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Article

Fluid Balance and Risk of Postoperative Atrial Fibrillation after On-pump Coronary Artery Bypass Grafting Surgery

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Abstract

Background: Postoperative atrial fibrillation (POAF) is a common complication after coronary artery bypass grafting (CABG) and is associated with increased adverse outcomes. However, the relationship of fluid balance and POAF is not clear yet. Accordingly, this study aims to study the relationship of fluid balance and POAF, and to evaluate the other risk factors of POAF in patients undergoing elective on-pump CABG with or without valve surgery in our center. **Methods**: A retrospective study between October 2018 and December 2022 including 261 patients who underwent CABG undergoing cardiopulmonary bypass was performed. The fluid balance on the first 4 days in the intensive care unit (ICU) and other potential perioperative risk factors for POAF were collected and analyzed using univariate and multivariate analyses to identify risk factors following CABG. The in-hospital adverse outcomes of POAF were also evaluated. **Results**: 261 adult CABG patients were evaluated, of whom 22 were excluded due to a history of atrial fibrillation or other causes. Among them, 72 patients developed POAF (30.1%). The mean fluid balance was negative on the first 3 days. Negative fluid balance was less on postoperative day 0 (POD 0) in those developing POAF than in those not developing POAF (–12.88 ± 12.47 *vs*. –17.48 ± 10.03 mL/kg, p = 0.003). No differences were noted for POD 1 and POD 2. Multiple logistic regression analysis showed age >60 years (adjusted odds ratio (OR), 3.86 [95% confidence interval (CI): 1.99 to 7.48]), left atrial antero-posterior (AP) dimension >42 mm (adjusted OR, 2.68 [95% CI: 1.45 to 4.93]), total blood transfusions >400 mL (adjusted OR, 1.96 [95% CI: 1.05 to 3.63]), and positive fluid balance on POD 0 (adjusted OR, 2.93 [95% CI: 1.01 to 8.51]) were independent perioperative risk factors for POAF. **Conclusions**: The incidence of POAF is not significantly reduced even with a fluid restriction strategy after CABG, and positive fluid balance on the day of surgery is a risk factor for POAF, rather than on POD 1 and POD 2. In addition, advanced age, left atrial enlargement, and increased perioperative blood transfusion are all risk factors for POAF.

Keywords

fluid balance; postoperative atrial fibrillation; coronary artery bypass grafting; blood transfusion; risk factor

Introduction

Postoperative atrial fibrillation (POAF) is a common complication in patients undergoing cardiac operations. It occurs in 30%–50% of patients after coronary artery bypass grafting (CABG) surgery with or without valve surgery [1] and is associated with extended in-hospital stay and increased adverse outcomes, including death and stroke [2–4].

The underlying mechanisms behind POAF are not yet fully understood. Many perioperative factors have been suggested to increase the incidence of POAF after CABG, such as advanced age, obesity [5], hypertension, respiratory complications, and bleeding [6].

A previous study showed that administration of fluids postoperatively, especially when creating a hypervolemic state, was associated with POAF [7]. However, in our center, a restrictive fluid strategy was routinely performed after CABG surgery, nevertheless, POAF still occurred frequently in patients who were severely fluid restricted. The relationship of fluid balance and POAF is not yet clear. It is thought that negative fluid balance may also increase the incidence of POAF.

In this study, we studied the relationship between fluid balance and POAF and evaluated risk factors for POAF in patients undergoing elective on-pump CABG with or without valve surgery in our center.

Methods

Ethical Statement

In this retrospective study, 261 consecutive adult patients underwent elective on-pump CABG were analyzed, between October 2018 and December 2022, in Peking University International Hospital in Beijing, China. The study protocol was approved by our hospital's institutional review board. Because of the retrospective nature of the study, requirement for informed consent was waived.

Patients were excluded based on the following criteria: (a) had a history of atrial fibrillation before surgery; (b) off-pump CABG; (c) died within 48 h after surgery; (d) had infective endocarditis before surgery.

Primary Endpoint

The primary endpoint of the analysis was the occurrence of POAF defined as a new onset of atrial fibrillation (AF) sustained for 30 seconds or more [8]. Information about the occurrence of POAF was extracted from the medical records. Detection of POAF was based on documentation of AF episodes by continuous electrocardiograph (ECG) monitoring or continuous telemetry throughout the hospitalization.

Data Collection

The data set included demographic information such as age, gender and weight at admission. Preoperative factors included preoperative comorbidities, echocardiography parameters. Intraoperative factors included type of surgery, cardiopulmonary bypass time, aortic cross-clamp time and volume of blood transfusion. Postoperative factors included re-exploration, use of the Intra-aortic balloon pump (IABP), fluid balance on the first four days in the intensive care unit (ICU). In addition, laboratory indices such as estimated glomerular filtration rate (eGFR), serum creatinine, serum albumin, hemoglobin, white blood cell (WBC) count, and C-reactive protein (CRP) were also extracted for each patient.

Clinical outcome characteristics such as duration of mechanical ventilation, ICU length of stay, hospital length of stay, in-hospital mortality, occurrence of bleeding, pulmonary complications, ventricular arrhythmias and stroke, and the need for renal replacement therapy were also investigated.

Fluid balance (mL/kg) was calculated as follows: Fluid balance = [(amount of crystalloids + colloids + packed red cell + plasma + platelets + enteral nutrition) – (blood loss + urine output +gastrointestinal losses + drain losses + dialysis or ultrafiltrate)]/weight.

Statistical Analysis

Statistical analyses were performed using the SPSS 21.0 statistical software package (SPSS, Inc., Chicago, IL, USA). All p values < 0.05 were considered statistically significant. Descriptive statistics are expressed as median (25th percentile, 75th percentile) or the means $\pm$ standard deviation (SD) for continuous variables and as n (%) for categoric variables. Univariate analysis, of pre-, intra- and post-operative variables for the occurrence of POAF using the Student t-test or the Mann–Whitney U test to compare continuous variables and the χ^2 test or Fisher's exact test to compare percentages, were performed to assess statistically significant variables. Stepwise multivariate logistic regression was also performed. Variables were entered into the model based on a univariable analysis with a significance threshold of $p < 0.1$. Collinearity between variables was assessed by Pearson correlation coefficient and variance inflation factors (VIF) statistics; r >0.7 and VIF >10 were cut-off values for multicollinearity in the regression model. All continuous variables were transformed into categorical variables before logistic regression analysis. The cut-off was considered as the 50th percentile of the recorded values or nearby clinically appropriate. The Hosmer-Lemeshow goodness-of-fit test was used to assess the validity of the regression model. Good calibration was indicated by a low χ^2 and a high p value > 0.05.

Results

During the study period, 261 adult CABG patients were evaluated, of whom 22 were excluded due to a history of atrial fibrillation or other causes. Ultimately, 239 patients were included in the analysis. Among them, 72 patients developed POAF. The patients were divided into a without POAF group (n = 167, 69.9%) and with POAF group (n = 72, 30.1%) (Fig. 1).

The timing of POAF is summarized in Fig. 2. Among the patients who had POAF, the highest incidence of POAF was on postoperative day (POD) 2, followed by POD 1, POD 3 and POD 4 after surgery.

The majority of patients were male (195 patients, 81.6%) with a median age of 62 years. Patients with POAF were significantly older compared to patients without POAF (median 68.5 years *vs*. 60 years, $p < 0.001$). The percentage of males was lower in patients with POAF than patients without POAF. No differences in weight and body mass index (BMI) between these two groups were observed. Patients with POAF were more likely to have hypertension and less likely to have diabetes. POAF patients showed an increased left atrial antero-posterior (AP) dimension (median 44.5 mm *vs*. 41 mm; $p = 0.002$). Patients who also had concomitant valve surgery, and with more blood transfusions and re-explorations were more likely to develop POAF, similarly, preoperative anemia and low eGFR were also prone to POAF. WBC was higher in patients with POAF on POD 2 than in patients without POAF, however, there was no difference in WBC on POD 1 and there was also no difference in CRP (Table 1).

Fluid balance was observed for 4 days after surgery. The mean fluid balance was negative on the first 3 PODs, both in the POAF group and No POAF group. Negative fluid balance was less in the POAF group than the No POAF group on POD 0 (–12.88 $\pm$ 12.47 *vs*. –17.48 $\pm$ 10.03

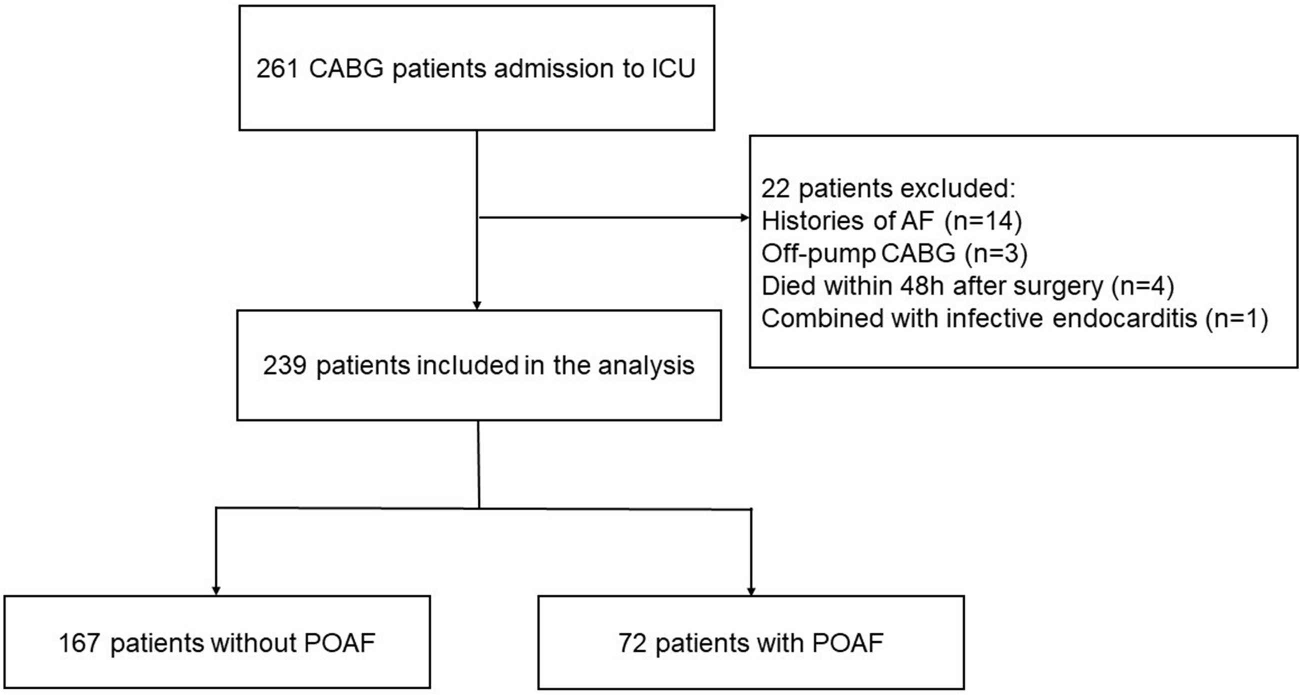

Fig. 1. Overview of study population and subgroups for analysis. After excluding 22 patients, 239 patients were analyzed in total. Subjects were allocated to 2 groups based on the occurrence of postoperative atrial fibrillation (POAF) or not. AF, atrial fibrillation; CABG, coronary artery bypass grafting; ICU, intensive care unit.

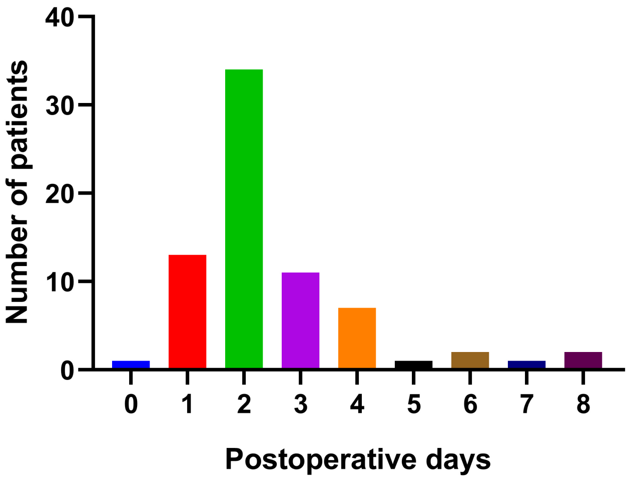

Fig. 2. Time of initial occurrence for postoperative atrial fibrillation.

mL/kg, $p = 0.003$), however, no differences were noted on POD 1 and POD 2 (Table 2, Fig. 3). For the first 2 PODs, negative fluid balance was also less in the POAF group than in the No POAF group (–23.44 ± 17.64 *vs.* –28.37 ± 14.29 mL/kg, $p = 0.0224$). On POD 3, the mean fluid balance was negative in the POAF group while positive in the No POAF group (median –6.85 *vs.* 0.16, $p = 0.003$). Overall, there were no differences in cumulative fluid balance between these two groups for the first 3 and first 4 PODs (Table 2, Fig. 4).

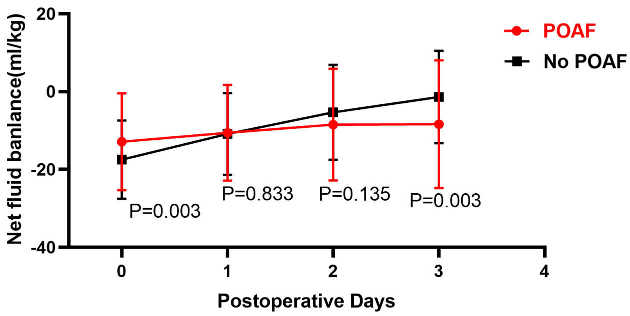

Fig. 3. Net fluid balance on each postoperative day (POD) in those who did and did not develop postoperative atrial fibrillation.

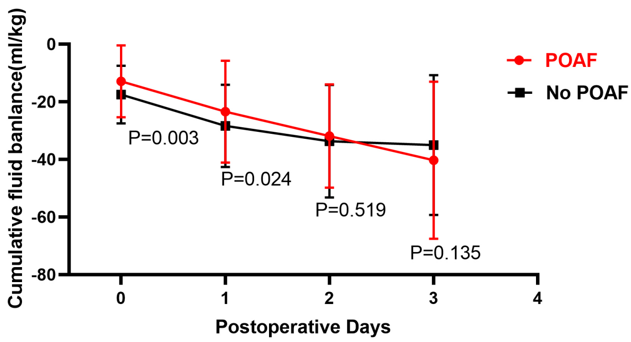

Fig. 4. Cumulative fluid balance for first 4 PODs in those who did and did not develop postoperative atrial fibrillation.

Table 1. Demographic and clinical characteristics.

Variable	Total cohort (N = 239)	POAF (N = 72)	No POAF (N = 167)	p value
Age (years)	62 (57, 69)	68.5 (62, 73)	60 (55, 66)	<0.001
Gender (% male)	195 (81.6)	53 (73.6)	142 (85.0)	0.037
Weight (kg)	71 (63, 78)	70 (59, 80)	71 (65, 78)	0.180
BMI (kg/m^2)	25.1 ± 3.05	24.9 ± 2.80	25.1 ± 3.16	0.522
Comorbidities				
Hypertension (%)	140 (58.6)	48 (66.7)	92 (55.1)	0.096
Diabetes (%)	111 (46.4)	27 (37.5)	84 (50.3)	0.069
COPD (%)	4 (1.7)	2 (2.8)	2 (1.2)	0.586
Prior myocardial infarction (%)	107 (44.8)	31 (43.1)	76 (45.5)	0.726
Previous cardiac surgery (%)	6 (2.5)	0 (0)	6 (3.6)	0.182
LVEF (%)	60 (46, 67)	60 (46, 70)	60 (47, 67)	0.791
Left atrial AP dimension (mm)	42 (38, 45)	44.5 (39, 48)	41 (38, 44)	0.002
LVEDD (mm)	50 (46, 57)	50 (47, 47)	51 (46, 57)	0.890
Type of surgery				0.069
CABG only	175 (73.2)	47 (65.3)	128 (76.6)	
CABG+valve	64 (26.8)	25 (34.7)	39 (23.4)	
CPB time (min)	175 (140, 227)	183 (142, 249)	174 (137, 220)	0.254
Aortic cross-clamp time (min)	122 (94, 164)	117 (101, 174)	123 (91, 158)	0.337
Transfusion				
Red blood cell (IU)	2 (0, 4)	4 (0, 4)	0 (0, 4)	0.003
Plasma (mL)	0 (0, 400)	400 (0, 600)	0 (0, 400)	0.004
PLT (IU)	0 (0, 0)	0 (0, 0)	0 (0, 0)	0.897
Total (mL)	400 (0, 1080)	870 (0, 1360)	340 (0, 1020)	0.002
Re-exploration (%)	13 (5.4)	8 (11.1)	5 (3.0)	0.026
IABP use (%)	12 (5.0)	6 (8.3)	6 (3.6)	0.192
eGFR (mL/min)	87.5 (71.5, 97.2)	81.3 (69.8, 93.5)	91.0 (72.8, 98.3)	0.006
Scr (μmol/L)	78 (68, 93)	78 (68, 95)	79 (68, 92)	0.986
Serum albumin (g/L)	40.2 ± 3.39	39.9 ± 3.37	40.3 ± 3.40	0.495
Hemoglobin (mg/dL)	138 (126, 147)	136 (121, 146)	139 (127, 148)	0.088
WBC count (baseline, ×10^9/L)	6.6 (5.5, 7.5)	6.5 (5.5, 7.4)	6.6 (5.5, 7.6)	0.607
WBC count (POD 1, ×10^9/L)	11.8 (9.7, 14.2)	12.1 (10.1, 14.3)	11.8 (9.6, 14.2)	0.607
WBC count (POD 2, ×10^9/L)	14.0 (10.9, 16.6)	14.3 (12.2, 18.6)	13.9 (10.7, 16.2)	0.027
CRP (POD 1, mg/L)	82.2 (60.7, 104.0)	84.1 (61.3, 103.4)	80.9 (60.2, 104.0)	0.841
CRP (POD 2, mg/L)	162.6 (124.0, 209.9)	170.3 (125.2, 216.0)	161.2 (120.6, 207.9)	0.378

POAF, postoperative atrial fibrillation; BMI, body mass index; COPD, chronic obstructive pulmonary disease; LVEF, left ventricular ejection fraction; AP, antero-posterior; LVEDD, left ventricular end diastolic diameter; CABG, coronary artery bypass grafting; CPB, cardiopulmonary bypass; PLT, platelet; IABP, intra-aortic balloon pump; eGFR, estimated glomerular filtration rate; Scr, serum creatinine; WBC, white blood cell; POD, postoperative day; CRP, C-reactive protein.

There was a total of 16 variables in Table 1 and Table 2 with $p < 0.1$, 12 variables were entered into the multivariate analysis, after red blood cell and plasma transfusion, fluid balance on the first 2 PODs were removed from the model because of multicollinearity, fluid balance on POD 3 was also removed because it had little value in predicting POAF. Results of the multivariable logistic regression models for POAF were shown in Table 3. The model discriminated between POAF and No-POAF fairly well (area under the receiver operator characteristic curve 0.746) (Fig. 5), and the model calibration was good (Hosmer-Lemeshow [goodness-of-fit test]: p = 0.86). Predictors of POAF included age >60 years (adjusted odds ratio (OR), 3.86 [95% confidence interval (CI): 1.99 to 7.48]), left atrial AP dimension >42 mm (adjusted OR, 2.68 [95% CI: 1.45 to 4.93]), total blood transfusions >400 mL (adjusted OR, 1.96 [95% CI: 1.05 to 3.63]), and positive fluid balance on POD 0 (adjusted OR, 2.93 [95% CI: 1.01 to 8.51]). Gender, hypertension, concomitant valve surgery, re-exploration, eGFR, and WBC count were no longer significant predictors.

POAF was associated with worse clinical outcomes as indicated by significantly increased duration of mechanical ventilation, ICU length of stay, and hospital length of stay. POAF patients were more likely to develop bleeding, pulmonary complications and ventricular arrhythmias in the

Table 2. Perioperative fluid balance.

Fluid balance (mL/kg)	Total cohort (N = 239)	POAF (N = 72)	No POAF (N = 167)	*p* value
POD 0	–16.09 ± 11.00	–12.88 ± 12.47	–17.48 ± 10.03	0.003
POD 1	–10.79 ± 11.06	–10.56 ± 12.32	–10.89 ± 10.51	0.833
POD 2	–4.38 (–13.37, 3.37)	–5.13 (–16.05, 1.90)	–4.01 (–11.95, 3.75)	0.135
POD 3	–2.11 (–10.90, 5.55)	–6.85 (–16.35, 5.04)	0.16 (–7.60, 6.25)	0.003
First 2 PODs	–26.88 ± 15.50	–23.44 ± 17.64	–28.37 ± 14.29	0.024
First 3 PODs	–33.15 ± 19.07	–31.93 ± 17.96	–33.67 ± 19.56	0.519
First 4 PODs	–34.58 (–53.29, –18.96)	–39.60 (–57.24, –21.72)	–33.14 (–52.02, –16.50)	0.135

POAF, postoperative atrial fibrillation; POD, postoperative day.

Table 3. Multivariate analysis of perioperative factors for POAF occurrence.

Variable	OR	95% CI	*p* value
Age >60 years	3.86	1.99–7.48	<0.001
Left atrial dimension >42 mm	2.68	1.45–4.93	0.002
Total blood transfusions >400 mL	1.96	1.05–3.63	0.033
Fluid balance >0 mL/kg on POD 0	2.93	1.01–8.51	0.048
Constant	0.073		<0.001

POAF, postoperative atrial fibrillation; POD, postoperative day; OR, odds ratio.

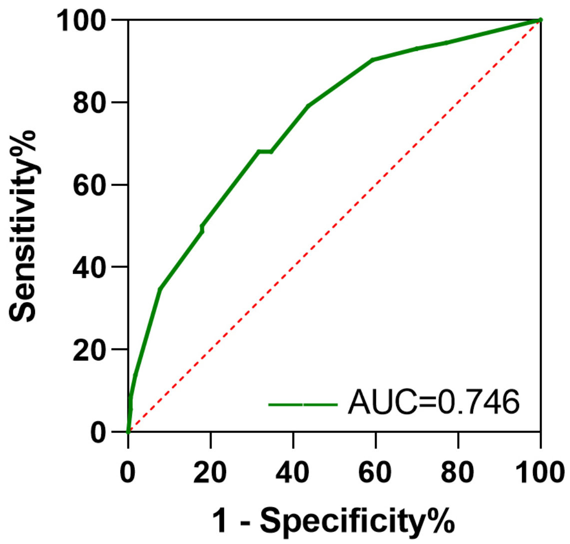

Fig. 5. Accuracy of the model: the receiver operating characteristic (ROC) curve of logistic regression model showing the area to be 0.746. AUC, area under the curve.

ICU compared to patients without POAF. However, there was no significant difference in in-hospital mortality, continuous renal replacement therapy (CRRT) and Stroke (Table 4). The risk of in-hospital adverse events was compared between the POAF and No POAF group (Fig. 6). Compared with patients in the No POAF group, patients with POAF had a more than 3-fold relative increased risk of in-hospital adverse events (hazard ration (HR), 3.33 [95% CI, 1.75–6.33]).

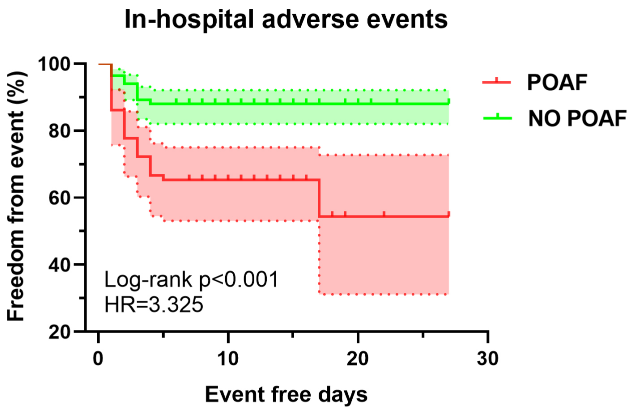

Fig. 6. Comparing of in-hospital adverse events between the POAF and No POAF group. HR, hazard ration.

Discussion

This study demonstrated that the mean fluid balance was negative on the first 3 PODs in both groups. Negative fluid balance was less on postoperative day 0 (POD 0) and first 2 PODs in the POAF group compared to the No POAF group. Positive fluid balance on POD 0 was strongly associated with POAF among patients undergoing CABG. However, there were no difference in cumulative fluid balance between these two groups for the first 3 and 4 PODs. This result differs from previous reports, which strongly implies fluid overload is a key player in the initiation of POAF [7,9–11]. Age over 60 years, left atrial AP dimension greater than 42 mm, and total blood transfusions greater than 400 mL are independent risk factors for POAF

Table 4. Postoperative outcomes.

Variable outcome	POAF (N = 72)	No POAF (N = 167)	*p* value
Duration of MV (hour)	20 (17, 44.75)	17 (15, 20)	<0.001
ICU LOS (day)	4 (2, 5)	2 (2, 4)	<0.001
Hospital LOS (day)	19 (15, 26)	17 (14, 22)	0.016
In-hospital mortality	2 (2.8)	0 (0)	0.090
Bleeding	12 (16.7)	5 (3.0)	<0.001
Pulmonary complication	12 (16.7)	12 (7.2)	0.025
Ventricular arrhythmia	9 (12.5)	3 (1.8)	0.002
CRRT	5 (6.9)	3 (1.8)	0.101
Stroke	0 (0)	1 (0.6)	1.000

Data were presented as median (25th percentile, 75th percentile) or n (%). MV, mechanical ventilation; ICU, intensive care unit; LOS, length of stay; CRRT, continuous renal replacement therapy.

after on-pump CABG surgery. We also showed that the occurrence of POAF was associated with increased hospital adverse events and increased resource utilization as defined by duration of mechanical ventilation, ICU length of stay (LOS) and hospital LOS, but not in-hospital mortality.

In 2004, Kalus *et al*. [7] studied the relationship between fluid balance and POAF. They observed that fluid balance and volume administered on POD 2 was greater in patients who developed POAF than in those who did not. They also found that net fluid balance on POD 2 was an independent predictor of POAF. This suggests that increased fluid balance is associated with the risk of POAF. However, in our study, there were no difference in fluid balance on POD 2, instead, the differences exist on the day of surgery. Furthermore, mean fluid balance was negative on the first 3 PODs, both in the POAF group and the No POAF group. There were no differences in cumulative fluid balance for the first 3 and 4 PODs. Therefore, we considered that the relationship of fluid balance and POAF was not simply hypervolemia or hypovolemia. In our study, the excess water caused by cardiopulmonary bypass were eventually excreted, the patients who excreted fluid slowly were more likely to develop POAF. Higher filling pressures of the left atrium and atrial distention did not explain this finding, since POAF should have been increased on the day of surgery, when the patients' blood volume was at its highest. Furthermore, there was no direct documentation of elevations in atrial pressure or size after surgery. Excess fluid may be distributed in the peripheral tissue space rather than within the blood vessels. It is possible that there are other factors involved in the occurrence of POAF, such as the inflammatory response, which are more important than fluid balance.

As previously reported, advanced age has been the most consistent predictor of POAF [6,12,13]. In our study, aged older than 60 years significantly increased the odds of POAF by more than three-fold (OR = 3.86; $p < 0.001$). These results are consistent with those of Todorov *et al*. [10] who found age to be the most powerful predictor of POAF (OR = 1.448 per decade increase ($p < 0.0001$)). The effect of ageing on the incidence of POAF may be caused by age related atrial fibrosis and is associated with conduction disturbances [14].

Left atrial enlargement is related to the risk for atrial fibrillation in individuals in the general population, particularly for those with mitral valvular disease or ventricular systolic dysfunction [15]. Left atrial enlargement is also a predictor of POAF with CABG in some studies [16–18], consistent with our results. It has been shown that left atrial AP dimension >42 mm has a 2.68-fold higher risk of developing POAF than with ≤42 mm. Mean left atrial dimension in the POAF group was 3.5 mm greater than the group who did not develop POAF. Moreover, patients who developed POAF had larger left atrial volumes [19,20].

This study showed that perioperative transfusion was significantly associated with POAF among patient undergoing CABG. Specifically, both red blood cell and frozen plasma transfusions perioperatively were increased in patients with POAF than in those without POAF. Total blood transfusions greater than 400 mL perioperatively significantly increased the odds of POAF by 96% (OR, 1.96, 95% CI: 1.05 to 3.63; $p = 0.033$), adjusting for other patient and clinical characteristics. These results are consistent with previous studies [21,22] which found red blood cell transfusion is associated with increased occurrence of POAF after cardiac surgery. The transfusion of red blood cell can cause an increased postoperative inflammatory response which contributes to the development of POAF. Ferraris *et al*. [23], found that the amount of blood transfused during intraoperative blood transfusions was a significant predictor for the development of the systemic inflammatory response syndrome (odds ratio, 2.2; $p < 0.0001$). Inflammatory mechanisms have been proposed as the main pathogenesis for POAF [6,24]. The inflammatory pathways facilitate the reentry mechanism in the atrium [25]. Furthermore, inflammatory markers such as the WBC count and CRP were found to be associated with POAF. Increased WBC count has been associated with a high incidence of POAF [26–28]. The preoperative levels [29] and peak of postoperative CRP levels were higher in patients with POAF [30]. However, increased WBC count on POD2 were not significantly associated with POAF in the multivariable model despite significant differences in the univariate analyses in our study, and there were no significant differences in postoperative CRP values, which might be due to other confounding factors and need further investigation.

In conclusion, our study showed that the incidence of POAF is not significantly reduced even with a fluid restriction strategy after on-pump CABG, although positive fluid balance on the day of surgery is a risk factor for POAF. The relationship of fluid balance and POAF is not as simple as fluid overload and needs further investigation. In addition, advanced age, left atrial enlargement, and increased perioperative blood transfusion are all risk factors for POAF. Given the adverse outcome of POAF, preventive measures for these high-risk patients need to be developed and will be the subject of future studies.

Limitations

This study is limited by being a retrospective single-center, observational cohort study, with a small sample size. Therefore, unobserved confounding effects on the results cannot be excluded. Furthermore, there were no information in the data set regarding the use of inotropes and vasopressors which would be associated with POAF. Additionally, we only reported preoperative left atrial dimension, but lack postoperative dynamic changes of the left atrial diameter or pressure, which cannot explain the potential mechanism of fluid balance and POAF. Finally, due to the potential for undiagnosed paroxysmal atrial fibrillation (PAF), it may be difficult to completely exclude patients with a history of PAF from the study group.

Conclusions

Our study found that even with a fluid restriction strategy after on-pump CABG, the occurred of POAF was still approximately 30%. Positive fluid balance on the day of surgery was a risk factor for POAF, rather than on POD1 and POD2. There were no differences in cumulative fluid balance for the first 3 and 4 PODs. The relationship of fluid balance and POAF was not simple like that fluid overload is associated with the development of POAF. The excess water caused by cardiopulmonary bypass is eventually excreted. Patients who undergo more prolonged fluid excretion were more likely to develop POAF. The mechanism of this is not clear and needs to be further studied.

Availability of Data and Materials

The datasets presented in this article are not readily available because of local data security restrictions. Requests to access the datasets should be directed to xiaoni2345@sina.com.

Author Contributions

YX: Conception and design of the work, data collection, interpretation of data, and writing of manuscript. CZ: Data collection and interpretation of data. JX: Provision of study materials or patients, data collection, manuscript editing. GP: Data collection and interpretation of data. All authors contributed to editorial changes in the manuscript. All authors read and approved the final manuscript. All authors have participated sufficiently in the work to take public responsibility for appropriate portions of the content and agreed to be accountable for all aspects of the work in ensuring that questions related to its accuracy or integrity.

Ethics Approval and Consent to Participate

The study protocol was approved by the Institutional Review Board of Peking University International Hospital (Approval Number 2023-KY-0052-03). Because of the retrospective nature of the study, requirement for informed consent was waived.

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Conflict of Interest

The authors declare no conflict of interest.

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