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The Incidence and Risk Factors of Acute Kidney Injury After Coronary Artery Bypass Graft Surgery

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Abstract

Background: Acute Kidney Injury (AKI) is a prevalent and important complication of cardiac surgery, which is associated with significant morbidity and mortality. Identification of risk factors associated with AKI will help it's prevent.
Objectives: The objective of the present investigation was to identify risk factors for acute kidney injury in patients who underwent coronary artery bypass graft (CABG) surgery at a tertiary care center for cardiovascular patients in Iran.
Patients and Methods: From March 2014 to April 2015, 490 consecutive patients who underwent On-pump CABG at Rajaie cardiovascular medical and research center were assessed. Baseline variables and perioperative data were collected and their association with the development of AKI was evaluated.
Results: Patients' mean age was of 67.9 (SD = 12.5) years. From these patients 353 (72%) were male and 137 (28%) were female. Six deaths (1.3%) occurred among patients. Thirteen patients (2%) had AKI. The baseline serum creatinine concentrations in patients with AKI were significantly higher than other patients ($P = 0.04$). Volume of transfused red blood cells and hemoglobin value were different, associated with AKI ($P < 0.05$), while systemic arterial oxygen saturation and pressure values were not associated with AKI ($P > 0.05$). Mean arterial pressure (MAP) was not different in patients with AKI ($P = 0.85$). The mean pump time in patients with AKI was significantly higher than the other patients ($P = 0.02$). Postoperative Left ventricle ejection fraction (LVEF) in patients who developed AKI was significantly reduced compared with patients without AKI ($P = 0.01$). The in-hospital mortality of patients who developed AKI was 7.69% compared with 1.04% among those who did not (P = 0. 01).
Conclusions: Acute kidney injury is the important postoperative organ dysfunction in patients who underwent CABG and preoperative elevated serum creatinine concentration, cardiopulmonary bypass time > 120 minutes, intraoperative anemia and blood transfusion were serious risk factors associated with AKI.

Keywords: Acute Kidney Injury, Coronary Artery Bypass Grafting, Risk Factors

1. Background

Acute kidney injury (AKI) occurs in up to 30% of all patients following coronary artery bypass graft (CABG), which is associated with a high mortality, a prolonged hospital stay and a higher risk for infection (1).

The pathogenesis of AKI involves hemodynamic, inflammatory and nephrotoxic factors, which lead to kidney injury (1). Antibiotics, anesthetic agents, contrast media such as exotoxins, myoglobin such as endotoxin, and history of chronic kidney disease are predisposing factors for acute postoperative renal failure (2).

There are many risk factors associated with the development of AKI after CABG (2). In almost all studies, certain risk factors have been repeatedly associated with an increased risk for AKI including female gender, reduced left ventricular function, diabetes, peripheral vascular disease, preoperative use of an intra-aortic balloon pump and an elevated preoperative serum creatinine (1, 3-5).

2. Objectives

The aim of this study was to evaluate the incidence of AKI following on-pump CABG surgery and to identify the impact of cardiopulmonary bypass on postoperative AKI.

3. Patients and Methods

3.1. Study Design

From March 2014 to April 2015, 640 consecutive patients, who underwent coronary bypass graft at Rajaie cardiovascular medical and research center, the main tertiary care hospital for cardiovascular patients in Tehran (Iran), were enrolled. Within our population, 150 patients who underwent CABG with the off-pump technique or required dialysis or were aged less than 18 years and had other concurrent types of cardiac surgery were excluded.

Baseline variables and perioperative data were collected and their association with the development of AKI was evaluated. acute kidney injury was defined as an increase in serum creatinine concentration

of more than 0.5 mg/dL compared with the baseline value, a 50% decrease in the calculated creatinine clearance, or a change in serum creatinine concentration of greater than 0.3 mg/dL within 48 hours of an acute insult, or using RIFLE or AKIN scores rather than an increase of serum creatinine of greater than or equal to 50% compared to preoperative values (6, 7).

3.2. Operative Procedure

All patients received a standard premedication (morphine 0.1 mg/kg intramuscularly), administered one hour prior to the surgery. The peripheral vein and radial artery were cannulated before induction of anesthesia. Intraoperative hemodynamic monitoring including arterial blood pressure, central venous pressure and an electrocardiogram was done for all patients. Additionally, pulse oximetry, capnometry and urine output were monitored during the surgery.

For all patients, anesthesia was induced by benzodiazepine (midazolam 0.05 to 0.1 mg/Kg), opioids (fentanyl 25 to 40 μg/Kg or sufentanil 2.5 to 4 μg/Kg), and muscle relaxants (atracurium 0.5 mg/ Kg or pancuronium 0.1 mg/ Kg) before tracheal intubation. Next, anesthesia was maintained with midazolam, sufentanil, atracurium and isoflurane up to 1%. All operations were performed with cardiopulmonary bypass (CPB) at mild to moderate core hypothermia (28 to 32°C).

Surgery was performed through a median sternotomy. Non-pulsatile CPB flow was maintained between 2 and 2.8 L/min/m^2 using a membrane oxygenator. A standard crystalloid prime and mannitol 18% (0.5 g/kg) to achieve a hematocrit of 18% or more was used in the Cardiopulmonary Bypass (CPB) circuit. Myocardial protection was achieved with a solution of cardioplegia. Patient's core temperature was maintained at 28 to 32°C. Active rewarming to 37°C was completed before aortic cross-clamp removal.

The intra-arterial mean arterial pressure (MAP) value was recorded immediately after cannulation of the aorta and then every 20 seconds until the end of the CPB. The MAP in all patients was preserved greater than 60 mm Hg. Transfusion of packed red blood cells was used when the hemoglobin level was measured to be < 7 g/dL (4.4 mmol/L).

3.3. Statistics

Mean value, standard deviation (SD) and frequency was used for descriptive analysis. For evaluation of the distribution of data, one-sample Kolmogorov-Smirnov test was used. Qualitative data were compared with Chi square or Fisher's exact test. Independent T test or Mann Whitney U test was used to compare quantitative variables. All data were analyzed using the SPSS software, version 11.0 (SPSS Inc., Chicago, IL, USA). A value of $P < 0.05$ was considered statistically significant.

4. Results

The study sample included 490 patients, who underwent on-pump CABG. Mean age of the study population was 67.9 (SD = 12.5) years. From these patients 353 (72%) were male and 137 (28%) were female. The demographic and perioperative characteristics of all patients are shown in Table 1.

Any death that occurred during the 30 days of hospitalization was defined as hospital mortality. Six deaths (1.3%) occurred among patients. Of all patients, 13 subjects (2%) had AKI.

The measured perioperative variables and their association with occurrence of AKI are shown in Table 2.

There were no significant associations between perioperative variables and AKI except pump time. The mean pump time in patients with AKI was significantly higher than the other patients ($P = 0.02$).

Postoperative LVEF in patients who developed AKI was significantly reduced compared with patients without AKI ($P = 0.01$).

The in-hospital mortality of patients, who developed AKI was 11.1% compared with 1.1% among those who did not (P = 0. 01).

The AKI was strongly associated with baseline renal insufficiency (Table 3). The baseline serum creatinine concentrations in AKI patients were significantly higher than the other patients ($P = 0.04$). It was expected for postoperative creatinine concentration in AKI patients to be higher than patients without AKI.

Intraoperative risk factors are depicted in Table 4. Volume of transfused red blood cells and hemoglobin value were differently associated with AKI ($P < 0.05$) while systemic arterial oxygen saturation and pressure values were not associated with AKI ($P > 0.05$). The MAP was also not different in AKI ($P = 0.85$).

Table 1. Demographic and Perioperative Data of all Patients (n = 490)

Variables	Values[a]
Gender	
Male	353 (72)
Female	137 (28)
Age, y	67.9 ± 12.5
DM	186 (38)
CKD	52 (10.6)
MI	70 (14.9)
Emergency surgery	27 (5.5)
Number of graft	
1	14 (2.8)
2	44 (9)
3	245 (50)
4	167 (34.1)
5	19 (3.9)
6	1 (0.2)
Pump time, min	
< 120	389 (79.4)
≥ 120	101 (20.6)
LVEF, %	45.90 ± 7.13
Preop-Cr, mg/dL	1.23 ± 0.3
Postop-Cr, mg/dL	1.24 ± 0.75
Death	6 (1.3)

Abbreviations: CKD, chronic kidney disease; Cr, creatinine; DM, diabetes mellitus; LVEF, left ventricle ejection fraction; MI, Myocardial infarction; min, minute; M, mean; N, number; SD, standard deviation.
[a]Values are expressed as No. (%) or mean ± SD.

Table 2. Perioperative Variables and Their Association With the Development of ARF Following Coronary Artery Bypass Graft (CABG) Surgery[a]

Variables	AKI (n = 13)	No AKI (n = 477)	P Value
Gender (M/F)	6/3	324/129	0.74
Age, y	65.70 ± 8.7	60.68 ± 9.7	0.48
CKD	2 (15.3)	49 (10.2)	0.28
DM	4 (30.7)	176 (36.8)	0.73
MI	3 (23.0)	65 (13.6)	0.11
Emergency surgery	0	27 (5.66)	0.51
Number of graft			0.40
1	0	14 (2.93)	
2	1 (7.69)	33 (6.91)	
3	4 (30.7)	231 (48.4)	
4	3 (23.0)	158 (33.1)	
5	1 (7.69)	16 (3.35)	
6	0	1 (0.20)	
Pump time, min	132.9 ± 36	92.4 ± 39.1	0.02
Preop-LVEF, %	42.08 ± 5.9	45.18 ± 3.5	0.30
Postop-LVEF, %	35 ± 7.4	43.25 ± 8.8	0.01
MV time, min	24.85 ± 40.7	20.88 ± 42.2	0.48
Death	1(7.69)	5 (1.04)	0.01

Abbreviations: CKD, chronic kidney disease; Cr, creatinine; DM, diabetes mellitus; LVEF, left ventricle ejection fraction; MI, myocardial infarction; min, minute; MV, mechanical ventilation.
[a]Values are expressed as No. (%) or mean ± SD.

Table 3. Serum Creatinine Before and Seventy-Four Hours After Surgery Associated With Acute Kidney Injury

Variable	AKI (n = 13)	No AKI (n = 477)	P Value
Baseline serum creatinine, mg/dL	1.5 ± 1.1	0.9 ± 1.1	0.04
Serum creatinine after 72 hours, mg/dL	2.27 ± 0.9	1.1 ± 0.6	0.001

5. Discussion

In different studies, the risk of ARF after cardiac surgery has been reported from 1% to 30%, based on the criteria used to define this complication (2, 5, 8). In our population, the incidence of AKI was 1.9% and it was lower than that reported in other studies probably due to the improvement of CABG technique and intensive care in our center and maybe because of minor risk of CABG procedures compared to valvular procedures.

This study investigated perioperative variables associated with postoperative acute renal complications. Among pre and intra-operative variables, only pump time was known as an influential risk factor for postoperative renal failure.

Rodrigues et al. assessed 381 patients that had undergone CABG, 339 valve surgery and 49 that had undergone both simultaneously and concluded that renal dysfunction was the most frequent postoperative organ dysfunction in patients who underwent CABG and/or valve surgery and cardiopulmonary bypass time of > 120 minutes is one of the risk factors independently associated with AKI (9).

Prolonged pump time is associated with the generation of free hemoglobin and iron through hemolysis that typically occurs during the surgery. Hemolysis may contribute to oxidative stress and renal tubular injury (1, 10, 11).

Patients who enter CPB often have received minor or major renal dysfunction. In the study of Conlon et al. there was a significant relationship between CPB time and ARF

Table 4. Intraoperative Variables Associated With Acute Kidney Injury

Variable	AKI (n = 13)	No AKI (n = 477)	P Value
SaO_2, %	99.7 ± 0.03	99.7 ± 0.01	0.94
PaO_2, mmHg	325 ± 2.1	318 ± 1.9	0.43
MAP, mmHg	68.6 ± 12.3	66.2 ± 10.0	0.85
Arterial O_2 content, mL/dL	12.3 ± 1.3	13.7 ± 1.0	0.004
Hemoglobin concentration, g/dL	8.0 ± 0.5	9.1 ± 0.7	< 0.001
Red blood cell transfusion, mL	750 ± 205	500 ± 200	< 0.001

Abbreviations: MAP, mean arterial pressure; PaO_2, oxygen pressure of arterial blood; SaO_2, oxygen saturation of arterial blood.

(12).

Patients with reduced left ventricular function and reduced renal perfusion or patients in cardiogenic shock, who will require inotropic support or an intra-aortic balloon pump or patients who use diuretics, non-steroidal anti-inflammatory drugs (NSAID), Angiotensin-converting enzyme inhibitors (ACEI), or angiotensin receptor blockers (ARB) and patients with preoperative hypotension are very prone to the risk of renal failure (13, 14) All these factors become more important if CPB is prolonged.

Age is still a controversial risk factor as a number of studies have shown that ARF is more common in elderly patients because of losing functional reserve of kidneys by age, while others do not (2, 15). In our investigation, we did not find a significant association between age and developing AKI.

In our study, preoperative LVEF was not significantly association with developing AKI in contrast with the study of Landoni et al. that reported an association between preoperative low ejection fraction and emergency surgery were expression of hemodynamic instability (2). We demonstrated that postoperative LVEF decreased in patients with AKI, which is considered to be a marker of renal hypo perfusion in patients with reduced left ventricular function. Kochi et al. (16) showed that ventricular dysfunction and myocardial infarction were independently associated with postoperative renal dysfunction.

In our study, pre-operative elevated serum creatinine was associated with AKI. Several studies have suggested that preoperative renal dysfunction is the most common predictive risk factor of renal replacement therapy and requires dialysis after cardiac surgery. Even minimal changes in serum creatinine significantly increase post-operative mortality and morbidity. Indeed, Serum creatinine is a reliable biomarker for the assessment of AKI (17). Thakar et al. (18) stated that preoperative serum creatinine, as an equivalent for renal dysfunction, is an important risk for predicting the need for dialysis after cardiac surgery. Armstrong et al. (19) reported that, patients with a pre-operative serum creatinine of > 125 mmol/L have a 4.3-fold risk of acute kidney injury and a 9.5-fold risk of requiring hemofiltration compared with those with a pre-operative serum creatinine of < 124 mmol/L.

We found that a reduction in hemoglobin concentration was associated with AKI, however arterial pressure of oxygen and arterial oxygen saturation and also MAP had no association with AKI. Several studies have investigated intraoperative risk factors such as MAP, hemoglobin concentration, O_2 saturation and intraoperative transfusion of red blood cells for AKI after CPB (20-22). Our findings on reduced intraoperative hemoglobin and increased use of blood products as independent risk factors for AKI are in line with other studies. The importance of intra and post-operative anemia for AKI was highlighted (20).

To maintain renal function, MAP should preserve near the minimum levels during CPB and any further disturbance may lead to ischemia and cellular damage (20). There were no deleterious effects of a low intraoperative perfusion pressure on post-operative renal function or mortality (21).

Furthermore, we evaluated other perioperative risk factors of AKI including diabetes mellitus, gender and chronic kidney disease, and also intraoperative variables such as number of graft and mechanical ventilation time. Interestingly, we showed that there was no association between incidence of AKI and these variables.

In conclusion, acute kidney injury is an important postoperative organ dysfunction in patients who underwent CABG and preoperative elevated serum creatinine concentration, cardiopulmonary bypass time of > 120 minutes, intraoperative anemia and blood transfusion are serious risk factors associated with AKI.

5.1. Study Limitation

In this study, there were some limitations regarding the evaluation of GFR as an important index of renal function after open-heart surgery, including 24-hour urine volume or intraoperative two-hour urine output estimation. These limitations were due to the use of diuretics such as mannitol and volume of liquid for prime CBP circuit, which prevents accurate calculation of GFR.

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Footnotes

Authors' Contribution: Samira Tabiban, conducting the project: Seyed Mostafa Alavi and Turaj Babaee, revising the manuscript: Behshid Ghadrdoost and Rasool Ferasatkish, collecting the data and review of the literature: Mohsen Ziyaeifard and Ali Sadeghpour Tabaei, data analysis and preparation of the Manuscript:Hooman Bakhshandeh, Zahra Faritous and Maziar Mahjoubifard revising the manuscript: Behshid Ghadrdoost and Mostafa Alavi; collecting the data and review of the literature: Mohsen Ziyaeifard, Ali Sadeghpour Tabaei and Rasoul Farasatkish; data analysis and preparation of the manuscript: Behshid Ghadrdoost and Hooman Bakhshandeh.

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