RIFLE Classification Did Not Have Satisfactory Predictive Value for Septic Patients with High Severity Scores

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Background: Predicting the outcome of patients with severe sepsis is important. The RIFLE classification has been evaluated for its ability to predict mortality. The aim of this study was to compare the predictive value of 3 scoring systems: the Acute Physiology and Chronic Health Evaluation (APACHE) II score, the Multiple Organ Dysfunction Score (MODS), and the Risk, Injury, Failure, Loss of kidney function, and End-stage kidney disease (RIFLE) classification.

Patients and methods: Seventy-one severe septic patients admitted to intensive care units (ICU) directly from the emergency department were enrolled into this study. The APACHE II score, MODS, and RIFLE classification were calculated within 24 hours after admission. Areas under the receiver operating characteristic (ROC) curves were computed in order to analyze the discriminatory power of these 3 scoring systems.

Results: The value of the APACHE II score and the MODS in the non-survivors was statistically significantly higher than that in the survivors. The RIFLE classification showed no significant difference between survivors and non-survivors. Areas under the ROC curves were 0.801, 0.715, and 0.602, respectively, for the APACHE II score, the MODS, and the RIFLE classification. The APACHE II score and the MODS were better tools for outcome prediction, compared with the RIFLE classification. The discriminatory power of the RIFLE classification did not have significance (p = 0.226) for outcome prediction in severe septic patients.

Conclusions: The APACHE II score and the MODS were useful tools in patients with severe sepsis. The RIFLE classification did not show satisfactory power in predicting 28-day mortality in more severe septic patients. ***(Thorac Med 2010; 25: 230-237)***

Key words: severe sepsis, mortality, RIFLE, APACHE II, MODS

Introduction

Severe sepsis is not only a common health-care problem but also a frequently fatal condition, and is still a predominant problem in intensive care units (ICUs) [1-2]. Sepsis may have a

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progressive course and result in multiple-organ dysfunction, which is the leading cause of mortality in ICU patients. We need tools such as the Acute Physiology and Chronic Health Evaluation (APACHE) II score and the Multiple Organ Dysfunction Score (MODS) to evaluate the severity of illness and risk of mortality for these patients [3-4]. Prognostic tools should have the following features: ease of use and clinical applicability, and high sensitivity and specificity for a variety of populations [5].

Acute kidney injury (AKI) is an important issue, and increases mortality among patients with severe sepsis [6]. The Acute Dialysis Quality Initiative (ADQI) proposed a consensus definition for the Risk, Injury, Failure, Loss of kidney function, and End-stage kidney disease (RIFLE) classification for acute kidney injury, grading the severity into risk, injury, and failure. Recently, several studies have used the RIFLE for outcome prediction in ICU patients, and its practicability is still under discussion [7-11].

The purpose of this study was to compare the efficacy of these 3 scoring systems (APACHE II score, MODS, and RIFLE criteria) for outcome prediction in patients with severe sepsis.

Materials and Methods

Patients

Patient data from our previous prospective study [12] were used for analysis. The RIFLE classification was added retrospectively. From October 2003 to September 2005, 71 patients who were admitted to the emergency department and soon transferred to the ICU at Chang Gung Memorial Hospital due to severe sepsis were enrolled into this study. Exclusion criteria included a history of renal replacement therapy for end-stage renal disease. The ICU is a closed-format unit covered by medical intensivists. The following patient data were recorded within the first 3 days after admission: age, gender, medical history, infection source, and co-morbidity. Standard treatment, including fluid resuscitation, broad-spectrum antibiotics, drainage, and basic support, were provided to all patients. Antibiotics and fluid resuscitation were started as soon as possible after the sepsis was diagnosed [13]. Pneumonia was diagnosed based on new abnormal infiltration shown on the chest radiograph with fever or respiratory symptoms. Urinary tract infection was diagnosed based on the presence of pyuria and positive bacteria culture.

Severe sepsis and septic shock were defined according to the criteria of the Consensus Conference [14]. Systemic inflammatory response syndrome (SIRS) was defined as 2 or more of the following criteria: (1) body temperature $> 38^{o}C$ or $< 36^{o}C$; (2) respiratory rate > 24 breaths/min; (3) heart rate > 90 beats/min; and (4) white blood count > 12,000/μl or < 4,000/μl or > 10% bands. Sepsis was defined as SIRS according to a confirmed or suspected microbial etiology. Severe sepsis was defined as sepsis with 1 or more of organ dysfunction or hypotension. Septic shock was defined as sepsis with hypotension unresponsive to fluid resuscitation, which further required vasopressors to maintain blood pressure on the emergency department admission day. The survivors were defined as patients who were still alive 28 days after hospital admission. Disease severity was assessed by the APACHE II score, MODS, and RIFLE classification using the data within 24 hours of admission. Both the serum creatinine and urine output criteria were used to determine the

RIFLE classification of all patients. The criteria that led to the worst possible classification was used. Because some patients (n = 25, 35%) did not have baseline renal function, a hypothetical baseline serum creatinine was estimated for a given patient, assuming a normal glomerular filtration rate (75 ml/min per 1.73 m^2) with the modification of diet in renal disease (MDRD) formula, as recommended by the ADQI workgroup [15-16]. Patients were classified into 1 of the first 3 levels: risk (1 point), injury (2 points), and failure (3 points) according to the RIFLE classification. The non-AKI group was classified as 0 points [9].

Statistical analysis

Differences in age, APACHE II score, MODS, and RIFLE categories between the survivors and non-survivors were analyzed by T-test. Differences for categorical variables of gender, medical history, infection source, and co-morbidity between survivors and non-survivors were compared using the Chi-square test. Areas under the receiver operating characteristic (ROC) curves were calculated in order to analyze the discriminatory power of the scoring systems for outcome prediction. All statistical tests were 2-tailed and a *p* value less than 0.05 was considered statistically significant.

Results

Seventy-one patients were enrolled into this study and 15 patients (21.1%) died. The clinical characteristics and demographic data of the patients are shown in Table 1. The value of the APACHE II score and the MODS in the non-survivors was statistically significantly higher than that in the survivors. The RIFLE classification did not show a significant difference between the survivors and non-survivors. There were no significant differences in history and infection source between the survivors and non-survivors. The proportions of septic shock and gastrointestinal bleeding in the non-survivors were significant higher than in the survivors.

The ROC curves of the APACHE II score, the MODS, and the RIFLE classification are shown in Figure 1. Table 2 compares the discriminatory power of the 3 scoring systems. The areas under the ROC curves of the APACHE II score and the MODS were significantly different than 0.5, and that of RIFLE classification was not.

Discussion

In recent years, several scoring systems, such as the APACHE II and the MODS, have been used extensively to describe the severity of illness and predict the outcome of ICU patients. Besides, these systems can also be used to assist in clinical trials and to compare the quality of care in different ICUs [3-4]. Nevertheless, we still need a simple, fast, and accurate tool to predict the prognosis of ICU sepsis patients.

In 2004, the ADQI workgroup published a classification system for acute kidney injury. The system was given the acronym RIFLE (Risk, Injury, Failure, Loss of kidney function, and End-stage kidney disease). Recently, the RIFLE classifications ‘‘risk,’’ ‘‘injury,’’ and ‘‘failure’’ have been used to evaluate and predict the outcome of critically ill patients [16-17]. Several large retrospective and prospective studies have shown that the RIFLE classification was an independent risk factor for the hospital mortality of ICU patients [8, 10-11]. The studies of Lopes *et al*. and Chen *et al*. showed that the RIFLE classification is predictive of

Table 1. Clinical characteristics of severe sepsis patients (mean ± standard error mean, number and percentage).

Characteristic	Survivors (n = 56)	Non-survivors (n = 15)
Age (years)	70.2 ± 1.9	72.1 ± 3.3
Gender		
Male	32 (57.1)	7 (46.7)
Female	24 (42.9)	8 (53.3)
APACHE II score	22.3 ± 0.9	30.1 ± 2.0*
MODS	6.1 ± 0.3	7.9 ± 0.6*
RIFLE	0.8 ± 0.1	1.3 ± 0.3
History		
Chronic lung disease	17 (30.4)	5 (33.3)
Chronic renal disease	7 (12.5)	2 (13.3)
Liver cirrhosis	1 (1.8)	0 (0)
Diabetes mellitus	15 (26.8)	6 (40.0)
Heart failure	5 (8.9)	2 (13.3)
Old cerebrovascular accident	35 (62.5)	7 (46.7)
Hypertension	28 (50.0)	7 (46.7)
Source of sepsis		
Pneumonia	48 (85.7)	11 (73.3)
Urinary tract infection	6 (10.7)	3 (20.0)
Others	2 (3.6)	1 (6.7)
Co-morbidity		
Septic shock	19 (33.9)	11 (73.3)*
Bacteremia	10 (17.9)	4 (26.7)
Jaundice	10 (17.9)	3 (20.0)
Thrombocytopenia	23 (41.1)	8 (53.3)
Gastrointestinal bleeding	14 (25.0)	10 (66.7)*

* Statistical significance based on Chi-square test or Fisher's exact test for categorical variables, T-test for continuous variables.

Abbreviations: APACHE = Acute Physiology and Chronic Health Evaluation; MODS = Multiple Organ Dysfunction Score; RIFLE = Risk, Injury, Failure, Loss of kidney function, and End-stage kidney disease

Table 2. The areas under the ROC (mean ± standard error mean) analysis of the 3 scoring systems.

	Areas under ROC	95% CI	*p* value
APACHE II	0.801 ± 0.064	0.675 – 0.926	< 0.001
MODS	0.715 ± 0.068	0.582 – 0.848	0.011
RIFLE	0.602 ± 0.087	0.432 – 0.773	0.226

Abbreviations: ROC = receiver operating characteristic; CI = confidence interval; APACHE = Acute Physiology and Chronic Health Evaluation; MODS = Multiple Organ Dysfunction Score; RIFLE = Risk, Injury, Failure, Loss of kidney function, and End-stage kidney disease

mortality in patients with severe sepsis [7, 9].

In our study, all patients were recruited from the emergency department and the mean of the APACHE II score was 23.9 (survivors: 22.3, non-survivors: 30.1). We found that the APACHE II score and the MODS were still

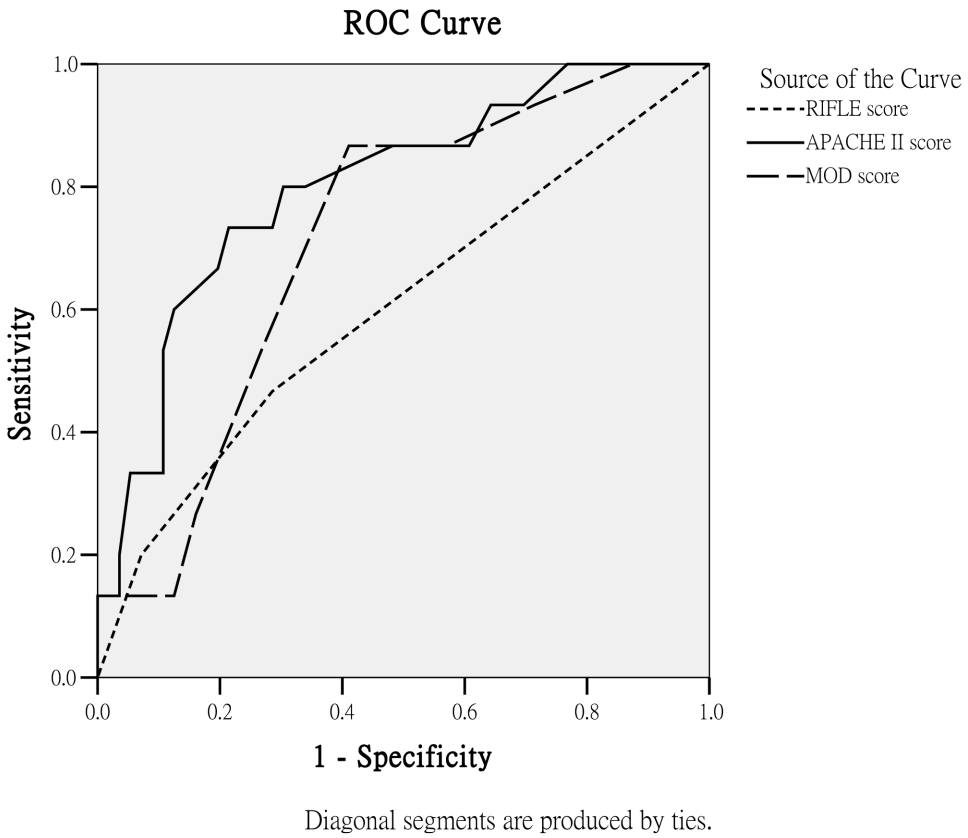

Fig. 1. ROC (receiver operating characteristic) curves of the APACHE (Acute Physiology and Chronic Health Evaluation) II score, MODS (Multiple Organ Dysfunction Score), and RIFLE (Risk, Injury, Failure, Loss of kidney function, and End-stage kidney disease) classification.

useful prognostic tools in this group. Nevertheless, the RIFLE classification did not have good discriminative power for hospital mortality in more severe sepsis patients (mean APACHE II score: 23.9). Ahlstrom *et al*. also found that the RIFLE score did not have good discriminative power (AUROC: 0.653) regarding hospital outcome in critically ill patients [8]. Contrary to our results, Ostermann *et al*. performed a retrospective analysis of a database of 41,972 patients admitted to 22 ICUs. He concluded that the RIFLE classification was proper for defining AKI in the ICU, and was associated with hospital outcome. However, the level of severity of the patients in the study was relatively low (median APACHE II score of the survivors: 12, non-survivors: 21) [11]. Similarly, Chen *et al*. reported that the RIFLE classification could predict prognosis in ICU sepsis patients. The survivors and non-survivors had mean APACHE II scores of 18 and 23, respectively [9].

The patient populations were different in the above studies. The patient population we enrolled had been admitted to the ICU directly from the emergency department. The Ostermann *et al*. and Chen *et al*. studies enrolled patients from both the emergency department and medical wards [9, 11], which might have led to different results. According to the APACHE

scoring system, the severity of disease in our patients was greater. It seems that the RIFLE classification did not have satisfactory predictive power for hospital mortality in patients with severe sepsis with a high APACHE II score. The RIFLE classification may be able to predict exactly the outcome of patients with a relatively low APACHE II score, but not the outcome of patients with a high APACHE II score.

There are some limitations to this study. First, some patients did not have available baseline creatinine to calculate the proportional decrease of renal function. Thus, we used an estimated baseline creatinine, based on the MDRD equation proposed by the ADQI in previous studies [8-10]. Second, Cruz *et al*. found that serum creatinine criteria appeared to be a better predictor than urine output criteria. Increased serum creatinine is an earlier sign of deterioration of renal function than oliguria [10]. These limitations may have influenced the results to a certain degree.

In conclusion, the APACHE II scores and the MODS differed between the survivors and non-survivors with severe sepsis. Nevertheless, the RIFLE classification did not provide satisfactory power to predict mortality in patients with severe sepsis with a high APACHE II score.

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在高嚴重程度分數的嚴重敗血症病人身上使用 RIFLE classification 沒有令人滿意的預測價值

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前言：預測嚴重敗血症病人的結果是重要的。RIFLE classification已經被拿來評估預測病人死亡的能力。本研究的目標是使用3個評分系統包括APACHE (Acute Physiology and Chronic Health Evaluation) II score、MODS (Multiple Organ Dysfunction Score)、及RIFLE (Risk, Injury, Failure, Loss of kidney function, and End-stage kidney disease) classification來比較其預測結果的價值。

方法：這個研究收集了71個從急診部門直接住到加護病房的嚴重敗血症病人。他們的APACHE II score、MODS、及RIFLE classification在住院後的24小時內就計算好。我們也估算了ROC (receiver operating characteristic) 的曲線下面積來分析這3個評分系統的辨識能力。

結果：非存活者的APACHE II score及MODS的數值皆顯著高於存活者的平均分數，但RIFLE classification在非存活者及存活者之間並沒有統計上的差異。APACHE II score、MODS、及RIFLE classification的ROC曲線下面積分別是0.801、0.715及、0.602。APACHE II score及MODS比起RIFLE classification而言，是用來預測結果比較好的工具。RIFLE classification的辨識能力在預測嚴重敗血症病人的結果上並沒有顯著意義 ($p = 0.226$)。

結論：APACHE II score及MODS對於嚴重敗血症病人而言是有用的工具。而RIFLE classification使用在相對嚴重的敗血症病人來預測28天的死亡率並沒有令人滿意的預測能力。*(胸腔醫學 **2010; 25: 230-237**)*

關鍵詞：嚴重敗血症，死亡率，RIFLE，APACHE II，MODS

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