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New onset of atrial fibrillation in acute coronary syndromes

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Klíčová slova:
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SOUHRN

Kontext: S akutními koronárními syndromy (AKS) a s fibrilací síní (FS) se lze v portugalské populaci setkat často. V některých případech může první epizoda FS proběhnout v rámci AKS. Zdá se přitom, že nově vzniklá FS (nFS) v přítomnosti AKS je spojena s nepříznivou prognózou.
Cíle: Popsat různé charakteristiky pacientů s nFS při AKS a posoudit prediktory nFS.
Metody: Multicentrická prospektivní studie používající údaje portugalského Národního registru akutních koronárních syndromů získané od 29 851 pacientů přijatých pro AKS v období od 1. října 2010 do 4. září 2019 a klasifikovaných podle přítomnosti nebo nepřítomnosti nFS během hospitalizace. Pacienti s dřívějšími epizodami FS nebyli do studie zařazeni.
Výsledky: K nFS došlo u 1 067 pacientů (4,1 %), většinou starších osob, s několika komorbiditami jiné než kardiovaskulární etiologie, se sníženou ejekční frakcí levé komory (EF LK) a s komplexnějším postižením koronárních tepen. U pacientů s nFS se častěji prováděla antiarytmická terapie, avšak pouze 21,5 % jich užívalo trojkombinaci antitrombotik a 30,3 % duální antitrombotickou léčbu. Tato skupina vykazovala i vysoký výskyt komplikací a úmrtí během hospitalizace. Podle vícečetné logistické regrese byly prediktory nFS v přítomnosti AKS věk nad 75 let, prodělaná cévní mozková příhoda, vysoká třída klasifikace podle Killipa a Kimballa, hemoglobin < 12 g/dl a EF LK < 50 %. Při kontrolním vyšetření po jednom roce predikovalo skóre CHA_2DS_2-VASc nový vznik FS v rámci AKS (poměr šancí 2,07; $p < 0,001$), opětovný příjem do nemocnice z kardiovaskulárních příčin ($p < 0,001$) a opětovnou hospitalizaci z jakýchkoli příčin ($p < 0,001$).
Závěr: Prognóza pacientů s nFS v přítomnosti AKS je nepříznivější než prognóza pacientů se sinusovým rytmem. Ukázalo se, že skóre CHA_2DS_2-VASc použité pro hodnocení rizika vzniku tromboembolie představuje středně spolehlivý prediktor nFS.

Keywords:
Acute coronary syndromes
CHA_2DS_2-VASc
Mortality
New-onset atrial fibrillation

ABSTRACT

Background: Acute coronary syndrome (ACS) and atrial fibrillation (AF) are common in the Portuguese population. In some cases, AF first episode can occur in ACS context. Nevertheless, the impact of new-onset AF (nAF) in the setting of ACS seems to be associated with a poor prognosis.
Objectives: To understand different characteristic in nAF patients with ACS and to evaluate the predictors of nAF.
Methods: Multicenter retrospective study based on the Acute Coronary Syndrome Portuguese National Registry, including 29 851 patients admitted for ACS between 1/10/2010–4/09/2019, classified according to the presence or absence of nAF during the hospitalization. Patients with previous AF were excluded.
Results: nAF was identified in 1067 patients (4.1%), mostly older, presenting more non-cardiovascular comorbidities, decreased left ventricular ejection fraction (LVEF) and a more complex coronary disease. nAF patients received more anti-arrhythmic therapy, but just 21.5% had triple anti-thrombotic therapy and 30.3% had dual anti-thrombotic therapy. This group also presented high rates of in-hospital complications and death. Multiple logistic regression revealed that age >75 years old, previous stroke, higher Killip–Kimball class, haemoglobin <12g/dL and LVEF <50% were predictors of nAF in the setting of ACS. CHA_2DS_2-VASc score was a predictor of nAF in the setting of ACS (odds ratio 2.07, p <0.001), of cardiovascular re-admission (p<0.001) and all-cause of re-admission (p <0.001) at one year follow-up.
Conclusions: Patients with nAF in the setting of ACS have a worse prognosis when compared to sinus rhythm patients. CHA_2DS_2-VASc score used for thromboembolic risk assessment was noted to be a moderate predictor of nAF.

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Introduction

Atrial fibrillation (AF) is the most common sustained cardiac arrhythmia affecting over 30 million people in developed countries. It has been estimated that the prevalence of AF will double over the next 50 years.[1] AF reduces quality of life and is associated with higher hospitalization and mortality rates, especially cardiovascular mortalities due to sudden death, heart failure or stroke.[1]

The presence of AF in patients admitted with acute coronary syndrome (ACS) is common. Nevertheless, the AF type, namely permanent or paroxysmal, pre-existing or new-onset, may have a different impact on the patients, especially when associated with ACS.[2,3] The management and implications regarding the approach of AF in ACS are a challenge since no randomized trials were designed for this population and all the available evidence is based on subgroup analyses.

Several mechanisms can explain an increased occurrence of AF in ACS, such as ischemia and reduction on 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. Different studies reported the AF in ACS incidence, with values ranging between 2 to 25%, and its incidence increases with the severity of myocardial infarction.[4] Other potential risk factors are older age, tachycardia, and heart failure signs.[5] It is yet to be clarified if the occurrence of AF on the setting of ACS is a prognostic marker of ACS or related to other comorbidities.[6] The presence of permanent AF in the setting of ACS is a direct predictor of mortality in the short and the long term,[2–4] and new-onset AF (nAF) may have a worse prognosis comparing with history of permanent AF in the setting of ACS.[4,7] A fact that this work pretends clarify. The main goal of this study was to analyse the rate, clinical features, therapeutic approach, complications and in-hospital mortality of nAF in the setting of ACS in a real-world scenario using data from the Portuguese Registry of Acute Coronary Syndromes.

Methods

Pro-ACS registry design

The Portuguese Registry of Acute Coronary Syndromes (Pro-ACS – ClinicalTrials.gov NCT 0162329) is a continuous, nationwide, prospective, observational registry launched in 2002. Data is uploaded by participating centres 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.[8] 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 a 1-year of follow-up.

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. AF identification cannot represent 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. We defined two groups: patients that presented nAF during hospitalization and patients without AF.

Study population

A total of 29 851 validated episodes in the Pro-ACS registry between 1 October 2010 and 4 September 2019 were accessed; 1 067 were defined as nAF (4.1%) in ACS context. 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 were excluded. The nAF was analysed according to the ACS presentation, as STEMI or NSTEMI. Patients with previous AF documented were also excluded.

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., Chicago, IL, USA) 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 nAF and sinus rhythm was performed using odds ratios (OR) and 95% confidence intervals (95% CI), as well as independent--samples t-test for continuous variables and chi-square test for categorical variables. Chi-square and Fisher exact tests, as well as univariate logistic regression, were used to assess in-hospital outcomes (categorical variables) as appropriate. Survival analysis for 1-year outcomes was performed using Kaplan-Meier curves and log-rank test. *p*-values are two-sided, and a threshold of 0.05 indicates statistical significance in all tests.

Ethical approval

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).[9] This way, ensuring the protection of human rights in Portugal, the confidential and anonymous information of every patient, in compliance with the Declaration of Helsinki. Informed consent was obtained to all the participants.

Results

Population clinical features

A total of 1 067 patients were categorized as having a nAF in the setting of ACS. Patients with nAF were old, with a low body mass index and a high prevalence of cardiovascular conditions and other comorbidities, including previous heart failure history, valvular heart disease, pe-

ripheral arterial disease, chronic obstructive pulmonary disease, dementia and previous stroke (Table 1). Previous medications are represented in Table 1.

Patients with nAF were more frequently admitted directly to the catheterization laboratory, while sinus rhythm patients to the emergency room. Other patterns of hospital admission were similar (Supplemental Table 1). Patients with nAF had similar symptoms onset to first medical contact time (p = 0.379) but had a shorter first medical contact to admission time (p = 0.006). Table 2 illustrates the clinical presentation features. Sinus rhythm patients frequently presented chest pain as the main symptom. As expected, Killip–Kimball (KK) class at admission was higher in nAF patients nevertheless, just 18.1% with KK ≥ II presented nAF at admission. Furthermore, nAF patients had high left or right-bundle branch block patterns, ST-segment depression and ST-segment elevations, and had less frequently normal ST-segment. Additionally, nAF presented increased brain natriuretic peptide (BNP), glycated haemoglobin and creatinine levels, as well as decreased haemoglobin levels.

Table 3 depicts clinical management features. nAF patients had a poor left ventricular ejection fraction (LVEF) (p <0.001). On the other hand, the complex coronary disease was common in nAF patients, including left main and two- and three-vessel disease. Curiously, the left anterior descending artery was the most frequently revascularized vessel in nAF patients. No differences were found between groups regarding the performance of percutaneous coronary intervention (PCI) (odds ratio [OR]: 1.06, p <0.001, confidence interval [CI] 0.93–1.21), nevertheless, nAF patients were less likely to have planned revascularization (OR: 0.47, p <0.001, CI 0.37–0.58). Concerning the planned revascularization strategy, coronary artery bypass grafting (CABG) was

Supplement table 1 – Admission, laboratory, and electrocardiogram characteristics regarding the rhythm, in percentage

	SR	AF	*p*
Admission emergency room	57.3	51.3	<0.001
Admitted directly to cath lab	10.4	18.8	<0.001
Admission for intensive care unit	31.5	29.0	0.088
Symptoms onset to first medical contact time	380±157	423±161	0.379
First medical contact to admission time	263±132	202±100	0.006
Left bundle branch block	3.6	6.4	<0.001
Right bundle branch block	5.2	9.8	<0.001
ST elevation	39.2	52.9	<0.001
ST depression	16.8	20.4	<0.001
Normal ST	23.5	10.8	<0.001
Haemoglobin	13.8±1.9	13.2±2.0	<0.001
HbA_{1c}	6.6±1.6	7.1±2.1	0.201
BNP	412±718	979±1309	<0.001

SR in acute coronary syndrome (ACS) – sinus rhythm; atrial fibrillation (AF) – new onset of AF in the setting of ACS.

Table 1 – Population characteristics regarding the rhythm, in percentage

	SR	AF	*p*
Smoking	27.0	17.8	<0.001
Arterial hypertension	70.4	75.6	<0.001
Diabetes mellitus	31.4	34.6	0.029
Dyslipidaemia	61.8	56.4	<0.001
Familiar cardiovascular history	7.7	2.5	<0.001
Angina	28.7	24.0	<0.001
Previous acs	20.6	18.2	0.062
Valvular pathology	3.7	5.7	<0.001
Previous heart failure	5.7	11.5	<0.001
Previous stroke	7.0	11.3	<0.001
Peripheral arterial disease	5.4	8.1	<0.001
Chronic kidney disease	7.1	4.7	0.001
Neoplasia	4.9	5.6	0.327
Chronic obstructive pulmonary disease	4.2	9.1	<0.001
Dementia	1.6	4.5	<0.001
Haemorrhage	1.5	1.5	0.833
Acid acetylsalicylic	30.8	33.9	0.033
Other antiplatelet	14.2	13.3	0.439
Beta block	25.2	27.2	0.159
Angiotensin converting enzyme inhibitors/angiotensin ii receptors blockers	47.2	51.9	0.003
Statin	39.1	39.8	0.642
Calcium channel blockers	18.9	20.5	0.181
Ivabradine	1.4	2.4	0.009
Mineralocorticoid receptor antagonists	2.1	3.0	0.039
Diuretic	24.2	32.6	<0.001
Anti-arrhythmic therapy	1.5	2.0	0.176
Insulin	7.7	8.5	0.327
Oral antidiabetic drugs	21.3	23.3	0.114

SR in acute coronary syndrome (ACS) – sinus rhythm; atrial fibrillation (AF) – new onset of AF in the setting of ACS.

Table 2 – Clinical presentation characteristics regarding the rhythm, in percentage

	SR	AF	*p*
Chest pain	92.9	81.9	<0.001
Dyspnoea	3.2	9.2	<0.001
Syncope	1.4	2.8	<0.001
Cardiac arrest	0.5	1.0	0.007
Killip–Kimball class >I	14.3	35.6	<0.001
AF at admission	0	78.2	<0.001

SR in acute coronary syndrome (ACS) – sinus rhythm; atrial fibrillation (AF) – new onset of AF in the setting of ACS.

Table 3 – Clinical management, angiography, and revascularization characteristics regarding the rhythm

	SR	AF	*p*
Left ventricular ejection fraction (LVEF)	51±12	46±13	<0.001
Quantification of LVEF	93.3%	96.5%	<0.001
Angiography	84.5%	82.7%	0.101
Radial access	69.7%	69.0%	0.658
Multivessel disease	51.5%	56%	0.001
Culprit lesion: anterior descending artery	37.2%	40.9%	0.045
Culprit lesion: unknown	16.8%	11.7%	<0.001
Percutaneous coronary intervention	70.2%	79.5%	<0.001
Coronary artery bypass grafting	8%	7.4%	0.554
Hybrid strategy	0.7%	2.1%	<0.001

SR in acute coronary syndrome (ACS) – sinus rhythm; atrial fibrillation (AF) – new onset of AF in the setting of ACS.

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

	SR	AF	*p*
Mortality	3.4	11.0	<0.001
Reinfarction	0.8	2.5	<0.001
Heart failure	14.3	45.7	<0.001
Cardiogenic shock	3.6	16.1	<0.001
Mechanical complication	0.6	1.8	<0.001
Complete atrioventricular block	2.2	8.0	<0.001
Sustained ventricular tachycardia	1.1	7.8	<0.001
Cardiac arrest	2.4	9.2	<0.001
Stroke	0.6	1.9	<0.001
Major haemorrhagic events	1.4	4.2	<0.001

SR in acute coronary syndrome (ACS) – sinus rhythm; atrial fibrillation (AF) – new onset of AF in the setting of ACS.

planned irrespective of the rhythm, although a hybrid revascularization strategy (PCI + CABG) was chosen more frequently in nAF patients. No differences were found regarding success rates.

Therapy

No differences were found regarding therapy with P2Y12 blockers or GP IIb/IIIa receptor inhibitors, as well as dual-antiplatelet therapy. nAF patients were more frequently given aspirin, any heparin/heparin-related-agent, enoxaparin, and vitamin K antagonists. Nonetheless, they were likely to receive less in-hospital beta-blockers and angiotensin converting enzyme inhibitors (ACEI)/angiotensin II receptors blockers (ARB). nAF patients were more frequently given ivabradine, mineralocorticoid receptor antagonists, diuretics, amiodarone, digoxin, others antiarrhythmic drugs and inotropes.

At discharge, nAF patients were less frequently prescribed with aspirin or ticagrelor, but the rates of clopidogrel prescription were higher. As expected, nAF patients had high prescription of vitamin K antagonists or any of the new anticoagulants. Interestingly, in the nAF group, just 21.5% of the patients had prescribed triple antithrombotic therapy and 30.3% had dual antithrombotic therapy. Nonetheless, nAF patients receive high percentage of mineralocorticoid receptor antagonists, diuretics, amiodarone, digoxin and other antiarrhythmic drugs.

Concerning patients discharged with triple antithrombotic therapy, follow-up at one year (32.5% of all the patients had follow at one year) revealed no statistical significance in mortality rates ($p = 0.578$), re-admission for cardiovascular causes ($p = 0.301$) and re-admission for all causes ($p = 0.431$).

Prognosis

Patients with nAF in the setting of ACS had increased in-hospital all-cause of death (OR: 3.47 [2.83–4.25], p <0.001), as well as higher rates of re-infarction, congestive heart failure, cardiogenic shock, mechanical complications, AV block, sustained ventricular tachycardia, aborted cardiac arrest, stroke and major bleeding (p <0.001 for all comparisons) (Table 4). nAF patients also exhibited longer in-hospital stay (p <0.001). nAF patients had high rates at 1-year of re-admission for all-cause, as well as cardiovascular hospitalization and all-cause of death.

Multiple logistic regression revealed age >75 years old (odds ratio [OR] 2.07, p <0.001, confidence interval [CI] 1.74–2.47), previous stroke (OR 1.40, $p = 0.019$, CI 1.06–1.85), KK >1 (OR 2.10, p <0.001, CI 1.72–0.56), haemoglobin <12 g/dL (OR 1.29, $p = 0.018$, CI 1.04–1.59), admission glycemia (OR 1.84, p <0.001, CI 1.52–2.22) and LVEF <50% (OR 1.91, p <0.001, CI 1.60–2.27) as the predictors of nAF in ACS.

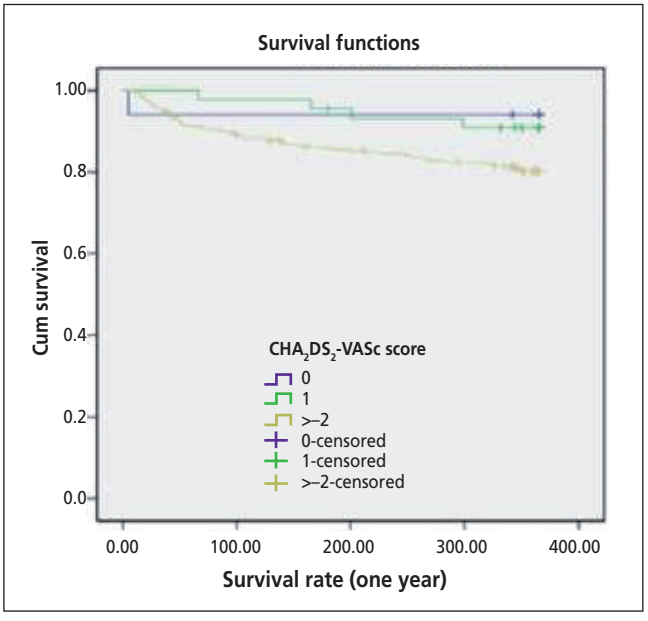

Fig. 1 – Representation with the Kaplan–Meier test of survival rates at one year of follow-up according to CHA_2DS_2-VASc punctuation, 0, 1, and ≥ 2.

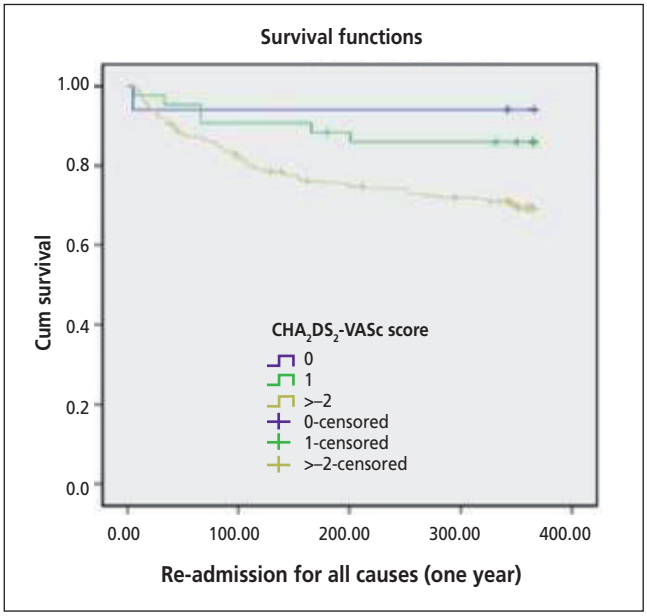

Fig. 2 – Representation with the Kaplan-Meier test of re-admission for all causes at one year of follow-up according to CHA_2DS_2-VASc punctuation, 0, 1, and ≥ 2.

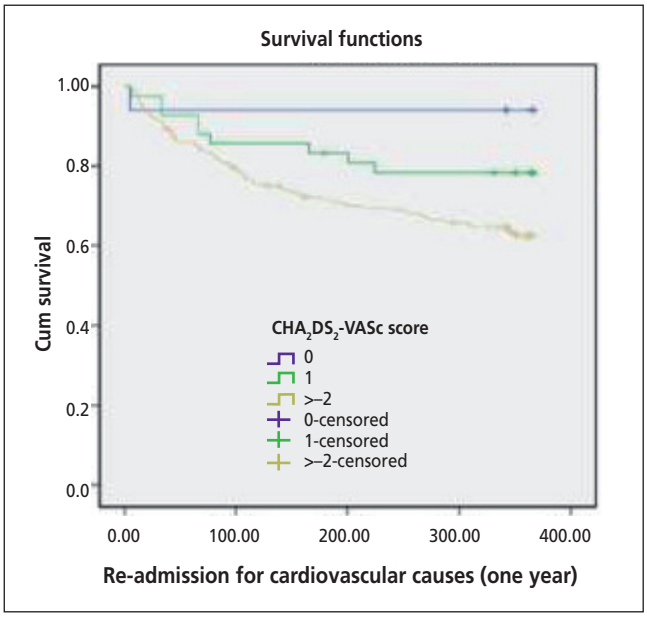

Fig. 3 – Representation with the Kaplan–Meier test of re-admission for cardiovascular causes at one year of follow-up according to CHA_2DS_2-VASc punctuation, 0, 1, and ≥ 2.

CHA_2DS_2-VASc score

Logistic regression analysis revealed that the CHA_2DS_2-VASc score was a median predictor of nAF in ACS (OR: 2.07, p <0.001, CI 1.74–2.47; Area Under Curve: 0.642, CI 0.625–0.659), with a 66.7% sensibility and 55.1% specificity. Mortality analysis at one year of follow up revealed higher mortality rates associated with higher CHA_2DS_2-VASc punctuation, although this association did not achieve statistical significance, p = 0.099 (Fig. 1). On the other hand, the score exhibited a statistically significant value (p = 0.016), at the re-admission for all causes (Fig. 2), according to its punctuation of 0, 1 or ≥2. Regarding re-admission for cardiovascular causes (Fig. 3), higher rates of readmission at 1-year follow-up were associated with a higher score classification, with a Kaplan–Meier test of p = 0.013.

Discussion

nAF is a frequent finding in ACS, and the ACS can be considered as a trigger to arrhythmias.[10] Our study reveals that nAF in the setting of ACS reflects several clinical characteristics and therapeutic implications and represents one of the largest analysis of nAF in the setting of ACS.

Patients with nAF, in general, have a higher prevalence of cardiovascular risk factors, coronary disease, chronic kidney disease and heart failure. This group has also low percentages of evidence-based medical therapies,[11] which is in line with our findings, suggesting that the identification of nAF in the setting of ACS is frequently in patients with more comorbidities, which have more propension to arrhythmia's development.

The arrhythmia contributes to several hemodynamic alterations, like fast ventricular rates, hypoxia, hypotension or hypertension, adrenergic discharge, the loss of atrial contraction and atrioventricular synchrony (which promote an imbalance between myocardial oxygen supply and demand). All of these hemodynamic alterations can be associated with exacerbation of acute ischemia and heart failure.[7] Therefore, and according to some authors,[7] the presence of AF should be interpreted as a sign or at least a trigger of hemodynamic compromise. Our results showed that patients with nAF presented higher Killip–Kimball (KK) class, less time until the first medical contact, worst left ventricular function, and were referred more frequently to the catheterization laboratory, which proves the direct hemodynamic impact the arrhythmia, being in agreement with the previous study. On the other hand, it was expected that patients admitted with STEMI presented higher hemodynamic compromise, thus presenting higher rates of nAF when compared to NSTEMI patients, which was not proved in our findings.

Curiously, the anatomical location of the infarction seems not to be related to the prevalence of AF in the setting of ACS, and patients with undefined ACS location had a higher prevalence of AF.[12] nAF patients, in our results, had a more complex multivessel and critical anatomical coronary disease, a finding very frequently in patients diagnosed with undefined ACS location.

Another problematic issue in patients with AF in the setting of ACS is the need of a percutaneous coronary intervention, which may imply the necessity of triple therapy with oral anticoagulation in patients with CHA_2DS_2VASc scores ≥2 and dual anti-aggregation in patients submitted to percutaneous coronary intervention (PCI).[13] Triple therapy is associated with a higher haemorrhagic risk and more difficult therapy management.[2,13] In our study, only 21.5% of the patients with nAF in the setting of ACS received triple therapy during hospitalization, and even considering that some may not have anticoagulati-

on criteria, a very significant percentage of patients did not receive the recommended therapy.

A study including over 69 000 patients[14] found that less than half of the patients received triple therapy because of the haemorrhagic risk associated. In another report, older patients were prescribed with dual antiplatelet therapy without anticoagulation,[15] for the same reason. Thus, the high rate of haemorrhagic incidents during the hospitalization in our patients may have influenced the physicians' decision on whether prescribing triple therapy.

In dual therapy (an anticoagulant and one antiplatelet), clopidogrel is preferred to other antiplatelet agents, because it has a lower haemorrhagic risk, explaining the higher prescription of clopidogrel and less acetylsalicylic acid in our group of nAF patients. A very curious finding in our study is the absence of prognostic significance of triple therapy in mortality and readmission rates at 1 year follow-up, contrary the major literature described,[14] a fact that maybe justify the physicians' decision on double therapy.

Beta-blockers were less used during hospitalization, probably due to the increased KK class in the ACS presentation, being nAF patients more frequently submitted to anti-arrhythmic therapy. Interestingly, we observed a diminished use of beta-blockers at discharge in the AF group, which can be justified by the arrhythmia presence. In fact, the nAF patients demonstrated a frequent left ventricular dysfunction and would consequently benefit from beta-blockers therapy. However, in our study, this did not occur requiring further investigation.

Considering that ivabradine is recommended in sinus rhythm patients only, an interesting result was the higher prescription of this medication to nAF patients. These last two arguments, prove the difficult and a complex therapeutic approach in nAF patients.

Lopes RD et al. [3] did not find an association between nAF in the setting of ACS and short-term mortality; despite that, higher rates of in hospital complications such as heart failure, acute mitral regurgitation, sustained hypotension, cardiogenic shock and strokes were found. Several studies concluded that the presence of nAF, comparing to sinus rhythm, is associated with a higher in-hospital and long term follow up mortalities.[16,17] These conclusions seem to be independent of AF onset (paroxysmal, chronic or new-onset).[2,17] These findings are in line with our results that confirmed that nAF patients had worse short-term prognosis (considering the complications during hospitalization) as well as mortality rates compared to sinus rhythm in the setting of ACS. On the other hand, other results[6,18] did not report that nAF in the setting of ACS was an independent predictor of mortality.

Nonetheless, for the majority of authors, it was not clear if the arrhythmia was a direct complication of the ACS or a risk marker of severity.[2] Some authors identified the following characteristics as risk factors to nAF in the setting of ACS: female gender, higher Killip-Kimball class, worse renal function, higher BNP and CK-MB, electrocardiogram and echocardiogram alterations.[19,20] Our results are in agreement that a higher KK class, age, and echocardiogram alterations are predictors of nAF. On the other hand, it suggests that a previous stroke, lower haemoglobin levels and higher glycaemic levels are also significant predictors of arrhythmia. Then it is imperative to identify risk factors to predict the development of AF during the hospitalization and therefore, develop preventive measures. The role of revascularization in nAF in the setting of ACS is not completely clarified.[7]

CHA_2DS_2-VASc score is used to estimate the stroke or thromboembolic risk in patients with AF and to decide the introduction of anticoagulant therapy. As so, this score was not developed to predict mortality, nevertheless the practical utility of this simple's score may be applied in the risk stratification of other clinical diseases. For example, CHA_2DS_2-VASc score was used in the general population to predict AF.[21] When analysing the score, we identified several cardiovascular risk factors, like hypertension, diabetes, heart failure, age, all of them significantly associated with worse outcomes in the follow up of ACS.[22] There are limited evidence on the use of the CHA_2DS_2-VASc score as a prognostic tool in ACS[23] being associated with long-term cardiovascular events prediction and as a good predictor of STEMI occurrence.[24] Our results are in line with these findings, suggesting that the CHA_2DS_2-VASc score is also able to predict re-admissions of nAF hospitalized for ACS.

To the best of the authors' knowledge, there are no publications that use the CHA_2DS_2-VASc score as a prognostic tool to identify patients at risk of developing nAF in the setting of ACS. Considering that the CHA_2DS_2-VASc score is easily calculated, it may be useful to evaluate the risk of nAF in patients presenting with ACS, allowing the physicians to prevent the occurrence of AF and/or to provide a faster response to the arrhythmia.

Limitations

There are several limitations to be considered in the study interpretation. This was observational and non-randomized study, which can have associated confounders that can 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 in 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. Another potential 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.

Conclusion

Our results are in accordance with several publications that suggested that nAF is a major complication of ACS with an important clinical impact. It should be considered a prognostic marker, and an active approach and therapy must be performed in these patients. Despite the di-

fferent characteristics between the groups, our analysis suggested that the presence of comorbidities favours the occurrence of nAF in the setting of ACS and that there is a bidirectional relationship between AF and ACS. Further investigation should focus on the determination of whether nAF can be considered a risk marker of prognosis or a direct mortality factor. The CHA_2DS_2-VASc score may be a useful tool to predict the occurrence of nAF in the setting of ACS, allowing a better approach to patients with increased risk.

Conflict of interest

The authors declare that there is no conflict of interest.

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