scientific reports

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Predictors of long-term atrial fibrillation following percutaneous coronary intervention in acute coronary syndrome

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The development of atrial fibrillation (AF) has important prognostic implications in patients undergoing percutaneous coronary intervention (PCI), due to the concurrent need for both antiplatelet and anticoagulant therapies. This study aimed to evaluate the long-term incidence and predictors of AF in patients with acute coronary syndrome (ACS) undergoing PCI. We prospectively enrolled 337 consecutive ACS patients in sinus rhythm who underwent PCI and did not develop AF during hospitalization. Patients were followed every six months for up to 72 months. Follow-up data were available for 300 patients (89%); 37 patients were lost to follow-up. At the end of follow-up, 34 patients (11.3%) had developed AF. Kaplan–Meier analysis demonstrated that mitral annular calcification (MAC) was significantly associated with an increased incidence of AF from the early stages (χ^2 = 24.620, log-rank $p < 0.001$). Multivariate Cox regression identified body mass index (BMI) (HR: 1.070; 95% CI: 1.010–1.130; $p = 0.022$), left ventricular ejection fraction (LVEF) (HR: 0.942; 95% CI: 0.918–0.916; $p < 0.001$), mitral annular late diastolic velocity (Am) (HR: 0.785; 95% CI: 0.707–0.872; $p < 0.001$), and mitral annular calcification (MAC) (HR: 4.066; 95% CI: 1.976–8.368; $p < 0.001$) as independent predictors. These findings provide important insights into the long-term risk of AF after PCI in ACS patients and may support early identification and management of high-risk individuals.

Keywords Atrial fibrillation, Percutaneous coronary intervention, Acute coronary syndrome, Mitral annular calcification, Body mass index, Left ventricular ejection fraction, Late diastolic velocity

Atrial fibrillation (AF) is one of the most clinically significant arrhythmic complications following percutaneous coronary intervention (PCI) in patients with acute coronary syndrome (ACS), occurring in approximately 5–10% of cases and substantially increasing both short-term and long-term morbidity and mortality[1]. The development of AF in this clinical setting is particularly concerning, as it not only reflects underlying cardiac structural and functional abnormalities but also serves as an independent predictor of adverse cardiovascular outcomes, including stroke, heart failure progression, and death[2,3].

The pathophysiological mechanisms underlying AF development following PCI in patients with ACS are multifactorial and complex. Acute ischemic insult, hemodynamic stress, inflammatory cascade activation, and procedure-related factors collectively create a substrate conducive to atrial arrhythmogenesis[4]. Furthermore, the coexistence of coronary artery disease and AF presents unique therapeutic challenges, particularly regarding optimal anticoagulation strategies and the balance between thrombotic and bleeding risks[5].

Recent large-scale registry studies have demonstrated that both pre-existing and incident AF significantly impact clinical outcomes in patients with ACS undergoing PCI. Notably, de novo AF, representing approximately 40% of AF cases during ACS hospitalization, carries a particularly high in-hospital mortality risk compared to pre-existing AF[4]. This finding underscores the importance of identifying patients at the highest risk of developing AF following PCI, as early recognition and appropriate management may improve clinical outcomes.

Current evidence suggests that several clinical, echocardiographic, and laboratory parameters may serve as predictors of long-term AF development following PCI in patients with ACS. Advanced age, heart failure with

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reduced ejection fraction, left atrial enlargement, prior myocardial infarction, and hemodynamic compromise have emerged as consistent independent predictors in multiple cohort studies[6,7]. Additionally, inflammatory markers, renal function parameters, and specific echocardiographic indices of diastolic dysfunction have shown promise as potential risk stratification tools[8].

Despite these advances, comprehensive risk prediction models that incorporate multiple clinical and imaging parameters remain limited, and the relative importance of various predictors in the long-term setting has not been fully established. The identification of robust predictors of long-term AF development is crucial for several reasons: it enables targeted surveillance strategies, guides prophylactic interventions, informs anticoagulation decision-making, and facilitates patient counseling regarding prognosis and lifestyle modifications.

Therefore, there is a pressing need for studies that systematically evaluate multiple clinical, echocardiographic, and laboratory parameters to develop comprehensive risk stratification tools for long-term AF prediction following PCI in patients with ACS. Such studies would contribute to personalized medicine approaches, optimize post-PCI surveillance protocols, and potentially improve clinical outcomes through targeted intervention. The present study aimed to address this knowledge gap by identifying independent predictors of long-term AF development in ACS patients undergoing PCI, with the goal of providing evidence-based tools that can be readily implemented in clinical practice.

Methods

This study was conducted as an observational and single-center study. We included consecutive patients with sinus rhythm at baseline who were hospitalized for ACS and underwent PCI between January 2019 and December 2024. The demographic data of all patients were recorded using a pre-prepared questionnaire, and biochemical examinations were performed after at least 8 h of fasting after coronary care unit (CCU) admission. To determine body mass index (BMI), one must divide a person's mass in kilograms (kg) by the square of their height in meters (m). The formula is expressed as BMI = mass [kg] / (height [m])^2. Patients were classified as having hypertension (HT), diabetes mellitus (DM), or hyperlipidemia (HPL) if they had been on medication for these conditions for a minimum of two weeks prior to their admission to the CCU or if they met the criteria outlined in current guidelines[8]. Individuals who had consumed at least one cigarette within the past 30 days were categorized as smokers. These patients were followed-up at 6-month intervals for a total of 72 months. During follow-up, a 72-hour rhythm Holter was applied to patients presenting with palpitations, and those with AF episodes lasting at least 30 s were classified as having AF. Participants were also diagnosed with AF if the ECG at the time of presentation to the outpatient clinic confirmed its presence. Subsequently, the study population was divided into two cohorts—patients with AF and patients without AF—for statistical evaluations.

Exclusion criteria

The study excluded participants who met any of the following criteria: failure to attend at least two subsequent follow-up visits, documented history of AF, the occurrence of AF during the index hospitalization, rheumatic mitral valve disease, any degree of mitral valve stenosis, or other severe valvular regurgitation or stenosis as detected by echocardiography, previous valvular heart surgery, hypertrophic cardiomyopathy, diagnosed endocrinological disorders, prior pulmonary thromboembolism, malignancy, active inflammatory or infectious conditions, severe chronic obstructive pulmonary disease, obstructive sleep apnea syndrome, and refusal to participate. Figure 1 illustrates the flow diagram of patient selection for the study.

Gensini score

The Gensini score was calculated based on the location and severity of coronary artery stenosis[9]. A scoring system was applied based on the degree of narrowing as follows: 1 point for < 25%, 2 points for 26–50%, 4 points for 51–75%, 8 points for 76–90%, 16 points for 91–99%, and 32 points for complete blockage. These scores were then multiplied by predetermined coefficients to reflect the importance of each vessel's position in the coronary system. The coefficients were 5 for left main coronary lesions, 2.5 for proximal left anterior descending (LAD) and left circumflex (LCx) arteries, 1.5 for middle LAD lesions, 1 for first diagonal branch, obtuse marginal branches, and right coronary artery (RCA), and 0.5 for second diagonal and posterolateral LCx branches. The final Gensini score for each patient was calculated by adding the weighted values.

Echocardiographic evaluation

Six months after discharge, all patients underwent a comprehensive transthoracic echocardiography (TTE) examination. Evaluation was performed by a single echocardiographer with ≥ 5 years of experience, utilizing a Philips Epiq 7 device (Philips Medical Systems, Andover, MA, USA) equipped with a 1–5 MHz X5-1 probe. Interobserver variability was not assessed. The echocardiographic findings have also been documented.

The modified Simpson method was employed to calculate the LVEF for each patient. Measurements of LA dimensions, left ventricular end-diastolic diameter (LVEDD), end-systolic diameter (LVESD), and left ventricular (LV) septal and posterior wall thicknesses were obtained in accordance with the current guidelines.

In the apical four-chamber (A4C) view, pulse-wave Doppler was used to evaluate mitral E- and A-wave velocities by positioning the sample volume at the mitral valve cusps. Additionally, tissue Doppler echocardiography was performed in the same view to measure early mitral annular diastolic velocity (e) by placing the cursor on the septal and lateral mitral annuli.

The area-length method, utilizing A4C and A2C views, was employed to determine the LA volume, excluding LA appendages and pulmonary veins. The study assessed various LA volumes, including the maximum volume (observed at the end of ventricular systole, just before the mitral valve opens), the minimum volume (recorded at the conclusion of ventricular diastole, when the mitral valve closes), and the pre-A volume (noted prior to

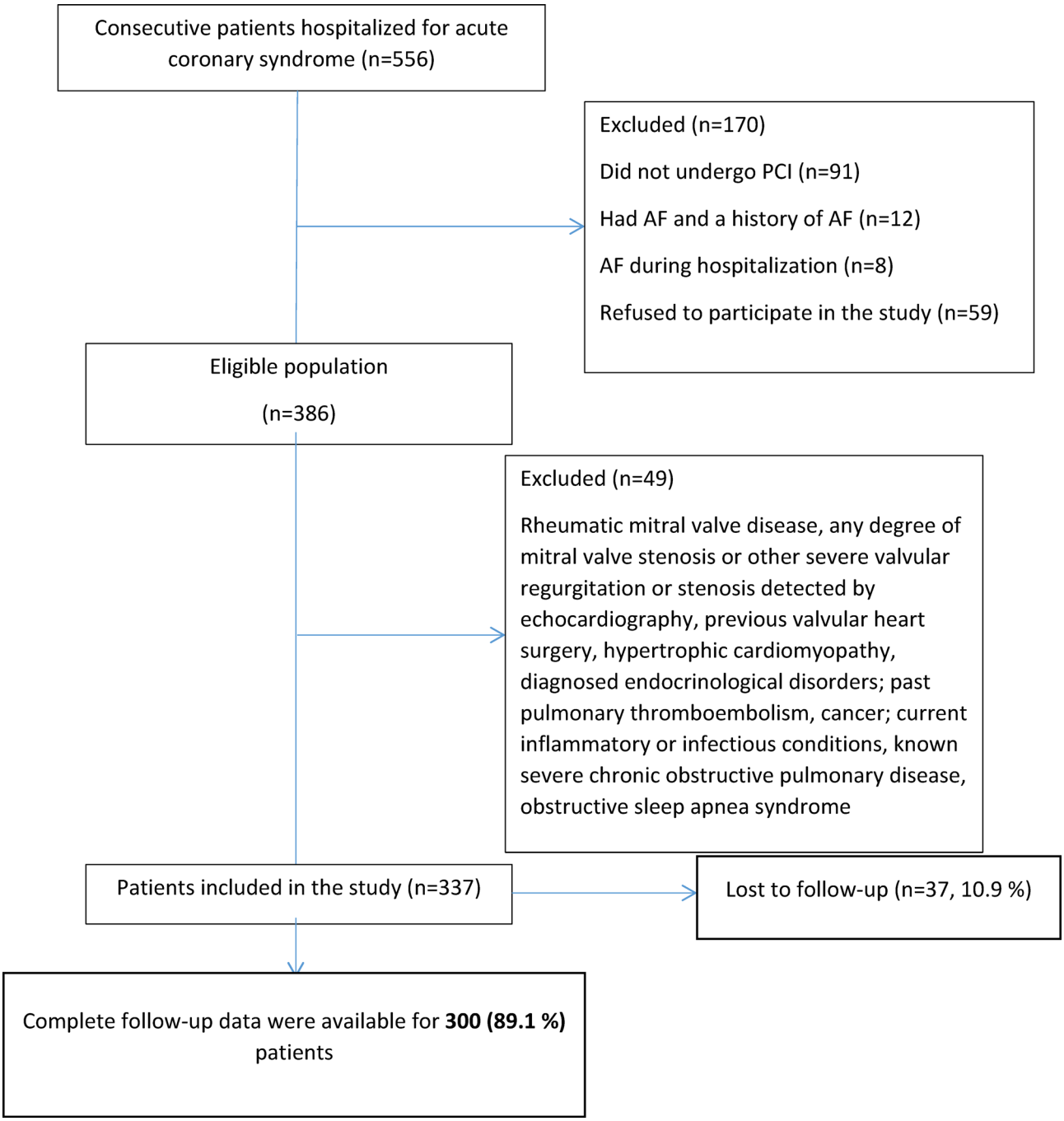


Fig. 1. Flow diagram of patient selection for the study.

atrial contraction, preceding the P wave on the electrocardiogram). Left atrial volume index (LAVI) (ml/m2) was computed by dividing the left atrial volume by body surface area[10].

Various echocardiographic views were used to evaluate the appearance, structure, and function of the aortic valve (AV) and diagnose aortic valve sclerosis (AVS). AVS was characterized by a peak transaortic velocity of 2.5 m/s or less and increased AV leaflet thickness or echogenicity on continuous wave Doppler examination, without rheumatic AV[11].

Mitral annular calcification (MAC) was defined as an echogenic, dense structure at the mitral annulus with acoustic shadowing, identified in the parasternal long-axis view. MAC was considered present if the calcified area measured ≥ 5 mm in thickness and showed characteristic posterior shadowing on 2D echocardiography, in accordance with previous literature[12].

Using the A4C view on two-dimensional M-mode echocardiograms, Tricuspid annular plane systolic excursion (TAPSE) was evaluated. The measurement involved placing the cursor on the lateral tricuspid annulus close to the free right ventricular (RV) wall and aligning it as accurately as possible towards the apex[10].

Ethical approval

The study was conducted in accordance with the principles outlined in the Declaration of Helsinki. Ethics approval was obtained from the Ethics Committee at the Faculty of Medicine, Recep Tayyip Erdoğan University in Rize, Turkey. All participants provided written informed consent before inclusion.

Statistical analysis

Data analysis was conducted using the Statistical Package for the Social Sciences (SPSS) (version 26, created by SPSS Inc. [Chicago, Armonk, NY, USA]). To assess the normality of variable distributions, researchers employed both visual and analytical approaches. Visual methods included examining histograms and probability plots, while analytical techniques involved the application of Kolmogorov-Smirnov and Shapiro-Wilk tests. For normally distributed continuous variables, results are expressed as mean ± standard deviation, while categorical variables are presented as percentages. Non-normally distributed continuous variables are reported using median values of the 25th and 75th percentiles. Comparisons between groups for normally distributed variables were conducted using Student's t-test, whereas the Mann-Whitney U test was applied for non-normal distributions. Chi-squared or Fisher's exact chi-squared tests were used to compare categorical variables, depending on sample size. Initially, variables showing statistically significant differences in the univariate analysis were evaluated using univariate Cox regression to assess their association with AF occurrence. Subsequently, variables marked with an asterisk (*) that remained significant were included in the multivariate Cox regression analysis (backward conditional method). The findings are expressed as 95% confidence intervals (CI) and hazard ratios (HR). To assess the predictive capability of AF, the researchers utilized the area beneath the receiver operating characteristic (ROC) curve. Kaplan-Meier curves were constructed to illustrate the percentiles of MAC presence or absence in predicting AF incidence over a 72-month follow-up period. To reduce potential confounding, propensity score matching was conducted using R for SPSS Statistics (via XQuartz, https://www.xquartz.org), with groups matched for age and BMI. A p-value < 0.05 was considered statistically significant.

Results

A total of 337 patients were initially enrolled in the study. Complete follow-up data were available for 300 patients (89%), while 37 patients were lost to follow-up due to death ($n = 19$), relocation ($n = 13$), or withdrawal of consent ($n = 5$). Among the 19 patients who died during follow-up, 9 deaths were attributed to cardiovascular causes (including acute myocardial infarction and sudden cardiac death), while 10 were due to non-cardiovascular causes, such as infections and other systemic conditions. Consequently, 300 patients were included in the final analysis, of whom 56 (18.6%) were women. In total, 98 patients had ST-segment elevated myocardial infarction (STEMI), 125 had non-ST elevated myocardial infarction (NSTEMI), and 77 had unstable angina pectoris (UAP). A total of 145 patients underwent urgent PCI, while the other patients underwent PCI within 24 h. After a total follow-up of 72 months, AF developed in 34 of the 300 (11.3%) patients.

Patients with AF had significantly higher rates of female gender (38.2% vs. 16.2%, $p = 0.004$), HT (76.5% vs. 57.5%, $p = 0.034$), HPL (58.8% vs. 38.3%, $p = 0.018$), history of PCI (32.4% vs. 17.3%, $p = 0.035$), and insulin use (20.6% vs. 6.1%, $p = 0.009$) compared to patients without AF. They also exhibited higher mean age (67.1 ± 10.1 vs. 62.2 ± 11.7 years, $p = 0.019$), BMI (31.5 ± 6.01 vs. 28.9 ± 4.50 kg/m^2, $p = 0.003$), Gensini score (1.70 ± 0.90 vs. 1.39 ± 0.64, $p = 0.013$), serum creatinine (1.1 ± 0.37 vs. 0.97 ± 0.30 mg/dL, $p = 0.027$), mitral E velocity (88.02 ± 31.1 vs. 69.80 ± 19.1 cm/s, $p < 0.001$), AVS (88.2% vs. 64.9%, $p = 0.003$), MAC (50.0% vs. 16.2%, $p < 0.001$), and LAVI (38.4 ± 16.1 vs. 28.4 ± 11.5 mL/m^2, $p < 0.001$). Conversely, estimated glomerular filtration rate (e-GFR) (66.3 ± 23.3 vs. 80.1 ± 20.5 mL/min/1.73 m^2, $p < 0.001$), mitral Am velocity (5.7 ± 4.1 vs. 8.5 ± 2.4 cm/s, $p < 0.001$), mitral A velocity (62.3 ± 46.7 vs. 85.1 ± 24.1 cm/s, $p < 0.001$), LVEF (47.2% ± 14 vs. 53.2% ± 10, $p = 0.002$), and TAPSE (21.5 ± 4.6 vs. 23.4 ± 4.5 mm, $p = 0.023$) were significantly lower in patients with AF (Table 1).

Kaplan–Meier survival analysis demonstrated a significantly higher incidence of AF in patients with MAC compared to those without MAC (Fig. 2). The mean AF-free survival time was 59.5 months (95% CI: 53.6–65.3) in the MAC-positive group and 68.3 months (95% CI: 66.5–70.1) in the MAC-negative group, with a statistically significant difference between the groups (log-rank test, $\chi^2 = 24.620$, $p < 0.001$).

Based on the CHA_2DS_2-VASc score, patients were stratified into three groups: scores of 0 ($n = 26$), 1 ($n = 46$), and > 1 ($n = 228$). The incidence of AF increased progressively across categories, occurring in none of the patients with a score of 0, 6.5% ($n = 3$) of those with a score of 1, and 13.5% ($n = 31$) of those with a score > 1 ($p = 0.016$) (Fig. 3).

Cox regression analysis with the backward elimination method was performed to identify the independent predictors of new-onset AF. In the univariate analysis, several clinical and echocardiographic parameters were significantly associated with AF, including BMI, HT, HPL, Gensini score, LVEF, mitral E and A velocities, mitral Am velocity, E/Em ratio, aortic sclerosis, MAC, LAVI, and eGFR. In the final multivariate model using backward selection, BMI (HR 1.070, 95% CI 1.010–1.130, $p = 0.022$), reduced LVEF (HR 0.942, 95% CI 0.918–0.916, $p < 0.001$), lower mitral Am velocity (HR 0.785, 95% CI 0.707–0.872, $p < 0.001$), and the presence of MAC (HR 4.066, 95% CI 1.976–8.368, $p < 0.001$) remained independent predictors of AF (Table 2).

Receiver operating characteristic (ROC) curve analysis was performed to evaluate the predictive performance of the significant variables for new-onset AF. The results are presented in Fig. 4. For BMI, the area under the curve (AUC) was 0.630 (95% CI: 0.519–0.742, $p = 0.022$). For LVEF, the AUC was 0.650 (95% CI: 0.557–0.743, $p = 0.002$). For MAC, the AUC was 0.670 (95% CI: 0.564–0.777, $p = 0.002$). For mitral Am velocity, the AUC was 0.295 (95% CI: 0.190–0.399, $p < 0.001$).

After performing 1:1 propensity score matching for age and BMI, 34 patients with AF and 34 without AF were compared (Table 3). Following adjustment, patients who developed AF continued to demonstrate significantly lower LVEF (44.5 ± 14.7% vs. 51.2 ± 10.1%, $p < 0.001$), a higher prevalence of MAC (50.0% vs. 17.6%, $p < 0.001$),

Variable	Patients without AF ($n=266$)	Patients with AF ($n=34$)	P
Female gender n (%)	**43 (16.2)**	**13 (38.2)**	**0.004**
Age (year)	**62.2 ± 11.7**	**67.1 ± 10.1**	**0.019**
BMI (kg/m^2)	**28.9 ± 4.5**	**31.5 ± 6.01**	**0.003**
Office SBP (mmHg)	132.4 ± 22	133.6 ± 24.9	0.776
Office DBP (mmHg)	77.7 ± 13.4	74.5 ± 14.7	0.200
HT n (%)	**152 (57.5)**	**26 (76.5)**	**0.034**
DM n (%)	102 (38.2)	16 (47.1)	0.216
HPL n (%)	**102 (38.3)**	**20 (58.8)**	**0.018**
Current smoking n (%)	116 (43.6)	10 (29.4)	0.080
CVA history n (%)	13 (4.9)	3 (8.8)	0.267
STEMI n (%)	111 (41.7)	15 (44.1)	0.465
CABG history n (%)	14 (5.3)	5 (14.7)	0.050
PCI history n (%)	**46 (17.3)**	**11 (32.4)**	**0.035**
Gensini score	**1.39 ± 0.64**	**1.70 ± 0.90**	**0.013**
ASA n (%)	266 (100)	33 (97.1)	0.113
Beta blocker n (%)	226 (85)	29 (85.3)	0.598
ACE-i/ARB n (%)	241 (90.9)	29 (82.4)	0.107
Statin n (%)	262 (98.5)	34 (100)	0.616
CCB n (%)	37 (13.9)	7 (20.6)	0.212
Aldosterone antagonist n (%)	12 (4.5)	4 (11.8)	0.094
Insulin n (%)	**16 (6.1)**	**7 (20.6)**	**0.009**
OAD n (%)	66 (24.8)	10 (29.4)	0.347
Glucose (mg/dL)	152.4 ± 76.2	155.2 ± 75.2	0.839
Serum creatinine (mg/dL)	**0.97 ± 0.30**	**1.1 ± 0.37**	**0.027**
eGFR (ml/min/1.73 m^2)	**80.1 ± 20.5**	**66.3 ± 23.3**	**< 0.001**
25-hydroxy vitamin D (ng/mL)	14.7 ± 13.7	15.2 ± 7.8	0.837
Glycosylated hemoglobin (%)	6.63 ± 1.6	6.85 ± 1.7	0.475
WBC (10^3/μL)	10.1 ± 3.3	10.01 ± 3.9	0.803
Hemoglobin (g/dL)	14.2 ± 1.8	13.7 ± 2.5	0.137
LV EF (%)	**53.2 ± 10**	**47.2 ± 14**	**0.002**
Interventricular septum (mm)	11.9 ± 1.8	12.01 ± 1.5	0.720
Posterior wall (mm)	11.01 ± 1.5	11.1 ± 1.5	0.568
Mitral E (cm/sec)	**69.8 ± 19.1**	**88.02 ± 31.1**	**< 0.001**
Mitral A (cm/sec)	**85.1 ± 24.1**	**62.3 ± 46.7**	**< 0.001**
DT (ms)	218 ± 45.5	209.1 ± 45.8	0.279
Mitral Am (mm)	**8.5 ± 2.4**	**5.7 ± 4.1**	**< 0.001**
Mitral Em (mm)	6.4 ± 2.06	6.7 ± 2.2	0.481
TAPSE (mm)	**23.4 ± 4.5**	**21.5 ± 4.6**	**0.023**
Aortic sclerosis n (%)	**172 (64.9)**	**30 (88.2)**	**0.003**
MAC n (%)	**43 (16.2)**	**17 (50)**	**< 0.001**
LAVI (ml/m^2)	**28.4 ± 11.5**	**38.4 ± 16.1**	**< 0.001**

Table 1. Comparison of basic demographic, clinical, biochemical and echocardiographic data between groups. A: Late diastolic peak flow velocity, ACE-i: Angiotensin converting enzyme inhibitor, Am: Late diastolic velocity, ARB: Angiotensin receptor blocker, BMI: Body mass index, CABG: Coronary artery bypass graft operation, CCB: Calcium channel blocker, CVA: Cerebrovascular accident, DBP: Diastolic blood pressure, DM: Diabetes mellitus, DT: Deceleration time, E: Early diastolic peak flow velocity, eGFR: Estimated glomerular filtration rate, Em: Early diastolic velocity, HPL: Hyperlipidemia, HT: Hypertension, LAVI: Left atrial volume index, LDL: Low-density lipoprotein, LV EF: Left ventricular ejection fraction, MAC: Mitral annular calcification, OAD: Oral anti-diabetic, PCI: Percutaneous coronary intervention, SBP: Systolic blood pressure, STEMI: ST segment elevation myocardial infarction, TAPSE: Tricuspid annular plane systolic excursion, WBC: White blood count.

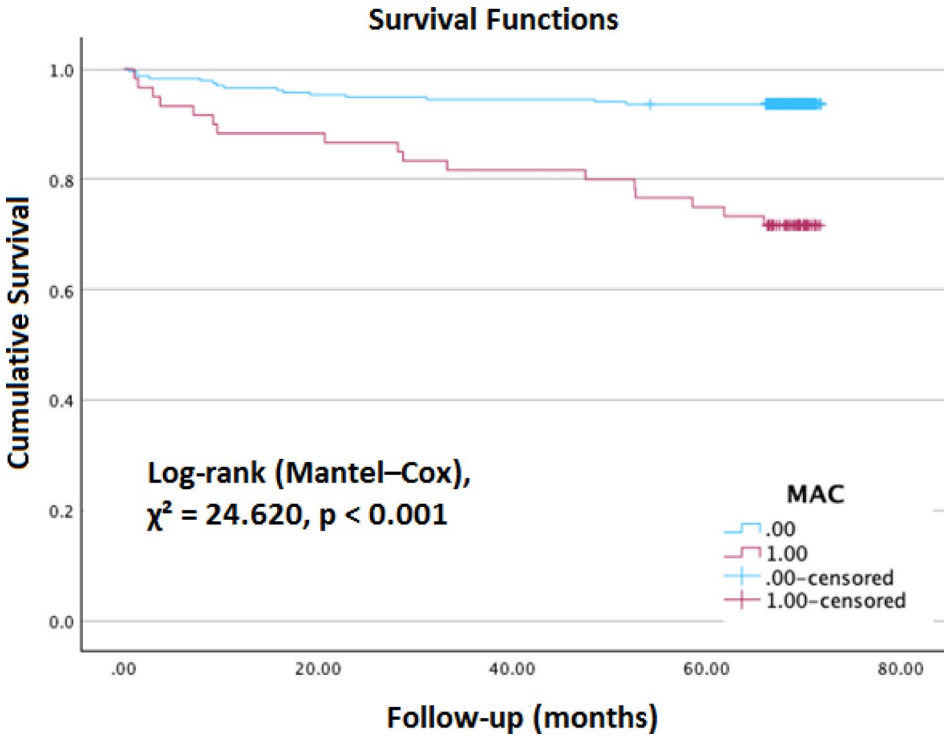


Fig. 2. Kaplan–Meier survival curves for AF-free survival in patients with and without MAC. Kaplan–Meier survival analysis demonstrated a significantly higher incidence of AF in patients with mitral annular calcification (MAC) compared to those without MAC. The mean AF-free survival time was 59.5 months (95% CI: 53.6–65.3) in the MAC-positive group and 68.3 months (95% CI: 66.5–70.1) in the MAC-negative group, with a statistically significant difference between groups (log-rank test, $\chi^2 = 24.620$, $p<0.001$).

and reduced Am (5.7 ± 4.2 vs. 8.6 ± 2.7 cm/s, $p = 0.005$) compared with those without AF. These findings further support the independent associations identified in the multivariate Cox regression analysis.

Discussion

To our knowledge, this is the first study to evaluate the long-term incidence and independent predictors of AF in patients with ACS undergoing PCI. Over a 72-month follow-up, we found that higher BMI, reduced LVEF, reduced mitral Am velocity, and the presence of MAC were independently associated with incident AF. These findings underscore the importance of comprehensive echocardiographic and clinical assessment during early post-PCI evaluation to identify patients at higher risk for developing AF in the long term.

The number of patients with AF continues to rise with increasing life expectancy and the growing prevalence of associated risk factors in the population. Although AF is not an acutely fatal arrhythmia, it significantly impairs quality of life and is associated with increased morbidity, mortality, and healthcare costs. This is largely due to its role in raising the risk of serious conditions such as ischemic stroke, all-cause mortality, heart failure (HF), and HF progression[13]. In patients undergoing PCI, the development of AF may lead to more severe consequences than in the general population, due to the need for concomitant use of anticoagulants and antiplatelet agents, the advanced age and frailty of this patient cohort, and the additional morbidities associated with AF[14]. Therefore, it is especially important to identify the incidence and predictors of AF in this population.

In the present study, the incidence of AF was 11.3% in the study population. In contrast, a recent population-based study reported an AF incidence of 322 per 100,000 person-years[15]. In a study by Saliba et al., approximately one million individuals aged ≥ 50 years with no history of AF were followed for three years (equivalent to three million person-years), during which more than 23,000 incident AF cases were identified. This corresponded to an AF incidence rate of 0.76 per 100 person-years. The study also demonstrated that the incidence of AF increased progressively with higher CHA_2DS_2-VASc scores[16]. Applying this calculation to our cohort, 300 patients were followed for six years (1,800 person-years), and 34 new cases of AF were identified, yielding an AF incidence rate of 1.88 per 100 person-years. Consistent with the findings of Saliba et al., our study also showed that the AF incidence increased in parallel with rising CHA_2DS_2-VASc scores. The higher incidence observed in our cohort—nearly doubles that of the general population—can be attributed to the high-risk profile of our participants, namely patients with ACS undergoing PCI, many of whom also had common risk factors such as HT and DM. Moreover, the longer follow-up duration and more intensive clinical surveillance in our study may have increased the likelihood of detecting AF. Taken together, these factors explain why the incidence observed in our cohort exceeded that of population-based studies, while still demonstrating a risk-dependent gradient consistent with the prior literature. A meta-analysis by Noubiap et al. indicated that approximately 11%

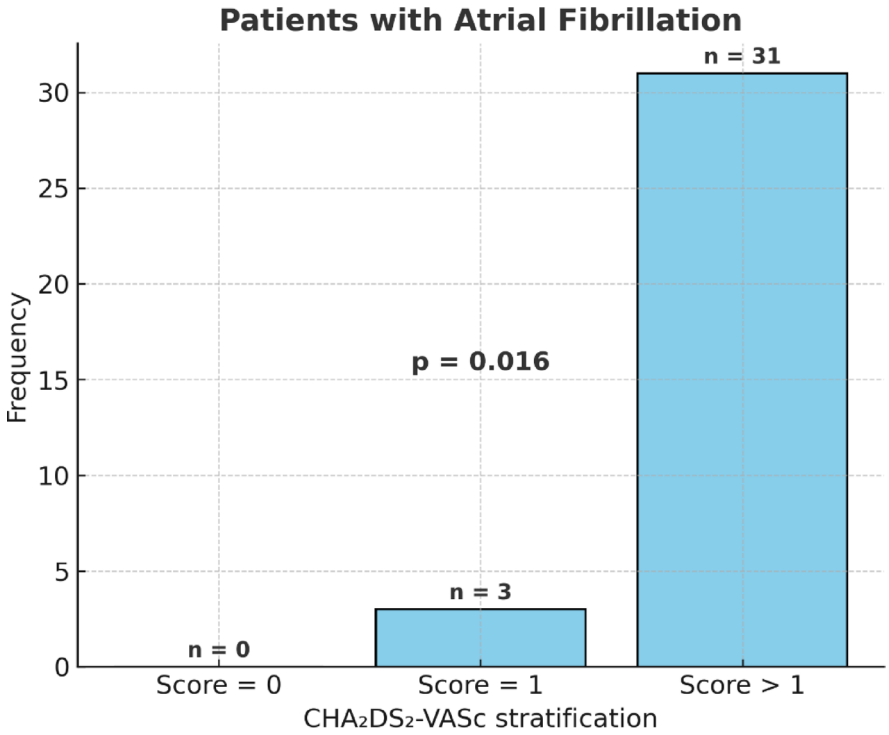


Fig. 3. Incidence of atrial fibrillation stratified by CHA_2DS_2-VASc score. Based on CHA_2DS_2-VASc scoring, patients were stratified into three groups: score of 0 (n=26), score of 1 (n=46), and score >1 (n=228). The incidence of AF increased progressively across categories, occurring in none of the patients with a score of 0, in 6.5% (n=3) of those with a score of 1, and in 13.5% (n=31) of those with a score >1 (p = 0.016).

of patients with acute myocardial infarction experience AF, with a substantial proportion being newly diagnosed cases[1]. Importantly, it should be noted that only AF events occurring after hospital discharge were systematically recorded in our cohort. Consequently, patients who developed AF during the index hospitalization were excluded. Therefore, our findings specifically reflect the incidence and predictors of long-term, post-discharge AF, and do not allow direct comparison with early, in-hospital AF.

The reported prevalence of MAC ranges from 5% to 47% and has been associated with adverse cardiovascular events and an increased risk of stroke[17,18]. In a large prospective, community-based cohort, Fox et al. demonstrated that MAC was a strong predictor of incident AF over a 16-year follow-up period[19]. Similarly, a systematic review by Li et al., which included over 21,000 patients, confirmed the association between MAC and AF, and further revealed that AF patients with MAC were at higher risk for both cardiovascular and cerebrovascular events[18]. Our findings support these associations and further extend them to a unique patient population that underwent PCI. Given that ACS itself confers a heightened risk of AF due to ischemic stress, inflammation, and elevated atrial pressure, which may have amplified the association between MAC and AF in this setting. Importantly, unlike previous studies, we focused on long-term AF development and examined the predictive role of MAC in addition to other echocardiographic parameters.

Recent evidence by Yao et al. further reinforces the significance of MAC, showing that it is independently associated with an increased risk of AF recurrence after successful ablation[20]. Additionally, the Multi-Ethnic Study of Atherosclerosis (MESA) demonstrated an association between computed tomography (CT)-detected MAC and incident AF[21]. A subsequent study in 2017, which followed patients for an average of 8.6 years, found that those with MAC progression had a higher risk of AF compared to those without progression[22]. The mechanisms underlying the association between MAC and AF are likely multifactorial. These may include structural remodeling of the LA due to increased wall stress, conduction abnormalities, and mitral valve dysfunction. Common risk factors in PCI patients—such as HT and DM—may also contribute to the pathogenesis of both MAC and AF. The mitral annulus plays a critical role in maintaining leaflet coaptation[23]. When the annular ring becomes stiffened due to calcification, this can lead to mitral regurgitation, resulting in LA volume and pressure overload, LA enlargement, and increased susceptibility to AF[19]. Furthermore, MAC-related conduction abnormalities across the interatrial septum may further predispose to AF. The identification of MAC through routine echocardiography may therefore serve as a simple, non-invasive marker for AF risk stratification.

Our findings also highlight the contribution of both systolic and diastolic dysfunction to AF development. Reduced LVEF and mitral Am velocity —indicators of impaired ventricular function and increased filling pressures—reflect structural and electrical atrial remodeling, which facilitate arrhythmogenesis. These results align with previous research linking heart failure and diastolic dysfunction to AF onset[24,25]. Extensive population-based and epidemiological research has shown that HF significantly increases the likelihood of developing new-onset AF (NOAF), with the risk being 2 to 6 times higher than that in individuals without HF[26].

	Univariate			Multivariate		
Variable	HR	95% CI	P	HR	95% CI	P
Female sex *	**0.306**	**0.151–0.621**	**0.001**			
Age*	**1.032**	**1.002–1.062**	**0.034**			
BMI*	**1.093**	**1.032–1.158**	**0.002**	**1.070**	**1.010–1.130**	**0.022**
HT*	**2.452**	**1.060–5.669**	**0.036**			
HPL*	**2.210**	**1.091–4.475**	**0.028**			
PCI history	2.006	0.950–4.236	0.068			
Gensini score*	**1.609**	**1.025–2.526**	**0.039**			
LVEF*	**0.962**	**0.941–0.984**	**0.001**	**0.942**	**0.918 – 0.916**	**< 0.001**
Mitral E*	1.028	1.016–1.040	< 0.001			
Mitral A*	0.978	0.968–0.988	< 0.001			
Mitral Am*	**0.722**	**0.701–0.850**	**< 0.001**	**0.785**	**0.707–0.872**	**< 0.001**
E/A ratio	**2.425**	**1.108–5.309**	**0.025**			
E/Em ratio*	**1.116**	**1.048–1.189**	**0.001**			
TAPSE	0.932	0.861–1.009	0.083			
Aortic Sclerosis *	**3.456**	**1.212–9.855**	**0.020**			
MAC*	**4.888**	**2.440–9.791**	**< 0.001**	**4.066**	**1.976–8.368**	**< 0.001**
LAVI*	**1.040**	**1.022–1.059**	**< 0.001**			
eGFR*	**0.975**	**0.960–0.989**	**0.001**			
Serum Creatinine	2.063	1.059–4.019	0.033			

Table 2. Univariate and multivariate Cox regression analysis. A: Late diastolic peak flow velocity, Am: Late diastolic velocity, BMI: Body mass index, DT: Deceleration time, E: Early diastolic peak flow velocity, eGFR: Estimated glomerular filtration rate, Em: Early diastolic velocity, HPL: Hyperlipidemia, HT: Hypertension, LAVI: Left atrial volume index, LV EF: Left ventricular ejection fraction, MAC: Mitral annular calcification, PCI: Percutaneous coronary intervention, TAPSE: Tricuspid annular plane systolic excursion. Variables demonstrating statistically significant differences in univariate analysis were evaluated using univariate Cox regression to assess their relationship with AF occurrence. Subsequently, multivariate Cox regression analysis with the backward elimination method was conducted on parameters labelled by "*" that maintained significance. Only statistically significant parameters are presented in the multivariate analysis table.

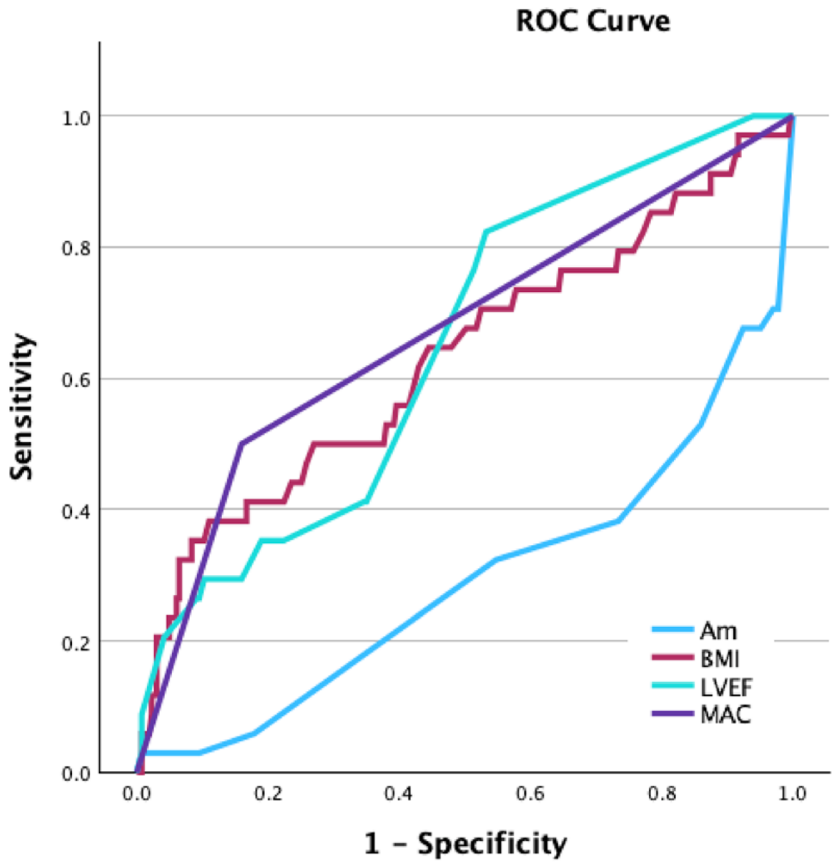
Ulus et al. compared patients with ACS undergoing PCI who developed NOAF during hospitalization with those who did not[6]. Prior myocardial infarction and a higher monocyte-to-high density lipoprotein ratio were found to be strong predictors of NOAF. A review has shown that 30–40% of individuals with LV dysfunction and systolic HF, regardless of etiology, develop AF as their condition progresses[27]. AF is associated with increased morbidity and mortality, and this relationship applies not only to systolic but also to diastolic LV dysfunction[28]. Isolated diastolic dysfunction may predispose to AF, likely due to shared risk factors such as older age and HT[13]. Combined LV systolic and diastolic dysfunction reflects elevated LV filling pressure, leading to increased LA pressure and wall stress. This contributes to structural and electrical atrial remodeling, which facilitates the development of AF[29]. Supporting our findings, Biccirè et al. found that in patients with ACS, NOAF was significantly associated with clinical scores that included HF parameters[7].

Numerous studies have demonstrated a strong association between obesity and AF[30]. A recent meta-analysis by Folli et al., involving over 15 million patients, confirmed this link and additionally showed that obesity is associated with a higher risk of AF recurrence following successful catheter ablation[31]. The considerable impact of obesity on the AF substrate is largely driven by atrial electro-structural remodeling, which may result from multiple mechanisms, including neurohormonal dysregulation, adipocyte-derived cytokine release, systemic inflammation, and abnormalities in calcium ion handling[30].

Obesity also shares common pathophysiological pathways with AF and various comorbid conditions, such as HT, DM, metabolic syndrome, coronary artery disease, and obstructive sleep apnea syndrome[32]. Supporting this, a prospective study by Foy et al. involving over 67,000 participants found that obesity was independently associated with NOAF, even after adjusting for age, sex, HT, and DM[33]. Consistent with the literature, BMI was a strong predictor of AF incidence in our study. The identification of obesity as a modifiable risk factor reinforces the need for weight management in secondary prevention strategies among ACS patients post-PCI.

Limitations of the study

Although our study provides valuable insights, several limitations should be acknowledged. Our study design did not capture AF episodes occurring during the index hospitalization for ACS, as only post-discharge AF events were prospectively recorded. This limits our ability to differentiate between early and late AF onset and explore potential differences in their underlying mechanisms. We did not perform a competing risk analysis (e.g., Fine–Gray regression), which may limit the assessment of predictors in the presence of mortality as a competing factor. The limited number of AF events restricted the statistical power of the multivariable models.



Variable	AUC	95% CI	p-value
BMI	0.630	0.519–0.742	0.022
LVEF	0.650	0.557–0.743	0.002
MAC	0.670	0.564–0.777	0.002
Am velocity	0.295	0.190–0.399	<0.001

Fig. 4. ROC curves of BMI, LVEF, MAC, and Am velocity for predicting new-onset AF. AUC = area under the curve; BMI = body mass index; LVEF = left ventricular ejection fraction; MAC = mitral annular calcification; Am = late diastolic velocity.

A. Baseline characteristics after matching				
Group	**Mean BMI (kg/m²)**	**Median BMI (kg/m²)**	**Mean age (years)**	**Median age (years)**
Patients without AF (*N* = 34)	32.3 ± 7.1	31.6	65.2 ± 11.4	65.5
Patients with AF (*N* = 34)	31.5 ± 6.0	30.8	67.2 ± 10.1	68.0
B. Echocardiographic predictors after matching				
Variable	**Patients without AF (*N* = 34)**	**Patients with AF (*N* = 34)**	**p-value**	
LVEF (%)	51.2 ± 10.1	44.5 ± 14.7	< 0.001	
MAC, n (%)	6 (17.6)	17 (50.0)	< 0.001	
Am (cm/s)	8.6 ± 2.7	5.7 ± 4.2	0.005	

Table 3. Propensity score matching (1:1) analysis of patients with and without AF.

Although penalized regression techniques, such as LASSO, were considered, they could not be reliably applied. Instead, a reduced Cox regression model and propensity score–matched analyses were performed to minimize the risk of overfitting; however, residual model instability could not be entirely excluded.

In our study, Kaplan–Meier survival analysis was performed for MAC because it emerged as the strongest and most consistent echocardiographic predictor of new-onset AF in both the univariate and multivariate models. Although other parameters, such as left ventricular function or diastolic indices, also showed significant associations with AF risk, the limited number of AF events precluded the performance of additional reliable subgroup survival analysis. Therefore, we focused on MAC for survival curve analysis to highlight its prognostic value, while acknowledging that larger cohorts are needed to validate the time-dependent effects of other predictors.

The study was conducted at a single center with a relatively modest sample size, which may limit generalizability.

Echocardiographic measurements were performed by a single observer, and inter-observer variability was not assessed.

An important limitation of our study is that the detection of AF was based on symptom-driven ECG and Holter monitoring, which may have underestimated the true incidence of AF by missing subclinical or asymptomatic AF episodes. Although this limitation could not be quantified within our dataset, it should be acknowledged that continuous or implantable monitoring strategies would likely provide a more accurate assessment of the overall AF burden in the long term. Future prospective studies incorporating systematic rhythm surveillance are warranted to better delineate the incidence of both clinical and subclinical AF in this population.

Finally, residual confounding cannot be entirely excluded despite multivariable adjustment.

Conclusion

In ACS patients with sinus rhythm undergoing PCI; higher BMI, impaired LVEF, elevated E/A ratio, and presence of MAC were strong predictors of AF incidence during long-term follow-up. These findings emphasize the prognostic utility of routine echocardiographic assessment and clinical risk profiling in this high-risk population. Early identification of individuals at increased risk for AF may allow for tailored surveillance, targeted interventions, and optimized secondary prevention to improve cardiovascular outcomes after PCI.

Data availability

The datasets used and/or analyzed during the current study available from the corresponding author on reasonable request.

Received: 5 July 2025; Accepted: 30 September 2025
Published online: 06 November 2025

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Author contributions

Hu.D. and M.C. wrote the main manuscript text and E.E. prepared Figs. 1, 2, 3 and 4. AGO prepared tables. All authors reviewed the manuscript.

Funding

No financial support was received from any institution for this study.

Declarations

Competing interests

The authors declare no competing interests.

Additional information

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