Annals of Medical Research
DOI: 10.5455/annalsmedres.2019.10.629 2019;26(10):2432-6

Original Article

Is preoperative anemia a risk factor of new-onset atrial fibrillation in patients underwent isolated coronary artery bypass surgery?

Baris Akca

Inonu University, Faculty of Medicine, Department of Cardiovascular Surgeon, Malatya, Turkey

Abstract

Aim: The impact of preoperative anemia in coronary artery bypass surgery (CABG) remains controversial and mostly associated with worse outcomes. Also, relationship between anemia and new on-set Atrial Fibrillation (NOAF) is still uncertain in patients who underwent CABG. This study aimed to investigate the anemia whether a risk factor of NOAF in patients who underwent isolated CABG.

Material and Methods: Between March 2007 - December 2017 data of patients who underwent isolated CABG were retrospectively examined and 2027 patients included in study. Anemia was defined as hemoglobin level < 13 g/dl for men and <12 g/dl for women. Patients were grouped as non-AF (n=1772) and AF (n=255) according to development of NOAF after CABG or not. Multivariate logistic regression analysis was performed to determine AF risk factors.

Results: Overall anemia incidence of this study was 25.8% (n= 522). Also, anemia was observed in 17.4% of males and 52.2% of females. The incidence of anemia was similar in both groups; AF group 29% (n=74), non-AF group 25.3% (n=448) (p = 0.202). The mean hemoglobin and mean hematocrit level of AF and non-AF groups were similar (p=0.749, p=0.954 respectively) and 13.88 ± 1.77 g/dl, 13.84±1.63 g/dl and 41.13±5.48 %, 41.15±4.97 % respectively. Multivariate logistic regression analysis revealed that the parameters of mean hemoglobin, mean hematocrit and preoperative anemia were not NOAF risk factors after CABG. The parameters of carotid artery disease (OR=1.996), low LVEF (OR=1.429), BUN (OR=1.019), Euroscore (OR=1.151), need of inotrop (OR=2.270), mean perfusion time (OR=1.008), mean crosclamp time (OR=1.007) and mean ventilation time (OR=1.030) were independent risk factors of NOAF after CABG. Postoperative early mortality of groups were similar (p=0.299).

Conclusion: Preoperative anemia was not a risk factor of NOAF in post-CABG patients. In addition, the mortality-enhancing effect of preoperative anemia was not detected in AF patients.

Keywords: Coronary artery bypass; atrial fibrillation; anemia; risk factors.

INTRODUCTION

New on-set Atrial Fibrillation (NOAF) is the most frequent arrhythmia after coronary artery bypass surgery (CABG) with an incidence between 15-50% and also associated with increased mortality, morbidity, and prolonged hospital stay (1-3). One of the determined risk factor of cardiovascular disease outcome is anemia and also related with rising rates of morbidity and mortality in the elderly population with coronary artery disease and congestive heart failure, especially in patients with acute coronary syndrome (4-6).

Various studies investigated the relation between anemia and cardiovascular outcome in patients with AF (7). Furthermore, some of the previous studies were reported the preoperative anemia as an independent risk factor of morbidity and in-hospital mortality after CABG or valve surgery (8-13). Nevertheless, some studies did not reveal significant difference in adverse outcomes in patients who underwent CABG with low and normal hemoglobin levels (14,15).

Thus, the impact of preoperative anemia in CABG remains controversial. Therefore, the association between anemia

Received: 25.09.2019 **Accepted:** 21.10.2019 **Available online:** 24.10.2019
Corresponding Author: Barış Akca, Inonu University, Faculty of Medicine, Department of Cardiovascular Surgeon, Malatya, Turkey
E-mail: dr.baris.akca@yandex.com.tr

and increased risk of NOAF is still uncertain in patients underwent CABG. In this study, we aimed to investigate the anemia whether a risk factor of NOAF in patients who underwent isolated CABG.

MATERIAL and METHODS

The patient records and hospital database were retrospectively examined between March 2007 and December 2017. Among the patients who underwent CABG, 2027 of them with full data were included in this study. The patients were grouped as non-AF (n=1772) and AF (n=255) according to development of NOAF after CABG or not. The anemia and other patient parameters were examined whether a risk factor of post CABG NOAF or not. Additionally, the predictive power of determined risk factors were calculated.

Patients with accompanying valve pathologies, hypothyroidism, all kinds of arrhythmia, hyperthyroidism, history of temporary and/or persistent pacemakers, history of AF, concomitant valve surgery during the CABG, redo operations and post-MI ventricular septal defect were excluded from the study.

This study was conducted with the research ethics committee approval (report number: 2019/373) in agreement with the principles of the Declaration of Helsinki. The written informed consent form was acquired from each patient.

Anesthesia and Surgical technique

All patients were monitored during the operating theater period. Peripheral arterial oxygen saturation was observed via a pulse oximetry probe from the monitor. A 20G branule mostly positioned in the right radial artery for both monitoring systemic arterial blood pressure and arterial blood gas analysis. CABG was performed via median sternotomy with general anesthesia. The selection of surgical technique (off-pump or on-pump) was depended on the surgeon's decision. All patients who underwent standard on-pump CABG in which a roller pump system, non-heparin coated oxygenator, two-stage venous cannula, and polyvinylchloride tubing set were used for cardiopulmonary bypass (CPB). The details about surgical technique, induction of general anesthesia and how it maintains furthermore preoperative and postoperative medication protocols of patients was as defined in previous report of us (3).

Data collection and definitions

Preoperative, perioperative and postoperative data of patients were collected retrospectively from the hospital database and patient records. A total of 2027 patients included in the present study. The number of patients with anemia in the overall study population, also in male and female patients were initially calculated and compared between non-AF and AF groups. Anemia was defined as hemoglobin level < 13 g/dl for men and <12 g/dl for women as stated by the World Health Organization.

Preoperative parameters of the patients included in the study were age, sex, comorbidities like hypertension, obesity, diabetes mellitus (DM), chronic obstructive pulmonary disease (COPD), hyperlipidemia, blood sample results of hemoglobin, hematocrit, Leucocyte, triglyceride and glucose levels, presence of renal insufficiency (serum creatinine level ≥ 1.5 mg/dL), peripheral vascular disease (PVD), carotid artery disease and unstable angina, prior percutaneous transluminal coronary angioplasty (PTCA), myocardial infarction and previous cerebrovascular event, body mass index (BMI), body surface area (BSA), blood urea nitrogen (BUN) levels, history of smoking and family history of coronary artery disease, presence of left main coronary artery (LMCA) and right coronary artery (RCA) disease, left ventricular ejection fraction (LVEF) and European System For Cardiac Operative Risk Evaluation Score (EuroSCORE).

Perioperative parameters of the patients included in the study were the type of surgery (on/off pump), elective or emergent CABG, graft types of each operation (left internal mammarian artery (LIMA), radial artery) and the period of CPB and aortic cross-clamp, also performed concomitant procedures like left ventricle aneurysmectomy.

Postoperative parameters of the patients included in the study were need of inotropic drugs (at least 24 h), mechanical ventilation time (VT), prolonged VT (≥6h), intraaortic balloon pump (IABP) support, reoperation for cardiac tamponade or bleeding, length of hospital stay, intensive care unit (ICU) stay and in-hospital mortality (postoperative 30 days).

Rhythm monitoring was done continuously during the ICU stay. A twelve lead electrocardiogram (ECG) of patients was performed immediately in ICU and on postoperative days 1, 2, 4, and before the hospital discharge. After ICU follow up patients transferred to the inpatient clinic. In a suspicious situation of arrhythmia, a twelve lead ECG performed quickly. If twelve lead ECG revealed fibrillatory p waves varying in size, shape, and timing or absence of p waves with irregular QRS complexes lasting more than 5 min was diagnosed as AF. All patients with AF were treated with a standard protocol of anticoagulation and amiodarone.

Statistical analysis

SPSS for Windows version 24.0 software (IBM Corp., Armonk, NY, USA) was used in this study. Shapiro-Wilk test was used for the normality assumption. The independent samples t-test was utilized for normally distributed parameters and expressed in mean ± standard deviation (SD). Categorical parameters were analyzed using the chi-square and Fisher's exact tests, where appropriate. If a parameter having a $p \leq 0.20$ in the univariate analysis, further analyzed with multiple logistic regression analysis. The multiple logistic regression model was confirmed using the Omnibus test and Hosmer-Lemeshow method. A $p < 0.05$ was considered statistically significant with 95% confidence interval (CI).

RESULTS

In the present study, the incidence of NOAF after CABG was 12.5 % (255/2027).

The mean age of patients in AF group was 65.37±8.22 years and the mean age of the non-AF group was 60.22±9.77 years. In the comparison of groups, the mean age was significantly higher in the AF group (p=0.0001) and also was found to be a risk factor of NOAF after CABG. Also, the number of patients with advanced age (Age ≥ 65 years) in the AF group (n=147, 57.6%) was significantly higher than the non-AF group (n= 652, 36.8%) and advanced age was found to be a risk factor of NOAF after CABG. Preoperative demographics, operative and postoperative parameters predisposing to NOAF development were compared between the AF group and the non-AF group in Table 1 and Table 2. Postoperative early mortality of groups were similar (non-AF (n= 21, 1.2%) AF (n=5, 2%) (p=0.299).

Table 1. Preoperative demographic, patient and disease-related parameters predisposing to post-CABG AF. (Data expressed as mean ± SD or n (%))

Variables	Non-AF group (n = 1772)	AF group (n = 255)	p Value
Age (years)	60.22±9.77	65.37±8.22	**0.0001**
Age ≥ 65 years	652 (36.8%)	147 (57.6%)??	**0.0001**
Female	421 (23.8%)	64 (25.1%)	0.639
Anemia	448 (25.3%)	74 (29%)	0.202
Unstable angına	289 (16.3%)	51 (20%)	0.317
History of smoking	1013 (57.3%)	140 (54.9%)	0.464
Diabetes mellitus (DM)	472 (26.7%)	50 (19.6%)	**0.016**
Hypertension	647 (36.5%)	104 (40.8%)	0.182
Obesity bmi≥30	360 (20.3%)	43 (16.9%)	0.196
Family history of CAD	570 (32.2%)	74 (29%)	0.310
COPD	258 (14.6%)	51 (20%)	0.147
Prior myocardial infarction	983 (55.5%)	153 (60%)	0.173
Prior PTCA	179 (10.1%)	22 (8.6%)	0.457
Renal insufficiency	39 (2.2%)	8 (3.1%)	0.353
Hyperlipidemia	686 (38.7%)	94 (36.9%)	0.890
Prior stroke	28 (1.6%)	5 (2%)	0.711
Carotid artery disease	147 (8.3%)	39 (15.3%)	**0.001**
Peripheral vascular disease	43 (2.4%)	9 (3.5%)	0.298
Emergency operation	64 (3.6%)	10 (3.9%)	0.805
Low LV EF (≤40)	390 (22%)	73 (28.7%)	**0.040**
RCA disease	1088 (61.4%)	163 (63.9%)	0.439
LMCA disease	66 (3.7%)	11 (4.3%)	0.614
Euroscore	3.92±2.59	5.06±3.07	**0.001**
BUN (mg/dl)	18.93±8.26	20.90±13.08	**0.001**
Platelet count	259.10±73.72	243.19±69.21	**0.001**
BSA (m2)	1.79±0.19	1.78±0.16	0.434
BMI (kg/m2)	26.73±3.86	26.41±3.88	0.213
Hemoglobin (g/dl)	13.84±1.62	13.877±1.77	0.749
Hematocrit (%)	41.15±4.97	41.13±5.48	0.954
LV EF (%)	49.67±9.83	48.25±10.50	0.066
Leucocyte count	8.88±7.53	10.42±23.03	0.076
Triglyceride (mg/dl)	180.26±96.83	162.71±92.29	**0.007**
Blood glucose (mg/dl)	135.91±71.94	126.10±66.16	**0.041**

BSA: Body Surface Area, BMI: Body Mass Index, CAD: Coronary Artery Disease, COPD: Chronic Obstructive Pulmonary Disease, PTCA: Percutaneous Transluminal Coronary Angioplasty, LMCA: Left Main Coronary Artery, LV EF: Left Ventricular Ejection Fraction, RCA: Right Coronary Artery, BUN: Blood Urea Nitrogen

Table 2. Operative and post-operative parameters of groups

Variables	Non-AF group (n = 1772)	AF group (n = 255)	p Value
LIMA usage	1687 (95.2%)	245 (96.1%)	0.536
Beating Heart	277 (15.6%)	35 (13.7%)	0.430
LV aneurysm repair	97 (5.5%)	21 (8.3%)	0.081
Need of Inotrop	116 (6.5%)	36 (13.7%)	**0.0001**
IABP usage	25 (1.4%)	6 (2.4%)	0.252
Bleeding- reoperation	21 (1.2%)	3 (1.2%)	0.927
Pleural effusion	53 (3%)	7 (2.8%)	0.827
Mortality (early)	21 (1.2%)	5 (2%)	0.299
Perfusion time	87.33±25.85	92.79±25.81	**0.009**
Crosclamp time	73.81±21.69	77.37±22.16	**0.044**
ICU stay (day)	2.40±1.35	3.43±1.52	**0.001**
Ventilation time (h)	7.75±5.47	9.27±8.03	**0.001**
Hospital stay (day)	6.77±1.78	7.43±1.67	**0.001**

LIMA: Left internal mammarian artery, LV: left ventricle, IABP: Intraartic balloon pump, ICU: Intensive care unit,

Overall anemia incidence of this study was 25.8% (n= 522). Also, anemia was observed in 17.4% of males and 52.2% of females. The incidence of anemia was similar in both groups; AF group 29% (n=74), non-AF group 25.3% (n=448) (p = 0.202). The mean hemoglobin level of AF

Table 3. Multivariate logistic regression risk analyze results of groups

Variables	Non-AF group (n = 1772)	AF group (n = 255)	p Value	Odds Ratio (95% CI)
Need of inotrop	116 (6.5%)	36 (13.7%)	**0.0001**	2.270 (1.516-3.397)
Carotid artery disease	147 (8.3%)	39 (15.3%)	**0.001**	1.996 (1.364-2.920)
Low LV EF (≤40)	390 (22%)	73 (28.7%)	**0.040**	1.429 (1.015-2.012)
Age ≥ 65 years	652 (36.8%)	147 (57.6%)	**0.0001**	2.336 (1.790-3.049)
Age (years)	60.22±9.77	65.37±8.22	**0.0001**	1.061 (1.045-1.077)
BUN (mg/dl)	18.93±8.26	20.90±13.08	**0.001**	1.019 (1.007-1.032)
Euroscore	3.92±2.59	5.06±3.07	**0.001**	1.151 (1.093-1.211)
Perfusion time (min)	87.33±25.85	92.79±25.81	**0.009**	1.008 (1.002-1.013)
Crosclamp time (min)	73.81±21.69	77.37±22.16	**0.044**	1.007 (1.000-1.014)
Ventilation time (h)	7.75±5.47	9.27±8.03	**0.001**	1.030 (1.011-1.048)

LV EF: Left ventricle ejection fraction,
BUN: Blood Urea Nitrogen.

group and the non-AF group were 13.88±1.77 g/dl, 13.84±1.63 g/dl respectively. The mean hemoglobin level of groups showed no statistically significant difference (p=0.749). The mean hematocrit level of AF group and the non-AF group were 41.13±5.48 %, 41.15±4.97 % respectively. The mean hematocrit level of AF and non-AF groups were similar (p = 0.954). Multivariate logistic regression analysis revealed that the parameters of mean hemoglobin, mean hematocrit and preoperative anemia were not NOAF risk factors after CABG.

The parameters of platelet count, DM, blood glucose and triglyceride levels were revealed a statistically significant difference between groups but they did not determine as risk factors of NOAF after CABG according to the results of multivariate logistic regression analysis.

Multivariate logistic regression risk analyze results of groups revealed that the parameters of carotid artery disease (OR=1.996), low LVEF (OR=1.429), BUN (OR=1.019), Euroscore (OR=1.151), need of inotrop (OR=2.270), mean perfusion time (OR=1.008), mean crosclamp time (OR=1.007) and mean ventilation time (OR=1.030) were independent risk factors of NOAF after CABG as shown in Table 3.

DISCUSSION

As it is the most common arrhythmia after CABG, studies still ongoing about the development, risk factors, and prevention of AF. Multiple factors were associated with the development of postoperative NOAF and various reports showed that the preoperative anemia was a risk factor of morbidity and mortality in patients underwent CABG (8-10,13,14,16-18), still some studies did not reveal a significant difference in adverse outcomes in patients who underwent CABG with low and normal hemoglobin levels (14,15). A recent study of taurien et al reported that the preoperative anemia was not realted with an increased mortality risk when adjusted for the severity of perioperative bleeding in patients who underwent CABG (19).

Furthermore, general population studies assessed the relationship between anemia and NOAF. In a report of Ganga et al, the relationship between chronic anemia and NOAF evaluated in aged people in a community setting and prevalence of chronic anemia seems to be more frequent, however, the incidence of AF was not significantly different (20).

Anemia is frequent in patients with AF and also associated with increased comorbidity and adverse results like mortality in patients with AF (21), although several mechanisms described about the affect of anemia in development of postoperative NOAF but it is not clear yet and suggested that anemia while accompanying with hypovolemia and hypoxia may cause of NOAF by myocardial injury (18). Rarely, NOAF may be one of the earliest sign of postoperative bleeding, however required optimal postoperative hgb level is also important because it determines the amount of transfusion which associated with postoperative AF by transfusion related inflammatory response in cardiothoracic surgery (18,22).

This study evaluated the preoperative anemia as a postoperative NOAF risk factor in patients underwent CABG and revealed that preoperative anemia, the mean hemoglobin, and the mean hematocrit levels were not NOAF risk factors.

In accordance with previous reports, this study showed that the carotid artery disease, low LVEF, high BUN level, Euroscore, the need of inotropes, mean perfusion time, mean cross-clamp time and mean ventilation time were independent risk factors of NOAF after CABG (3,23-26). Surprisingly, RCA disease was similar in both groups.

Platelet count, DM, blood glucose and triglyceride levels were higher in non-AF group contrary to expectations and revealed a statistically significant difference between groups yet they did not determine as risk factors of NOAF after CABG.

Study limitations

Retrospective analysis of a single-center data was the main limitation of this study. Patients who had asymptomatic paroxysmal atrial arrhythmia with preoperative sinus rhythm may be missed and included in study. Also, postoperative AF episodes without complaints may be missed after ICU stay. Results of the study could be analyzed better with the data of postoperative bleeding and transfusion.

CONCLUSION

This study revealed that preoperative anemia, the mean hemoglobin, and the mean hematocrit levels were not NOAF risk factors in patients undergoing isolated CABG.

Nevertheles, prospective randomized trials with the classification of anemia as acute, chronic and also with the data of postoperative bleeding and transfusions can offer different results.

Competing interests: The authors declare that they have no competing interest.
Financial Disclosure: There are no financial supports .
Ethical approval: This study was conducted with the research ethics committee application (report number: 2019/373) in agreement with the principles of the Declaration of Helsinki.

Baris Akca ORCID: 0000-0001-9154-4764

REFERENCES

1. Erdem K, Yazıcı M, Öztürk S, et al. Usefulness of CHA2DS2-VASc scoring system in predicting atrial fibrillation after coronary artery bypass grafting. Turk Gogus Kalp Dama 2016;24:27-33.
2. Kaireviciute D, Aidietis A, Lip GY. Atrial fibrillation following cardiac surgery: clinical features and preventative strategies. Eur Heart J 2009;30:410-25.
3. Akça B, Erdil N, Colak MC, et al. Is There Any Difference in Risk Factors between Male and Female Patients in New-Onset Atrial Fibrillation after Coronary

Artery Bypass Grafting? Thorac Cardiovasc Surg 2018;66:483-90.
4. Sarnak MJ, Tighiouart H, Manjunath G, et al. Anemia as a risk factor for cardiovascular disease in the Atherosclerosis risk in communities (ARIC) study. J Am Coll Cardiol 2002;40:27-33.
5. Tang YD, Katz SD. Anemia in chronic heart failure: prevalence, etiology, clinical correlates, and treatment options. Circulation 2006;113:2454-61.
6. Younge JO, Nauta ST, Akkerhui KM, et al. Effect of anemia on short- and long-term outcome in patients hospitalized for acute coronary syndromes. Am J Cardiol 2012;109:506-10.
7. Sharma S, Gage BF, Deych E, et al. Anemia: An independent predictor of death and hospitalizations among elderly patients with atrial fibrillation. Am Heart J 2009;157:1057-63.
8. Zindrou D, Taylor KM, Bagger JP. Preoperative haemoglobin concentration and mortality rate after coronary artery bypass surgery. Lancet 2002;359:1747-88.
9. Karkouti K, Wijeysundera DN, Beattie WS.Risk associated with preoperative anemia in cardiac surgery: A multicenter cohort study. Circulation 2008;117:478-84.
10. van Straten AH, Hamad MA, van Zundert AJ, et al. Preoperative hemoglobin level as predictor of survival after coronary artery bypass grafting: a comparison with the matched population. Circulation 2009;120:118-25.
11. Cladellas M, Bruguera J, Comín J, et al. Is pre-operative anaemia a risk marker for in-hospital mortality and morbidity after valve replacement? Eur Heart J 2006;27:1093-9.
12. Ranucci M, Di Dedda U, Castelvecchio S, et al. Impact of preoperative anemia on outcomes in adult cardiac surgery: a propensity-matched analysis. Ann Thorac Surg 2012;94:1134-41.
13. Miceli A, Romeo F, Glauber M, et al. Preoperative anemia increases mortality and postoperative morbidity after cardiac surgery. J Cardiothorac Surg 2014;9:137.
14. Bell ML, Grunwald GK, Baltz JH, et al. Does preoperative hemoglobin independently predict short-term outcomes after coronary artery bypass graft surgery? Ann Thorac Surg 2008;86:1415-23.
15. Carrascal Y, Maroto L, Rey J, et al. Impact of preoperative anemia on cardiac surgery in octogenarians. Interact Cardiovasc Thoracic Surg 2010;10:249-55.
16. Boening A, Boedeker RH, Scheibelhut C, et al. Anemia before coronary artery bypass surgery as additional risk factor increases the perioperative risk. Ann Thorac Surg 2011;92:805-11.
17. Kulier A, Levin J, Moser R, et al. Impact of postoperative anemia on outcome in patients undergoing coronary artery bypass graft surgery. Circulation 2007;116:471-9.
18. Chelazzi C, Villa G, De Gaudio AR. Postoperative atrial fibrillation. ISRN Cardiol 2011;2011:203179.
19. Tauriainen T, Koski-Vähälä J, Kinnunen EM, et al. The Effect of Preoperative Anemia on the Outcome After Coronary Surgery. World J Surg 2017;41:1910-18.
20. Ganga HV, Kolla N, Zimmerman MB, et al. Impact of Chronic Anemia on the New-Onset Atrial Fibrillation in the Elderly: It May Not Be What We Have Thought. J Atr Fibrillation 2012;4:515.
21. Ali AN, Athavale NV, Abdelhafız AH. Anemia: An Independent Predictor Of Adverse Outcomes In Older Patients With Atrial Fibrillation. J Atr Fibrillation 2016;8:1366.
22. Sood N, Coleman CI, Kluger J, et al. The association among blood transfusions, white blood cell count, and the frequency of post-cardiothoracic surgery atrial fibrillation: a nested cohort study from the Atrial Fibrillation Suppression Trials I, II, and III. J Cardiothorac Vasc Anesth 2009;23:22-7.
23. Almassi GH, Schowalter T, Nicolosi AC, et al. Atrial fibrillation after cardiac surgery: a major morbid event? Ann Surg 1997;226:501-511.
24. Mathew JP, Parks R, Savino JS, et al. Atrial fibrillation following coronary artery bypass graft surgery: predictors, outcomes, and resource utilization. MultiCenter Study of Perioperative Ischemia Research Group. JAMA 1996;276:300-6.
25. Aranki SF, Shaw DP, Adams DH, et al. Predictors of atrial fibrillation after coronary artery surgery. Current trends and impact on hospital resources. Circulation 1996;94:390-7.
26. Ismail MF, El-Mahrouk AF, Hamouda TH, et al. Factors influencing postoperative atrial fibrillation in patients undergoing on-pump coronary artery bypass grafting, single center experience. J Cardiothorac Surg 2017;12:40.