Acute Renal Failure in Adult Patients after Cardiac Surgery: Incidence, Risk Factors, and Associated Mortality Rate in Critical Care Unit

AHMED A. OSMAN, M.D.*; MOHSEN S. ABD EL-AZEEM, M.D.*; AKRAM ALLAM, M.D.** and FAREED KHOUQEER, M.D.***

The Departments of Critical Care Medicine, Cairo University*, Cardiothoracic Surgery, Alexandria University** and Cardiothoracic Surgery, King Faisal Hospital***

Abstract

Background: Acute renal failure (ARF) requiring continuous renal replacement therapy (CRRT) is a devastating complication post cardiac surgery, with an estimated incidence of 2-15% and is associated with high in-hospital mortality.

Aims of the Study: To determine the incidence, main risk factors, and in-hospital morbidity and mortality rate for patients who developed acute renal failure post cardiac surgery and who had normal renal profile preoperatively.

Methods: A retrospective, comparative case-control study was implemented between January 01, 2007 and June 30, 2008. A total of 680 consecutive adult patients who underwent cardiac surgery with cardiopulmonary bypass (CPB) at the King Faisal Heart Institute (KFHI) were retrospectively reviewed. Of these, 42 patients (6%) were identified as having renal impairment after cardiac surgery. However, only 29 patients met the inclusion criteria for the study, since 13 patients had pre-operative renal impairment and hence, were excluded from any subsequent analysis. As a control group, we randomly selected 51 patients who did not develop renal failure after cardiac surgery.

Results: Twenty-two patients (75.9%) in the study group underwent elective surgery. Valve surgery was the most common procedure in both groups (12, 41% for the study group and 28, 54.9% for the control group). CABG surgery was performed in 9 patients (31%) in the study group compared with 18 patients (35.3%) in the control group; valve surgery plus CABG was performed in 5 patients (17.2%) in the study group compared with one patient (2%) in the control group. In the study group the incidence of acute ARF after cardiac surgery was 4.3% (29/680). Of those, 25 out of 29 patients required continuous renal replacement therapy (CRRT) after surgery due to persistent oliguria, metabolic acidosis, hypervolemia, and hyperkalemia that did not respond to other forms of therapy. The in-hospital mortality was high 69% (20 patients died out of 29). Preoperative variables that were significantly associated with ARF were advanced age, history of congestive heart failure with low ejection fraction, high Euro Score, and high normal pre-operative serum creatinine level. Significant operative and post-operative variables associated with development of postoperative ARF were emergency surgery, the use of Intra-aortic balloon pump (IABP), prolonged cardiopulmonary bypass time (CPB) and cross clamping time, hemodynamic complications (low cardiac output, hypoperfusion with requirement for inotropic support and/or vasopressors), development of systemic sepsis, post-operative bleeding, and prolonged ventilation. Preventive measures can be planned ahead in order to achieve better results, diminish these complications, reduce mortality, save hospital costs and decrease total hospital stay.

Conclusions: The development of ARF after cardiac surgery is associated with high mortality. Preoperative risk factors associated with postoperative development of ARF include advanced age, history of congestive heart failure with low ejection fraction, high EuroScore, and high normal pre-operative serum creatinine. The operative and post-operative risk factors include emergency surgery, the use of IABP, prolonged CPB and cross clamping time, hemodynamic complications (low cardiac output, hypoperfusion), development of systemic sepsis, postoperative bleeding, and prolonged ventilation. Preventive measures can be planned ahead in order to achieve better results, diminish these complications, reduce mortality, save hospital costs and decrease total hospital stay.

Key Words: Acute renal failure – Cardiac surgery – Incidence – Risk factors – In-hospital mortality.

Introduction

ACUTE Renal Failure (ARF) requiring Continuous Renal Replacement Therapy (CRRT) is a devastating complication post cardiac surgery, with an estimated incidence of 2-15% and in-hospital mortality of more than 40%. When renal failure develops following cardiac surgery and is severe and associated with the need for continuous renal replacement therapy, including hemodialysis support, it is associated with high mortality, increased healthcare resource utilization, and prolonged length of intensive care and hospital stay [II].
Advances have been achieved in cardiac surgery through improvements in operative techniques, post surgery intensive care, and through a safer and more efficient use of cardiopulmonary bypass circuit. Despite these advances, renal failure requiring Continuous Renal Replacement Therapy (CRRT) remains a problem incurring increased morbidity and mortality [2]. The renal dysfunction is usually moderate in approximately 80-90% of cases; severe dysfunction occurs in about 10% of cases. The incidence of ARF requiring dialysis (RF-D) is approximately 2% [3].

Acute kidney injury is diagnosed on the basis of clinical history and laboratory data. A diagnosis is made when there is rapid reduction in kidney function, as measured by serum creatinine, or based on a rapid reduction in urine output, termed oliguria. Introduced by the Acute Kidney Injury Network (AKIN), specific criteria exist for the diagnosis of AKI, as rapid time course (less than 48 hours); reduction of kidney function as rise in serum creatinine more than or equal to 50% (1.5-fold from baseline), and reduction in urine output, defined as <0.5ml/kg/hr. For more than 6 hours [4,5].

The etiology of renal insufficiency following cardiac surgery is poorly understood, but it is believed that ischemic injury of the kidney resulting from inadequate perfusion is a major factor, although renal injury by exotoxins (e.g. antibiotics, anesthetic agent, contrast media, and diuretics) or endotoxins (e.g. myoglobin) may also be involved. Some studies have shown that a decrease in Glomerular Filtration Rate (GFR) of more than 20% from baseline commonly occurs in patients following cardiac surgery [6].

Aim of study:

This study aimed to evaluate the incidence, main risk factors, and in-hospital morbidity and mortality rate for patients who developed acute renal failure post cardiac surgery, having normal renal function preoperatively and to compare these patients with a control group who did not develop renal failure. This will help identify how dealing with such a complication could be planned for in advance, thereby leading to potentially better outcomes and decreased associated mortality and costs.

Material and Methods

The present study followed a retrospective, comparative case-control study design. Between January 01, 2007 and June 30, 2008, the records of 680 consecutive adult patients who underwent cardiac surgery with Cardio Pulmonary Bypass (CPB) at the King Faisal Heart Institute (KFHI), Riyadh, Kingdom of Saudi Arabia were analyzed.

Inclusion criteria:

All patients over the age of 18 years who underwent cardiac surgery, having normal renal function preoperative and who developed acute renal failure postoperatively were included in the study. The diagnosis of acute renal failure based on rising serum creatinine to > 50% (1.5-fold from baseline), and reduction in urine output, defined as <0.5ml/kg/hr. For more than 6 hours, and or anuria despite having adequate filling pressure and cardiac output [7,8].

Patients were identified through the King Faisal Heart Institute (KFHI) Apollo Database for inclusion in the study. All data collected were entered into case report forms designed for the study. Patients suitable for historical control group who did not develop ARF post-operatively.

Exclusion criteria:

Patients with preoperative renal impairment, either on conservative treatment or on regular dialysis, were excluded from the subsequent analysis.

Study samples:

A total of 42 patients (6%) were identified as having renal impairment post cardiac surgery. Of those, 13 patients excluded from the study because of their preoperatively impaired renal function with high serum creatinine. Thus, 29 (4.3%) patients with normal renal function preoperatively, the mean preoperative serum creatinine 86.8 ± 13 g/mol/l, and mean postoperative serum creatinine 180±55 γmol/l (range: 135-233 γmol/l), were enrolled for subsequent analysis. Of those, 25 patients required CRRT after surgery due to one or more than of the following parameters (persistent oliguria, metabolic acidosis, hypervolemia, and hyperkalemia) that not responded to other forms of therapy. CRRT was commenced through nephrologist consultation. Only 4 patients were managed conservatively without dialysis.

Following a simple random sampling technique, we selected 51 patients, who underwent cardiac surgery during the same period, and did not develop renal failure postoperatively as controls. The sample size for the control group was determined according to Kasiulevičius, et al. [9].

Approval to conduct the study was granted by the Hospital’s Research Advisory Council.
Study variables:

A- Pre-operative variables:
1. Age.
2. Gender.
3. Euro SCORE [10].
5. Preoperative ejection fraction (EF%).
6. Operative priority either elective or emergency.
7. Intra-aortic balloon pump insertion (IABP).
8. Preoperative creatinine level.

B- Intra-operative variables:
1. Cardiac procedure (CABG, Valve, Both, other).
2. Cardiopulmonary bypass time.
3. Aortic cross-clamp time.

C- Post-operative variables:
1. Hours ventilated.
2. Postoperative complications, including i.e. Systemic sepsis, renal failure, re-exploration for bleeding and major hemodynamic complications.

Statistical analysis:
The Statistical Package for Social Sciences (SPSS, ver. 16.0) was used for data entry and analysis. Descriptive statistics were applied (i.e., frequency, percentage, mean and standard deviation. Testing statistical significance of differences between variables within the two study groups were compared using the Chi-square/Fisher’s exact test for categorical variables and by t-test for continuous variables. For each of these tests, a two-sided significance level of 5% was used for calculation.

Ethical considerations:
This study was conducted in accordance with the ethical principles contained in the Declaration of Helsinki (2000), the ICH Harmonized Tripartite Good Clinical Practice Guidelines, the policies and guidelines of the Research Advisory Council (RAC) of the KFSH and RC, and the laws of Saudi Arabia. As this is a retrospective study and does not involve any direct contact with patients or their families and does not pose any risk to patients, we consider the benefit to risk ratio to be favorable. A waiver of written, informed consent was obtained from the Research Advisory Council.

Results

Patient's characteristics and pre-operative data:
All patients, 18 years of age or older, with normal renal function, who underwent cardiac surgery at our Institute, and developed ARF post-operatively were included in the study. The patients' demographic characteristics, risk factors, cardiovascular diagnosis and pre-operative serum creatinine are presented in (Table 1). The average pre-operative EuroScore for the study group was 14.2 ± 11.9, compared with 4.8 ± 3.8 for the control group (p<0.001). Thirteen patients (44.8%) in the study group had coronary artery disease (CAD) and 12 patients (41.4%) had rheumatic heart disease. In the control group, 20 patients (39.2%) had CAD and 27 patients (52.9%) had rheumatic heart disease. Previous cardiac surgery had been performed in 12 study patients (41.4%) and in 13 (25.5%) control patients.

Table (1): Patients’ pre-operative baseline characteristics.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Cases n=29</th>
<th>Controls n=51</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>59.1±16.2</td>
<td>50.6±14.9</td>
<td>0.020</td>
</tr>
<tr>
<td>Gender</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>16 (55.2%)</td>
<td>23 (45.1%)</td>
<td>0.386</td>
</tr>
<tr>
<td>Female</td>
<td>13 (44.8%)</td>
<td>28 (54.9%)</td>
<td></td>
</tr>
<tr>
<td>Pre-op EuroScore</td>
<td>14.2±11.9</td>
<td>4.8±3.8</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>History of</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>12 (41.4%)</td>
<td>21 (41.2%)</td>
<td>0.986</td>
</tr>
<tr>
<td>Hypertension</td>
<td>13 (44.8%)</td>
<td>21 (41.2%)</td>
<td>0.751</td>
</tr>
<tr>
<td>Congestive heart failure</td>
<td>8 (27.6%)</td>
<td>2 (3.9%)</td>
<td>0.002</td>
</tr>
<tr>
<td>Pre-op ejection fraction (%)</td>
<td>44.5±12.6</td>
<td>52.8±10.5</td>
<td>0.002</td>
</tr>
<tr>
<td>Pre-op diagnosis</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CAD</td>
<td>13 (44.8%)</td>
<td>20 (39.2%)</td>
<td>0.521</td>
</tr>
<tr>
<td>Valve</td>
<td>12 (41.4%)</td>
<td>27 (52.9%)</td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>4 (13.8%)</td>
<td>4 (7.8%)</td>
<td></td>
</tr>
<tr>
<td>Previous surgery</td>
<td>12 (41.4%)</td>
<td>13 (25.5%)</td>
<td>0.140</td>
</tr>
<tr>
<td>Pre-op creatinine</td>
<td>86.9±13.0</td>
<td>68.6±15.8</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Intra-operative data:
The basic operative data of the patients included in the study are outlined in (Table 2). The majority of patients (n=22, 75.9%) in the study group and all patients in the control group (n=51, 100%) underwent elective surgery. Valve surgery, either valve replacement or repair, was the most common surgery performed in both groups, (12, 41.4% for the study group and 28, 54.9% for the control group). Difference between groups was statistically significant (p<0.001). As regard type of surgery, coronary artery bypass grafting (CABG) surgery was performed in 9 cases (31%) in the study group and 18 (35.3%) in the control group. Differences were not statistically significant. The need for intra-aortic balloon pump (IABP) insertion was high in the study group (8, 27.6%) compared with
only one case (2%) in the control group. Difference between both groups was statistically significant ($p<0.001$). Interestingly, the cardio-pulmonary bypass (CBP) time and cross-clamp time during surgery were significantly higher in the study group than the control group. In the study group, the average CPB time and cross clamp time were 193.3±94.4 min and 118.8±70 min, respectively, while the control group's average CPB time and cross clamp times were 99.9±63.5 min and 62.2±46.1 min, respectively.

The operative data of the patients are shown in (Table 2). The following factors were significant predictors of renal failure post-operatively: Emergency surgery which was exclusively observed among the study group (7, 24.1% Vs. 0, 0%, $p<0.001$); the use of IABP ($p<0.001$); prolonged CPB time, 193.3±94.3 minutes Vs. 99.9±63.5 minutes ($p<0.001$); and cross clamping time, 118.8±70 minutes Vs. 62.2±46.1 minutes ($p<0.001$).

The postoperative data of the patients and control cases are shown in (Table 3). The following factors were significant predictors of renal failure post-operatively: Hemodynamic complications (e.g., low cardiac output, hypo-perfusion, need for inotropic support and/or vasopressors) were significantly high in the study patients (22, 75.9% Vs. 0, 0.0%, respectively; $p<0.001$); development of systemic sepsis (7, 24.1% Vs. 0, 0.0%, respectively; $p<0.001$); post-operative bleeding necessitating re-exploration (10, 34.5% Vs. 0, 0.0%, respectively; $p<0.001$); and prolonged duration of ventilation i.e., more than 24 hours (23 79.3% Vs. 1, 2%, respectively; $p<0.001$).

Continuous renal replacement therapy (CRRT) was maintained in 25 patients (82.2%) while only 4 patients were managed conservatively without dialysis. The in-hospital postoperative mortality was high in patients who developed ARF; the cause of death was multi-organ failure, secondary to systemic sepsis, severe heart failure, and renal failure.

### Table (2): Operative data.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Cases n=29</th>
<th>Controls n=51</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Operative priority:</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Elective</td>
<td>22 (75.9%)</td>
<td>51 (100%)</td>
<td>$&lt;0.001$</td>
</tr>
<tr>
<td>Emergency</td>
<td>7</td>
<td>0 (0%)</td>
<td></td>
</tr>
<tr>
<td><strong>Type of surgery:</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CABG</td>
<td>9 (31.0%)</td>
<td>18 (35.3%)</td>
<td></td>
</tr>
<tr>
<td>Valve</td>
<td>12 (41.4%)</td>
<td>28 (54.9%)</td>
<td></td>
</tr>
<tr>
<td>Both</td>
<td>5 (17.2%)</td>
<td>1 (2.0%)</td>
<td></td>
</tr>
<tr>
<td>Others</td>
<td>3 (10.3%)</td>
<td>4 (7.8%)</td>
<td>0.083</td>
</tr>
<tr>
<td>IABP-insertion</td>
<td>8 (27.6%)</td>
<td>1 (2.0%)</td>
<td>$&lt;0.001$</td>
</tr>
<tr>
<td>CPB time (min)</td>
<td>193.3±94.4</td>
<td>99.9±63.5</td>
<td>$&lt;0.001$</td>
</tr>
<tr>
<td>Cross-clamp time (min)</td>
<td>118.8±70.0</td>
<td>62.2±46.1</td>
<td>$&lt;0.001$</td>
</tr>
</tbody>
</table>

### Post-operative data:

Postoperative morbidities assessed for the study group are outlined in (Table 3). Morbidities included hemodynamic complications (low cardiac output which needed inotropic support and/or vasopressors), development of systemic sepsis, re-exploration for significant bleeding post-operatively, duration of mechanical ventilation, the development of acute renal failure, and in-hospital mortality.

The incidence of ARF after cardiac surgery was 4.3% (29/680), the mean serum creatinine was 180±55 μmol/l (range: 135-233 μmol/l). The in-hospital mortality among patients who developed postoperative ARF was quite high (20/29, 69%). The following pre-operative variables were significantly associated as predictors of ARF after surgery: Age: The patients who developed renal failure were older than the patients is the control group, 59.1±16.2 years Vs. 50.6±14.9 years ($p=0.02$); high Euro SCORE 14.2±11.9, Vs. 4.8±3.8, respectively ($p<0.001$); history of congestive heart failure ($p=0.002$); pre-operative low ejection fraction, 44.5±12.6% Vs. 52.8±10.5% ($p=0.002$); and high normal preoperative creatinine: 86.9±13 μmol/l Vs. 68.6±15.7 μmol/l ($p<0.001$).
Discussion

Renal insufficiency after cardiac surgery remains one of the most clinically significant causes of morbidity, mortality, prolonged intensive care unit stay and increase health care cost, particularly if there is requirement for hemodialysis. Renal failure is known to develop in 5-30% of patients who have cardiac surgery [11]. And the development of acute renal failure has been identified as the strongest risk factor for death [12].

Most of the previously reported studies have focused on patients with impaired renal function before surgery [13]. In this study, we investigated a group of patients who had normal renal function preoperatively and attempted to correlate and predict risk factors (preoperative, intra-operative, and early postoperative) that may cause acute renal failure and the need for renal replacement therapy. By identifying those risk factors, preventive measures can be planned in advance to improve outcomes and a more efficient use of hospital and intensive care resources.

The incidence of acute renal failure after cardiac surgery in our study was 4.3% (29/680), and the in-hospital mortality among these patients was quite high (20/29, 69%). Previous studies have demonstrated that a postoperative need to initiate renal dialysis occurs in 1.1% to 3.0% of cardiac surgery, importantly, these studies indicate that the minority of patients who require dialysis after cardiac surgery have significantly longer in-hospital length of stay and extremely high mortality, with 63% to 100% of patients dying before leaving the hospital [14].

In this study, older age, higher Euro score, preoperative congestive heart failure with low ejection fraction, and a high normal creatinine level were associated with a higher risk of developing acute renal failure requiring continuous renal replacement therapy.

Advanced age have been shown to be associated with glomerular sclerosis or disease, which increases the risk of renal failure in general and make subjects more susceptible to ischemic insults during cardiopulmonary bypass [15].

This study showed no difference between males and females in developing ARF and no difference in patients with diabetes or hypertension. Diabetes has been shown in some studies to be a high risk for developing acute renal failure, while other studies have failed to show an association with ARF [16].

Patients who developed renal failure had a higher mean Euro SCORE than patients who did not develop acute renal failure, (14 Vs. 4.8). Applying the Euro SCORE can be a useful aid in predicting acute renal failure, as well as other postoperative complications, and can be used to guide the physicians in avoiding drugs that may damage the kidneys. Patients with higher creatinine preoperative levels (“high normal”) are at a higher risk for developing postoperative acute renal failure [17].

Operative factors that are associated with ARF included prolonged CPB time (p<0.001), and long cross clamping time (p<0.001). This is in agreement with that of Kishore, et al. [18].

Cardiopulmonary bypass circuits had the capability to activate systemic inflammatory cascade and induce endothelial cell-neutrophil adhesion has been well established, these changes promote leukocyte sequestration and adhesions to capillary bed in the kidneys with subsequent release of cytokines and oxygen free radicals causing renal injury [19]. These findings are supported by the observation that the incidence of ARF post off-pump CABG is 50% less than that of on-pump CABG [17].

The insertion of IABP intraoperative or postoperatively which is usually due to severe hemodynamic instability, increased the risk of renal failure (p<0.001), and this is in agreement with that of Ostermann ME, et al. [20]. And whether the surgery is elective or emergency (p=0.0002) this might be in part due to the prolonged cardiopulmonary bypass time, prolonged hypo-perfusion of the renal medulla and the increased levels of vasoconstrictors (e.g. catecholamines, aldosterone, angiotensin) to maintain hemodynamic stability [21].

Complex cardiac cases and long cases, such as valve replacement associated with CABG, carry a high risk, as illustrated in Kishore, et al. 2007 study, but these factors did not reach statistical significance in our series.

In the postoperative period, 25 cases (86%) with ARF required dialysis. Also, 23 patients required prolonged intubation and ventilation, (more than 24 hours) which made them at higher risk to develop infections, especially in the lungs, and also increasing the risk of developing ARF, that may be attributed to the degree of illness, high Euro SCORE, hemodynamic instability and other co morbidities.

In the study group, twenty patients died (69%) and only 9 patients survived, while in the control
group with no renal impairment, there was no mortality. The higher in-hospital mortality in the ARF has been reported to be multifactorial as dialysis-induced effects on inflammatory and immune responses predisposing to activation of cytokines induced systemic sepsis, hemodynamic instability, microcirculatory failure, visceral ischemia and progression to multiorgan failure [22].

Conclusions:

In conclusion, we have identified some of the risk factors that could lead to postoperative acute renal failure in patients with normal preoperative renal function. Preventive measures can be planned ahead in order to achieve better results, diminish this complications, reduce mortality, save hospital costs and decrease total hospital stay. These measures should include pre-operative nephrology consultation, adequate hydration, maintenance of adequate cardiac output (volume and inotropic support), and early hemofiltration postoperatively. By applying these measures, a decrease in morbidity and mortality can be expected in high-risk patients.

Disclosures:

Authors declare no conflict of interest.

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References


