Acute kidney injury in adult postcardiotomy patients with extracorporeal membrane oxygenation: evaluation of the RIFLE classification and the Acute Kidney Injury Network criteria

Xiaolei Yan, Shijie Jia, Xu Meng, Ping Dong, Ming Jia, Jiuhe Wan, Xiaotong Hou

Abstract

Introduction: Acute kidney injury (AKI) is one of the major complications in adult postcardiotomy patients on extracorporeal membrane oxygenation (ECMO) support. The RIFLE (the Risk of renal failure, Injury to the kidney, Failure of kidney function, Loss of kidney function and End-Stage Kidney Disease) classification and the Acute Kidney Injury Network (AKIN) criteria were proposed to identify and classify AKI recently. This study aims to evaluate the occurrence of AKI during the initial 48 h of ECMO support by using both the RIFLE classification and the AKIN criteria, and to determine which scoring tool has better capability for predicting hospital mortality of adult postcardiotomy patients with ECMO support.

Methods: From 2004 to 2008, 67 patients (≥18 years) who received extracorporeal membrane oxygenation support after undergoing cardiac surgery were enrolled and retrospectively evaluated. Results: The average age was 50.5 ± 13.6 years; 48 patients (72%) were male. According to the RIFLE classification and the AKIN criteria, the incidence of AKI during first 48 h after receiving ECMO support was 81% and 85%, respectively. The overall mortality was 51% and the hospital mortality was much higher among patients who received renal replacement therapy (RRT) than in patients not receiving RRT (73% vs 32%, p = 0.001). Either class-Failure for the RIFLE classification (odds ratio (OR) = 12.6, 95% confidence interval (CI) = 2.2—72.3, p = 0.005) or the Stage 3 for the AKIN (OR = 30.8, 95% CI = 3.3—287.2, p = 0.003) was found to be independently associated with the hospital mortality. The area under the receiver operator characteristic (ROC) curve for hospital mortality was 0.738 for the RIFLE classification (p = 0.001) and was 0.799 for the AKIN criteria (p < 0.001). No significant differences were found in both the incidence of AKI and the hospital mortality of AKI by using the RIFLE/AKIN criteria.

Conclusions: Acute kidney injury is a major complication and associated with high mortality in adult patients who received ECMO support after undergoing cardiac surgery. Both the RIFLE classification and the AKIN criteria have good short-term prognostic capability in these populations and either class-Failure for the RIFLE classification or the Stage 3 for the AKIN were found to be independently associated with the hospital mortality. However, it does not seem that the AKIN criteria have greater sensitivity and specificity, compared with the RIFLE classification in this study population.

Keywords: Postoperative complications; Acute kidney injury; Cardiac surgery; Extracorporeal membrane oxygenation

1. Introduction

Extracorporeal membrane oxygenation (ECMO) can provide a temporary support for postcardiotomy patients who have refractory cardiac and/or pulmonary dysfunction unresponsive to conventional treatment [1—4]. Previous studies showed a poor prognosis for adult patients with ECMO support and AKI, which is one of the major complications that contributes to a high mortality in adult patients following cardiac surgery [1,4—7].

The RIFLE (the Risk of renal failure, Injury to the kidney, Failure of kidney function, Loss of kidney function and End-Stage Kidney Disease) classification [8] and the Acute Kidney Injury Network (AKIN) criteria [9,10], which were modified from the RIFLE classification, were proposed to identify and classify AKI recently. The RIFLE classification has been widely validated and has become an acceptable, uniform and evidence-based definition for AKI, as well as demonstrated to have clinical relevance for the diagnosis of AKI, classifying the severity of AKI and for monitoring the progression of AKI whereas the AKIN criteria might need further confirmation [11—16], although in recent studies [9,17], it does not seem that the AKIN criteria improve on the ability of the RIFLE classification.

Abbreviations: AKI, acute kidney injury; 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 Disease; AKIN, Acute Kidney Injury Network; APACHE, Acute Physiology and Chronic Health Evaluation; SORF, Sepsis-related Organ Failure Assessment; GFR, glomerular filtration rate; RRT, renal replacement therapy.

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classification in predicting hospital mortality. Meanwhile, it is currently unknown whether the proposed modifications of the AKIN criteria improve the ability to identify and classify postcardiotomy adult patients with ECMO support into categories of different severity of renal injury.

Hence, this study aims to evaluate the occurrence of AKI during the initial 48 h of ECMO support by using both the RIFLE classification and the AKIN criteria and to determine which scoring tool has better capability for predicting hospital mortality of adult postcardiotomy patients with ECMO support.

2. Materials and methods

A retrospective cohort was constructed to analyse the incidence of AKI and compare the RIFLE classification with the AKIN criteria during the study period (from 2004 to 2008) in the Beijing Anzhen Hospital, Capital Medical University. A total of 67 adult patients (≥18 years) who received ECMO support after undergoing cardiac surgery were enrolled in this study. Patients were excluded if they had undergone dialysis or renal transplantation before the open-heart operation.

Demographic and clinical data were collected from the hospital records, including gender, age, type of surgery, duration of ECMO support, urine output and hospital mortality. The laboratory information was obtained from a computer database. Plasma values of creatinine, which were measured instead of serum values and evaluated to correspond to each other, were used in our hospital laboratory [18]. The baseline of creatinine concentration was the first measurement available for every patient hospitalised. Urine output was recorded hourly and plasma creatinine was measured at least once per day when the patients were on ECMO support.

The study endpoints were the day of demise or discharge from hospital.

2.1. The RIFLE classification and the AKIN criteria

The RIFLE classification system [8] was established in 2002 and offers the scoring tools to categorise and stratify a population of patients based on their glomerular filtration rate (GFR) criteria and urine output criteria. According to the RIFLE classification, patients were classified into three grades of acute renal failure (ARF) severity (the Risk of renal failure, Injury to the kidney, Failure of kidney function) and two clinical outcomes (Loss of kidney function and End-Stage Kidney Disease).

The AKIN criteria [9,10] defined three stages of AKI which were modified from the RIFLE classification. A slight increase in creatinine concentration (≥26.2 μmol l⁻¹) within 48 h, a percentage increase in serum creatinine ≥50% (1.5-fold from the baseline) or a reduction in urine output of less than 0.5 ml kg⁻¹ h⁻¹ for more than 6 h was used to define AKI and identify patients with Stage 1 of AKIN criteria. Stages 2 and 3 were identical to Injury and Failure of RIFLE classification, respectively; all patients requiring RRT for AKI were categorised into Stage 3. Two clinical outcomes (Loss, End-Stage Kidney Disease) of the RIFLE classification were removed from the AKIN criteria [9,10].

In this study, the RIFLE classification and the AKIN criteria were evaluated during the initial 48 h of ECMO support based on the worst of either glomerular filtration rate criteria or urine output criteria and recorded as RIFLE₀₄₈ h and AKIN₀₄₈ h. In addition, no patient was categorised into the two clinical outcomes for RIFLE classification.

2.2. Statistical analyses

Descriptive continuous data are expressed as mean with standard deviation or the median (interquartile range) and categorical variables are presented as the percentage of the number of cases. Normal distribution was tested by using the Kolmogorov–Smirnov test. The unpaired t-test was used to compare the means of continuous variables and normally distributed data; otherwise, the Mann–Whitney U test was used. The Pearson’s chi-square test and McNemar test were applied to test categorical data, as well as the chi-square test for trend (χ² for trend) were used to evaluate the hospital mortality according to either RIFLE classification or the AKIN criteria. Calibration of the model was evaluated by the goodness-of-fit test using the Hosmer–Lemeshow statistic. Discrimination capability was evaluated by using the area under the receiver operator characteristic (AUCoRC) curve. Data are presented as odds ratios (ORs) with 95% confidence intervals (CIs). Logistic regression models are performed to evaluate the association of each RIFLE and AKIN category/stage with hospital mortality, and data are presented as ORs with 95% CIs.

The statistical package SPSS (Version 12.0 for Windows) was used for all statistical analyses, and two-tailed p value less than 0.05 was considered statistically significant.

3. Results

The study population included 67 postcardiotomy patients receiving ECMO support from 2004 to 2008. Average age was 50.5 ± 13.6 years; 48 patients (72%) were males and 19 (28%) were females. Mean duration of ECMO support was 74.4 ± 50.4 h, and 51 patients (76%) were weaned from ECMO support successfully. The main cardiac surgical procedures were coronary artery bypass grafting (CABG) and/or valve operation in 49 patients, heart transplantation in 9 patients, congenital heart disease correction in 4 patients and other operations in 5 patients. Among all the patients, 18 need intra-aortic balloon pump (IABP) support, and 30 patients received RRT. Demographic data and clinical characteristics of all the patients are shown in Table 1.

3.1. Incidence of AKI

According to the RIFLE classification, AKI occurred in 54 patients (cumulative incidence, 81%) during the first 48 h of ECMO support, and 16% of patients were classified as having Risk, 28% having Injury and 36% having Failure (Table 2). Stratified by the AKIN criteria, the incidence of AKI during the first day was 76% (51/67); it increased to 85% (57/67) within the 48 h on ECMO support; and 19% of the patients were stratified for Stage 1, 18% for Stage 2 and 48% for Stage 3 (Table 2).
Table 1
Demographic data and clinical characteristics of hospital survivors and non-survivors.

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>All patients (n = 67)</th>
<th>Survivors (n = 33)</th>
<th>Non-survivors (n = 34)</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (year)</td>
<td>50.5 ± 13.6</td>
<td>47.6 ± 13.0</td>
<td>53.3 ± 13.8</td>
<td>NS (0.085)</td>
</tr>
<tr>
<td>Male, n (%)</td>
<td>48 (72)</td>
<td>24 (73)</td>
<td>24 (71)</td>
<td>NS (0.846)</td>
</tr>
<tr>
<td>LVEF</td>
<td>0.47 ± 0.16</td>
<td>0.44 ± 0.15</td>
<td>0.50 ± 0.16</td>
<td>NS (0.158)</td>
</tr>
<tr>
<td>IABP (yes/no)</td>
<td>18/49</td>
<td>5/28</td>
<td>13/21</td>
<td>0.033</td>
</tr>
<tr>
<td>RRT (yes/no)</td>
<td>30/37</td>
<td>8/25</td>
<td>22/12</td>
<td>0.001</td>
</tr>
</tbody>
</table>

Renal function on admission
Creatinine (μmol l⁻¹) 78.1 ± 18.5 78.7 ± 20.5 77.4 ± 16.5 NS(0.782)
Urea (mmol l⁻¹) 7.7 ± 2.6 7.7 ± 2.3 7.5 ± 2.8 NS(0.337)

Renal function on ECMO 24 h
Creatinine (μmol l⁻¹) 168.8 ± 89.2 133.8 ± 70.8 201.6 ± 93.1 0.002
Urea (mmol l⁻¹) 13.2 ± 5.6 11.9 ± 5.0 14.3 ± 6.0 0.099

Renal function on ECMO 48 h
Creatinine (μmol l⁻¹) 228.5 ± 137.5 171.8 ± 97.9 281.6 ± 149.1 0.001
Urea (mmol l⁻¹) 20.4 ± 12.5 17.4 ± 9.8 23.3 ± 14.1 0.061

ECMO support
Duration of ECMO support 74.4 ± 50.4 60.0 ± 35.8 90.4 ± 59.3 0.016
Mean of (yes/no) 51/16 33/0 18/16 <0.001
APACHE III score on ECMO 48 h 62.2 ± 18.1 53.2 ± 13.1 70.6 ± 18.3 <0.001

LVEF: left ventricular ejection fraction; NS: not significant; SD: standard deviation; ECMO: extracorporeal membrane oxygenation; APACHE: Acute Physiology and Chronic Health Evaluation.

Table 2
Incidence of AKI according to different criteria.

<table>
<thead>
<tr>
<th>RIFLE48 h classification</th>
<th>Incidence of AKI, n (%)</th>
<th>AKIN48 h criteria</th>
<th>Incidence of AKI, n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-AKI</td>
<td>13 (19)</td>
<td>Non-AKI</td>
<td>10 (15)</td>
</tr>
<tr>
<td>Risk</td>
<td>11 (16)</td>
<td>Stage 1</td>
<td>13 (19)</td>
</tr>
<tr>
<td>Injury</td>
<td>19 (28)</td>
<td>Stage 2</td>
<td>12 (18)</td>
</tr>
<tr>
<td>Failure</td>
<td>24 (36)</td>
<td>Stage 3</td>
<td>32 (48)</td>
</tr>
<tr>
<td>Any category in AKI</td>
<td>54 (81)</td>
<td>Any category in AKI</td>
<td>57 (85)</td>
</tr>
</tbody>
</table>

AKI: acute kidney injury; RIFLE: Risk of renal failure, Injury to the kidney, Failure of kidney function, Loss of kidney function and End-Stage Renal Disease; AKIN: Acute Kidney Injury Network.

Table 3
Hospital mortality according to different criteria.

<table>
<thead>
<tr>
<th>RIFLE48 h</th>
<th>Hospital mortality (%)</th>
<th>AKIN48 h</th>
<th>Hospital mortality (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-AKI</td>
<td>15</td>
<td>Non-AKI</td>
<td>10</td>
</tr>
<tr>
<td>Risk</td>
<td>27</td>
<td>Stage 1</td>
<td>23</td>
</tr>
<tr>
<td>Injury</td>
<td>63</td>
<td>Stage 2</td>
<td>42</td>
</tr>
<tr>
<td>Failure</td>
<td>71</td>
<td>Stage 3</td>
<td>78</td>
</tr>
<tr>
<td>Any category in AKI</td>
<td>59</td>
<td>Any category in AKI</td>
<td>58</td>
</tr>
</tbody>
</table>

AKI: acute kidney injury; ARF: acute renal failure; ARI: acute renal injury; ARFS: acute renal failure syndrome; SARFS: severe acute renal failure syndrome; RIFLE: Risk of renal failure, Injury to the kidney, Failure of kidney function, Loss of kidney function and End-Stage Renal Disease; AKIN: Acute Kidney Injury Network.

Although 4% more patients were identified as having any category of AKI by the AKIN criteria than by the RIFLE criteria during the first 48 h with ECMO, no statistically significant differences were found (85% vs 81%, p = 0.250).

3.2. Mortality

The overall hospital mortality was 51% (34 of 67 patients) and mortality was significantly higher for AKI patients compared with non-AKI patients defined by either the RIFLE classification or the AKIN criteria. Multiplication of hospital mortality rate was observed in 10% (non-ARF), 23% (Stage 1), 41% (Stage 2) and 78% (Stage 3) of patients based on the

Table 4
Logistic regression analysis of the risk factors for hospital mortality.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Odds ratio (95% CI)</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>RIFLE criteria (reference: non-AKI)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Risk</td>
<td>2.1 (0.3—15.4)</td>
<td>0.480</td>
</tr>
<tr>
<td>Injury</td>
<td>8.6 (1.4—51.2)</td>
<td>0.018</td>
</tr>
<tr>
<td>Failure</td>
<td>12.6 (2.2—72.3)</td>
<td>0.005</td>
</tr>
<tr>
<td>Constant</td>
<td>0.2</td>
<td>0.027</td>
</tr>
<tr>
<td>AKIN criteria (reference: non-AKI)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stage 1</td>
<td>2.7 (0.3—30.8)</td>
<td>0.424</td>
</tr>
<tr>
<td>Stage 2</td>
<td>5.1 (0.5—56.9)</td>
<td>0.182</td>
</tr>
<tr>
<td>Stage 3</td>
<td>30.8 (3.3—287.2)</td>
<td>0.003</td>
</tr>
<tr>
<td>Constant</td>
<td>0.1</td>
<td>0.037</td>
</tr>
</tbody>
</table>

AKIN: Acute Kidney Injury Network; RIFLE: Risk of renal failure, Injury to the kidney, Failure of kidney function, Loss of kidney function and End-Stage Renal Disease; 95% CI: 95% confidence interval.

a Adjusted for gender, age, creatinine on admission and urea on admission.
class-Failure for the RIFLE classification or the Stage 3 for the AKIN were found to be independently associated with the hospital mortality, after adjusting age, gender and renal function on admission (i.e., urea and creatinine). Results of ROC analysis (AuROCs and 95% CIs) were listed in Fig. 1, which confirmed the good discriminative power of both the AKIN criteria and the RIFLE classification for hospital mortality.

4. Discussion

Although surgical technique, cardiac anaesthesia, myocardial protection and intensive care have improved over the past decades, approximately 0.5—1% of all patients undergoing cardiac surgery have refractory cardiac and/or pulmonary dysfunction unresponsive to conventional treatment [1—4]. ECMO has been widely practiced in critically ill patients to provide a temporary support in recent years. However, ECMO in adults has met with less success compared with ECOM in newborns, infants or children; previous studies showed a poor prognosis for adult patients with ECMO support [1], and AKI, which is one of major clinical disorders, contributes to a high morbidity and mortality in adult postcardiotomy patients [4]. The clinical data of 67 adult patients with ECMO support following cardiac surgery are analysed and two recently proposed staging systems for AKI, that is, the RIFLE classification and AKIN criteria are evaluated in this study. Analytical results show that hospital mortality is 51%. According to either the RIFLE classification or the AKIN criteria, the incidence of AKI in this study cohort is grave, and the observations reveal that patients with AKI have a higher mortality than those without AKI.

Recently, the RIFLE classification [8], which became an acceptable, uniform and evidence-based definition for AKI, has been evaluated in many clinical studies and has been generally found to have the relevance for the diagnosis of AKI, classifying the severity of AKI, as well as having a modest predictive capability for mortality. The ability of the RIFLE classification for identifying and classifying the AKI and capability for prediction of hospital mortality were confirmed in this study. The incidence of AKI within 48 h following ECMO support was based on the RIFLE classification to the extent of 54%; each subsequent stage of AKI showed higher hospital mortality than the previous stage. This is in accordance with the previous reports in which a greater degree of kidney dysfunction was associated with greater mortality [19].

More recently, accumulating evidence suggests that even small changes in creatinine concentrations are associated with increased inpatient mortality [11, 20]. Based on these findings, the AKIN criteria, as the modification of the RIFLE classification, were proposed and defined AKI as an abrupt (within 48 h) reduction in kidney function, currently defined as an absolute increase in serum creatinine concentrations of more than or equal to 26.4 μmol l⁻¹, or a percentage increase in serum creatinine concentrations of more than or equal to 50% or a reduction in urine output of less than 0.5 ml kg⁻¹ h⁻¹ for more than 6 h, and classified as Stage 1 of the AKIN criteria. Those who are classified as having ‘Injury’ and ‘Failure’ categories map to Stages 2 and 3 of the AKIN criteria. Furthermore, Stage 3 was revised now to include any patient receiving RRT [9, 10, 21].

In a report by Lopes et al. [17], although AKIN criteria could improve the sensitivity of acute kidney injury diagnoses, it does not seem to improve on the ability of the RIFLE classification in predicting hospital mortality. Bagshaw et al. [9] used a large multicentre clinical database in their recent study and found no statistically significant differences regarding terms of incidence of AKI and mortality by either the RIFLE classification or the AKIN criteria in the first 24 h after admission. However, it is currently unknown whether proposed modifications of AKIN criteria improve the ability to identify and classify postcardiotomy adult patients with ECMO support into categories of different severity categories as regards renal injury.

Analytical results in this study revealed that the incidence of AKI was 85% and a trend was observed towards significant increase in hospital mortality according to the AKIN criteria. The discriminative power of the AKIN criteria for hospital mortality was confirmed as being similar to the RIFLE criteria by using ROC analysis. The principal aim for these new criteria amended from the RIFLE classification was to improve the sensitivity and reproducibility of the criteria for defining and classifying AKI [17]. Having compared the performance of the RIFLE and AKIN systems in adult postcardiotomy patients with ECMO support, although 4% more patients were identified as having any category of AKI by the AKIN criteria than by the RIFLE classification during the first 48 h with ECMO, unfortunately, no statistically significant differences were found. Meanwhile, no material differences in terms of hospital mortality were also proven.

The postoperative AKI has been a well-recognised problem in patients undergoing cardiac surgery, but whether it directly produces adverse clinical outcomes remains unclear [4]. Despite the considerable therapeutic progress and technolo-
gical improvement observed in recent years, the prognosis of AKI is still unfavourable [4,22]. Reported mortality rate in postcardiotomy patients with AKI necessitating renal replacement therapy remained impressively high, between 40% and 90% [11,23]. The incidence of AKI in this study was grave: 45% of the patients needed RRT and 22 died. The hospital mortality was much higher among patients who received RRT than in patients not receiving RRT (73% vs 32%, p = 0.001). Previous retrospective studies in patients with AKI following cardiac surgery revealed improved survival with earlier initiation of RRT, and showed the most important issue in AKI treatment was the diagnosis and the initiation of the RRT [24,25]. However, there is no consensus on the exact indications for RRT in terms of the RIFLE/AKIN criteria [11]. The present study only confirmed patients with class-Failure for RIFLE classification or Stage 3 for AKIN criteria. The patients incur a significant increased risk of hospital mortality compared with those who do not develop AKI or who are only classified into class-Risk for RIFLE classification or Stage 1 for AKIN criteria. This current study has some limitations. First, it is a retrospective analysis performed in a small cohort of patient at a single medical centre, which may limit the generalisation of results. Second, the prognosis of patients receiving RRT was poor in this cohort; however, it was not possible to figure out the timing of the beginning of RRT due to the limited patient population. Third, the endpoints of this study are demise or discharge from the hospital; therefore, it lacks the relationship between the prognosis and RIFLE/AKIN criteria for long-term survival in this population.

5. Conclusions

Acute kidney injury is one of the major complications and is associated with increased hospital mortality in adult patients who receive ECMO support following cardiac surgery. Both the RIFLE classification and the AKIN criteria have good short-term prognostic capability in critically ill patients. Either class-Failure for the RIFLE classification or the Stage 3 for the AKIN were found to be independently associated with hospital mortality. However, it does not seem that the AKIN criteria have greater sensitivity and specificity, by comparison with the RIFLE classification in this study population. More studies are necessary, especially associated with the timing of initiation of RRT and the indications for RRT in AKI.

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References