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Urine Output during Cardiopulmonary Bypass Predicts Acute Kidney Injury after Coronary Artery Bypass Grafting

Mehmet Yilmaz, MD,[1] Rezan Aksoy, MD,[2] Vildan Kilic Yilmaz, MD,[3] Canan Balci, MD,[1] Cagri Duzyol, MD,[2] Atike Tekeli Kunt, MD[2]

Departments of [1]Anesthesiology and Reanimation and [2]Cardiovascular Surgery, Derince Research and Education Hospital Kocaeli; [3]Anesthesiology and Reanimation Department, Kocaeli State Hospital, Kocaeli, Turkey

ABSTRACT

Objective: This study evaluated the relationship between the amount of urinary output during cardiopulmonary bypass and acute kidney injury in the postoperative period of coronary artery bypass grafting.

Methods: Two hundred patients with normal preoperative serum creatinine levels, operated on with isolated CABG between 2012-2014 were investigated retrospectively. The RIFLE (Risk, injury, failure, loss of function, and end-stage renal disease) risk scores were calculated for each patient in the third postoperative day. Patients were distributed into two groups in relation to the presence of acute kidney injury or not and these two groups were compared.

Results: The urinary output (mL/kg/hour) during cardiopulmonary bypass in the acute kidney injury negative group was significantly higher than in the acute kidney injury positive group ($P = .022$). In case of a urinary output value 3.70 and lower to predict acute kidney injury positivity, sensitivity was detected as 71.43%. Results of the analysis for urinary output predict positivity of acute kidney injury.

Conclusion: We suggest that urine output during cardiopulmonary bypass is a significant criteria that could predict acute kidney injury following coronary artery bypass grafting with cardiopulmonary bypass. Attempts to increase the urine output during cardiopulmonary bypass could help to maintain the renal functions during and after surgery.

INTRODUCTION

Cardiopulmonary bypass (CPB) is frequently used in the treatment of coronary artery, valvular, and congenital heart diseases. Despite the improvements in cardiac surgery with cardiopulmonary bypass, there is still a possibility for various organ dysfunctions to occur.

Cardiopulmonary bypass triggers systemic inflammatory response syndrome (SIRS) [Cremer 1996]. The possible reasons for SIRS during CPB are contact of blood with the artificial surfaces of CPB circuit, ischemia-reperfusion injury, endotoxemia, nonpulsatile blood flow, and former left ventricular dysfunction [Czerny 2000]. One or more of the following can be seen in SIRS by various mechanisms: renal, pulmonary, central nervous system, gastrointestinal system and myocardial function disorders, coagulopathy, vasodilatation, hemolysis, increase in capillary permeability, fever or infection [Fransen 1998]. Acute kidney injury (AKI) of various grades may develop following cardiopulmonary bypass in 1% to 30% of patients [Bove 2004; Thakar 2003]. Only 5% of patients with AKI require renal replacement therapy (RRT) [Loef 2005]. However, the mortality rate for patients with renal replacement therapy reaches 40-60% [Bove 2004; Provenchère 2003]. Hourly urinary output volume is an important criteria for the follow up of renal functions. In general, an output of 0.5-2 mL/kg/h is accepted as normal. Urinary output lower than 0.5 mL/kg/h is evaluated as oliguria, which is a messenger of AKI [Buğra 2014]. Despite the fact that there are lots of reasons that affect renal perfusion during CPB and AKI potentially occuring at a serious rate following CPB, there are not many reports regarding the amount of urinary output, which is suggestive of AKI during CPB.

In this study, we evaluated the relationship between the amount of urinary output during CPB and AKI in the postoperative period in patients undergoing elective coronary artery bypass grafting (CABG) operated on in our clinic.

MATERIALS AND METHODS

Three hundred and twenty five patients who were operated on with open heart surgery in our clinic between January 2012 and July 2014 were evaluated retrospectively, and 200 of these patients who underwent isolated coronary bypass gratfing were included in the study. Only patients without formerly known renal failure and with normal preoperative serum creatinine levels (creatinine level <1.4 mg/dL, glomerular filtration rate >60 mL/dk/m^2) were included. Patients who had been given diuretics or inotropic drugs intraoperatively were excluded from the study. EuroSCORE values of all of the patients were evaluated; patients at high risk were not included in the study. Patients with an increase of more than 1.5 times the preoperative creatinine values on their third postoperative day were evaluated as AKI according to RIFLE criteria. Patients were divided into two groups regarding presence of AKI or not, and these two groups were compared.

Demographic variables (age, sex) and body mass index (BMI) of the patients in both groups were recorded and the presence of diabetes mellitus (DM) and hypertension (HT)

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Correspondence: Mehmet Yilmaz, MD, İbni Sina Mah, Sopalı Mevki Lojman Sok, Derince Merkez, Derince, Kocaeli, Turkey; +90-505-217-44-32; fax: +90-262-233-55-40 (e-mail: drmyilmaz33@mynet.com).

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Table 1. Demographic Data of the Groups

	AKI (-) (n = 186)	AKI (+) (n = 14)	P
Age, y	61.50 ± 9.73 (62)	65.64 ± 11.02 (65)	.219
Sex			
Male	134 (93.7)	9 (6.3)	.547
Female	52 (91.2)	5 (8.8)	
BMI, kg/m2	28.63 ± 4.62 (27.74)	26.47 ± 4.76 (25.39)	.121
EF, %	56.85 ± 7.71 (60)	54.46 ± 10.47 (60)	.459
Diabetes			
-	120 (96.0)	5 (4.0)	.032*
+	66 (88.0)	9 (12.0)	
Hypertension			
-	109 (94.0)	7 (6.0)	.529
+	77 (91.7)	7 (8.3)	
EuroSCORE			
2	66 (94.3)	4 (5.7)	.928
3	93 (92.1)	8 (7.9)	
4	27 (93.1)	2 (6.9)	

AKI: Acute Kidney Injury; BMI: Body Mass Index; EF: Ejection Fraction. The median values were written in parenthesis. Significant p values were marked with '' * ''.

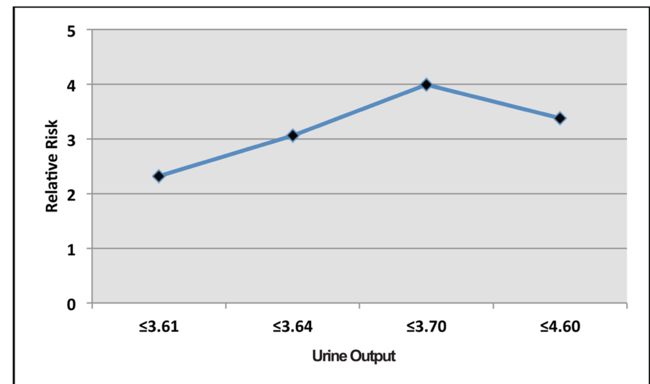
Table 2. Operative Variables of the Groups

	AKI (-) (n = 186)	AKI (+) (n = 14)	P
Duration of CPB, min	115.15 ± 39.95 (113.5)	134.36 ± 54.84 (130)	.178
Duration of aortic cross clamping, min	67.24 ± 24.23 (66)	71.21 ± 32.45 (73.5)	.714
CPB temperature, ºC	30.44 ± 1.60 (30)	29.64 ± 1.15 (30)	.117
Number of blood products used, units	0.87 ± 0.87 (1)	0.5 ± 0.85 (0)	.161
Intraoperative fluid balance, mL	850.80 ± 231.99	4.95 ± 2.39 (4.65)	.840
Urine output during CPB (mL/kg/hour)	860.71 ± 259.59	3.63 ± 1.77 (3.15)	.022*

CPB: Cardiopulmonary Bypass; UO: Urine Output; AKI: Acute Kidney Injury. The median values were written in parenthesis. Significant p values were marked with '' * ''.

were sought. Ejection fraction (EF), duration of CPB and aortic cross clamping, and temperature during CPB were recorded. Preoperative and intraoperative mean arterial pressures, pCO_2, pO_2 and hemoglobin values were obtained from blood gas analysis. Patients requiring blood transfusion and the amount of blood products required were recorded. Blood urea and creatinine levels of both groups were compared on the third postoperative day. The requirement of hemofiltration during CBP and ocurrance of postoperative complications in both groups were compared.

All operations were performed in a standardized approach by a Terumo roller pump (Terumo Advanced Perfusion System 1), membrane oxygenators (Dideco Compactflo Evo), mild to moderate (28-32°C) hypothermia, and continuous flow of 2.2-2.4 L/m². Priming solution included 150 mL of 20% mannitol in both groups. Myocardial protection was achieved with tepid antegrade blood cardioplegia and a "hot shot" (250-500 mL) was delivered just prior to the removal of the aortic cross-clamp. The perfusion pressure was kept over 70 mmHg at all times. Standard anaesthetic induction with intravenous propofol, fentanyl, and rocuronium bromide was performed in all patients. The anesthetic management was made using inhalation of 60% oxygen and 6% desflurane. All operations were performed by the same surgical team. Activated coagulation time (ACT) was kept in between 480 to 600 seconds by heparin infusion. A protamine dose of 0.8 mg/kg was administered to neutralize heparin. Additional protamine



Cutoff point for urine output.

was given until the ACT reached 130 seconds.

Exlusion criteria from the study was as follows: patients with an EF of 35% or lower detected with preoperative echocardiography; known renal failure; applied coronary angiography and/or percutaneous coronary intervention in the final 3 days prior to CABG; and patients who needed positive inotropic agents and intraaortic baloon pump counter pulsation (IABP) following CPB and furosamide intravenous bolus during CPB.

Statistical Analysis

Number Cruncher Statistical System software (NCSS, 2007, Kaysville, Utah, USA) was used for statistical analysis. For evaluation of study data, besides definitive statistical methods (mean, standard deviation, median, incidence, and rate), the one-way ANOVA test and Tukey HDS test were used for

Table 3. Evaluation of Diagnostic Tests to Determinate Cutoff Point for Urine Output Acute Kidney Injury (AKI)

UO	Sensitivity	Specificity	PPV	NPV	Accuracy	RR
≤3.61	57.14	65.05	10.96	95.28	64.50	2.32
≤3.64	64.29	65.05	12.16	96.03	65.00	3.06
≤3.70	71.43	63.98	12.99	96.75	64.50	3.99
≤4.60	78.57	50.00	10.58	96.88	52.00	3.38

UO: Urine Output; PPV: Positive Predictive Value; NPV: Negative Predictive Value; RR: Relative Ratio.

Table 4. Comparison of values of blood gas analysis and blood pressures between groups

	AKI (-) (n = 186)	AKI (+) (n = 14)	*P*
Preoperative MAP	82.37 ± 7.06 (80)	79.29 ± 6.16 (80)	.165
Intraoperative	64.38 ± 5.40 (65)	65.00 ± 5.55 (62.5)	.707
Preoperative PO_2	88.80 ± 32.23 (82)	94.60 ± 19.47 (85)	.063
Intraoperative	291.17 ± 47.38 (296)	282.30 ± 71.15 (276)	.417
Preoperative PCO_2	31.63 ± 3.95 (32)	30.84 ± 4.02 (31)	.466
Intraoperative	30.91 ± 5.58 (29)	30.51 ± 4.92 (30.5)	.849
Preoperative HGB	12.79 ± 2.22 (13)	8.07 ± 1.08 (7.9)	.879
Intraoperative	13.25 ± 1.52 (13)	8.23 ± 1.12 (7.7)	.877

MAP: Mean Arterial Pressure; HGB: Hemoglobin; AKI: Acute Kidney Injury. The median values were written in parenthesis.

numeric data matching normal distribution; the Kruskal-Wallis test and Mann-Whitney U test were used for numeric data unmatching normal distribution. Paired sample t test was used for comparison of parameters with normal distribution inside a group; Wilcoxon signed rank test was used for comparison of parameters without normal distribution inside a group. The Pearson chi-square test, Yates continuity correction test and Fisher exact test were used for categorical data. The results were evaluated with a 95% confidence interval and a *P* value of less than .05 was considered statistically significant.

RESULTS

The demographic variables (sex, age, BMI, hypertension, EF and EuroSCORE) were similar among groups. The incidence of AKI in patients with diabetes mellitus was statistically significantly higher than in patients without diabetes mellitus (*P* = .032) (Table 1).

Among the 200 patients included in the study, 14 patients were considered to have AKI according to the RIFLE criteria regarding 1.5 times more elevated serum creatinine levels than the baseline.

The CPB and cross clamping times, body temperatures, and the amount of blood products used were similar between the groups (*P* > .05) (Table 3). The urinary output during CPB (UO) (mL/kg/hour) of the AKI(-) group was significantly higher than the AKI(+) group (*P* = .022) (Table 2).

In case of a UO value less than 3.70 to predict AKI positivity, sensitivity was detected as 71.43%, specificity was detected as 63.98%, PPV was detected as 12.99%, NPV was detected as 96.75%, accuracy was detected as 64.50%, and relative risk was detected as 3.99 (Table 3) (Figure).

The mean arterial pressure levels and pO_2 and pCO_2 values of arterial blood gas analysis were similar among groups in the preoperative and intraoperative periods (Table 4).

None of the patients in either group required renal replacement therapy.

DISCUSSION

Acute kidney injury following CPB is an important cause of morbidity and mortality [Cruz 2010]. In the recent literature, there are many studies present regarding early diagnoses of AKI and prevention from the inflammation processs, an accepted cause of AKI [Buğra 2014; Cagli 2005; Zhang 2005; Boldt 2001; Loef 2004; Tossios 2003; Sucu 2004; Kshirsagar 2004]. However, the number of studies regarding the relationship between urine output during CPB and postoperative AKI are limited. In our study, 200 patients who were operated on with isolated elective CABG, who didn't have a history of known renal disease, and who had creatinine levels in normal range and GFR over 60 mL/min/m^2 were investigated retrospectively for the analysis of the effect of hourly urine output volume during CBP on postoperative AKI.

Acute kidney injury following cardiac surgery is multifactorial. The known risk factors are advanced age, diabetes, low preoperative GFR (<60 mL/min/m^2), low EF (<35%), early surgery following myocardial infarction, early surgery following percutaneous cardiac intervention, and administration of nephrotoxic agents. Taking into account all of this information, the patients with known renal disease, operated on in the 72 hours following percutaneous cardiac intervention, having acute myocardial infarction, aged over 75 years, and using angiotensin converting enzyme inhibitors or angiotensin receptor blockers were excluded from the study. There was no statistically significant difference between the study groups regarding demographic variables and risk factors for AKI following CABG, such as hypertension, EF, and EuroSCORE values. The incidence of AKI was found to be higher in patients with DM in our study in parallel with the literature [Bove 2004; Maitra 2009; Karkouti 2005].

It has been shown in the studies that longer CPB and cross clamp times, hemodilution, hemolysis, systemic inflammatory response, usa of excess blood products, and hemodynamic instability causing renal hypoperfusion are risk factors for AKI following open heart surgery [Bove 2004; Maitra 2009; Karkouti 2005]. The duration of CPB and cross clamp, bladder temperatures during CPB, and measured mean arterial pressure levels during the operation between the groups

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were similar in our study. Although the groups were similar in terms of presence of HT and length of CPB time in univariate analysis, these parameters were determined as risk factors in multivariate analysis in parallel with the literature.

In the studies where cross clamp time and the incidence of AKI were compared, the risk for AKI to occur were found to be higher, particularly in patients with cross clamp time over 70 minutes [Boldt 2003; Fischer 2002]. In our study, we found statistically significant differences in the postoperative period between the two groups regarding the amount of urinary output during CPB.

Preoperative and intraoperative values of hemoglobin and hematocrit play roles in the occurrence of AKI following CPB by various mechanisms. The risk for AKI was reported to increase by hemodilution, which lowers the hemoatocrit values under 25%. Furthermore, the blood products used for the patient may interfere both with hemoglobin and hematocrit levels and renal perfusion directly by various mechanisms [Karkouti 2005]. In our study, there were no statistically significant differences in the levels of hemoglobin, pO_2 and pCO_2 in the preoperative and intraoperative periods.

Accompanied by all these data, the effects of inflammation and systemic hemodynamic changes due to CPB on renal functions are controversial. In a study by Kron and colleagues in 1985, hypothermia was reported to possibly impair renal function [Kron 1985]. However, in another study reported in 1995, which investigated the renal functions in temperatures of 28, 32 and 37°C, no significant differences in renal functions were found at different temperature levels [Regragui 1995]. Pressure in CPB pump circuits during CPB causes hemolysis, which may result in hemoglobinuria, anemia, and therefore AKI [Karkouti 2005].

The effects of partial arterial oxygen pressure on tissue perfusion are known. Both hypoxemia by reducing the amount of oxygen carried to renal cells and hyperoxemia by changing the rheologic characteristics of erytrocytes influence microcirculation and therefore renal perfusion [Toraman 2007].

In a study on patients with normal preoperative renal functions in which the patients were divided into two groups, one with a mean arterial pressure adjusted to 50-60 mmHg during CPB and the other adjusted over 70 mmHg, there were no differences regarding postoperative renal functions, although intraoperative creatinine clearance values were higher in the group with mean arterial pressure over 70 mmHg [Urzua 1992].

In the literature as far as we have scanned, we did not find any study on the relationship between the UO during CPB and postoperative AKI. In our study, the difference between the groups in terms of UO was statistically significant (P = .022) with univariate analysis. When the risk factors for AKI were evaluated, the difference in UO values between the groups was not found so far from the significant level (P = .083). We think that the UO variable might have been significant if our sample size had been greater; therefore, we suggest greater sample sizes for future studies.

There are some limitations of our study. This study was designed as a retrospective study rather than a randomized trial. The second limitation is that although the power calculation of the study is satisfactory regarding the number of patients in the study groups, a larger number of patients and a multicentre study could increase the value of our hypothesis.

In conclusion, to the best of our knowledge, our study seems to be the first that deals with the urine output during CPB and AKI occurrence following CABG. We suggest that urine output during CPB is a significant criteria that could predict AKI following CABG with CPB. Attempts to increase the urine output during CPB could help maintain renal functions during and after surgery.

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