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EDITORIAL

Acute kidney injury classification: AKIN and RIFLE criteria in critical patients

Chan-Yu Lin, Yung-Chang Chen

Chan-Yu Lin, Yung-Chang Chen, Kidney Institute, Department of Nephrology, Chang Gung Memorial Hospital, Chang Gung University College of Medicine, Taipei 105, Taiwan, China
Author contributions: Lin CY and Chen YC contributed equally to this manuscript.
Correspondence to: Yung-Chang Chen, MD, Kidney Institute, Department of Nephrology, Chang Gung Memorial Hospital, 199 Tung Hwa North Road, Taipei 105, Taiwan, China. cyc2356@adm.cgmh.org.tw
Telephone: +886-3-3281200 Fax: +886-3-3282173
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Abstract

Acute kidney injury (AKI) is a common and serious complication in critically ill patients. The mortality rate remains high despite improved renal replacement techniques. A possible cause of the high mortality rate is that intensive care unit patients tend to be older and more debilitated than before. Pathophysiological factors associated with AKI are also implicated in the failure of other organs, indicating that AKI is often part of a multiple organ failure syndrome. Until recently, there was a lack of consensus as to the best definition, characterization, and evaluation of acute renal failure. This lack of a standard definition has been a major impediment to progress in clinical and basic research. The introduction of the risk, injury, failure, loss, and end-stage kidney disease criteria and the modified version proposed by the Acute Kidney Injury Network have increased the conceptual understanding of AKI syndrome, and these criteria have been successfully tested in clinical studies. This article reviews current findings concerning the application of these criteria for assessing epidemiology and predicting outcome in specific homogeneous critically ill patient groups.

Key words: Acute kidney injury; Extracorporeal membrane oxygenation; Cirrhosis; Sepsis; Acute respiratory distress syndrome; Intensive care unit

Peer reviewers: Manu L Malbrain, MD, PhD, Department of Intensive Care, ZNA Stuivenberg, Lange Beeldekensstraat 267, 2060 Antwerpen, Belgium; Xu-Lin Chen, Professor, Department of Burns, The fiirst affiliated hospital of Anhui Medical University, 218 Jixi Road, Hefei 230022, Anhui Province, China; Hideo Inaba, Professor, Department of Emergency Medical Science, Kanazawa University Graduate School of Medicine, 13-1 Takaramachi, Kanazawa 920-8641, Japan

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INTRODUCTION

Acute kidney injury (AKI) is well recognized for its impact on intensive care unit (ICU) patient outcomes[1-3]. In an international survey, more than 200 different definitions of AKI were reported[4]. The numerous definitions cause clinical confusion and complicate data comparison[5,6]. The risk of renal failure, injury to the kidney, failure of kidney function, loss of kidney function, and end-stage renal failure (RIFLE) criteria was published by the Acute Dialysis Quality Initiative group in 2004, in an attempt to standardize AKI research[1]. It classified AKI into three categories (risk, injury, and failure) according to the status of serum creatinine (SCr) and urine output (UO) (Table 1).

In 2007, the Acute Kidney Injury Network (AKIN) group proposed a modified version of the RIFLE criteria. In AKIN stage-1 (analogous to RIFLE-Risk), a smaller change within 48 h in SCr of over 0.3 mg/dL (≥ 26.2 μmol/L) was suggested as the threshold for AKI

(Table 1). Additionally, patients receiving renal replacement therapy were re-classified as AKIN stage-3 (RIFLE-Failure). Finally, the loss and end-stage kidney disease categories were eliminated in the AKIN classification[7].

To date, the use of the consensus definitions of AKI (RIFLE and AKIN) in the literature has increased substantially[8]. Both classifications have been proven to be useful for diagnosing and classifying the severity of AKI in critical patients. This study reviews their use and validation in specific diagnostic groups.

PATIENTS ON EXTRACORPOREAL MEMBRANE OXYGENATION

Extracorporeal membrane oxygenation (ECMO) is effective in treating severe, reversible myocardial dysfunction (e.g., myocarditis, cardiomyopathy, or postoperative cardiogenic shock) and for providing a bridge to another treatment modality. AKI developing during ECMO is associated with very poor outcome[9,10], possibly due to accumulated extravascular fluid causing interstitial overload, impaired oxygen transport through tissues, and subsequent organ dysfunction, particularly of the heart, lungs, and brain[11,12].

Lin *et al*[9] retrospectively applied the RIFLE criteria to evaluate forty-six critically ill patients treated by ECMO, most of whom had postcardiotomy cardiogenic shock. The RIFLE was determined only during the first day of ECMO support. A progressive and significant increase in mortality was associated with increasing RIFLE categories among all patients.

The authors further retrospectively reviewed the medical records of seventy-eight critical ill patients on ECMO support[10]. The RIFLE criteria classified 78.2% of the patients as having AKI. Multivariate analysis indicated that acute physiology, age, chronic health evaluation (APACHE) IV and RIFLE classification had independent prognostic significance.

Chen *et al*[13] retrospectively evaluated the outcomes of 102 patients treated with ECMO and identified the relationship between prognosis and AKIN scores obtained at pre-ECMO support (AKIN0-h), and at 24 h (AKIN24-h) and 48 h (AKIN48-h) post-ECMO support. The overall mortality rate was 57.8%. The AKIN0-h, AKIN24-h, and AKIN48-h scoring systems also had excellent discrimination power according to analysis of areas under the receiver operating characteristic curves (AUROC). Furthermore, multiple logistic regression analysis indicated that AKIN48-h, age, and Glasgow Coma Scale score on the first day of ICU admission were independent risk factors for hospital mortality. During ECMO support, the AKIN48-h scoring system proved to be a reproducible evaluation tool with excellent prognostic abilities for these patients.

CRITICALLY ILL CIRRHOTIC PATIENTS

A feature of liver cirrhosis is the disturbed systemic circulation characterized by marked arterial vasodilatation occurring principally in the splanchnic circulation. These disturbances may reduce total peripheral vascular resistance and arterial pressure and cause a secondary increase in cardiac output. These abnormalities can cause major cirrhotic complications such as severe liver damage with jaundice, coagulopathy, hepatic encephalopathy, hepatorenal syndrome, hepatocardiac syndrome, and hepatopulmonary syndrome. Renal failure is the most clinically relevant of these conditions as its appearance generally indicates very poor prognosis[14-16].

As demonstrated in a previous prospective study performed by Jenq *et al*[17], the predictors of RIFLE criteria and sequential organ failure assessment (SOFA) score were independently associated with hospital mortality in 134 cirrhotic patients admitted to the ICU. Progressive and significantly elevated mortality correlated with increasing RIFLE criteria severity among all patients. The RIFLE criteria classified 60.4% of ICU cirrhotic patients with varying severity of AKI.

In order to identify specific predictors of hospital mortality in critically ill cirrhotic patients with AKI, Fang *et al*[18] evaluated 111 critically ill cirrhotic patients with AKI (RIFLE-R, I, or F) or a rise in SCr level over 1.5 mg/dL (132.6 μmol/L) using prospectively collected data. Mean arterial pressure (MAP), serum bilirubin, acute respiratory failure, and sepsis on the first day in ICU were significantly related to prognosis. The best Youden index yielded cutoff points of 80 for MAP (in mmHg) and 80 for serum bilirubin (in μmol/L) (or 4.7 mg/dL), and indicated acute respiratory failure and sepsis. A simple model for mortality is developed on the basis of these four readily available parameters on day 1 of ICU admission. The new score (MBRS score: MAP + bilirubin + respiratory failure + sepsis) displays an excellent AUROC (0.898 ± 0.031, $P < 0.001$). The mortality rate exceeds 90% when the MBRS score is 2 or higher.

Moreover, Tu *et al*[19] prospectively evaluated 202 consecutive cirrhotic patients admitted to the ICU during a 2-year period and revealed AKIN, SOFA and the model for end-stage liver disease (MELD) scores showing good discriminative power in predicting hospital mortality in cirrhotic patients admitted to the ICU. The AKIN scoring system proved to be a reproducible evaluation tool with excellent prognostic abilities for these patients.

SEVERE SEPSIS AND SEPTIC SHOCK

The high incidence of sepsis and associated mortality risk in ICU patients are constant concerns[20,21]. Sepsis is also a well-known risk factor for AKI; 35%-50% of AKI cases in ICUs are attributable to sepsis[18,22,23]. Severe sepsis and septic shock are defined according to modified the American College of Chest Physicians and Society of Critical Care Medicine consensus criteria[24]. Patients with proven or suspected infection, two or more systemic inflammatory response syndrome criteria and an infection-induced organ dysfunction are classified as having severe sepsis.

Table 1 Risk of renal failure, injury to the kidney, failure of kidney function, loss of kidney function, and end-stage renal failure and Acute Kidney Injury Network classification schemes for acute kidney injury

	GFR criteria	Urine output criteria
RIFLE (an acute rise in SCr over 7d)		
Risk	Increase in SCr ⩾ 1.5 × baseline or decrease in GFR ⩾ 25%	UO < 0.5 mL/kg per hour × 6 h
Injury	Increase in SCr ⩾ 2.0 × baseline or decrease in GFR ⩾ 50%	UO < 0.5 mL/kg per hour × 12 h
Failure	Increase in SCr ⩾ 3.0 × baseline or SCr ⩾ 4.0 mg/dL (354 μmol/L) or decrease in GFR ⩾ 75%	UO < 0.3 mL/kg per hour × 24 h or anuria × 12 h
Loss	Complete loss of kidney function > 4 wk	
ESKD	End stage renal disease (> 3 mo)	
AKIN (an acute rise in SCr within 48 h)		
Stage 1	Same as RIFLE-Risk plus increase in SCr ⩾ 0.3 mg/dL (⩾ 26.4 μmol/L)	Same as RIFLE
Stage 2	Same as RIFLE-Injury	
Stage 3	Same as RIFLE-Failure plus initiation of RRT	

AKIN: Acute Kidney Injury Network; ESKD: End-stage kidney disease; GFR: Glomerular filtration rate rate; RIFLE: Risk of renal failure, injury to the kidney, failure of kidney function, loss of kidney function, and end-stage renal failure; RRT: Renal replacement therapy; SCr: Serum creatitine; UO: Urine output.

Septic shock is diagnosed when the systolic arterial blood pressure remains < 90 mmHg or shows a reduction of > 40 mmHg from baseline, despite adequate volume resuscitation, in the absence of other causes for hypotension[25].

Chen *et al*[26] studied a total of 121 sepsis patients admitted to the ICU using prospectively collected data. Mortality of these patients was significantly increased as RIFLE score increased. Septic shock, RIFLE criteria, and number of organ system failures on the first day of ICU admission were independent predictors of hospital mortality according to multiple logistic regression analysis. The RIFLE criteria classified 56.2% of ICU septic patients with varying severity of AKI. Excluding patients who died within 6 mo, the percentage of AKI patients who achieved full recovery of renal function was very high (85%). Of the few studies reporting renal recovery in AKI patients, most indicated that patients usually recover adequate renal function[26,27].

Although RIFLE classification was independently predictive of mortality, the leading causes of death associated with AKI were non-renal complications, typically those related to multi-organ dysfunction. During septic shock, global tissue hypoxia caused by imbalance between systemic oxygen delivery and oxygen demand resulted in renal tubular necrosis, multiple organ failure, and increased mortality[28].

ACUTE RESPIRATORY DISTRESS SYNDROME

Acute respiratory distress syndrome (ARDS) is commonly diagnosed in ICUs and is frequently associated with AKI. The clinical definition of ARDS is the acute onset of bilateral pulmonary infiltrates, a ratio of arterial partial pressure of oxygen (PaO_2) to fraction of inspired oxygen (FiO_2) of ⩽ 200 mmHg, and pulmonary artery occlusion pressure ⩽ 18 mmHg or no evidence of left atrial hypertension[29]. Numerous risk factors, such as pneumonia, sepsis, and aspiration, are associated with ARDS onset. Although recent reports reveal improving mortality rates in ARDS patients[30,31], morbidity and mortality are still high.

Using retrospectively collected data, Lin *et al*[32] earlier reported that a maximum RIFLE (RIFLEmax) score on ICU days 1 and 3 and on the day of open lung biopsy (OLB) improves the accuracy of outcome prediction in ARDS patients undergoing OLB. To compare the predictive value of outcome scoring systems (APACHE IV, earlier APACHE models, SOFA, RIFLE criteria, Acute Lung Injury score) the authors further retrospectively abstracted data from the medical records of 135 critically ill ARDS patients[33]. Overall mortality rate was 65%. Forward conditional logistic regression identified APACHE IV, alveolar-arterial O2 tension difference, age, sepsis, and RIFLEmax score on ICU days 1 and 3 to be independent predictors of hospital mortality. The APACHE IV score and RIFLEmax score were predictors of hospital mortality in ARDS patients, with APACHE IV demonstrating good prognostic accuracy.

The ARDS patient group represented a population with a high risk of AKI. Clearly, significant crosstalk occurs between the lung and other organs. Ischemia/reperfusion injury to the kidney increases pulmonary vascular permeability[34,35]. Furthermore, ventilator-associated lung injury causes AKI in animal models[36]. Regarding the effect of ARDS on the kidney, mechanical ventilation can induce acute tubular necrosis leading to AKI[37]. In addition, the harmful effects of mechanical ventilation are exacerbated by comorbidities. Renal blood flow is further compromised by a reduced cardiac output, resulting from a high intrathoracic pressure. Moreover, the impact of biotrauma is not limited to the lungs and may cause a systemic inflammatory reaction. Sepsis may increase the severity of these effects. This series of events probably reflects a multifactorial process that can eventually cause AKI.

Of note, intra-abdominal pressure (IAP) has recently been included in the consensus statement as the possible

missing link explaining deterioration of renal function in critically ill patients[38,39]. IAP is an independent risk factor for AKI development and may also explain the cardiorenal syndrome[40-43]. Dalfino *et al*[44] put IAP into relation with RIFLE criteria by showing intra-abdominal hypertension to be an independent predictive factor of acute renal failure, defined as failure class of RIFLE criteria[45,46].

COMPARISON OF AKIN AND RIFLE CRITERIA IN GENERAL ICU

The few studies[47,48] that have compared the AKIN and RIFLE criteria have revealed no substantial differences. Chang *et al*[49] retrospectively investigated 291 critically ill patients and compared performance of the RIFLE and AKIN criteria for diagnosing and classifying AKI and for predicting hospital mortality. Overall mortality rate was 60.8%. Increased mortality was progressive and significant based on the severity of AKIN and RIFLE criteria. The AKIN and RIFLE scoring systems displayed good AUROC (0.720 ± 0.030, P = 0.001; 0.738 ± 0.030, P = 0.001, respectively). Compared with RIFLE criteria, this study indicated that the AKIN classification does not improve the sensitivity and accuracy of outcome prediction in critically ill patients.

REVIEW OF CLINICAL LITERATURE ON AKI AS DEFINED BY THE RIFLE AND AKIN CRITERIA

Ricci *et al*[50] published a systematic review of 24 studies. The majority of the studies looked at patients in general or specialized ICU. Most studies were retrospective in design, and used only the creatinine/GFR criterion. In only 12% of the analyzed population were the creatinine and UO criteria used together. The analysis of pooled data showed a stepwise increase in relative risk for death with increasing AKI severity (Risk, 2.40; Injury, 4.15; Failure, 6.37, with respect to non-AKI patients)[50].

Generally speaking, studies that have used the AKIN criteria rather than the RIFLE criteria did not seem to show any improvement in the sensitivity, robustness and predictive ability in the definition and classification of AKI[51]. The RIFLE and AKIN criteria can detect AKI with high sensitivity and high specificity and describe different severity levels that aim to predict the prognosis of affected patients. They are easy to use in a variety of clinical and research settings, but have several limitations. Both utilize an increase in SCr level from a hypothetical baseline value and a decrease in UO, but these surrogate markers of renal impairment manifest relatively late after injury has occurred and do not consider the nature or site of the kidney injury. New biomarkers such as neutrophil gelatinase-associated lipocalin, interleukin-18, kidney injury molecule-1 and cystatin C have shown promise for early diagnosis and prediction of the prognosis of AKI. As more data become available, they could be incorporated into improved definitions or criteria for AKI in the future[51-53].

CONCLUSION

The RIFLE and AKIN criteria have increased the conceptual understanding of AKI syndrome. They have been successfully tested in clinical studies and used to predict the prognosis of critical patients with AKI. Compared with RIFLE criteria, AKIN criteria do not improve the sensitivity and ability to predict outcome in critically ill patients according to present data.

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