**Title: Impact of Emergency Department Admission Time on Clinical Outcomes among Septic Patients Admitted to the Medical Intensive Care Unit**

Erika Yoo, MD

**Study Purpose and Rationale**

The clinical syndrome of sepsis is characterized by the host's inflammatory response to severe infection. As defined by the American College of Chest Physicians/Society of Critical Care Medicine, it is considered to be part of a continuum of disease severity that progresses from sepsis to severe sepsis to septic shock [1]. The clinical implications of the sepsis continuum are substantial, accounting for a notable proportion of admissions to an intensive care unit (ICU) with a historical mortality rate as high as 60 percent [2]. Though updated data from the United States demonstrate that sepsis is associated with an in-hospital mortality rate of near 20 percent [3], its burden on patient survival remains considerable.

Since the publication of clinical trials showing the benefits of early goal-directed resuscitation in improving mortality [4], the focus of sepsis treatment has been on early recognition and early intervention. For those patients admitted to the ICU directly from the emergency department (ED), the task of early optimization of patient care would fall on ED physicians. However, in a recent study out of England, only 18 percent of emergency departments were able to begin the pathway to early goal-directed therapy in patients with sepsis [5]. Similarly, a Finnish study confirmed the poor implementation of such a protocol in septic patients admitted directly from the ED to the ICU from November 2004 to February 2005 [6].

This unreliable initiation of well-circumscribed care in the ED calls for more timely admissions to the ICU in order to ensure the best possible provision of care. A retrospective study in the *Journal of Emergency Nursing* was able to show an increase in mortality rate the longer it took to leave the ED after an ICU admission order [7]. This phenomenon was also observed in a UK confidential inquiry into the quality of a series of adult ICU admissions when over half of patients were judged to have received suboptimal ED care, and of these 69 percent were deemed to have been admitted late with a 53.5 percent contribution to morbidity or mortality [8]. Though the aforementioned studies are not diagnosis-limited, we propose that patients with an admitting or secondary diagnosis along the sepsis continuum whose ED triage to ICU admission time is delayed have worse clinical outcomes than those who spend less time in the ED.

**Study Design and Statistical Analysis**

We have designed a longitudinal study involving the retrospective review of patients with the clinical diagnosis of sepsis admitted to the medical intensive care unit of Columbia Presbyterian Medical Center directly from the emergency department over a period of 9-12 months. All patients with the admitting or secondary diagnosis of sepsis upon ICU admission who are sent directly from the ED will be included in the study. In order to account for potential covariates, we also plan to collect demographic data (age, gender, and ethnicity), co-morbid illnesses (AIDS, cirrhosis, cancer, etc.), severity of sepsis (need for intubation, need for vasopressors, antibiotic regimens utilized, infectious source if known, APACHE II score), and clinical outcomes (number of organ system failures, duration of vasopressor therapy or mechanical ventilation, ICU and in-hospital lengths of stay, and ICU and in-hospital mortality rates), in

addition to ED admission time as defined as time from ED triage to ICU arrival. The primary outcome that will be studied is the rate of in-hospital mortality among the selected patient cohort.

In order to address the principal potential confounder of clinical condition upon ED triage, ICU-bound patients who are identified as septic will be assigned a category that has been shown to accurately quantify disease severity contributing to disposition and estimate mortality. Based on data from chart-review, patients will be given a score on the Emergency Severity Index (ESI), a 5-level ED triage algorithm designed to categorize patients in a clinically relevant fashion by both acuity and resource needs [9,10]. Higher acuity patients would be categorized as ESI levels 1 and 2 and would thus be the levels most relevant to this study. For example, in a European validation of the ESI, 56% of ESI-2 patients were admitted (compared to <1% of ESI-5), 26% to a critical care bed [11]. Within each ESI level (namely levels 1 and 2), the mean admission time of the patients who died over the course of their hospitalization will be compared to the mean admission time of those patients who survived sepsis. These means will be compared using an unpaired t-test.

The medical ICU (MICU) at Columbia Presbyterian Medical Center (CPMC) admits approximately 90 patients monthly, 30% of which are admitted (or subsequently diagnosed) with sepsis. Preliminary data show that approximately 40% of these patients are admitted from the ED. Though various studies report average ICU bed wait times from 4-5 hours [7,12], at CPMC this mean value has been determined to be 12 hours with a standard deviation of 6 hours. Given that the mortality benefit of early-goal directed therapy in Rivers' seminal 2001 study occurred in the initial 6 hours, the expected effect, or postulated group difference, that will be used in the power calculation is 6 hours. Therefore, for an 80% power, 17 subjects will be needed in each group within each relevant ESI level, summing to a total of approximately 70 patients, with an ultimate goal of about 100. It is expected that data on at least 100 patients can be collected over 9-12 months of MICU admissions.

Given the hypothesis of this longitudinal study, there are a number of variables that in and of themselves may be predictive of the primary outcome, that is, sepsis-related mortality. Such covariates include age, ethnicity, presence of hypothermia or leukopenia, comorbid conditions, site of infection, organism isolated, and appropriateness of antimicrobial therapy. These will be accounted for using a multiple logistic regression analysis.

**Study Procedure**
Given that this is an observational investigation, there will be no procedures performed over the course of the study other than routine retrospective review of WebCIS and hospital charts.

**Study Drugs**
There will be no drugs administered in this study.

**Medical Device**
There will be no investigational devices used in this study.

**Study Questionnaires**
There will be no questionnaires administered during this study.

**Study Subjects**
*Inclusion criteria*: Patients 18 years and older admitted to the medical intensive care unit (MICU) at Columbia Presbyterian Medical Center from the emergency department with the admitting or secondary diagnosis of sepsis.

*Exclusion criteria*: Patients younger than 18 years, patients admitted to the MICU from outside hospitals or from the floor, and patients in whom the diagnosis of sepsis is not applicable.

**Recruitment of Subjects**
No subjects will be approached for recruitment over the course of this study.

**Confidentiality of Study Data**
All patient-related data will be stored in an Access database on a password-protected computer in the Primary Investigator's laboratory. Only screened study personnel will be granted access to the database. All patient information, once collected, will be de-identified and subsequently linked by an assigned study number in lieu of name and medical record number.

**Potential Conflict of Interest**
There are no conflicts of interest warranting disclosure.

**Location of the Study**
Primary data collection and analysis will be conducted on the campus of Columbia Presbyterian Medical Center.

**Potential Risks**
The proposed study is minimal risk.

**Potential Benefits**
Though the patients included in the database will not benefit directly from this study, the results of the study may have implications for improving both efficiency and treatment efficacy of the emergency department at Columbia Presbyterian Medical Center. It also has the potential to stimulate further inquiries in health services research.

**Alternative Therapies**
Not-applicable

**Compensation to Subjects**
Not-applicable

**Costs to Subjects**
Not-applicable

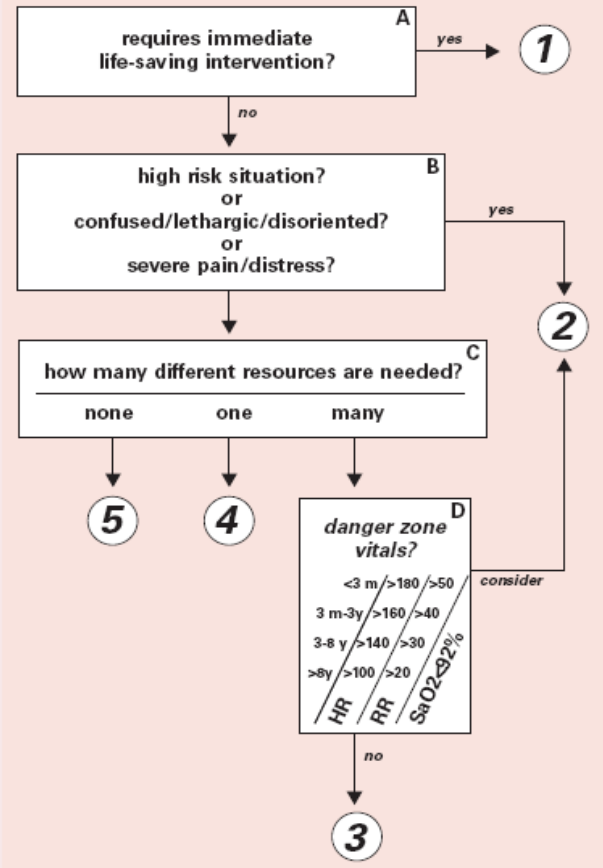
**Minors as Research Subjects**
The patients included in the database are only those admitted to the adult Medical Intensive Care Unit of Columbia Presbyterian Medical Center.

**Radiation or Radioactive Substances**
Not-applicable

**References**


1. American College of Chest Physicians/Society of Critical Care Medicine. Consensus Conference: Definitions for sepsis and organ failure and guidelines for the use of innovative therapies in sepsis. Crit Care Med 1992; 20:864.
2. Annane, D, Aegerter, P, Jars-Guincestre, MC, Guidet, B. Current Epidemiology of Septic Shock: The CUB-Rea Network. Am J Respir Crit Care Med 2003; 168:165.
3. Martin, GS, Mannino, DM, Eaton, S, Moss, M. The epidemiology of sepsis in the United States from 1979 through 2000. N Engl J Med 2003; 348:1546.
4. Rivers, E, Nguyen, B, Havstad, S, Ressler, J, Muzzin, A, Knoblich, B, Peterson, E, Tomlanovich, M. N Engl J Med. 2001 Nov 8;345(19):1368-77.
5. Sivayoham, N. Management of severe sepsis and septic shock in the emergency department: a survey of current practice in emergency departments in England. Emerg Med J. 2007 Jun;24(6):422.
6. Varpula, M. Implementation of early goal-directed therapy in Finland. Critical Care 2007, 11(Suppl 2)**:**69.
7. Clark, K, Normile, LB. Influence of time-to-interventions for emergency department critical care patients on hospital mortality. J Emerg Nursing 2007;33:6-13.
8. McQuillan, P, Pilkington, S, Allan, A, Taylor, B, Short, A, Morgan, G, Nielsen, M, Barrett, D, Smith G, Collins CH. Confidential inquiry into quality of care before admission to intensive care. BMJ. 1998;316:1853–1858.
9. Tanabe, P, Gimbel, R, Yarnold, PR, Kyriacou, DN, Adams, JG. Reliability and validity of scores on The Emergency Severity Index version 3. Acad Emerg Med. 2004 Jan;11(1):59-65.
10. Wuerz, R. Emergency severity index triage category is associated with six-month survival. ESI Triage Study Group. Acad Emerg Med. 2001 Jan;8(1):61-4.
11. Elshove-Bolk, J, Menel, F, van Rijswijck, B, Simons, M, van Vugt, A. Validation of the Emergency Severity Index (ESI) in self-referred patients in a European emergency department. Emerg Med J 2007;24:170-174.
12. McCaig, L, Burt, C. National Hospital Ambulatory Medical Care Survey: 2001 Emergency Department Summary Advance Data from Vital and Health Statistics, Centre for Disease Control and Prevention, National Centre for Health Statistics, 2003 Report No 335.

## Figure 3-1a. ESI Triage Algorithm




A. Immediate life-saving intervention required: airway, emergency medications, or other hemodynamic interventions (IV, supplemental O2, monitor, ECG or labs DO NOT count); and/or any of the following clinical conditions: intubated, apneic, pulseless, severe respiratory distress, $SPO_2$<90, acute mental status changes, or unresponsive.

Unresponsiveness is defined as a patient that is either:
(1) nonverbal and not following commands (acutely); or
(2) requires noxious stimulus (P or U on AVPU) scale.

B. High risk situation is a patient you would put in your last open bed.

Severe pain/distress is determined by clinical observation and/or patient rating of greater than or equal to 7 on 0-10 pain scale.

C. Resources: Count the number of different types of resources, not the individual tests or x-rays (examples: CBC, electrolytes and coags equals one resource; CBC plus chest x-ray equals two resources).

| *Resources* | *Not Resources* |
|---|---|
| • Labs (blood, urine)<br>• EKG, X-rays<br>• CT-MRI-ultrasound-angiography | • History & physical (including pelvic)<br>• Point-of-care testing |
| • IV fluids (hydration) | • Saline or heplock |
| • IV or IM or nebulized medications | • PO medications<br>• Tetanus immunization<br>• Prescription refills |
| • Specialty consultation | • Phone call to PCP |
| • Simple procedure =1 (lac repair, foley cath)<br>• Complex procedure =2 (conscious sedation) | • Simple wound care (dressings, recheck)<br>• Crutches, splints, slings |

D. Danger Zone Vital Signs
Consider uptriage to ESI 2 if any vital sign criterion is exceeded.

Pediatric Fever Considerations
1 to 28 days of age: assign at least ESI 2 if temp >38.0 C (100.4F)

1-3 months of age: consider assigning ESI 2 if temp >38.0 C (100.4F)

3 months to 3 yrs of age: consider assigning ESI 3 if: temp >39.0 C (102.2 F), or incomplete immunizations, or no obvious source of fever