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

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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 of kidney function, and end-stage renal failure (RIFLE) criteria was published by the Acute Kidney Injury Network (AKIN) in 2007, in an attempt to standardize AKI research. It classified AKI into three categories (risk, injury, and failure) according to the status of serum creatinine (SCr) and urine output (UO) (Table 1).

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

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INTRODUCTION

Acute kidney injury (AKI) is well recognized for its impact on intensive care unit (ICU) patient outcomes. In an international survey, more than 200 different definitions of AKI were reported. The numerous definitions cause clinical confusion and complicate data comparison. 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. 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[11-14].

Lin et al[11] 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[12] 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 discriminative 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.

**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.
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, 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[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[26,27].

### 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 (PaO₂) to fraction of inspired oxygen (FiO₂) of ≤ 200 mmHg, and pulmonary artery occlusion pressure ≤ 18 mmHg or no evidence of left atrial hypertension[28]. Numerous risk factors, such as pneumonia, sepsis, and aspiration, are associated with ARDS onset. Although recent reports reveal improving mortality rates in ARDS patients[29,30], 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[31]. 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. IAP is an independent risk factor for AKI development and may also explain the cardiorenal syndrome. Dalfino et al. 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.

COMPARISON OF AKIN AND RIFLE CRITERIA IN GENERAL ICU

The few studies that have compared the AKIN and RIFLE criteria have revealed no substantial differences. Chang et al. 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. 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).

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. 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.

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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