

ORIGINAL ARTICLE

POSTOPERATIVE ATRIAL FIBRILLATION AFTER CORONARY BYPASS SURGERY IN PATIENTS HAVING PRE-OPERATIVE HYPOALBUMINEMIA

Asaf Shah, Rizwan Aziz Memon, Zara Shirazi, Muhammad Ishaq

National Institute of Cardiovascular Diseases (NICVD), Karachi-Pakistan

Background: Hypoalbuminemia commonly occurs in cardiac patients, especially in elderly patients and those with chronic congestive heart failure, and it has been associated with adverse events such as atrial fibrillation. The study aimed to determine the incidence of postoperative atrial fibrillation (POAF) in patients undergoing coronary bypass surgery (CABG) with pre-operative hypoalbuminemia in a major cardiac surgery institute in Karachi, Pakistan. **Methods:** This descriptive cross-sectional study included patients of any gender, aged between 30–80 years, who underwent CABG surgery and had hypoalbuminemia at the time of pre-operative assessment. Hypoalbuminemia was defined as a serum albumin level less than 3.8 mg/dL (normal range: 3.8–4.5 mg/dL). We recorded routine daily 12-lead ECGs and monitored the occurrence of POAF within 72 hours of surgery. **Results:** A total of 144 patients were included in the study, of which 77.8% (112) were male, and the mean age was 58.1±8.4 years. The average serum albumin levels before surgery were 3.5±0.2 mg/dL. The majority of patients, 71.5% (103), had three-vessel disease (3VD), and 20.8% (30) had 3VD with left main (LM) disease. Hypertension was observed in 70.1% (101) of the patients, diabetes in 52.1% (75), and prolonged CBP time in 61.8% (89). The frequency of POAF was 10.4% (15), and it was significantly higher in non-hypertensive and non-diabetic patients, with a crude odds ratio of 4.19 [1.39–12.65] and 8.47 [1.84–39.09], respectively. **Conclusion:** The study found that approximately one in every ten patients undergoing CABG experienced POAF. Surprisingly, the rate of POAF was higher among non-hypertensive and non-diabetic patients.

Keywords: Hypo-albuminuria; Coronary bypass surgery; Postoperative atrial fibrillation.

Citation: Shah A, Memon RA, Shirazi Z, Ishaq M. Postoperative atrial fibrillation after coronary bypass surgery in patients having pre-operative hypoalbuminemia. J Ayub Med Coll Abbottabad 2023;35(4):574–8.

DOI: 10.55519/JAMC-04-11891

INTRODUCTION

Hypoalbuminemia commonly occurs in cardiac patients, especially in elderly patients and those with chronic congestive heart failure, and it has been associated with adverse events such as atrial fibrillation.¹ Previous studies have shown that hypoalbuminemia can lead to various complications, including pulmonary congestion, diuretic resistance, fluid overload, and reduced antioxidant and anti-inflammatory functions.¹ Additionally, hypoalbuminemia serves as a marker for heart, liver, and kidney diseases, endothelial dysfunction, and subclinical systemic inflammation.² Albumin, being the predominant serum protein, is known for its strong antioxidant nature and its ability to protect against ischemia-reperfusion injury.³ Furthermore, it has been noted as a natural angiotensin-converting enzyme inhibitor (ACE), exerting cardio-protective effects on coronary circulation. Therefore, our study primarily focuses on determining whether albumin deficiency can affect the development of postoperative atrial fibrillation due to its role in coronary circulation.⁴

Coronary artery bypass surgery (CABG) is one of the most common cardiac surgeries worldwide,⁵ which can lead to various complications, including impaired heart function and hemodynamic parameters. To mitigate these

risks, two techniques have been developed: off-pump CABG and cardioplegia solution, which stops the heart and prevents ischemic injury.⁶

Post-operative atrial fibrillation (POAF) is one of the most common and serious complications occurring after CABG. It may cause cerebrovascular accidents (CVA), respiratory infections, cardiopulmonary failure, prolonged hospital and intensive care unit (ICU) stays compared to those without the event, increased healthcare expenditure, and mortality.⁷ POAF usually develops in the first week after heart surgery, with approximately 70% of cases occurring within the first 3 days.⁸ Various factors have been implicated in POAF, with cardiopulmonary bypass (CPB) time consistently associated with its occurrence. Studies show that reducing cardiopulmonary bypass time may reduce the incidence of POAF.^{9–11}

The frequency of POAF associated with hypoalbuminemia varies in different studies, ranging from 39.2–70.03%.^{12,13} This study was planned to find out the exact frequency of POAF following CABG associated with pre-operative hypoalbuminemia in our population.

MATERIAL AND METHODS

A descriptive cross-sectional study was conducted on 144 patients over a period of 6 months at the cardiac surgery

unit of the "National Institute of Cardiovascular Diseases (NICVD), Karachi, Pakistan," the largest cardiovascular healthcare institute in Karachi. The inclusion criteria were established as patients undergoing CABG surgery of any gender, aged between 30 to 80 years, and having hypoalbuminemia at the time of pre-operative assessment. Hypo-albuminemia was defined as a serum albumin level less than 3.8 mg/dl (normal range: 3.8–4.5 mg/dl).

Patients who refused to give consent to participate, those with congenital heart diseases or concomitant valvular heart disease (based on history, clinical examination, and echocardiogram), hyperthyroidism, obstructive sleep apnoea, chronic obstructive pulmonary disease (COPD), acute illness, and patients with a history of atrial fibrillation were not included in the study. Additionally, patients with uncontrolled hypertension (> 160/90 mmHg), uncontrolled diabetes (HbA1c >8%), and moderate-to-severe underweight (body mass index <17 kg/m²) were excluded from the analysis based on clinical assessment.

The study was conducted after obtaining approval from the ERC (ethical review committee) of NICVD. Patients eligible for CABG were briefed about the study and its purpose, and verbal consent was obtained for their participation and the publication of the data obtained from them. To minimize intra-operative and post-operative complications, admitted patients were medically optimized through a multidisciplinary approach.

Demographic details such as gender, age (years), body mass index (BMI kg/m²), smoking, alcohol intake, hypertension, diabetes mellitus, renal dysfunction, left ventricular (LV) dysfunction, prolonged CBP time, and post-operative hypokalaemia were all noted according to the operational definitions.

All surgeries were performed by authorized cardiac surgeons, and CBP time (minutes) was recorded following clinical practice guidelines and institutional protocols. After the procedure, patients were moved to the ICU where they were continuously monitored using invasive blood pressure measurement and cardiac rhythm monitoring. As nearly 70% of POAF events are reported to occur within the first 3 days (72 hours) after surgery,⁸ all patients were kept under continuous ECG monitoring during this period, and any event of POAF was recorded. To minimize observation bias, 12-lead ECGs were interpreted by two independent consultant cardiologists, and the agreement of any two was taken as the final finding. A principal investigator recorded all collected data on a predesigned proforma. Confounding variables were controlled by strictly adhering to the inclusion and exclusion criteria, and patient information was kept secure and accessible only to authorized individuals. Data analysis was performed using SPSS version 21. The normality of the distribution of continuous variables such as age (years) and CBP time (minutes) was assessed using the Shapiro-Wilk test, and descriptive statistics such as

mean±SD/median (IQR) were computed. Frequencies and percentages were calculated for qualitative variables like gender, age, smoking, alcohol intake, hypertension, diabetes mellitus, renal dysfunction, LV dysfunction, prolonged CBP time, post-operative hypokalaemia, and POAF. Effect modifiers like gender, age group, smoking, alcohol intake, hypertension, diabetes mellitus, renal dysfunction, LV dysfunction, post-operative hypokalaemia, and prolonged CBP were controlled through stratification. Post-stratification Chi-square test/Fisher's exact test was applied, and two-sided *p*-values of ≤0.05 were considered statistically significant.

RESULTS

The study included a total of 144 patients, out of which 77.8% (112) were male, and the mean age was 58.1±8.4 years. Prior to the surgery, the average serum albumin levels were 3.5±0.2 mg/dL. The majority of patients, 71.5% (103), had the three-vessel disease (3VD), and 20.8% (30) had 3VD plus left main (LM) disease. Hypertension was observed in 70.1% (101) of the patients, diabetes in 52.1% (75), and prolonged CBP time in 61.8% (89) (Table-1).

The frequency of POAF was observed to be 10.4% (15) and it was found to be significantly higher in non-hypertensive and non-diabetic patients with a crude odds ratio of 4.19 [1.39–12.65] and 8.47 [1.84–39.09], respectively (Table-2).

Table-1: Distribution of patient and procedure-related factors and frequency of postoperative atrial fibrillation

	Summary N (%) / mean±SD
Total (N)	144
Gender	
Male	112 (77.8%)
Female	32 (22.2%)
Age (years)	58.1 ± 8.4
Serum albumin (mg/dL)	3.5 ± 0.2
Body mass index	
Underweight	10 (6.9%)
Normal weight	75 (52.1%)
Overweight	37 (25.7%)
Obese	22 (15.3%)
Diagnosis	
Single vessel disease	2 (1.4%)
Two vessel disease	8 (5.6%)
Three vessel disease	103 (71.5%)
Left main + three-vessel disease	30 (20.8%)
Smoking	
Non-smoker	109 (75.7%)
Current smoker	14 (9.7%)
Ex-smoker	21 (14.6%)
Alcohol	0 (0%)
Hypertension	101 (70.1%)
Diabetes	75 (52.1%)
Left ventricular dysfunction	51 (35.4%)
Renal Dysfunction	11 (7.6%)
Prolonged CBP time	89 (61.8%)
Hypokalaemia	48 (33.3%)
Post-operative atrial fibrillation	15 (10.4%)

CPB: cardiopulmonary bypass

Table-2: Frequency of postoperative atrial fibrillation by patient and procedure-related factors

	Base (N)	Incidence of postoperative atrial fibrillation		
		n (row %)	Crude Odds Ratio	p-value
Total	144	15 (10.4%)	-	-
Gender				
^Male	112	13 (11.6%)	0.51 [0.11–2.38]	0.389
Female	32	2 (6.3%)		
Age				
^≤ 60 years	91	8 (8.8%)	1.58 [0.54–4.63]	0.406
> 60 years	53	7 (13.2%)		
Obese				
^No	122	13 (10.7%)	0.84 [0.18–4]	0.825
Yes	22	2 (9.1%)		
Left main + three-vessel disease				
^No	114	9 (7.9%)	2.92 [0.95–8.98]	0.062
Yes	30	6 (20%)		
Smoking				
^No	109	9 (8.3%)	2.3 [0.76–6.99]	0.143
Yes	35	6 (17.1%)		
Hypertension				
^No	43	9 (20.9%)	0.24 [0.08–0.72]	0.011
Yes	101	6 (5.9%)		
Diabetes				
^No	69	13 (18.8%)	0.12 [0.03–0.54]	0.006
Yes	75	2 (2.7%)		
Left ventricular dysfunction				
^No	93	11 (11.8%)	0.63 [0.19–2.1]	0.457
Yes	51	4 (7.8%)		
Renal Dysfunction				
^No	133	15 (11.3%)	-	-
Yes	11	0 (0%)		
Prolonged CBP time				
^No	55	5 (9.1%)	1.27 [0.41–3.92]	0.683
Yes	89	10 (11.2%)		
Hypokalaemia				
^No	96	9 (9.4%)	1.38 [0.46–4.13]	0.564
Yes	48	6 (12.5%)		

^reference category, CPB: cardiopulmonary bypass

DISCUSSION

The POAF is characterized by abnormal, uncoordinated electrical activation of the atrium, leading to ineffective contractility of the atrium and resulting in deranged heart and hemodynamic parameters. Our study aimed to evaluate the frequency of POAF in a cohort of patients with hypoalbuminemia undergoing CABG. The incidence rate of POAF was observed to be one in every ten cases, and it was found to be higher among non-hypertensive and non-diabetic patients. Previous studies have reported a wide range of incidence rates of POAF, with some studies reporting rates of up to 5–40% in the early postoperative period.^{14–18}

Interestingly, the incidence of POAF in our population undergoing CABG appears to be lower compared to developed countries. This difference could be attributed to factors such as younger age, ethnicity, consideration of only new-onset early postoperative atrial fibrillation, absence of alcohol intake history, and exclusion of diseases like COPD, valvular, and congenital heart diseases.^{19–21}

The relationship between hypertension and POAF is complex, with some studies showing a strong predictive link, while others, including our study, find an inverse relationship, possibly influenced by preoperative beta-blocker use. Our study observed a higher risk of POAF among non-hypertensive patients.²²

Similarly, differing opinions and results exist in various studies concerning diabetes mellitus and HbA1c about POAF. Our study observed a higher occurrence of POAF in non-diabetic patients, contrasting with some studies suggesting diabetes is a significant risk factor for POAF. Additionally, HbA1c was labelled as a predictor of POAF in both diabetic and non-diabetic patients. However, other articles have shown that in the absence of valvular disease, diabetes is no longer a significant predictor for the development of AF, and HbA1c is not an independent predictor of POAF. These discrepancies highlight the importance of monitoring perioperative blood glucose regulation in all patients undergoing CABG surgery, regardless of their diabetes history. Further research

may be necessary to understand the factors contributing to these differences in outcomes.²³⁻²⁸

In this study, obesity, renal dysfunction, and LV dysfunction were analyzed as predictors of postoperative AF, but they did not achieve statistical significance. Other variables might have influenced the results.²⁹ The involvement of multiple factors in the development of postoperative atrial fibrillation is reflected in the higher incidence observed in normotensive and non-diabetic patients.²⁹ Patients with these mentioned risk factors were relatively more likely to develop atrial fibrillation, emphasizing not only the importance of these factors for the development of new-onset postoperative atrial fibrillation but also highlighting the significance of optimizing these factors to decrease events. Further research work may explore the role of these factors in isolation to better understand their impact on subsequent atrial fibrillation.

It is essential to consider these limitations when interpreting the study's findings. The study was conducted at a single institution with a small sample size and a short monitoring period, which may limit its generalizability to the broader population. More extensive and longer-term research would be beneficial for a more comprehensive understanding.

CONCLUSION

Interestingly, the study found a contrasting result to the commonly reported positive relationship between pre-operative hypoalbuminemia and postoperative atrial fibrillation. Instead, the incidence of atrial fibrillation was found in every tenth patient after routine CABG surgery, and it was most common in normotensive patients. Further research might be needed to understand these findings better.

AUTHORS' CONTRIBUTION

AS & RAM: Conceived the idea, and designed the study. AS, RAM, ZS: Data collection. AS, RAM, ZS, MI: Write-up, review. AS: Supervision.

REFERENCES

- Chien SC, Chen CY, Lin CF, Yeh HI. Critical appraisal of the role of serum albumin in cardiovascular disease. *Biomark Res* 2017;5(1):1-9.
- Ferencesy A, Diller GP, Alonso-Gonzalez R, Uebing A, Rafiq I, Li W, *et al.* Hypoalbuminaemia predicts outcome in adult patients with congenital heart disease. *Heart* 2015;101(9):699-705.
- Arques S, Ambrosi P. Human serum albumin in the clinical syndrome of heart failure. *J Card Fail* 2011;17(6):451-8.
- Fagyas M, Úri K, Siket IM, Fülöp GÁ, Csato V, Daragó A, *et al.* New perspectives in the renin-angiotensin-aldosterone system (RAAS) II: albumin suppresses angiotensin converting enzyme (ACE) activity in human. *PLoS One* 2014;9(4):e87844.
- D'Agostino RS, Jacobs JP, Badhwar V, Fernandez FG, Paone G, Wormuth DW, *et al.* The society of thoracic surgeons adult cardiac surgery database: 2018 update on outcomes and quality. *Ann Thorac Surg* 2018;105(1):15-23.
- Guajardo Salinas GE, Nutt R, Rodriguez-Araujo G. Del Nido cardioplegia in low risk adults undergoing first time coronary artery bypass surgery. *Perfusion* 2017;32(1):68-73.
- Aranki SF, Shaw DP, Adams DH, Rizzo RJ, Couper GS, VanderVliet M, *et al.* Predictors of atrial fibrillation after coronary artery surgery. Current trends and impact on hospital resources. *Circulation* 1996;94(3):390-7.
- Shen J, Lall S, Zheng V, Buckley P, Damiano RJ, Jr Schuessler RB. The persistent problem of new-onset postoperative atrial fibrillation: a single-institution experience over two decades. *J Thorac Cardiovasc Surg* 2011;141(2):559-70.
- Badhwar V, Rankin JS, Ad N, Grau-Sepulveda M, Damiano RJ, Gillinov AM, *et al.* The society of thoracic surgeons adult cardiac surgery database: 2019 update on outcomes and quality. *Ann Thorac Surg* 2019;107:24-32.
- Lee EH, Kim WJ, Kim JY, Chin JH, Choi DK, Sim JY, *et al.* Effect of Exogenous Albumin on the Incidence of Postoperative Acute Kidney Injury in Patients Undergoing Off-pump Coronary Artery Bypass Surgery with a Preoperative Albumin Level of Less Than 4.0 g/dl. *Anesthesiology*. 2016;124:1001-11.
- Berbel-Franco D, Lopez-Delgado JC, Putzu A, Esteve F, Torrado H, Farrero E, *et al.* The influence of postoperative albumin levels on the outcome of cardiac surgery. *J Cardiothorac Surg* 2020;15(1):78.
- Hussain SM, Zia K, Mangi AR, Shirazi Z, Ahmed A, Kumar K, *et al.* Operative Mortality of Coronary Artery Bypass Grafting in Patients with Low Serum Albumin after Nutritional Support. *Pak Heart J* 2021;54(03):235-8.
- Akgul E, Parlar AL, Erkul G, Erkul Sİ, Cekirdekci AH. Investigation of the effect of preoperative hypoalbuminemia, blood urea nitrogen and creatinine levels on postoperative atrial fibrillation on off-pump coronary bypass surgery patients. *Heart Surg Forum* 2020;23(5):E641-6.
- Mostafa A, El-Haddad MA, Shenoy M, Tulliani T. Atrial fibrillation post cardiac bypass surgery. *Avicenna J Med* 2012;2(3):65-70.
- Engelman DT, Ali WB, Williams JB, Perrault LP, Reddy VS, Arora RC, *et al.* Guidelines for perioperative care in cardiac surgery: enhanced recovery after surgery society recommendations. *JAMA Surg* 2019;154(8):755-66.
- Yadava M, Hughey AB, Crawford TC. Postoperative atrial fibrillation: incidence, mechanisms, and clinical correlates. *Heart Fail Clin* 2016;12:299-308.
- Zakkar M, Ascione R, James AF, Angelini GD, Suleiman MS. Inflammation, oxidative stress and postoperative atrial fibrillation in cardiac surgery. *Pharmacol Ther* 2015;154:13-20.
- Li N, Qiao H, Guo JF, Yang HY, Li XY, Li SL, *et al.* Preoperative hypoalbuminemia was associated with acute kidney injury in high-risk patients following non-cardiac surgery: a retrospective cohort study. *BMC Anesthesiol* 2019;19(1):171.
- Mathew JP, Fontes ML, Tudor IC, Ramsay J, Duke P, Mazer CD, *et al.* A multicenter risk index for atrial fibrillation after cardiac surgery. *JAMA* 2004;291(14):1720-9.
- Nazeri A, Razavi M, Elayda MA, Lee VV, Massumi A, Wilson JM. Race/ethnicity and the incidence of new-onset atrial fibrillation after isolated coronary artery bypass surgery. *Heart Rhythm* 2010;7(10):1458-63.
- Rader F, Van Wagoner DR, Ellinor PT, Gillinov AM, Chung MK, Costantini O, *et al.* Influence of race on atrial fibrillation after cardiac surgery. *Circ Arrhythm Electrophysiol* 2011;4(5):644-52.
- Benjamin EJ, Levy D, Vaziri SM, D'Agostino RB, Belanger AJ, Wolf PA. Independent risk factors for atrial fibrillation in

- a population-based cohort: the Framingham Heart Study. JAMA 1994;271(11):840–4.
23. Tadic M, Ivanovic B, Zivkovic N. Predictors of atrial fibrillation following coronary artery bypass surgery. Med Sci Monit 2011;17(1):CR48–55.
 24. Mueller XM, Tevæarai HT, Ruchat P, Stumpe F, Von Segesser LK. Atrial fibrillation and minimally invasive coronary artery bypass grafting: risk factor analysis. World J Surg 2002;26(6):639–42.
 25. Kalus JS, White CM, Caron MF, Coleman CI, Takata H, Kluger J. Indicators of atrial fibrillation risk in cardiac surgery patients on prophylactic amiodarone. Ann Thorac Surg 2004;77(4):1288–92.
 26. Kinoshita T, Asai T, Suzuki T, Kambara A, Matsubayashi K. Preoperative hemoglobin A1c predicts atrial fibrillation after off-pump coronary bypass surgery. Eur J Cardiothorac Surg 2012;41(1):102–7.
 27. Zhao H, Liu M, Chen Z, Mei K, Yu P, Xie L. Dose-response analysis between hemoglobin A1c and risk of atrial fibrillation in patients with and without known diabetes. PLoS One 2020;15(2):e0227262.
 28. Abbaszadeh S, Shafiee A, Bina P, Jalali A, Sadeghian S, Karimi A. Preoperative hemoglobin A1c and the occurrence of atrial fibrillation following on-pump coronary artery bypass surgery in type-2 diabetic patients. Crit Pathw Cardiol 2017;16(1):37–41.
 29. Malhotra P, Pande S, Mahindru S, Thukral A, Kotwal AS, Gupta RP, *et al.* Postoperative atrial fibrillation in coronary artery bypass grafting herald poor outcome. Ann Card Anaesth 2021;24:464–9.

Submitted: March 14, 2023

Revised: August 3, 2023

Accepted: September 4, 2023

Address for Correspondence:

Dr. Asaf Shah, Resident of Cardiac Surgery, National Institute of Cardiovascular Diseases (NICVD), Rafiqui (H.J.) Shaheed Road, Karachi-75510, Pakistan.

Email: asifshahkmc@gmail.com