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The relationship between fluid balance and the incidence of post-operative acute kidney injury during and 24 hours after coronary artery bypass graft surgery

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ABSTRACT

Introduction: Around 30% of patients undergoing cardiac surgery experience acute kidney injury (AKI).
Objectives: The purpose of this study was to determine the relationship between fluid overload and serum creatinine changes in patients undergoing coronary artery bypass grafting (CABG) surgery.
Patients and Methods: a total of 130 patients undergoing CABG surgery were entered into the study using cardiopulmonary bypass (CPB). The fluid balance for each patient was calculated for 24 hours after surgery. Each patient was classified into one of these three groups; 1) Patients with a fluid balance of less than 2000 mL; 2) Patients with fluid balance of 2000 to 3000 mL; 3) Patients with a fluid balance of more than 3000 mL. Serum creatinine changes and renal failure were studied in these three groups.
Results: After multivariate analysis of the factors affecting the incidence of AKI, we found a significant relationship between the administration of inotrope and AKI incidence (P=0.001, 75.1875 to 847.5, 95% CI, 664/89, OR). However, there is no significant relationship between the incidence of AKI and the high fluid balance.
Conclusion: There are many interactions between renal function and fluid balance during a cardiovascular-pump. According to the results of our study, the high fluid balance in patients has a minor effect on serum creatinine.

Implication for health policy/practice/research/medical education:
Implications of this study include 1) Reducing the length of stay of kidney patients undergoing heart surgery in the intensive care unit; 2) Satisfaction of kidney patients, especially those undergoing heart surgery; and 3) Reducing hospital costs and improve the quality of life of kidney patients undergoing heart surgery.
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Introduction

Coronary artery disease (CAD) is one of the main causes of human mortality in the world and coronary artery bypass grafting (CABG) is the mainstay treatment method for CAD (1). Over the past 50 years, cardiopulmonary bypass (CPB) and open heart surgery have led to significant advances in surgical methods throughout the world (2). Although CABG with the help of CPB is a common method for treating CAD, this procedure causes multiple complications after surgery. Acute kidney injury (AKI) is a common complication of cardiac surgery (3). Age, body mass index (BMI), ejection fraction, number of involved vessels, exogenous circulation time, aortic cross-clamp (X-clamp) (min), hemoglobin and serum creatinine levels are associated with post-operative complications (4).

Many of these factors are not modifiable. However, serum creatinine is a moderately regulated agent that is widely used to evaluate renal function in patients undergoing bypass surgery. One of the most important post-operative complications is the accumulation of fluids

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Original

in the body (5-8). Several factors are considered as the cause of fluid accumulation, including the induction of systemic inflammatory responses of the body as a result of the use of CPB and increased vascular permeability (9,10). On the other hand, over-administration of fluids including crystalloids, colloids, blood and blood products during and after surgery can cause fluid buildup in the body and tissue edema. Serum creatinine changes and renal failure are some of the most common complications after CABG surgery. Overflow fluid induces more renal perfusion and glomerular filtration rate (9, 10). A recent study showed a slight increase in serum creatinine (0.5-0.5 mg/dL) was associated with mortality in patients within 30 days after cardiac surgery (11,12). On the one hand, fluid accumulation is associated with heart failure in patients. In fact, the overdrive fluids are a new biomarker for cardiac and renal function. Serum creatinine is considered a good indicator of kidney function. However, the creatinine range remains normal until about half of the kidney function is lost. AKI is defined as increasing serum creatinine of greater than or equal to 0.3 mg/dL or an increase of 50%-200% of creatinine from an initial value.

Objectives

The purpose of this study was to determine the relationship between fluid overload and serum creatinine changes in patients undergoing CABG surgery.

Patients and Methods

Study design

The present prospective study was carried out at the Rajaee Cardiovascular Center, Tehran over a six-month period (2016). The study included 130 adult patients who were candidates for CABG surgery by CPB. The criteria for entering the study included; adult patients (over 18 years old), elective surgery, all the patients who underwent CABG surgery "on-pump", not redo CABG surgery, no combined valve+ CABG surgery and not having preoperative renal failure (patients with creatinine above 2 mg/dL were excluded from the study). Other patients regardless of gender, racial or social status were included in the study. In this research, easy sampling was conducted. In an easy sampling, the patients were randomly assigned to the operating room for CABG surgery, and provided that they had input criteria. All information was collected and recorded before, during and after the operation of each patient, and then the patients were followed up on the day of discharge from the hospital. For each patient, the fluid balance was calculated and finally, based on the fluid balance, each of them was placed in one of the following three groups:

- Group I; patients whose balance of fluids was less than 2000 mL for 24 hours after surgery.
- Group II; patients whose fluid balance was between 2000 and 3000 mL up to 24 hours after surgery.
- Group III; patients whose balance of fluids exceeded 3000 mL for up to 24 hours after surgery.

The equilibrium fluid formula was calculated using the formula conducted by Stein et al, as follows:

Fluid balance = (intravenous fluids + cardioplegia + fluid in the pump unit) - (urine output + filtered fluid from the pump + drainage fluid in the chest tube).

Blood loss on gases, as well as inaccurate liquids disposal, are not included in this calculation, however it can be assumed that this value is the same for all groups and does not play a role in the balance of fluids (12). The post-operative AKI was considered as a consequence of the study between the time after the completion of the operation and hospital discharge.

First, sampling started in the operating room where the researcher or colleagues were present from the beginning to the end of the surgery. Then, demographic data, risk factors, laboratory results and echocardiography reports of patients were recorded according to the contents of the case file in the study forms. They also recorded the exact amount of fluid intake and disposal of the patient, the amount of fluid in the pump device and the volume of filtered liquid. Other information about the patient's presence in the operating room until the end of the surgery was recorded too. After the surgery, patients were transferred to the ICU and the second stage of data collection began at the moment of entering. From the arrival of the patient to the special section, up to 24 hours afterwards, the amount of fluids, blood and blood products received. Additionally, the amount of urine output, discharge and bleeding of drains and chest tube drainage was carefully recorded in the forms. Simultaneously, the researcher recorded the complications and consequences of the ICU. The possible outcomes of surgery were recorded since the admission to discharge of the patient from the hospital.

Ethical approval

The protocol of the study has been approved by the Ethics Committee of Rajaie Cardiovascular Medical and Research Center, Iran University of Medical Sciences (RHC.AC.IR.1395.53), Tehran, Iran and has therefore been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki and its later amendments. The protocol of the study was clarified to all participants and written informed consent was obtained from the patients. Besides, this study was extracted from the M.D, thesis of Elham Shahidi at this University (Thesis# PP; 94/37).

Data analysis

One sample of Kolmogorov Smirnov was used to determine the normal variables. In numerical variables after data normalization test, in the case of normal, independent t-test and in case of non-normalization, Mann Whitney U test was used. Mann Whitney U test was used to compare the rank and file variables between the two groups. To compare numerical variables, two groups of Pearson's chi-square or Fisher's exact test were used. Binary logistic regression was used for multivariate analysis.

Results

At the end of the sampling period, 130 forms were collected. No patient was excluded from the study. Around 67.7% of men (88 subjects) were included in this study. Age of subjects varies from 40 to 81 years (mean of 62.31 ± 9.20 years). Calculation of the fluid balance in the samples shows that the minimum and maximum volume of balance is 500 mL and 6200 mL respectively. Demographic data and risk factors for preoperative factors are presented in Table 1. No significant difference in CPB time, cross-clamping time, surgical length and inotrope and baseline creatinine in all three groups was detected (Table 2). According to Figure 1, the number of days in the hospital was evaluated. We found a significant relationship between days of hospital stay and fluid balance ($P < 0.001$). Using the Mann Whitney U test for post-hoc comparison between two groups, we found, the average amount of hospital stay in the third group was significantly higher than the first group. Considering the data in Table 3, no significant relationship between the percent of AKI of patients with their fluid balance in all three groups ($P = 0.186$) was seen. After multivariate analysis of the factors affecting the incidence of AKI, a significant relationship between the use of inotrope and the incidence of AKI was found ($P = 0.001$, 121.75 to 847.5, 95% CI, 664/89, OR; Table 4). In addition, there is no significant relationship between the incidence of AKI and the high fluid balance.

Discussion

According to Table 3, there were 9 patients out of a total of 130 patients with AKI (One patient in the first equilibrium group, two patients in the second group and six patients in the third equilibrium group). No significant relationship between equilibrium volume and prevalence of AKI among them was found. The smaller sample size in this study as well as the separate study of AKI as a complication could be due to differences in the results of this study with the study by Morin et al (13). However, in the study by Toraman et al (14) a correlation between fluid balance and postoperative complications was detected. They found renal complications were not significantly associated with equilibrium volume. There are many interactions between renal function and fluid balance during a cardiovascular pump. CPB causes fluid shifts, electrolyte imbalances and inflammation throughout the body. Acute exacerbation of cardiac output is the most common and most important risk factor for the development of acute renal damage (13).

Hemodilution caused by fluid overload in the body

Table 1. Demographic characteristics and preoperative risk factors by groups

Variable	Groups (n = 130)			*P* value
	Balance group <2000 mL (n=44)	Balance group = l000-3000 mL (n=36)	Balance group >3000 mL (n=52)	
Age (years)[a]	60 (57-68)	61 (54.75-65.25)	64 (56.25-72)	0.383
Gender (female/male)	33.11	25.9	30.22	0.120
BMI (kg/m^2)[a]	75 (70-82.75)	75 (68.75-84.25)	69.50 (60.50-80)	0.057
The median left ventricular ejection fraction (%)[a]	50 (45-50)	45 (35-50)	45 (41.25-55)	0.240
Diabetes[b]	13 (29.5%)	12 (35.3%)	25 (48.1%)	0.150
Blood pressure[b]	16 (36.4%)	22 (64.7%)	34 (65.4%)	0.008
Smoking history[b]	23 (52.3%)	16 (46%)	12 (23.1%)	0.007
High blood lipids[b]	9 (20.5%)	15 (44.1%)	22 (43.3%)	0.039
Thyroid dysfunction[b]	1 (2.3%)	4 (11.8%)	5 (9.6%)	0.140
Recent MI history[b]	4 (9.1%)	11 (32.3%)	7 (13.7%)	0.053
Cerebrovascular accident history[b]	2 (4.5%)	2 (5.9%)	3 (5.8%)	0.955
Lung disease[b]	0 (0.0%)	1 (2.9%)	3 (5.8%)	0.264
Drug addiction[b]	8 (18.2%)	11 (33.3%)	7 (13.5%)	0.139
Functional class NYHA				
1	3 (6.8%)	1 (2.9%)	5 (9.6%)	0.023
2	39 (88.6%)	24 (70.6%)	41 (78.8%)	
3	2 (4.5%)	8 (23.5%)	6 (11.5%)	
4	0 (0.0%)	1 (2. 9%)	0 (0.0%)	

NYHA, New York Heart Association; BMI, body mass index;
[a] Descriptive information (Interquartile range) is provided on a median basis
[b] Descriptive information is presented in frequency (percentage).
P<0.05 was considered statistically significant.

Table 2. Comparison of intraoperative parameters in patients divided into three groups

Variable	Groups (n = 130)			*P* value
	Balance group <2000 mL (n=44)	Balance group = l000-3000 mL (n=36)	Balance group >3000 mL (n=52)	
Elective surgery	38 (86.4%)	33 (97.1%)	46 (88.5%)	0.264
Emergency surgery	6 (13.6%)	1 (2.9%)	6 (11.5%)	
Duration of pulmonary pump (min)	75 (52-88.75)	75 (58.75-105)	75 (60-110)	0.775
Aorta X-clamp time (min)	41 (31.50-50)	35 (30-54.25)	4.45 (26-56)	0.649
Duration of surgery (h)	5 (4.03-5.11)	42.32 (4-5.47)	4.45 (4-5.52)	0.964
Use of inotrope	3 (6.8%)	4 (11.8%)	12 (23.1%)	0.964
Hemoglobin before surgery	13.5 (13-14.3)	13 (11.6-14.5)	13 (12.1-14.1)	0.139
Creatinine Before Surgery	1 (0.82-1.1)	1 (0.87-1.2)	1 (0.80-1.1)	0.139
Number of grafts				
1	0	1 (2.9%)	2 (3.8%)	
2	9 (20.5%)	9 (26.5%)	14 (26.9%)	
3	20 (45.5%)	13 (38.2%)	17 (32.7%)	0.801
4	14 (31.8%)	9 (26.5%)	15 (28.8%)	
5	1 (2.3%)	2 (5.9%)	4 (7.7%)	
Use of packed-cell	16 (36.4%)	14 (41.2%)	31 (59.6%)	0. 055

The number index (percent) in the ordinal and nominal variables, Mean ± SD for numerical variables with normal distribution and median (25th percentile -75th percentile) is used for variables with abnormal distribution. $P<0.05$ was considered statistically significant.

Table 3. Comparison of the incidence of acute renal injury (AKI) in each of the groups

Variable	Groups (130 = n)			*P* value
	Balance group <2000 mL (n=44)	Balance group = l000-3000 mL (n=36)	Balance group > 3000 mL (n=52)	
AKI	1 (2.3%)	2 (5.9%)	6 (11.8%)	0.186

$P<0.05$ was considered statistically significant.

by reducing oxygen supply to tissues increases lactate production and increase the risk of developing AKI (15). In a study by Lassnigg et al, a slight increase in serum creatinine (0.1-5 mg/dL) was associated with mortality in cardiac surgery patients(11). They identified AKI as an increase in serum creatinine of greater than or equal to 0.3 mg/dL, or an increase of 50%-200% of serum creatinine from an initial amount. However, the prevalence of acute renal damage is different in patients with a reduction in cardiac output, as other risk factors also contribute to kidney damage. Morin et al classified renal injury along with complications such as death, heart disease, tamponade and low cardiovascular disease in the major complications group (14). After analyzing, they found a significant relationship between the incidence of major complications and those who had overweight over five kg due to fluid accumulation.

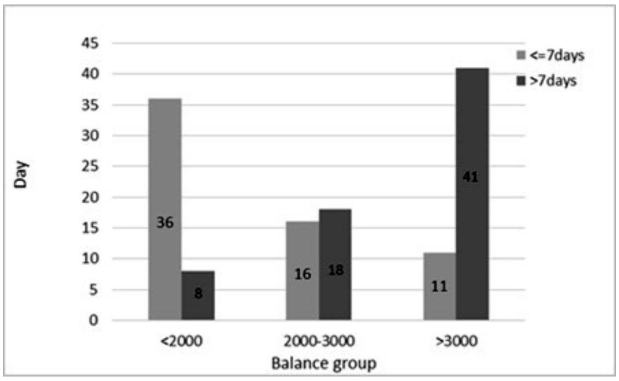

Figure 1. Comparison of the number of days in the hospital in all three groups.

Conclusion

Our study showed, the relationship between fluid overload and serum creatinine changes in patients undergoing CABG surgery. On the other hand, high fluid balance in patients had a minor effect on serum creatinine.

Limitations of the study

This study was primarily limited by its small sample size, therefore it cannot be generalized to other populations. Lack of follow-up of patients is another limitation of this study.

Authors' contribution

SMA; study concept and design, acquisition of data, analysis and interpretation of data, drafting of the manuscript,

Table 4. Effective factors in causing acute renal injury (AKI) (multivariate analysis)

Variable	Coefficient	SE	P Value	OR	95% CI for OR	
					Lower limit	Upper limit
Balance <3000 mL	1.875	1.141	0.100	6.521	0.697	61.049
Age	0.110	0.071	0.119	1.116	0.972	1.282
Gender	-1.151	1.553	0.459	0.316	0.015	6.638
BMI (kg/m^2)	0.042	0.051	0.410	1.043	0.944	1.152
Diabetes	0.919	1.155	0.426	0.399	0.042	3.836
High blood lipids	0.469	1.153	0.667	1.642	0.171	15.746
High blood pressure	1.101	1.360	0.418	3.008	0.209	43.223
Myocardial infarction	0.479	0.391	0.220	1.614	0.751	3.470
Bypass time	-0.030	0.020	0.145	0.971	0.933	1.010
Mechanical ventilation> 10 h	-0. 012	0.097	0.899	0.988	0.817	1.194
Smoking	1. 578	1.276	0.216	4.846	0.398	59.074
NYHA	1. 324	1.031	0.199	3.757	0.498	28.353
Use of inotrope	4. 496	1.393	0.001	89.664	5.847	75.121

NYHA, New York Heart Association; SE, standard error; OR, odds ratio; BMI, body mass index.
$P < 0.05$ was considered statistically significant.

critical revision of the manuscript for important intellectual content, statistical analysis, administrative, technical, and material support, and study supervision. ES; acquisition of data, analysis and interpretation of data, drafting of the manuscript, statistical analysis. HS; acquisition of data, analysis and interpretation of data, drafting of the manuscript, statistical analysis. MZ; acquisition of data, analysis and interpretation of data, drafting of the manuscript, statistical analysis. SSB; acquisition of data, analysis and interpretation of data, drafting of the manuscript, statistical analysis. Drafting of the manuscript, critical revision of the manuscript for important intellectual content. MF; acquisition of data, analysis and interpretation of data, drafting of the manuscript, statistical analysis. MS; acquisition of data, analysis and interpretation of data, drafting of the manuscript, statistical analysis.

Conflicts of interest

All authors declare no potential conflicts of interest.

Ethical considerations

Ethical issues including plagiarism, double publication, and redundancy have been completely observed by the authors.

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