The Influence of Acute Kidney Injury on Acute Cardiovascular Disease

Hsing-Shan Tsai,¹ Yung-Chang Chen²,³ and Pao-Hsien Chu¹,³,⁴

Acute kidney injury (AKI) is an important issue in the management of acute cardiovascular diseases. The risk, injury, failure, loss of kidney function, and end-stage renal failure (RIFLE) criteria, and acute kidney injury network (AKIN) criteria have been proposed to stage and predict the outcomes of patients with AKI. In this article, we review AKI in the context of a variety of acute cardiovascular diseases, e.g., acute myocardial infarction (AMI), myocarditis, aortic dissection, and post-cardiotomy cardiogenic shock. For earlier detection of AKI, numerous biomarkers have been proposed and Cystatin C has been shown to have predictive value for AKI in patients with AMI.

Key Words: Acute cardiovascular disease • Acute kidney injury

INTRODUCTION

Acute kidney injury (AKI) is characterized by the rapid loss of renal function, resulting in a number of complications including fluid imbalance, metabolic acidosis, and uremia. The causes of AKI are often categorized into pre-renal, renal, and post-renal. AKI is most commonly defined according to the risk, injury, failure, loss of kidney function, and end-stage renal failure (RIFLE) or acute kidney injury network (AKIN) criteria. As shown in Table 1, the RIFLE criteria classifies AKI based on the magnitude of elevation in either serum creatinine or urine output.¹ The AKIN criteria is an alternative definition of AKI using a simplified version of the RIFLE criteria (Table 1).

AKI frequently develops following rapid hemodynamic changes that occur in cardiovascular diseases. Cardiorenal syndrome (CRS) is the term used to define a condition characterized by renal failure and heart failure. CRS type 1 is characterized by the development of AKI following acute cardiac illness, especially acute heart failure.² This article reviews the interaction between cardiovascular disease and renal failure, with a focus on specific patient subgroups.

Acute myocardial infarction

Acute myocardial infarction (AMI) is defined as myocardial ischemia accompanied by myocardial injury. AKI may occur following rapid hemodynamic changes due to acute coronary syndrome. Previous studies have reported the importance of diagnosing renal dysfunction upon admission for an AMI, as well as the effect of AKI among hospitalized patients with an AMI.

Using RIFLE criteria, Hsieh et al. evaluated the impact of AKI severity on 613 AMI patients during the first week after hospitalization in Taiwan (Table 2).³ Independent of initial renal dysfunction on admission, AKI severity predicted the 2-year mortality in AMI patients who survived until discharge. The results of the study by Hsieh et al. are compatible with those of studies conducted in the United States, Italy, Israel, Brazil, Korea, Japan, and the multi-national cooperative cardiovascular...
The effect of AKI is also notable in the subgroup of patients with ST-segment elevation myocardial infarction (STEMI). The impact of AKI on after-AMI mortality was also noted during 4 years of follow-up in another study; AKI occurred in about 30-40% of patients with AMI. AKI during an AMI has been found to be strongly associated with long-term mortality. Proposed factors which may predict AKI after an AMI include age, Killip class, diabetes, and left ventricular systolic dysfunction.

Heart failure with acute decompensation

While no study has focused on the association between AKI and acute-decompensated heart failure in Taiwan, the importance of CRS type 1 has been studied. The pathophysiological mechanism underlying CRS type 1 is considered to be multifactorial. In China, Zhou et al. studied 1005 patients hospitalized for acute decompensated heart failure and found that pre-existing chronic kidney disease and AKI, as classified by RIFLE criteria, predicted in-hospital mortality. Similarly, Shirakabe et al. studied the 1-year and 2-year mortality rates of patients who were admitted to the intensive care unit (ICU) for acute heart failure. When AKI was defined using the AKIN classification, the incidence of AKI in patients with acute decompensated heart failure was above 70%. Risk of mortality during the ICU stay and in-hospital mortality were also higher among patients with advanced AKIN stage, especially stage 3. The development of AKI, as classified by RIFLE criteria, predicted both the 1-year and 2-year mortality. When AKI was defined using the AKIN classification, the incidence of AKI in patients with acute decompensated heart failure was above 70%. Risk of mortality during the ICU stay and in-hospital mortality were also higher among patients with advanced AKIN stage, especially stage 3.

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<tr>
<th>Table 1. RIFLE and AKIN classification schemes for AKI</th>
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<td><strong>GFR criteria</strong></td>
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<td><strong>RIFLE: an acute rise of SCr over 7 days</strong></td>
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<tr>
<td>Risk</td>
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<td><strong>Loss</strong></td>
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<td><strong>ESKD</strong></td>
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<td><strong>AKIN: an acute rise of SCr within 48 h</strong></td>
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<td>Stage 1</td>
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<td>Stage 3</td>
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AKI, acute kidney injury network; ESKD, end-stage kidney disease; GFR, glomerular filtration 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 creatinine; UO, urine output.

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<th>Table 2. Acute kidney injury following acute cardiac illness</th>
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<td><strong>Number</strong></td>
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<tr>
<td>AMI</td>
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<tr>
<td>Acute myocarditis</td>
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<td>Post aortic dissection surgery</td>
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<td>ECMO</td>
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AKI, acute kidney injury; AKIN, acute kidney injury network; AMI, acute myocardial infarction; CCU, coronary care unit; ECMO, extracorporeal membrane oxygenation; RIFLE, risk of renal failure, injury to the kidney, failure of kidney function, loss of kidney function, and end-stage renal failure.

* 2-year mortality; † 1-year mortality; ‡ 6-month mortality; § RIFLE; ¶ AKIN.
suggest that prevention, reduction, and adequate treatment of AKI may improve the mortality risk associated with heart failure.17-20

Myocarditis

Myocarditis is broadly defined as inflammation of the myocardium, and can lead to multiple organ failure in its most severe form. In a sample of 101 patients with acute myocarditis, Yang et al. found an AKI rate of 59% by 48 hours after hospitalization (Table 2).16 Additionally, a high mortality rate was noted in patients with AKIN stage 3. Sequential Organ Failure Assessment (SOFA) score is one of the ICU scoring systems used to evaluate a patient’s status, and is based on a 6-organ dysfunction score.21 A high SOFA score on admission was also associated with high in-hospital mortality risk. The retrospective study by Yang et al. was the only one conducted in recent years that examined the effect of AKI on myocarditis.16

Post aortic dissection surgery

Type A and complicated type B aortic dissections are surgical emergencies. Tasi et al. studied the 1-year survival of 268 patients with aortic dissection (Table 2).22 The incidence of AKI following aortic dissection in this and another similar study was between 53% and 54%.22,23 Additionally, AKI was an independent clinical predictor of mortality in these patients. Indeed, the survival rate post-surgery could be predicted by the RIFLE AKI criteria.22 Hypertension, blood culture documented sepsis, lower limb malperfusion, long bypass duration (>180 minutes), and preoperative serum creatinine level were proposed as independent risk factors for the development of AKI following aortic dissection repair.22,23

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 provides a bridge to another treatment modality. AKI which develops during ECMO is associated with a very poor outcome.24,25 This is possibly due to accumulated extravascular water resulting in interstitial overload, impaired oxygen transport through tissues, and subsequent organ dysfunction, particularly of the heart, lungs, and brain.26,27 Lin et al. retrospectively applied RIFLE criteria during the first day of ECMO support to evaluate 46 critically ill patients treated by ECMO, most of whom had post-cardiotomy cardiogenic shock (Table 2).25 A progressive and significant increase in mortality was associated with increasing RIFLE categories among all patients. Lin et al. further retrospectively reviewed the medical records of 78 critical ill patients on ECMO support, and RIFLE criteria classified 78.2% as having AKI.24 Multivariate analyses indicated that acute physiology, age, acute physiology and chronic health evaluation (APACHE) IV, and RIFLE classification had independent prognostic significance.

Chen et al. 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-hour), at post-ECMO support 24 hours (AKIN24-hour), and at post-ECMO support 48 hours (AKIN48-hour) (Table 2).28 The overall mortality rate was 57.8%, and the AKIN0-hour, AKIN24-hour, and AKIN48-hour scoring systems exhibited excellent discrimination power according to areas under the receiver operating characteristic curve (AUROC) analysis. Furthermore, multiple logistic regression analysis indicated that AKIN48-hour, 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-hour scoring system proved to be a reproducible evaluation tool with excellent prognostic abilities for these patients.

When AKI occurs in these critically ill ECOM patients, continuous arteriovenous hemofiltration (CAVH) is indicated. Tsai et al. reviewed the data of 123 patients receiving ECMO and CAVH at an ICU who developed cardiogenic shock and oliguria.14 The APACHE II score and organ system failure (OSF) score, 2 ICU scoring systems proposed by Knaus, showed adequate predictive ability in detecting a high risk of in-hospital mortality.29,30 Indeed, the 6-month survival rate was significantly different between patients with an OSF score > 4 versus those with a score ≤ 4.

Biomarkers for early prediction of AKI in cardiovascular disease

After reviewing past studies, it becomes evident that the presence and the severity of AKI play an impor-
tant role in the clinical course of numerous acute cardiovascular diseases. Many studies have attempted to identify a biomarker that could predict the occurrence of AKI in patients with acute cardiovascular diseases. Chen et al. analyzed a number of potential biomarkers including neutrophil gelatinase-associated lipocalin (NGAL), interleukin-18 (IL-18), and Cystatin C (CysC) in 150 patients on the first day after admission to a cardiac intensive care unit (Table 2). The most common cause of cardiac ICU admission was AMI. The results indicated that serum CysC was a significant predictor of AKI development, while NGAL and serum IL-18 were the strongest correlates of 6-month mortality. Hsiao et al. studied 96 patients with AMI verified by coronary angiography, and reported an AKI rate of 18% within 48 hours. Multivariate analysis revealed that thrombolysis in myocardial infarction (TIMI) flow and a serum CysC level over 1364 mg/L were important predictors of AKI. In another study of 100 post-AMI patients in an ICU, baseline CysC was superior to baseline serum creatinine in predicting the incidence of AKI.

Prophylactic hemodialysis

AKI is a significant predictor of morbidity and mortality among patients with acute cardiovascular diseases, and the treatment and prevention of AKI has been studied. Since the pathophysiology of CRS type 1 is complicated, methods of AKI prevention may differ between diseases. To date, there is no conclusive evidence for the use of prophylactic hemodialysis immediately after contrast infusion for coronary angiography or percutaneous intervention.

In this section, we review the effect of prophylactic hemodialysis. Although many papers have studied the effect of prophylactic hemodialysis, overall the results are inconclusive. In 2004, Hsieh et al. reviewed the clinical course of patients with a serum creatinine level between 2.5 and 5.5 mg/dl who underwent coronary angiography or intervention, and found that prophylactic hemodialysis failed to affect the 1-year outcome. In 2007, Lee et al. reported the results of a randomized control trial conducted to study the effect of prophylactic hemodialysis after coronary angiography or percutaneous coronary intervention in 82 patients with a mean baseline serum creatinine of 4.9 mg/dl. The control group had a > 1 mg/dl increase in creatinine from baseline in comparison to the intervention group (37% vs. 5%, respectively; p < 0.01). Additionally, more patients in the control group as compared to the intervention group needed long-term dialysis (13% vs. 0%, respectively). The sample size of the study (82 patients), however, was relatively small. In general, intensive monitoring, optimizing volume status, the use of diuretics, and minimizing contrast volume are the most effective way to reduce the risk of AKI. The best way to protect renal function may be through the avoidance of risk factors.

CONCLUSIONS

The presence of AKI after acute cardiovascular disease is a significant risk factor for in-hospital and long-term mortality. This article provided a concise review of CRS type 1 in different acute cardiovascular diseases. As classified according to the RIFLE criteria, AKI severity is a direct predictor of in-hospital and 2-year mortality among AMI patients. The use of RIFLE and AKIN criteria can also help predict mortality among patients with acute decompensated heart failure. AKI also influences the mortality risk associated with myocarditis. In addition, AKI severity predicts 1-year mortality after emergent aortic dissection repair. APACHE II and OSF scores are alternative predictive tools used for very critically-ill patients with cardiogenic shock and oliguria. Although a variety of biomarkers for AKI have been proposed in patients with acute cardiovascular diseases, CysC appears to be the most sensitive. The pathophysiology of CRS type 1 is complicated, and its management remains a challenge.

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AKI and CVD (Acute Kidney Injury and Cardiovascular Disease)