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The Correlation between the Severity of Coronary Artery Disease and Coronary Collateral Circulation and Atrial Fibrillation after Coronary Artery Bypass Surgery: A Cross-Sectional Study

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ABSTRACT

Background: Post-Operative Atrial Fibrillation (POAF) is the most common cardiac arrhythmia, which occurs in nearly 15 - 40% of patients after Coronary Artery Bypass Graft (CABG) surgery. However, the exact mechanism of POAF development is unclear.
Objectives: The present study aimed to investigate whether ischemic severity and preoperative coronary collateral circulation grade were associated with the development of POAF.
Methods: This cross-sectional, observational study assessed 246 patients who underwent CABG surgery from September 2017 to September 2019. The patients were divided into two groups according to the development of POAF; 51 patients in the POAF group and 195 patients in the group without POAF. Clinical variables were recorded. Additionally, coronary collateral circulation and the severity of coronary artery disease were assessed and recorded for each patient according to Rentrop classification and Gensini score.
Results: POAF was observed in 51 patients (20.7%). The results of multivariate analysis showed that chronic obstructive pulmonary disease (OR = 5.4, CI = 1.17 - 25.1, P = 0.03) was the independent predictor of POAF development. However, no significant association was found between the development of POAF and coronary collateral circulation (OR = 0.82, CI = 0.44 - 1.52, P = 0.54) and severity of coronary artery disease (OR = 0.98, CI = 0.42 - 2.29, P = 0.97). Furthermore, the coronary collateral circulation status was poorer in patients with the history of chronic obstructive pulmonary disease who developed POAF.
Conclusions: Preoperative coronary collateral circulation and severity of coronary artery disease were not associated with the development of POAF. However, patients with the history of chronic obstructive pulmonary disease who developed POAF had poorer coronary collateral circulation, indicating that hypoxia might play a role in the development of POAF.

1. Introduction

Atrial Fibrillation (AF) is the most common cardiac arrhythmia in the general population whose prevalence increases with age after cardiac surgery (1, 2). Annually, almost 800,000 patients undergo isolated Coronary Artery Bypass Graft (CABG) surgery, and Post-Operative AF (POAF) occurs in around 15 - 40% of post-CABG cases. POAF is an independent predictor of numerous adverse outcomes including renal insufficiency, heart failure, stroke, morbidity, and mortality and is associated with a significant financial burden (3-6).

The exact mechanism by which POAF evolves is unknown. POAF has been thought to be multifactorial, with certain surgical and non-surgical risk factors such as obesity, history of hypertension, diabetes mellitus, and chronic pulmonary disease, atrial factors (such as atrial dilatation, hypertrophy, and fibrosis), post-operative inflammation, pericarditis,

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autonomic imbalance, atrial incision, and perioperative ischemia (7). Ischemic mechanisms in the development of POAF have been discussed by comparing off-pump and on-pump coronary bypass grafting. Nevertheless, there is a paucity of data about Coronary Collateral Circulation (CCC) (8, 9). The severity of Coronary Artery Disease (CAD) and CCC indirectly indicate ischemia. CCC is another source of blood supply to the at-risk myocardium and is one of the most important defense mechanisms of the heart against ischemia (10, 11).

2. Objectives

The present study aims to investigate whether ischemic severity and preoperative CCC grade are associated with POAF development.

3. Patients and Methods

3.1. Patient Selection

This cross-sectional, observational study was conducted on the patients who underwent CABG surgery from September 2017 to September 2019. The inclusion criterion of the study was undergoing elective CABG surgery. The exclusion criteria were emergency cardiac surgery (e.g., acute myocardial infarction), history of prior cardiac surgery, hemodynamic instability, concomitant valvular surgery, severe enlargement ≥ 5.2 cm in males and ≥ 4.7 cm in females, hyperthyroidism, preoperative history of AF, history of implantation of pacemaker or other intra-cardiac devices, and history of digoxin or amiodarone consumption. The study endpoints were the correlation between the development of AF rhythm and the coronary collateral status defined by the Rentrop grade and the severity of CAD defined by the Gensini scoring system.

This study was conducted at the Cardiovascular Surgery Department and Cardiology Department at Buali Research and Training Hospital in Qazvin, Iran. This study was approved by the Institutional Ethics Committee, and written consent was obtained from the participants.

3.2. Data Collection

In the first two post-operative days, the patients underwent continuous ECG monitoring regarding AF rhythm development. The development of AF rhythm was diagnosed by expert ICU nurses, and 12-lead ECG was obtained from the patients who developed AF to confirm the rhythm abnormalities. AF was described as an abnormal ventricular rhythm with no P-wave before the QRS complex, which was confirmed with a 12-lead ECG on the rhythm strip.

Considering the Rentrop grade, the CCC status was graded from 0 to 3 as follows: grade 0: none, grade 1: filling of the side branches of the artery by collateral vessels without the visualization of the epicardial segment, grade 2: partial filling of the major epicardial coronary artery by collateral vessels, and grade 3: complete filling of the major epicardial coronary artery by collateral channels (12). According to the Rentrop grade, the patients were classified as poor CCC (grades 0 and 1) and good CCC (grades 2 and 3).

Based on the Gensini scoring system, the severity of CAD was calculated as the sum of the severity scores by multiplying functional significance scores for each epicardial coronary artery segment. The severity score indicated the percentage of coronary artery lumen obstruction, with scores 1, 2, 4, 8, 16, and 32 representing 25%, 50%, 75%, 90%, 99%, and 100% stenosis, respectively. The functional significance score indicated the importance of the area supplied by the location of the lesion. The score ranged from 0.5 for side branches to 5 for major epicardial coronary arteries (13). Overall, Gensini scores ≤ 40, between 40 and 100, and above 100 were considered non-severe, advanced, and heavy CAD, respectively.

The patients' demographic and clinical data including traditional cardiovascular risk factors, history of Chronic Obstructive Pulmonary Disease (COPD), and Left Ventricular Ejection Fraction (LVEF) were obtained from their medical records.

3.3. Statistical Analysis

Statistical analyses were performed using the SPSS 16.0 software (SPSS Inc. for Windows, version 16.0. Chicago, USA). The data were assessed by descriptive statistics (frequency, percentage, mean, and standard deviation). Student t-test was used to analyze the normally distributed quantitative variables, and Mann–Whitney test was employed for non-normally distributed ones. Additionally, categorical variables were analyzed by chi-square test or Fisher's exact test, as appropriated. Moreover, a binary logistic regression test was used for multivariate analysis. $P < 0.05$ (two-sided) was considered statistically significant, and 95% Confidence Interval (CI) was reported for each variable.

4. Results

This study was conducted on 246 patients; 51 in the POAF group and 195 in the group without POAF. The mean age of the patients was 63.3 ± 9.8 years, and 87 patients (35.5%) were female. During the study period, 51 patients (20.7%) developed AF rhythm. The baseline demographic and clinical characteristics of the patients regarding the development of AF rhythm have been presented in Table 1. Accordingly, the two groups were homogeneous regarding the distribution of sex and clinical characteristics, except for the history of COPD that was significantly higher in the AF group ($P = 0.03$). However, the results revealed no statistically significant difference between the two groups regarding the Rentrop grade and the Gensini score ($P = 0.4$ and $P = 0.6$, respectively) (Figures 1 and 2).

The results of univariate analysis showed no statistically significant difference between the two groups, except for the history of COPD. A binary logistic multivariable regression model with backward elimination was applied to find the independent predictors of POAF development. The findings indicated that the history of COPD was an independent predictor of POAF development (OR = 5.4, CI = 1.17 - 25.1, $P = 0.03$) (Table 2).

4.1. Subgroup Analysis

The subgroup analysis of the patients with POAF demonstrated that the male patients and those with a history

Table 1. The Baseline Demographic and Clinical Characteristics

Variable		All Study Population (n = 246)	POAF		P-value*
			Yes (n = 51)	No (n = 195)	
Age		63.3 ± 9.85	64.1 ± 10.2	63.1 ± 9.7	0.61
Sex)Female)		87 (35.5)	14 (27.5)	73 (37.4)	0.21
HTN		150 (61)	31 (60.8)	119 (61.1)	0.97
DM		100 (40.6)	18 (35.3)	82 (42.1)	0.42
DLP		38 (15.4)	5 (9.8)	33 (16.9)	0.27
Smoker		69 (28)	10 (19.6)	59 (30.3)	0.16
COPD		7 (2.8)	4 (7.8)	3 (1.5)	0.03
CVA		12 (4.9)	2 (3.9)	10 (5.1)	1
MI		20 (8.1)	3 (5.9)	17 (8.7)	0.58
CABG	On-pump	185 (75.2)	35 (68.6)	150 (76.9)	
	Off-pump	61 (24.7)	16 (31.4)	45 (23.1)	0.22
LVEF		46.2±10	46.7 ± 9.8	46.1 ± 10.1	0.78

The data represent the number of patients (%) or mean ± standard deviation.
Abbreviations: HTN, hypertension; DM, diabetes mellitus; DLP, dyslipidemia; COPD, chronic obstructive pulmonary disease; CVA, cerebrovascular accident; MI, myocardial infarction; CABG, coronary artery bypass graft; AF, atrial fibrillation; LVEF, left ventricular ejection fraction.

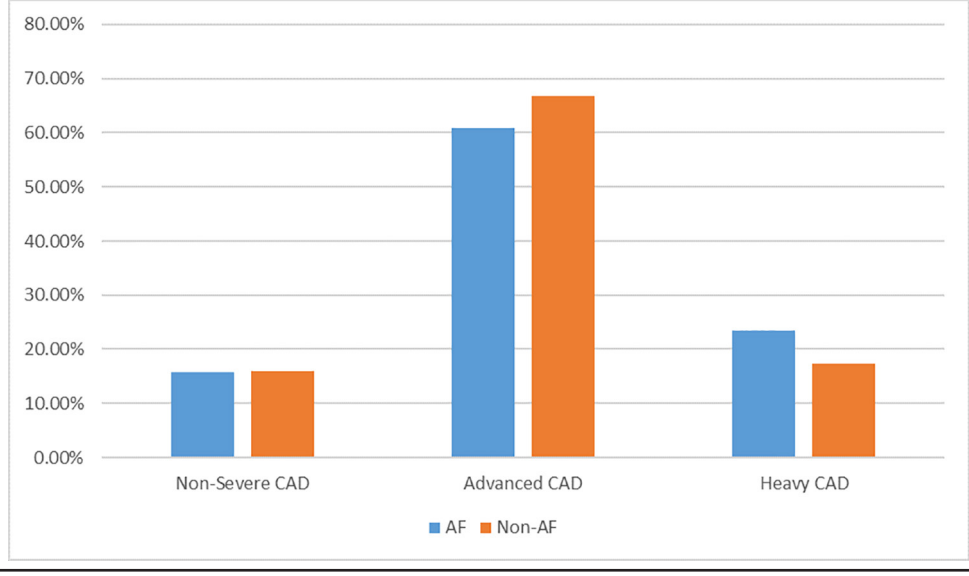

Figure 1. Frequency of Coronary Artery Disease Severity Defined by Gensini Score in Patients with and without Post-Operative Arterial Fibrillation

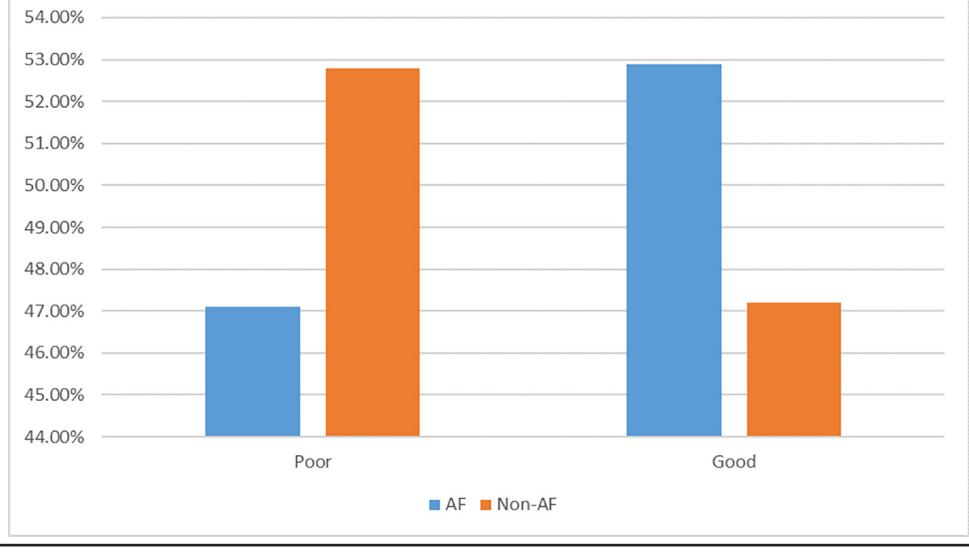

Figure 2. Frequency of Coronary Collateral Circulation defined by Rentrope grade in Patients with and without POAF

of COPD had inadequate coronary collateral status scores (P = 0.03 and P = 0.04, respectively). However, the subgroups were not significantly different in terms of the severity of CAD defined by the Gensini score (Tables 3 and 4).

Table 2. The Predictors of POAF Development

Variable	Odds ratio (CI)	P-value
Age (≥ 60)	1.29 (0.66 - 2.3)	0.47
Sex)male)	1.53 (0.77 - 3.04)	0.21
HTN	0.98 (0.52 - 1.86)	0.97
DM	0.75 (0.39 - 1.42)	0.38
DLP	0.53 (0.19 - 1.44)	0.21
Smoker	0.56 (0.26 - 1.19)	0.13
COPD	5.4 (1.17 - 25.1)	0.03
MI	0.65 (0.18 - 2.31)	0.51
Number of grafts	1.7 (0.81 - 3.7)	0.15
LVEF (≤30%)	1.04 (0.4 - 2.7)	0.93
Rentrope grade	0.82 (0.44 - 1.52)	0.54
Gensini score	0.98 (0.42 - 2.29)	0.97

Abbreviations: HTN, hypertension; DM, diabetes mellitus; DLP, dyslipidemia; COPD, chronic obstructive pulmonary disease; CVA, cerebrovascular accident; MI, myocardial infarction; CABG, coronary artery bypass graft; AF, atrial fibrillation; LVEF, left ventricular ejection fraction.

Table 3. The Baseline Characteristics of the Patients with Post-Pperative Atrial Fibrillation based on the Rentrope Score

Variable	Renetrope Grade		P-value
	Poor 0-1 (n = 24)	Good 2-3 (n = 27)	
Sex (male)	14 (58.3)	23 (85.2)	0.03
HTN	16 (66.7)	15 (55.6)	0.56
DM	8 (33.3)	10 (37)	1
DLP	2 (8.3)	3 (11)	1
Smoker	2 (8.3)	8 (29)	0.08
COPD	4 (16.7)	0	0.04
CVA	2 (8.3)	0	0.21
MI	3 (12.5)	0	0.09

Abbreviations: HTN, hypertension; DM, diabetes mellitus; DLP, dyslipidemia; COPD, chronic obstructive pulmonary disease; CVA, cerebrovascular accident; MI, myocardial infarction.

Table 4. The Baseline Characteristics of the Patients with Post-Operative Atrial Fibrillation based on the Gensini Score

Variable	Gensini Score			P-value
	Score ≤ 40 (n = 8)	Score = 40 - 100 (n = 31)	Score > 100 (n = 12)	
Sex (male)	5 (62.5)	23 (74.1)	9 (75)	0.82
HTN	4 (50)	19 (61.3)	8 (66.7)	0.84
DM	1 (12.5)	15 (48.4)	2 (16.7)	0.054
DLP	0	4 (12.9)	1 (8.3)	0.71
Smoker	1 (12.5)	5 (16.1)	4 (33.3)	0.53
COPD	1 (12.5)	2 (6.5)	1 (8.3)	1
CVA	0	1 (3.2)	1 (8.3)	1
MI	0	2 (6.5)	1 (8.3)	1

Abbreviations: HTN, hypertension; DM, diabetes mellitus; DLP, dyslipidemia; COPD, chronic obstructive pulmonary disease; CVA, cerebrovascular accident; MI, myocardial infarction; Gensini score ≤ 40, non-severe CAD; Gensini score = 40-100, advanced CAD; Gensini score > 100, heavy CAD.

5. Discussion

This study investigated whether ischemic severity and preoperative CCC grade were associated with the POAF development. The Rentrop grade and Gensini score were used to evaluate the extent of CAD and collateral circulation, respectively. The results revealed no significant relationship between the Rentrop grade and Gensini score and the development of POAF in univariate and multivariable analyses. Among the patients with POAF, however, males and those with a history of COPD had poorer CCC.

AF is the most common cardiac arrhythmia in the general population whose incidence is high after cardiac surgery, with an average incidence of approximately 15 - 45% (1, 2). POAF is an independent predictor of numerous adverse outcomes including renal insufficiency, heart failure, stroke, morbidity, and mortality and is associated with a significant financial burden (3-5). Given the large number of patients undergoing CABG surgery each year and the high incidence of POAF in these patients, finding a reliable criterion for identifying high-risk patients and focusing on preventive treatments can significantly reduce the treatment costs.

The mechanism of POAF is complex and involves a large number of clinical and perioperative factors (14). Recently, some studies have evaluated the association between the

severity of preoperative ischemia and the development of POAF. Myocardial ischemia may provoke electrical instability that initiates AF. Previous studies demonstrated that good CCC was a preventative factor in ischemia (15). In this regard, the severity of coronary atherosclerotic disease and CCC have been considered indirect criteria for the severity of preoperative ischemia, and their relationships with the incidence of POAF have been evaluated. For instance, Ducceschi et al. conducted a study on 150 patients and disclosed that the extension of CAD was a predictor of the POAF development (16). Gungor et al. also reported that preoperative poor CCC was an essential predictor of the POAF development (10). However, the present study findings revealed no significant relationship between the incidence of POAF and Gensini score. The results also showed no statistically significant difference between the two groups regarding the CCC based on the Rentrop scoring system. Similarly, Sahin et al. (17) and Polat et al. (18) indicated that Gensini and Rentrop scores were not associated with the development of POAF. In the present study, male sex, history of smoking, and COPD were the independent predictors of POAF, which was consistent with the results of the previous studies (3, 7, 19).

Atrial arteries provide atrial blood supply through high take-off branches from the Left Circumflex (LCX) coronary artery or the Right Coronary Artery (RCA). Intraoperative atrial wall ischemia has been considered one of the pathophysiological mechanisms for POAF development (9). Even in severe CAD, if atrial branches are not involved, the atrial blood supply is not affected and the severity of CAD may not be associated with the POAF development. Thus, the impact of CCC on atrial blood flow has yet to be determined. CCC is prominent in the distal part of coronary arteries, and Rentrop scoring is used to evaluate the retrograde blood flow. However, atrial branches usually separate from the initial part of the coronary arteries. The current study findings also showed no significant association between the severity of coronary atherosclerotic disease and the development of POAF, suggesting inadequate collateral retrograde blood flow to the atrial branches.

Topsakal et al. (20) demonstrated a higher development of CCC in patients with a history of COPD, which might be related to the presence of chronic hypoxia in these patients. In the present research, however, the patients with a history of COPD who developed POAF had a poorer CCC status. This suggested that hypoxia, exacerbated by COPD and poor CCC, might play a role in the development of POAF. Nonetheless, the limited number of patients with COPD who developed POAF restricted the obtained results, showing the necessity to conduct a more rigorous study to validate them.

5.1. Limitations of the Study

There were some obvious limitations in this study, the first of which being the utilization of the traditional coronary angiographic method rather than such specific techniques as Intravascular Ultrasound (IVUS) or Optical Coherence Tomography (OCT) for evaluating the severity of coronary atherosclerotic disease and the CCC status. Another drawback of the research was the absence of ECG Holter monitoring of the patients to detect AF.

5.2. Conclusion

This study showed that the prevalence of POAF was 21% in patients with stable hemodynamic status. There was no significant association between the severity of CAD and POAF development. However, the patients with a history of COPD who developed POAF had a poorer CCC status. Further case-control studies on larger populations can be helpful for confirming the relationship between CCC and the development of POAF.

5.3. Ethical Approval

IR.QUMS.REC.1395.148

5.4. Informed Consent

Written informed consent was obtained from the participants.

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Authors' Contribution

Study concept and design: S.F. and H.J.; analysis and interpretation of data: S.R. and Z.M.; drafting of the manuscript: Z.M. and S.R.; critical revision of the manuscript for important intellectual content: N.N. and E.A.; statistical analysis: S.R. and E.A.

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All the authors declare no conflict of interests regarding this work.

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