The Clinical Outcome of Acute Kidney Injury in Critically Ill Thai Patients Stratified with RIFLE Classification

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Objective: *The Acute Dialysis Quality Initiative (ADQI) Group published a consensus definition (the RIFLE criteria) for acute renal failure. We sought to assess the ability of the RIFLE criteria to predict mortality in critically ill Thai patients with acute kidney injury (AKI).*

Material and Method: *We performed a retrospective cohort study, in Siriraj Hospital (a large single tertiary care academic center in Thailand) on 121 patients admitted during November 2005-November 2006. We classified patients according to the maximum RIFLE class (class R, class I or class F) reached during their hospital stay. Demographic data, hospital mortality, hospital length of stay, and need of renal replacement therapy was collected.*

Results: *Patients with maximum RIFLE class R, class I and class F had hospital mortality rates of 35.7%, 35.7% and 65.9%, respectively, compared with 20% for patients without acute kidney injury. Overall hospital mortality of the patients in AKI group (Risk, Injury, Failure group) was increased when compared with no AKI group (Odds ratio = 4.2; 95% Confidence Interval, 1.6-10.6; p =0.003). Mortality was not significantly different among those with the "Risk" and "Injury" class of RIFLE AKI compared with those without AKI, but mortality increased significantly with the "Failure" class (Odds ratio = 7.7; 95% Confidence Interval, 2.7-21.8; p < 0.001). There was the highest rate of renal replacement therapy in the failure group (52.3%) compared with no AKI group (5.7%), and injury group (7.1%) (p < 0.001).*

Conclusion: *Acute kidney injury 'risk, injury, failure', as defined by the newly developed RIFLE classification, is associated with increased hospital mortality and renal replacement therapy in critically ill Thai patients.*

Keywords: *Critical illness, Injuries, Kidney, Kidney failure, Acute, Mortality, Severity of illness index*

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The clinical syndrome of acute renal failure (ARF) is a common condition in intensive care unit (ICU) patients, with a reported incidence of 1-25% depending on the setting and the definition used[1,2]. Hospital mortality for patients with ARF has been reported to vary widely ranging from 28% to 90%[3,4]. One of the major reasons for such variability is that there has been no consensus definition for ARF. A recent survey revealed the use of at least 35 definitions in the literature, creating confusion and making comparisons among the studies difficult[5]. This situation has impaired the study of ARF as well as the development of possible treatments[6].

The Acute Dialysis Quality Initiative (ADQI) represents the efforts of a workgroup seeking to develop consensus and evidence-based statements in the field of ARF[7,8]. To establish a uniform definition for acute kidney injury, ADQI has recently published a consensus definition of ARF, using a set of criteria called the RIFLE (Risk, Injury, Failure, Loss, and End stage) criteria[9].The RIFLE criteria classify ARF into three groups (Risk, Injury, and Failure) according to relative changes of serum creatinine and urine output. In particular, this group has proposed the term 'acute kidney injury (AKI)' to define the entire spectrum of acute renal dysfunction from its earliest and mildest

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forms to the need for renal replacement therapy (RRT). The last two groups, classed as Loss and End-Stage Kidney Disease, were the outcome of kidney dysfunction.

The ultimate value of this new definition for AKI should be determined by its utility. A classification scheme for AKI should be sensitive and specific, and also be predictive of relevant clinical outcomes such as mortality, use of dialysis and length of hospital stay. In addition, the new classification should be validated in different population groups. A number of papers have been published the application of the RIFLE criteria[10]. The clinical characteristics and predictive ability of this classification have not, however, been clinically validated in an Asian population. The aims of this study were therefore to characterize acute kidney injury defined by the maximum RIFLE classification, to relate this classification to the hospital mortality, the hospital length of stay, and the need of renal replacement therapy in a cohort of Thai critically ill patients.

Material and Method

Study population

We conducted a retrospective cohort study. We included adult critically ill patients admitted to the medical intensive care unit (ICU) and general medical wards during November 2005-November 2006 at the Siriraj Hospital (a large tertiary care academic center with 1,200 beds in Bangkok, Thailand). Patients were excluded if they were younger than 15 years old, if they were ESRD, on chronic dialysis or had had kidney transplant, and if they did not have the complete database.

The patient data, including demographic, administrative, physiologic, laboratory and hospital outcome information, were retrieved from medical notes or a computer database. The demographic data included age, sex, type of ward admission (*i.e* general wards or ICU), baseline serum creatinine (Cr), peak serum Cr during admission, severity scores (*i.e* APACHE II[11], SAPS II[12], SAPS III[13]), and the mortality probabilities predicted by such scoring systems. The study protocol was approved by the local ethics committee. The need for informed consent was waived because the study required no intervention and no breach of privacy or anonymity as such projects are considered quality improvement activities by the Institutional Ethics Committee.

RIFLE criteria

The RIFLE criteria[9] are shown in Table 1. We classified patients according to the maximum RIFLE class (class R, class I or class F) reached during their hospital stay. We did not evaluate the outcome classes of RIFLE. In the original criteria, the RIFLE class was determined based on the worst measurement of either glomerular filtration rate (GFR) criteria or urine output criteria. In the present study, we used the GFR criterion only because only a minority of general ward patients has a urinary catheter in situ. Even when they do, hourly or six-hourly measurement of urine output is uncommon.

To classify patients according to one of the RIFLE criteria, peak and baseline creatinine were collected from the computerized laboratory database. Patients who met any of the criteria of the RIFLE classification were classified as acute kidney injury patients. The peak creatinine was defined as the

Table 1. The RIFLE criteria

	GFR criteria	Urine output criteria
Risk	Increased SCreat x 1.5 orGFR decrease > 25%	UO < 0.5 ml/kg/hr x 6 hr
Injury	Increased SCreat x 2 orGFR decrease > 50%	UO < 0.5 ml/kg/hr x 12 hr
Failure	Increased SCreat x 3 GFR decrease 75%	UO < 0.3 ml/kg/hr x 24 hr
	or SCreat ≥ 4 mg/dlAcute rise ≥ 0.5 mg/dl	or Anuria x 12 hr
Loss	Persistent ARF = complete loss of kidney function > 4 weeks	
ESKD	End Stage Kidney disease (> 3 months)	

Adapted from reference 9

SCreat: serum creatinine; UO: urine output; GFR: glomerular filtration rate; ARF: acute renal failure; ESKD: end-stage kidney disease

highest creatinine during their hospital stay. The baseline creatinine was defined in two ways. For patients without a baseline creatinine value as reported in the medical history, we calculated a serum creatinine level using the modification of diet in renal disease (MDRD) equation[14], (CrMDRD), as recommended by the ADQI, by solving the MDRD equation for serum creatinine assuming a glomerular filtration rate of 75 ml/minute/1.73 m^2. For patients for whom we had the previous creatinine data, the baseline creatinine was defined as the lowest serum creatinine within the 3 months before their admission.

Severity of illness

The calculations of the individual scoring models were based upon the most deranged physiological value within the first 24 hr of ICU or medical ward admission for APACHE II and SAPS II, and within the first 1 hr after admission for SAPS III, as described in the original studies[12-14]. The mortality probabilities for APACHE II, SAPS II and SAPS III were calculated using the original regression equations.

Outcome

The primary outcome of this study was the hospital mortality according to RIFLE classification (class R, class I or class F). The secondary outcomes were length of hospital stay and the need for renal replacement therapy related to this classification.

Statistical analysis

The clinical parameters were reported as mean $\pm$ standard deviation (SD), the median (interquartile range) for non-normality, frequencies and percent. We compared quantitative data (normality) using the ANOVA F-test with Bonferroni post hoc test and quantitative data (non-normality) using Kruskal-Wallis H test. We analyzed qualitative data including hospital mortality and the need for RRT using the Chi-Square test. The hospital mortality between groups was compared by odds ratio and 95% confidence interval (OR, 95%CI). A double-sided p-value of less than 0.05 was considered significant. Analysis was performed with the statistical software package SPSS 11.5 (SPSS Inc., Chicago, IL, USA).

Results

A total of 121 patients was evaluated. The baseline characteristics of the patient cohort are presented according to the maximum RIFLE class in Table 2. The mean age of the "no AKI" group was 53.1 years, of the Risk group was 59.5 years, of the Injury

Table 2. Baseline characteristics of patients classified according to the maximum risk, injury, failure, loss, and end-stage kidney (RIFLE) class

	Mean $\pm$ SD or number (%)				
	No AKI (C) (n = 35)	Risk (R) (n = 14)	Injury (I) (n = 28)	Failure (F) (n = 44)	p-value
Demographic data					
No. of patients	35	14	28	44	
Age (yr)	53.1 $\pm$ 22.1	59.6 $\pm$ 16.1	62.7 $\pm$ 17.1	58.0 $\pm$ 19.8	0.28
Sex (% men)	15 (42.9%)	7 (50%)	14 (50%)	23 (52.3%)	0.87
ICU (%)	19 (54.3%)	7 (50%)	22 (78.6%)	33 (75%)	
Baseline creatinine (mg/dl)	0.7 $\pm$ 0.4	0.9 $\pm$ 0.3	0.8 $\pm$ 0.4	1.0 $\pm$ 0.7	0.06
Scoring systems					
APACHE II score	16.4 $\pm$ 7.7	21.8 $\pm$ 8.4	21.8 $\pm$ 8.2	27.1 $\pm$ 9.4	<0.001[#]
APACHE II prob. of death (%)	28.7 $\pm$ 20.8	42.8 $\pm$ 26.2	42.1 $\pm$ 22.9	58.5 $\pm$ 26.2	<0.001[@]
SAPS II score	33.8 $\pm$ 12.9	42.9 $\pm$ 20.2	43.2 $\pm$ 16.02	54.1 $\pm$ 18.9	<0.001[#]
SAPS II prob. of death (%)	20.3 $\pm$ 18.7	34.7 $\pm$ 31.9	33.4 $\pm$ 26.9	51.5 $\pm$ 31.1	<0.001[@]
SAPS III score	54.0 $\pm$ 14.5	64.0 $\pm$ 18.3	70.0 $\pm$ 18.2[#]	74.4 $\pm$ 17.9	<0.001[$]
SAPS III prob. of death (%)	31.9 $\pm$ 24.3	45.6 $\pm$ 28.9	53.5 $\pm$ 26.4[#]	59.3 $\pm$ 25.2	<0.001[$]

[#] $p < 0.05$ for C vs. F
[@] $p < 0.05$ for C vs. F, I vs. F
[$] $p < 0.05$ for C vs. I, C vs. F

group was 62.7 years, and of the Failure group was 58.0 years (p = 0.28). The percentage of males among studied groups was not different. (p = 0.87). Baseline serum creatinine were 0.7 ± 0.4 mg/dl, 0.9 ± 0.3 mg/dl, 0.8 ± 0.4 mg/dl, 1.0 ± 0.7 mg/dl (p = 0.06) in no AKI, Risk, Injury, and Failure group. There was no significant difference among study groups for demographic variables.

General scoring systems

As expected, the patients in failure group (RIFLE-F) had greater APACHE II and SAPS II scores than those in no AKI group (RIFLE -0) (p < 0.001). Like the scores, estimated probabilities of death predicted by APACHE II and SAPS II were significantly higher in RIFLE-F group compared with RIFLE-I and RIFLE-0 groups (p < 0.05, and p < 0.001, respectively). Mean SAPS III score and its predicted mortality were significantly higher for patients with RIFLE-F and RIFLE-I than those with RIFLE-0 (Table 2).

Primary outcome

Patients with maximum RIFLE class R, class I and class F had hospital mortality rates of 35.7%, 35.7% and 65.9%, respectively, compared with 20% for patients without acute kidney injury (p < 0.05) (Table 3). We also found that, the unadjusted odds ratios (95% confidence interval) for hospital mortality for acute kidney injury and RIFLE class R, class I and class F were, respectively, 2.2 (0.5-8.7, p = 0.25), 2.2 (0.7-6.8, p = 0.17) and 7.7 (2.7-21.8, p < 0.001). In terms of AKI, patients with AKI had OR of hospital mortality of 4.2 (95% CI 1.6, 10.6, p = 0.003) than those without AKI.

Secondary outcome

There was the highest rate of renal replacement therapy (RRT) in the failure group (52.3%) as compared with the no AKI group (5.7%), and the injury group (7.1%) (Table 3). We can't evaluate the Risk group because there was no RRT in this group. Patients with maximum RIFLE class R, class I and class F had median hospital lengths of stay of 14.5 days, 12.5 days and 17 days, respectively, compared with 16 days for patients without acute kidney injury (p = 0.68) (Table 3).

Discussion

We conducted a study of Thai patients admitted in a teaching hospital and validated the ability of the RIFLE criteria, a recently published consensus definition of ARF, to predict hospital mortality, the need of RRT, and length of hospital stay. The RIFLE classification predicted the probability of making the need for RRT, and in-hospital mortality. It did not, however, predict the length of hospital stay. We found that acute kidney injury, defined by the RIFLE classification was associated with an increased risk for hospital mortality and renal replacement therapy compared with those who never developed acute kidney injury. We also found that in our patients the presence of such renal impairment was strongly predictive of an increased odds ratio (OR) for death, especially in the RIFLE-F group.

RIFLE provided a well-balanced classification system for determination of patients with different severity of acute kidney injury. It provided even more sensitive criteria for AKI and more specific criteria than some traditional criteria, such as a 25% increase of serum creatinine or need for RRT. We found that small decreases in kidney function are important. Similar to previous studies, Levy et al[15] found that a 25% increase of serum creatinine after administration of radio contrast was associated with a worse outcome compared with those who did not experience a 25% or

Table 3. Outcomes for all patients and for patients classified according to RIFLE classification

	Mean ± SD or number (%)				
	No AKI (C) (n = 35)	Risk (R) (n = 14)	Injury (I) (n = 28)	Failure (F) (n = 44)	p-value
Peak serum creatinine (mg/dl)	0.8 ± 0.5	1.6 ± 0.8	2.0 ± 1.1	4.8 ± 2.4	<0.001
Renal replacement therapy (%)	2 (5.7)	0 (0)	2 (7.1)	23 (52.3)	<0.001[@]
Hospital LOS (days): median (IQR)	16 (8-27)	14.5 (8-46)	12.5 (9-23.5)	17 (8-32.5)	0.68
Hospital mortality (%)	7 (20.0)	5 (35.7)	10 (35.7)	29 (65.9)□	<0.001
OR (95% CI)	1	2.2 (0.5, 8.7)	2.2 (0.7,6.8)	7.7 (2.7,21.8)	

[@] p < 0.05 for C vs. F, I vs. F

greater increase. Chertow et al[16] defined hospital acquired acute kidney dysfunction as an increase of serum creatinine of above 0.3 mg/dl and found that this was independently associated with mortality. In a cohort study of Lassnig et a[17], patients who underwent cardiac surgery, that developed acute kidney dysfunction, defined as an increase of serum creatinine of 0.5 mg/dl or above or a decrease greater than 0.3 mg/dl, were associated with worse survival.

Not surprisingly, the occurrence of acute kidney injury and maximum RIFLE class F was associated with increased severity of general scoring systems (APACHE II, SAPS II, and SAPS III). It may be because all scoring systems included renal dysfunction determined by plasma creatinine as a powerful physiologic variable[12-14]. The ICU patients are sicker, older, and have more co-morbidities. Acute kidney injury mostly occurs as part of multi-organ dysfunction syndrome in critically ill patients.

Unlike the recent studies[10,18,19], there was no significant difference of length of hospital stay in all groups; this may be due to the small number of patients in the present study.

The present study has a number of limitations. First, the population was relatively small, and reflective of a single center. Next, we couldn't estimate the incidence of AKI. Thirdly, like previous studies[20-22], we used the GFR criterion only because the urine output criteria had some limitations in our population, although their use is common practice worldwide in AKI patients, with the reported incidences of use of 59-70%[23,24]. The urine output criteria can only be accurately assessed in patients with a urinary catheter. Thus, the use of urine output criteria may be limited to the ICU cohort of our patients. These data may, however, also prompt us to reconsider and improve the rigor by which urine output is currently collected and measured in most areas outside the ICU. The final limitation is that, we didn't follow up long term outcomes, such as 60-day or 90-day mortality.

Conclusion

Applying the new ADQI group classification system (RIFLE) helped us establish that patients with AKI had the worst prognostic factors for patient and kidney survival. ARF should be managed as early as possible in an ICU setting because it is an independent risk factor for death. That mortality was much greater in RIFLE category failure when compared with other groups and may support previous research showing that an early start of RRT can be beneficial. Thus, renal protection strategies should be implemented early in the ICU.

RIFLE represents a superior model to apply to all patients with ARF in the critically ill patient in the ICU's and general wards. RIFLE classification can guide the timing of initiation of RRT, which may lead to improved survival. RIFLE also can assist in the prediction of prognosis of patients with ARF, which may help in the decision-making process.

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ผลทางคลินิกของภาวะไตวายเฉียบพลันในผู้ป่วยวิกฤติชาวไทยจำแนกโดยใช้ RIFLE classification

รณิษฐา รัตนะรัต, ฉัตรี หาญทวีพันธุ์, ณัฐกานต์ ตังควัฒนกุล, ไชยรัตน์ เพิ่มพิกุล

วัตถุประสงค์: *เพื่อประเมินอัตราการเสียชีวิตในโรงพยาบาลของผู้ป่วยวิกฤตซึ่งมีภาวะไตวายเฉียบพลัน (acute kidney injury, AKI) โดยใช้ RIFLE Criteria ซึ่งเป็นคำจำกัดความใหม่สำหรับภาวะไตวายเฉียบพลัน*

วัสดุและวิธีการ: *คณะผู้นิพนธ์ได้ทำการศึกษาชนิด Cohort ในผู้ป่วยวิกฤติ 121 ราย ของภาควิชาอายุรศาสตร์ โรงพยาบาลศิริราช ตั้งแต่ พฤศจิกายน พ.ศ. 2548 - พฤศจิกายน พ.ศ. 2549 โดยแบ่งผู้ป่วยเป็นกลุ่มตามระดับ RIFLE ที่สูงที่สุด ระหว่างรับการ รักษาในโรงพยาบาล (R, I, F) รวมทั้งเก็บข้อมูลพื้นฐานผู้ป่วย อัตราการเสียชีวิตในโรงพยาบาล ระยะเวลาการรักษาตัว ในโรงพยาบาล และอัตราการรักษาทดแทนไต*

ผลการศึกษา: *ผู้ป่วยที่มีระดับ RIFLE สูงสุดที่ระดับ R, I และ F มีอัตราการเสียชีวิตในโรงพยาบาลที่ 35.7%, 35.7% และ 65.9% ตามลำดับ เทียบกับผู้ป่วยที่ไม่มีภาวะ AKI ซึ่งมีอัตราการเสียชีวิตที่ 20% โดยพบว่าผู้ป่วยซึ่งมี AKI มีอัตราการเสียชีวิตในโรงพยาบาลเป็น 4.2 เท่า (OR 4.2, 95% CI 1.6-10.6, p = 0.003) เทียบกับกลุ่มที่ไม่มี AKI โดยอัตราการเสียชีวิตมีค่าเพิ่มขึ้นสูงสุดในกลุ่ม F (Failure) (OR = 7.7, 95% CI 2.7-21.8, p < 0.001) สำหรับการรักษาทดแทนไตมีอัตราสูงสุดในกลุ่ม F (52.3%) เทียบกับกลุ่มซึ่งไม่มี AKI (5.7%) และกลุ่ม I (7.1%) (p < 0.001)*

สรุป: *ภาวะไตวายเฉียบพลันหรือ AKI ซึ่งแบ่งผู้ป่วยเป็นกลุ่ม Risk (R), Injury (I) และ Failure (F) ตาม RIFLE criteria มีความสัมพันธ์กับอัตราการเสียชีวิตในโรงพยาบาลของผู้ป่วยวิกฤติในประเทศไทย*