

The effect of perioperative mean arterial pressure and fluid management on postoperative acute kidney injury: Prospective evaluation of 219 coronary artery bypass cases

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Abstract

Aim: In this article, we evaluated risk factors associated with cardiac surgery-related AKI, including the pathophysiology, potential causes of injury, and preventing modalities. Acute kidney injury (AKI) is a significant obstacle that is of remarkable attention after cardiac surgical procedures. Perioperative AKI is independently correlated with an increase in morbidity, costs of treatment, prolonged hospitalization and increase in mortality.

Material and Methods: Two hundred and nineteen patients who underwent coronary artery bypass grafting surgery from April through June 2019 were enrolled in this prospective study. Left ventricle ejection fraction, complete blood count, and kidney function test (KFT) were evaluated preoperatively. And, in perioperative evaluation, aortic cross-clamp time, minimum hemoglobin value, and mean arterial pressure, the perioperative fluid type used were recorded. KFT were recorded at postoperatively and, patients with AKI were identified using Kidney Disease Improving Global Outcomes classification.

Results: Left ventricle ejection fraction of the patients who did not have AKI was significantly higher ($p=0.009$). A higher rate of AKI was observed in perioperative colloid used patients ($p=0.004$). Perioperative MAP values were significantly lower in patients having AKI ($p=0.002$). There is also a positive correlation between the decrease in MAP value and the development of AKI.

Conclusion: Improving factors effecting arterial blood flow of the kidney such as preoperative hemoglobin value, perioperative mean arterial pressure may restrain the risk of cardiac surgery-related AKI. Also, we found that the use of colloid solutions while cardiac surgery was associated with more AKI. Based on this result; it is crucial managing perioperative fluid therapy more targeted and considering the personal data of the patients.

Keywords: Acute kidney injury; cardiac surgery; bypass, colloid; mean arterial pressure

INTRODUCTION

Cardiovascular diseases are widespread all over the world and are one of the leading causes of death. However, epidemiological studies conducted over the last decade have shown that the incidence of cardiovascular system death has decreased in many countries (1). The decrease in the rate of death is the result of the development of medical and surgical treatment methods. Therefore, every factor that will affect the success of perioperative treatment

methods is investigated in detail. Acute kidney injury (AKI) is one of these factors and increases postoperative mortality-morbidity rates in patients (2,3). Therefore, AKI is one of the most important factors to be investigated.

The incidence of AKI after coronary artery bypass grafting (CABG), ranges from 5 to 30% depending on the definition (4). Patients with AKI following CABG require dialysis have an unacceptably high mortality rate that approaches 68%. The development of AKI also

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is associated with a significant increase in infectious complications and an increase in hospitalization time (4,5).

Some parameters are used to predict the development of AKI. Advanced age, high preoperative creatinine levels, diabetes mellitus, congestive heart failure, emergency surgery, perioperative intra-aortic balloon pump use, prolonged cardiopulmonary bypass, postoperative low cardiac output syndrome are the most predicted risk factors (6). Despite the deleterious consequences of AKI after CABG, its pathophysiology remains not entirely understood.

In the present study, our primary aim is to determine factors that may influence the development of AKI after CABG. Our second aim is to evaluate the importance of perioperative fluid replacement in CABG related AKI.

MATERIAL and METHODS

Patient selection

A total of 219 patients who underwent CABG, consequently by the same surgical team from April 2019 through June 2019 were enrolled in this prospective observational cohort study. Scheme of the present study is shown in Figure 1.

Exclusion criteria

Patients aged under 18 years (n=6), history of chronic renal failure (n=6), preoperative elevated blood urea nitrogen (BUN) and creatinine values (n=11), previous CABG or cardiac valve surgery (n=27) were excluded from the study protocol.

Preoperative evaluation

Patients' demographics, body mass index, comorbidities, left ventricle ejection fraction, complete blood count, and blood urea nitrogen (BUN), creatinine levels were evaluated. Beta-blocker treatment was continued before surgery if there were no contraindications. Antiplatelet agents were discontinued at least five days before surgery but continued as high-risk patients. Since oral antidiabetic drugs could cause lactic acidosis and hypoglycemic complications, they were terminated before cardiac surgery and insulin treatment initiated.

Perioperative evaluation

Aortic cross-clamp time, minimum hemoglobin value, and mean arterial pressure during on-pump (MAP), blood products transfusion requirement, inotropic

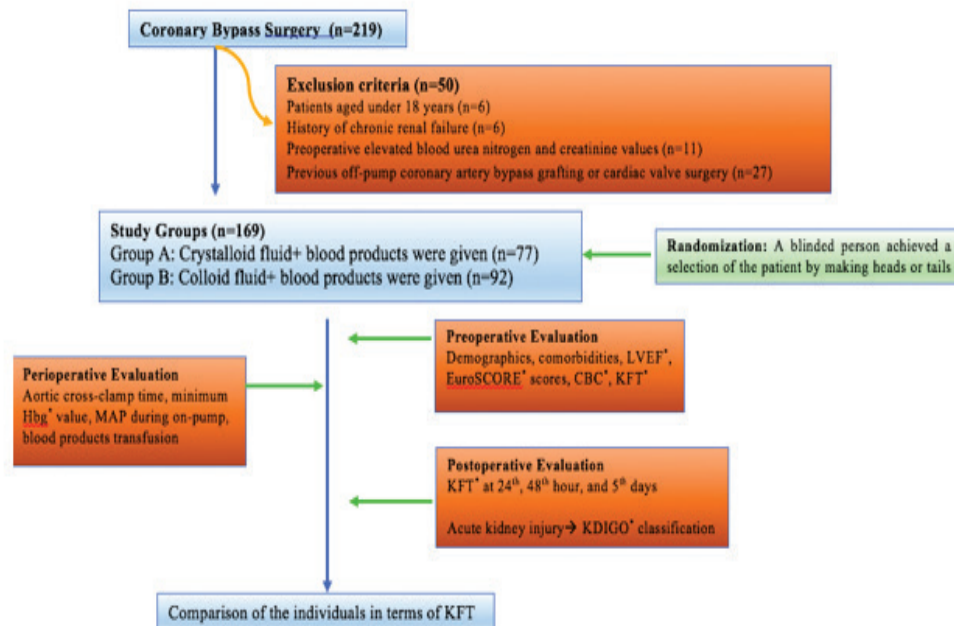


Figure 1. Scheme of the present study

*LVEF: Left ventricle ejection fraction, EuroSCORE: European System for Cardiac Operative Risk Evaluation, CBC: Complete blood count, KFT: Kidney function tests (Blood urea nitrogen and creatinine), Hbg: Haemoglobin, MAP: Mean arterial pressure, KDIGO: Kidney disease improving global outcomes

drug requirement, central venous pressure values, the perioperative fluid type used were recorded.

Postoperative evaluation

BUN-creatinine values were recorded at postoperative 24th, 48th hour, and 5th days and, patients with AKI were identified using Kidney Disease Improving Global Outcomes (KDIGO) classification (7).

Anesthesia technique

In the operation room; 5-lead ECG, noninvasive blood pressure, pulse oximeter, and temperature probe were used for monitoring. After the peripheral venous catheter was inserted, lactated ringer solution was started at a dose of 10 mL/kg. A radial arterial catheter was placed under local anesthesia to observe arterial blood pressure

before induction of general anesthesia, and a central venous catheter was positioned after induction of general anesthesia. Both arterial and central venous pressure values were followed and noted, continuously. Antibiotic prophylaxis was performed before the incision by two grams of intravenous cefazolin sodium. Clindamycin 900 mg was used intravenously if the patient was allergic to penicillin. Cefazolin was repeated every 4 hours, and clindamycin was repeated every 3 hours.

Midazolam 0.1-0.2 mg/kg, fentanyl 3-10 mcg/kg, propofol 1-2 mg/kg, rocuronium 0.3-1.2 mg/kg were administered intravenously for anesthesia induction. Pulmonary ventilation was performed with mechanical ventilator at 8-10mg/kg tidal volume and 50-50% oxygen-air mixture to achieve partial arterial carbon dioxide pressure (PaCO₂) of 35-40 mmHg. After endotracheal intubation, anesthesia was maintained with propofol 20-120 mcg/kg/min., fentanyl 0.03-0.1 mcg/kg/min. and sevoflurane 0.5-2%.

Following standard median sternotomy and pericardiectomy, 300 units/kg heparin was induced for ACT to be over 450 seconds. The postoperative heparin effect was reversed using protamine sulfate at a ratio of 1: 1-1: 1.

Power analysis

G*Power, Statistical Power Analyses (v3.1.9.2) program was applied to determine the number of individuals. The power of the research was settled as 1- (= probability of type II error) and was estimated at 80%. Based on the the study of Yates et al. (8), we accepted significance at a minimum of one unit with 0.7 units of standard deviation (SD). The resultant calculated effect size was $d=1.319$. To obtain 20% type II error (power is 80%) at $\alpha=0.05$ level, it was decided to involve at least 350 individuals to the study protocol.

Ethical Approval

All procedures performed in studies involving human

participants were following the Helsinki declaration and its later amendments or comparable ethical standards. The study was also approved and reviewed by the ethics committee of Health Sciences University, Haydarpasa Numune Training and Research Hospital (March 12, 2018/38).

Informed Consent

All patients provided written informed consent to participate in the study, and additional informed consent was obtained before any surgical procedure.

Statistical analysis

IBM SPSS Statistics 22 for statistical analysis (SPSS IBM, Turkey) program was used. The suitability of the parameters to normal distribution was evaluated by Shapiro Wilks test. Student's t-test was used for the comparison of the normally distributed parameters between the two groups, and Mann Whitney U test was used for the comparison of the non-normally distributed parameters between the two groups. Friedman test was used for intragroup comparisons of parameters not showing normal distribution, and Wilcoxon sign test was used to determine the period that caused the difference. The paired sample t-test was used for in-group comparisons of quantitative data showing normal distribution, and the Wilcoxon Signed Ranks Test was used for in-group comparisons of non-normal distribution parameters. Fisher's Exact test and Continuity (Yates) Correction were used to compare qualitative data. Significance was evaluated at $p < 0.05$.

RESULTS

A total of 169 of 219 patients included, 53 (34.3%) were female, and the mean age was 61.63 ± 9.65 years. Thirty-eight (22.5%) cases had postoperative AKI according to KDIGO criteria.

The assessment of preoperative parameters was shown in Table 1. The patients who had AKI was younger ($p=0.009$).

Table 1. Assessment of demographics and preoperative parameters

		Acute kidney injury (-) (n=131)	Acute kidney injury (+) (n=38)	p
Age (year)	Min-Max (Median)	47-72 (57.5)	14-19 (17)	^a 0.009*
	Average \pm SD	60.6 \pm 9.7	65.2 \pm 8.6	
Gender; n (%)	Female	48 (36.6)	10 (26.3)	^c 0.324
	Male	83 (63.4)	28 (73.7)	
Diabetes Mellitus; n (%)	Yes	64 (48.9)	21 (55.3)	^a 0.609
	No	67 (51.1)	17 (44.7)	
Hypertension; n (%)	Yes	110 (84)	36 (94.7)	^b 0.151
	No	21 (16)	2 (5.3)	
Blood Urea Nitrogen (mg/dl)	Average \pm SD	15.7 \pm 3.1	15.5 \pm 3.2	^b 0.988
Creatinine (mg/dl)	Average \pm SD	0.69 \pm 0.18	0.71 \pm 0.19	^b 0.633
Ejection Fraction (%)	Average \pm SD	55.4 \pm 7.2	52.6 \pm 8.3	^a 0.046
Mean arterial pressure (mmHg)	Average \pm SD	95.06 \pm 11.07	98.79 \pm 11.16	^a 0.070
Haematocrite (%)	Average \pm SD	36.7 \pm 4.06	36.8 \pm 4.2	^b 0.561
^a Student's t-test	^b Mann-Whitney U Test	^c Fisher's Exact Test	^d p < 0.05	

And the left ventricle ejection fraction of the patients who did not have AKI was significantly higher than the patients who had AKI ($p=0.009$).

A higher rate of AKI was observed in colloid solution used patients ($p=0.004$). In addition, intraoperative aortic cross-clamp time was longer in patients with AKI ($p=0.001$) (Table 2).

Perioperative MAP values were significantly lower in patients having AKI ($p=0.002$) (Table 2). There is a positive correlation between the decrease in MAP value and the development of AKI (Table 3). In addition, in cases with a MAP value of 60 or less; the incidence of AKI was significantly higher in perioperative colloid solution used patients (Table 4).

Table 2. Assessment of perioperative parameters

		Acute kidney injury (-) (n=131)	Acute kidney injury (+) (n=38)	p
Mean arterial pressure (mmHg)	Average \pm SD	66.52 \pm 8.22	61.92 \pm 6.72	^a 0.002*
Central venous pressure (mmHg)	Average \pm SD	6.27 \pm 3.28	7.13 \pm 3.63	^a 0.168
Haematocrite (%)	Average \pm SD	27.1 \pm 3.2	26.3 \pm 3.8	^b 0.218
Cross clamp time (minutes)	Average \pm SD	58.24 \pm 17.08	75.5 \pm 26.76	^b 0.001*
Intraoperative fluid; n (%)	Crystalloid	68 (51.9)	9 (23.7)	^c 0.004*
	Colloid	63 (48.1)	29 (76.3)	
Blood transfusion; n (%)	Yes	68 (51.9)	16 (42.1)	^c 0.379
	No	63 (48.1)	22 (57.9)	
Positive inotropic agent; n (%)	Yes	50 (38.2)	8 (21.1)	^c 0.078
	No	81 (61.8)	30 (78.9)	

^aStudent's t-test ^bMann-Whitney U Test ^cYates Continuity Correlation *p <0.05

Table 3. Assessment of acute kidney injury in terms of mean arterial pressure

		Acute kidney injury (-) n (%)	Acute kidney injury (+) n (%)	p
Mean arterial pressure (mmHg)	\leq 60	33 (25.2)	51 (30.2)	^a 0.028*
	61-69	47 (35.9)	58 (34.3)	
	\geq 70	51 (38.9)	60 (35.5)	

^aStudent's t-test ^bMann-Whitney U Test ^cYates Continuity Correlation *p <0.05

Table 4. Assessment of acute kidney injury in terms of intraoperative fluid usage in patients having mean arterial pressure \leq 60 mmHg

		Acute kidney injury (-) n (%)	Acute kidney injury (+) n (%)	p
Intraoperative fluid; n (%)	Crystalloid (+)	13 (100)	0 (0)	^a 0.002*
	Colloid(+)	20 (52.6)	18 (47.4)	

^aStudent's t-test ^bMann-Whitney U Test

DISCUSSION

In this prospective observational study, 47.7% of cardiac surgical patients given colloid solutions perioperatively presented with AKI according to KDIGO criteria. The outcomes of the present study show that a perioperative fluid management strategy has an influence on kidney function after CABG.

The incidence of AKI following cardiac surgery ranges between 5% to 30% alternately according to the definition (9,10). And, dialysis therapy is required in %6-20 of these patients (11,12). In addition, the short term

and long term mortality rates increase to 12% to 64% in patients experienced AKI after cardiac procedures (10-13). However, the mortality rate is between 1 to 5 % in patients not developing AKI. The situation is so severe that, even minor elevations of the serum creatinine levels increase the mortality rate, surpassing 50% in patients needing hemodialysis therapy (10). In the present study, 38 patients (22.5%) were found to develop AKI. We think that the differences in the results obtained from the different studies may be due to the criteria used in the identification of AKI, and the differences in the patient population.

Our analysis revealed the mean preoperative ejection fraction was $55.42 \pm 7.26\%$ in patients without AKI, and $52.63 \pm 8.36\%$ of patients with AKI. We found preoperative ejection fraction was significantly lower in patients with AKI. ($p=0.046$). Low ejection fraction increases the risk of poor renal perfusion (14-16). Kandler et al. observed that just 12% of patients with a preoperative ejection fraction under 30% did not develop AKI (16). However, contrary to literature knowledge, Delgado et al. claimed that the preoperative ejection fraction had no impact on the post-cardiac surgery AKI (17). Unlike Delgado et al., we think, the insufficient arterial flow of the kidney is associated with kidney insufficiency. In addition, it is a known fact that endothelial dysfunction is the primary determinant of peripheral vascular disease and coronary artery disease (18). These two determinants are indirectly linked to insufficient arterial blood flow of the kidney. We also hypothesized that a stronger impact of arteriosclerosis in CABG patients is also connected with peripheral vascular disease and with endothelial injury in the arteries of the kidney, which eventually predisposes to AKI.

Another perioperative factor associated with impaired postoperative kidney function is prolonged cross-clamp time. It is obvious that prolonged cross-clamp time impairs arterial perfusion of the kidney. In results suggest mean cross-clamp time of the patients having postoperative AKI were higher than those without AKI. ($p: 0.001$). Our finding is compatible with previous studies (19-23).

MAP is another determinant of impaired kidney perfusion during CABG. Our findings suggest that MAP measurements of the patients having AKI are lower than patients not having AKI ($p=0.002$). Our results are in line with previous studies (24-26). MAP values in CABG are usually close to the minimum levels required to support the optimal arterial flow of the kidney, and any additional irregularity may cause renal ischemia and cellular injury (27). In contrast with the literature, in the study of Urzua et al., which compares the hypertensive blood pressure with the hypotensive blood pressure group, no adverse effect of low perioperative perfusion pressure was observed on postoperative kidney function (28). Researches advocating that low MAP values have no adverse impact on kidney perfusion are found in the literature (28-31). We think the technological limitations of previous studies (manually measured and possibly inadequate and biased MAP measurements) may impede their correctness and statistical power. These limitations make it challenging to determine the predictors of postoperative AKI correctly. However, most studies support that low MAP value may adversely affect kidney function; it is evident that the issue mentioned above needs further investigations.

Many clinical studies have been conducted on the perioperative use of crystalloid and colloid solutions in CABG, and the development of postoperative AKI and different outcomes have been reached. In our study, when the patients were assessed in terms of the type of solution

used perioperatively; It was found that colloid fluids were used more in patients with AKI than those without AKI ($p: 0.004$). Consistent with our findings, Lagny et al. investigated the risk of AKI in 606 patients undergoing CABG and had perioperative colloid replacement; found that 25.1% of patients had colloid solutions experienced AKI, but only 9.5% of patients had crystalloid solutions had AKI. Also, patients with perioperative colloid replacement, a higher rate of postoperative revision surgery due to bleeding were reported (32). In the study of Momeni et al., investigating the incidence of colloid fluid and postoperative AKI in cardiac surgery, they found a positive correlation between the amount of perioperative colloid solution used and the development of AKI (33). Tobey et al. studied the relationship between perioperative use of colloid solutions and postoperative AKI in patients having CABG. The amount of colloid solution was below 1000 milliliters in 47% of the patients, and more than 1000 milliliters in 53% of the patients. Tobey et al. advocated that there is no difference according to the amount of colloid solution in terms of AKI development. Nevertheless, in accordance with our study and literature, they reported that the incidence of AKI in colloid-treated patients was less than that of crystalloid-treated patients. Besides, they did not find a difference in terms of mortality between those who used colloids or crystalloids (34). In contrast to our study, in a prospective study conducted by Ryhammer et al. with 17,742 patients, it was shown that perioperative colloid solution use did not affect the need for new dialysis (35). In the review of Bignami et al. about fluid management in cardiac surgery, they showed the results, a-) there is no data showing the superiority of different fluid types b-) continuing monitoring should be used for proper fluid management in cardiac surgery c-) purpose-directed fluid management should be achieved rather than uniform fluid preference (36). It is evident that investigators do not conclude about perioperative proper fluid replacement and that there is a need for more comprehensive and more participatory studies.

LIMITATIONS

The present research has some definite weaknesses. The datum is obtained from a single center; therefore, our study protocols need to be experimented at multiple centers to be confirmed for general applicability. In addition, any irregularities in kidney function results between the groups could probably be due to unmeasured severity-of-illness variations. Further prospective, randomized investigations are expected to advance an understanding of the determinants may lead to AKI after CABG. Hence, our findings should be evaluated with attention, and more randomized controlled investigations are required.

CONCLUSION

Based on the findings of the present study, a-) age is an essential factor in the development of AKI after CABG b-) incidence of AKI decreases in patients $> EF > 55\%$. c-) maintaining perioperative MAP values within certain limits (55-60 mm Hg) and preventing excessive deviations from

basal values prevents AKI. d-) kidney functions were better preserved in patients with not prolonged CABG and cross-clamp times. e-) There is no definite conclusion about the colloid use in patients undergoing CABG. However, based on our findings, we found that the use of colloid solutions while CABG was associated with more AKI. Based on this result; it is crucial managing perioperative fluid therapy more targeted and considering the personal data of the patients.

Competing interests: The authors found that the conflict of interest did not fully coincide.

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Ethical approval: The study was also approved and reviewed by the ethics committee of Health Sciences University, Haydarpasa Numune Training and Research Hospital (March 12, 2018/38).

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