EIA. Data are presented as mean ± SD; statistical analyses were performed by ANOVA.

Results Both groups were comparable regarding risk factors for CAD and a history of previous myocardial infarction. No group differences were observed in cardiac output, mean arterial blood pressure, heart rate, and central venous pressure. U-II plasma levels and pulmonary artery pressures are presented in Table 1.

Conclusions Extending previous observations in patients during CABG surgery, these findings suggest that the plasma levels of U-II in humans with CAD are related to left ventricular filling pressures and, hence, left ventricular diastolic dysfunction, further supporting a role of urotensin II in heart failure.

Reference

1. Heringlake M, Eleftheriadis S, Bahlmann L, Klaus S, Eichler W, Schumacher J, Heinzinger M, Kraatz E, Schmucker P: **The relationship between plasma urotensin II (hU-II) and pulmonary artery occlusion pressure during cardiac surgery: further evidence, that hU-II is influenced by cardiac filling pressures [abstract].** *Crit Care* 2002, **6(suppl 1)**:P146.

P204 Prognostic value of cardiac Troponin I after cardiac surgery: comparison with two different assays

S Provenchère[1], A Mongredien[1], P Verpillat[2], JM Desmonts[1], I Philip[1], M Dehoux[3]
[1]Département d'Anesth-Réanimation, [2]Département de Biostatistique, and [3]Laboratoire de Biochimie A, Hôpital Bichat, 46 rue Henri Huchard, 75018, Paris, France
Critical Care 2003, **7(Suppl 2)**:P204 (DOI 10.1186/cc2093)

Introduction After adult cardiac surgery, the inhospital prognostic value of cTnI, measured at 20 hours after the end of surgery, has been demonstrated [1]. Various cardiac troponin I (cTnI) assays are available but the lack of standardization renders difficult any comparative study [2]. The aim of this study was therefore to determine cTnI concentration after cardiac surgery using two different assays, and to evaluate their correlation and their respective prognostic values.

Materials and methods After approval by the local ethic committee and informed consent, 167 consecutive patients undergoing either coronary artery bypass grafting ($n=80$) or valve surgery ($n=87$) were prospectively studied. The cTnI was measured by an immunoenzymatic method at 10 and 20 hours after the end of surgery (H10 and H20) on two analyzers: RXL® (Dade Behring) and AxSym® (Abbott). For each patient, the occurrence of a cardiac event (CE+) was defined as: prolonged low cardiac output (more than 4 hours), Q-wave perioperative myocardial infarction, cardiac death.

Results A good correlation was found between assay at H10 ($r^2=0.81$; $P<0.0001$) and at H20 ($r^2=0.80$; $P<0.0001$). However, the slopes of the regression equation were different at H10 (3.8) and at H20 (5.6). In the CE+ group, cTnI concentrations were significantly higher at H10 and H20 for both assays (at H20; Dade, 16.3 [28]* vs 3.3 [3.6] cTnI in ng/ml; Abbott, 50.0 [117.9]* vs 9.6 [14.1] cTnI in ng/ml; median [interquartile range], *$P<0.0001$, Mann–Whitney test, CE+ vs CE–). Using ROC curve analysis, no difference was found in area under the curve (AUC) at both H10 and H20 between assays, even if at H10 the AUC found with the Dade assay tended to be higher than that of the Abbott assay (0.91 vs 0.80, $P=0.06$).

Conclusion Both assays were found to be well correlated, but the correlation differed with time. cTnI was associated with CE in both assays, with a similar predictive value at H20.

References

1. Lasocki S: *Anesthesiology* 2002, **97**:405-411.
2. Jaffe A: *Circulation* 2000, **102**:1216-1220.

P205 Changes in brain natriuretic peptide concentrations after cardiac surgery: kinetics and prognostic value

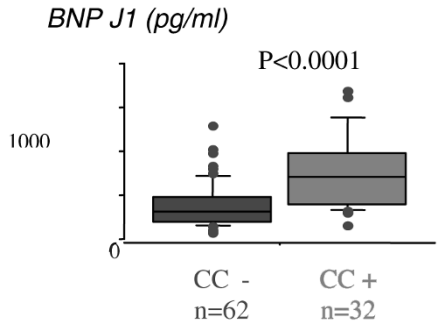
S Provenchère[1], N Merniz[1], D Shouperlieva[1], JM Desmonts[1], I Philip[1], J Benessiano[2]
[1]DAR and [2]CIC, Hôpital Bichat, 46 rue Henri Huchard, 75018 Paris, France
Critical Care 2003, **7(Suppl 2)**:P205 (DOI 10.1186/cc2094)

B-type natriuretic peptide (BNP) is a cardiac neurohormone specifically secreted from the ventricles in response to volume expansion and pressure overload. Plasma levels of BNP have been shown to be elevated in patients with left ventricular dysfunction and correlate with prognosis. The purpose of the present study was to determine the variations of BNP levels in cardiac surgery patients and to look for a possible association between BNP levels and perioperative cardiac complications.

Methods After ethics committee approval and patient informed consent, we studied 94 consecutive patients undergoing elective coronary artery (36) or valve surgery (58). BNP was measured using a fluorescence immunoassay Test (Triage, Biosite Inc) before surgery (day 0), and at days 1 and 5 after surgery. Anesthesia and cardiopulmonary bypass management was standardized for all patients. Postoperative cardiac complication (CC) was defined as hemodynamic instability requiring inotropic support >4 hours, congestive heart failure in ward and cardiac death.

Results At day 0, the levels of BNP were significantly associated with the NYHA class ($P=0.003$) and LVEF ($P=0.002$), but neither with the type of cardiac disease nor with preoperative pulmonary artery catheter measurements. BNP concentrations increased in all patients at day 1 and remained elevated in plateau at day 5. At

Figure 1



day 1, BNP concentrations were associated with the occurrence of cardiac complications (Fig. 1) and length of stay in intensive care unit. Using ROC curve analysis, the best predictive value (for cardiac complications) of BNP at day 1 was 450 pg/ml.

Conclusion Plasma BNP levels increased in all patients after cardiac surgery and remained elevated until day 5. High BNP levels at day 1 were significantly associated with postoperative cardiac complications.

P206 Correlation of lactate, pHi and oxygen extraction ratio with cardiac index in ICU patients after aortic surgery

E Kiparissi[1], E Andoniadou[1], S Vassiliagou[1], P Papagiannopoulou[1], A Bekridelis[1], S Koutsias[2], G Vretzakis[2], D Papadimitriou[2]
[1]ICU Department and [2]Vascular Surgery Department, General Hospital 'G. Gennimatas', 41 Ethnikis Aminis str, 54635 Thessaloniki, Greece
Critical Care 2003, **7(Suppl 2)**:P206 (DOI 10.1186/cc2095)

Introduction Investigation of the relationship among Lac acid, pHi and O_2ER with cardiac index (CI) and determination of the early indicator of hemodynamic compromise in patients undergoing aortic surgery during the first 24 hours of their stay in a multidisciplinary ICU.

Methods Our prospective study included 17 patients after aortic aneurysm surgery. They were all men of mean age 70.5 ± 5.56 with admission mean APACHE II score 16.2 ± 3.96. In all cases the duration of cross-clamping was 2–3 hours. The following parameters were recorded: CI, PCWP, Hb, DO_2, VO_2, SaO_2, SvO_2, O_2ER, Lac acid and sigmoid pHi. The pHi was monitored continuously with the TONOCAP–™ monitor for regional tonometry. All the other parameters were recorded at the admission in the ICU and every 4 hours for 24 hours. Regression analysis and curve estimation were performed among CI and pHi, Lac and estimated O_2ER every 4 hours. Level of significance was $P<0.05$.

Results At admission in ICU there was correlation between CI and Lac ($r^2=0.6$, $P<0.05$). At the first 8 hours there was a statistically significant inverse correlation between CI and levels of Lac ($r^2=0.68$, $P<0.008$). After the 8 hours until the end, pHi was then statistically correlated to CI ($r^2=0.65$, $P<0.01$). It is noticeable that O_2ER was strongly inversely correlated to CI ($r^2=0.91$, $P<0.008$) during the whole study at any phase of the study.

Conclusions According to our data until now, it seems that the levels of Lac during the first 8 hours reflect early hemodynamic instability while the sigmoid pHi, indicating local microcirculation and reperfusion phenomena, is correlated with CI at later stages during the cardiovascular and metabolic stabilisation. Finally, O_2ER is the most powerful indicator of the hemodynamic status.

Reference
1. Kellum JA: **Lactate and pHi: our continued search for markers of tissue distress.** *Crit Care Med* 1998, **26**:1783-1784.

P207 Prognostic value of gastric tonometry in patients with intestinal obstruction

RR Gubaidullin, AV Butrov
City Clinical Hospital No. 64, Medical Faculty of Russian People's Friendship University, Russia, Moscow
Critical Care 2003, **7(Suppl 2)**:P207 (DOI 10.1186/cc2096)

Background and goals Intestinal failure can be accompanied by intra-abdominal hypertension (IAH) [1]. Gastrointestinal ischaemia occurs particularly because of IAH [2]. The index of gut luminal PCO_2 referenced to arterial PCO_2 ($PgCO_2$–$PaCO_2$) reflects an adequacy of splanchnic tissue perfusion and is a predictor of any later complications [3].

Materials and methods We studied 24 patients with diagnosis of intestinal obstruction. The survey patients were nearly homogeneous on age (average age 46 ± 4 years) and preoperative condition (APACHE II score 18 ± 1.8). One-half of patients were males. The same technique of anesthesia was carried out in all the patients. IAP and $PgCO_2$–$PaCO_2$ (kPa) were measured by TRIP NGS catheter and Tonocap monitor preoperatively. Cluster analysis was performed on the base of preoperative differences between IAP and $PgCO_2$–$PaCO_2$.

Results On the results of cluster analysis, the patients were allocated into two groups. In 14 patients (group 1) the mean of preoperative IAP was 1.82 ± 0.14 kPa. IAP was 0.41 ± 0.06 kPa in 10 patients of the second group ($P<0.05$). Patients with higher IAP had 2.24 ± 0.42 $PgCO_2$–$PaCO_2$ vs 1.49 ± 0.32 in group 2 ($P<0.05$). Study of outcomes revealed that six patients of the group 1 had different serious complications and seven died. Eight patients from group 2 recovered without complications.

Conclusion A higher level of $PgCO_2$–$PaCO_2$ because of increased IAP in patients with intestinal obstruction may have a prognostic value.

References
1. Malbrain MLNG: *Curr Opinion Crit Care* 2000, **6**:17-29.
2. Diebel L, Saxe J, Dulchavsky S: *Am Surg* 1992, **58**:573-576.
3. Hamilton MA, Mythen MG: *Curr Opin Crit Care* 2001, **2**:122-127.

P208 Critical role of capsaicin-sensitive sensory neurons in gender difference in the stress-induced gastric mucosal injury in rats

N Harada, K Okajima, M Uchiba
Department of Laboratory Medicine, Kumamoto University School of Medicine, Kumamoto 860-0811, Japan
Critical Care 2003, **7(Suppl 2)**:P208 (DOI 10.1186/cc2097)

Introduction Recent studies have demonstrated that the outcome of critically ill patients is better in females than in males. Although estrogen has been shown to be critically involved in regulation of immune responses, the detailed mechanism(s) underlying such gender differences has yet to be fully understood. Since proinflammation plays a critical role in the development of the organ dysfunction seen in such critically ill patients, estrogen might show any anti-inflammatory effects to attenuate such inflammatory responses. We previously reported that capsaicin-sensitive sensory neurons (CSSN), nociceptive neurons, play an important role in attenuating inflammatory responses by releasing calcitonin gene-related peptide (CGRP), which promotes the endothelial production of prostacyclin, one of the anti-inflammatory prostaglandins [1]. Since estrogen increases the synthesis of nerve growth factor, which increases the CGRP production, estrogen might attenuate inflammatory responses by promoting CGRP release from CSSN. We examined this possibility in the present study.

Methods and results Gastric accumulation of neutrophils as well as gastric mucosal injury were significantly less in female rats than in male rats subjected to water-immersion restraint stress (WIRS). Gastric levels of CGRP and 6-keto-PGF1α, a stable metabolite of PGI_2, were significantly higher in female rats than those in male rats subjected to WIRS. Administration of capsazepine, a vanilloid receptor-1 antagonist, markedly reduced the gastric levels of CGRP and 6-keto-PGF1α in female rats subjected to WIRS. Both gastric accumulation of neutrophils and gastric mucosal injury in female rats pretreated with capsazepine were comparable with those seen in male rats.

Conclusions These results suggest that CGRP release from CSSN is more marked in female rats than male rats, contributing to differences in the gastric tissue levels of PGI_2 in rats subjected to WIRS. This difference in the regulatory function for inflammatory responses might at least partly explain the gender difference in the development of stress-induced gastric mucosal injury in rats.

Reference
1. Harada N, *et al.*: *Gastroenterology* 2001, **120(suppl)**:A-148.

P209 Gastric residual volume and the paracetamol gastric motility test in critically ill patients

V Zidianakis, Th Niarchou, P Miriantheus, E Mboutzouka, G Baltopoulos
Athens University School of Nursing ICU at KAT Hospital, 2 Nikis Street Kifisia, Athens 14561, Greece
Critical Care 2003, **7(Suppl 2)**:P209 (DOI 10.1186/cc2098)

Objective To evaluate the paracetamol absorption test in comparison with the clinical test of gastric residual volume, as indicators of gastric motility, in order to initiate peros feeding in critically ill patients.

Design A prospective self-controlled study, evaluating a clinical and a laboratory test.

Setting An adult medical–surgical university ICU.

Patients and methods All patients were studied in three steps. *Step I*. The gastric residual volume was measured 1 hour (by aspiration of the gastric content) after the delivery of 200 ml D_5W (gastric residual volume test [GRVT]) via a nasogastric tube in 18 mechanically ventilated critically ill trauma patients (mean age ± SEM 51.31 ± 4.92 years). *Step II*. One gram of paracetamol was delivered via the nasogastric tube, and blood samples were drawn at time (t) 0 and 30, 60 and 90 min post paracetamol administration. The paracetamol was administered immediately after step I. *Step III*. A try (commercial liquid food) of peros feed was given in all studied patients right after the 90 min blood sample was drawn.

All patients were divided in two groups. Group A ($n=10$): patients tolerated the peros feeding and were successfully fed peros thereafter. Group B ($n=8$): patients not tolerated the peros feeding. The peros feeding was not achieved the day of the study.

Results The mean (± standard error) GRV and paracetamol serum levels were as presented in Table 1. In all Group A patients the residual gastric volume was ≤100 ml (mean ± standard error =58.0 ± 9.5), whereas in all Group B patients it always was >100 ml (mean ± standard error =208.0 ± 18.7). All Group A patients were successfully fed whereas no one of the Group B was successfully fed the day of the study.

No statistically significant differences (Mann–Whitney U test) were observed in blood paracetamol levels between groups at baseline, 30 and 60 min. A statistically significant difference was observed at 90 min, reflecting the higher blood paracetamol levels of Group A, which was the successfully peros-fed group.

Conclusions The GRVT is a fast (within 1 hour) clinical tool for decision making to peros feed a critically ill patient. A gastric resid-

Table 1

	GRV (ml)	0 min	30 min	60 min	90 min
Group A	58.0 ± 9.5	0.11 ± 0.08	2.79 ± 0.83	3.69 ± 0.89	4.17 ± 0.88
Group B	208.0 ± 18.7	0.67 ± 0.26	3.01 ± 1.8	2.91 ± 1.36	2.35 ± 0.96
P value*	< 0.0001	> 0.05	> 0.05	> 0.05	< 0.05

GRV, gastric residual volume. * Between Groups A and B, Mann–Whitney U test.

ual volume <100 ml is indicative of a successful peros feeding in our critically ill patients. The higher paracetamol blood levels at 90 min post paracetamol administration does not seem to be a useful tool in the peros feeding decision-making process. It happens because on one hand it is a time-consuming and work-consuming process and on the other hand there is not a cutoff paracetamol serum level, which separates the peros food-tolerating patients.

P210 Interleukin-18 levels reflect the severity of acute pancreatitis

H Abe[1], S Imai[1], N Sato[1], Y Inoue[1], Y Fujino[1], M Onodera[1], T Ikeda[2], K Ikeda[2], S Endo[1]
[1]Department of Critical Care Medicine, Iwate Medical University, Uchimaru 19-1, Morioka 020-8505, Japan; [2]Hachioji Medical Center, Tokyo Medical University, Tatemachi 1163, Hachioji 193-0998, Japan
Critical Care 2003, **7(Suppl 2)**:P210 (DOI 10.1186/cc2099)

Background and goal of study IL-18 is mainly produced by macrophages, especially by the Kupffer cells of the liver. When anti-IL-18 antibodies were administered before challenge with LPS 1 week after the injection of *P. acnes*, the development of liver tissue necrosis and the associated increase in serum GOT and GPT levels were prevented. We therefore studied the correlation between the serum IL-18 levels, severity of the disease, and the development of liver dysfunction in cases of acute pancreatitis.

Materials and methods Seventeen patients with acute pancreatitis treated at our center from the early stage of the disease, were enrolled in this study. The disease state was mild in four patients, moderate in five, and severe in eight patients. The IL-18 and TNF-α levels in the serum were determined by ELISA. The correlations between the maximum serum IL-18 level and the corresponding serum TNF-α, IL-6, and IL-8 levels were studied.

Results The levels of IL-18 were 4.3 ± 5.3 pg/ml in the mild group, 18.7 ± 67.1 pg/ml in the moderate group, and 269.6 ± 2482.1 pg/ml in the severe group. The IL-18 levels increased significantly corresponding to the severity of the disease. The group in which the complication of MODS developed showed significantly higher IL-18 levels than that in which this complication did not develop. The IL-18 levels in the survivor group were 132.0 ± 130.7 pg/ml, and those in the nonsurvivor group were 3028.6 ± 2480.8 pg/ml, the levels being significantly higher in the nonsurvivor group. Significant correlations were observed between the total bilirubin and IL-18 levels (r=0.617, P=0.0003).

Conclusion In this study, the severity of acute pancreatitis was significantly correlated with the serum IL-18 levels; conversely, increased serum IL-18 levels reflected the severity of the disease. Since significant correlations between the serum IL-18 levels and APACHE II scores were also observed in cases of sepsis, such a correlation may not be specific to only acute pancreatitis.

P211 Incidence of organ failure in patients with severe acute pancreatitis

S Lapauw, A Wilmer, H Bobbaers
MICU, UZ Gasthuisberg, Herestraat 49, B-3000 Leuven, Belgium
Critical Care 2003, **7(Suppl 2)**:P211 (DOI 10.1186/cc2100)

Introduction The clinical course of severe acute pancreatitis (SAP) may be complicated by a variety of organ failures, an ominous evolution associated with high mortality rates. We aimed to describe a population of patients with SAP and to quantify the type and frequency of organ failures in these patients.

Methods Retrospective analysis of all medical records of patients admitted to the MICU between January 1995 and January 2001 due to SAP. SAP was defined as acute pancreatitis associated with at least one organ failure. Organ failure was defined as a score of 3 or 4 according to the SOFA score.

Results Seventy-two patients (44 male, 61%) met the criteria of SAP. The mean age was 54 (range 24–90) years. The average length of stay in the MICU was 21 days (range 3–133). Average SAPS II score at admission was 42 (range 19–83), and SOFA score was 8 (range 1–22). Thirty-six per cent were referred from other ICUs in other hospitals. The most frequent causes of SAP were gallstones (32%), alcohol (24%), idiopathic (13%), hyperlipidemia (10%), and post-ERCP pancreatitis (8%). Forty patients (56%) developed respiratory failure with need for mechanical ventilation; nine out of these patients developed ARDS. Thirty-one patients (43%) developed renal failure, 24 of these patients required renal replacement therapies. Fifty-one per cent of patients developed cardiovascular failure with need for vasopressors. Thrombocytopenia <50,000/ml occurred in 14 patients (19%), and hepatic failure in 15 patients (21%). Eight patients (11%) developed two organ failures, 16 patients (22%) developed three organ failures and 15 patients (21%) developed four or more.

Bacteremia was detected in 32 patients (44%), and in 13 patients the positive blood cultures were interpreted as contaminants. According to computertomographic criteria, 54 patients (75%) were diagnosed with pancreatic necrosis. Pancreatic cultures were obtained in 30 patients. Microbes were cultured from necrotic areas in 17 of these patients. Seventeen patients (24%) underwent surgery (on average, two interventions, range 1–6) because of infected necrosis or progressive organ failure. Mortality in patients requiring surgery was 53%; that in those not requiring surgery 20%. Overall mortality was 28%.

Conclusions In an unselected population of patients with SAP, of which 75% also had acute necrotising pancreatitis, organ failure is common. Respiratory failure is most common (56%), followed by cardiovascular failure (51%), renal failure (43%), hepatic failure (21%) and coagulopathy in 19% of patients. At 28%, mortality in these patients remains high.

P212 Extrapancreatic microcirculatory injury in acute experimental pancreatitis in the rat

H Freise, LG Fischer, V Hlouschek, MM Lerch, H Van Aken, A Sielenkaemper
Department of Anaestheseiology and Intensive Care, University Hospital of Muenster, Albert Schweitzer Strasse 33, 48149 Muenster, Germany
Critical Care 2003, **7(Suppl 2)**:P212 (DOI 10.1186/cc2101)

Background The clinical course of acute pancreatitis is determined by acute lung injury, systemic inflammatory response syndrome and septic complications. Microcirculatory dysfunction in both the intestinal and the pulmonary vessels might be partly responsible for this process.

Methods Fourteen male Sprague–Dawley rats were randomly assigned to two groups: acute pancreatitis (AP) was induced by IV infusion of 10 µg/kg cerulein; control rats (CON) received saline infusion. Four hours later, intravital microscopy of the distal ileum mucosa was performed. In six villi, the intercapillary area of all capillaries (ICA total) and of continuously perfused capillaries only (ICA cont) was measured. Terminal arteriolar flow was calculated from arteriolar diameter and plasma flow velocity. In a second set of experiments, pulmonary endothelial function was assessed in isolated perfused lungs (IPL) in 10 rats using the same study design and treatment. After 4 hours of treatment, IPL was established (flow 16 ml/min, hematocrit 10%). After stabilization, endothelium-independent (hypoxic pulmonary vasoconstriction, 3% O_2 [HPV]) as well as endothelial-dependent (bradykinin 6 µg [BK]) responses were determined as differences in pulmonary arterial pressure. Statistical analysis included ANOVA and the Student–Newman–Keuls test.

Results Acute pancreatitis significantly increased the ICA total, thereby indicating a loss in capillary perfusion. HPV after AP was not different from control. In contrast, BK induced pulmonary vasoconstriction after AP compared with control (* $P<0.05$ vs control).

Conclusion During AP, the mucosal microcirculation showed increased arteriolar blood flow and decreased capillary perfusion, indicating increased intramucosal shunt. This may lead to critical mucosal hypoxia. Furthermore, pulmonary vascular reactivity was altered in AP. Mechanisms of AP-induced extrapancreatic microvascular injury need to be further investigated to develop treatment options in the prevention of severe AP-related complications.

Table 1

	ICA total (µm²)	ICA cont (µm²)	Diameter (µm)	Velocity (µm/s)	Flow (nl/s)	ΔPAP HPV (mmHg)	ΔPAP BK (mmHg)
AP	874 ± 79	1355 ± 148*	7.0 ± 1.4	729 ± 64*	3.58 ± 0.31*	7.17 ± 1.89	1.5 ± 0.43*
CON	773 ± 45	932 ± 46	7.6 ± 1.1	541 ± 50	2.61 ± 0.31	9.63 ± 1.91	0.57 ± 0.3

P213 Acute renal failure as a risk factor associated with acute pancreatitis

M Alvarenga[1], V Segura[1], H Marroquin[2], M Guevara[1]
[1]Unidad de Medicina Critica Hospital Medico Quirurgico Instituto Salvadoreño del Seguro Social (ISSS), San Salvador, El Salvador; [2]Sala de Terapia Intensive Hospital San Juan de Dios, Santa Ana, El Salvador
Critical Care 2003, **7(Suppl 2)**:P213 (DOI 10.1186/cc2102)

Background With a retrospective study previously published by our team, we found that acute renal failure in patients with pancreatitis had a high mortality rate. The objective was to make a prospective study in which we could demonstrate whether renal failure was either associated with a deficit in cardiac preload or with hypotension.

Methods A prospective study was conducted in all patients with diagnosis of acute pancreatitis that were admitted to the intensive care unit during the time of the study, and the following variables were evaluated at the moment of admittance: RANSON SCORE, APACHE II, SOFA, age, MAP, CVP, diuresis/hour, creatinin and BUN. The statistical analysis was realized by Student *t* test, values of $P<0.05$ were considered significant.

Results During the period of investigation 2449 patients were admitted to our intensive care unit, of which 46 were diagnosed with acute pancreatitits (1.8%) with a mortality of 30.4% ($n=14$). In the group of deceased patients, the variables age, MAP, SOFA score and APACHE II score were not statistically significant, and therefore no difference was found between this group and those who stayed alive. On the contrary, we observed that the deceased patients presented lower diuresis and higher BUN retention. The mean arterial pressure (MAP) showed no difference between both group, and its values were found to be in normal ranges, which discards the possibility that the presence of hypotension causes

Table 1

Variable	Alive	Dead	*P*
Age	56.04	48.37	NS
MAP	88.57	86.78	NS
RANSON	2.72	3.93	< 0.01
SOFA	3.4	4.9	NS
APACHE II	6.4	8.5	NS
CVP	9.84	13.07	< 0.02
Diuresis/hour	42.63	78.79	< 0.006
Creatinin	1.06	1.7	< 0.05
BUN	15.2	40.2	< 0.03

acute renal failure. No decrease of preload volume was found, which suggests that the acute renal failure is caused by an intrinsic renal dysfunction, which should be studied in later investigations.

Conclusions In patients with acute pancreatitis in our study, the acute renal failure seems to be a factor associated with mortality, and it does not seem to be conditioned by a diminished preload or hypotension, which suggest the possibility that an intrinsic renal damage is associated with acute pancreatitis.

Reference

1. Segura V, *et al.*: **Shock, acute renal failure and MODS as mortalaity indicator in acute pancreatitis.** *Crit Care* 2001, **5(suppl 1)**:P211.

P214 CVVH versus IHD in patients with multiple organ failure

V Gašparović[1], I Filipović-Grčić[1], I Višnja[2], V Vesna[2], P Zoran[1]
[1]Department of Internal Intensive Care and [2]Department of Surgical Intensive Care, Zagreb, Croatia
Critical Care 2003, **7(Suppl 2)**:P214 (DOI 10.1186/cc2103)

The place and role of continuous renal replacement therapy (CRRT) has recently been evaluated in comparison with intermittent hemodialysis (IHD) in patients with multiple organ failure (MOF). The emphasis is on removal of a number of inflammatory cytokines, not only correction of azotemia which can be achieved with dialysis.

Patients and methods The randomized prospective study on 104 patients with MOF investigated circulatory stability, survival after 28 days, and total survival. Intermittent hemodialysis was performed every day, during 3–4 hours with blood flow rate 200–250 ml/min and dialysate flow rate 500 ml/min, using a biocompatible polysulfone membrane with surface area 1.4–1.6 m^2, most frequently without heparin utilization. CVVH was procedure of continuous venovenous hemofiltration, where in the first 33 patients 18 ml/kg per hour were replaced (low volume hemofiltration) and, subsequently, 35 ml/kg per hour (high volume hemofiltration). The membrane used for CVVH was of polysulfone. MOF was defined as a severe deterioration of at least two organ systems. Circulatory instability was defined by blood pressure fall up to 10 mmHg or over 10 mmHg.

The etiology of MOF was sepsis (52 patients), septic shock (28 patients) renopulmonary syndrome (five patients), hemorrhagic fever (seven patients), rhabdomyolysis (five patients), and ishemic cardiomyopathy (seven patients).

Results Comparison of scoring systems of both patient groups showed no statistically significant difference: (HD:HF arithmetic means ± SD) APACHE II_0 (20.3 ± 8.4 vs 21.9 ± 8.8, P=NS), MARSHALL II_0 (8.3 ± 4.0 vs 9.6 ± 3.5, P=NS), $SOFA_0$ (9.2 ± 4.6 vs 10.6 ± 3.8, P=NS), APACHE II_3 (16.4 ± 7.5 vs 18.3 ± 8.2, P=NS), $MARSHALL_3$ (7.1 ± 3.8 vs 8.1 ± 3.7, P=NS), $SOFA_3$ (7.7 ± 4.6 vs 9.3 ± 4.2, P=NS), APACHE II_7 (15.5 ± 8.2 vs 18.2 ± 8.5, P=NS), $MARSHALL_7$ (6.1 ± 3.9 vs 7.3 ± 4.1, P=NS), $SOFA_7$ (6.6 ± 4.3 vs 8.5 ± 4.6, P=NS). No statistically significant difference in 28-day survival between IHD and CRRT was seen (23/52 vs 17/52, P=NS). No statistically significant difference in total survival between IHD and CRRT was seen (21/52 vs 15/52, P=NS). Survival of patients on low versus high volume hemofiltration was studied (9/31 vs 6/21, P=NS). The number of hypotensive attacks, defined by blood pressure fall up to and over 10 mmHg in the group of patients on continuous procedures, was not significantly smaller (Rank Sum 2664.5 vs 2795.5, P=NS)

Conclusion In this randomized prospective study, survival of patients with MOF after 28 days, total survival, and circulatory instability were not significantly related to the type of procedure. In our patients no difference in survival was reached with regard to the use of low volume versus high volume hemofiltration.

P215 Very high volume haemofiltration (VHVHF) (8.75 l/hour) sustained during a 4 hour period of time can remove by filtration significantly higher amounts of cytokine compared with low volume haemofiltration (LVHF) (1 l/hour) and is accompanied by a significant drop in cytokines only in haemodynamical responders and survivors during early severe septic shock

PM Honoré[1], Y Ernst[1], J Jamez[2], M Lemaire[2], B Pirenne[1], C Lebaupin[3], JP Pelgrim[3], Th Dugernier[1], JC Renauld[4]
[1]Intensive Care Unit, [2]Nephrology Unit, [3]Emergency Unit St Pierre and [4]ICP UCL Bruxelles, St Pierre Hospital, Ottignies-Louvain-La-Neuve, Belgium
Critical Care 2003, **7(Suppl 2)**:P215 (DOI 10.1186/cc2104)

Background and objectives It has been speculated that the beneficial effects of VHVHF in refractory septic shock [1] could be explained or not by cytokine removal. We compared the cytokine removal in 16 patients with early severe septic shock: eight were held with VHVHF and were compared with a historical cohort treated with LVHF.

Setting General intensive care unit, regional centre.

Design Comparative study: 16 patients in early septic shock. Eight patients were put on VHVHF (8.75 ml/hour) and were compared in term of cytokine filtration with a historical cohort of eight patients who were treated with low volume haemofiltration (1 l/hour).

Results VHVHF was able to remove a significantly higher amount of IL-6 when compared with LVHF. The total amount removed in 1 hour by VHVHF was 40 µg/hour, significantly higher than the amount removed by LVHF, which was about 1 µg/hour (P<0.01).

The extremely important removal was accompanied in patients treated by VHVHF by a significant drop in serum IL-6 only in responders and survivors (two out of eight). No decrease was observed in nonresponders and nonsurvivors (six out of eight) and was very minimal in the group of LVHF.

During VHVHF, serum IL-10 never dropped, whatever the outcome of the patient. These results were in agreement with two recent studies [2,3] where the IL-6 clearance in LVHG was between 15 and 30 µg/day.

Conclusion The beneficial effect of VHVHF in refractory septic shock can be explained at least in part by a significantly higher

removal of proinflammatory cytokines compared with LVHF. In responders and survivors, this was accompanied by a significant decrease in serum proinflammatory cytokines levels, whereas IL-10 levels did not change at all.

References
1. Honoré P, *et al.*: *Crit Care Med* 2000, **28**:3581-3587.
2. Bellomo R, *et al.*: *Crit Care Med* 1993, **21**:522-526.
3. De Vrien A, *et al.*: *J Am Soc Nephrol* 1999, **10**:846-853.

P216 Effect of continuous hemodiafiltration (CHDF) on vascular endothelial cell function in sepsis patients

K Ikeda[1], T Ikeda[1], H Taniuchi[1], H Suzuki[1], M Nagura[1], K Ooshima[1], Y Kuroki[1], S Endo[2]
[1]Division of Critical Care and Emergency Medicine, Hachoji Medical Center, Tokyo Medical University, 1163-Tatemachi, Hachioji, Tokyo 193-0994, Japan; [2]Department of Critical Care Medicine, Iwate Medical University, Uchimaru 19-1, Morioka, Japan
Critical Care 2003, **7(Suppl 2)**:P216 (DOI 10.1186/cc2105)

Objectives To remove humoral mediators in sepsis patients, continuous hemodiafiltration (CHDF) was performed and its effect on vascular endothelial cell function was examined.

Subjects and methods The study subjects were 10 patients with sepsis who received CHDF for more than 3 days at our facility. A PMMA membrane was used as a hemofilter, and nafamostat mesylate was administered as an anticoagulant. Measurements were performed before CHDF and 30 min and 24, 48 and 72 hours after CHDF, of granulocytic elastase, PAI-I, IL-6, IL-1ra, ELAM-1, endothelin-1, and NOx. The survival group (six cases) and nonsurvival group (four cases) were separated according to the outcome at 2 weeks after CHDF and were separately analyzed.

Results Before CHDF treatment, granulocytic elastase, PAI-I and NOx were significantly higher in the survival group than in the nonsurvival group. Starting 48 hours after CHDF, granulocytic elastase decreased significantly in the survival group and increased significantly in the nonsurvival group. PAI-I was significantly lower 24 and more hours after CHDF in the survivors, whereas it rather increased in the nonsurvivors. In both groups, IL-6, IL-1ra and NOx were significantly decreased by CHDF. ELAM-1 and endothelin-1 appeared to decrease in both groups, although there was no statistical significance. There was no significant difference in BNP between the groups.

Discussion PAI-I, which is associated with activation of vascular endothelial cells, and granulocytic elastase, which is associated with neutrophil activation, were significantly higher in the survival group before CHDF. After CHDF, they significantly decreased in the survival group and rather increased in the nonsurvival group. These data suggest that vascular endothelial cell damage was suppressed by CHDF in the survival group. In the nonsurvival group, cytokines decreased while granulocytic elastase and PAI-I did not decrease, suggesting that it is more important to control vascular endothelial damage in sepsis patients. The NO metabolite NOx, a vascular endothelial relaxation factor, endothelin-1, a contraction factor, and ELAM-1, an adhesion factor, decreased during CHDF, but showed no difference between the two groups of patients.

Conclusion The results suggest the possibility that CHDF suppresses vascular endothelial cell damage in sepsis patients.

P217 Is it true that PMX-DHP can improve lung oxygenation?

T Ikeda[1], K Ikeda[1], H Suzuki[1], H Taniuchi[1], M Nagura[1], K Ohshima[1], Y Kuroki[1], N Matsuno[2]
[1]Division of Critical Care and Emergency Medicine, and [2]5th Department of Surgery, Hachioji Medical Center, Tokyo Medical University, 1163-Tatemachi, Hachioji, Tokyo, 193-0994, Japan
Critical Care 2003, **7(Suppl 2)**:P217 (DOI 10.1186/cc2106)

Polymyxin B immobilized fiber (PMX-R; Toray industries, Inc) has been developed in Japan for direct removal of endotoxin (PMX-DHP). PMX-DHP is used for treatment of patients with sepsis and septic shock primarily caused by Gram-negative infections, and its effectiveness of hemodynamic changes has been evaluated. In 119 cases (62 ± 16 years old, 82 men and 37 women) treated with PMX-DHP, changes in pulmonary oxygenation before and after PMX-DHP were examined, using PaO_2/FiO_2 as an oxygenation indicator, separately according to the outcome (80 survivors and 39 who died). Improvement of PaO_2/FiO_2 was identified in 64% of all cases. In the survival group, there appeared to be a trend for PaO_2/FiO_2 improvement as blood pressure increased. In the nonsurvival group, however, no improvement of PaO_2/FiO_2 was obtained, regardless of an increase of blood pressure. There was no significant correlation between PaO_2/FiO_2 and the rate of change in endotoxin levels, TNF-α, and IL-6. Granulocyte elastase increased significantly after PMX-DHP treatment in both groups. In the survival group, PaO_2/FiO_2 appeared to increase as macrophage inflammatory protein (MIP-1) 1-α decreased, suggesting the possibility that changes in MIP-1-α influenced PaO_2/FiO_2. As the mechanism for the improvement of pulmonary oxygenation by PMX-DHP has been shown clearly, it remains to be examined further.

P218 Plasmafiltration in septic shock: a review of 15 cases

P Campos, A Maia-Goncalves, A Paiva, C Granja, J Pina
Intensive Care Unit, Hospital Pedro Hispano, Matosinhos, Portugal
Critical Care 2003, **7(Suppl 2)**:P218 (DOI 10.1186/cc2107)

Introduction Plasmafiltration is a nonselective method with the potential of removing harmful mediators, and is being used as salvage therapy and suggested to play an important role in severe infection. This study aims to evaluate efficacy and safety of plasmafiltration used as salvage therapy in septic shock in our ICU.

Methods This study enrolled 15 adult patients admitted from January 1998 to December 2000 to our eight-bed mixed-case ICU of a tertiary care hospital, with septic shock refractory to conventional therapy. A plasmafiltration session with albumin-electrolyte replacement solution was initiated for each patient. Demographic

and clinical data were collected from clinical registries. Variables such as systolic pressure, inotropes, oxygen saturation, oxygen inspiration fraction, PEEP, platelets, and coagulation were collected before plasmafiltration and 6 and 24 hours after. SPSS for Windows was used for data analysis.

Results From the 15 patients enrolled, 47% were male and mean age was 53 years; mean APACHE II was 25. Pneumonia was the primary infection in 40% of patients; peritonitis in 20%. All patients were under adrenaline or noradrenaline infusion. Twenty-seven per cent experienced minor hemorrhagic complications during plasmafiltration; no fatal complications were attributed to plasmafiltration. A trend towards lowering inotrope dose was noticed, without statistic significance. Thirty-three per cent of patients recovered and were discharged alive from the ICU.

Conclusions Plasmafiltration seems to have an important role in septic shock, delaying the process of organ dysfunction and allowing treatment of the underlying cause. Moreover, it is a safe procedure. Further investigation is still needed on this subject.

References

1. Busund R, Koukline V, Utrobin U, Nedashovsky E: **Plasmapheresis in severe sepsis and septic shock: a prospective, randomised, controlled trial.** *Intensive Care Med* 2002, **28**:1434-1439.
2. Reeves JH, *et al*., and the Plasmafiltration in Sepsis Study Group: **Continuous plasmafiltration in sepsis syndrome.** *Crit Care Med* 1999, **27**:2096-2104.

P219 Retrospective study of continuous haemofiltration on patients with acute liver failure with renal dysfunction

H Antoniades, A Antoniou, G Auzinger, J Wendon
Institute of Liver Studies, King's College Hospital, Denmark Hill, London SE5 9RS, UK
Critical Care 2003, **7(Suppl 2)**:P219 (DOI 10.1186/cc2108)

Introduction Continuous venovenous haemofiltration (CVVHF) is commonly instituted in patients with renal dysfunction in acute liver failure (ALF), the latter carrying a high mortality rate unless patients undergo liver transplantation. In this cohort, the prognostic significance varying doses of CVVHF has not been established. A retrospective analysis of 73 patients admitted to a specialist Liver Intensive Care Unit.

Methods All patients admitted with acute liver failure and receiving continuous haemofiltration were studied. We analysed data that had been acquired between January 1999 to November 2002 utilising the Riyadh ICU programme. The variables analysed were bilirubin, lactate, creatinine, APACHE II score, noradrenaline, and mechanical ventilation. Patients were divided into three groups. Group 1, low volume (LV) CVVHF (<2 l exchange); Group 2, high volume (HV) CVVHF (>2 l exchange); and Group 3, combination of HV and LV CVVHF. These three groups were subdivided as to whether they were receiving noradrenaline, mechanical ventilation or a combination of both.

Results The survival rate of patients receiving LV or HV CVVHF or a combination was 50%. The subgroup survival is presented in Table 1.

Table 1

	ICU survival (%)/number of patients			
	Noradrenaline		Ventilation	
	Yes	No	Yes	No
Low volume	72 (8/11)	83 (10/12)	50 (5/10)	100 (13/13)
High volume	10 (1/10)	0 (0/1)	9 (1/11)	0
Combination	42 (13/31)	50 (4/8)	40 (14/35)	75 (3/4)

Patients receiving LV CVVHF, on noradrenaline, had significantly higher APACHE II ($P<0.03$) and creatinine ($P<0.003$) levels when compared with those not on noradrenaline. Ventilated patients, on LV CVVHF, had a significantly higher APACHE II score than those not ventilated ($P<0.001$). Twenty-eight per cent of patients with ALF underwent transplantation.

Conclusion This study shows a more favourable outcome when compared with similar patients in a general ICU setting. As expected, patients on HV CVVHF had higher mortality, which is attributable to their underlying physiology. These patients were selected for HV CVVHF at the physician's discretion. The timing of initiation of HV CVVHF did not affect the outcome of these patients. This may be related to the fact that standard CVVHF was initiated early in the time course of the disease.

P220 Retrospective study of the effect of haemofiltration on the outcome of patients with chronic liver disease with renal dysfunction

A Antoniou, H Antoniades, G Auzinger, R Sutcliffe, J Wendon
Institute of Liver Studies, King's College Hospital, Denmark Hill, London SE5 9RS, UK
Critical Care 2003, **7(Suppl 2)**:P220 (DOI 10.1186/cc2109)

Introduction Renal dysfunction is common in critically ill patients with chronic liver disease (CLD). The outcome of patients with CLD requiring ITU care with associated renal failure is poorly defined, as is their response to dose of renal replacement (CVVHF). We performed a retrospective study of 80 patients with CLD admitted to a specialist Liver Intensive Care Unit.

Methods All patients admitted with chronic liver disease and receiving continuous haemofiltration were studied. We analysed data that had been acquired between January 1999 and November 2002 utilising the Riyadh ICU programme. The variables analysed were bilirubin, lactate, creatinine, APACHE II score, noradrenaline, and mechanical ventilation. Patients were divided into three

groups. Group 1, low volume (LV) CVVHF (<2 l exchange); Group 2, high volume (HV) CVVHF (>2 l exchange); and Group 3, combination of HV and LV CVVHF. These three groups were subdivided as to whether they were receiving noradrenaline, mechanical ventilation or a combination of both.

Results The survival rate in patients receiving LV and HV CVVHF or a combination of both was 9%. The subgroup survival is presented in Table 1.

Patients receiving HV CVVHF, on noradrenaline, had a statistically significant higher lactate ($P<0.003$) and APACHE II ($P<0.005$) score when compared with those not on noradrenaline. Ventilated patients, on combination CVVHF, had significantly higher lactate ($P<0.02$) and creatinine ($P<0.001$) than nonventilated patients. There was no difference between early or late initiation of HV CVVHF. No patient with a lactate of greater than 3 mmol/l survived.

Conclusions The outcome in our cohort of patients with chronic liver disease and receiving haemofiltration is extremely poor (9% survival). Our data shows the subgroup of patients on HV haemofiltration had 100% mortality rate. We have also shown that patients who require noradrenaline and ventilation in addition to RRT have a worse outcome. In addition, the timing of initiation of HV CVVHF does influence survival.

Table 1

	ICU survival (%)/number of patients			
	Noradrenaline		Ventilation	
	Yes	No	Yes	No
Low volume	31 (5/16)	22 (2/9)	25 (5/20)	40 (1/5)
High volume	0 (0/8)	0 (0/3)	0 (0/10)	0 (0/0)
Combination	4 (1/24)	15 (3/20)	5 (2/40)	50 (2/4)

P221 Creatinine index in acute renal failure: an outcome and nutritional indicator

L Amigues[1], S Canet[2], K Klouche[1], P Massanet[1], B Canaud[2], JJ Beraud[1]
[1]Intensive Care Unit and [2]Nephrology Care Unit, Lapeyronie University Hospital, 371 avenue du Doyen G Giraud, 34295 Montpellier, France
Critical Care 2003, **7(Suppl 2)**:P221 (DOI 10.1186/cc2110)

Normalized creatinine production (creatinine index [CI]) has been shown to reflect protein nutritional status and outcome in chronically hemodialysis patients, but such has not yet been established in acute renal failure (ARF). We therefore investigated CI as an indicative parameter of protein denutrition and outcome in ARF requiring extrarenal replacement therapy (ERRT).

Methods Twenty-four patients (APACHE II score 29.6 ± 5.7) with ARF treated by intermittent hemodialysis or continuous venovenous hemofiltration (CVVHF) have been studied along 7 days from the first ERRT session (D_1–D_7). Weight, diuresis, BUN, creatinemia, urinary urea nitrogen and creatinine were collected daily, before and after each ERRT. During CVVHF, fractional ultrafiltrant urea nitrogen and creatinine collections were also collected. Normalized protein catabolism rate (nPCR) and nitrogen supply were estimated daily and an average of 7 days (D_1–D_7) was calculated. CI was calculated at D_1 and D_7 according to the formula CI (mg/kg per 24 hours) = $\{[(Cb_{T2} - Cb_{T1}) \times \text{weight} \times 0.6] / T + (Cu \times Vu) / T + (Cuf \times Vuf) / T\} \times 0.113 \times 1440 / \text{weight} + [(Cb_{T1} + Cb_{T2}) / 2] \times 0.0429$, where C = creatinine in blood (b), in urine (u) and in ultrafiltrant (uf), V = volume of urine (u) and ultrafiltrant (uf), and T = time in minutes from T1 to T2. The CI changing rate from D_1 to D_7 was calculated according to $cCI = (D_7CI - D_1CI) \times 100 / D_1CI$. From ICU survival, two groups were individualized and compared.

Results The mean CI was 28.3 ± 9.6 at D_1 and 22.2 ± 9.4 mg/kg per day at D_7 ($P<0.05$); the mean cCI was −21.5 ± 26.6%. The average nPCR was 1.87 ± 0.77 g/kg per day, whereas the average nitrogen supply was 0.14 ± 0.06 g/kg per day. ICU survival rate was 50%.

No correlation was found between nPCR and CI, nor between nPCR and nitrogen supply.

Conclusion We conclude that CI before and 7 days after initiation of ERRT is a predictive factor of outcome in ARF, and that a dramatic decrease of CI after the first week of ERRT worsens significantly the outcome. These results would also suggest that, in ARF patients, CI and CI changes are better indicative of protein denutrition than nPCR.

Table 1

	Deceased (12 patients)	Survived (12 patients)	*P*
CI D_1 (mg/kg per 24 hours)	24.0 ± 9.6	32.7 ± 7.9	0.02
CI D_7 (mg/kg per 24 hours)	16.8 ± 6.6	27.5 ± 8.8	0.006
cCI (%)	−29.7 ± 11.8	−13.3 ± 27.9	0.02
nPCR (g/kg per 24 hours)	2.0 ± 0.9	1.7 ± 0.6	NS
Nitrogen supply (g/kg per 24 hours)	0.16 ± 0.06	0.13 ± 0.07	NS

Correction (10 March 2003)

The original published version of the abstract (as shown above) included incorrect data in the 5th sentence of the Methods section. The sentence should read as follows:

CI was calculated at D_1 and D_7 according to the formula CI (mg/kg per 24 hours) = $\{[(Cb_{T2} - Cb_{T1}) \times \text{weight} \times 0.6] / T + (Cu \times Vu) / T + (Cuf \times Vuf) / T\} \times 0.113 \times 1440 / \text{weight} + [(Cb_{T1} + Cb_{T2}) / 2] \times 0.00429$, where C= creatinine in blood (b), in urine (u) and in ultrafiltrant (uf), V = volume of urine (u) and ultrafiltrant (uf), and T = time in minutes from T1 to T2.

P222 Immediate effects of a bolus of furosemide on hemodynamics in critically ill patients

N Markou, D Hroni, H Koumoudiou, M Kanata, P Zaglavira, B Talou, H Apostolakos
ICU-B, Athens Trauma Hospital KAT, Athens, Greece
Critical Care 2003, **7(Suppl 2)**:P222 (DOI 10.1186/cc2111)

Purpose To study the immediate effects of a bolus of furosemide on hemodynamics, in critically ill patients, before the appearance of a significant increase in diuresis.

Methods A double-blind, placebo-controlled study in 34 critically ill patients; 28 of them with sepsis. All patients participating in the study had adequate diuresis (at least 0.5 ml/min) and none had received a diuretic in the past 8 hours. All patients randomly received either a bolus of 40 mg furosemide or 4 ml N/S (placebo). Eight hours later there was crossing over to the other branch of the study. The physician recording the changes in physiologic parameters was blinded as to the substance infused. We recorded CVP, systolic and diastolic blood pressure and diuresis per minute at t0 (the time of infusion), t1 (5 min from infusion) and t2 (15 min from infusion).

Results In the intervention group, CVP at t0 was 11.35 ± 4.80 mmHg (mean ± SD) and there was no significant difference in CVP from t0 to t2 (paired *t* test). No significant difference was also observed in systolic and diastolic blood pressure and in heart rate. Although there was an increase in diuresis at t2 compared with t0, it did not reach statistical significance. Additionally, the observed changes at t1 and t2 in CVP, blood pressure and diuresis in the intervention group did not differ from changes observed in the placebo group.

Conclusion Before an obvious effect on diuresis has become obvious, a bolus of furosemide has no immediate effect in CVP or blood pressure in critically ill patients. Furosemide has no immediate hemodynamic effects independent of its diuretic action.

P223 Comparison between continuous versus bolus furosemide administration in oliguric postoperative paediatric cardiac patients

D Taylor, A Durward, A Mayer, C Turner, SM Tibby, IA Murdoch
Paediatric Intensive Care Unit, Guy's Hospital, St Thomas Street, London SE1 9RT, UK
Critical Care 2003, **7(Suppl 2)**:P223 (DOI 10.1186/cc2112)

Objective To compare the efficacy of continuous versus bolus furosemide administration on urinary output, sodium and furosemide excretion following paediatric cardiac surgery.

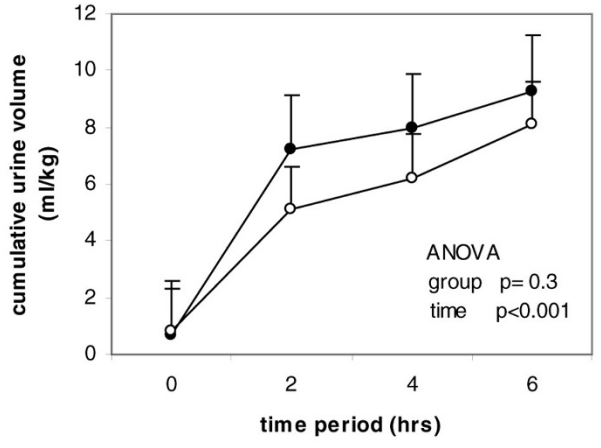
Design Prospective, double-blinded, randomised crossover study.

Patients Fifteen infants with postoperative oliguria (urine volume <1 ml/kg per hour) unresponsive to 10 ml/kg 0.9% saline bolus were enrolled in the study. Time of enrolment was between 16 and 24 hours post-PICU admission, which is the period of least ADH-mediated antidiuresis. Diagnostic groups included Tetralogy of Fallots ($n=7$), Norwood Stage 1 ($n=2$), VSD and arch repair ($n=2$), and other ($n=4$).

Interventions Patients were randomly assigned to receive an equivalent dose of furosemide either as a single bolus dose (1 mg/kg) with a placebo saline infusion or a continuous furosemide infusion (0.2 mg/kg bolus followed by 0.125 mg/kg per hour) and studied over a 6 hour period. After a 2 hour 'washout' period, the patients were crossed over and the study repeated with the alternative administration method. Urine was collected every 2 hours for electrolytes and urinary furosemide concentration (measured by high-performance liquid chromatography) [1].

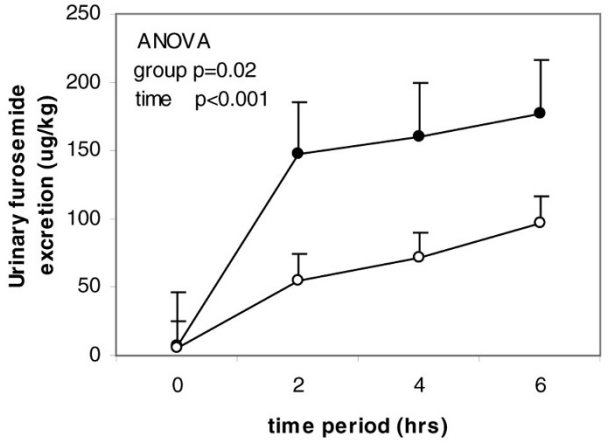
Measurements and results The median age (IQ) was 4.1 months (0.1–7.6), weight 6.3 kg (3.5–7.1) and duration of cardiopulmonary bypass ($n=13$) was 99 min (74–112).

Figure 1



Cumulative urine output over time. Bolus therapy (closed circles), and continuous infusion (open circles). Mean/SEM.

Figure 2



Cumulative furosemide excretion over time. Bolus therapy (closed circles), and continuous infusion (open circles). Mean/SEM.

Cumulative urine output (Fig. 1) and Na excretion were similar between both groups (ANOVA, $P=0.3$) over the 6 hour study period. However, cumulative tubular furosemide excretion (Fig. 2) was significantly greater following furosemide bolus (ANOVA group effect, $P<0.02$). Additionally, cumulative K excretion was similar between both treatment methods (ANOVA, $P=0.3$). No differences were observed between treatment groups for the following haemodynamic parameters; heart rate (ANOVA, $P=0.9$), mean BP (ANOVA, $P=0.9$) or CVP (ANOVA, $P=0.8$).

Conclusion Furosemide administration by continuous infusion is effective as bolus therapy in its diuretic and natriuretic effects in oliguric infants following cardiac surgery. The continuous furosemide infusion produces a greater diuresis per urinary tubular furosemide concentration.

Reference

1. Mills J, *et al.*: **Quantification of furosemide from serum and tissues using HPLC.** *J Chromatogr B* 1997,**701**:65-70.

P224 Hypokalemia, magnesium and high creatinine

A Aaron[1], MM Bahadur[2], A Bachwani[3], KM Mody[1], DM Gamadia[1], CB Wadia[1], BS Pardiwadia[1], JD Sunavala[1], BB Ichhaporia[1], SA Golwalla[1], JA Chichgar[1], CB Kohiar[1]

[1]Intensive Care Unit, Parsee General Hospital, 400026 Mumbai, India; [2]BAM Railway Hospital, 400018 Mumbai, India; [3]BARC Hospital, 400094 Mumbai, India

Critical Care 2003, **7(Suppl 2)**:P224 (DOI 10.1186/cc2113)

Introduction Magnesium has been used since ancient times as a purgative and uterine relaxant. We obtained excellent results in a selected group of hypokalemic patients with impaired renal function by constantly monitoring serum levels of magnesium and creatinine. The results were unexpectedly encouraging and prompted us to use magnesium on these types of patients more often.

Selection criteria Severe hypokalemia ($K<3$); baseline urine output 5 ml/kg per hour and more; serum creatinine 2–5. Anuric and chronic renal failure patients were excluded from this study.

Methods Five grams of magnesium is administered in D5W over 8 hours for a period spanning up to five consecutive days monitoring parameters such as urine output, creatinine, serum magnesium/potassium, deep tendon reflexes and patient outcome.

Results Total patients, $n=55$ (Fig. 1 and Table 1).

Conclusions Magnesium was given to treat hypokalemia refractory and otherwise; patients responded very well.

Urine output increased substantially, through indirect diuretic action of magnesium. Substantial decrease in the creatinine in selected patients; an event quite unexplainable and contrary to conventional wisdom, probably another salutary action of magnesium, more work is needed on this aspect. Reduction in creatinine could not be achieved in septic/septic shock patients.

Figure 1

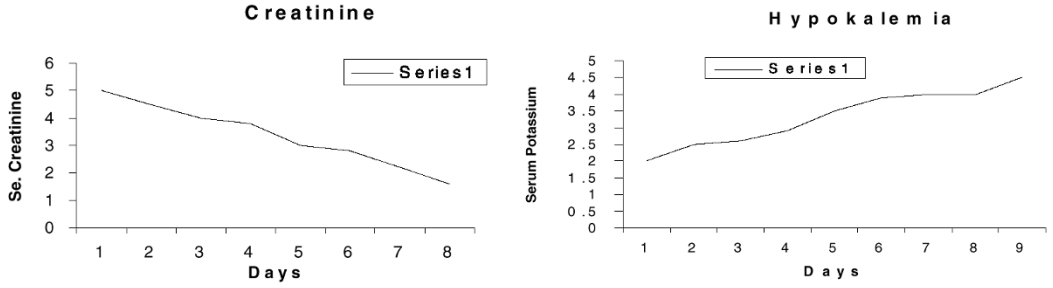


Table 1

Conditions	*n*	Serum K before Mg	Serum K after Mg	Creatinine before Mg	Creatinine after Mg	Urine output before Mg (ml/kg per hour)	Urine output after Mg (ml/kg per hour)
Dehydration	25	1.5–3	4.5–5	1.4–5	0.8–1.4–1.6	0.5–1	1–3
CHF/LVF	16	2.5–3	3.6–4.5	2–7	1–1.5	0.5–1	1–2
Refractory hypokalemia K	14	2–3	4–4.5	0.8–1.2	0.8–1.2	1	1–3

P225 Outcome from acute renal failure complicating critical illness is influenced by age

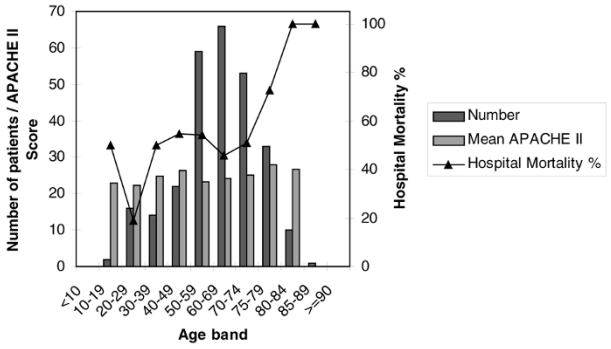
MJ Garfield, JM Dixon
Consultants in Intensive Care Medicine, Ipswich Hospital NHS Trust, Heath Road, Ipswich, Suffolk IP1 3QY, UK
Critical Care 2003, **7(Suppl 2)**:P225 (DOI 10.1186/cc2114)

Acute renal failure is a common complication of critical illness. Renal replacement therapy with continuous venovenous haemofiltration (CVVH) is now a routine element of the organ support provided to these patients. The decision to initiate therapy is made on the basis of fluid balance, electrolytes, the degree of accumulation of urea and creatinine and, importantly, on the likely benefit to the patient.

In order to help inform this decision we conducted a retrospective audit of the outcome in terms of hospital mortality of patients receiving CVVH in our district hospital general intensive care unit.

Records were reviewed covering a period of 7 years; September 1995–November 2002. Over this period of time there was a total of 3848 admissions, with a mean APACHE II score of 16.2; these patients had a mean hospital mortality of 26%. Over the same period of time, 276 patients received CVVH. These patients had a mean APACHE II score of 24.8 and a mean hospital mortality of 53.3%. Examination of the data by age group showed that, up to the age of 75 years, the mortality rate was around the average. From 75 years onwards, however, mortality increased rapidly, with those aged 75–80 years having a mortality rate of 73%, and those older than 80 years having 100% mortality.

Figure 1



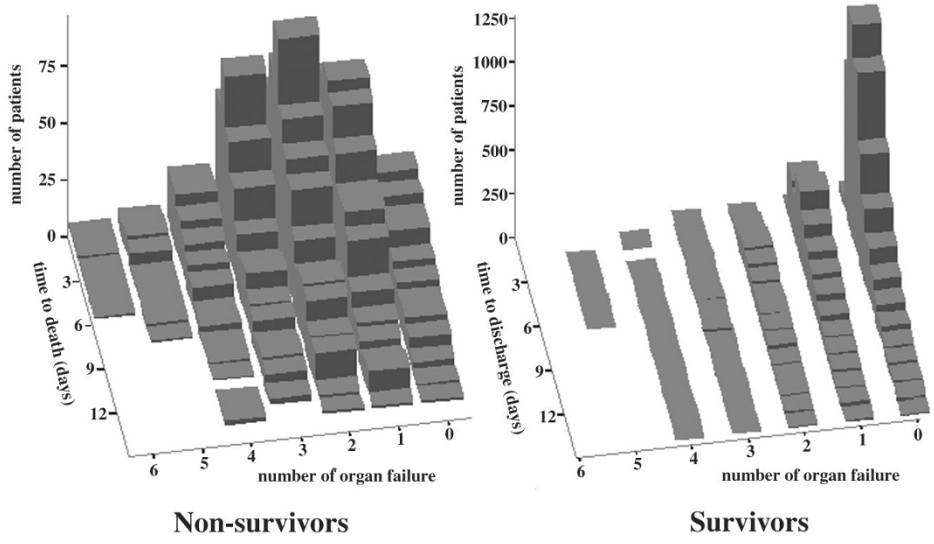
Intensivists require a performance audit of this kind if they are to establish reasonable limits to the extent of organ support. We contend that this provides valuable information for clinicians at the bedside and in discussions with patients and their relatives.

P226 Time course of organ dysfunction comparing survivors and nonsurvivors: results of the multicentric study 'Sepsis occurrence in the acutely ill patients' (SOAP)

H Gerlach, O Ahlers, Y Sakr, J-R Le Gall, M Ranieri, C Sprung, D Payen, K Reinhart, R Moreno, J Carlet, J-L Vincent, on behalf of the SOAP investigators
Department of Anesthesiology and Intensive Care Medicine, Vivantes-Klinikum Neukölln, Berlin, Germany
Critical Care 2003, **7(Suppl 2)**:P226 (DOI 10.1186/cc2115)

Introduction Multiple organ dysfunction syndrome (MODS) is the main reason for death in septic patients. Most scoring systems are aimed to calculate a sum parameter for estimating the individual risk of the patient. This analysis describes the time course of organ dysfunction comparing survivors and nonsurvivors.

Figure 1



Methods A total of 3147 patients (198 centers from 24 countries) were included. The time period preceding the day of fatal outcome (nonsurvivors) or ICU discharge (survivors) was analyzed and plotted versus the severity of organ dysfunction (SOFA) and the number of patients (3D histogram). In addition, the SOFA points of each organ system were calculated over time, considering reproducible time patterns of survivors versus nonsurvivors.

Results The ICU mortality rate was 18.5%. The overall time course of organ dysfunction was as shown in Fig. 1.

Analysis of single organ scores revealed that a cardiac failure was preceding in the majority of nonsurvivors, whereas other early organ dysfunctions were only rarely found. In contrast, the severity of organ dysfunction decreased towards discharge in surviving patients.

Conclusion This analysis demonstrates that 1) most survivors had only minor organ dysfunction (one or two organ failures), and 2) early cardiac failure is typical in nonsurvivors.

P227 Is MMODS better than SOFA?

M Zuleika[1], D Tjan[2], M Shoukri[3], T Mphanza[2], S Al Sammarai[2]
[1]Royal Surrey County Hospital, Guildford, Surrey, UK; [2]Riyadh Armed Forces Hospital, Riyadh, Saudi Arabia; [3]King Faisal Specialist Hospital, Riyadh, Saudi Arabia
Critical Care 2003, **7(Suppl 2)**:P227 (DOI 10.1186/cc2116)

MMODS is a simple modification of the Multiple Organ Dysfunction Score (MODS). MMODS is calculated by summing up MODS with the Organ Support Score (OSS). OSS is a dichotomous score of one or none, given to each organ support the patient received, namely: ventilation, inotropes and renal replacement therapy (CVVH). The maximum score a patient could receive was 3. The above modification was made as MODS variables do not account for the above therapeutic interventions, but can be affected by them. This could result in an apparent false improvement in the organ dysfunction parameters, which can affect quantification of organ dysfunction and thus fail to describe organ dysfunction precisely.

Objective To compare the sensitivity of MMODS with Sequential Organ Failure Assessment (SOFA).

Design A prospective trial in a tertiary referral multidisciplinary intensive care setting.

Patients and methods All critically ill patients admitted to the ICU were studied. All necessary data to calculate daily MMODS and SOFA were collected and entered into a dedicated database. ICU outcomes of all patients were also recorded. The sensitivity of both MMODS and SOFA were compared and the statistical significance established using appropriate statistical tests.

Results Ninety-two patients were studied with a male to female ratio of 2:1 and a mean length of stay of 8.72 ± 8.0 days. The mean age was 47.62 ± 22.1. The mean MMODS for all patients was 6.41 ± 3.74 and the mean SOFA was 6.66 ± 3.72. The mean MMODS for survivors was 5.23 ± 2.70 and that of nonsurvivors was 9.02 ± 4.34 ($P \leq 0.00$). The mean SOFA for survivors was 5.61 ± 2.86 and that for nonsurvivors was 8.97 ± 4.32 ($P \leq 0.00$). The contribution to ICU outcome (alive/dead) by both SOFA and MMODS was evaluated by determining their coefficients in a logistic regression model as shown in Table 1.

Table 1

Variable	β coefficient	Wald	Significance	Exponential β
MMODS	0.304	34.994	0.000	1.355
SOFA	0.004	0.007	0.935	1.004
Constant	–2.891	183.401	0.000	0.056

The performance of the logistic model was determined by the area under the Receiver Operating Characteristic (ROC) curve. MMODS demonstrated a significant effect on the ICU outcome with an area under the ROC curve of 0.766 in comparison with that of SOFA (0.726) ($P \leq 0.002$).

Conclusion The sensitivity of MMODS was significantly better than SOFA. Increased sensitivity can augment the efficacy of a scoring system and thus the evaluation of novel ICU therapies. Further addition of the simple dichotomous OSS did not compromise the simplicity of the original MODS.

P228 Variation of results of the SMR using APACHE II, APACHE III and SAPS II

A Orellana[1], V Segura[2]
[1]Department of Internal Medicine and [2]Intensive Care Unit, Medico-Quirurgico Hospital, ISSS, Boulevard Juan Pablo II, San Salvador, El Salvador
Critical Care 2003, **7(Suppl 2)**:P228 (DOI 10.1186/cc2117)

Introduction The Standardized Mortality Ratio (SMR) has been designed as a measurement of the clinical performance in the intensive care units (ICUs), because it compares the actual mortality rate with the predicted mortality for each group of patients in the ICU. However, due to the existence of many scoring systems, an approach that allows one to settle which scoring system better shows the real performance of the ICU when it is used in the SMR does not exist. Therefore, we defined as our objective to establish a comparison between the results of the SMR using three different scoring systems (APACHE II, APACHE III, SAPS II).

Methods We determined the severity of disease or injury of the patients admitted to the ICU, using APACHE II, APACHE III, and SAPS II. We also determined the crude mortality for each interval of patients. Then we calculated the real mortality of each interval and we obtained the SMR using the risk of mortality assessed by APACHE II, APACHE III and SAPS II, divided by the crude mortality. Finally, we elaborated the curves of risk of death using the results of each scoring system.

Results In a prospective study, we collected data from 161 patients admitted in the ICU during 4 months (1 May 2002–30 August 2002). We included in our study 157 patients, with an average age of 55 years. Seventy-two per cent ($n=113$) of the patients included in our study were men, and 28% ($n=44$) were women. Most of the patients came from the Emergency Room: 51% from Maximum Urgency, and 20.4% from the Emergency Operation Room. We obtained a crude mortality of 28%. The averages of the scores were: APACHE II, 15; APACHE III, 44.7; SAPS II, 35.6. The tendencies of SMR using APACHE II, APACHE III and SAPS II were compared. The tendencies obtained from SMR using APACHE II and APACHE III showed a bigger dispersion of the results, especially in the intervals of more severity when they were compared with the tendency of SMR using SAPS II. From the three scoring systems used, APACHE II showed higher values of SMR than those from APACHE III and SAPS II, which demonstrate the inconsistency of the SMR when we use different scoring systems to determine it.

Table 1

APACHE II	1–7	8–14	15–21	22–28	29–35
Risk of mortality	4.82	12.92	27.43	46.54	68.25
Crude mortality	0	12.7	42.5	60.7	50
SMR	0	0.982972	1.549398	1.304254	0.73260

Conclusion Inconsistency exists in the SMR when we use the different scoring systems, especially when we analyze the higher scores. We should carry out larger studies to define which scoring system is the one that provides better information about the clinical performance of ICU, when it is used in the SMR.

Table 2

APACHE III	1–15	16–30	31–45	46–60	61–75	76–90	91 and more
Risk of mortality	1.7	3.21	7.12	13.94	26	45.13	70.3
Crude mortality	0	12	12.5	20	67.7	53.3	100
SMR	0	3.738318	1.755618	1.43472	2.603846	1.181033	1.422475

Table 3

SAPS II	1–10	11–20	21–30	32–40	41–50	51–60	61 and more
Risk of mortality	0.9	3.06	7.47	18.06	36.6	57.9	80.3
Crude mortality	0	3.03	17.9	20	37.03	70	88.9
SMR	0	0.990196	2.396252	1.10742	1.011749	1.208981	1.107098

P229 An upper estimate of the attributable mortality and cost of severe sepsis in surgical patients

WT Linde-Zwirble[1,2], LM Cooper[3], DC Angus[2]
[1]HPM LLC, Doylestown, PA, USA; [2]The CRISMA Laboratory, Department of Critical Care Medicine, University of Pittsburgh, Pittsburgh, PA, USA; [3]Eli Lilly and Co, Indianapolis, IN, USA
Critical Care 2003, **7(Suppl 2)**:P229 (DOI 10.1186/cc2118)

Introduction Although patients developing severe sepsis (SS) incur high mortality and costs, the extent to which these events are attributable to SS is unclear, especially in surgical patients. We conducted a retrospective analysis of the US Medicare hospital discharge database to estimate the resource use and mortality attributable to SS in patients >65 years old.

Methods We selected all major surgical prospective payment system (PPS) discharges from the FY 2000 Medicare hospital discharge database. Costs were calculated by multiplying charges by institution-specific cost to charge ratios. We defined SS as documented infection plus acute organ dysfunction using ICD-9-CM-based criteria. We calculated hospital mortality, length of stay (LOS), ICU LOS, and total cost for those with and without SS within each surgical DRG. Attributable outcomes were defined as differences in absolute outcomes between those with and without SS within DRG.

Results There were 2.88 million major surgery PPS discharges, of whom 99.903 (3.4%) developed SS. There were 834,722 discharges that incurred ICU care, of whom 66,222 (7.9%) developed SS. In the entire SS cohort, the actual mortality was 26.4%, the expected mortality was 4.8%, and the potential attributable mortality was 21.6% ($n=21,628$). In the ICU SS cohort, the actual mortality was 31.1%, the expected mortality was 8.4%, and the potential attributable mortality was 22.6% ($n=15,057$). The additional SS deaths represented 23.7% of all surgical deaths and 25.3% of all surgical ICU deaths. SS was also responsible for 825,870 hospital days (4.2% of all), 443,113 ICU days (12.6% of all), and US$1,812,415,000 hospital costs (4.7% of all costs). This represents an additional 4.4 ICU days, 3.9 floor days, and US$18,142 per patient.

Discussion The attributable mortality of severe sepsis in elderly surgical patients appears to be as much as 22%. The only factors

reducing this rate would be concomitant conditions that covaried with SS and were not captured in our case-mix adjustment. Importantly, the attributable rate was so high that SS, although occurring in only a small number of patients, resulted in one-quarter of all surgical deaths. The attributable costs and resource use were also very high.

P230 Modelling the cost-effectiveness of treatment of septic patients in intensive care units in Hungary

G Hoffer[1], L Kardos[2], A Csomós[3]
[1]Contract Health Economist, School of Public Health, Kassai út 26, 4029 Debrecen, Hungary; [2] Contract Medical Statistician and [3]Intensive Care Unit, Markhot Teaching Hospital, 3300 Eger, Széchenyi út 27, Hungary
Critical Care 2003, **7(Suppl 2)**:P230 (DOI 10.1186/cc2119)

Introduction Sepsis is among the most lethal diseases in Hungary. While there were 2659 septic events treated in intensive care units (ICU) in Hungary in 2001, 42.7% of the treated patients died owing to sepsis. Obviously, this figure calls attention to the need of measuring the effectiveness and efficiency of sepsis treatment. There is a considerable amount of information related to the effectiveness of different treatment alternatives. In our study we aimed to assess the cost-effectiveness of sepsis treatment in Hungary for the year 2001.

Methods To calculate the average efficiency of treatment of a septic patient in an ICU in Hungary, we constructed a model. This model was made up of three parts. In the first part we defined a septic patient cohort based on the age and gender distribution of all the septic cases treated in ICUs in Hungary in 2001. This patient cohort entered into the second part of the model, where we developed a time-dependent Markov model to describe and analyse the route of Hungarian septic cases through a 28-day-long period. We defined three Markovian states: survival in the ICU, leaving the ICU or the hospital alive, and death in or out of the ICU. Transfer probabilities were defined for each of the 28 days on the basis of data collected for all septic events treated in ICUs in Hungary in 2001 (data were provided by Hungarian governmental health care information suppliers 'GYOGYINFOK'). In the third phase, patients' life-long survival was modelled based on the average age-specific life expectancy of the Hungarian population (data source: Hungarian Central Statistical Office). Survival of the septic patients was corrected by a factor of 0.51 taken from the international literature. Cost data of treatment of septic patients was collected in a nonrandom sample of six Hungarian ICUs. Microcosts of the ICU treatment of 70 septic patients were collected in 2002. Collection and analysis of cost data were described in a detailed manner in another report. Cost per years of survival was selected as a cost-effectiveness measure. During the calculation of efficiency, we used a societal and a Health Insurance Fund viewpoint.

Results The average survival of a septic patient was 8.6 years in Hungary. The average cost of treatment was 1,036,474 HUF from a societal and 462,765 HUF from a Health Insurance Fund (HIF) viewpoint. Average cost-effectiveness of sepsis treatment was 120,458 HUF per life years saved from a societal view. The corresponding figure was 53,765 HUF per life years saved from a HIF viewpoint.

Conclusion Considering all the factors, we found that our model can assess the efficiency of sepsis treatment in Hungary in a valid and reliable way.

P231 Outcome and cost of sepsis in intensive care units in Hungary

A Csomós[1], G Hoffer[2], L Kardos[3]
[1]Intensive Care Unit and [3]Contract Medical Statistician, Markhot Teaching Hospital, 3300 Eger, Széchenyi út 27, Hungary; [2]Contract Health Economist, School of Public Health, Kassai út 26, 4029 Debrecen, Hungary
Critical Care 2003, **7(Suppl 2)**:P231 (DOI 10.1186/cc2120)

Introduction Septic patients do not just have higher than average mortality, but the cost implications of their treatment are significant as well. In this study we report the incidence of sepsis among patients treated in intensive care units (ICU) in Hungary in 2001. We also describe and analyse the outcome and cost of ICU treatment of sepsis in Hungary.

Methods Our study consisted of two parts. In Part 1, we collected data on nationwide incidence and mortality of sepsis cases treated in ICUs in Hungary in 2001. We used secondary data provided by the National Health System database ('GYOGYINFOK'). All patients were selected who complied with the following two criteria: the patient was treated in an ICU and at least one septic ICD-10 code was included in the diagnostic code list. In Part 2, we conducted cost data collection and analysis based on the Cost Block Method [1]. We selected a nonrandom sample of six intensive care units where cost data of 10 severe sepsis patients were collected consecutively from 15 August 2002 backwards. Inclusion criteria were as described in a sepsis definition paper [2]. In order to validate these data, the participating units performed a prospective observational data collection between 15 August and 14 September 2002. Resource consumption of clinical support services, consumables and cost of medical and nursing staff were collected on a daily basis.

Results We identified 2659 admissions with a septicaemia diagnosis code to ICUs in 2001. Mortality was 42.7%; the average length of stay was 14.46 days (SD 17.44 days; median value 9) among patients diagnosed with sepsis. After the intensive treatment, patients remained treated in other inpatient units for a further 18.14 days on average (SD 18.05; median 12). Cost questionnaires based on 70 patients were returned, 60 with retrospective and 10 with prospective cost evaluation of severe sepsis. The average daily cost of sepsis was 101,737 HUF (412 €), higher on days 1–3 than later. The main cost drivers were consumables (42%), clinical support services (19%) and staff cost (18%).

Conclusion The incidence and outcome of severe sepsis in Hungary is similar to international data. Compared with our previous study [3], the cost per patient-day of severe sepsis is over three times more (112 € vs 412 €) than that of average intensive care patients. In proportion to total cost, we spend much more on drugs and less on personnel.

References
1. *Anaesthesia* 1999, **54**:110-120.
2. *Crit Care Med* 1992, **20**:864-874.
3. *Int Care Med* 2002, **28**:S66.

P232 Cost-effectiveness of early goal-directed therapy in the treatment of severe sepsis and septic shock

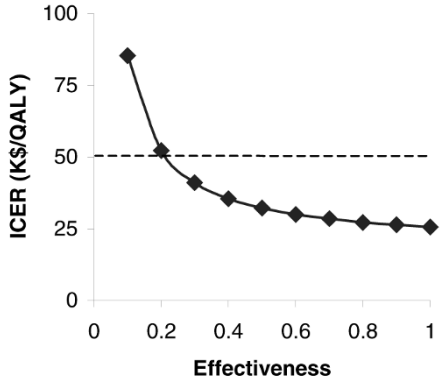
DT Huang[1], DC Angus[1], TT Dremsizov[1], EP Rivers[2], G Clermont[1]
[1]CRISMA Laboratory, Department of Critical Care Medicine, University of Pittsburgh, Pittsburgh, PA, USA; [2]Departments of Emergency Medicine and Surgery, Henry Ford Hospital, Case Western Reserve University, Detroit, MI, USA
Critical Care 2003, **7(Suppl 2)**:P232 (DOI 10.1186/cc2121)

Introduction Early goal-directed therapy (EGDT) for severe sepsis and septic shock has been shown to significantly decrease 60 day mortality and survivor hospital length of stay [1]. However, concern exists over the additional resources and personnel required for this labor-intensive therapy.

Methods We conducted a cost-effectiveness analysis of EGDT from the US societal perspective, based on the results of a recent randomized trial [1]. In constructing the reference case, estimates of short-term effectiveness were based on 60 day survival. Short-term costs were estimated from mechanical ventilation duration, hospital length of stay, and the additional requirements for blood, personnel and capital costs of EGDT. We estimated long-term survival from prior observational data in sepsis patients and long-term costs using age-specific annual health care costs from the National Center of Health Statistics' Medical Expenditure Survey and published costs of nursing homes.

Results The incremental cost-effectiveness ratio (ICER) of EGDT over standard care was $25,600/QALY (quality-adjusted life-year) (95% CI: $20,500–78,600/QALY). In multiway sensitivity analyses, 94% of simulations had an ICER below $50,000/QALY. EGDT was cost-effective (<$50,000/QALY) as long as patient volume exceeded 16/year. Cost-effectiveness increased with greater annual patient volume, decreased long-term survival, decreased annual health care costs, and decreased capital costs. EGDT remained cost-effective even if its 60 day mortality effectiveness was only 20% of that reported by Rivers *et al*. [1] (Fig. 1).

Figure 1



Discussion EGDT is cost-effective for severe sepsis and septic shock over a wide range of assumptions.

Acknowledgement Sponsored by NIH grant 02-T32HL07820-06.

Reference

1. Rivers E, Nguyen B, Havstad S, Ressler J, Muzzin A, Knoblich B, Peterson E, Tomlanovich M, for the Early Goal-Directed Therapy Collaborative Group: **Early goal-directed therapy in the treatment of severe sepsis and septic shock.** *N Engl J Med* 2001, **345**:1368-1377.

P233 Effect of socioeconomic deprivation on intensive care mortality

M Booth[1], S Murray[2], L Plenderleith[3], C Howie[4], F MacKirdy[5]
[1]Department of Anaesthesia, Royal Infirmary, Castle Street, Glasgow, UK; [2]Public Health Medicine, Dalian House, St Vincent Street, Glasgow, UK; [3]Western Infirmary, Dumbarton Road, Glasgow, UK; [4]Department of Anaesthesia, Victoria Infirmary, Langside Road, Glasgow, UK; [5]Scottish Intensive Care Society Audit Group, Department of Anaesthesia, Victoria Infirmary, Langside Road, Glasgow, UK
Critical Care 2003, **7(Suppl 2)**:P233 (DOI 10.1186/cc2122)

Introduction The effect on health of socioeconomic deprivation has been demonstrated in many areas such as risk for myocardial infarction [1]. There is little data on its effect on intensive care mortality. The Scottish Intensive Care Society Audit is a computer-based audit system that all 26 adult general ICUs in Scotland contribute to. Consequently there is a database for the whole country. In Scotland, the socioeconomic deprivation category (DepCat) can be designated by postcode using the Carstairs score [2]. This is based on housing density, car ownership, male unemployment and the head of the household's social class, and ranges from 1 (most affluent) to 7 (most deprived).

Methods Between 1 January 1995 and 31 December 2000, audit data were collected prospectively on 44,000 consecutive admissions to all adult general ICUs in Scotland. The Information and Statistics Division of NHS Scotland undertook the linkage of the ICU data to hospital activity episodes (Scottish Morbidity Records) and Registrar General death records. All data were standardised for age and sex. The Standardised Mortality Rate (SMR) by DepCat was calculated by comparing the expected and observed mortality for each DepCat. This enabled us to assess the impact of socioeconomic deprivation on outcome of ICU admissions.

Results A total of 33,337 case records were able to be allocated a DepCat score. The SMR for these patients ranged from 0.97 for DepCat 1 to 1.32 for the most deprived in DepCat 7 (see Table 1).

Conclusions Socioeconomic deprivation appears to affect ICU mortality with a worsening mortality with worsening deprivation. The exact causes for this are unclear but may be due to a multitude of small chronic comorbidities such as smoking, obesity, poor nutrition, alcohol abuse, drug misuse rather than severe chronic ill health. More work is, however, required to further evaluate this.

Table 1 Standardised ICU mortality by deprivation category

DepCat group	1	2	3	4	5	6	7
SMR	0.97	0.93	0.88	0.99	1.0	1.1	1.32

References
1. Macintyre K, Stewart S, Chalmers J, *et al.*: **Relation between socioeconomic deprivation and death from a first myocardial infarction in Scotland: population based analysis.** *BMJ* 2001, **322**:1152-1153.
2. Carstairs V, Russell M: *Deprivation and Health in Scotland*. Aberdeen: Aberdeen University Press; 1991.

P234 On call physiotherapy: the impact of outreach services

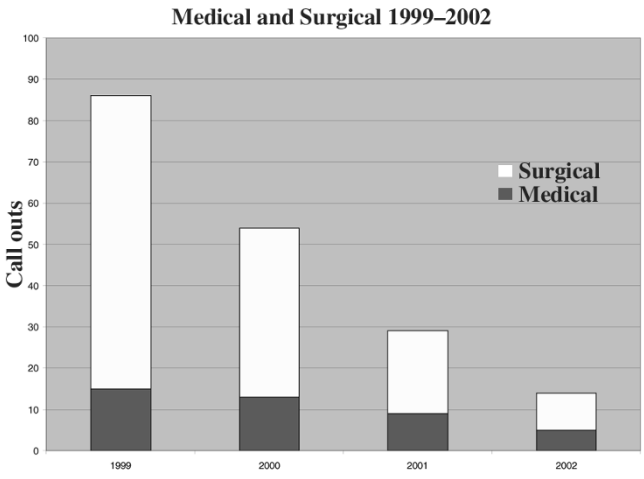
LJ Lees, SJ Coates
Department of Intensive Care, Queens Hospital, Burton on Trent DE13 ORB, UK
Critical Care 2003, **7(Suppl 2)**:P234 (DOI 10.1186/cc2123)

The Modified Early Warning System (MEWS) was introduced in 1998 to aid in the detection of critical illness within the ward setting. Strong links were forged between outreach, physiotherapy and surgery from 1998, as the critical care physiotherapist covered both areas. Formalisation of multidisciplinary outreach was achieved in June 2001, with the appointment of an outreach physiotherapist whose role includes not only critical care patients, but also hospital-wide, ward-based, outreach. Retrospective audit data on frequency of callout by speciality was collected over 4 month snapshot periods (April, May, June, and July) for the years 1999–2002 in order to analyse outreach physiotherapy impact on emergency physiotherapy callouts.

The hospital has a total of 575 beds, of these 424 are inpatient with 60 acute surgical and 114 acute medicine. The majority of callouts were to the acute surgical wards (142) in contrast to acute medicine (42). Evening callouts to acute surgery showed a consistent decline, as did the frequency of weekend daytime on call requests. This finding is not surprising, as multidisciplinary outreach intervention has been embraced primarily within surgery. Figure 1 demonstrates the reduction in callouts over the past 4 years. Further audit over the winter period is necessary.

Monitoring the number of out-of-hours physiotherapy callouts is one way of assessing the impact of specific physiotherapist roles within outreach.

Figure 1



Reference
1. Stenhouse C, *et al.*: *Br J Anaesth* 2000, **84**:663.

P235 Principles for improving the standards for drug-help in the intensive care units

T Lugovkina[1], V Mikhilov[1], V Nevzorova[1], B Richards[2]
[1]Fund of Compulsory Medical Insurance of Sverdlovsk Area, Pharmaceutical Center, 60A Lenin Prospect, 620062 Ekaterinburg, The Urals, Russia; [2]Department of Medical Informatics, UMIST, Sackville Street, Manchester M60 1QD, UK
Critical Care 2003, **7(Suppl 2)**:P235 (DOI 10.1186/cc2124)

Introduction It is very important to maintain the balance between the clinical and the economical vectors in the situation of strictly limited resources in the real clinical practice in Russia. The system of clinical governance must be called into play for this purpose. The most important sector in the use of clinical governance is the intensive care units.

Materials and methods Using a computer, the analysis of the quality of drug-prescribing in the intensive care units of the Sverdlovsk Area in Russia was carried out by the experts in clinical pharmacology. The methodology of constructing the models of drug help standards for the intensive care units by computer was based on the hierarchical principle of structured organization of the 'elementary syndromes' and the corresponding 'elementary standard drug protocols'. Databases were set up containing (a) a list of all drugs and their current market prices, and (b) protocols for the list of drugs allowed for a given diagnosis on a patient in intensive care. It became mandatory to use only those drugs in the list.

Results It was established that 20% of drugs used in the intensive care units had no proven effectiveness and were therefore not included in the standards of drug help in the Government Programme. In 10% of clinical cases, when antibiotics were used, the choice of antibiotics was not optimal and rational. In order to regulate the quality and rationality of fulfilling the drug help standards within the framework of the Area Government Programme, stricter guidelines were laid down. These resulted in a 20–25% reduction in costs of the drugs used in intensive care. The strict protocol for using antibiotics has reduced the length of stay for patients in the ITU. Errors in prescribing have been prevented. This new system was welcomed by the clinicians.

P236 Implementation of a computerized bedside data management program in the ICU

E Grozovski, D Garji, J Cohen, M Shapiro, O Benshimon, P Singer
General Intensive Care Unit, Rabin Medical Center, Campus Beilinson, Petah Tikva, and Sackler School of Medicine, Tel Aviv University, Israel
Critical Care 2003, **7(Suppl 2)**:P236 (DOI 10.1186/cc2125)

Intensivists are reluctant to take the step into paperless documentation in the ICU mainly due to uncertainty concerning the time investment, the impact of a radical change in documentation method on the staff as well as reliability of the software and hardware involved. We describe the implementation of a computerized data collection and management system – 'Metavision' (IMD-Soft®) – in a 10-bed general ICU (admission rate 750 patients/year) of a 1200-bed tertiary care medical center.

Methods Metavision, which is Windows™ (Microsoft®) based, is a program charting patient clinical data, including monitoring parameters, medical and nursing treatment orders, treatment reports, diagnoses, followup documentation and laboratory results, which are inserted either automatically or manually. The system data collection is based on a central server for data storage connected via the intranet with bedside terminals and other user stations in the ward. Most of the medical and nursing staff were computer users with basic knowledge of Windows™, while 20% had no computer experience at all.

Implementation was divided into three phases, Phase 1 (3 weeks), project manager and superusers were trained, and the database was customized to local ICU needs. Phase 2 (4 weeks), configuration and programming of interphases as well as staff training (12 doctors, 51 nurses, a pharmacist, a physiotherapist, a social worker and a respiratory technician underwent 45 min of individual teaching and 45 min of exercise training). The project manager invested 240 hours in training and customization. Phase 3 Go-live (105 days after start day), documentation was switched to computerized charting with no double charting. No major difficulties were registered. Since then all data collection is automated and the documentation is paperless.

Conclusion: A paperless documentation data collection program in a 10-bed ICU can be implemented in a relatively short period with no major difficulties.

P237 Comparison of general medical and general surgical nursing intervention following Early Warning Score triggers

S Ingleby, D Conway
Intensive Care Unit, Manchester Royal Infirmary, Oxford Road, Manchester M13 9WL, UK
Critical Care 2003, **7(Suppl 2)**:P237 (DOI 10.1186/cc2126)

Introduction The Early Warning Score (EWS) [1] has been delivered within the trust for 2 years. In our institution, the EWS protocol has been modified to allow a nurse intervention when EWS = 3 (Appendix 1). The aim of the study was to look at the efficacy of nursing interventions in medical and surgical patient groups.

Method Data were prospectively collected within the surgical and medical wards over a period of 10 weeks. We recorded information for any patient who triggered EWS ≥ 3. The person performing the first intervention and the prevention of further triggers was noted.

Table 1

	Patients on medical ward	Patients on surgical ward	Fisher's exact test, *P*
Total triggering	500	398	
Nurse therapy as first intervention	301 (60%)	42 (16%)	< 0.0001
EWS successfully reduced by nurse therapy	188 (62%)	42 (61%)	NS
Patients who retrigger following nurse therapy	110	18	NS

Appendix 1

Early Warning Score used in Central Manchester and Manchester Children's University NHS Trust

	3	2	1	0	1	2	3
HR		≤ 40	40–50	51–100	101–110	111–129	≥ 130
SBP	≤ 70	71–80	81–100	101–199		≥ 200	
RR		≤ 8		9–14	15–20	21–29	≥ 30
Temperature (°C)		≤ 35.0	35.1–36.0	36.1–37.9	≥ 38–38.9	≥ 39	
CNS				Alert	Voice	Pain	Unconscious

Alert, patient is alert and orientated; Voice, patient responds to voice; Pain, patient responds to painful stimuli; Unconscious, patient is unconscious.

Results Nurses caring for acutely unwell medical patients were able to intervene in 60% of initial triggers without having to call for a doctor (Table 1). These interventions successfully reduced the score in 60% of cases. By contrast, in the surgical group, 16% of triggers were initially dealt with by the nursing staff, and these interventions were successful in 60% of cases.

Conclusion A number of factors could explain these differences: the intensive education package that accompanied the introduction of the score into medicine, differences within the patient groups, and the use of medical ward nurses assisting in the implementation of the score into their areas. Nursing intervention appears effective as first-line treatment for a trigger in many medical patients and we believe it is a useful part of the EWS protocol.

Reference

1. Morgan RJM, Williams F, Wright MM: **An early warning scoring system for detecting developing critical illness [abstract].** *Clin Int Care* 1997, **8**:100.

P238 Evaluating knowledge in acute illness: Critical Care Educational Project

S Ingleby[1], J Eddleston[1], S Naylor[2]
[1]Intensive Care Unit, Manchester Royal Infirmary, Oxford Road, Manchester M13 9WL, UK; [2]Clinical Audit Department, Maternity Annex, The Pennine Acute Hospitals NHS Trust, Birchill Hospital, Rochdale OL12 9QB, UK
Critical Care 2003, **7(Suppl 2)**:P238 (DOI 10.1186/cc2127)

Aim Clinical knowledge and its application underpins delivery of adult care in our hospitals. Such deficits are well recognised [1,2]. The Greater Manchester Network assessed clinical knowledge and its application within the trusts in our area.

Method Eleven hospitals were involved in the design and application of a questionnaire that asked specific questions in relation to applied physiology and care of acutely ill patients.

The questionnaire was distributed to coordinators in 11 hospitals across the network. There were 240 replies (72% response) and they were completed by: nurses $n=134$; medical staff $n=42$; physiotherapists $n=48$; and 24 other/unrecorded. The specialities of those questioned varied with the majority from medical and surgical areas; $n=79$ and $n=72$, respectively. The questionnaire contained questions relevant to basic and applied physiology (25); and qualitative questions pertinent to their perception of their ability to deal with ill patients

Results Respiratory system; 16% recognised all the signs of respiratory distress; 22% did not know how much oxygen was in room air; 27% correctly identified factors relevant to the measurement of oxygen saturation. Forty-eight per cent recognised what respiratory rate reflects; 50% failed to recognise the role of supplementary oxygen in an acute asthmatic attack. Forty-two per cent knew when to take a manual pulse. Eighty-seven per cent knew the normal range for potassium; 31% recognised the implications of hypokalaemia and 54% knew what caused hyperkalaemia. Interestingly, even though the questionnaire had areas that required intensive teaching, 71% of the participants said they felt confident in looking after acutely ill patients.

Conclusion To address this deficit, education and training had commenced in all the trusts surveyed. A central training centre has opened within the network and a shared programme of education has been instituted. The schools of nursing have been approached to look at preregistration training to try to address these issues earlier, and the same is to occur with the other training institutions.

Acknowledgement With thanks to the Greater Manchester Network Outreach Forum.

References

1. Daffurn K, Lee A, Hillman KM, Bishop GF, Bauman A: **Do nurses know when to summon emergency assistance.** *Intensive Crit Care Nurse* 1994, **10**:115-120.
2. McQuillan O, Pilkington S, Allan A, *et al.*: **Confidential inquiry into quality of care before admission to intensive care.** *Br Med J* 1998, **316**:1853-1858.

P239 Critical care training needs analysis for ward staff

S Quinton, Y Higgins
Critical Care Outreach Team, Birmingham Heartlands & Solihull NHS Trust, Birmingham B9 5SS, UK
Critical Care 2003, **7(Suppl 2)**:P239 (DOI 10.1186/cc2128)

Introduction Our Trust recently established a critical care outreach service. The objectives of the team are to enhance the quality and continuity of care for critically ill patients and to share critical care skills with ward staff. Historically, critical care areas within the Trust have experienced a reluctance from ward nursing staff to accept patients back into the ward area who still require a high level of nursing intervention. It became apparent that skill deficits existed among the ward staff and highlighted the need for more skills training. The aim of this study was to conduct a training needs analysis to ensure that future skills training was based on the ward staff's perceived needs as opposed to those perceived by the outreach team.

Table 1

	Central lines (%)	CVP monitoring (%)	Tracheostomy (%)	CPAP (%)	ECG monitoring (%)	Airway suction (%)	O_2 therapy (%)
Frequency > monthly	41	28	11	15	66	49	0
Frequency < monthly	59	72	89	85	34	51	100
Confidence (high/very high)	38	36	18	12	41	83	59

Method A questionnaire was distributed to a random sample of 139 nursing staff of all grades across the Trust. It asked respondents to report knowledge, competence and confidence in the following areas of care: tracheostomy, central lines, CVP monitoring, CPAP, ECG monitoring, airway suction and oxygen therapy. Respondents were also asked to report on the frequency with which they used these skills.

Results Responses were received from 71 staff (51%). The frequency with which skills were used by ward staff and their self-reported confidence are displayed in Table 1.

Discussion Apart from ECG monitoring and airway suction, respondents performed the remaining interventions infrequently. Lack of knowledge, confidence and competence in performing a skill may lead to a reluctance to perform that skill. Similarly, infrequent opportunities to practice a skill can lead to low levels of confidence. A self-sustaining vicious circle of low utilisation and poor confidence can then be generated. Following the results of the initial questionnaire, the Outreach Team implemented a variety of educational activities including a Critical Care Skills Day and the multidisciplinary ALERT course in order to address the low levels of confidence among ward staff. Access to work-based education and training is essential for ward nurses in ensuring they are competent to assess and manage acutely ill patients who are at risk of deterioration. Further work to evaluate the impact of this educational package is now required.

P240 A modification of the blood sampling technique in critical care to reduce blood wastage

PS Hegde, K Tarsey, MC Blunt
Queen Elizabeth Hospital, Kings Lynn, Norfolk PE30 4ET, UK
Critical Care 2003, **7(Suppl 2)**:P240 (DOI 10.1186/cc2129)

Introduction Diagnostic blood sampling is an indispensable and effective tool for assessing critically ill patients. However, the amount of blood drawn daily can be substantial and deleterious to patient care [1]. A recent survey [2] on arterial blood sampling practices in the ICU in England and Wales concluded that blood conservation is underused. There is commercially available equipment to assist in this by ensuring that the amount of blood disposed during sampling could be kept to a minimum. This equipment significantly increases the cost of most critically ill patients. We therefore designed, taught and assessed a sampling technique that could be performed without modification of the standard transducer connection, in which any blood returned was always contained within the closed sterile environment of the transducer tubing.

Method Blood was initially drawn form the distal three-way tap through the 120 cm extension tubing. As soon as blood reached this three-way tap, a total of 2.8 ml had been withdrawn and a further 0.2 ml was withdrawn from the proximal tap, followed by the sample in the usual way. The blood still within the tubing could be flushed back to the patient. In this way we were able to reduce blood wastage from 3 ml to 0.2 ml per sample. We trained all staff for a 2 month period and then proceeded to audit the use of this technique, allowing us to estimate the amount of blood wastage that was saved over a 2 month period.

Results During the study period, 949 separate sampling episodes occurred in 63 patients. All staff confirmed that they had followed the new technique during this period, and daily observation by the authors failed to identify any episode when this was not the case. During the study period, the technique reduced blood wastage during sampling by 2657 ml.

Conclusions This technique is a simple cost-effective approach that minimises blood wastage which could be successfully taught and is feasible for everyday use in the critical care environment.

References

1. Andrews T, Waterman H, Hillier V: *J Adv Nursing* 1999, **30**:851-857.
2. O'Hare D, Chilvers R: *Anaesthesia* 2001, **56**:568-584.

P241 Education reduces unnecessary diagnostic blood sampling in the intensive care unit (ICU)

PS Hegde, K Tarsey, MC Blunt
Queen Elizabeth Hospital, Kings Lynn, Norfolk PE30 4ET, UK
Critical Care 2003, **7(Suppl 2)**:P241 (DOI 10.1186/cc2130)

Introduction Diagnostic blood sampling is an indispensable and effective tool for assessing critically ill patients. It has been demonstrated that a substantial blood volume is drawn daily from these patients [1]. A recent review of UK practice suggested a number of measures to reduce this [2]. Furthermore the recent introduction of an integrated electronic record-keeping system in our unit ensured that maximum information could be derived from each sample. In order to assess whether it is possible to optimise the amount of blood sampled, we performed a prospective cohort controlled study to compare blood volumes used for sampling before and after a 2 month education period.

Method Sample frequency for both laboratory investigations and near-patient testing (NPT) was derived from the electronic record for all patients treated in our ICU during two periods of 2 months. Education included information on unit guidelines on sample requirements, demonstration of the benefit of end-tidal measurements and oximetry, the accuracy of near-patient equipment, as well as education of a new technique designed to minimise blood wastage. Cost per sample was provided by the laboratory management. All sample data were evaluated on a per patient-day basis.

Results There was a significant reduction in total volume, blood wastage, the frequency of laboratory and near-patient tests performed and overall cost following education (Table 1). Demographics were not significantly different in the two groups.

Conclusions Education can significantly reduce the volume of blood used for sampling by ensuring that full use is made of all information. Our data suggest that this volume is clinically important and, furthermore, that this approach can also produce substantial cost saving.

Table 1

	Before education ($n = 43$)	After education ($n = 63$)
Patient-days (total)	263.1	221.5
APACHE II	21 (6–36)	19 (3–36)
Volume sampled (ml/day)	93.5 (76.4–110.5)	46.0 (36.9–55.1)**
NPT (*n*/day)	7.1 (6.1–7.9)	5.1 (4.2–6.0)*
Laboratory tests (*n*/day)	8.7 (6.2–11.3)	5.2 (4.3–6.1)*
Blood discarded (ml/day)	20.9 (18.2–23.6)	1.0 (0.8–1.2)**
Costs (€/day)	94.36 (71.81–116.91)	59.24 (50.13–68.35)*

Data presented as mean (95% confidence intervals), except APACHE as median (range). * $P < 0.01$, ** $P < 0.001$.

References
1. Andrews T, Waterman H, Hillier V: *J Adv Nursing* 1999, **30**:851-857.
2. O'Hare D, Chilvers R: *Anaesthesia* 2001, **56**:568-584.

P242 The efficacy of high performance liquid chromatography (HPLC) for the diagnosis of intoxication patients in the emergency room and ICU

J Yuzawa, T Suzuki, M Ishikawa, M Takeda, S Hanafusa, K Imai
Department of Emergency and Critical Care Medicine, Tokyo Women's Medical University, 8-1 Kawada-cho, Shinjuku-ku, Tokyo, 162-8666, Japan
Critical Care 2003, **7(Suppl 2)**:P242 (DOI 10.1186/cc2131)

Background After the chemical weapon terrorism with SARIN (methyphosphonofluoridic acid 1-methyl-ethyl ester), a nerve agent used in Tokyo, Japan in 1995, the Ministry of Health and Welfare set up the chemical material's analyzers for countermeasure immediately at 73 emergency centers in Japan. On the other hand, there are no rare intoxication patients who are transferred to the emergency center and admitted in the ICU because of unconsciousness and critical cases. It is important to judge chemical materials for intoxication cases immediately and also to discriminate what cause to unconsciousness by intoxication or other diseases. The purpose of this study is to assess the efficacy of HPLC in the emergency room and ICU for the unconscious and critical patients caused by intoxication compared with Triage® (Biosite Diagnostics, San Diego, CA, USA), which is the usual method.

Materials and Methods The clinical records of 120 intoxication patients who underwent treatment in our emergency room and ICU between 1999 and 2002 were reviewed retrospectively. These patients included 40 men and 80 women ranging in age from 17 to 84 years (mean 33 ± 2.1 years).

To evaluate the usefulness and efficacy of HPLC for the critical cases, we surveyed the detective ability, the duration of examination, the expense per sample and the technical skill of HPLC compared with Triage®.

Results The drugs and poisons that patients took are presented in Table 1. Table 2 shows characteristics of HPLC and Triage®. 44.8% of drugs and poisons were detected only by Triage® and they are some benzosiazepines, hemp and stimulants. Also, HPLC was not useful for them. 25.4% of materials were positive by HPLC but negative by Triage®. These chemicals were carbamazepine, levomepromazine, bromovalerylurea and agricultural chemicals. 9.7% were detected with both of HPLC and Triage®, but 20.1% were not detected with either HPLC or Triage®. These chemicals were nicotine, magic mushrooms, bleach, lithium carbonate, and insecticide (Table 3).

Discussion HPLC is superior to specify the chemicals compared with Triage®, which can detect only the metabolized products. Moreover, since HPLC has begun use in our institution, the percentages of detection of chemical materials has elevated more than 25%. However, HPLC takes a long time to get the results, at much expense and requires more technical skills. Therefore, to improve the diagnosis for intoxication patients in critical cases, we should examine with both HPLC and Triage®. But first, Triage® should be done and, if its result is negative, afterwards HPLC should be carried out. Furthermore, it was not able to detect around 20% using both HPLC and Triage®. This result suggests we have to take into consideration HPLC is not enough equipment for all chemical materials and we should consider the countermeasure for negative materials.

Table 1

Chemical	Number of cases
Medicine	100
Amphetamine	6
Agricultural chemicals	5
Nicotine	2
Cocaine	2
Magic mushroom	1
Hemp	1
Bleach	1
Kmarine	1
Adhesive agent	1

Table 2

	HPLC	Triage®
Kinds of samples	Urine, blood, gastric juice	Only urine
Duration (min)	120–180	15
Cost ($/sample)	165	37
Technical skill	Difficult	Easy

Table 3

	HPLC-positive (%)	HPLC-negative (%)
Triage®-positive	9.7	44.8
Triage®-negative	25.4	20.1

References
1. West A, Frost M, *et al.*: *Int J Legal Med* 1997, **110**:251-253.
2. Schwartz JG, Hurd IL, *et al.*: *Am J Emerg Med* 1994, **12**:513-516.

P243 Admission to an adult intensive care unit for poisoning: a review of 230 cases

K Mehmet, S Murat, D Nazim, K Husnu
Ataturk University Hospital, Department of Anaesthesiology and Reanimation, Erzurum, Turkey
Critical Care 2003, **7(Suppl 2)**:P243 (DOI 10.1186/cc2132)

Background Poisoning remains a serious public health problem despite regulatory interventions and medical advances.

Objective To evaluate epidemiological features of poisoning in our adult ICU (AICU).

Patients and methods We reviewed all patients treated for poisonings in the AICU of University Hospital in Ezurum, Turkey, between May 1997 and October 2002. A retrospective study was conducted.

Results Reasons for admission to the AICU were the need for ventilator treatment or invasive monitoring of vital functions. Two hundred and thirty patients (126 men [57%], 104 women [43%], mean age 34 years) were treated for poisoning in the AICU. Specific poisons have been presented in Table 1.

Seventy-three per cent of the patients (n=168) had attempted suicide, most of them using drugs (n=123). Eleven patients (6.5%) died. Twenty-seven per cent of the patients (n=62) were admitted because of accidental poisoning, most of them expected to be CO intoxications (n=30). Eleven patients (17.7%) died. The most common cause of death was methyl alcohol poisoning (death rate 42.8%).

Conclusions In adults, self-poisoning is usually deliberate (suicide or parasuicide) [1]. Although advanced life support and antidotal treatments were available, mortality was high. Concrete preventive measures are mandatory to prevent loss of life and health care resources.

Table 1

Causes of poisoning	Number	Recovered	Died	Agent death rate (%)	Total death rate (%)
Drugs	123	114	9	7.3	4
Organophosphate	46	44	2	4.4	0.87
Carbon monoxide	30	28	2	6.66	0.87
Methyl alcohol	14	8	6	42.8	2.6
Botulism	8	6	2	25	0.87
Mushrooms	6	5	1	16.6	0.34
Sulphur	2	2	–	–	–
Lithium	1	1	–	–	–
Total	230	208	22	–	9.55

Reference
1. Ellenhorn MJ: *Ellenhorn's Medical Toxicology*, second edition. Williams & Wilkins; 1997:5-6.

P244 Organophosphate poisoning in the intensive care unit

H Sungurtekin, C Balcý
Department of Anesthesiology and Reanimation, Pamukkale University School of Medicine, Tokat Cad No 41-8, Özkan Apt., Denizli, Turkey
Critical Care 2003, **7(Suppl 2)**:P244 (DOI 10.1186/cc2133)

Introduction Organophosphate pesticides are widely used agricultural products that act as acetycholinesterase inhibitors. This study aimed to describe the presentation and management of organophosphate poisoning (OPP) in the intensive care unit (ICU).

Method Retrospective examination of medical records from 25 patients with OPP, who were admitted to the ICU and remained for ≥24 hours. Diagnosis was performed from the history taken either from the patients or from the patient's relatives. Demographic, survival data and day 1 APACHE II, APACHE III and Glasgow Coma Scale (GCS) scores were recorded.

Results There were 20 female and five male patients. Twenty-two of 25 patients (88%) attempting suicide were admitted to the ICU, with a mean stay of 11.9 days (range 1–61 days). The organophosphates were parathion, fenthion, malathion, and diazinon. Gastric lavage was performed, and activated charcoal was administered to all patients. Atropine sulphate was administered

intravenously in repeated doses or infusion to all patients with bradycardia, diarrhea, salivation, and miosis. Pralidoxime was used for 24 patients. Mechanical ventilation was required by 68% of patients because of bronchial secretions, altered conscious level and paralysis. The mean APACHE II and APACHE III scores were 9.4 ± 5.9 and 34.5 ± 17.5, respectively. Intermediate syndrome was observed in two patients. Four patients died from ARDS, and three died from septic shock. Serum cholinesterase level at admission was well correlated with APACHE II, APACHE III and GCS scores.

Discussion Ingestion of organophosphate compounds in an attempt at suicide is a major problem, especially in developing countries because of the wide availability of pesticides as result of extensive use in agriculture, and uncontrolled sale of these agents all over the country. OPP is a serious condition that needs rapid diagnosis and treatment. Delay in discovery of poisoning and in seeking medical assistance, inadequate airway management and severity of OPP may contribute to mortality in these patients.

Reference

1. Sungur M, Güven M: *Crit Care* 2001, **5**:211-215.

P245 Intensive care expenditure on overdose admissions

MA Staber, JL Plenderleith, ES Wilson, AR Binning
Department of Anaesthesia and Intensive Care, Western Infirmary, Glasgow, UK
Critical Care 2003, **7(Suppl 2)**:P245 (DOI 10.1186/cc2134)

Introduction In Scotland, 3% of intensive care admissions relate to drug overdoses. In Greater Glasgow, £12 million are annually spent on drug misuse services. UK studies have related a therapeutic intervention scoring system (TISS) to expenditure [1]. We investigated the costs of overdose admissions in a teaching hospital intensive care unit (ICU) from 1 January 1997 to 31 December 2000.

Method Data were collected prospectively for all overdose admissions to the intensive care unit using Ward Watcher software (Critical Care Audit Ltd, Yorkshire, UK).

Result A total of 3.8% ($n = 70$) of all ICU admissions ($n = 1846$) were due to overdoses. During the same period, the Accident & Emergency Department admitted 4097 patients with the same diagnosis. Comparing overdose patients with the whole ICU population, the mean age was 36.6 years versus 56.5 years; mean stay was 1 day (median 0.8) versus 4.02 days (median 1.8); TISS score was 41.8 ± 30.3 versus 144.7 ± 171.7; and available APACHE scores were 15 ± 6.5 versus 18.84 ± 7.48. Overdose mortality was 3%. Overall ICU mortality was 23%.

Over the 4 years, the whole ICU population accumulated a TISS score of 266,360. On a basis of £25–31 per TISS point, this relates to an expenditure of £6.7–8.3 million. The overdose group collected a score of 2926, giving an overall cost of £0.07–0.09 million.

Conclusion Drug overdoses accounted for 3.8% of ICU admissions but only for 1.1% of the overall treatment costs. Only 1.7% of overdose hospital admissions required ICU admission. Nevertheless, drug overdose admissions are a significant component of the workload and costs of our ICU.

References

1. Dickie H, Vendo A, Dundas R, Treacher DF, Leach RM: **Relationship between TISS and ICU cost.** *Intensive Care Med* 1998, **24**:1009-1017.

Table 1

Cost

	Mortality (%)	Stay in days (mean [median])	APACHE score (mean [SD])	TISS score (mean [SD])	Cost	
					£ million	€ million
All ICU admissions ($n = 1846$)	23	4.0 (1.8)	18.84 (7.48)	144.7 (171.7)	6.7–8.3	10.4–12.9
Overdose admissions ($n = 70$)	3	1.0 (0.8)	15.0 (6.5)	41.8 (30.3)	0.07–0.09	0.11–0.14

P246 Adverse incidents in a paediatric ICU: a model to identify latent risk factors

SM Tibby, J West, L Ferguson, A Durward, IA Murdoch
Department of Paediatric Intensive Care, Guy's Hospital, London SE1 9RT, UK
Critical Care 2003, **7(Suppl 2)**:P246 (DOI 10.1186/cc2135)

Introduction Successful risk management requires a robust system for adverse incident (AI) reporting and analysis. Although many ICU studies have focused on AI categorisation and examination of factors immediately preceding the AI, few have investigated the potential contribution from latent or hidden factors (e.g. poor staff supervision). This phenomenon is well known in other complex, nonmedical systems such as the aviation and nuclear industries.

Aim To establish latent risk factors for AI occurrence in a tertiary PICU.

Methods Data were collected prospectively from 730 consecutive, 12-hour nursing shifts over a 12-month period (816 patient episodes, standardised mortality ratio 0.77). Incidents were reported and categorised using a standardised format. Factors potentially contributing to the occurrence of an AI were classified

according to temporal aspects (time of day, weekend, etc.), bed occupancy, patient dependency, patient flux, nursing and medical skill-mix, junior medical staff supervision, nursing agency (locum) use and a weighted, composite score quantifying several factors that may compromise the clinical supervisory role of the nurse in charge (e.g. patient death on a shift, logistical issues with support staff such as porters, coverage of meal breaks, etc.). Two logistic regression models were constructed: one examining the relationship between these variables and the type of AI; the second examined potential interaction effects between clinically related variables (e.g. 'patient workload' combines bed occupancy with patient dependency).

Results Two hundred and eighty-four AI occurred during 30% (220/730) of shifts, of which 181 were patient related and 103 unit or staff related. Patient-related AI were categorised as: drug errors (55), intravenous/arterial line problems (37), equipment issues (32), patient injury (26), standard of care (21) and self-extubation (10). One hundred and thirty-four (74%) of the patient-related CIs resulted in actual harm to the patient, of which 49 (27%) were deemed serious.

Both unit-related and patient-related AI were more common during the day shift (the period of greatest ICU activity). Unit-related AI were also associated with factors compromising the senior nurses' supervising role, OR 1.31 (95% CI 1.03–1.68), while patient-related AI were less common with increased junior doctor supervision, OR 0.61 (95% CI 0.40–0.91). Factors associated with the various categories of patient AI (drug errors, self-extubation, etc.) included: patient dependency, bed occupancy, number of admissions/discharges per shift, increased nursing agency use, and absence of a senior sister on the shift. The second regression model, examining interaction effects, demonstrated an interaction between nursing supervision factors for unit-related AI, and patient workload factors for patient-related AI. Both models demonstrated excellent goodness of fit (Hosmer Lemeshow $P > 0.10$).

Conclusion AI are common and are associated with many latent factors including time of day, nursing and medical supervision, and patient workload. This model may provide a focus for strategies aimed at reduction in AI.

P247 Iatrogenic complications in the ICU: prospective study during 10 months

S Abdellatif[1], H Ksouri[1], A Ben Hamida[2], R Nasri[1], S Alaya[1], H Ben Mokhtar[1], S Ben Lakhal[1]
[1]Medical Intensive Care Unit, Rabta Hospital, Jabbari, 1007 Tunis, Tunisia; [2]Department of Epidemiology, University of Medicine, 1007 Tunis, Tunisia
Critical Care 2003, **7(Suppl 2)**:P247 (DOI 10.1186/cc2136)

Introduction Iatrogenic complications (IC) are defined as an adverse event that occurs independently of the underlying disease. In fact, in the USA, IC are noted in 4% of hospitalised patients leading to death in 14% of cases.

Aim To evaluate the incidence and types of IC in the ICU, their repercussions on morbidity and mortality rates and to identify the associated factors of risk.

Materials and methods A prospective study, performed between February 2002 and November 2002. All episodes of IC are recorded. The type, the cause and the repercussions are noted. IC were divided, according to their consequences, into three categories: major, moderate and minor.

Results One hundred and thirty-two patients were hospitalised during the period of study with mean age 45 ± 19 years, sex ratio = 1.6, SAPS II = 37 ± 18, APACHE II = 18 ± 10, MacCabe = 0.95 ± 0.89, LOD = 6.5 ± 3.75. Fifty-four per cent needed mechanical ventilation. One hundred and thirty-nine episodes of IC occurred in 59 patients. Incidence 44.7%, prevalence 42.5% and density of incidence of 101/1000 day stay in the ICU. Cardiovascular complications are the most frequent ones, including mainly hypotension and arrhythmia (54%). The incidence was judged major in 26 cases, leading to death in four cases, moderate in 60 cases and minor in 53 cases. Risk factors retained are: prognosis indices (SAPS II, APACHE II), a high or excessive nursing workload expressed by the OMEGA score, duration of mechanical ventilation and length of stay in the ICU.

Discussion IC are frequent, they are induced by the development of invasive techniques of investigation and monitoring, human errors and a high or excessive nursing workload. Their pathogenesis is related to the acute disease and the characteristics of the ICU.

Conclusion To decrease IC incidence, human and material resources must be optimised and the indications of invasive investigations and monitoring must be more rigorous.

P248 Near-miss maternal mortality in North Greece during the past decade

C Kydona[1], Ch Timiliotou[1], E Papazafiriou[1], N Gritsi-Gerogianni[1], A Papanikolaou[2]
[1]Intensive Care Unit and [2]4th Department of Obstetrics & Gynecology, 'Hippokration' General Hospital, Konstantinoupoleos 49, 54642 Thessaloniki, Greece
Critical Care 2003, **7(Suppl 2)**:P248 (DOI 10.1186/cc2137)

Introduction The aim of this study was to determine the level of 'near-miss maternal mortality', due to severe obstetrical complications or maternal disease, in the largest public hospital of Greece. The objective was also to identify risk factors and outcome of pregnant women who required intensive care.

Methods During the period 1990–2001 (12 years), all pregnant patients who were transferred from the Department of Obstetrics to the ICU of 'Hippokration' General Hospital of Thessaloniki, were retrospectively included into the study. A 'near-miss' describes a patient with an acute organ system dysfunction that, if not treated appropriately, could result in death. The cases fitting this definition and all maternal deaths were analysed. Several factors were looked for and noted: a) the demographic characteristics of the patients, b) the diagnosis at admission in the obstetric unit, c) the indications for admission in the ICU, d) the type of surgery, e) the consultation of other specialities in the management of the critically ill, f) the time of hospitalization, and g) the outcome.

Results Over 12 years there were 43,754 deliveries in a general hospital with four university obstetric clinics, which covers the area of North Greece with a population of nearly 3 million habitants. One hundred and twenty-two women required transfer for critical care in the ICU (0.28%); of these, 21% had no medical insurance and were immigrants. Mean age was 29.1 years. The main causes of admission in ICU were respiratory insufficiency (32.8%), hypovolemic shock due to hemorrhage (27.1%), hypertension (26.3%), and sepsis (7.4%). Mean time of hospitalization in the ICU was 4.9 days. Several complications, such as DIC, ARDS, acute renal failure, cerebral hemorrhage, and cardiac dysfunction, needed the contribution of other specialities. The majority required ventilatory support, vasoactive drugs and blood transfusions. There were 12 deaths (mortality rate 9.8%).

Conclusions The term 'near-miss mortality' implicates the potentially mortal complications of pregnancy that needed admission in the ICU. In our study it is 0.28%, and it shows the risks of pregnancy nowadays and indicates the quality of the obstetric care in our country.

P249 Stress and other personality traits in ICU staff

A Bekridelis[1], E Antoniadou[1], M Stougianni[1], A Kiparissi[1], S Vasiliagou[1], S Skordi[2], P Grigoriadou[2]
[1]NHS General ICU and [2]Psychology, General Hospital 'G. Gennimatas', 41 Ethikis Aminis str., Thessaloniki 54635, Greece
Critical Care 2003, **7(Suppl 2)**:P249 (DOI 10.1186/cc2138)

Introduction This pilot study aims to find stress (S) and other personality traits (physical symptoms [PS], anger [A]) among the ICU staff, and any existing correlation between them and length of working time (LWT) in the ICU and with educational level (EDL).

Materials and methods The staff (university degree doctors [UDD], university degree nurses [UDN], technician nurses [TN] and lower degree staff) of the General ICU (GICU), $n=32$, and the respective of the Medical ICU (MICU), $n=15$, answered the SCL-90-R questionnaire (a short type of the Minnesota Personality Inventory) in association with LWT in the ICU, with EDL and demographic data. We evaluated mean values of scoring points for stress (S), physical symptoms (PS) and anger (A), between the two ICU's staff and LWT and EDL.

Results MICU pathologic scoring: 2/15, 13.3%. PSa: 11.6 points, PSb: 26 points, Sa: 8.2 points, Sb: 9 points, Aa: 5.25 points, Ab: 9 points. EDL MICU: 2/2 LDS. LWT mean in years: 9. GICU pathologic scoring: 3/32, 9%. PSa: 10.5, PSb: 14.25, PSc: 10.5, Sa: 6.5, Sb: 7.5, Sc: 7.5, Aa: 4.6, Ab: 3.5, Ac: 3. EDL GICU: UDD 1/3, UDN 1/3, TN 1/3. LWT GICU mean: 11 years.

Conclusion Between individuals of the two ICUs, it seems that MICU staff with a lower degree of education experienced more stress, anger and physical symptoms than GICU staff.

P250 ICU staff level of depression

A Bekridelis[1], E Antoniadou[1], T Georgiadou[1], A Kiparissi[1], S Vasiliagou[1], S Skordi[2], P Grigoriadou[2]
[1]NHS General ICU and [2]Psychology, General Hospital 'G. Gennimatas', 41 Ethnikis Aminis str., Thessaloniki 54635, Greece
Critical Care 2003, **7(Suppl 2)**:P250 (DOI 10.1186/cc2139)

Introduction This pilot study aims to define the occurrence of depression in ICU staff in relation with length of working time (LWT) in the ICU and with educational level (EDL) (university degree doctor [UDD], university degree nurse [UDN], technician nurse [TN], lower degree staff [LDS]).

Materials and methods The staff of the General ICU (GICU: $n=32$) and the staff of the Medical ICU (MICU: $n=15$) answered the BDI-II questionnaire, which measures depression, in correlation with EDL, LWT and demographic data. Depression score: 10–17 points = mild, 18–30 points = moderate, >30 points = major.

Results Total depression in GICU 37.5% (12/32) and in MICU 26.6% (4/15). Mild: GICU (*n*, %): 6/12, 50%; MICU (*n*, %): 2/4, 50%. Moderate: GICU (*n*, %): 4/12, 33%; MICU (*n*, %): 0.25, 25%. Major: GICU (*n*, %): 2/12, 16%; MICU (*n*, %): 1/4, 25%. Individuals in depression A: EDL GICU: 4/12 UDD, 3/12 UDN, 4/12 TN, 1/12 LDS; EDL MICU: 1/4 TN, 3/4 LDS; LWT mean value in GICU: UDD 14 years, UDN–TN 2 years LDS 3 years. B: LWT mean value in MICU: UDN–TN 8 years, LDS 2 years.

Conclusion Results showed a higher rate of depression occurrence in GICU and especially to individuals bearing a university degree and having more than 10 years LWT in the ICU.

P251 Intensive care nurses' attitudes to withdrawal of treatment

T Dean[1], A Williams[2], B Regan[1], R Beale[1]
[1]Adult ICU, Guy's and St Thomas' Hospital, London SE1 7EH, UK; [2]Florence Nightingale School of Nursing & Midwifery, King's College, London, UK
Critical Care 2003, **7(Suppl 2)**:P251 (DOI 10.1186/cc2140)

Introduction Withdrawal of active treatment (WoT) is increasingly important as the mode of dying for patients treated in intensive care units (ICUs). The objective of this study was to ascertain whether ICU nurses feel adequately prepared to meet the challenges this presents.

Method The study was performed in the 30-bed general adult ICU of an academic medical centre, using a self-administered, cross-sectional survey, comprising mainly closed questions and Likert scale responses to set statements, allowing numeric values to be assigned and an overall 'confidence score' to be calculated. Content and face validity of the tool were appraised through a pilot study. The following key factors were addressed: nurses' previous education regarding WoT, how beneficial they believed this to have been, their previous experiences of WoT, their confidence in their ability to communicate within the multidisciplinary team (MDT)

and with relatives, their knowledge of the legal issues raised during WoT, and their priorities for strategies to improve the WoT process.

Results One hundred and twenty-seven nurses were surveyed and 94 (74%) responded, of whom 91 (97%) had experienced withdrawal of treatment (WoT). The mean overall confidence score was 2.78 ± 0.5, but this was significantly higher (i.e. more confident) by nursing grade, previous experience and previous education ($P < 0.0005$ for all). Sixty-two per cent of nurses felt able to represent their own views and 81% the patient and/or family's views within the MDT, while 64% felt confident communicating with the family. Forty-three per cent of nurses had received some form of education addressing WoT, but only 55% felt it had benefited their practice. Fifty per cent were unsure of the legal issues surrounding WoT, and 72% felt unclear of the correct process for WoT. The three strategies felt most likely to improve WoT were written guidelines (74%), full supervision of first experience of WoT (79%) and a rostered study day (86%).

Conclusion This survey shows that ICU nurses are uncertain about their own abilities and the process when addressing WoT. It confirms that both experience and education increase confidence and perceived knowledge, but suggests that education should be more effective. A more structured approach to WoT may also be of benefit.

P252 Predictors of clinician discomfort with daily life support plans for mechanically ventilated patients

L Griffith[1], D Cook[1,2], S Hanna[1], G Rocker[3], P Sjokvist[4], P Dodek[5], J Marshall[6], M Levy[7], J Varon[8], S Finfer[9], R Jaeschke[2], L Buckingham[1], G Guyatt[1,2]

[1]Department of Clinical Epidemiology and Biostatistics, and [2]Department of Medicine, McMaster University, Hamilton, Ontario, Canada; [3]Department of Medicine, Dalhousie University, Halifax, Nova Scotia, Canada; [4]Department of Anesthesia & Intensive Care, Huddinge University, Stockholm, Sweden; [5]Program of Critical Care Medicine, University of British Columbia, Vancouver, British Columbia, Canada; [6]Department of Surgery, University of Toronto, Toronto, Ontario, Canada; [7]Department of Medicine, Brown University, Providence, Rhode Island, USA; [8]Department of Medicine, Baylor College of Medicine, Houston, Texas, USA; [9]Intensive Care Unit, Royal North Shore Hospital, University of Sydney, Sydney, Australia

Critical Care 2003, **7(Suppl 2)**:P252 (DOI 10.1186/cc2141)

Objective To examine the incidence and predictors of clinician discomfort about daily advanced life support plans for ICU patients.

Design Prospective international cohort study.

Setting Thirteen university-affiliated ICUs in Canada, the United States, Australia and Sweden.

Patients Six hundred and thirty-three mechanically ventilated adults with an expected ICU length of stay of 72 hours or more.

Measurements We documented the daily plan for advanced life support and asked the bedside nurse, ICU resident and physician how comfortable they were with this plan. If they were uncomfortable, they stated whether the plan was too technologically intense or not intense enough, and why. We used hierarchical logistic regression to examine predictors of discomfort.

Results Of 15,800 observations, 1294 (8.2%) indicated discomfort with the life support plan. At least one clinician was uncomfortable on at least one occasion for 295 (46.6%) patients. Discomfort occurred more often when the plan was too intense than when the plan was not intense enough (94.7% vs 5.3%, $P < 0.001$). We found the following factors independently predicted discomfort because the plan was too intense: patient age (odds ratio [OR] 1.19, 95% CI 1.07–1.33 for 10 year intervals), APACHE II score (OR 1.23, 1.09–1.38 for five-point intervals), medical admission (OR 2.66, 1.65–4.29), poor prior functional status (OR 3.52, 1.98–6.26 compared with good functional status), daily organ dysfunction (OR 1.60, 1.25–2.04 for each five-point interval), dialysis in the ICU (OR 3.09, 2.05–4.66), plan to withhold dialysis (OR 2.03, 1.52–2.70), plan to withhold mechanical ventilation (OR 0.20, 0.06–0.65), first week in the ICU (OR 1.76, 1.40–2.22), clinician (OR 1.92, 1.75–2.10 for nurse versus resident and OR 1.57, 1.43–2.1 for attending physician versus resident), and city.

Conclusions Clinicians often experience discomfort about life support plans for mechanically ventilated patients. Discomfort occurs more often among nurses and is more likely for older, more severely ill medical patients developing acute renal failure, and for extubated patients for whom there are no plans to withhold ventilation.

P253 Attitudes and practices about do-not-resuscitate orders in Turkey

L Ýyilikçi[1], S Erbayraktar[2], N Gökmen[1], H Ellidokuz[3], HC Kara[1], A Günerli[1]

[1]Department of Anesthesiology and [2]Department of Neurosurgery, School of Medicine, Dokuz Eylül University, Turkey; [3]Department of Public Health, School of Medicine, Kocatepe University, Turkey

Critical Care 2003, **7(Suppl 2)**:P253 (DOI 10.1186/cc2142)

Objective To determine attitudes and practices of the Turkish anesthesiologists about Do-Not-Resuscitate (DNR) orders and to recommend educational programs to improve the understanding of the role of the anesthesiologist in end-of-life care.

Design An anonymous questionnaire consisting of 18 questions was mailed to 439 members of the Turkish Society of Anesthesiology and Reanimation, and 369 returned responses were evaluated.

Results Three hundred and sixty-nine questionnaires were returned (84% response). Of the respondents, 56% were male 44% female. Over 90% of the respondents indicated that they were Muslim. One-half of respondents work in hospitals with more than 800 beds; 49.1% of respondents had an intensive care unit facility of seven to 12 beds. We found that 66% of respondents had initiated written or oral (94.2%) DNR orders most frequently after discussing with colleagues (82.7%). Clinical scenarios provided specific examples of the decision-making challenges facing the anesthesiologist. In these examples, support was most often continued even when

the patient had no chance of meaningful recovery no matter whether the patient had family or not. In this situation, male physicians and physicians having intensive care unit experiences of less than 5 years showed significantly high rates of maintaining full life support (62.1% and 61.0%, respectively), even when the family desired that support be withdrawn. Experience also influenced decision-making independence. Physicians with less experience indicated that decisions should be made by concensus more often than did those with over 5 years of experience in intensive care medicine. Younger physicians also indicated a greater concern about the potential to be punished for decisions to withhold or withdraw care than did those with more years of experience.

Conclusions This study defined the attitudes of Turkish anesthesiologists about end-of-life care and DNR orders. While a number of similarities were found between Turkish physicians and those from other countries, some specific differences could be identified, particularly related to concensus decision making and to sharing information with other providers and the value of ethics committees in the decision-making process, even when the family and physicians concur on the plans for further care.

References

1. Vincent JL: **Foregoing life support in western European intensive care units: the results of an ethical questionnaire.** *Crit Care Med* 1999, **27**:1626-1633.
2. Stevens L, Cook D, Guyatt G, *et al.*: **Education, ethics, and end-of-life decisions in the intensive care unit.** *Crit Care Med* 2002, **30**:290-296.

P254 Influencing advance directive completion rates in nonterminally ill patients: a systematic review

R Patel[1], T Sinuff[1], D Cook[1,2]
[1]Department of Medicine and [2]Department of Clinical Epidemiology and Biostatistics, McMaster University, Hamilton, Ontario, Canada
Critical Care 2003, **7(Suppl 2)**:P254 (DOI 10.1186/cc2143)

Introduction Advance directives (AD) in the form of cardiopulmonary resuscitation orders are a specific set of interventions in response to a cardiopulmonary arrest. *A priori* documentation and subsequent availability of ADs at the point of care increases the probability that diagnostic, therapeutic and palliative interventions will be administered to patients within the framework of these preferences.

Objectives We conducted a systematic review of educational advance care planning interventions for adults without terminal illness to determine their influence on the completion rate of advance directives for cardiopulmonary resuscitation.

Methods We searched MEDLINE, the Cochrane Library, all retrieved trials and pertinent reviews for trials published between 1981 and September 2002. We included randomized trials enrolling patients ≥18 years of age, evaluating an educational intervention comprised of at least one of: written, audio, or video materials, or direct counseling, and whether an outcome included the completion rate of an advance directive. We appraised the quality of each trial in terms of methodology and reporting transparency (quality score range 0–10).

Results We included nine randomized trials enrolling 3206 patients. A variety of interventions were evaluated, primarily among Caucasian patients, including direct individual counseling, brochures, both direct counseling and brochures, and direct counseling plus brochures with a video presentation. Some trials included reminders as part of the intervention. Overall, the methodologic quality and reporting transparency were poor, reflected in a median composite quality score of 5 (interquartile range 4.5–6.0). The odds ratios for the completion rate of an advance directive ranged from 0.41 to 106.0 across the trials (test of heterogeneity $P<0.001$). The summary odds ratio for these educational interventions was 3.71 (95% CI 1.46, 9.40). Trials with greater methodologic rigor and reporting transparency were associated with a more conservative estimate of the effect, 2.42 [0.96, 6.10], compared with 28.69 [5.08, 162.06] for less rigorous and poorly reported trials ($P=0.013$ for the difference).

Conclusions Busy clinicians may use simple educational interventions to increase the completion rate of advance directives documenting patient preferences for cardiopulmonary resuscitation. Understanding the influence of these interventions on other clinically important outcomes is worthy of further research.

P255 Lifestyle adaptation of the patient post coronary artery bypass surgery (CABG)

C Du Toit, J Bornman, C van Belkum
Technikon Pretoria, Private Bag X680, Pretoria 0001, Republic of South Africa
Critical Care 2003, **7(Suppl 2)**:P255 (DOI 10.1186/cc2144)

Background Many patients have an unrealistic gloomy perception of their prognosis despite realistic appraisals, together with an understandable explanation of the pertinent clinical features of the disease. It has been established that the incidence of psychological complications and postoperative psychosis is higher in cardiac surgery.

Long-term cognitive changes post CABG has received less attention and, as up to 42% patients perform below baseline level, it is understandable that doubt and uncertainty becomes part of their lives. Patient-perceived quality of life after CABG proved about one-quarter of the interviewed expressed dissatisfaction concerning their present quality of life. The aim is to determine whether an effective lifestyle adaptation program post CABG could enhance the quality of life of the CABG patient.

Methods A qualitative study in which the experiences, as lived, of the patient and his/her family postoperatively was described in naïve sketches. The approach was phenomenological This was completed in a period 2 weeks–2 years post CABG. In the naïve sketch, the patients were asked to summarize their anxieties, uncertainties and new demands after the CABG.

Results Among the patients studied, the context being a cardiothoracic unit where the patients received assistance in the recuperative phase, 57% summarized anxieties, 37% summarized uncertainties and 60% summarized new demands post CABG.

Conclusion The major surgical intervention, the coronary artery bypass surgery, the operation procedure itself, engrosses the

patients' psyche in such a manner that limitation of space is left for the thought of lifestyle adaptation thereafter. If intensive care is truly to develop as a speciality it has to understand the complete path of the illness process. The critical care nurses are the lifelines in these criteria. More time should be spent and more support should be provided in the recuperative phase post CABG. A rehabilitation program is warranted.

References
1. Anderson G, Felecke E, Perski A: **Patient-perceived quality of life after coronary bypass surgery.** *Scand J Caring Sci* 1999, **13**:11-17.
2. Selnes OA: **Neurobehavioural sequelae of cardiopulmonary bypass.** *The Lancet* 1999, **353**:1601-1605.
3. Griffiths R, Jones C: *Intensive Care Aftercare*. [www.elsevier-health.com] Butterworth Heineman; 2002.

P256 Late sequaela of primary post-traumatic ARDS

I Fichtel, M Baake, R Stiletto
Department of Trauma Surgery/ICU, Philipps-University-Marburg, Baldinger Strasse, 35033 Marburg, Germany
Critical Care 2003, **7(Suppl 2)**:P256 (DOI 10.1186/cc2145)

Introduction Post-traumatic lung injuries with consecutive ALI and ARDS are frequent injuries in trauma populations. There is only a small body of literature dealing with late sequaela of ALI and ARDS. To evaluate the long-term disability and disorders of lung function in these patients, we initiated a prospective, nonrandomised study.

Patients and methods The study population was recruited from a group of 111 patients from a former study dealing with position therapy for the treatment of acute lung injuries. Patients were included if they survived the initial injuries and were avaliable for pulmonary function testing and had a minimal followup of 1 year. In all included patients the pulmonary function were tested in the laboratory with a bodyplethysmograph from Jaeger (Wuerzburg, Germany). The bellows function included vital capacity (VC [l]) and forced expiratory volume in 1 s (FEV1 [l]). In addition, blood samples for the calculation of capillary blood oxygenation were collected. The pO_2/FiO_2 rational was calculated. The respiratory data were compared with a control group from historical literature-based data including 49 patients. $n = 19$ patients were avaliable for physical evaluation.

Statistics The initial ISS of the population was 40 (15–59), age 40.5 years (19–71), the initial paO_2/FiO_2 was 286 (95–466). Time on the respirator was 14.3 days (3–31).

Table 1

Laboratory data	G1[a]	G2 [1]	G3 [2]	Statistical significance
VC (l)	89.0	87.0	81.0	NS
FEV1 (l)	79.3	88.0	81.0	NS

[a] Author study group. NS, not significant.

Results The results of the laboratory examination are presented in Table 1.

Discussion: The presented study demonstrates a moderate reduction in respiratory function (VC, FEV1) 1 year after severe chest injury. Our pulmonary outcome data could not demonstrate a significant difference to the historical control group. Blood gas analysis and cardiopulmonary function were normal with the exception of one case. In conclusion, we postulate that severe injury to the chest leads to a moderate decrease of pulmonary function in polytrauma patients with ALI and ARDS.

References
1. Svennevig: *Injury* 1989, **20**:253-256.
2. Livingston: *J Trauma* 1990, **30**:562-567.

P257 Changes of health-related quality of life in survivors of acute respiratory distress syndrome

M Wehler[1], A Geise[1], D Hadziomerovic[1], U Reulbach[2], EG Hahn[1], R Strauss[1]
[1]Department of Medicine I and [2]Department of Medical Informatics, Biometry and Epidemiology, University Erlangen-Nuremberg, 91023 Erlangen, Germany
Critical Care 2003, **7(Suppl 2)**:P257 (DOI 10.1186/cc2146)

Introduction Few studies have analyzed health-related quality of life (HRQOL) in survivors of acute respiratory distress syndrome (ARDS) taking prehospitalization baseline data into account.

Patients and methods From June 1997 to May 1999, all admissions (≥18 years) to our medical intensive care unit (ICU), an academic referral center, who developed ARDS according to the American–European Consensus Conference definition were eligible. Baseline HRQOL measures were collected by interview during the first 24 hours of the ICU stay and 6 months after admission using a HRQOL questionnaire specifically designed for critically ill patients [1]. A clinically relevant change score was determined by survivors ratings of global health change since ICU admission.

Results The 265 enrolled patients had a mean age of 59 ± 16 (± SD) years, median 62 years; 58% were male. The mean ICU length of stay was 19 ± 23 days, median 11 days; the mean APACHE II score after 24 hours was 27 ± 9, mean time requiring mechanical ventilation was 17 ± 22 days, median 9 days. The most prevalent predisposing conditions for ARDS were pneumonia and severe sepsis. Cumulative mortality rates were 51% in the ICU, 59% in the hospital, and 65% at 6 months followup. At followup, HRQOL data could be obtained in 87 ARDS survivors; six patients were lost to followup. A change score of −15% was considered as a relevant deterioration using survivors ratings of health transition. Compared with baseline data, a relevant deterioration of HRQOL was reported by 18 (21%) patients in the domain basic physiologic activities, by 31 (35%) patients in the domain activities of daily life, and by 29 (33%) patients in the mental health domain. The majority of the survivors (84%) were living at home and 76% of those previously in employment had returned to their former work. Eighty-one survivors (93%) reported that they

would be willing to undergo intensive care again if medically necessary in the future.

Conclusion Compared with prehospitalization HRQOL, about one-third of our ARDS survivors reported a relevant deterioration in various HRQOL domains. Satisfaction with care and the return-to-work rate was high in our sample of medical ARDS survivors.

Reference

1. Fernandez RR, *et al.*: *Intensive Care Med* 1996, **22**:1034.