IJKD KIDNEY DISEASES

Fluid Balance Has Effects on the Length of Hospital Stay After Coronary Artery Bypass Grafting Surgery

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Introduction. A vast range of factors cause adverse outcomes after coronary surgery. The goal of this study was to figure out if there was a relation between large volumes of fluid balance in patients who underwent coronary surgery and common complications after CABG.

Methods. 130 candidates for on-pump CABG were enrolled in our study at Rajaie Cardiovascular Medical and Research Center in 2016. After calculating balance volume for each patient, they were divided into 3 groups; Group (1): fluid balance < 2000 mL, Group (2): fluid balance 2000-3000 mL, Group (3): fluid balance > 3000 mL. Some of the post-surgery complications were studied in these 3 groups. Since in similar studies, fluid overload has been investigated based on the patient's weight gain after surgery or only on the basis of the patient's fluid intake, we designed a study based on an accurate fluid balance measurement, which included the subtraction of the patient's outputs and losses from their intakes.

Results. Logistic Regression showed that fluid balance > 3000ml was the predictor of long mechanical ventilation [(Odds Ratio (95% CI) = 4.6 (1.9 - 11.5), $P < .05$], more than 3 days of ICU stay [(Odds Ratio (95% CI) = 3.2 (1.09 - 9.6), $P < .05$], and longer hospital stay [Odds Ratio (95% CI) = 5.2 (1.9 - 14.08), $P < .05$]. There was no significant relation between AKI and fluid balance.

Conclusion. Administration of large fluid volumes in CABG patients would lead to fluid accumulation and independently associated with prolonged mechanical ventilation, longer ICU stays and extended hospital stays.

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INTRODUCTIONS

Although the coronary artery bypass grafting along with cardiopulmonary bypass (CPB) reduces angina in patients with coronary diseases, this method can cause significant complications such as fluid overload.[1-4] Different mechanisms have been postulated as possible causes for this hypervolemia. For instance, CPB can cause an inflammatory response throughout the body and capillary permeability and fluid leakage in the extravascular space would increase as a result.[5,6] On the other hand prescription of the large volume of fluids containing crystalloids, colloids, packed cells and other blood products during and after surgery augments fluid aggregation which result in widespread tissue edema and more need for oxygenation.[7,8] Moreover, fluid overload exerts greater venous pressure on the kidney perfusion and glomerular filtration.[9-11]

It seems onset of the complications after

CABG can lead to extend ICU stay and lengthy hospitalization.

This study was designed to assess the relationship between fluid balance and long ICU stay, long mechanical ventilation, acute kidney injury, and long hospital stay in patients undergoing CABG surgery.

MATERIALS AND METHODS

Study Design

We conducted a historical cohort study, which lasted 6 months in the year 2016. 130 patients were drawn from adult patients (over 18 years of age) who had undergone coronary artery bypass grafting involving cardiopulmonary bypass (CPB) at Rajaie Cardiovascular Medical and Research Center, a tertiary care hospital for cardiovascular patients in Tehran, Iran. The odds ratio of the fluid balance and postoperative complications was calculated 4.43. So, considering $\alpha = 0.05$ and $\beta = 0.2$; using the GPower 3.1 software, the sample size was determined at least 120 people. The Sample size formula was as below:

$$N = \frac{\left\{z_{0.975} + z_{0.9}\exp(-\beta_2^2/4)\right\}^2}{\exp(\beta_1)\beta_2^2}\left\{1+2\exp\left(\beta_1\right)\delta\right\}$$

$$\delta = \frac{1+\left(1+\beta_2^2\right)\exp\left(5\beta_2^2/4\right)}{1+\exp\left(-\beta_2^2/4\right)}$$

Inclusion criteria were as follows: adult patients (over 18 years of age), on-pump surgery, elective surgery, isolated CABG (not valve and other surgeries simultaneously), not being redone surgery, patients with no history of renal failure (creatinine above 2 mg/dL). Other patients have no more limitation to enter the study and were included in the study regardless of sexual, racial or social status. This research protocol was approved by the ethics committee of Rajaie Cardiovascular Research Center.

Data Collection

The operating room was the primary location for our survey. Researchers were present from the beginning to the end of the surgery. Preoperative demographic indicators and risk factors were obtained from medical records. They contained age (in full years), gender, weight (kg), history of smoking and opioid, diabetes, dyslipidemia, pulmonary diseases, thyroid diseases, cerebrovascular disease, hypertension, recent MI and New York Heart Association (NYHA) functional classification. Baseline serum creatinine (mg/dL) and primary ejection fraction (%) were also extracted from records. During surgery, total CPB time (minutes), operation time, amount of fluid administrated (mL), amount of packed cells and blood products received (mL), prime volume (mL), the amount of cardioplegia and other fluids added to the CPB (mL), urine output (mL), amount of filtrated fluid from CPB (mL), use of inotropes, the need to use intra-aortic balloon pump (IAB) were evaluated. After the surgery, the patient was transferred to the ICU. The second stage of data collection began at the moment the patient entered the ICU. During postoperative follow up all fluid administrated and fluid excreted (mL) containing the volume of serums, packed cells, blood products, urine output, drainage of chest bottles and drains until 24 hours after surgery were included. It is worth noting determination for prescribing fluids was not affected by study researchers. The following formula[12-4] was applied to calculate the fluid balance for each patient:

Fluid Balance = [Intravenous Fluids + Cardioplegia + Prime and Fluids in CPB] – [Urine Output + Filtered Fluid + Drainage Fluid]

According to their fluid balance up to 24 hours post-surgery, patients were classified into three groups: Group 1) patients with less than 2000 mL fluid balance, Group 2) patients with 2000 to 3000 mL fluid balance, and Group 3) patients with more than 3000 mL of fluid balance. Blood loss in surgical gauzes was not calculated in fluid balance formula, but can be assumed to be equal for the three groups.

We considered long ICU stay (> 4 days),[15,16] long mechanical ventilation (> 10 hours), long hospital stay (> 7 days) [16] and AKI as post-operative complications in the analysis of the study outcome. Abrupt reduction in kidney function currently defined as an absolute increase in serum creatinine of 0.3 mg/dL or more (≥ 26.4 μmol/L) or a percentage increase in serum creatinine of 50% or more.[17]

Statistical Analysis

Quantitative data were described using mean ± standard deviation for normally distributed variables or the median (interquartile range) when there was skewness. One sample of Kolmogorov Smirnov was used to determine the fitness of data to normal distribution. Qualitative data were described as count (%) was used to express its value. The accuracy of the data was controlled. Data were compared among the fluid-balance groups via Kruskal Wallis test for interval and Pearson chi-square (or Fisher's exact) test for nominal variables. Mann Whitney U test (with Bonferroni correction) was used for post-hoc comparison between groups. We performed multivariate analysis using binary logistic regression models to investigate the adjusted associations between the study outcomes and different predictors. The significance level was considered as .05. IBM SPSS Statistics 21 for Windows (IBM Inc., Armonk, NY) was applied for the statistical analysis.

RESULTS

After the end of the sampling period, one hundred and thirty forms were collected. No patient was excluded. Eighty-eight male and forty-two female were operated and admitted to the ICU, so we studied them prospectively. Age findings showed that the age of subjects varied from 40 years to 81 years and had a mean of 62.31 ± 9.20. Calculation of the fluid balance in the samples showed that the minimum volume of fluid balance was 500 mL while the maximum was 6200 mL. Preoperative demographic and risk indicators are shown in Table 1. We also observed that there was no significant difference in CPB time, cross-clamp time, operation time, baseline creatinine, and using inotropes between three groups. Evaluating the days of ICU stay, we found a significant relationship between ICU stay days and fluid balance ($P < .05$). Utilising the Mann Whitney U test and Bonferroni's correction for post-hoc comparison between groups in two to two, it was found that the average number of ICU stay days was significantly higher in group 3 than in group 1 (Table 2). We found that patients with more than 3000 mL fluid balance (group 3) had more length of hospital stay than patients with 2000-3000 mL balance (group 2), and patients in group 2 stay longer in hospital than patients in group 1 (Figure 1). Furthermore, there was a significant association between prolonged mechanical ventilation in the intensive care unit

Table 1. Comparison of Patients' Characteristics and Preoperative Risk Factors in the Study Groups

Variables	Groups (n = 130)			*P*
	Balance Group < 2000 mL (n = 44)	Balance Group = 2000-3000 mL (n = 34)	Balance Group > 300 mL (n = 52)	
Age*, year	60 (57 – 68)	61 (54.75 - 65.25)	64 (56.25 - 72)	> .05
Gender, Male/Female	33/11	25/9	30/22	> .05
Weight*, kg	75 (70 - 82.75)	75 (68.75 - 84.25)	69.50 (60.50 - 80)	> .05
LVEF*, %	50 (45 - 50)	45 (35 - 50)	45 (41.25 - 55)	> .05
Diabetes**	13 (29.5%)	12 (35.3%)	25 (48.1%)	> .05
Hypertension**	16 (36.4%)	22 (64.7%)	34 (65.4%)	< .05
Smoking**	23 (52.3%)	16 (46%)	12 (23.1%)	< .05
Hyperlipidemia**	9 (20.5%)	15 (44.1%)	22 (43.2%)	< .05
Thyroid Disease**	1 (2.3%)	4 (11.8%)	5 (9.6%)	> .05
Recent MI**	4 (9.1%)	11 (32.3%)	7 (13.7%)	> .05
CVA**	2 (4.5%)	2 (5.9%)	3 (5.8%)	> .05
Lung Disease**	0 (0.0%)	1 (2.9%)	3 (5.8%)	> .05
Opium Addiction**	8 (18.2%)	11 (33.3%)	7 (13.5%)	> .05
NYHA Functional Class**				< .05
1	3 (6.8%)	1 (2.9%)	5 (9.6%)	
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%)	

The significance level in this analysis is considered less than 0.05
*Descriptive information is presented as median (inter-quartile range).
**Descriptive information is presented as frequency (percent).
LVEF, left ventricular ejection fraction; CVA, cerebrovascular accident

Table 2. Comparison of Length of ICU Stay in Groups

Variables	Groups (n = 130)			P
	Balance Group < 2000 mL (n = 44)	Balance Group = 2000-3000 mL (n = 34)	Balance Group > 300 mL (n = 52)	
Days of ICU Stay	3 (3-3)	3 (3-3)	3 (3-4)	< .05

The significance level in this analysis is considered less than .05.

and high fluid balance (Figure 2). The association between AKI and balance volume was shown that there was no significant relationship between the incidence of acute renal injury after surgery and fluid balance ($P > .05$) (Table 3).

After multivariate analysis of the factors

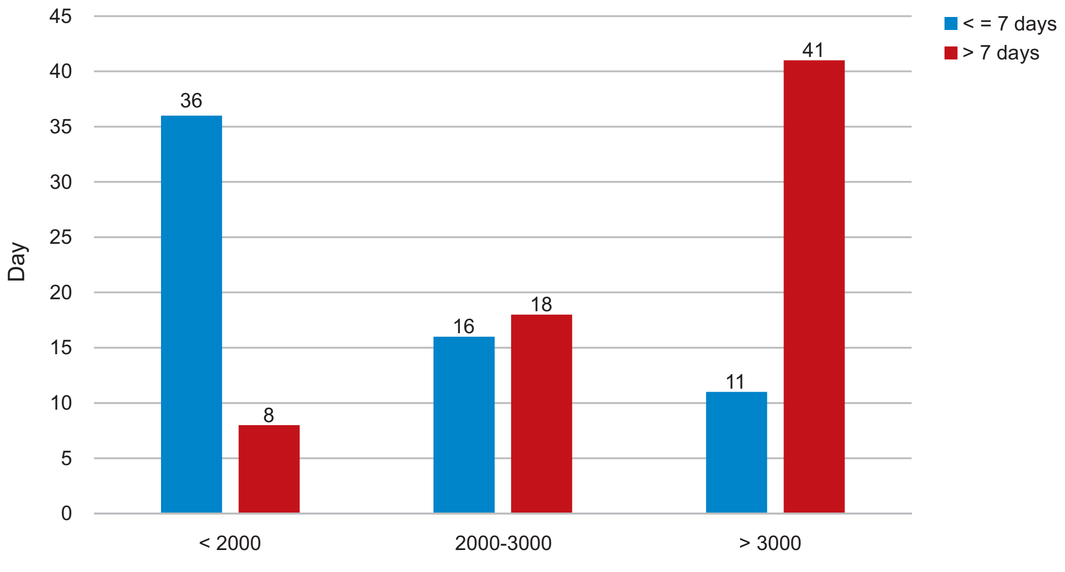

Figure 1. It mentions the comparison of the long hospital stay (> 7 days) among the groups.

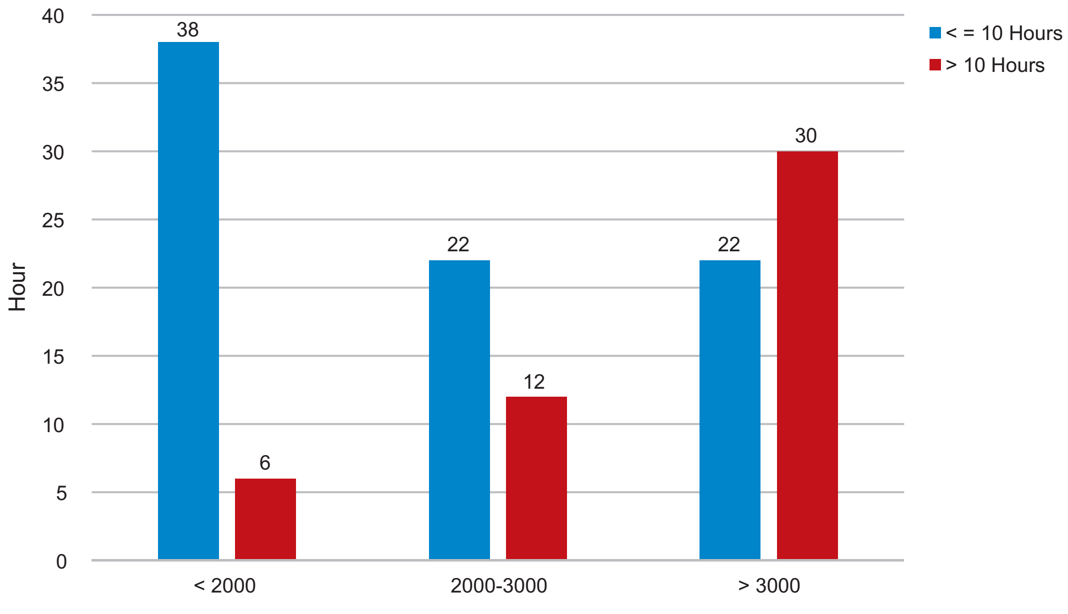

Figure 2. It determines the comparison of the prolonged mechanical ventilation time in ICU among the groups.

Table 3. Comparison of Acute Kidney Injury (AKI) in Groups

Variables	Groups (n = 130)			*P*
	Balance Group < 2000 mL (n = 44)	Balance Group = 2000-3000 mL (n = 34)	Balance Group > 300 mL (n = 52)	
AKI	1 (2.3%)	2 (5.9%)	6 (11.8%)	> .05

The significance level in this analysis is considered less than .05.

affecting the long-term hospitalisation, there is a significant relationship [Odds Ratio (95% CI) = 5.2 (14.8 - 1.9), $P < .05$] between more than 3000 mL of fluid balance and more than 10 days of hospital stay. Among other effective factors, mechanical ventilation more than 10 hours [Odds Ratio (95% CI) = 1.31 (1.6 - 1.7), $P < .05$], prolongs the patient's residence time in the hospital (Table 4). On the other hand, the balance of more than 3000 mL directly effects on prolongation of mechanical ventilation [Odds Ratio (95% CI) = 4.6 (11.5 - 1.9), $P < .05$].

In the study of effective factors in long-term ICU stay, we also found that fluid balance of more than 3000 mL [(Odds Ratio (95% CI) = 3.24 (1.09 - 9.6), $P < .05$], and using inotropes [Odds Ratio (95% CI) = 3.95 (1.1 - 13.9), $P < .05$] increases the time patients have to stay in ICU (Table 5).

Table 4. Logistic Regression Model for the Association Between Long-term Hospitalization and Fluid Balance Adjusted for the Other Factors

Variables	Odds Ratio (OR)	95% CI for OR		*P*
		Upper Limit	Lower Limit	
Fluid Balance > 3000 mL	5.29	14.09	1.99	< .05
Age	1.02	1.08	0.97	> .05
Gender	1.19	3.44	0.41	> .05
Weight	1.00	1.04	0.97	> .05
Diabetes	0.94	1.82	0.49	> .05
Hyperlipidemia	2.43	6.55	0.90	> .05
Hypertension	1.70	4.31	0.67	> .05
MI	1.68	3.48	0.81	> .05
Bypass Time	1.01	1.02	0.99	> .05
Mechanical Ventilation > 10h	1.32	1.62	1.07	< .05
Smoking	1.21	3.21	0.46	> .05
NYHA	0.95	2.46	0.37	> .05
Use of Inotropes	3.61	16.12	0.81	> .05

The significance level in this analysis is considered less than 0.05

Table 5. Logistic Regression Model for the Association Between Long-term ICU Stay and Fluid Balance Adjusted for the Other Factors.

Variables	Odds Ratio (OR)	95% CI for OR		*P*
		Upper Limit	Lower Limit	
Fluid Balance > 3000 mL	3.25	9.64	1.09	< .05
Age	0.99	1.05	0.94	> .05
Gender	1.56	5.49	0.44	> .05
Weight	1.01	1.05	0.97	> .05
Diabetes	1.15	2.31	0.57	> .05
Hyperlipidemia	0.91	2.80	0.30	> .05
Hypertension	1.49	4.54	0.49	> .05
MI	0.96	2.57	0.36	> .05
Bypass time	1.00	1.02	0.99	> .05
Mechanical Ventilation > 10h	1.23	1.53	0.99	> .05
Smoking	1.37	4.40	0.43	> .05
NYHA	1.37	4.29	0.44	> .05
Use of Inotropes	3.95	13.95	1.12	< .05

The significance level in this analysis is considered less than .05.

DISCUSSION

The present study demonstrates an association between fluid balance after CABG surgery and some postoperative adverse outcomes. There were significant differences in the prevalence of hypertension, smoking, hyper-lipoproteinemia (HLP) and NYHA in these three groups. However, after the logistic regression, the effect of the above variables was not significant. In other words, there was no significant correlation between the balance of fluid and the history of hypertension, smoking, HLP, and NYHA classification by eliminating the effects of confounding variables. Considering this relationship seems logical when deciding to administrate fluids to these patients. Toraman *et al.* showed that in advanced age patients, patients with diabetes mellitus or chronic obstructive pulmonary disease (COPD), the need for replacement of preoperative fluid is greater.[18]

The findings of this research illustrate that the fluid balance of 3000 mL has a significant and independent effect on the long mechanical ventilation, long ICU and long hospital stay. Since in similar studies, fluid overload has been investigated based on the patient's weight gain after surgery or only based on the patient's fluid intake, we designed a study based on an accurate fluid balance measurement, which included the subtraction of the patient's outputs and losses from their intakes.

The prolonged intubation time after surgery was investigated in this research as a particular complication, while, in Morin's survey[21] prolonged intubation time has been studied along with death, cardiac arrest and respiratory failure in the same category of major complications.

Furthermore, no studies have been done on this issue in Iran so far.

Body fluids are affected by the difference in hydrostatic and oncotic pressure between the interstitial space and the capillary vessel space.[19,20] Changes in plasma proteins or intravascular volume cause water and electrolyte imbalances.[7] According to Bellomo,[1] the use of CPB exposes the patients to a large volume of fluids such as CPB pump prime, cardioplegia and other fluids given to compensate hypotension during surgery.[1] Patients undergoing cardiac surgery often experience heart failure or renal failure, and there are some degrees of fluid overload in their bodies, which will worsen when using CPB.[21] Regardless of the situation, fluid overload can often play a role in the pathogenesis of postoperative hypoxemia, myocardial edema, and organs oedema.[22,23] Studies show iatrogenic myocardial edema formation and a rise in extravascular lung water occur during CPB.[12,13,22,24] This condition can be responsible for delaying the recovery of cardiac surgery patients.

On the other hand, it is explained that the use of a cardiopulmonary pump in cardiac surgeries activates the systemic inflammatory response syndrome (SIRS) in the body.[5] Excessive fluid intake also increases vascular permeability. Increasing vascular permeability, along with activation of systemic inflammatory responses, leads to fluid accumulation and pulmonary edema.[25] The reasons given above can justify the prolongation of the mechanical ventilation time in patients with balance volume of more than 3000 mL in this study. We have assumed mechanical ventilation of more than 10 hours for long-term ventilation. In 2011, Morin *et al.* reported that the risk of major complications (such as prolonged intubation) significantly differed for high fluid overload compared to medium and low fluid overload.[21]

In this study, the relationship between balance groups and days of admission in ICU was compared. The average days of ICU stay in group 3 were higher than those in group 1. This is consistent with the study by Stein *et al.*[14] Stein considers the fluid overload and serum creatinine changes after cardiac surgery alone as an indicator for long-term ICU stay.[14] It should be noted that in the Stein study, the average days of ICU stay were considered 2 days (48 hours) while in our study, most patients experience 72 hours of ICU stay. The impact of other factors affecting the prolongation of ICU stays, such as the need for Inotropes, age and diabetes and hypertension complications have been investigated, and results are shown in Table 5.

There are many interactions between renal function and fluid balance during CPB. CPB causes fluid shifts, electrolyte imbalances and inflammation throughout the body.[16] Acute reduction in cardiac output immediately after surgery is the most common and, at the same time, the most critical risk factor for the development of acute kidney injury.[21] Hemodilution that is caused by fluid overload in the body results in increased lactate production and an increased risk of developing

AKI by reducing the oxygenation of the tissues.[8] In this study, 9 patients out of 130, have experienced AKI: one patient in group1, two patients in the second group, and six patients in the third group. However, after statistical analysis, there was no significant relationship between balance volume and prevalence of AKI. Morin[21] classifies kidney injury along with complications such as death, MI, tamponade and low cardiac output syndrome in the group of major complications. After analysing, he found a significant relationship between the incidence of major complications and those who had overweight over 5 kg due to fluid accumulation. The evaluation of AKI as an outcome individually in our survey could be the reason for the difference between the present study and research mentioned above.

In this study, there is a significant relationship between balance volumes and days of hospital stay ($P < .05$). This result is consistent with other similar studies.[14,21,26] In the follow-up studies, multivariate analysis of effective factors on outcomes had been investigated. In fact, at this stage of the research, confounding variables were eliminated by statistical methods to determine which factors directly affect the long ICU stay, long hospital stay, prolonged mechanical ventilation and AKI. The result of the study demonstrates that fluid balance of more than 3000 mL was the direct cause for the long ICU stay, long hospital stay, and prolonged mechanical ventilation. The use of Inotropes also directly affected acute kidney injury.

In the end, the study suggests that fluids should be administered, taking into account the central venous pressure and blood transfusion should be done according to hematocrit. Assessing pulse pressure variations and Stroke volume variations help to determine the hemodynamic status of the patients. Another effective method for continuous hemodynamic examination of patients during and after surgery is using bioimpedance analysis. It is also appropriate to use echocardiogram for intermittent measurement of fluid volume. Also, less CPB prime is used to reduce hemodilution, and If possible, hemofiltration should be done to minimise postoperative complications resulting from fluid accumulation.

LIMITATIONS

In this study, the precise details of patients' intakes and outputs should be recorded, and follow up of patients in several different wards required the assistance of more colleagues. So there is a risk of data log bias. The ability to accurately measure the amount of blood loss during surgery was not provided by the calculation of blood-stained gauzes and long gauzes, as well as the exact amount of blood remaining in the suction and CPB tubes, so it is likely that the calculation of fluid balance volumes in all patients was not possible with 100% accuracy. Obviously, if the sample size were more extensive, the probability of other predictive variables would also be possible.

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CONFLICT OF INTEREST

We hereby declare that this study was an independent research, and there was no conflict of interest with other organisations or individuals.

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