



## Silent Atrial Fibrillation Complicating Acute Coronary Syndrome: Determinants and Prognosis

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### Abstract

**Introduction:** Silent atrial fibrillation (AF) has been suggested to be frequent after acute coronary syndrome. Continuous ECG monitoring (CEM) has been shown to improve AF screening in patients at risk of stroke.

**Objectives:** We aimed to assess the incidence and prognosis of silent AF in patients with acute coronary syndrome.

**Methods:** All the consecutive patients with acute coronary syndrome were prospectively analyzed by CEM  $\geq$  24h after admission at intensive care of cardiology department CHU IBN ROCHD Casablanca. Silent AF was defined as asymptomatic episodes lasting at least 30s. The population was divided into three groups: no-AF, silent AF and symptomatic AF.

**Results:** Among the 84 patients, 13 (16%) developed silent AF and 5 (5%) symptomatic AF. Compared with the no-AF group, patients with silent AF were markedly older (70 vs. 55 years,  $p < 0.001$ ), more frequently women (45% vs. 25%,  $p = 0.006$ ) and less likely to be smokers (25% vs. 30%,  $p < 0.001$ ). They had impaired left ventricular ejection fraction (LVEF) and left atrial (LA) enlargement. By multivariate analysis, age, history of AF, indexed LA area and LVEF were identified as independent predictors of silent AF. In-hospital heart failure and death rates were markedly higher in silent AF group when compared with no-AF patients (40% vs. 20.0% and 10% vs. 2%, respectively).

**Conclusion:** Our large prospective study showed for the first time that silent AF is more frequent than symptomatic AF after acute coronary syndrome. Our work suggests that indexed LA area could help to predict the risk of developing silent AF. Moreover, the onset of silent AF is associated with worse hospital prognosis.

**Keywords:** Silent Atrial Fibrillation; Acute Coronary Syndrome; Echocardiography, Prognosis

### Abbreviations

AF: Atrial fibrillation; CEM: Continuous ECG Monitoring; LA: Left Atrial; LVEF: Left Ventricular Ejection Fraction; USIC: Cardiac Intensive Care Unit; MI: Myocardial Infarction

### Introduction

Atrial fibrillation (AF) is a disorder of the supra-ventricular rhythm that consists of loss of the atrial systole. It is the most frequent arrhythmia in patients with and without structural heart disease, with an increasing incidence mainly due to the aging of the population [1-3]. Data from large epidemiological studies has clearly shown that AF is associated with increased mortality and morbidity. The combination of atrial fibrillation and congestive heart failure is of particular concern since it appears that the onset of either condition has a marked negative impact on the death of the other patient [4,5].

Atrial fibrillation can also complicate acute coronary syndromes, particularly STEMI. In this clinical context, the occurrence of AF is of particular importance, since rapid and irregular ventricular rates during arrhythmia can lead to further deterioration of the coronary circulation and left ventricular function [6-8].

### Study Objectives

We therefore conducted this work to clarify the incidence, de-

terminants and the prognostic role of AF in the acute phase of myocardial infarction, whether silent or symptomatic.

### Materials and Methods

We therefore included, all patients hospitalized during the year 2018 in the cardiac intensive care unit (USIC) of the cardiology department of the Ibn Rochd University Hospital of Casablanca, for the management of an IDM in acute phase, to provided that they were over 18 years of age, that the duration of ECG monitoring by the scope was  $\geq$  24h and finally that they benefited from an ultrasound measurement of the LVEF and the parameters of the size of the LA (diameter, surface and volume).

The detection of AF episodes was done on the patient's scope by the doctors assigned to the USIC. The rhythm was recognized as AF on the complete irregularity of the RR intervals and was controlled by a resting ECG performed at the patient's bed, and only the episodes whose duration was greater than 30 seconds were qualifying and were therefore retained as AF episodes. The patients were then classified into three distinct groups: no AF, silent AF and symptomatic AF. In addition, each admission patient benefited from an ultrasound evaluation of the LVEF on the one hand, measured by the Simpson method in apical incidence 4 cavities (A4C) and 2 cavities (A2C) and size parameters on the other hand. This evaluation of

the MA was based on the measurement of the anteroposterior diameter in para-sternal long axis incidence, the area and the volume in A4C and A2C. All the values of these measurements were related to the body surface.

Continuous data are presented as the median (25<sup>th</sup> to 75<sup>th</sup> percentile) or mean ± standard error. A Kolmogorov-Smirnov test was carried out to test the normal distribution of the population. For the comparison of two groups of continuous data, the Mann-Whitney rank test or the Student’s t-test were used and a one-factor ANOVA or one-factor Kruskal Wallis analysis was performed for the comparisons between three groups.

The dichotomous data presented as a percentage were compared by the Chi square or Fisher test.

### Results

A total of 128 patients were candidates for inclusion, but only 84 met the inclusion criteria.

Among them, 18 patients developed at least one episode of AF during the acute phase of their MI, for a total incidence of 21.2%. 13 patients developed silent AF (16%) and 5 patients with symptomatic AF, 5%. Patients with AF episodes of any type were older (81 vs. 62 years), more often hypertensive, more likely to be female, and less prone to tobacco poisoning than patients without AF after MI.

They were also more likely to have a history of cardiovascular disease, including coronary artery disease (CAD), stroke, previous AF and kidney failure.

Therefore, they were more likely to take drugs that affect the cardiovascular system. Compared to patients with symptomatic AF, patients who developed silent AF were similar in age (~ 80 years), but were more frequently female, and significantly more likely to be smokers (5 versus 24% and 2 versus 7%, respectively). However, they were less likely to receive prior treatment for AF and AVK.

The GRACE risk score was much higher in patients with AF, regardless of the type of AF. The location and type of MI were similar for the three groups.

Patients with AF had lower creatinine clearance and higher CRP levels than patients without AF. Glucose levels gradually increased in all three groups. There was no difference between the three groups for the troponin peak Ic.

### Analysis of patient monitoring

According to monitoring data, patients with silent AF had higher heart rates, including maximum, median, and minimum heart rates, than patients without AF, but below those of patients with symptomatic AF.

SVES (Supraventricular extra-systole) episodes were more frequent in the FA groups.

The rates of occurrence of VT or VF in patients with silent AF were similar to those in patients without AF.

In contrast, patients with symptomatic AF had significantly more ventricular arrhythmias than patients with silent AF or without AF (24% versus 5.2% and 4.3%, respectively).

### Ultrasound analysis

The median LVEF gradually decreased in all three groups. In particular, the LVEF was more impaired in patients with silent AF than in those without AF (50% versus 55%).

Compared to the group without AF, patients with silent AF had significant left atrial enlargement (OG), including an indexed OG diameter (2.4 (2.0 - 2.8) versus 2, 1 (1.8 - 2.5) cm/m<sup>2</sup>), an indexed OG area (10.8 (8.6 - 12.6) vs 9.3 (7.5 - 11.0) cm<sup>2</sup>/m<sup>2</sup>) and the volume of the indexed OG (29.5 (21.3 - 43.8) vs 24.4 (18.2 - 33.1) cm<sup>3</sup>/m<sup>2</sup>).

On the other hand, the enlargement of the OG, including the area and the indexed volume in patients with silent AF was lower than in patients with symptomatic AF.

### Therapies introduced at the USIC

Patients with AF were less likely to receive beta blockers and an ACE inhibitor and to undergo percutaneous coronary intervention (b 0.001) (Table). However, they were more frequently treated with diuretics, amiodarone and AVK than patients without AF.

### Determinants of AF

In order to determine the factors associated with the onset of AF during the acute phase of MI, we performed a backward logistic regression analysis. After adjustment for the confounding variables, age, enlargement of the GO were identified as independent explanatory variables for the development of silent AF (Table 1). LVEF and heart rate were additional variables associated with symptomatic AF.

### Analysis of the results

Only a few patients developed stroke during their hospital stay, with a similar rate in all groups (without AF: 4 (0.6%), silent AF: 0 (0%), symptomatic AF: 1 (2.2%), p = 0.240).

Variables	Silent AF			Symptomatic AF		
	OR	95% IC	p	OR	95% IC	p
AF history	3.07	1.38 - 6.82	0.006	8.53	3.72 - 19.58	< 0.001
Age in year	1.06	1.04 - 1.07	< 0.001	1.05	1.02 - 1.08	0.003
LA area indexed in cm <sup>2</sup> /m <sup>2</sup>	1.11	1.04 - 1.18	0.002	1.23	1.08 - 1.41	0.002
FEVG < 40%	-	-	-	3.22	1.45 - 7.14	0.004
HR on admission	-	-	-	1.03	1.01 - 1.05	< 0.001

**Table 1:** Multivariate logistic regression analysis for the occurrence of silent or symptomatic AF.

Compared to patients without AF, symptomatic AF was associated with a significantly increased risk of heart failure and death during hospital stay (20% vs 2% and 38% vs 1.3%, respectively,  $p < 0.001$ ) (Table 2).

More surprisingly, patients with silent AF had a poorer hospital prognosis than patients without AF, characterized by a higher rate of CI episodes, which were twice as frequent in the silent AF group (41.8%, versus 21.0%, respectively). In addition, mortality was significantly higher in the silent FA group (10.4% versus 1.3%).

	No AF N = 66	Silent AF N=13	Symptomatic AF N = 5	p
Heart failure	2 (2%)	5 (38%)	1 (20%)	< 0.001
Intra-hospital mortality	1 (1%)	2 (16%)	0	< 0.001

**Table 2:** Evolution of patients.

A multivariate logistic regression analysis for mortality estimation was performed taking into account silent AF and symptomatic AF as qualitative variables without AF as a reference group (Table 3). The LVEF < 40% and the GRACE risk score were included as co-variables.

The final multivariate model showed that AF, symptomatic or not, and the GRACE risk score were independent explanatory variables for death in hospital after MI.

Silent AF was associated with a significantly increased risk of

Variable	OR	IC 95%	p
Symptomatic AF	5.22	(1.71 - 15.97)	0.004
Silent AF	3.65	(1.44 - 9.23)	0.006
GRACE score	1.03	(1.02 - 1.05)	< 0.001

**Table 3:** Multivariate logistic regression analysis for estimation of intra-hospital mortality.

death in hospital (OR (95% CI): 3.65 (1.44 - 9.23)), although the risk was lower than that of Symptomatic AF (OR (95% CI): 5.22 (1.71 - 15.97)). This model gave 96% of the correct classification. When individual variables associated with mortality were included in the model instead of the GRACE risk score, silent and symptomatic AF remained strongly associated with mortality (OR (95% CI): 3.34 (1.28 - 8.77) and 4.37 (1.41 - 13.59), respectively), beyond age and LVEF (OR (95% CI): 1.05 (1.01 - 1.10) and 0.93 (0.90 - 0.97), respectively).

**Discussion**

The appearance of symptomatic AF after MI is frequent, ranging from 2% to more than 20% [9-11]. Our study found a fairly low incidence of symptomatic AF (5%). This low rate could be explained by the duration of screening, which only covered the first 48 hours of hospitalization. In addition, as our study reflects current clinical practice, a greater proportion of patients have received chronic long-term treatment with cardioprotective drugs (beta-blockers, ACE inhibitors or statins) and acute strategies, particularly for

revascularization, compared to older studies. A decrease in the incidence of AF after MI over the past decade has been reported [12-14]. In accordance with data from the literature, our study encountered the main predictors of symptomatic AF, namely old age, history of AF, impaired LVEF, elevated heart rate and LA dilation [10]. To our knowledge, our study shows that the ultrasound markers of LA dilation are associated with the onset of AF after MI. Patients with symptomatic AF had a considerably higher risk of mortality (OR (95% CI): 5.22 (1.71 - 15.97)).

Our study showed that silent AF after MI is three times more frequent than symptomatic AF [8,9]. The measurement of the LA parameters, in particular of the indexed LA zone, could help predict the risk of developing silent AF after MI. Moreover, silent FA is associated with worse diagnosis, increased risk of heavy failure and death in hospital. It shares a similar risk factor with symptomatic AF [10], which includes old age and a history of AF. In addition, the analysis of the ultrasound parameters showed that patients in the silent AF or symptomatic AF groups had an altered FEVG and an enlarged LA. These results are in agreement with studies showing a relationship between dilation of LA and the onset of AF or recurrent AF after an ablation procedure [15-17]. However, in patients with silent AF, the LVEF was higher and LA enlargement was lower than in symptomatic AF patients. This progressive alteration of the LVEF and LA dilation reinforces the hypothesis that silent AF is an early stage before symptomatic disease.

One of the main conclusions of our study is that silent AF is associated with a dramatic worsening of the hospital prognosis in the acute phase of MI, characterized by a higher incidence of heart failure and a risk of death at excessive hospital. In the ASSERT population study, subclinical AF was associated with a worse prognosis, characterized by an increased risk of stroke or systemic embolism (HR (95% CI): 2.50 (1.28 4.89)) [8,18-20].

**Conclusion**

Silent AF is a frequent and serious event in the acute phase of MI that severely affects the prognosis of patients and which must be taken into account in the management of patients.

The main result of our work concerns the prognosis, since it provides proof of the negative prognostic impact of the occurrence of silent AF with hospital mortality.

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**Conflict of Interest**

None.

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