








Incidence and predictors of new-onset atrial fibrillation in ST-elevation myocardial infarction: A single-center study

Behrouz Zarei¹  | Ali Bozorgi²  | Mehran Khoshfetrat¹  |
Reza Arefizadeh¹  | Seyed Abolfazl Mohsenizadeh¹  | Seyed Hossein Mousavi¹ |
Arash Jalali³  | Akbar Shafiee³ 

¹Department of Cardiology, School of Medicine, AJA University of Medical Sciences, Tehran, Iran

²Department of Cardiology, Tehran Heart Center, Cardiovascular Diseases Research Institute, Tehran University of Medical Sciences, Tehran, Iran

³Cardiac Primary Prevention Research Center, Cardiovascular Diseases Research Institute, Tehran University of Medical Sciences, Tehran, Iran

Correspondence

Seyed Abolfazl Mohsenizadeh, Tehran Heart Center, North Kargar St., Tehran 1411713138, Iran.
Email: dr.mohseni959@gmail.com

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Abstract

Background and Aims: Atrial fibrillation (AF) is a common arrhythmia that occurs following ST-elevation myocardial infarction (STEMI) and can significantly impact clinical outcomes. We investigated the incidence and predictors of AF following STEMI in patients, as well as its association with major adverse cardiac and cerebrovascular events (MACCE).

Methods: We conducted a retrospective cohort study, including all STEMI patients who presented under code 247 to Tehran Heart Center between 2016 and 2020 and completed a 1-year follow-up. Patients were divided into two groups based on the development of AF during follow-up, and their baseline and clinical characteristics were compared. We used multivariable regression models to identify predictors of MACCE.

Results: Out of 3647 STEMI patients, 84 (2.3%) developed new-onset AF (NOAF). Patients with AF were significantly older and had lower levels of total and low-density lipoprotein cholesterol, triglyceride, and hemoglobin, but higher levels of fasting blood sugar and creatinine. AF patients were also more likely to have a history of hypertension, chronic kidney disease (CKD), congestive heart failure, and cerebrovascular accidents. The multivariable logistic regression model identified the CHA₂DS₂-VASc score and CKD as independent predictors of NOAF following primary percutaneous coronary intervention. Furthermore, the incidence of MACCE was higher in the AF group, and AF independently predicted MACCE with a hazard ratio of 2.766.

Conclusion: The CHA₂DS₂-VASc score and the presence of CKD can serve as useful predictors of NOAF among patients with STEMI. Early detection and appropriate management are crucial to improve outcomes.

KEYWORDS

atrial fibrillation, clinical outcome, primary percutaneous coronary intervention, ST-elevation myocardial infarction

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1 | INTRODUCTION

New-onset atrial fibrillation (NOAF) is a frequent complication, occurring in 3.6%–5.3% of patients diagnosed with ST-segment elevation myocardial infarction (STEMI) following primary percutaneous coronary intervention (PCI).¹ NOAF is associated with worse prognostic outcomes.² It has been associated with increased in-hospital complications and mortality.^{1,3} Furthermore, it has been linked to cardiac dysfunction and is independently associated with major adverse cardiac events.⁴ However, no significant differences in myocardial salvage, infarct size, or microvascular damage were found in patients with STEMI with or without AF.⁴

Several predictors for the development of NOAF have been identified, including age, prior stroke, inferior myocardial infarction (MI), chronic kidney disease (CKD), and complete atrioventricular block.^{3,5} In addition to individual predictors, risk scoring systems such as the CHA₂DS₂-VASc score have been proposed as potential predictors of cardiovascular outcomes in patients with NOAF.^{6,7} Nonetheless, the available data is still limited, necessitating further research to compile a comprehensive list of predictors for NOAF.

Cardiovascular diseases are increasingly recognized as conditions with a high inflammatory burden. Some studies highlighted the role of platelet distribution width, red blood cell distribution width, and other inflammatory markers in coronary artery disease.^{8–10} These studies collectively highlight the significant role of inflammation in the pathogenesis and progression of cardiovascular diseases and other related conditions. Therefore, understanding inflammation's role in cardiovascular diseases provides a strong rationale for investigating the factors associated with NOAF after STEMI.

Given that both AF and STEMI are conditions with a high inflammatory burden, it is reasonable to hypothesize that similar inflammatory markers could play a role in the development of AF post-STEMI.^{11,12} Therefore, studying these factors could potentially lead to improved prediction, prevention, and management strategies for patients at risk of developing AF after STEMI. This could ultimately contribute to better patient outcomes and advancements in cardiovascular medicine.

As NOAF remains a frequent complication of MI and is associated with a higher rate of complications and in-hospital mortality, we aimed to determine the incidence of NOAF in patients who presented to our center with STEMI and underwent primary PCI. We hypothesized that some clinical characteristics of the patients can predict NOAF and it can also reduce the survival of the patients. Therefore, we also investigated the predictors of NOAF and studied the association of NOAF with the clinical outcome of the patients.

2 | METHODS

In this study, we collected data from STEMI patients admitted to our center between 2016 and 2020 and underwent primary PCI. We excluded patients with a history of AF or atrial flutter, thyroid dysfunction, malignancy, incomplete clinical data, those who did not complete follow-

up, or those who passed away before the intervention from this analysis. The research board of the cardiology department and the ethics committee reviewed and approved the study protocol. Following our center's protocols, all patients consented to the anonymous use of their clinical data for research purposes. This study adheres to the Declaration of Helsinki and its subsequent updates.

We retrieved baseline, clinical, angiographic, and PCI data from the patient databank. Successful PCI was defined as a thrombolysis in myocardial infarction flow grade of 3, a myocardial blush grade of 3, or an ST-segment resolution of more than 50% 60 min postprocedure. Patients were divided into two groups based on the occurrence of AF, and we compared the study variables between them.

The primary study outcome was the occurrence of AF during hospitalization or within a 1-year follow-up period. The attending physician confirmed the presence of AF using electrocardiograms obtained during hospitalization or at follow-up visits, and this information was recorded in the datasheet. The secondary outcomes were the occurrence of major adverse cardiac and cerebrovascular events (MACCE), which were defined as target vessel revascularization, target lesion revascularization, coronary revascularization (either coronary artery bypass graft surgery or PCI), MI, cerebrovascular accidents, and death.

We identified predictors for the occurrence of AF in our study population using baseline characteristics that were significantly or partially different between the study groups. Subsequently, we compared the occurrence of MACCE between the study groups and tested the predictive effect of AF.

2.1 | Statistical analysis

Categorical variables were described using frequency and percentage and were compared between the patients with and without AF using the χ^2 test or Fisher's exact test, as appropriate. The normal distribution of continuous variables was tested using skewness. These variables were expressed as either mean \pm standard deviation (SD) or median with interquartile range. We compared these variables using the Student's *t* test or Mann–Whitney *U* test between patients with and without AF. We determined the predictors for the occurrence of AF using a modified logistic regression analysis. The effects were reported as an odds ratio (OR) with a 95% confidence interval (CI). Variables with *p* values less than 0.1 were included in the regression model to identify the independent predictors of AF. We evaluated the unadjusted and adjusted effect of AF on MACE using the COX regression model. The results were reported as a hazard ratio and 95% CI. We considered a *p* value of ≤ 0.05 as statistically significant. All statistical analyses were performed using IBM SPSS Statistics for Windows, version 24.0 (IBM Corp.).

3 | RESULTS

Out of 3647 STEMI patients who underwent PCI at our center and participated in this study, 84 (2.3%) cases had an AF rhythm. The mean (\pm SD) age of the patients in the AF- group was

62.09 ± 11.81 years, while it was 71.61 ± 12.48 years in the AF+ group. Male participants comprised 2787 (78.2%) of the cases in the AF- and 61 (72.6%) in the AF+ group. Obesity was present in 971 (27.6%) AF- patients, with a mean body mass index (BMI) of 27.82 ± 4.45, while 18 (23.1%) cases in the AF+ group were obese, with a mean BMI of 27.62 ± 4.61. Congestive heart failure (CHF) was present in 133 (3.7%) and 9 (10.7%) patients, alongside cerebrovascular disease (CVD) in 112 (3.7%) and 8 (9.5%) cases, respectively. Baseline characteristics and past medical history findings are presented in Table 1.

PCI was the most common type of previous revascularization with 388 (10.9%) cases in the AF- group, and 14 (16.7%) cases in the AF+ patients. Despite a lower ejection fraction (EF) in the AF group, a higher left atrial (LA) size was observed. The CHA₂DS₂-VASc score was also significantly higher in AF patients ($p < 0.001$). Neither the culprit vessel nor the severity of CAD affected the occurrence of AF. The success rate of revascularization was lower in the AF group ($p < 0.001$). Echocardiographic and laboratory findings are presented in Table 1.

A comparison of the baseline characteristics between the patients with and without AF showed that those with AF were significantly older, had lower levels of total and low-density lipoprotein (LDL) cholesterol, lower triglyceride, and hemoglobin levels, but higher levels of fasting blood sugar and creatinine. Moreover, patients with AF were significantly more likely to have a history of hypertension, CKD, CHF, and CVA.

Based on the multivariable logistic regression model, the CHA₂DS₂-VASc score and CKD were independent predictors of NOAF following primary PCI as presented in Table 2.

Overall, 13.4% of the study population developed MACCE. However, the incidence of MACCE was also higher in the AF group (35.7% vs. 14.9%; $p < 0.001$) and AF could independently predict MACCE with a hazard ratio of 2.766 ($p < 0.001$). The most common MACCE complication in total and AF- patients was the need for coronary revascularization, whereas death was the most common MACCE outcome among AF+ patients. Readmission due to decompensated heart failure (DHF) was recorded in 79 (2.2%) patients which was significantly higher in the AF group with an hazard ratio of 5.988 (2% vs. 10.9%, $p < 0.001$). Higher in-hospital and all-cause mortality rates were seen in the AF group with an imposed OR of 4.866 (3.3% vs. 14.3%, $p < 0.001$), and 4.768 (5.8% vs. 75%, $p < 0.001$) for in-hospital and all-cause mortality. Furthermore, hospitalization duration was also significantly higher among AF patients (4.00 vs. 6.00, $p < 0.001$). Risk estimation results are presented in Table 3.

Figure 1 depicts the findings of COX regression for survival analysis. Cumulative adjusted and unadjusted MACCE hazards during the follow-up period reveal significantly worse outcomes within the first months of STEMI in AF+ patients. Similar findings have been discovered for mortality rates, with cumulative mortality hazard revealing significantly worse outcomes within the first months of STEMI in AF+ patients.

Subpopulation analysis was also performed among AF group patients based on the time of AF development. Fifty patients

(59.52%) exhibited AF at admission (Group A), while 34 patients (40.48%) developed AF after admission (Group B), within 3–72 h. Patients with AF rhythm at admission had significantly higher rates of AF rhythm at the time of discharge (51.2% vs. 13.3%, $p = 0.001$). Moreover, they were treated with anticoagulant therapy significantly more than Group B (60% vs. 35%, $p = 0.045$). No significant difference was observed regarding DHF readmissions ($p = 0.475$) or intrahospital mortality ($p = 0.754$) between the two groups.

Patients in the AF group were significantly more likely to receive cardioversion after admission (44.1% vs. 8.5%, $p = 0.001$), with 12 (35.3%) pharmacologic, and three (8.8%) cases receiving electrical cardioversion. However, no significant difference was observed regarding MACCE incidences between the two groups (6 [31.6%], vs. 23 [37.1%] cases in patients with and without cardioversion [$p = 0.661$]).

4 | DISCUSSION

The primary objective of this study was to evaluate the prevalence and predictors of NOAF among patients with STEMI. The key findings of this study are

- (1) The CHA₂DS₂-VASc score and CKD are independent predictors of the development of NOAF in STEMI patients following PCI.
- (2) AF independently predicts higher mortality and MACCE rates.
- (3) Patients undergoing dual antithrombotic therapy regimens experience higher mortality and MACCE rates.

The development of NOAF in post-STEMI patients can lead to the deterioration of cardiac function¹³ through various mechanisms, including inflammatory, hemodynamic, and thrombotic effects.¹⁴ Coronary artery perfusion impairment during STEMI may result in ischemia of the sinus and atrioventricular nodes, leading to arrhythmias.

The literature suggests a prevalence of NOAF ranging from 6% to 21% among STEMI patients.¹⁵ In previous studies, the prevalence of NOAF varied, with reports of 9.3% and 10.1% by Khalfallah and Elsheikh¹³ and Aksoy et al.,⁷ respectively. Arsalan et al.¹⁶ reported a prevalence of 6.1%, and Selçuk et al.¹⁵ reported 8% among STEMI patients following primary PCI. However, Topaz et al.¹⁷ reported AF in 7.4% of cases, with only 2.8% representing NOAF. In our study, consistent with the findings of Topaz et al., NOAF was observed in 2.3% of cases, with 1.3% presenting with AF at admission and 1% developing AF following admission.

Studies evaluating the demographic characteristics of AF patients have demonstrated significant differences. Several studies have shown that NOAF patients are significantly older and, more frequently female.^{16–18} In this study, NOAF patients were significantly older, but there was no significant difference in sex. The variation in prevalence among different populations may be attributed to higher AF rates in older populations and populations with a lower male-to-female ratio.

TABLE 1 comparing the baseline and procedural characteristics between patients with and without atrial fibrillation.

Characteristics	AF negative (n = 3563; 97.7%)	AF+ positive (n = 84; 2.3%)	p Value
Age, year	62.1 (11.8)	71.7 (12.4)	<0.001
Male gender, n (%)	2787 (78.2)	61 (72.6)	0.22
BMI (kg/m ²)	27.82 (4.45)	27.62 (4.61)	0.69
Obesity, n (%)	971 (27.6)	18 (23.1)	0.38
Dyslipidemia, n (%)	1911 (53.6)	41 (48.8)	0.38
Diabetes mellites, n (%)	1444 (40.5)	41 (48.8)	0.13
Hypertension, n (%)	1664 (46.7)	59 (70.2)	<0.001
Current smoker, n (%)	1306 (36.7)	26 (31.0)	0.28
Opium user, n (%)	596 (16.7)	14 (16.7)	0.99
Previous MI, n (%)	231 (6.5)	8 (9.5)	0.27
Chronic kidney disease, n (%)	62 (1.7)	9 (10.7)	<0.001
Congestive heart failure, n (%)	133 (3.7)	9 (10.7)	0.005
History of CVA, n (%)	112 (3.1)	8 (9.5)	0.001
previous PCI, n (%)	388 (10.9)	14 (16.7)	0.09
Previous CABG, n (%)	171 (4.8)	7 (8.3)	0.14
Family history of CAD, n (%)	565 (15.9)	8 (9.5)	0.11
Total cholesterol (mg/dL)	158.2 (39.4)	139.5 (36.7)	<0.001
HDL (mg/dL)	37.6 (9.6)	38.8 (10.8)	0.25
LDL (mg/dL)	100.5 [78.0, 124.0]	81 [66.0, 110.0]	<0.001
Triglyceride (mg/dL)	123.0 [89.00–170.00]	94.0 [73.00–146.00]	0.002
Fasting blood glucose (mg/dL)	113.0 [96.00–153.00]	133.5 [112.00–165.00]	<0.001
Hemoglobin (mg/dL)	15.00 (1.92)	14.27 (1.77)	0.001
Creatinine (mg/dL)	0.90 (0.80–1.08)	1.09 (0.90–1.30)	<0.001
Ejection fraction (%)	42.16 (8.68)	34.52 (8.79)	<0.001
Left atrium size (mm)	38 (35–41)	41 (40–47)	<0.001
CHA ₂ DS ₂ -Vasc score	2.00 (1.00–3.00)	4.00 (3.00–5.00)	<0.001
Primary PCI for SVG, n (%)	101 (2.8)	3 (3.6)	0.51
Left main artery involvement, n (%)	12 (0.3)	0 (0.0)	0.60
Territory of culprit lesion, n (%)			
LAD	1760 (49.4)	36 (43.4)	
LCX	661 (18.6)	17 (20.5)	0.55
RCA	1142 (32.1)	30 (36.1)	
Revascularization success, n (%)	3403(95.5)	68 (81)	<0.001

Note: $p < 0.05$ was considered as statistically significant. Obesity was defined as BMI > 30 kg m².

Abbreviations: AF, atrial fibrillation; BMI, body mass index; CABG, coronary artery bypass graft surgery; CAD, coronary artery disease; CVA, cerebrovascular accident; HDL, high-density lipoprotein; LAD, left anterior descending artery; LCX, left circumflex artery; LDL, low-density lipoprotein; MI, myocardial infarction; PCI, percutaneous coronary intervention; RCA, right circumflex artery; SVG, saphenous vein graft.

Regarding underlying comorbidities, literature reports indicate that AF patients often have several comorbidities.¹⁹ Topaz et al.¹⁷ reported a higher prevalence of heart failure, hypertension, and prior MI among NOAF patients with lower tobacco use. Arsalan et al.¹⁶

found that hypertension was significantly higher among NOAF patients, while hyperlipidemia, systolic arterial pressure, and smoking were less common. In a similar vein, Aksoy et al.⁷ reported significantly higher rates of hypertension and lower rates of smoking

in NOAF patients. However, they observed no significant differences in terms of diabetes mellitus, obesity, and hyperlipidemia. In our study, we found hypertension to be significantly more prevalent among AF patients. Furthermore, we observed significant differences in the incidence of underlying conditions such as renal failure, CHF, and CVDs.

Determining predictors of NOAF has been an important focus of research. Previous studies have proposed older age,²⁰ and comorbidities,⁴ such as hypertension,²¹ diabetes mellitus,¹⁹ culprit lesion site,¹³ CKD,⁵ and neutrophil/lymphocyte ratio.²² Rene et al.¹⁸ reported age, and BMI as independent predictors for the development of AF following MI. Khalfallah and Elsheikh study identified age over 65, hypertension, LA volume index >34 mL/m², E/e ratio > 12, culprit lesion in the right coronary artery (RCA), and heart failure as independent predictors of NOAF. In this study, multivariate regression analysis revealed that CKD and the CHA₂DS₂-VASC score were predictors for the development of NOAF.

CKD has been suggested as a contributing factor to the development of NOAF. This is believed to occur through several mechanisms, including electrolyte disturbances, especially hyperkalemia, seen in CKD patients. Additionally, the inflammatory status observed across all stages of CKD is also thought to play a role.⁵

Another independent predictor of NOAF is the CHA₂DS₂-VASC score. This score integrates key risk factors for cardiac diseases and has a range of applications, including predicting the risk of AF development and stroke in AF patients. However, its effectiveness in

predicting AF among post-MI patients seems to be limited.²³ Arsalan et al.¹⁶ and Aksoy et al.⁷ reported significantly higher CHA₂DS₂-VASC scores in AF+ patients. Our study, consistent with previous investigations, found a significantly higher CHA₂DS₂-VASC score among AF patients.

Regarding laboratory findings, Aksoy et al.⁷ found that triglyceride levels were significantly lower in AF patients, with no significant differences in cholesterol patterns. Conversely, Arsalan et al.¹⁶ reported significantly lower total and LDL cholesterol levels, with no significant difference in triglycerides and glucose. Selçuk et al.¹⁵ reported no significant differences in the lipid profile. In our study, dyslipidemia did not significantly differ between patients with and without AF. However, in the AF group, total cholesterol, LDL, and triglyceride levels were significantly lower, while fasting blood sugar was significantly higher.

In terms of echocardiographic findings, Savic et al.¹⁹ observed a significantly lower EF among AF patients upon admission. This finding is echoed by Ling et al.² and Reinstadler et al.,⁴ who reported a significantly lower left ventricular EF in AF patients. The literature presents inconsistent findings regarding the LA diameter, with some studies reporting a significantly larger LA diameter in AF patients,^{2,7,24} while others found no significant difference.¹⁹ In our study, echocardiographic examinations revealed a significantly lower EF and a larger LA size among AF patients. Notably, a larger LA size was associated with an increased likelihood of AF development.

Ling et al.² reported no significant difference in the culprit coronary lesion, with the left anterior descending (LAD) artery being the most commonly affected vessel in both total and sinus rhythm patients. In contrast, the LAD and RCA were equally affected in NOAF patients. Khalfallah and Elsheikh¹³ reported a significantly higher involvement of the RCA and significantly lower involvement of the LAD among NOAF patients. In this study, no significant difference was observed regarding the location of the culprit lesion, with the LAD being the most affected location in both groups.

Regarding revascularization, Congo et al.³ found no significant difference in successful revascularization between patients with and

TABLE 2 Independent predictors of atrial fibrillation in ST-elevation myocardial infarction patients.

Characteristics	Odds ratio	Confidence interval (95%)	p Value
CHA ₂ DS ₂ -Vasc score	1.616	1.43, 1.827	<0.001
Chronic kidney disease	4.087	1.896, 8.808	<0.001

Note: $p < 0.001$ was considered as statistically significant.

TABLE 3 The incidence of major adverse cardiocerebrovascular events in the study population and the predictive role of atrial fibrillation.

Characteristic	Total subjects (n = 3647)	AF- patients (n = 3563)	AF+ patients (n = 84)	p Value	Hazard ratio
Myocardial infarction	71 (12.7)	67 (12.6)	4 (13.3)	-	-
Coronary revascularization	265 (47.3)	260 (49.1)	5 (16.7)	-	-
Stroke	19 (3.4)	17 (3.2)	2 (6.7)	-	-
Death	205 (36.6)	186 (35.1)	19 (63.3)	-	-
Total MACCE	560 (13.4%)	530 (14.9)	30 (35.7)	<0.001	2.766
DHF readmission	79 (2.2%)	70 (2%)	9 (10.7%)	<0.001	5.988
In-hospital mortality	130 (3.6%)	118 (3.3%)	12 (14.3%)	<0.001	4.866
All-cause mortality	228 (6.3%)	207 (5.8%)	21 (75%)	<0.001	4.768

Abbreviations: AF, atrial fibrillation; DHF, decompensated heart failure; MACCE, major adverse cardiac and cerebrovascular events.

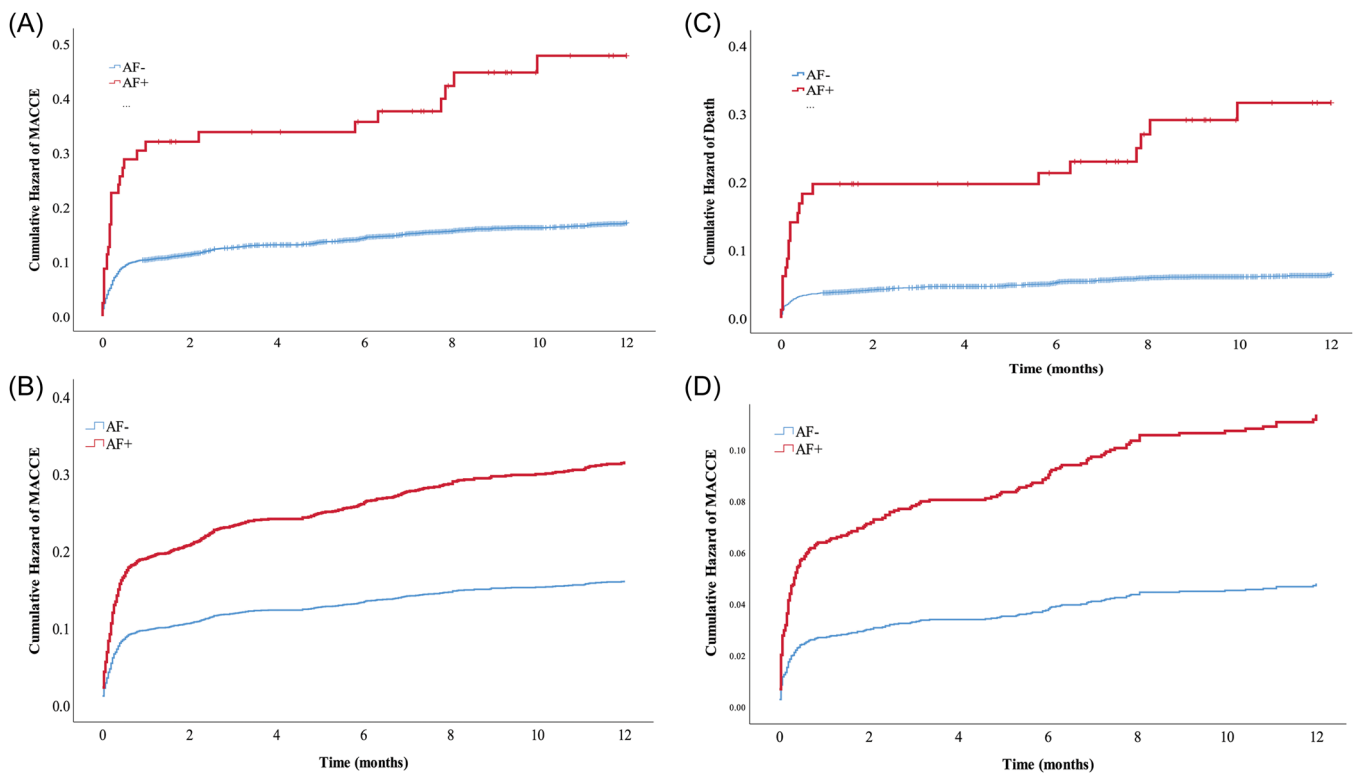


FIGURE 1 Kaplan-Meier curves depicting the cumulative hazard of major adverse cardiac and cerebrovascular events between atrial fibrillation (AF)+ and AF- groups before (A) and after adjustment (B) and for the cumulative hazard of death between AF+ and AF- groups before (C) and after adjustment (D).

without AF; however, the time to revascularization was significantly longer in AF- patients. In contrast to the Congo et al. study, we found significantly more successful revascularization in the AF- group.

The literature presents inconsistent outcomes. The global utilization of streptokinase and tissue plasminogen activator for occluded coronary arteries trial I trial reported higher mortality rates among patients who developed NOAF. Similarly, Madsen et al. found NOAF to be an independent predictor for long-term mortality.¹ However, Khalfallah and Elsheikh¹³ found no significant differences in mortality, recurrent infarction, and cerebral stroke rates between NOAF and sinus rhythm patients. In our study, NOAF patients had significantly worse outcomes, with higher rates of MACCE, readmission due to DHF, in-hospital mortality, and all-cause mortality.

4.1 | Study limitations

This study has several limitations. It is observational and retrospective and was conducted at a single center. Additionally, the lack of certain cardiac laboratory findings and the absence of data on the stage of kidney failure associated with NOAF are limitations. Our data regarding the timing of treatment delivery (i.e., door-to-balloon time or symptom-to-device time) was incomplete, which could potentially influence the occurrence of AF as well as the MACCE.

Further collaborative studies involving multiple centers, larger sample populations, and longer follow-up assessments could provide more definitive results.

5 | CONCLUSION

Overall, the CHA₂DS₂-VASc score and the presence of CKD can serve as predictors of NOAF among patients with STEMI. Early detection and appropriate management can significantly improve patients' mortality and MACCE rates. These findings provide valuable insights into the factors influencing the development of NOAF in STEMI patients and the associated outcomes. Further research is needed to validate these findings and develop effective strategies for managing these patients.

AUTHOR CONTRIBUTIONS

Behrouz Zarei: Conceptualization; data curation; visualization; writing—original draft; methodology; investigation. **Ali Bozorgi:** Conceptualization; supervision; investigation; methodology; validation; project administration. **Mehran Khoshfetrat:** Conceptualization; investigation; supervision; methodology; project administration. **Reza Arefizadeh:** Conceptualization; methodology; investigation; supervision; project administration. **Seyed Abolfazl Mohsenizadeh:** Conceptualization; data curation; formal analysis;

methodology; investigation; supervision; project administration; writing—review and editing; resources; validation. **Seyyed Hossein Mousavi**: Conceptualization; methodology; investigation; supervision. **Arash Jalali**: Data curation; formal analysis; software; visualization. **Akbar Shafiee**: Writing—original draft; writing—review and editing; visualization; software; validation.

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CONFLICT OF INTEREST STATEMENT

The authors declare no conflict of interest.

DATA AVAILABILITY STATEMENT

The data set of this work is available upon reasonable request from the corresponding author.

TRANSPARENCY STATEMENT

The lead author Seyed Abolfazl Mohsenizadeh affirms that this manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned (and, if relevant, registered) have been explained.


ORCID

Behrouz Zarei  <http://orcid.org/0000-0002-3150-5779>

Ali Bozorgi  <http://orcid.org/0000-0001-5586-6598>

Mehran Khoshfetrat  <http://orcid.org/0000-0002-6418-9979>

Reza Arefizadeh  <http://orcid.org/0000-0002-0369-164X>

Seyyed Abolfazl Mohsenizadeh  <http://orcid.org/0000-0001-7157-4675>

Arash Jalali  <http://orcid.org/0000-0003-3225-8498>

Akbar Shafiee  <http://orcid.org/0000-0001-6912-7788>

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