Predictive Value of Acute Kidney Injury in Medical Intensive Care Patients With Sepsis Originating From Different Infection Sites

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Abstract: *Introduction:* Sepsis is the most common noncoronary cause of mortality in intensive care units (ICUs). This study compared different systems for predicting outcomes in a population of critically ill patients with sepsis originating from different infection sites, including intra-abdominal and pulmonary infections. *Methods:* This *post hoc* analysis of an accumulated database enrolled 161 heterogeneous critically ill patients diagnosed as severe sepsis and septic shock patients admitted to medical ICUs from June 2005 to May 2007. Demographic characteristics, clinical and laboratory variables, comorbidities and infection source were prospectively recorded on the first day of ICU admission. Patient evaluations included acute physiology and chronic health evaluation (APACHE) II, APACHE III, sequential organ failure assessment scores, organ system failure and risk of renal failure, injury to kidney, failure of kidney function, loss of kidney function and end-stage renal failure (RIFLE) classification. *Results:* Regarding the different originating sites of severe sepsis, intra-abdominal infections and pulmonary infections had the highest mortality rates (83.3% and 48.5%, respectively; $P < 0.001$). The APACHE III was the best mortality predictor for the overall sepsis population [areas under the receiver operating characteristic curve (AUROC) 0.800], whereas RIFLE classification was the best predictor in those with intra-abdominal infection (AUROC 0.856). The AUROC analyses verified that RIFLE classification had significantly ($P < 0.05$) better discriminatory power for predicting hospital mortality in patients with intra-abdominal infections than in those with pulmonary infections (AUROC 0.545). *Conclusions:* This investigation confirms that different infection sites have different outcomes. In terms of mortality prediction, outcome scoring systems are significantly more accurate in patients with intra-abdominal infections than in those with pulmonary infections.

Key Indexing Terms: Acute kidney injury; Sepsis; RIFLE; Intensive care unit; Prognosis. **[Am J Med Sci 2012;344(2):83–89.]**

Sepsis is a constant concern in intensive care unit (ICU) patients, not only because of its high incidence but also owing to its high mortality rate.[1] In recent decades, various scoring systems have been used to predict outcome in critically ill septic patients.[2–5] However, it remains unclear whether these scoring systems should consider the specific cause of sepsis.

The acute physiology and chronic health evaluation (APACHE) II and III are physiologically based scoring systems, originally developed and modified by Knaus et al.[6,7] Sequential organ failure assessment (SOFA) was designed to describe morbidity. Although originally used for classifying severity of organ failure rather than for predicting outcome, the literature reveals a clear relationship between organ dysfunction and mortality.[8] The RIFLE classification (risk of renal failure, injury to the kidney, failure of kidney function, loss of kidney function and end-stage renal failure) system was first proposed by the acute dialysis quality initiative (ADQI) group to standardize the findings of acute kidney injury (AKI) research.[9] We reported earlier that RIFLE category accurately predicts in-hospital mortality and short-term prognosis in ICU sepsis patients.[10] Our objective in the current study was to compare the accuracy of the recently defined AKI (RIFLE classification), organ system failure (OSF) number[11] and the general ICU prognostic models APACHE II, APACHE III and SOFA in predicting in-hospital mortality in critically ill patients with sepsis resulting from different infection sites, including intra-abdominal and pulmonary tract infections. All assessment scores were calculated on ICU day 1.

MATERIALS AND METHODS

Patient Information and Data Collection

After obtaining approval from the local institutional review board, this study enrolled critically ill patients with severe sepsis who had been admitted to medical ICUs at Linkou Chang Gung Memorial Hospital between June 2005 and May 2007. All enrolled patients had received diagnoses of sepsis with organ failure. Patients who had developed septic shock in the emergency departments or medical wards were also included if they had been transferred to the medical ICU within 4 hours. Exclusion criteria were age younger than 18 years, hospital or ICU stay <24 hours, hospital readmission or any history of the following: renal replacement therapy for end-stage renal disease; pregnancy; acute cerebral or vascular event such as acute coronary syndrome, acute pulmonary edema, status asthmaticus or cardiac dysrhythmia; seizure; drug overdose or intoxication; burn injury; trauma requiring emergent surgical treatment; uncured cancer; current use of immunosuppressants or do-not-resuscitate status

This *post hoc* analysis of a prospectively accumulated database assessed the following variables on the first day of ICU admission: demographic data, clinical and laboratory variables, comorbidities and source of infection. The APACHE II,

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APACHE III, SOFA scores, OSF number and RIFLE category were assessed. Length of hospitalization and in-hospital outcome were also documented. When necessary, the hospital registry office provided information regarding patient survival or date of death.

Definitions

According to modified American College of Chest Physicians and Society of Critical Care Medicine consensus criteria, severe sepsis was defined as presence of 2 or more systemic inflammatory response syndrome criteria, proven or suspected infection and associated organ dysfunction.[11] Septic shock was defined as sepsis-induced hypotension with systolic arterial blood pressure (BP) <90 mm Hg despite adequate fluid (crystalloid or colloid) resuscitation.[11] Pulmonary infection was defined as presence of at least 2 of the following criteria: persistent (ie, duration at least 24 hours) temperature above 37.5°C, purulent sputum with 20% or larger increase in volume, radiologic evidence of new shadowing on chest radiograph and/or persistent (ie, 2 or more days) localized signs on chest examination (crackles, bronchial breathing, wheeze and/or pleural rub). Intra-abdominal infection was defined as infection of any intra-abdominal viscus, with or without overlying peritoneum involvement.[12]

The worst physiological and biochemical values on the first day of ICU admission were recorded. Neurological scoring was not performed in patients who were paralyzed or sedated because their conditions were not classified as neurological failure. The best verbal response for in-patients who had been intubated but not sedated was determined according to clinical judgment. Illness severity was assessed by the following scoring systems: APACHE II, APACHE III and SOFA. The number of organ failures was recorded within 24 hours of ICU admission. Organ failure was defined by criteria established by the consensus committee of the American College of Chest Physicians and Society of Critical Care Medicine: respiratory failure; need for mechanical ventilation; cardiovascular failure; systolic BP equal to or less than 90 mm Hg or mean arterial pressure equal to or less than 60 mm Hg for 1 hour despite fluid

TABLE 1. Patient demographic data and clinical characteristics according to different sites of infections

	Intra-abdomen (n = 60)	Pulmonary (n = 101)	*P*
Age (yr)	58.8 ± 1.7	69.7 ± 1.4	<0.001
Male	42 (70.0)	72 (72.3)	NS (0.757)
Length of ICU stay (d)	8.7 ± 1.3	15.5 ± 1.4	0.004
Length of hospital stay (d)	13.5 ± 1.7	34.5 ± 2.3	<0.001
Body weight on ICU admission (kg)	63.2 ± 2.0	55.2 ± 1.2	<0.001
GCS, ICU first day (points)	8.9 ± 0.6	10.4 ± 0.4	NS (0.084)
MAP, ICU admission (mm Hg)	71.3 ± 1.9	77.7 ± 1.7	0.044
Serum creatinine, ICU first day (mg/dL)	2.5 ± 0.3	2.1 ± 0.2	NS (0.583)
Arterial HCO_3^-, ICU first day	16.0 ± 0.8	23.6 ± 0.7	<0.001
Serum sodium, ICU first day (mg/dL)	133.2 ± 1.2	137.4 ± 0.8	0.016
Bilirubin, ICU first day (mg/dL)	12.9 ± 1.6	1.0 ± 0.2	<0.001
Albumin, ICU first day (g/L)	2.3 ± 0.1	2.4 ± 0.1	NS (0.496)
Blood sugar, ICU first day (mg/dL)	147.7 ± 8.3	158.9 ± 7.8	NS (0.246)
Hemoglobin, ICU first day (g/dL)	8.8 ± 0.3	10.1 ± 0.2	0.001
Platelets, ICU first day ($\times 10^3/\mu L$)	84.1 ± 9.9	219.3 ± 12.0	<0.001
Leukocytes, ICU first day ($\times 10^3/\mu L$)	14.3 ± 1.5	14.6 ± 0.7	NS (0.726)
PaO_2/FiO_2, ICU first day (mm Hg)	266 ± 16.0	249 ± 13.9	NS(0.302)
Septic shock, ICU first day	39 (65.0)	79 (78.2)	NS (0.067)
Mortality	50 (83.3)	49 (48.5)	<0.001
Chronic coexisting conditions			
Diabetes mellitus	12 (20.0)	29 (28.7)	NS (0.187)
Hypertension	9 (15.0)	24 (23.8)	NS (0.146)
Congestive heart failure	3 (5.0)	15 (14.9)	NS (0.095)
Liver cirrhosis	45 (75.0)	0 (0)	<0.001
Chronic renal failure	5 (8.3)	19 (18.8)	NS (0.173)
History of malignancy	2 (3.3)	32 (31.7)	<0.001
Score systems			
APACHE II, ICU first day (mean ± SE)	25.9 ± 1.1	20.8 ± 0.7	0.001
APACHE III, ICU first day (mean ± SE)	110.1 ± 4.8	75.3 ± 2.4	<0.001
SOFA, ICU first day (mean ± SE)	11.9 ± 0.3	6.8 ± 0.3	<0.001
OSF, ICU first day number (mean ± SE)	3.3 ± 0.2	2.7 ± 0.1	0.011
RIFLE, ICU first day (mean ± SE)	1.87 ± 0.2	1.2 ± 0.1	0.003

NS, not significant; M, male; F, female; ICU, intensive care unit; SE, standard error; PaO_2, arterial partial pressure of oxygen; FiO_2, fraction of inspired oxygen; $AaDO_2$, alveolar-arterial O_2-tension difference; GCS, Glasgow coma scale; MAP, mean arterial pressure. APACHE, acute physiology and chronic health evaluation; OSF, organ system failure; RIFLE, risk of renal failure, injury to the kidney, failure of kidney function, loss of kidney function and end-stage renal failure; SOFA, sequential organ failure assessment.