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Early and late new-onset of atrial fibrillation in acute coronary syndromes: Their differences in mortality and cardiac event

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Abstract

Background: In a stressful situation like acute coronary syndrome (ACS), the occurrence of the first episode of atrial fibrillation is more frequent. The impact of the timing occurrence of AF new-onset (nAF) in the setting of ACS is still debatable.

Methods: Multicenter retrospective study based on the Acute Coronary Syndrome Portuguese National Registry, including 29 851 patients admitted for ACS between 1/10/2010 and 4/09/2019. The group with early nAF - nAF in the first 48 h of hospitalization; and late nAF - patients with nAF after the first 48 h of in-hospital admission.

Results: New-onset AF was identified in 1067 patients, nonetheless, just 38.1% had late nAF. The group with late nAF presented more cardiovascular comorbidities and worse left ventricular ejection fraction. Late nAF patients received more antiarrhythmic therapy, and early nAF had a higher beta-block prescription. Early nAF had higher rates of in-hospital complications, on the other hand, late nAF group exhibited more mortality and readmission at one year follow-up. Multiple logistic regression revealed that symptoms onset to the first medical contact time, admission hemoglobin <12 g/dl, right bundle branch block at admission, and diuretic therapy during the hospitalization for ACS were predictors of late nAF in ACS.

Conclusions: The ACS population could be divided by the timing of nAF occurrence into the two groups with different characteristics, therapeutic approaches, and outcomes. Late nAF patients had a worse prognosis at 1 year follow-up, however, the early nAF group had more major adverse cardiac events during the hospitalization for ACS.

KEYWORDS
acute coronary syndromes, CHA_2DS_2-VASc, mortality, new-onset atrial fibrillation

1 | INTRODUCTION

Atrial fibrillation (AF) is the most prevalent arrhythmia in the general population and in some cases can appear for the first time in the context of an acute coronary syndrome (ACS), with a reported incidence between 6% and 21%.[1] The occurrence of this arrhythmia in critical cardiac care is frequent both in patients with a previous diagnosis of AF and in naïve patients.

Several mechanisms can explain an increased occurrence of AF in ACS, such as ischemia and reduction of the atrial blood flow, higher left ventricle end-diastolic and left atrial pressure, diastolic dysfunction and autonomic nervous system disorders. Other mechanisms,

such as neurohormonal activation and inflammation may also be involved.[2] The identification of the arrhythmia is critical since there are therapeutic and clinical implications for patients with AF, especially in new-onset AF (nAF) patients.

The register of nAF was directly associated with worse outcomes and long-term mortality rates, even in cases where the arrhythmia just had a few hours of duration.[3] Nonetheless, nAF in an early phase of ACS maybe had a different impact when compared with late nAF in ACS. Yet, limited evidence was published regarding the nAF in an early phase of ACS, the short duration of nAF, silent AF, and undetected nAF.[4]

The main goal of this study was to analyze the rate, clinical features, therapeutic approach, complications, and in-hospital mortality of early and late nAF in the setting of ACS in a real-world scenario using data from the Portuguese Registry of Acute Coronary Syndromes.

2 | METHODS

2.1 | ProACS registry design

The Portuguese Registry of Acute Coronary Syndromes (ProACS – ClinicalTrials.gov NCT 0162329) is a continuous, nationwide, prospective, observational registry launched in 2002. Data is uploaded by participating centers and managed by the Portuguese Society of Cardiology. All ACS patients older than 18 years are eligible for inclusion. ACS episodes are adjudicated according to current guidelines and based on electrocardiogram, myocardial necrosis biomarkers, and clinical status.[5] Data collected include patient demographics, baseline characteristics, presenting symptoms, biochemical, electro and echocardiography findings, clinical evolution, medical treatment (background, in-hospital, and post-discharge), coronary anatomy, revascularization procedures, and clinical outcomes. Outcome data were collected after hospital discharge and after 1-year of follow-up.

2.2 | Definition of new-onset AF

The nAF is defined as the first episode of AF that has not been diagnosed before, regardless of the arrhythmia's duration or the presence and severity of AF-related symptoms. All episodes of nAF admitted in this study were episodes of paroxysmal and persistent nAF. An AF episode may not correspond to its first occurrence, as sometimes episodes of silent AF have occurred before. Nonetheless, in this study, the first recorded AF episode was characterized as nAF. Then, we defined two groups of nAF: patients that presented nAF during hospitalization in the first 48 h of ACS (counting the time of admission as the first minute) – early nAF group, and patients that presented nAF during hospitalization after the first 48 h – late nAF group. The cut-off of 48 h was utilized since this it is the time that in clinical practice arrhythmias secondary to reperfusion are accepted.

2.3 | Study population

A total of 29 851 validated episodes in the ProACS registry between October 1, 2010, and September 4, 2019 were accessed. Each patient might have more than one episode of ACS. Patients with missing data regarding the ACS type and the rhythm at admission and during hospitalization, and patients with previously documented AF were excluded (total of 4124 patients). One thousand sixty-seven were defined as nAF (4.1%) in the ACS context, while 24 660 patients (82.6%) did not have any register of AF occurrence (Table S1), the rest of patients were excluded for previous AF register or lack of AF data information. Of the 1067 patients with nAF, 123 patients were excluded because did not present information regarding the admission rhythm and/or because the time when the nAF occur was not exactly clear and did not allow us to categorize them into one of the groups (Figure 1). Therefore, early nAF in the setting of ACS was registered in 584 patients (61.9%) and late nAF in ACS patients was identified in 360 patients (38.1%). All the patients that presented nAF included in this study had their first episode of paroxysmal or persistent AF.

Multivessel disease was defined as the presence of two or more coronary artery stenosis (>70%). Valvular heart disease was defined as severe valvular stenosis or regurgitation or previous valvular intervention. Familiar cardiovascular history refers to patients with at least one familiar that presented a previous cardiac event (including sudden cardiac arrest) before the age of 65. Chronic kidney disease was applied to all the patients with a creatinine level superior to 2 mg/dl or glomerular filtration rate inferior to 30 ml/min/1.73 m^2. Hybrid revascularization was defined as the revascularization technique that combines both percutaneous coronary intervention and coronary artery bypass.

2.4 | Statistical analysis

All statistical analyses were performed by a professional statistician within the National Centre for Data Collection in Cardiology (CNCDC), using SPSS software (SPSS Inc.) for Windows XP (version 20.0). Continuous variables are described as mean and standard deviation (SD) if normally distributed, or median and interquartile range (IQR) in case of skewed distribution. Categorical variables are described as absolute and relative frequencies. Hypothesis testing for differences between early and late nAF in ACS patients was performed using odds ratio (OR) and 95% confidence intervals (95% CI), as well as independent-samples t-test for continuous variables and chi-square test for categorical variables. In addition, a univariate logistic regression analysis was performed for each independent variable in order to assess the association between the nAF groups (Table S2). The independent variables with significant p values identified in the univariate analysis were then used to create a model in multivariate logistic regression, defining the predictors of late nAF. Survival analysis for 1 year outcomes was performed using Kaplan–Meier curves and

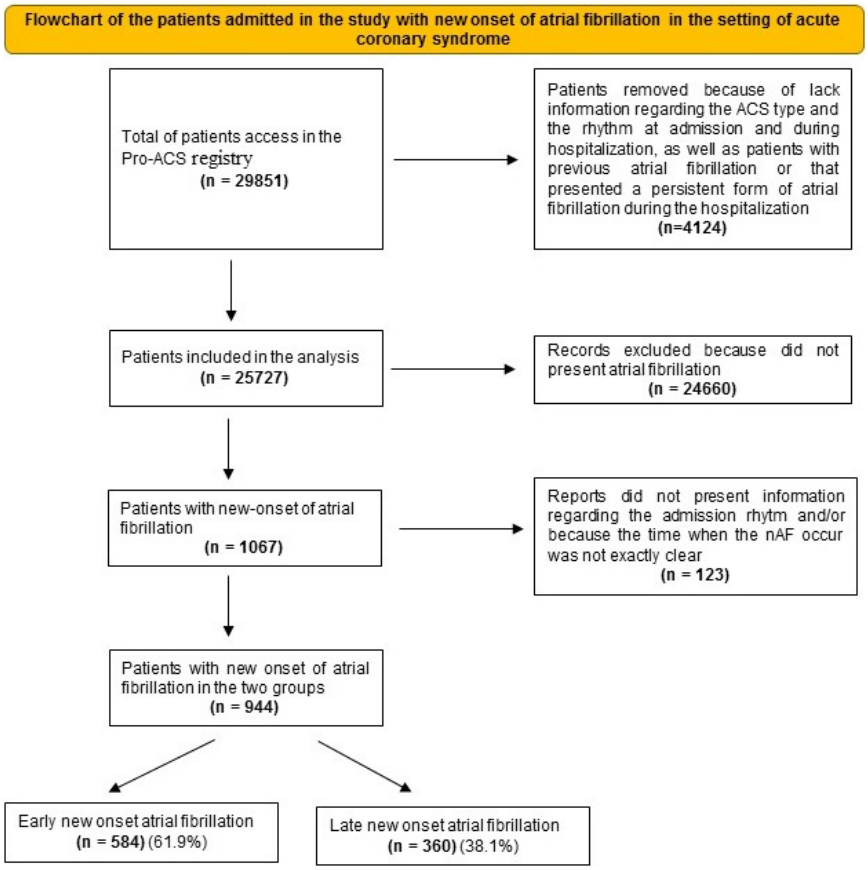


FIGURE 1 Flowchart of the patients admitted in the study with new-onset of atrial fibrillation in the setting of acute coronary syndrome

log-rank test. *p* values are two-sided, and a threshold of .05 indicates statistical significance was used in all tests.

2.5 | Ethical approve

Participation in the registry must be approved by the review board at each institution, the local ethics committee, and by the Portuguese Data Protection Authority (no. 3140/2010).[6] All ethical requirements in the Helsinki declaration of 1975 were met, nor involved any human and/or animal experimentation. Written informed consent for the introduction of patients' data into the registry is available since 2010 and has been applied after approval by the ethics committee of each hospital center.

3 | RESULTS

3.1 | Population clinical features

Patients without nAF were young and with less prevalence of cardiovascular conditions and other comorbidities (Table S1). Patients with nAF in the setting of ACS had increased in-hospital all-cause of death, as well as higher rates of major adverse cardiac events (reinfarction, congestive heart failure, cardiogenic shock, mechanical complications, AV block, sustained ventricular tachycardia, aborted cardiac arrest, stroke, and major bleeding), represented in the Table S1.

Patients with late nAF were older ($p < .001$) and presented a higher prevalence of cardiovascular conditions and other comorbidities, including, arterial hypertension, dyslipidemia, previous heart failure symptoms, valvular heart disease, peripheral arterial disease, chronic obstructive pulmonary disease, dementia, and previous stroke (Table 1), nonetheless only diabetes ($p = .002$), angina ($p = .001$), coronary artery disease ($p = .006$) and chronic kidney disease ($p = .015$) were significantly higher in late nAF. Previous medications are also represented in Table 1.

Patients with early nAF were more frequently admitted directly to the catheterization laboratory, while late nAF patients were admitted to the emergency room. Other patterns of hospital admission were similar and represented in Table S3. Patients with late nAF had a higher time from the onset of the symptoms to the first medical contact time ($p < .001$), as well, the time from the first medical contact to the admission time ($p < .001$). Curiously, late nAF presented a higher percentage of right bundle branch block on the first electrocardiogram ($p < .001$). Hemoglobin at admission was higher in early nAF, but both groups had a normal range of hemoglobin levels (Table S3).

Table 2 illustrates the clinical presentation features. Late nAF patients presented more frequently dyspnea as the main symptom ($p = .045$). Killip-Kimball (KK) class at admission was higher in late nAF patients nevertheless without significant differences between the groups. Furthermore, early nAF patients had a higher incidence of ST-elevation myocardial infarction.

Table 3 depicts clinical management features. Late nAF patients had a poor left ventricular ejection fraction (LVEF) ($p = .010$). On the

TABLE 1 Population characteristics regarding the rhythm, in percentage

	AF < 48 h	AF > 48 h	*p*-value
Age (years old)	73 ± 13	77 ± 10	<.001
Sex (male)	375 (64.2%)	232 (64.4%)	.942
Smoking	124 (21.3%)	43 (12.1%)	<.001
Arterial hypertension	427 (74.3%)	271 (75.9%)	.572
Diabetes *mellitus*	173 (30.2%)	142 (40.1%)	.002
Dyslipidaemia	304 (55.1%)	204 (59.0%)	.253
Familiar cardiovascular history	12 (2.5%)	6 (2.1%)	.684
Angina	125 (21.4%)	110 (30.8%)	.001
Previous ACS	90 (15.4%)	80 (22.5%)	.006
Valvular heart disease	26 (4.5%)	24 (6.8%)	.139
Previous Heart failure	60 (10.3%)	48 (13.4%)	.145
Previous stroke	65 (11.2%)	40 (11.2%)	.986
Peripheral arterial disease	40 (7.0%)	35 (9.9%)	.111
Chronic Kidney Disease	44 (7.6%)	44 (12.4%)	.015
Neoplasia	29 (5.0%)	24 (6.7%)	.273
Chronic Obstructive Pulmonary Disease	46 (8.0%)	38 (10.6%)	.174
Dementia	22 (3.9%)	16 (4.5%)	.649
Previous bleeding	11 (1.9%)	4 (1.1%)	.350
Acid acetylsalicylic	176 (30.8%)	133 (37.2%)	.044
Other antiplatelet	70 (12.6%)	63 (18.1%)	.028
Beta-block	154 (26.9%)	102 (28.7%)	.556
Angiotensin converting enzyme inhibitors/ angiotensin II receptors blockers	295 (51.6%)	189 (52.9%)	.685
Statin	214 (37.3%)	164 (45.8%)	.010
Calcium channel blockers	110 (19.3%)	74 (20.8%)	.572
Mineralocorticoid receptor antagonists	21 (3.6%)	9 (2.5%)	.340
Diuretic	172 (30.0%)	134 (37.5%)	.018
Anti-arrhythmic therapy	4 (0.7%)	4 (1.1%)	.490
Insulin	34 (5.9%)	41 (11.5%)	.002
Oral antidiabetic drugs	113 (19.6%)	101 (28.2%)	.002

Note: Atrial fibrillation (AF) – New-onset of AF in the setting of acute coronary syndrome (ACS), in number total of patients (and percentage).

TABLE 2 Clinical presentation characteristics regarding the rhythm, in percentage

	AF < 48 h	AF > 48 h	*p*-value
Chest pain	484 (83.0%)	288 (80.0%)	.242
Dyspnoea	44 (7.5%)	41 (11.4%)	.045
Syncope	21 (3.6%)	8 (2.2%)	.233
Cardiac arrest	4 (0.7%)	5 (1.4%)	.314
Killip-kimball class > I	188 (32.8%)	131 (37.0%)	.185
ST-elevation myocardial infarction	332 (56.8%)	169 (46.9%)	.003

Note: Atrial fibrillation (AF) – New-onset of AF in the setting of acute coronary syndrome, in number total of patients (and percentage).

other hand, in the early nAF group angiography was more frequently performed. Curiously, the right coronary artery was the most frequent culprit lesion and as a consequence the most revascularized vessel. Additionally, percutaneous coronary intervention (PCI) was more frequently performed for all lesions in early nAF ($p = .035$). Concerning the planned revascularization strategy, coronary artery bypass grafting (CABG) was planned irrespective of the time of nAF occurrence. No differences were found regarding success rates.

TABLE 3 Clinical management, angiography, and revascularization characteristics regarding the rhythm

	AF < 48 h	AF > 48 h	*p*-value
Left ventricular ejection function	47 ± 13	45 ± 13	.010
Angiography	499 (85.4%)	275 (76.4%)	<.001
Radial access	334 (69.7%)	178 (67.9%)	.614
Multivessel disease	253 (53.9%)	157 (61.3%)	.055
Culprit lesion: right artery	141 (32.9%)	46 (19.7%)	<.001
Percutaneous coronary intervention	388 (81.7%)	196 (75.1%)	.035
Coronary artery bypass grafting	31 (6.5%)	22 (8.4%)	.339

Note: Atrial fibrillation (AF) – New-onset of AF in the setting of acute coronary syndrome, in number total of patients (and percentage).

TABLE 4 In-hospital complications according to the rhythm, in percentage

	AF < 48 h	AF > 48 h	*p*-value
Mortality	56 (9.6%)	51 (14.2%)	.031
Reinfarction	6 (1.0%)	8 (2.2%)	.142
Heart failure	185 (32.1%)	61 (17.2%)	<.001
Cardiogenic shock	61 (10.5%)	28 (7.8%)	.173
Mechanical complication	10 (1.7%)	7 (1.9%)	.797
Complete atrioventricular block	33 (5.7%)	7 (1.9%)	.006
Sustained ventricular tachycardia	47 (8.1%)	12 (3.3%)	.004
Cardiac arrest	49 (8.4%)	11 (3.1%)	.001
Stroke	11 (1.9%)	5 (1.4%)	.565
Major haemorrhagic events	17 (2.9%)	9 (2.5%)	.703

Note: Atrial fibrillation (AF) – New-onset of AF in the setting of acute coronary syndrome, in number total of patients (and percentage).

3.2 | Therapy

No differences were found regarding therapy with P2Y12 blockers or GP IIb/IIIa receptor inhibitors, as well as dual-antiplatelet therapy (Table S4). Early nAF patients were more frequently given heparin/heparin-related-agent, nonetheless, regarding enoxaparin, and vitamin K antagonists administration, no differences were registered. Early nAF patients were likely to receive fewer in-hospital mineralocorticoid receptor antagonists, diuretic therapy, insulin, inotropic therapy, and oral antidiabetic therapy (Table S4).

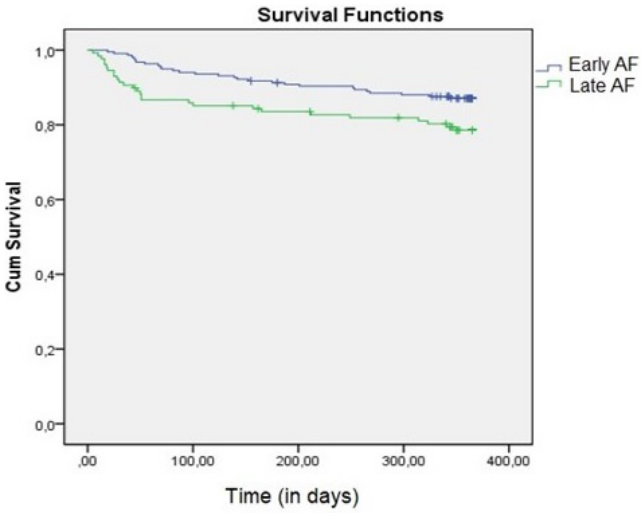
At discharge, no differences between the nAF groups were found concerning anticoagulation or antiplatelet therapy. Early nAF had a higher prescription of beta-block therapy. On contrary, amiodarone was prescribed more frequently in the late AF group (Table S5).

3.3 | Prognosis

Patients with late nAF in the setting of ACS had increased in-hospital all-cause of death (9.6 vs. 14.2%, $p = .031$). However, no significant differences were registered concerning reinfarction, cardiogenic shock, mechanical complications, stroke, and major bleeding. It was in the early nAF group that a higher percentage of major adverse cardiac events were listed, like congestive heart failure (32.1 vs. 17.2%, $p < .001$), atrioventricular block (5.7 vs. 1.9%, $p = .006$), sustained ventricular tachycardia (8.1 vs. 3.3%, $p = .004$) and aborted cardiac arrest (8.4 vs. 3.1%, $p = .001$) (Table 4). Late nAF patients exhibited longer in-hospital stay (7 ± 5 vs. 12 ± 8, $p < .001$).

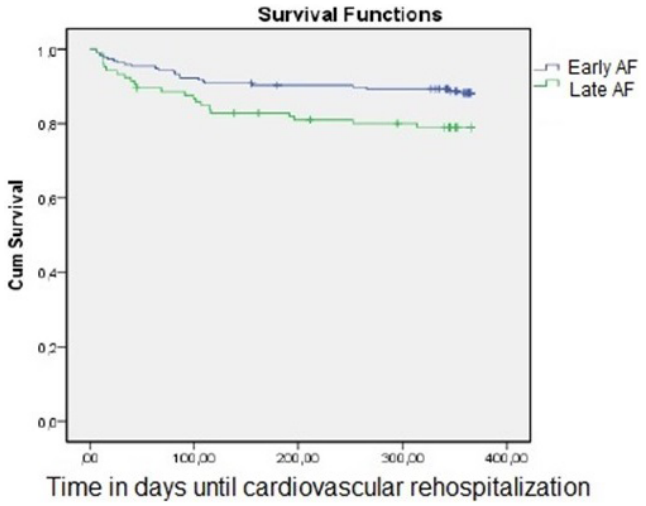
Late nAF patients had significantly higher rates of all-cause of mortality at 1-year of follow-up (log-rank test $p = .028$, Figure 2), as well as cardiovascular rehospitalization at 1-year of follow-up (log-rank test $p = .029$, Figure 3).

Between the several variables studied, the ones found predictive of late nAF in univariate analysis were used to create a model in multivariate analysis (Table S2). Multiple logistic regression revealed that symptoms onset to first medical contact time over 120 min (odds ratio (OR) 1.60, $p = .005$, confidence interval (CI) 1.15–2.22), hemoglobin <12 g/dl (OR 1.53, $p = .018$, CI 1.08–2.18), right bundle



New-onset atrial fibrillation (nAF)	Total of patients included	Mortality during the follow up		
		3 months	6 months	1 year
Early nAF	218	8	13	28
Late nAF	128	14	19	27

FIGURE 2 Representation of the Kaplan–Meier test of survival rates at 1 year of follow-up according to early or late new-onset of atrial fibrillation. Also, in a table, the number of patients included in the analyze in absolute frequency, and also in absolute frequency the number of the patients that died at the 3 and 6 months and at 1 year follow-up



New-onset atrial fibrillation (nAF)	Total of patients included	Cardiovascular rehospitalization during the follow up		
		3 months	6 months	1 year
Early nAF	197	14	20	23
Late nAF	106	11	17	22

FIGURE 3 Representation with the Kaplan–Meier test of readmission for cardiovascular causes at 1 year of follow-up according to early or late new-onset of atrial fibrillation. Also, in a table, the number of patients included in the analyze in absolute frequency, and also in absolute frequency the number of the patients that presented a cardiovascular rehospitalization at 3 and 6 months and at 1 year follow-up

branch block at admission (OR 1.72, $p = .043$, CI 1.02–2.92), and diuretic therapy during the hospitalization for ACS (OR 2.18, $p < .001$, CI 1.57–3.01) were predictors of late nAF in ACS comparing with patients without nAF.

Logistic regression analysis revealed that the CHA_2DS_2-VASc score was a median predictor of late nAF in ACS (Area Under Curve: 0.560, $p = .002$, CI 0.552–0.598), with a 72.8% sensibility and 38.1% specificity.

4 | DISCUSSION

Given that it is established that AF in the setting of ACS worsens prognosis compared to sinus rhythm, this study aimed to compare early and late aAF regarding impact on prognosis. Our main finding was that the early nAF group had more in-hospital complications and the late nAF had an overall worse prognosis.

AF and ACS had analogous risk factors, so the identification of nAF in the setting of ACS is a frequent finding. Our study reveals that nAF in the setting of ACS reflects several unique clinical characteristics. Our findings are in line with other authors[7] considering that ACS can be a trigger to arrhythmias. Our population had a 3.6% incidence of nAF during the hospitalization for ACS, with 2.0% the patients presenting early nAF, 1.2% with late nAF, and in the rest of the population was not possible to determine the timing of nAF occurrence. These findings are in line with several series in ACS patients.[1,8]

Patients with nAF had a hemodynamic impact on ACS, since it may lead to fast ventricular rates, hypoxia, hypotension, or hypertension, adrenergic discharge, the loss of atrial contraction, and atrioventricular synchrony (promoting an imbalance between myocardial oxygen supply and demand). All of these hemodynamic alterations can be associated with exacerbation of acute ischemia and heart failure.[3] Consequently, nAF in the setting of ACS has been recurrently associated with a higher number of AF episodes during the follow-up, increased risk of other comorbidities, and long and short mortality.[9,10]

Patients with late nAF had a higher prevalence of cardiovascular risk factors, coronary disease, chronic kidney disease and diabetes, as well, higher age. Our results are in line with reports that early nAF manifests more frequently in young patients, with ST-elevation myocardial infarction and higher left ventricular ejection fraction.[11,12] Our results showed also that patients with early nAF presented less time until the first medical contact, symptoms onset to first medical contact, and were referred more frequently direct to the catheterization laboratory, which suggested the direct hemodynamic impact the arrhythmia, being in agreement with a previous study.[3] These results confirm that ACS can be a trigger for nAF, namely in the early phase with less impact in the patient prognosis, namely in AF recurrence and stroke risk during the follow-up.[11] Interestingly, a culprit lesion on STEMI patients as a right coronary artery was higher in early nAF, a finding already reported,[12] that can justify the arrhythmia occurrence in a certain percentage of patients since the irrigation of the sinus node came commonly from this artery.

No differences were registered in our population regarding antiplatelet and anticoagulation therapy. Nonetheless, literature data concerning anticoagulation in nAF in the setting of ACS is not clear, since guidelines did not consider this as a special group of patients that deserve a different approach. A recent review article concluded that nAF in ACS patients is associated with a significant occurrence of ischemic stroke events during the follow-up,[13] yet some authors suggest that early nAF in ACS patients did not require long-term anticoagulation.[14] Even so, our data does not elucidate regarding the benefits of long-term anticoagulation therapy in these patients (independent of the time of the nAF occurrence).

Beta-blockers were more used in early nAF patients, probably due to a clinical interpretation that the arrhythmia occurred only in the ACS context. Interestingly and contrary to early nAF, the late nAF group had a high prescription of anti-arrhythmic therapy, we observed a diminished use of beta-blockers in this group, suggesting that late nAF was interpreted by the physician as a primary arrhythmia and not just an acute cardiac response to the ACS stress. Late nAF patients demonstrated more frequent left ventricular dysfunction and would consequently benefit from mineralocorticoid receptor antagonists, maybe this was the justification for the different prescription of this

drug in the two groups. Considering that late nAF patients had more frequent diagnosis of diabetes mellitus, was not surprised that this group in our population had more antidiabetic therapy.

The arrhythmia occurrence in the setting of ACS is certainly associated with higher rates of major adverse cardiac events (MACE)[15] and short and long-term mortality.[3] However, to the best authors' knowledge, no literature was published comparing the rates of MACE during the hospitalization for ACS between the two nAF groups. The loss of atrioventricular synchrony in an early phase with the ischemic stress can justify the higher rates of heart failure in the early nAF. The stress response to the acute ischemic can justify the early nAF manifestation and the higher incidence of MACE. Complete atrioventricular block in early nAF can be justified directly to an ischemic lesion in the vessel that irrigated the sinus node and the atrioventricular node. Curiously, we observed a higher mortality rate in the late nAF group. We hypothesized that the higher rates of comorbidities and frailty status may interfere with the response to the arrhythmia and the ACS, and be a cause of higher mortality in this group.

As previously mentioned, it is not surprising that cardiovascular readmission at 1 year follow-up is higher in late nAF patients in the setting of ACS. We did not know any comparison between these two nAF groups, but it was expected found higher values of cardiovascular readmission and mortality during the follow-up of late nAF since this group presented more comorbidities, higher time until revascularization, higher thrombolytic risk, and low left ventricular ejection fraction, all these variables were associated to worse prognosis during the ACS follow-up.[3] Very small series analyses the early nAF predictors, nevertheless to the best knowledge the authors, never MACE and follow-up in the late nAF group were investigated. Yet, our findings suggested that the time until adequate assistance and comorbidities can be directly associated with late nAF in the setting of ACS.

CHA_2DS_2-VASc score is a clinical tool used in clinical practice in patients with AF to estimate the stroke or thromboembolic risk. Considering the simplicity and utility of this score, it was applied in the prediction of several complications, diseases, and as a prognostic tool in ACS patients.[15] Our results are in line with these findings, that the CHA_2DS_2-VASc score is also capable to predict late nAF in hospitalized for ACS and can be useful in the stratification of these patients, however considering our results its application in the clinical practice seems to have just a modest predictor capacity.

5 | LIMITATIONS

There are several limitations to be considered in the study interpretation. This was an observational and non-randomized study, which could have associated confounders that could influence the outcomes. Some of the patients could have misclassified characteristics or incomplete records. Analysis of differences between patients with and without the combined endpoint was performed with univariable, non-adjusted models without correction of multiple inferential tests. Other complications, namely non-cardiovascular complications, can interfere with the patient's prognosis, but there were not considered in the registry. Even considering the high number of patients in the registry, just a few patients had a documented follow-up after the hospitalization. In the nAF episodes during the hospitalization, the duration of the episode was not considered, yet can interfere in some conclusions. Another limitation might be that the ProACS registry just allows considered the follow-up events as cardiovascular or all-cause readmission/mortality, lacking some detail regarding the events, namely for example the occurrence of thromboembolic events in this group of patients during the follow-up, as well a clear death cause.

6 | CONCLUSION

Our results suggest that the time occurrence of nAF in the setting of ACS can have different clinical and prognostic implications. Despite the different characteristics between early and late nAF, our analysis suggested that the presence of comorbidities favors the occurrence of late nAF in the setting of ACS and that these patients seem to have the worst prognosis. Further investigation should focus on the determination of whether the different types of nAF have clinical, prognostic, and therapeutic consequences. CHA_2DS_2-VASc score may be a useful tool to predict the occurrence of late nAF in the setting of ACS.

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CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

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SUPPORTING INFORMATION

Additional supporting information may be found in the online version of the article at the publisher's website.

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