ORIGINAL ARTICLE

Interventional lung assist enables lung protective mechanical ventilation in acute respiratory distress syndrome

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ABSTRACT

Background. The feasibility and safety of a pumpless arteriovenous extracorporeal lung assist system (pECLA) has been demonstrated in previous studies of patients with severe respiratory insufficiency. The aim of this report was to examine whether pECLA is feasible in a center that is new to the technology and to determine the positive and adverse effects associated with its use.

Methods. This was a retrospective case series of 13 consecutive patients with established acute respiratory distress syndrome (ICU patients with ARDS or ALI) at a university hospital. Management consisted of transcutaneous placement of a femoral arteriovenous pECLA to allow lung-protective ventilation. Nonparametric statistics were applied; all data are values and standard deviations (SD).

Results. Mean simplified acute physiology score (SAPS) II was 49.5 (26); ICU mortality was 54% (7/13). Mean length of ICU stay was 34.5 (65.3) days for survivors (S) and 36 (32.8) days for non-survivors (NS). Total time on arteriovenous pECLA was 12.0 (22.2) days (S) and 7.0(7.8) days (NS), total time on mechanical ventilation was 31.0 (28.2) (S) and 32.0 (15.2) days (NS). Hypercapnia was significantly ($P<0.05$) reduced from 80.0 (23.0) (pre-pECLA) to 48.0 (13.0) mmHg (day 7), as were minute ventilation and inspiratory pressure. pECLA was accompanied by a significant ($P<0.05$) increase in the PaO_2/fraction of inspired oxygen (P/F) ratio from 100.0 (28.9) (pre-pECLA) to 191.1 (114.3) mmHg after 7 days of treatment. Major complications were two inadvertent decannulations in the first two patients treated; there was one minor bleeding event in a patient seen subsequently.

Conclusion. pECLA is an effective and manageable technique to support gas exchange in ARDS patients. This retrospective case series demonstrates the feasibility of pECLA in a center that did not have prior experience with this technique. pECLA may decrease further lung injury by minimizing the amount of time for which the lung is exposed to high stress and/or strain. *(Minerva Anestesiol 2011;77:797-801)*

Key words: Respiratory distress syndrome, adult - Acute lung injury - Respiration, artificial - Extracorporeal membrane oxygenation.

The global mortality and morbidity in patients with acute respiratory distress syndrome (ARDS) or acute lung injury (ALI) who receive mechanical ventilation in intensive care units (ICUs) remain unacceptably high.[1, 2] Treatment focuses on maintaining gas exchange while attempting to avoid ventilator-associated complications.[3] Even though there is currently no clear proof that extracorporeal support systems *per se* have an impact on survival rates, it may be argued that they can be used to allow lung-protective ventilation in patients who have not

responded to conservative treatment.[4-7] Conventional pump-driven extracorporeal lung assist (ECLA) or extracorporeal membrane oxygenation (ECMO) have significant drawbacks such as the need for systemic anticoagulation and complications such as blood trauma, systemic inflammation and blood loss.[7,8] To overcome these drawbacks, a pumpless arteriovenous extracorporeal lung assist (pECLA) has been developed using a low-resistance, heparin-coated membrane with a pressure gradient and the patient's own cardiac output as its driving force.[9-11]

The aims of this study were to evaluate whether pECLA could be put into clinical practice in a center that was new to the technology and to determine the positive and adverse effects associated with its use in a consecutive series of mechanically ventilated ARDS patients.

Materials and methods

The local ethics committee approved this retrospective study and waived the need for informed consent. Electronic clinical records, into which data had been prospectively entered, of 13 consecutive adult patients from our surgical and medical ICUs were analyzed. ARDS and ALI were defined according to the American-European Consensus Conference.[12]

All patients received conventional therapy, including pressure-controlled ventilation, recruitment maneuvers for the titration of positive end-expiratory pressure (PEEP) to achieve maximal oxygenation at minimal inspiratory oxygen concentrations and kinetic therapy, such as prone positioning and/or continuous lateral rotation. Every attempt was made to limit tidal volumes to 6 ml/kg. However, pECLA was initiated when the patients fulfilled the entry criteria of persisting gas exchange impairment (partial pressure of oxygen in arterial blood (P_aO_2)/fraction of inspired oxygen (FiO_2) ≤200 mmHg with PEEP>10 cmH_2O and arterial pH ≤7.25 and plateau pressures of >30 cmH_2O for more than 12 h) in the absence of any contraindications.

Prior to insertion of the arteriovenous shunt, hemodynamic parameters were adjusted to a cardiac index of >2.7 L/min/m² and a mean arterial pressure of > 75 mmHg using dobutamine 3.2 ± 0.8 (mean ± SD) μg/kg/min and norepinephrine 0.45 ± 1.18 (mean ± SD) μg/kg/min where indicated. The diameters of the femoral vessels were determined by ultrasound. It was agreed that the minimal internal arterial diameter should exceed 7 mm for a 15-17 F cannula. The affected limb was left open for monitoring of color, skin temperature and assessment of distal pulses. Further technical details of the method are described elsewhere.[13, 14, 20] Minute ventilation was then reduced by adjusting frequency and inspiratory pressure. PEEP was increased to ventilate the patient with the least possible mechanical stress while maintaining a sufficient level of oxygenation (oxygen saturation by pulse oximetry [S_pO_2] ≥90%).

Weaning from pECLA was attempted when the following signs of an improvement in pulmonary function could be discerned over at least 24 h: decrease of F_iO_2 to <0.5 to maintain a P_aO_2 >80 mmHg, clearing of infiltrates, absence of severe respiratory acidosis, respiratory rate <35/min and tolerance of pressure support ventilation with a delta P≤10 cmH_2O. Gas flow to the oxygenator was then cautiously reduced while closely monitoring the partial pressure of carbon dioxide in arterial blood (P_aCO_2) and checking for signs of ventilatory exhaustion until zero gas flow through pECLA was reached. After a period of 24 h, the cannulae were removed openly in the operating room to control for bleeding and to surgically repair potential lesions to the

Table I.—*Baseline demographics, clinical characteristics and outcomes data.*

Characteristic	Data (N.=13)
Age (years; mean [SD])	52 (19)
Gender (male/female)	8/5
Surgical/medical	6/7
SAPS II (mean [SD])	49.5 (26)
Mortality in ICU (%)	7 (54%)
Bacterial pneumonia, sepsis	7
Viral pneumonia	4
Cystic fibrosis	1
Bronchiolitis	1

ICU: intensive care unit; SAPS II: simplified acute physiology score II.

Table II.—*Respiratory parameters before and during pECLA treatment (N.=13).*

Respiratory parameter	Before pECLA (baseline)	After insertion (Gas flow 8 l/min)	Day 1	Day 3	Day 7	Before decannulation
Tidal volume (mL)	292.5 (94.0)	188.0 (120.0)*	183.0 (67.0)*	177.5 (90.0)*	229.0 (82.7)	242.0 (123.0)
Pinsp (cmH_2O)	34.0 (3.0)	28.5 (3.0)*	28.3 (4.0)*	27.2 (4.0)*	28.0 (2.0)*	26.6 (6.0)*
Respiratory rate (L/min)	30.0 (7.0)	19.0 (14.0)	20.0 (11.0)	21.0 (5.0)	15.5 (8.3)	24.3 (11.0)
Minute ventilation (L/min)	10.2 (3.4)	3.7 (3.1)*	4.1 (3.0)*	3.25 (2.35)*	4.3 (2.0)*	6.4 (2.9)
PEEP (cmH_2O)	12.3 (5.0)	15.2 (4.0)*	16.2 (6.0)*	15.0 (4.0)*	13.0 (2.0)	11.0 (5.0)
Arterial pH	7.18 (0.22)	7.33 (0.19)	7.37 (0.09)	7.41 (0.1)	7.44 (0.07)	7.38 (0.3)
$PaCO_2$ (mmHg)	80.0 (23.0)	61.0 (113.0)*	54.0 (19.0)*	50.0 (8.1)*	48.0 (13.0)*	51.0 (19.0)*
FiO_2	0.70 (0.2)	0.70 (0.3)	0.70 (0.2)	0.50 (0.25)*	0.49 (0.25)*	0.45 (0.2)*
PaO_2 (mmHg)	71.5 (20.0)	75.3 (24.0)	79.0 (11.0)	79.5 (17.0)	88.0 (12.0)*	84.5 (13.0)
PF-Ratio (PaO_2/FiO_2, mmHg)	100.0 (28.9)	110.5 (51.4)	120.7 (51.2)	152.0 (55.1)	191.1 (114.3)*	192.5 (71.0)*

pECLA: pumpless arteriovenous extracorporeal lung assist system; FiO_2: fraction of inspired oxygen; $PaCO_2$: partial pressure of carbon dioxide in arterial blood; PaO_2: partial pressure of oxygen in arterial blood; PEEP: positive end-expiratory pressure; PF: ratio of arterial partial pressure of oxygen to the fraction of inspired oxygen; Pinsp: inspiratory pressure; *P<0.05 *vs* baseline (ANOVA). Data are presented as mean (SD).

vessels. We continued to record all clinical and laboratory data during weaning until discharge from the ICU or death.

Statistical analysis

Data were analyzed using SPSS version 18.0. Non-parametric statistics were used in all cases. Friedman's ANOVA for repeated measurements with a post-hoc Wilcoxon test and Bonferroni's adjustment for multiple testing were then used for comparisons of respiratory parameters before, during and after pECLA. Statistical significance was assumed if p-values were ≤0.05. All data are reported as mean values and standard deviation (SD).

Results

The baseline demographics and clinical characteristics of the 13 patients included in this study are reported in Table I. Four of the 13 patients had established ARDS and had been transferred from community hospitals for further treatment. Nine patients had acute renal failure with the need for continuous veno-venous hemofiltration. All but one patient were on norepinephrine for hemodynamic support with a mean dose (SD) of 0.45 (1.18) µg/kg/min before pECLA, which decreased during treatment to 0.09 (0.02) µg/kg/min (day 7). Nine patients needed hemodynamic support with dobutamine at an initial dose of 3.2 (0.8) µg/kg/min, which could be discontinued by day 7.

The mean time (SD) on mechanical ventilation before pECLA was 9.4 (10.2) days. The mean length of ICU stay was 34.5 (65.3) days for survivors and 36.0 (32.8) days for non-survivors. The mean duration of pECLA treatment was 12.0 (22.2) days for survivors and 7.0 (7.8) days for non-survivors. The mean total time on mechanical ventilation was 31.0 (28.2) days for survivors and 32.0 (15.2) days for non-survivors.

The most relevant respiratory parameters before and during pECLA treatment are summarized in Table II. The key changes when compared to baseline values were significant (P<0.05) decreases of inspiratory pressure, minute ventilation and respiratory rate, while P_aCO_2 values were significantly reduced.

There were two major complications in this study. These were two episodes of inadvertent cannula dislocations, which led to the termination of pECLA. However, acute respiratory insufficiency was avoided in these patients and

weaning was subsequently initiated. The cannula dislocations occurred in the first two patients of the series during partial mobilization and nursing procedures, respectively. Blood loss from the insertion sites was limited by compression using a mechanical compression device, and blood transfusions were not required. There was one minor complication in this study. This was an episode of superficial bleeding from the insertion site that required bedside surgical intervention. We did not observe limb ischemia or any thrombotic episode. All surviving patients (N=6) could be weaned from pECLA and were discharged from the ICU. Two patients died in the ICU from septic multi-organ failure after successful weaning. Five patients died from uncontrolled septic shock with pECLA still in place. In one patient (male, 21 years) with severe bronchiolitis, pECLA remained in place for 105 days, and the oxygenator had to be exchanged three times. Eventually, this patient was successfully weaned and transferred to a rehabilitation unit.

Discussion

This case series of 13 consecutive patients with ARDS/ALI describes the positive and adverse effects during implementation of pECLA in a center without prior experience with this technique. From the data shown, we first conclude that pECLA can effectively address the impaired gas exchange in ARDS; and secondly, that pECLA can be put into clinical practice, even in institutions with limited experience with this method.

The occurrence of ARDS in ICU patients is still a serious complication associated with a mortality of 40-80% and high comorbidity.[2, 3] The most important paradigm change in the management of ARDS has come from evidence that avoiding injury-causing mechanical ventilation may increase survival by reducing volu-, baro- and biotrauma.[3, 15-18] Consequently, extracorporeal support systems such as ECMO have been developed to keep the affected lung inflated and recruited, with the opportunity to heal in the absence of damaging ventilatory settings.[19] The drawbacks of ECMO include the lack of evidence for clinical efficacy, its inherent complexity, high cost, and prohibitive side effects such as blood loss, systemic inflammatory response syndrome (SIRS) and the need for therapeutic heparinization.[5] The development of a pumpless membrane ventilator expands extracorporeal life support options, due to the high efficacy of CO_2 removal without roller pumps, tubing, heat exchange and allows for minimal ventilation even below the ARDS-network requirement of 6 mL/kg tidal volume.[21] However, oxygenation capacity is inherently limited, and pECLA can only be used in the presence of sufficient cardiac output.

In this case series, we demonstrated that pECLA is an effective treatment option for the impaired gas exchange in ARDS. The reported cases were the first patients treated with pECLA at our institution, which at this time had only limited experience in conventional ECMO. Training by experienced medical technicians was provided by the manufacturer (Novalung GmbH, Talheim, Germany) and was performed on site shortly before pECLA was first used. We had to learn how to correctly secure the cannulae after problems with insufficient fixation of the cannulae in our first two patients. Therefore we recommend that great care should be taken to secure the cannulae *in situ* and that the insertion sites should be visible at any time during treatment. With regard to the unintended decannulations in our first two patients, we subsequently intensified training of the nursing staff and ensured that the following cannulations were performed by the same medical team.

The only vascular complication in this study was one case of minor bleeding at the insertion site. Following clamp release, the anticipated fall in peripheral vascular resistance could be antagonized by transient adjustments of the norepinephrine dose. In agreement with other groups, we noticed a steady and significant ($P<0.05$) improvement of the mean P/F ratio from 100.0 (28.9) at the beginning of pECLA to 192.5 (71.0) mmHg before removal (Table II).[19]

Our primary aim to establish less invasive mechanical ventilation by using pECLA was accomplished. However, pECLA alone does not treat the patient's underlying disease, which is reflected by the high ICU mortality in our group of patients. The intensity of the underlying disease in very sick patients will clearly limit clinical

outcomes so that the potential benefit of pECLA may not be apparent.

Limitations of the study

The primary limitations of this study are its retrospective design and the lack of a control group, both of which clearly limit the generalizability of the findings. Furthermore, the reported rate of complications may not reflect the actual rate of complications associated with pECLA, given that the presented case series represents the first set of patients treated with pECLA at our institution.

Conclusions

In conclusion, the present study demonstrates that pECLA can be put into clinical practice even in centers without extensive experience with this technique. The learning curve is relatively steep. Furthermore, special attention should be paid to correct fixation of the cannulae.

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