2016-2017

THÈSE

pour le

DIPLÔME D'ÉTAT DE DOCTEUR EN MÉDECINE

Qualification en Cardiologie et maladies vasculaires

New-onset atrial fibrillation as an independent prognostic marker after ST-segment elevation myocardial infarction: results from the RIMA registry

La survenue de fibrillation atriale comme marqueur pronostique indépendant après un syndrome coronarien aigu avec élévation du segment ST : résultats issus du registre RIMA

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Né le 11 Février 2017 à Lorient (56)

Sous la direction du Dr. BIERE Loïc

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Soutenue publiquement le :
12 Octobre 2017

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REMERCIEMENTS

Je remercie chaleureusement toutes les personnes qui m'ont aidé à l'élaboration de ma thèse, en commençant par mon directeur de thèse le Docteur Loic Bière, je te remercie pour ta grande disponibilité et ta bienveillance. Ton aide m'aura été très précieuse et j'ai apprécié ton humour autant que ta rigueur. Je voudrais également exprimer ma reconnaissance et mon grand respect au Professeur Furber, je vous remercie de m'avoir fait profiter de vos connaissances et de vos lumières éclairées, ce travail ne serait pas ce qu'il est sans votre aide. Un grand merci à ceux qui ont accepté de faire partie de ce jury : le Professeur Prunier, merci pour la qualité de votre enseignement et vos conseils avisés; le Docteur Desprets, futur collègue avec qui il me tarde de travailler ; et le Docteur Grall, spectateur de mes « premiers pas » jusqu'à ce jour et qui m'a beaucoup appris, je sais que ce ne fut pas toujours tâche facile !

Ce travail n'aurait pu être mené à bien sans la participation des centres hospitaliers de Cholet, Saumur et Château Gontier qui ont participé à l'élaboration du registre RIMA, de même que toutes les personnes qui ont participé au recueil des données, en particulier nos attachés de recherche clinique Charles et Jeremy. Merci également aux secrétaires de la cardiologie, pour leur gentillesse et leur compréhension à mon égard.

Merci à celles et ceux que je n'ai pas encore cité et qui m'ont formé tout au long de ces années au gré des services ou je passais : le Dr Brault, le Dr Delepine, le Dr Abi-Khalil, le Dr Rouleau, le Dr Laporte, le Dr Benard, le Dr Dupuis ; et celles qui sont devenues des amies, Marjorie, Sophie et Tin-Hinan, merci pour ces bons moments passés ensemble. Je n'oublie évidemment pas mes chers cointernes, j'ai adoré travailler dans la bonne humeur avec vous tous et je retiendrai de cet internat une grande convivialité et beaucoup de confraternité. Enfin, un bon travail d'équipe ne serait pas non plus possible sans toutes les équipes paramédicales, de jour comme de nuit, que je remercie pour leur aide et leur bonne humeur, sans oublier les pauses goûter qui sont toujours les bienvenues !

Je terminerai par celles et ceux qui ont bien voulu me supporter et me soutenir durant toutes ces années, bien qu'il soit difficile de citer tout le monde… Tout d'abord, à mes parents, que je ne remercierai jamais assez pour leur indéfectible amour et leur soutien, et je sais combien ils ont enduré et apprécié ces années avec moi. A mon frère Gaëtan, pour sa complicité de toujours et son écoute. A mes amies d'enfance, Maud, Marlène la brune, Marine, Marlène la blonde, vous avez été et serez toujours des amies fidèles quoiqu'il arrive. A mes compagnons de galère, Antoine, Alex, Alexis et Camille, sans qui je n'aurai peut-être pas eu le courage d'arriver jusque-là et qui me sont devenus chers. A mes copains guidelois, sur qui j'ai toujours pu compter quand il s'agissait de se changer les idées. A mes 2 meilleures amies et plus belles rencontres, Audrey et Charlotte, rien ne saurait défaire les liens qui ont été créés pendant cet internat et je ne réalise toujours pas la chance que j'ai eu de vous rencontrer. Ces quatre années m'auraient semblé bien longues et tristes sans vous, vivement celles à venir ! Enfin, à toi Benoit, tu as été aux premières loges tout au long de ce travail et c'est probablement le rôle le plus difficile, surtout lorsqu'on me connaît, mais tu as toujours su trouver les mots pour m'encourager et me redonner le sourire. Merci de m'avoir entouré de ton amour et de ta tendresse, merci pour tout.

Abbreviations list

AF	Atrial Fibrillation
STEMI	ST-Segment Elevation Myocardial Infarction
LA	Left Atrial
LV	Left Ventricular
HF	Heart Failure
CK	Creatin Kinase
LVEF	Left ventricular Ejection Fraction

Plan

New-onset atrial fibrillation as an independent prognostic marker after ST-segment elevation myocardial infarction: results from the RIMA registry

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Word count: 5053

ABSTRACT

Aims : Atrial Fibrillation (AF) is common in ST-segment elevation myocardial infarction (STEMI) but its influence on prognosis remains controversial, particularly considering timing of occurrence. Therefore, we examined the one-year prognostic value of AF in STEMI, distinguishing patients with prior AF, from patients with new-onset of AF (NOAF).

Methods : Between January 2004 and December 2015, 3173 patients with STEMI were consecutively and prospectively enrolled in the RIMA registry (Registre des Infarctus en Maine Anjou). They were divided into 3 groups according to the timing of AF occurrence: 1) patients free for AF; 2) patients with prior AF; and 3) patients with NOAF. We defined 3 primary outcomes at 1-year post-discharge**:** cardiovascular mortality, readmission for heart failure (HF) and stroke. The secondary included intra-hospital events and the assessment of temporal onset of NOAF: early NOAF <24h and late NOAF ≥24h.

Results : 158 patients (5%) had prior AF and 278 (8.8%) had NOAF. Prior AF patients were significantly older (81 [73;86] years) with more comorbidities but NOAF patients were more hemodynamically unstable with a greater creatin kinase (CK) peak and a lower left ventricular ejection fraction (LVEF) (44 [35;50]% versus 50 [40;55]%). At 1-year follow-up, rate of cardiovascular mortality were greater in case of AF (13.5% for prior AF vs 9.2% for NOAF, compared with 2.4% for free AF, p<0.001). After adjustment, only NOAF was related to cardiovascular mortality (hazard ratio 2.49; 95% CI 1.32 to 4.67; p=0.004), but the both types of AF were related to readmission for HF. There was no significant difference on stroke between prior AF, NOAF, and free AF (2.2%, 0.5% and 0.8% respectively, p=0.327). Finally, outcomes did not differ between early (n=127) and late (n=151) NOAF.

Conclusion : Only NOAF but not prior AF was associated with 1-year cardiovascular mortality. NOAF should not be considered as an intercurrent event of STEMI but rather as a strong prognostic marker. Whether a specific management of NOAF may improve the prognosis of these patients remains to be studied.

INTRODUCTION

Up to 2.5 to 12% of patients presenting with a ST-segment elevation myocardial infarction (STEMI) had a history of atrial fibrillation (AF), compared with a 2% prevalence in the general population. Likewise, new-onset of AF (NOAF) at the acute phase of STEMI is the most common rhythmic complication (28%) (1). Overall, the incidence of AF in STEMI patients ranges from 2% to 22% (2,3). Overall AF is established as a marker of outcomes in STEMI population (4–8). A point is still unclear in regard of NOAF occurring at the acute phase of STEMI. Some studies suggested that NOAF is an independent predictive factor of mortality at either short- or long-term (4,9–16), whereas prior AF is not (9,13,16,17). Prior AF and NOAF are two distinct events. While prior AF relates to the presence of previous diastolic dysfunction and cardiomyopathy, NOAF relates to acute changes at the time of STEMI, including left atrial (LA) ischemia or overload, so as neuroendocrine activation and tachycardia due to hemodynamic instability. Therefore, prior AF and NOAF may differentially influence outcomes. However, studies on the field broadly differ in term of sample size, STEMI characteristics and management, so as in AF diagnosis method. Therefore, they present conflicting results that we managed to stress by studying a prospective and consecutive cohort of real-life STEMI. (6,9,10,15,18–21).

The aim of the present study was to assess the one-year prognostic value of NOAF in patients with STEMI.

METHODS

Study population

This is a retrospective analysis based on the RIMA registry (Registre des infarctus en Maine-Anjou) (22). The RIMA prospectively included all consecutive patients admitted for STEMI at participating sites, including the University Hospital of Angers which is an angioplasty centre and three secondary care hospitals without angioplasty, France, between January 2004 and December 2015. STEMI was diagnosed based on the following symptoms suggestive of myocardial infarction: persistent ST elevation ≥0.1 mV in 2 contiguous peripheral leads and V5, V6, or ≥0.2 mV in 2 contiguous leads from V1 to V4, as well as elevation of cardiac biomarkers. Patients with cardiac surgery during hospitalization including coronary artery bypass grafting were excluded. 378 (11.9%) patients were lost at 1-year follow-up.

Atrial Fibrillation diagnosis

AF was defined as the absence of P waves, and atrial activity was represented by fibrillatory waves and irregular time elapsing between 2 consecutive R wave (RR) intervals. Atrial flutter on ECG recordings had to meet the following criteria: presence of regular P waves with a rate of 250 to 350/min and regular or irregular RR intervals. All patients were systematically monitored during their hospital stay in intensive care unit with an ECG that was routinely realized to monitor the ST segment and purposely when the diagnostic of AF was suspected.

Patients were classified into 3 groups: 1) patients free for AF; 2) patients with prior AF (permanent, persistent or paroxysmal) and 3) patients with NOAF developed from the first medical contact to the end of the hospitalization. Patients with atrial flutter were classified like AF. Finally, patients who developed NOAF were divided into 2 groups: Early NOAF

starting within 24 hours after the admission, late NOAF occurred after the first 24 hours. AF delay was calculated between the first chest pain until a discriminating ECG.

Patients were treated either with rate control only strategy or a rhythm control strategy using anti-arrhythmic medications (amiodarone mostly) and/or electrical cardioversion. Treatment decisions were made by the medical team.

Data collection

Basic demographics, cardiovascular risk factors, medication, biomarkers and hospitalization information were all prospectively collected. Left ventricular ejection fraction (LVEF) was assessed on echocardiography using biplane Simpson's method during the first 24 hours of hospitalization. In-hospital data on mortality, reinfarction, stent thrombosis, HF, severe ventricular arrhythmias and severe atrioventricular block, stroke and major bleedings according to BARC classification were recorded. The CHA2DS2-Vasc score was calculated for any patients. One-year follow-up was obtained and mortality, reinfarction, readmission for HF and stroke were collected. HF was defined clinically in accordance with the guidelines of the European Society of Cardiology (23). MACE was the combined event associating cardiovascular mortality, reinfarction, stroke, and readmission for HF. The data were collected during follow-up consultation at 1 year or by phone if the patient was followed up at a centre other than the participating centre. In-hospital and 1-year outcomes, so as cause of death, were systematically adjudicated by 2 blinded physicians. The study was performed in accordance with the Declaration of Helsinki and the protocol was approved by the ethics committee of University Hospital of Angers.

Outcomes

We have evaluated 3 primary outcomes at 1-year post-discharge**:** cardiovascular mortality, readmission for HF and stroke. The secondary included intra-hospital events and the assessment of temporal onset of NOAF: early NOAF <24h and late NOAF ≥24h.

Statistical analysis

All statistical tests were performed using SPSS Version 20.0 software for Windows (SPSS Inc., Chicago. Illinois. USA). Quantitative variables were expressed as median [IQR: interquartile range], and qualitative variables as numbers and percentages. Comparisons of quantitative variables were conducted by means of unpaired Student's t-test. Comparisons of qualitative variables were performed using chi-squared test or Fisher's exact test, where appropriate. Cox regression models were applied for the purposes of explaining 1-year mortality and 1-year hospitalisation for heart failure. We tested one by one the effect of NOAF and prior AF compared to free AF patients. Only significant univariate correlates ($p<0.05$) were included into the multivariate Cox models. The proportional-hazard assumptions were tested by analysing the Schoenfeld residuals. Statistical significance was set at $p<0.05$.

RESULTS

Population characteristics

Between January 2004 and December 2015, 3173 patients were hospitalized with an incident myocardial infarction. 2737 (86.2%) people were free of AF; 158 (5%) had a prior AF history; and 278 (8.8%) developed NOAF during hospitalization (figure 1). The median age at the time of myocardial infarction presenting with STEMI was 65 [53;78] years, and 72.8% of the patients were men.

Prior AF patients were significantly older (81 [73;86] years), had more comorbidities with high prevalence of hypertension (81%), of stroke (14.6%) and renal failure (9.9%). NOAF patients and free AF patients had similar percentage of anterior myocardial infarction (45.8% versus 45.7%; p=0.94) and similar timing to reperfusion (5 [4.3;8.3] versus 5.3 [3.5;8.8] hours; p=0.19) but NOAF patients had a higher creatin kinase (CK) peak and a lower LVEF (44 [35;50]% versus 50 [40;55]%); care was also different with less use of angioplasty (78.7% versus 84%) and longer hospital duration (10[5;16]days versus 5[4;8]days).

CHA2DS2-Vasc score was significantly greater in the prior AF group (5 [4;6]) and the NOAF group (4 [3;6]) compared to the free AF group (3 [2;4]); 22% of the NOAF patients had anticoagulant at discharge (table 1).

In-hospital and one-year events

During hospitalization, cardiovascular mortality was higher in case AF, respectively 17.1% for prior AF and 14.7% for NOAF, versus 5.7% for free AF patients (p<0.001). Table 2 shows in-hospital complications to be more frequent among the NOAF patients, particularly regarding in-hospital HF events with Killip ≥3 (33.5%), major bleedings (12.5%),

reinfarction (3.6%), severe ventricular arrhythmias (20.9%) and severe atrioventricular block (14.4%). Stroke rate was similar compared to free AF.

1-year cardiovascular mortality was greater in case of prior AF (20.6%) compared to NOAF (12.1%) and free AF patients (4.3%) with p<0.001. Hospitalization for HF was also higher (21.3% versus 13.8% and 4.2%; p<0.001). Stroke rate did not differ (p=0.327) (table 2).

The multivariate Cox regression model showed that only NOAF was associated with higher cardiovascular mortality (hazard ratio 2.485; 95% CI 1.323 to 4.67 with p=0.004). Prior AF was not related to cardiovascular mortality (p=0.09) but age, creatinine level, angioplasty and LVEF were. Both prior AF and NOAF were associated with readmission for HF (figure 2).

Timing of NOAF

Early NOAF occurred in 127 patients and late NOAF in 151 patients. Although the 2 groups of NOAF were not very different regarding the characteristics of myocardial infarction as regard as the CK peak (p=0.16) and anterior infarction (p=0.51); patients with late NOAF were significantly older, with median age 78 [70;84] years, 35.6% had a Killip class ≥ II at admission and they had lower LVEF (table 4). Importantly, the excess risk of 1-year post-discharge events conferred by NOAF did not differed markedly according to its timing. There was either no difference according to the persistence of AF at discharge in the 2 groups (p=0.59) (table 5). At discharge, 20 (8%) patients have persistent AF and 214 (84.6%) returned in sinus rhythm. Among the patients with persistent AF, we note nearly two-fold increased events in this group. There was significantly more cardiovascular death (15.8% versus 1.5%, p<0.001), readmission for HF (21.4% versus 13.1%, p<0.001) and MACE (35.3% versus 22.3%, p<0.001). Early or late timing of NOAF was not related to 1-year cardiovascular mortality and readmission for HF in multivariate analysis.

DISCUSSION

The main result of our study is that NOAF is an independent predictive factor of 1-year cardiovascular mortality, when prior AF was not. More, timing of NOAF has no incremental value on prognosis.

While our results are in line with Morishima *et al.* (10), our study is based on a longer follow-up and a greater number of patients. It is also concordant with some previous studies that were mostly post-hoc analyses of randomised clinical trials which were not specifically conducted to study AF, thereby their applicability to the community is uncertain (4,7,15,16,24,25). Recent studies that disagreed with our results varied in term of population characteristics, by including STEMI and non-STEMI (8,14), or either high rate of fibrinolysis use (26). On the contrary, our study is issued from the RIMA registry which is a real-life registry at the angioplasty era. Furthermore, all patients had continuous ECG monitoring during hospitalization, that allowed us not to underestimate AF prevalence and acutely determinate the timing of its onset.

NOAF

How STEMI relates to NOAF is poorly understood. Potential pathophysiologic mechanisms include: tachycardia with hemodynamic instability related to LV dysfunction and pump failure, myocardial ischemia and diastolic dysfunction with increased LA overload leading to LA enlargement, adrenal catecholamine discharge, electrolyte (e.g hypokaliemia) and acid-base disturbances. Likewise, NOAF was associated with markers of greater hemodynamic instability, namely greater infarct size and lower LVEF (13,24), as reported in our study (table 1). We also showed not only NOAF to be independently related to

cardiovascular mortality, but to a higher risk of in-hospital outcomes. Consequently, NOAF should not be considered as an intercurrent phenomenon of STEMI but as a strong prognosis marker. Whether NOAF actually effects on prognosis or how NOAF management might impact on outcomes need to be further investigated.

In the literature, data on temporal association between NOAF and prognosis are limited with heterogenous designs and conflicting results (18–21,26). Podolecki *et al*. found an excess mortality only for patient with early NOAF <24h (20), but their population was different with more severe presentation admission as cardiogenic shock (14,2%), a lower LVEF (36.9±8.1%) and an overall higher 1-year mortality rate.

Prior AF

While prior AF was not found as an independent risk marker (table 3) of cardiovascular mortality, it was a strong correlate of readmission for HF (hazard ratio 2.501; 95% CI 1.402 to 4.468) with p=0.001). A recent Canadian registry made similar findings, despite an older population, higher rates of comorbidities and lower use of angioplasty (27). Prior AF is a major component of diastolic dysfunction, associated with senescent myocardium and increased peripheral vascular resistance. It is thus assumed to be strongly related to heart failure morbidity and mortality. In this context, development of ischemic heart disease will play as an incremental risk factor, illustrated by the fact that 1-year outcomes were independently related to age, creatinine level, CK peak and LVEF (table 3).

Management: anticoagulation and rhythm control

Even paroxysmal AF that has reversed to sinus rhythm at the time of discharge will increase the risk for ischaemic stroke during follow-up (2). Interestingly, only 22% of our NOAF patients had anticoagulation at discharge even though their CHA2DS2-Vasc score was

high (4 [3;6]). Reasons why anticoagulation was not prescribed are unknown. However, we didn't find any difference based on in-hospital and 1-year stroke compared to free AF patients, with the exception for more major in-hospital bleeding events (12.4% versus 5.8%, p<0.001). According to current guidelines, patients with CHA2DS2Vasc ≥ 2 should receive a triple therapy combine aspirin, an ADP receptor antagonist and an oral anticoagulation. The aim is for reducing the burden of thromboembolic complications and minimizing the risk of stent thrombosis, with shortest possible duration to reduce the bleedings complications (1).

While restoring and maintaining sinus rhythm is an integral part of AF management (28), all trials that have compared rhythm control and rate control to rate control alone have resulted in neutral outcomes. For now, rhythm control therapy is indicated to improve symptoms in AF patients who remain symptomatic on adequate rate control therapy. The ESC guidelines for the management of acute myocardial infarction in patients presenting with STEMI (1) suggest that if the arrhythmia is well tolerated, no specific treatment is required, other than anticoagulation. Actually, there is a lack of studies on management of AF at the acute phase of myocardial infarction and little is known about the impact of AF treatment strategy on clinical outcomes in these patients (29–31).

Limitations

Several limitations must be considered, the first being inherent bias due to a retrospective and observational non-randomized study with 11.9% lost of follow-up. Secondly, more specific data on AF such as AF duration, LA enlargement, or therapeutical management or recidive of AF after discharge are lacking to fully comprehend these results.

CONCLUSION

NOAF was not only related with greater infarction and lower LV function after STEMI, but was independently associated with 1-year cardiovascular mortality. NOAF should not be considered as a benign intercurrent event of STEMI but rather as a strong prognostic marker. Whether a specific management of NOAF may improve the prognosis of these patients remains to be studied. Both NOAF and prior AF were independent predictors of post-discharge readmission for HF.

Figures

Figure 1. Flow chart

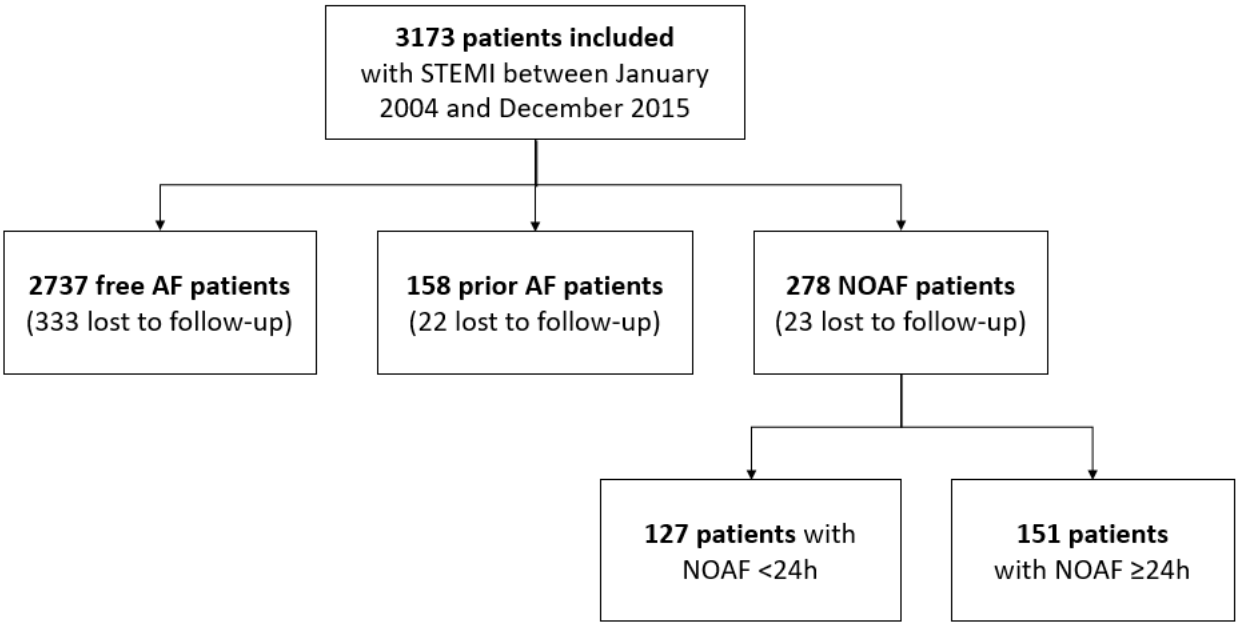
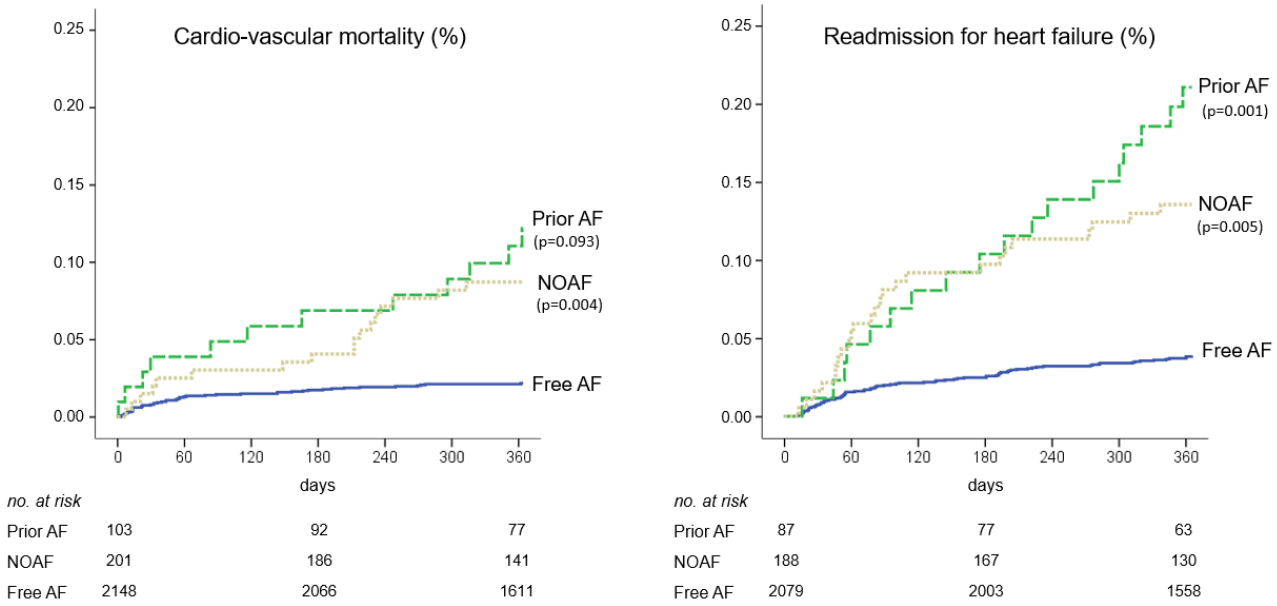


Figure 2. Survival curves



p values compare either prior AF and NOAF to AF free patients after multiple adjustments by Cox regression analysis.

Tables

Table 1. Characteristics of Patients With Myocardial Infarction According to the Presence of Atrial Fibrillation

	Total N=3173	Free AF N=2737	Prior AF N=158	NOAF N=278	p-value
Clinical history					
Age (years) *	65 [53;78]	62 [52;76] §¤	81 [73;86] ¤	77 [65;83]§	<0.001
Weight (kg) *	75 [65;85]	75 [66;85]§¤	72 [62;82]	72 [64;81]	<0.001
Male gender, n(%)	2311(72.8)	2016 (73.7)¤	106 (67.1)	189 (68)	0.032
History of hypertension, n(%)	1606 (50 .7)	1302 (47.7)§¤	128 (81)¤	176 (63.3)§	<0.001
History of diabetes mellitus, n(%)	700 (22.2)	595 (21.9)	37(23.6)	68 (24.5)	0.69
History of dyslipidemia, n(%)	1615 (51.2)	1398 (51.4)	71 (44.9)	146 (52.5)	0.28
Smoker, n(%)	1187 (37.2)	1107 (40.6)§¤	22 (14)	59 (21.4)	<0.001
History of myocardial infarction, n(%)	261(8.2)	213 (7.8)§	20 (12.7)	28 (10.1)	0.025
History of CABG, n(%)	59 (1.9)	44 (1.6)§	8 (5.1)	7 (2.5)	0.004
History of Angioplasty,(n%)	205 (6.5)	173 (6.3)	15 (9.5)	17 (6.1)	0.28
History of stroke, n(%)	145 (4.6)	100 (3.7)§¤	23 (14.6)¤	21 (7.6)§	<0.001
History of renal failure, n(%)	105 (3.3)	78 (2.9)§	15 (9.6)¤	12 (4.1)§	<0.001
Medical therapy at Admission					
Amiodarone, n(%)	42 (1.3)	13 (0.5)§	27 (17.1)¤	2 (0.7)§	<0.001
ACEI/ARBs, n(%)	861 (27.3)	686 (25.2)	80 (50.6)	95 (34.3)	<0.001
Beta-blockers, n(%)	642 (20.3)	494 (18.1)	78 (49.4)	70 (25.3)	<0.001
Statins, n(%)	693 (21.9)	582 (21.4)	48 (30.4)	63 (22.7)	0.027
Antiplatelet, n(%)	626 (19.8)	497 (18.2)§¤	52 (32.9)	77 (27.8)	<0.001
Anticoagulant, n(%)	118 (3.7)	37 (1.4)§	77 (48.8)¤	4 (1.3)§	<0.001
Charasteritics of qualifying myocardial infarction					
SBP at baseline (mmHg) *	138 [120;159]	140 [120;159]¤	134 [115;159]¤	128 [110;146]§	<0.001
HF at baseline (Killip ≥ II)	493 (15.7)	369 (13.3)§¤	51 (33.3)	83 (30.3)	<0.001
Creatinin value at baseline (µmol/L) *	82 [69;98]	81 [69;96]§¤	93 [76;121]	91 [75;116]	<0.001
CK peak (UI/L) *	1412 [597;2688]	1403 [607;2669]§¤	1053 [346;2143]¤	1767 [589;3438]§	<0.001
CRP max (mg/L) *	8 [3;42]	7 [3;32]§¤	22 [4;87]	32 [4 ;127]	<0.001
Anterior myocardial infarction, n(%)	1352 (45.8)	1175 (45.7)	63 (47.4)	114 (45.8)	0.93
Medical therapy, n(%)	399 (13.2)	326 (12.4)§	32 (22.7)	41 (16)	0.001
Fibrinolysis, n(%)	405 (12.8)	370 (13.5)§¤	11(7)	24 (8.6)	0.003
Angioplasty, n(%)	2602 (82.9)	2279 (84)§¤	109 (70.8)	214 (78.7)	<0.001
Multivessel disease, n(%)	1419 (48.1)	1301 (50.6)§¤	81 (60.9)	151 (60.9)	0.001
Time from symptoms to reperfusion (h) *	5.3 [3.5;8.7]	5.3 [3.5;8.8]	3.1 [1.4;6.4]	5 [4.3;8.3]	0.19
Complete revascularization, n(%)	1447 (52.5)	1300 (54.1)§¤	51 (39.5)	96 (42.5)	<0.001
LVEF, n(%) *	50 [40;55]	50 [40;55]§¤	45 [37;53]	44 [35;50]	<0.001
CHA2DS2-Vasc *	3 [2 ;5]	3 [2 ;4]§¤	5 [4 ;6]¤	4 [3 ;6]§	<0.001
Hosiptal duration (d) *	6 [4;9]	5 [4;8]§¤	7 [4;12]¤	10 [5;16]§	<0.001
Medical therapy at discharge					
Amiodarone, n(%)	174 (5.9)	38 (1.5)	45 (34.6)	91 (38.6)	<0.001
ACEI/ARBs, n(%)	2715 (92.5)	2408 (93.7)	112 (86.2)	195 (83)	<0.001
Beta-blockers, n(%)	2768 (87.2)	2448 (89.4)	113 (71.5)	207 (74.5)	<0.001
Statins, n(%)	2790 (87.9)	2462 (90)	119 (75.3)	209 (75.2)	<0.001
Antiplatelet, n(%)	2892 (98.6)	2552 (99.4)	112 (86.2)	228 (96.6)	<0.001
Anticoagulant, n(%)	206 (6.9)	85 (3.3)§¤	66 (50)¤	52 (22)§	<0.001

*Continuous variables given as median [IQR: 25;75]
CABG= Coronary Artery Bypass Grafting; ACEI= Angiotensin-Conversting-Enzym Inhibitor; ARBs= Angiotensin Receptor Blockers ; SBP= Systolic Blood Pressure ; HF= Heart Failure ; CK= Creatin Kinase ; LVEF= Left Ventricular Ejection Fraction
§ p<0.005 vs Prior AF
¤ p<0.005 vs NOAF

Table 2. Total population in-hospital and 1-year post-discharge events

	Free AF n=2737	Prior AF n=158	NOAF n=278	p-value
In-hospital Events				
All-cause mortality, n(%)	164 (6)§¤	28 (17.7)	42 (15.1)	<0.001
CV mortality, n(%)	156 (5.7)§¤	27(17.1)	41(14.7)	<0.001
Non CV mortality, n(%)	8 (4.9)	1 (3.6)	1 (2.4)	0.76
Reinfarction, n(%)	35(1.3)¤	4(2.5)	10(3.6)	0.007
Stroke, n(%)	45 (1.6)§	7(4.4)	9 (3.2)	0.011
Major bleeding (BARC 3 or 5), n(%)	155 (5.8)¤	14 (9.2)	34 (12.5)	<0.001
HF (Killip ≥3), n(%)	271 (9.9)§¤	41 (25.9)	93 (33.5)	<0.001
Severe Ventricular Arythmias, n(%)	219 (8)¤	16 (10.1)¤	58 (20.9)§	<0.001
Severe atrioventricular block, n(%)	150 (5.5)¤	11(7)¤	40 (14.4)§	<0.001
One-year post-discharge events				
All-causes mortality, n(%)	96 (4.3)§¤	22 (20.6)¤	25 (12.1)§	<0.001
CV mortality, n(%)	52 (2.4)§¤	14 (13.5)	19 (9.2)	<0.001
Non CV mortality, n(%)	37 (15.1)§¤	6 (5.6)	4 (1.9)	0.006
Readmission for HF, n(%)	91 (4.2)§¤	19 (21.3)	26 (13.8)	<0.001
MACE, n(%)	198 (9.8)§¤	34 (35.8)	46 (24.1)	<0.001
Reinfarction, n(%)	43 (2.1)	4 (4.5)	3 (1.7)	0.29
Stroke, n(%)	18 (0.8)	2 (2.2)	1 (0.5)	0.33
Severe Ventricular Arythmias, n(%)	12 (0.7)	2 (3.1)	2 (1.4)	0.08

CV= Cardiovascular; HF = Heart Failure ; MACE = Major Cardiovascular Events (cardiovascular mortality, Stroke, reinfarction, readmission for heart failure)
§ p<0.005 vs Prior AF
¤ p<0.005 vs NOAF

Table 3. Multivariate analysis predicitve factors 1-year events

A. Prior AF versus free AF

	CV mortality		Readmission for HF	
	HR (IC95%)	**p-value**	**HR (IC95%)**	**p-value**
Prior AF	**2.006 (0.889;4.528)**	**0.093**	**2.501 (1.402;4.463)**	**0.001**
Sexe male	1.46 (0.688;3.096)	0.32	0.704 (0.419;1.182)	0.18
Age (yrs)	1.053 (1.02;1.088)	0.001	1.066 (1.044;1.09)	<0.001
Weight (kg)	0.986 (0.962;1.01)	0.25	0.994 (0.98;1.009)	0.50
Hypertension	0.81 (0.408;1.604)	0.54	1.487 (0.899;2.459)	0.12
Current smoker	1.094 (0.475;2.523)	0.83	2.917 (1.723;4.938)	<0.001
History of stroke	2.043 (0.771;5.416)	0.15	1.078 (0.43;2.696)	0.87
SBP (mmHg)	0.991 (0.981;1.001)	0.10	1 (0.993;1.007)	0.91
Creatinin (µmol/L)	1.001 (1;1.003)	0.026	1.001 (1;1.003)	0.017
Angioplasty	0.443 (0.233;0.842)	0.013	1.31 (0.755;2.272)	0.33
CK peak (UI/L)	0.999 (0.999;1)	0.88	1 (1;1)	0.035
Killip ≥ III	1.957 (0.915;4.187)	0.08	2.173 (1.322;3.572)	0.002
LVEF (%)	0.966 (0.939;0.994)	0.020	0.933 (0.915;0.952)	<0.001

B. NOAF versus free AF

	CV mortality		Readmission for HF	
	HR (IC95%)	**p-value**	**HR (IC95%)**	**p-value**
NOAF	**2.485 (1.323;4.67)**	**0.004**	**1.97 (1.223;3.174)**	**0.005**
Sexe male	1.083 (0.563;2.083)	0.81	0.606 (0.376;0.977)	0.039
Age	1.059 (1.028;1.092)	0.000	1.058 (1.036;1.08)	<0.001
Weight	0.984 (0.962;1.006)	0.16	0.995 (0.981;1.01)	0.55
Hypertension	0.877 (0.456;1.686)	0.69	1.517 (0.947;2.43)	0.08
Smoke	1.235 (0.547;2.787)	0.61	2.249 (1.317;3.842)	0.002
Stroke	1.398 (0.542;3.606)	0.49	0.89 (0.384;2.061)	0.78
SBP	0.997 (0.988;1.006)	0.59	0.999 (0.993;1.006)	0.99
Creatinin	1.001 (1;1.003)	0.031	1.001 (1;1.002)	0.031
Angioplasty	0.355 (0.198;0.638)	0.000	1.674 (0.942;2.975)	0.07
CK peak (UI/L)	0.999 (0.999;1)	0.86	1 (1;1)	0.008
Killip ≥ III	1.813 (0.897;3.664)	0.10	1.641 (1.01;2.668)	0.045
LVEF	0.984 (0.956;1.012)	0.26	0.935 (0.917;0.953)	0.000

AF = Atrial Fibrillation ; NOAF = New Onset of AF; CV = Cardiovascular ; HF = Heart Failure ; HR = Hazard Ratio; SBP = Systolic Blood Pressure; CK = Creatin Kinase, LVEF = Left Ventricular Ejection fraction

Table 4. Baseline characteristics of NOAF population

	Total NOAF (n=278)	Early NOAF (n=127)	Late NOAF (n=151)	p-value
Baseline Characteristics				
Age (years) *	77 [64;83]	74 [56;82]	78 [70;84]	0.001
Weight (%) *	72 [64;81]	72 [63;82]	73 [65;81]	0.81
Male gender, n(%)	189 (68)	85 (67)	104 (68.9)	0.72
History of hypertension, n(%)	176 (63.3)	73 (57.5)	103 (68.2)	0.06
History of diabetes mellitus, n(%)	68 (24.5)	27 (21.3)	41 (27.2)	0.25
History of dyslipidemia, n(%)	146 (52.5)	65 (51.2)	81 (53.6)	0.68
Current smoker, n(%)	59 (21.4)	39 (30.7)	20 (13.4)	<0.001
History of myocardial infarction, n(%)	28 (10.1)	11 (8.7)	17 (11.3)	0.47
History of CABG, n(%)	7 (2.5)	2 (1.6)	5 (3.3)	0.35
History of Angioplasty, n(%)	17 (6.1)	7 (5.5)	10 (6.6)	0.70
History of stroke, n(%)	21 (7.6)	7 (5.6)	14 (9.3)	0.24
History of renal failure, n(%)	12 (4.3)	3 (2.4)	9 (6)	0.14
Medical therapy at admission				
Amiodarone, n(%)	2 (0.7)	0 (0)	2 (1.3)	0.19
ACEI/ARBs, n(%)	95 (34.3)	36 (28.6)	59 (39.1)	0.06
Beta-blockers, n(%)	70 (25.3)	28 (22.2)	42 (27.8)	0.28
Statins, n(%)	63 (22.7)	28 (22.2)	35 (23.2)	0.85
Antiplatelet, n(%)	77 (27.8)	31 (24.6)	46 (30.7)	0.26
Anticoagulant, n(%)	4 (1.3)	0 (0)	4 (2.7)	0.11
Charasteritics of qualifying myocardial infarction				
SBP at baseline (mmHg) *	128 [110;146]	130 [110;143]	127 [110;150]	0.87
HF at baseline (Killip ≥ II)	83 (30.3)	30 (24)	53 (35.6)	0.03
Creatinin value at baseline (µmol/L) *	91 [75;116]	89 [72;114]	90 [73;116]	0.81
CK peak (UI/L) *	1767 [589;3438]	1970 [822;3537]	1606 [465;3241)	0.16
CRP max (mg/L) *	32 [4;127]	14 [4;83]	54 [7;133]	0.00
Anterior myocardial infarction, n(%)	114 (45.8)	51 (43 .6)	53 (47.7)	0.51
Medical therapy, n(%)	41 (16)	14 (11.8)	27 (19.7)	0.01
Fibrinolysis, n(%)	24(8.6)	14(11)	10 (6.6)	0.19
Angioplasty, n(%)	214 (78.7)	106 (85.5)	108 (73)	0.012
Multivessel disease n(%)	151 (60.9)	66 (56.4)	85 (64.9)	0.172
Time from symptoms to reperfusion (h) *	5 [4.3;8.3]	4.7 [4.2;7.9]	6.4 [4.5;10.7]	0.24
Complete revascularization, n(%)	97 (42.9)	51(45.9)	46 (40)	0.36
LVEF (%) *	45 [35;50]	45 [38;50]	40 [35;50]	0.035
Hosiptal duration (d) *	9 [5 ;15]	7 [4;13]	11 [7 ;18]	<0.001
Medical therapy at discharge				
Amiodarone, n(%)	91 (38.6)	33 (30.3)	58 (45.7)	0.015
ACEI/ARBs, n(%)	195 (83)	93 (86 .1)	102 (80.3)	0.23
Beta-blockers, n(%)	202 (87.7)	98 (89.9)	109 (85.8)	0.34
Statins, n(%)	209 (88.6)	96 (88.1)	113 (89)	0.82
Antiplatelet, n(%)	228 (96.6)	105 (96.3)	123 (96.9)	0.82
Anticoagulant, n(%)	52 (21.8)	19 (16.7)	33 (26)	0.07

*Continuous variables given as median [IQR: 25;75]
CABG= Coronary Artery Bypass Grafting; ACEI= Angiotensin-Converting-Enzym Inhibitor; ARBs= Angiotensin Receptor Blockers ; SBP= Systolic Blood Pressure ; HF= Heart Failure ; CK= Creatin kinase ; LVEF= Left Ventricular Ejection Fraction

Table 5. New AF patients in-hospital and one-year post-discharge events

	Early NOAF (n=127)	Late NOAF (n=151)	p-value
In-hospital Events			
All-causes mortality, n(%)	18 (14.2)	24 (15.9)	0.69
CV mortality, n(%)	18 (14.2)	23 (15.2)	0.80
Non CV mortality, n(%)	0 (0)	1 (4.2)	0.35
Reinfarction, n(%)	4 (3.1)	6 (4)	0.71
Stroke, n(%)	4 (3.1)	5 (3.3)	0.94
Major bleeding (BARC 3 or 5), n(%)	15 (12.2)	19 (12.8)	0.87
HF (Killip max ≥3), n(%)	35 (27.6)	58 (38.4))	0.056
Severe Ventricular Arythmias, n(%)	28 (22)	30 (19.9)	0.65
Severe atrioventricular block, n(%)	15 (11.8)	25 (16.6)	0.26
Persistant AF at discharge, n(%)	8 (6.3)	12 (7.9)	0.59
One-year post-discharge events			
All-causes mortality, n(%)	11 (11.3)	14 (12.7)	0.76
CV mortality, n(%)	8 (8.2)	11 (9.9)	0.67
Non CV mortality, n(%)	3 (3.1)	1 (8.3)	0.23
Readmission for HF, n(%)	10 (11.2)	16 (16.2)	0.32
MACE, n(%)	18 (20.5)	28 (27.2)	0.27
Reinfarction, n(%)	2 (2.5)	1 (1.1)	0.48
Stroke, n(%)	0 (0)	1 (1)	0.34
Severe Ventricular Arythmias, n(%)	0 (0)	2 (2.5)	0.19

CV= Cardiovascular; HF = Heart Failure ; MACE = Major Cardiovascular Events (cardiovascular mortality, Stroke, reinfarction, readmission for heart failure)

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La survenue de fibrillation atriale comme marqueur pronostique indépendant après un syndrome coronarien aigu avec élévation du segment ST: résultats issus du registre RIMA

ABSTRACT

Introduction : La fibrillation atriale (FA) est une complication fréquente après un syndrome coronarien aigu avec sus-décalage du segment ST (SCA ST+) mais son influence pronostique reste controversée, en particulier en regard de son délai de survenue. L'objectif de cette étude était donc d'étudier la valeur pronostique à 1 an de la FA après un SCA ST+, en distinguant les patients avec antécédent de FA de ceux avec survenue de FA post SCA ST+ (FA de novo).

Methodes : Entre janvier 2004 et décembre 2015, 3173 patients avec un SCA ST+ ont été consécutivement et prospectivement inclus dans le registre RIMA (Registre des Infarctus en Maine Anjou). Ils ont été divisés en 3 groupes selon la survenue de FA: 1) patients sans FA; 2) patients avec antécédent de FA; et 3) patients avec FA de novo. Nous avons définis 3 critères de jugements principaux à 1 an : la mortalité cardio-vasculaire, la réhospitalisation pour insuffisance cardiaque (IC) et la survenue d'un AVC. Les critères d jugements secondaires incluaient la survenue de complications intra-hospitalières et l'évaluation du délai de survenue de la FA de novo : survenue précoce <24h et survenue tardive ≥24h.

Resultats : 158 patients (5%) avaient des antécédents de FA et 278 (8.8%) ont développé une FA de novo. Les patients avec antécédents de FA étaient plus âgés (81[73;86] ans) avec plus de comorbidités mais les patients avec FA de novo étaient plus instables hémodynamiquement avec un pic de CPK plus élevé et une FEVG plus altérée (44[35;50]% versus 50[40;55]%). A 1 an, le taux de mortalité cardio-vasculaire était plus élevé en cas de FA (13.5% pour les antécédents de FA vs 9.2% pour la FA de novo, et 2.4% pour les patients sans FA, p<0.001). Après ajustement, seule la FA de novo était associée à la mortalité cardio-vasculaire (odd ratio 2.49; IC 95% 1.32-4.67; p=0.004), mais les 2 types de FA étaient associées à la réhospitalisation pour IC. Il n'y avait pas de différence sur la survenue d'AVC entre les antécédents de FA, la FA de novo et les patients sans FA (2.2%, 0.5% et 0.8% respectivement, p=0.327). Enfin, il n'y avait pas de différence en regard du délai de survenue de la FA de novo, qu'elle soit précoce (n=127) ou tardive (n=151).

Conclusion : Seule la FA de novo était associée à une mortalité cardio-vasculaire à 1 an plus importante. La FA de novo ne devrait donc pas être considérée comme un simple évènement intercurrent du SCA ST+ mais comme un marqueur pronostic fort. Une prise en charge plus spécifique de la FA de novo pour améliorer le pronostic de ces patients reste à étudier.

Mots clés: fibrillation atriale, SCA ST+, pronostic, mortalité cardio-vasculaire

New-onset atrial fibrillation as an independent prognostic marker after ST-segment elevation myocardial infarction: results from the RIMA registry

ABSTRACT

Aims : Atrial Fibrillation (AF) is common in ST-segment elevation myocardial infarction (STEMI) but its influence on prognosis remains controversial, particularly considering timing of occurrence. Therefore, we examined the one-year prognostic value of AF in STEMI, distinguishing patients with prior AF, from patients with new-onset AF (NOAF).

Methods : Between January 2004 and December 2015, 3173 patients with STEMI were consecutively and prospectively enrolled in the RIMA registry (Registre des Infarctus en Maine Anjou). They were divided into 3 groups according to the timing of AF occurrence: 1) patients free for AF; 2) patients with prior AF; and 3) patients with NOAF. We defined 3 primary outcomes at 1-year post-discharge**:** cardiovascular mortality, readmission for heart failure (HF) and stroke. The secondary included intra-hospital events and the assessment of temporal onset of NOAF: early NOAF <24h and late NOAF ≥24h.

Results : 158 patients (5%) had prior AF, and 278 (8.8%) had NOAF. Prior AF patients were significantly older (81[73;86] years) with more comorbidities but NOAF patients were more hemodynamically unstable with a greater creatin kinase (CK) peak and a lower left ventricular ejection fraction (LVEF) (44[35;50]% versus 50[40;55]%). At 1-year follow-up, rate of cardiovascular mortality were greater in case of AF (13.5% for prior AF vs 9.2% for NOAF, compared with 2.4% for free AF, p<0.001). After adjustment, only NOAF was related to cardiovascular mortality (hazard ratio 2.49; 95% CI 1.32 to 4.67; p=0.004), but the both types of AF were related to readmission for HF. There was no significant difference on stroke between prior AF, NOAF, and free AF (2.2%, 0.5% and 0.8% respectively, p=0.327). Finally, outcomes did not differ between early (n=127) and late (n=151) NOAF.

Conclusion : Only NOAF but not prior AF was associated with 1-year cardiovascular mortality. NOAF should not be considered as an intercurrent event of STEMI but rather as a strong prognostic marker. Whether a specific management of NOAF may improve the prognosis of these patients remains to be studied.

keywords : atrial fibrillation, STEMI, prognosis, cardiovascular mortality

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