Abstract:

Determining the optimal cardiac output during critical illness that will improve clearance of lactic acidemia and/or prevent acute kidney injury among sepsis patients is a significant problem in ICU. Early studies showed not outcome benefit for supraphysiologic cardiac output using inotropes and blood transfusion interventions. The contribution of blood pressure on clinical outcomes after adjusting for the illness acuity and the treatments remains uncertain. Instead of assessing optimal heart rate and blood pressure independently, this study investigates whether there is an optimal cardiac output, estimated as heart rate multiplied by pulse pressure, for sepsis patients using the MIMIC II database.

Current question:

1. Optimal cardiac output during sepsis in regards to clearance of lactic acidema and/or prevention of progression of acute kidney injury among sepsis patients.

Confounders:

- Lactate: Adequate perfusion but ? mitochondrial dysfunction

- For renal failure (as below), multiple confounders

- Dynamic process: The hemodynamic alterations with sepsis are exceedingly complex and include volume depletion, depressed myocardial function, and altered microvascular flow. These changes are dynamic; it has been reported that patients with preserved ventricular function may progress to develop severely depressed contractility  (Source 1)



Reference:

1. Surviving sepsis: going beyond the guidelines

http://www.annalsofintensivecare.com/content/1/1/17

Prior literature searches regarding heart rate, lactate, and acute kidney injury below.

**ICU HEART RATE PROJECT**

**Key points**

1. Determine final clinical question and patient population

2. Discuss optimal strategy for heart measurement

3. Discuss limitations of heart signal and ways to account for noise

4. Discuss desired outcomes

**I. Introduction**

Derangements in heart rate are common in the intensive care unit (ICU). Heart rate is a variable in ICU mortality scoring symptoms such as SAPSII and APACHEII.

Prior literature on heart rate in the ICU:

- Sepsis induced myocardial dysfunction limits the increase in contractility that can occur with neurohumeral activation, so heart rate becomes a more critical component of adaptation.

- Trauma study

- Heart rate variability

**II. Clinical question**

A. Primary: Is elevated or slow HR during the first 6 hours of an ICU admission indicative of mortality.

Is this information of prognostic significance?

? Or should we limit the clinical question initially to a specific subset of patients such as sepsis.

B. Secondary:

This is some other random stuff I thought about:

Is heart rate “inappropriate” in certain patient populations in the ICU.

Model:

Patients with pulmonary artery catheter measuring hemodynamic variables

CO (use derived data) = HR x SV (? Use model to estimate EF)

HR = CO/SV

Does HRcalculated match HRactual

III. Methods

**Heart Rate**

1. Time period: First 6 hours after ICU admission



Example of Heart rate graph from Korean study ([J Crit Care.](http://www.ncbi.nlm.nih.gov.ezp-prod1.hul.harvard.edu/pubmed?term=Significance%20of%20new-onset%20prolonged%20sinus%20tachycardia%20in%20a%20medical%20intensive%20care%20unit%3A%20a%20prospective%20observational%20study.) 2011 Oct;26(5):534.e1-8) regarding sinus tachycardia

B. Heart Rate Measurement

1. Source: Signal from telemetry

Issues: Signal noise and false alarms

Source: <http://www.bme.sdu.edu.cn/qiaoli/Suppress%20false%20arrhythmia%20alarms%20of%20ICU%20monitors%20using%20heart%20rate%20estimation%20based%20on%20combined%20arterial%20blood%20pressure%20and%20ECG%20analysis.pdf>

This paper examined the high rate of false alarms when physiological signals were severely corrupted by noise. It designed an ABP signal quality index (SQI) based upon the combination of two previously reported signal quality measures.

? a-line measurements were used in addition to ECG monitoring data. Would we need to limit study to patients with a-line to ensure a good signal and reduce false alarms.

2. Definitions used in other studies of increased HR (per Korean study)

a) HR > 95 bpm for at least 12 hours OR

b) acute change of 20 %.

c) Other comments: Data limited regarding critical threshold and duration of acute increases in HR.

3. Concepts regarding HR measurement (excluding heart rate variability)

a) Frequency of measurement: ? minute to minute

b) Absolute rate

b) Other measures of rate

i) slope

ii) Max, median, average, low

iii) Integration of heart rate area over time period (see figure below)

For instance, a large or small volume may indicate mortality (always fast or always slow – may be inappropriate response)



|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Heart Rate**(bpm) | HR < 60 | 60 ≤ HR < 100 | 100 ≤ HR < 120 | HR ≥ 120 |
| **Expected Area**  **Over 6 hour period**  **(heart beats)** | <21600 | 21600-36000 | 36000-43200 | >43200 |
|  |  |  |  |  |

iv) “Tempo”

This technique or above integration scheme could account for variability in a case like sick sinus syndrome but is different than integration because it would give certain bursts a qualitative level.

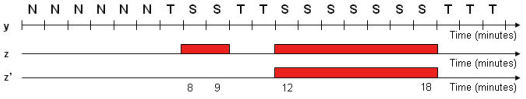
For example, someone with sick sinus might get tachycardiac to 120 and then bradycardia to 30 – this might even out with averages/median values or canceled out with integration.

This technique may be too similar to heart rate variability but provides slightly different information.

Example: Assigning qualitative variable

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Heart Rate**(bpm) | HR < 60 | 60 ≤ HR < 100 | 100 ≤ HR < 120 | HR ≥ 120 |
| **Qualitative Label** | B (Bradycardia) | N (Normal) | T (Tachycardia) | S (Severe Tachycardia) |

Example: Time graph of qualitative variable



Source: <http://www.hcklab.org/projects/tempo/index.htm>

An example of this was used in the poster presentation from *Critical Care Medicine* Vol 39, Issue 12

This could then be converted to percentages for each category reminiscent of a patient who has a pacemaker interrogated.

Patient X:

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Heart Rate**(bpm) | HR < 60 | 60 ≤ HR < 100 | 100 ≤ HR < 120 | HR ≥ 120 |
| **Qualitative Label** | B (Bradycardia) | N (Normal) | T (Tachycardia) | S (Severe Tachycardia) |
| **Percentage of time over 6 hour period** | 0 % | 15% | 70% | 15 |
|  |  |  |  |  |

**Criteria**

Inclusion criteria

- Anyone admitted to the ICU with a stay over 6 hours (or whatever time window we would use)

Exclusion criteria

- permanent pacemaker or temporary pacer

- CMO

- post-cardiac surgery

- post cardiac arrest

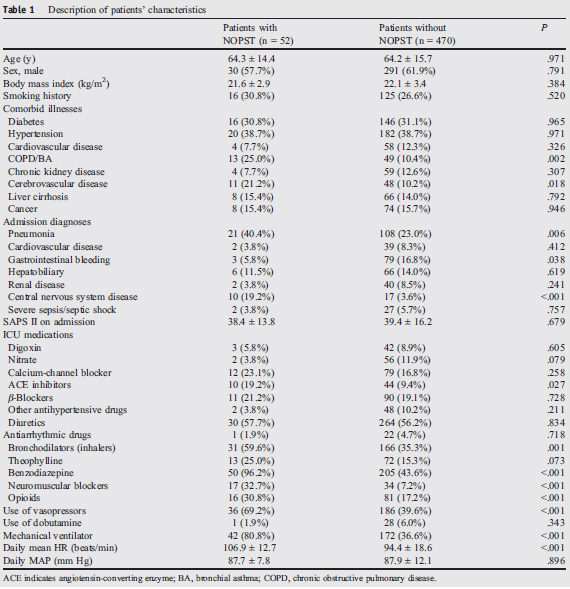
- significant arrhythmia requiring electrical or chemical cardioversion secondary to hemodynamic instability

- significant loss of signal (> 30 minutes). Ex. Patient at HD, procedure, etc.

- death within six hours of admission

**Variables**

The table 1 from the Korean study on sinus tachycardia is below.



One problem is that the SAPSII score has HR as a variable.

I think the standard variables such as age, gender, admission diagnosis, comorbid illness, medications are a good start.

Additional vital signs and laboratory data would supplement.

**Confounders** (anything that could cause abnormal heart rate)

A. Medications

- cardiovascular medications such as beta-blockers, CCB

- medications that cause tachycardia (e.g. albuterol)

- pressor infusion

B. Intrinsic pacing

C. Cardiac issues

- LVEF

- arrhythmia

- hypovolemia 🡪 can use length of stay fluid balance

D. Vital signs

- fever

- hypoxemia

E. Laboratory

Electrolytes imbalance

F. Procedure/ICU machines

- CVC insertion

- ventilator dysfunction

G. Patient factors

- pain/anxiety

- aspiration

H. Death

IV. Results

Comparison of hospital outcomes between patients within different HR ranges or heart rate area (basically heart beats)

Variables \* HR < 60 60-80 81-100 HR 101 – 119 HR > 120

ICU LOS

ICU Mortality

In-hospital mortality

x-day mortality

\* Or could consider other strategies of heart rate measurements as above in methods

V. Conclusions

VI. Limitations

- Heart rate was considered as a variable and not rhythm. Rhythm may be an important factor with hemodynamic significance such as a heart failure patient that converts into atrial fibrillation after developing sepsis.

- Study was performed at only one institution

- etc

**Source 1**: Review of pathophysiology of HR in critical illness

1. Magder, Sheldon A. MD. Critical Care Medicine:

January 2012 - Volume 40 - Issue 1 - p 239–245

<http://journals.lww.com/ccmjournal/Abstract/2012/01000/The_ups_and_downs_of_heart_rate.35.aspx>

2. Critical Care Medicine:

December 2011 - Volume 39 - Issue 12 - p 148

Poster presentation

THE EFFECT OF HEART RATE ON SURVIVAL FROM ICU

Tara Quasim, Colette Lange, University of Glasgow, Kathryn Henderson, NHS

Greater Glasgow and Clyde, Laura Moss, John Kinsella, University of Glasgow

Introduction: As tachycardia may contribute to a worse outcome in the critically

ill we examined the effect of heart rate on the outcome of critically ill patients.

Hypothesis: We hypothesised that a persistent sinus tachycardia in the critically

ill is associated with a higher mortality. Methods: Patients admitted to a tertiary

referral hospital between January 2009 -January 2010 were studied. Exclusions

included: a stay 48 hours, any arrhythmia during their stay, readmissions and

patients with incomplete information. Data collected included: age, gender, admission diagnosis, length of ICU stay, APACHE II and predicted hospital mortality. Individuals’ hourly heart rates were categorised as 90 bpm, between 90 –120 bpm or 120 bpm. Patients were further categorised into one of three groups: heart rate always 90 bpm throughout their ICU stay, heart rate always 120 bpm or a third mixed group with heart rates in all 3 categories. The patients were then quantified into time spent in each heart rate category. Data was evaluated using binary logistic regression. Odds ratios were used to confirm the strength of association between the variables. Results: After exclusions, 136 patients were studied. Only 2 patients always had a heart rate 90 bpm whilst 134 were in the mixed group. For every additional 10% of time spent with a heart rate 90 bpm, there was a 22% increase in survival from ICU (p 0.026). For every additional 10% of time spent with a heart rate 90 bpm, there was a 20% increase in hospital survival (p 0.011). For every additional 10% of time spent with a heart rate 120 bpm, there was a 31% reduction in survival from ICU (p 0.001). For every additional 10% of time spent with a heart rate 120 bpm there was a decrease in hospital survival by 25% (p 0.007). For every additional

10% of time spent with a heart 90 bpm there was an 18% decrease in ICU surviva (p 0.025). Conclusions: There is an association between the time spent with a heart rate 120 bpm and mortality and an association between time spent with a heart rate 90 bpm and survival. This was independent of illness

severity. This observation may have prognostic and intervention implications.

Source 3:

[Acute Card Care.](http://www.ncbi.nlm.nih.gov/pubmed/22142200) 2011 Dec;13(4):205-10.

# Admission heart rate as a predictor of mortality in patients with acute coronary syndromes.

[Timóteo AT](http://www.ncbi.nlm.nih.gov/pubmed?term=%22Tim%C3%B3teo%20AT%22%5BAuthor%5D), [Toste A](http://www.ncbi.nlm.nih.gov/pubmed?term=%22Toste%20A%22%5BAuthor%5D), [Ramos R](http://www.ncbi.nlm.nih.gov/pubmed?term=%22Ramos%20R%22%5BAuthor%5D), [Oliveira JA](http://www.ncbi.nlm.nih.gov/pubmed?term=%22Oliveira%20JA%22%5BAuthor%5D), [Ferreira ML](http://www.ncbi.nlm.nih.gov/pubmed?term=%22Ferreira%20ML%22%5BAuthor%5D), [Ferreira RC](http://www.ncbi.nlm.nih.gov/pubmed?term=%22Ferreira%20RC%22%5BAuthor%5D).

### Source

Cardiology Department, Santa Marta Hospital, Centro Hospitalar de Lisboa Central, EPE Lisbon, Portugal. ana\_timoteo@yahoo.com

### Abstract

#### INTRODUCTION:

Heart rate (HR) is a prognostic factor in stable angina. However, in the context of acute coronary syndromes (ACS), it is less studied.

#### AIMS:

To evaluate the influence of admission HR as a prognostic factor in patients with ACS.

#### METHODS:

We evaluated in-hospital, 30-day and one-year mortality in patients with ACS, according to admission HR.

#### RESULTS:

We analysed 1126 patients, 69% males, mean age 64 years, 59% with ST-segment elevation acute myocardial infarction and 15% on medication with a beta-blocker. On admission, 14% presented signs of heart failure. In 10%, left ventricular ejection fraction was < 35%. In-hospital mortality was 7.1%, 30-day mortality 9.1% and one-year mortality 10.7%. The best cut-off of HR to predict mortality was 80 bpm (sensitivity 64-66% and specificity 54-55%). By multivariate analysis, a heart rate ≥ 80 bpm was an independent predictor of all-cause mortality (HR 1.50, 95% CI: 1.01-2.23, P = 0.047).

#### CONCLUSIONS:

In a population with ACS, a higher admission HR is an independent predictor of short- and medium-term prognosis, which is also independent of left ventricular function.

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Eur Heart J (May 2005) 26 (10):943-945.

# Heart rate: a strong predictor of mortality in subjects with coronary artery disease

**This editorial refers to ‘Long-term prognostic value of resting heart rate in patients with suspected or proven coronary artery disease’** [†](http://eurheartj.oxfordjournals.org.ezp-prod1.hul.harvard.edu/content/26/10/943.long#fn-1)**by A. Diaz** **et al., on page 967**

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[J Trauma Acute Care Surg.](http://www.ncbi.nlm.nih.gov.ezp-prod1.hul.harvard.edu/pubmed/22491609) 2012 Apr;72(4):943-7.

# Admission heart rate is a predictor of mortality.

[Ley EJ](http://www.ncbi.nlm.nih.gov.ezp-prod1.hul.harvard.edu/pubmed?term=%22Ley%20EJ%22%5BAuthor%5D), [Singer MB](http://www.ncbi.nlm.nih.gov.ezp-prod1.hul.harvard.edu/pubmed?term=%22Singer%20MB%22%5BAuthor%5D), [Clond MA](http://www.ncbi.nlm.nih.gov.ezp-prod1.hul.harvard.edu/pubmed?term=%22Clond%20MA%22%5BAuthor%5D), [Ley HC](http://www.ncbi.nlm.nih.gov.ezp-prod1.hul.harvard.edu/pubmed?term=%22Ley%20HC%22%5BAuthor%5D), [Mirocha J](http://www.ncbi.nlm.nih.gov.ezp-prod1.hul.harvard.edu/pubmed?term=%22Mirocha%20J%22%5BAuthor%5D), [Bukur M](http://www.ncbi.nlm.nih.gov.ezp-prod1.hul.harvard.edu/pubmed?term=%22Bukur%20M%22%5BAuthor%5D), [Margulies DR](http://www.ncbi.nlm.nih.gov.ezp-prod1.hul.harvard.edu/pubmed?term=%22Margulies%20DR%22%5BAuthor%5D), [Salim A](http://www.ncbi.nlm.nih.gov.ezp-prod1.hul.harvard.edu/pubmed?term=%22Salim%20A%22%5BAuthor%5D).

### Source

Los Angeles, California From the Division of Trauma and Critical Care, Department of Surgery, Cedars-Sinai Medical Center, Los Angeles, California.

### Abstract

#### BACKGROUND:

: The association between admission heart rate (AHR) and mortality after trauma can assist initial emergency department triage and resuscitation. In addition, increased AHR is often associated with sympathetic hyperactivity which may require targeted treatment. We determined whether AHR was a predictor for mortality in trauma patients.

#### METHODS:

: The Los Angeles County Trauma System Database was queried for all injured patients admitted between 1998 and 2005 (n = 147,788). Traumatic brain injury (TBI) patients (head Abbreviated Injury Scale score ≥3) were excluded. Demographics were compared at various AHR subgroups (<50, 50-59, 60-69, 70-79, 80-89, 90-99, 100-109, and ≥110). Mortality was compared at various AHR ranges, and logistic regression was performed to determine significance.

#### RESULTS:

: After exclusions, 103,799 trauma patients requiring admission were identified; overall mortality was 1.4%. AHR 80 to 89 demonstrated a statistically significant lower mortality (0.5%) compared with all other AHR ranges, except AHR 70 to 79 (0.6%). In trauma patients who requiredadmission, AHR 70 to 79 and 80 to 89 were predictors of lower mortality. Mortality for 22,232 moderate to severely injured patients was 5.5% and AHR 80 to 89 demonstrated a statistically lower mortality (2.0%) than all other AHR ranges, except AHR 70 to 79 (1.9%). After moderate to severe trauma, AHR <60 and ≥100 were associated with significantly higher mortality.

#### CONCLUSION:

: Mortality after trauma increases outside the AHR range of 70 to 89 beats per minute. AHR ranges previously considered "normal" were associated with significantly increased mortality. Prospective research is required to evaluate if resuscitation goals should target heart rate at the 70 to 89 range.

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[J Crit Care.](http://www.ncbi.nlm.nih.gov.ezp-prod1.hul.harvard.edu/pubmed?term=Significance%20of%20new-onset%20prolonged%20sinus%20tachycardia%20in%20a%20medical%20intensive%20care%20unit%3A%20a%20prospective%20observational%20study.) 2011 Oct;26(5):534.e1-8. Epub 2011 Mar 3.

# Significance of new-onset prolonged sinus tachycardia in a medical intensive care unit: aprospective observational study.

[Park S](http://www.ncbi.nlm.nih.gov.ezp-prod1.hul.harvard.edu/pubmed?term=%22Park%20S%22%5BAuthor%5D), [Kim DG](http://www.ncbi.nlm.nih.gov.ezp-prod1.hul.harvard.edu/pubmed?term=%22Kim%20DG%22%5BAuthor%5D), [Suh GY](http://www.ncbi.nlm.nih.gov.ezp-prod1.hul.harvard.edu/pubmed?term=%22Suh%20GY%22%5BAuthor%5D), [Park WJ](http://www.ncbi.nlm.nih.gov.ezp-prod1.hul.harvard.edu/pubmed?term=%22Park%20WJ%22%5BAuthor%5D), [Jang SH](http://www.ncbi.nlm.nih.gov.ezp-prod1.hul.harvard.edu/pubmed?term=%22Jang%20SH%22%5BAuthor%5D), [Hwang YI](http://www.ncbi.nlm.nih.gov.ezp-prod1.hul.harvard.edu/pubmed?term=%22Hwang%20YI%22%5BAuthor%5D), [Han SJ](http://www.ncbi.nlm.nih.gov.ezp-prod1.hul.harvard.edu/pubmed?term=%22Han%20SJ%22%5BAuthor%5D), [Jeong HH](http://www.ncbi.nlm.nih.gov.ezp-prod1.hul.harvard.edu/pubmed?term=%22Jeong%20HH%22%5BAuthor%5D), [Lee CH](http://www.ncbi.nlm.nih.gov.ezp-prod1.hul.harvard.edu/pubmed?term=%22Lee%20CH%22%5BAuthor%5D), [Jung KS](http://www.ncbi.nlm.nih.gov.ezp-prod1.hul.harvard.edu/pubmed?term=%22Jung%20KS%22%5BAuthor%5D).

### Source

Division of Pulmonary, Allergy and Critical Care Medicine, Department of Internal Medicine, Hallym University Sacred Heart Hospital, 896 Anyang, Gyeonggi-do, Republic of Korea.

### Abstract

#### OBJECTIVE:

Few data are available on sinus tachycardia among medical intensive care unit (ICU) patients. We investigated new critical illnesses related to new-onset prolonged sinus tachycardia (NOPST) and the relationship of NOPST with ICU mortality.

#### METHODS:

The heart rate (HR) of all enrolled patients was monitored hourly over a 12-month period, and NOPST was defined as sinus tachycardia(>100 beats/min) with an increase in HR of more than 20% from the baseline value lasting longer than 6 hours.

#### RESULTS:

Among the 522 patients enrolled, the average mean HR was 96.1 ± 18.4 beats/min. Fifty-two (10.0%) patients met the criteria for NOPST; pneumonia, delirium, septic shock, acute respiratory distress syndrome, catheter-related infections, and mechanical ventilator-related problems were related to the occurrence of NOPST. The ICU mortality rate in patients with a NOPST duration of more than 72 hours was higher compared with other patients with NOPST (60.0% vs 18.5%; P = .002). A high daily mean HR rather than NOPST was a significant predictor of ICU mortality (odds ratio, 1.415; 95% confidence interval, 1.177-1.700).

#### CONCLUSIONS:

Although NOPST was not associated with ICU mortality, it indicates the presence of new critical events in the medical ICU setting.

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**Clinical review: A review and analysis of heart rate variability and the diagnosis and prognosis of infection**

<http://ccforum.com/content/13/6/232>

**Cardiac Uncoupling and Heart Rate Variability Stratify ICU Patients by Mortality**

**A Study of 2088 Trauma Patients**

<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC1570581/>

Hemodynamic Monitoring for detection of acute kidney injury in ICU patients

I. Introduction

Acute renal failure (ARF) is common in the intensive care unit (ICU); however, it is difficult to predict which patients will develop ARF.

ARF is an important issue as it is an independent risk factor for mortality **[1].**  A common contributing factors to ARF in a multinational, multicenter study with severe ARF was septic shock (47.5 %) with approximately 30 % of patients having preadmission renal dysfunction **[2].** Thirty-four percent of ARF was associated with major surgery, 27 % was related to cardiogenic shock, 26 % was related to hypovolemia, and 19 % of ARF was potentially drug-related. Prevalence estimates vary with prevalence ranging 1.4 % to 25.9 % across all study centers **[2]** Other concern is contrast-associated acute kidney injury (CA-AKI). One retrospective analysis cohort showed that CA-AKI occurred in 16.3 % receiving such radiological examinations **[6]**.

Prior studies summarized below have focused on laboratory and clinical data but not hemodynamic data. A prospective cohort study **[3]** found that decreased levels of serum albumin concentration, increased A-a gradient, and presence of active cancer predicted which patients who were admitted to the ICU will develop acute renal failure. Another prospective, multicenter, observational cohort study **[4]** found that the most important risk factors for development of ARF present on admission were acute circulatory or respiratory failure, age more than 65 years, presence of infection, past history of chronic heart failure (CHF), lymphoma or leukemia, or cirrhosis with conclusion that most important risk factors for ARF or mortality from ARF are often present on admission. A prospective observational study tailored to septic patients admitted to the ICU **[8]** showed that AKI development was independently associated with delay to initiation of adequate antibiotics, intra-abdominal sepsis, blood product transfusion, use of angiotensin-converting enzyme inhibitor/angiontensin-receptor blocker, and body mass index. Higher baseline GFR and successful early goal directed resuscitation were associated with decreased risk of AKI. It was concluded that both patient and health care delivery risk factors seemed important for AKI development.

The clinical significance of this study would be the implementation of physiological data to calculate an “abnormal physiology score.” In essence, these data could explore if hypotension is a risk factor for acute renal failure in critically ill patients.

II. Methods

A. Obtaining variables

The BIDMC ICU database would be utilized to explore the above question.

Acute renal failure would be determined by AKIN criteria using both creatinine and urine output as variables. One limitation is that baseline creatinine cannot be extracted from the database, so admission creatinine would be used for baseline creatinine.

Blood pressure data would be extracted from those patients only with arterial lines as non-invasive readings may not be accurate. Blood pressure data would then be integrated based on hourly measurements.

****

**Figure:** The above red area is an integrated area where the blood pressure is below an optimal MAP target of 65 mm Hg.

These are preliminary variables in the model.

a) Win\_minimum = lowest blood pressure in window

b) Win\_median = median blood pressure in window

c) Win\_average = average blood pressure in window

d) Win\_delta\_min = maximum blood pressure drop in window

e) nsamps = TBD

f) win\_slope = slope of window trend

g) median\_pp = median pulse pressure

h) min\_pp = minimum pulse pressure

i) max\_pp = max pulse pressure

k) MAP\_x\_Z (where x = 90,80,75,70)

Laboratory data would also be extracted with preliminary variables consisting of albumin among other variables to be determined.

Clinical data would also be extracted such as length of stay fluid balance (LOS), CVP, radiology studies, BMI, age, APS, etc.

The primary reason for admission would be determined from review of discharge summaries and categorized (e.g. sepsis, heart failure, decompensated cirrhosis, active cancer).

Certain high-risk medications would also be included such as blood product transfusion, ACEi/ARB, pressor usage.

Co-founders such as admission Cr, age, SAP, presence of CRF, hypertension, DM, CAD, CHF, and sepsis will be adjusted for.

B. Design/Setting

This data is derived from a retrospective cohort based on data extracted from the BIDMC ICU database.

C. Patient Population

Inclusion criteria would be all ICU patients (medical or surgical) that have an arterial line for invasive blood pressure measurements.

Exclusion would be patients without an arterial line such as only non-invasive blood pressure measurements. Patients with CKD Stage V (on hemodialysis) or patients on HD or CVVH are also excluded.

D. Control population

Techniques for generating a control population are being planned.

III. Outcomes

In the database, about 11,000 controls can be extracted, and about 6900 patients were determined to have acute renal failure with the above definitions. These were both patients with non-invasive and invasive hemodynamic monitoring.

The database was used to generate initially a multivariate model; however, it was decided to try a net reclassification model.

The original outcome would be with a ROC curve to evaluate the clinical utility of the model with the curve assessing how well the model discriminates between ARF and non-ARF with resultant AUC calculation (c-statistic) along with calibration to measure whether the predicted probabilities agree with the observed proportions.

The ROC curve and c-statistic are insensitive in assessing the impact of adding new predictors (e.g. the above physiological variables such as the integrated blood pressure readings) to a predictive model of ARF. Therefore, a net reclassification model will be utilized to address this issue. We are working to determine the modeling for this.

**References**

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2. JAMA. 2005 Aug 17;294(7):813-8.

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8. Clin J Am Soc Nephrol. 2011 Jul;6(7):1744-51.

Other:

[Curr Opin Crit Care.](http://www.ncbi.nlm.nih.gov.ezp-prod1.hul.harvard.edu/pubmed/22027404) 2011 Dec;17(6):548-55.

Lactate Prediction

Introduction

Millions of cases of severe sepsis occur annually with resultant ICU admissions. The Surviving Sepsis Campaign (1) was developed to improve the management, diagnosis, and treatment of sepsis including treatment bundles. After sepsis is diagnosed clinically by the SIRS criteria and suspected source of infection, antimicrobial therapy is initiated along with cardiovascular and respiratory support. The pathophysiology of sepsis is complex that includes a pro-inflammatory state, enhanced coagulation, and impaired thrombolysis. As a result, patients may experience decreased perfusion of organs resulting in severe sepsis. In addition to goal-directed resuscitation, antimicrobial therapy, and source control, determination of tissue oxygen delivery can be measured. Two laboratory tests to evaluate tissue oxygen delivery are measurement of serum lactate or ScVO2, which are included in the Surviving Sepsis Campaign bundle. Measurement of ScVO2 is technically difficult compared to measurement of lactate. Hyperlactatemia is typically present in patients with severe sepsis or septic shock and may be secondary to anaerobic metabolism due to hypoperfusion (1).

From the surviving sepsis corresponding bundle element (serum lactate measurement):

<http://www.survivingsepsis.org/Bundles/Individual_Changes/Pages/serum_lactate.aspx>

**Background**  
   
Hyperlactatemia is typically present in patients with severe sepsis or septic shock and may be secondary to anaerobic metabolism due to hypoperfusion.  The prognostic value of raised blood lactate levels has been well established in septic shock patients [1], particularly if the high levels persist. [2,3]  In addition, blood lactate levels have been shown to have greater prognostic value than oxygen-derived variables. [4]  Obtaining a lactate level is essential to identifying tissue hypoperfusion in patients who are not yet hypotensive but who are at risk for septic shock.  
   
**Limitations**  
  
However, the interpretation of blood lactate levels in septic patients is not always straightforward.  A number of studies have suggested that elevated lactate levels may result from cellular metabolic failure in sepsis rather than from global hypoperfusion.  Elevated lactate levels can also result from decreased clearance by the liver.  Although blood lactate concentration may lack precision as a measure of tissue metabolic status, elevated levels in sepsis support aggressive resuscitation.  
   
**Implications**  
Given the high risk for septic shock, all patients with elevated lactate >4 mmol/L (36 mg/dL) enter the early goal-directed therapy portion of the Severe Sepsis Resuscitation Bundle, regardless of blood pressure.    
   
This approach is consistent with the trial that established the value of early goal-directed therapies, Rivers et al. [5]  
   
**Turnaround Time**  
  
Serum lactate must be available in your institution with rapid turnaround time (within minutes) to effectively treat severely septic patients.  An arterial blood gas analyzer located in the clinical laboratories usually accomplishes this.  However, any means of rapid turnaround time will be acceptable.  It is essential for hospitals to invest in adequate equipment in order to meet present standards of care for septic patients.   
   
The technique of obtaining serum lactate by venipuncture typically carries a 24- to 48-hour turnaround time and will not be suitable to care for septic patients.  This technique also requires special collection conditions, such as without the use of tourniquet, hindering clinical care.

**Arterial vs. Venous Lactate**  
  
In the course of the Campaign the question has been raised many times as to whether an arterial or venous lactate sample is appropriate.  While there is no consensus of settled literature on this question, an elevated lactate of any variety is typically abnormal, although this may be influenced by other conditions such as a variety of medications, hepatic insufficiency, or hyperlactatemia due to primarily cardiac causes of hypoperfusion.

A recent non-inferiority randomized controlled trial (2) investigated lactate clearance vs. central venous oxygen saturation as goals of early sepsis therapy. Lactate clearance is derived from calculating the change in lactate concentration from 2 blood specimens drawn at different times, which is a more accessible method to assess tissue oxygen delivery.

Objective of this project would be lactate lab predictions based on physiological variables (HR, BP), laboratory data, and patient characteristics.

Design:

A. Retrospective cohort study

B. Inclusion criteria

All ICU (MICU, SICU, CCU, CSRU) patients admitted to ICU, septic

C. Exclusion Criteria

- CMO, ? liver failure patients (affect lactate),asthma exacerbation (albuterol 🡪 type 2 lactic acidosis)

D. Definition of Septic shock

Septic shock was defined according to the American College of Chest Physicians/Society of Critical Care consensus conference criteria (see sepsis definition reference). The onset of septic shock was determined when, in a patient suspected infection, two consecutive measurements revealed the following:

1. Two systemic inflammatory response syndrome criteria
2. temperature > 38.3 deg C or < 35.6 deg C
3. HR > 90 beats/minute
4. RR 20 per minute OR arterial partial pressure of CO2 less than 32 mmHg

Some critical case texts suggest a minute volume of > 10 L/min in intubated patients

1. WBC > 12.0 x 103 or < 4.0 x 103 or the presence of greater than 10 % of immature neutrophils [band forms]

AND

1. Hypoperfusion as evidenced by
2. systolic BP < 90 mm Hg OR
3. mean arterial pressure (MAP) < 60 mm Hg OR
4. a fall of > 40 mm Hg from baseline despite a 20 mL/kg fluid bolus OR
5. serum lactate >/= 4 mmol/L regardless of blood pressure

The MIMICII Database was assessed for vital sign data (RR, HR, arterial and central venous pressures [CVP], urine output, laboratory findings, infusions, and other treatments to determine the time when criteria for septic shock were present.

Blood pressure measurements

E. Cohort characteristics

F. Physiological Variables

Setting

Outcomes

Results

References:

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Sepsis Definition

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