

## Research Article

# Typical Atrial Flutter in acute coronary syndrome with ST segment elevation: incidence, predictive factors and related mortality.

Hanane ZOUZOU

Professor in cardiology, Department of Medicine Batna 2 university Algeria

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### Abstract:

**Background:** Typical Atrial Flutter in acute coronary syndrome with ST segment elevation is very rare and never reported as a separate electrocardiographic entity, but associated with atrial fibrillation.

Its incidence isn't reported in the literature, and no data about its predictive factors or related mortality, also its epidemiological data is lacking in Algeria.

**Aims:** The main objective of our study is the determination of the frequency of typical atrial flutter in acute coronary syndrome with ST segment elevation, the secondary objective was the analysis of its predictive factors, and related mortality.

**Methods and materials:** In this prospective study, conducted in the cardiology department of Hussein Dey hospital (Algiers-Algeria), 467 patients with acute coronary syndrome with elevated ST segment (87 women and 380 men) were enrolled between 28 February 2014 and 16 July 2015. The average age is  $60 \pm 13$  years; at admission, a Holter recorder was attached for continuous ECG monitoring during 48 hours

Kruskal's ANNOVA or H tests were used for comparison of quantitative variables,  $\chi^2$  test or Fisher's exact test, were used for qualitative variables, all tests were performed with 1<sup>st</sup> species risk of 5%.

**Results:** The frequency of typical atrial flutter is 0.4 % (2 patients), CI 95%: [0%-1%], multivariate analysis identified right heart failure as the only predictive factor.

The risk of mortality expressed by Hazard Ration (HR) is 27 (CI95%: [3.5-207],  $p = 0.001$ ); right heart failure is the only predictive factor of mortality identified in our study.

**Conclusion:** typical atrial flutter is very rare in acute coronary syndrome with elevated ST segment, its predictive factor according to our study is right heart failure, and its occurrence increases the risk of hospital mortality.

**Keywords:** Acute Coronary Syndrome, typical atrial flutter, Right heart failure.

## Introduction

Typical Atrial Flutter in acute coronary syndrome with ST segment elevation is very rare and never reported as a separate electrocardiographic entity, but associated with atrial fibrillation.

Atrial flutter with rapid ventricular response may be dangerous and causing hemodynamic instability.

Several mechanisms have been proposed to explain atrial flutter like ischemia and/or necrosis.

Its incidence isn't reported in the literature, and no data about its predictive factors or related mortality, also its epidemiological data is lacking in Algeria.

The main objective of our study is to determine the frequency of typical atrial flutter in acute coronary syndrome with ST segment elevation, during the first 48 hours of hospitalization, while the secondary objective is the analysis of its predictive factors and the related mortality.

## Methods and materials

We prospectively studied a group of 467 consecutive patients (380 men and 87 women; mean age  $60 \pm 13$  years) who presented acute coronary syndrome with ST segment elevation and admitted in cardiology department of Hussein-Dey hospital (Algiers, Algeria), between 28th February 2014 and 16th

August 2015.

At emergency department admission, an ECG Holter recorder was attached for continuous ECG monitoring during 48 hours, the 17-leads surface ECG recorded at admission and repeated during hospitalization, Doppler Echocardiography, coronary angiography, and biological assessment were performed in the majority of patients.

The most important rhythm and conduction disorders were identified, the patients with the same type of disorder are grouped together, and the name assigned to each group is that of the disorder that characterizes it; there are overlaps between the groups, so that several disorders may exist in the same patient.

The constitution of each group of the rhythm disorder implies the constitution of the opposite group without the corresponding disorder, the latter group is used for the comparative study; each group is therefore described and then compared to the corresponding opposite group.

In this sub study, the group of patients with typical atrial flutter was compared to the rest of patients without typical atrial flutter.

## Statistical analysis

Data are presented as mean  $\pm$  SD, median, or frequency

(percentage) where appropriate. Continuous variables were compared using the ANNOVA test, or H Kruskal Wallis test.  $\chi^2$  tests and Fisher's exact test were performed to distinguish differences between categorical variables. Statistical significance was defined as  $p < 0.05$ . In this first step, we used EPI-info version 6.0. A multivariate Binary regression was performed to determine the predictor factors of arrhythmias, and Cox regression was performed to identify the predictor factors of mortality.

The magnitude of the relationship between typical atrial flutter and their predictive factors is estimated by the Cramer V coefficient, a coefficient lower than 0.2 is in favor of a weak link, between 0.2 and 0.5: moderate link, greater than 0.5: strong link.

The statistical analysis was performed using SPSS Statistics (release 17).

## Results

**Incidence:** The characteristics of the 467 patients included in our study are shown in Table 1; Two patients had presented typical atrial flutter at admission or during hospitalization, so its frequency in this present study is 0.4 % (2 patients), CI 95% [0%-1%].

This group of patients included a 72-year-old woman and a 56-year-old man. The mean age was  $64 \pm 11.31$  years;

The woman had presented typical atrial flutter at admission, with rapid ventricular response (heart rate: 150 beats /min); the man had presented atrial flutter one hour after the beginning of the continuous ECG recording, the duration of the episode was 8 hours 15 minutes, with variable ventricular conduction 2/1, 3/1, et and heart rate varied between 100 and 150 beats/min. [Figure1]

Cardiovascular risk factors, clinical characteristics, medical history, treatment and evolution are shown in Table 1.

The Surface ECG had shown, inferobasal ACS in the two patients, the woman had also presented right ventricular extension.

The duration of the QRS complex was 100 msec in the woman, and 60 msec in the man, the mean amplitude of the ST segment elevation was 2 mm, the mean amplitude of the ST segment depression was 1 mm in the two patients, the amplitude of the T wave was 2 mm in the woman and 3 mm in the man, the corrected QT was 421 msec in the woman and 439 msec in the man.

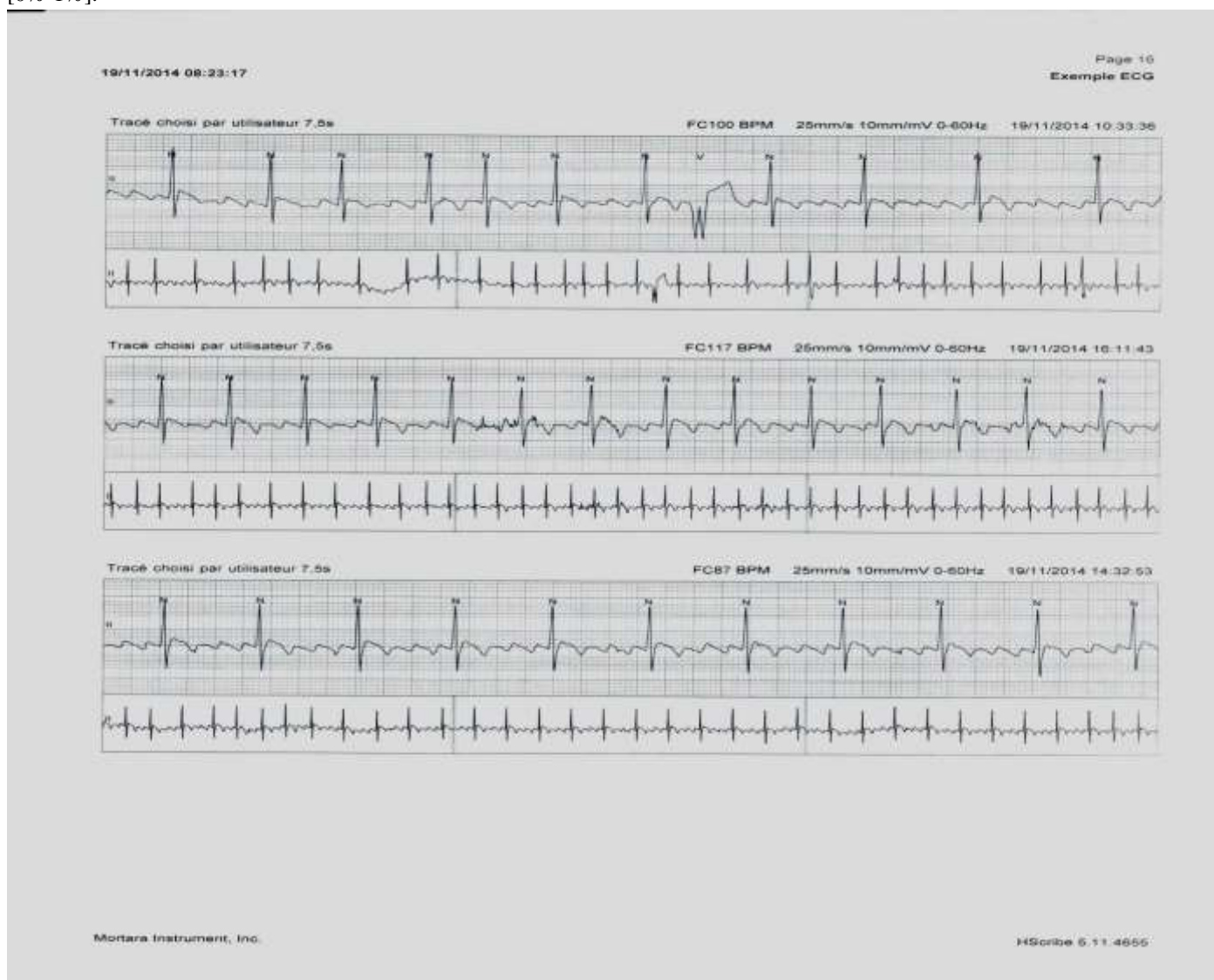


Figure 1: Holter ECG showed typical atrial flutter in acute coronary syndrome with ST segment elevation with variable ventricular conduction 2/1 and 3/1.

<b>Table 1: Characteristics of the study patients.</b>				
	Patients with typical atrial flutter (n = 2)	Patients without typical atrial flutter (n = 465)	P-value	
Mean age	64.00	60.103	0.668	NS
Females	1	86	0.338	NS
Early consultation (within 6 hours)	1/2	342/460	0.449	NS
Hypertension	2/2	207/465	0.199	NS
Diabetes	1/2	155/465	0.556	NS
Current smoking	0/2	235/465	0.246	NS
hyperlipidemia	0/2	67/462	0.731	NS
GRACE score $\geq$ 155	1/2	166/464	0.588	NS
Cardiogenic shock	1/2	17/465	0.075	NS
Left heart failure	0/2	63/465	0.748	NS
<b>Right heart failure</b>	<b>1/2</b>	<b>10/465</b>	<b>0.046</b>	<b>S</b>
Persistence of chest pain	1/2	27/465	0.116	NS
Mean SBP	90.00	130.561	0.060	NS
Mean DBP	55.00	77.596	0.051	NS
Hospital mortality (first 48 hours)	1/2	16/465	0.071	NS
Previous myocardial infraction	0/12	21/455	0.571	NS
<b>Electrocardiogram</b>				
Right ventricular ACS	1/2	41/465	0.171	NS
Extensive anterior ACS	0/2	168/465	0.409	NS
Inferior ACS	0/2	110/465	0.057	NS
Infero basal ACS	2/2	110/465	0.057	NS
Average QTc	430.000	417.667	0.690	NS
Persistence of ST segment elevation	1/2	29/463	0.125	NS
<b>Other associated arrhythmias</b>				
Atrial tachycardia	0/2	1/465	0.911	NS
Bursts of PAC	1/1	157/447	0.352	NS
Bursts of PVC	0/1	205/447	0.542	NS
<b>Medication before ACS</b>				
Beta blockers	0/2	36/428	0.851	NS
ARB	0/2	67/464	0.732	NS
ACE-inhibitor	0/2	35/464	0.855	NS
Lipid-lowering drugs	0/2	33/464	0.863	NS
Antiplatelet agents	0/2	40/464	0.835	NS
<b>Treatment at admission</b>				
Thrombolysis	2/2	404/465	0.755	NS
Primary or rescue percutaneous coronary intervention	0/1	14/328	0.957	NS
Beta blockers	1/2	185/465	0.638	NS
ACE-inhibitor	1/2	260/465	0.688	NS
Sympathomimetic agents	1/2	14/464	0.063	NS
Atropine	1/2	21/465	0.092	NS
<b>Echocardiography</b>				
Ejection fraction of left ventricle < 40 %	0/1	63/446	0.215	NS
Mean left atrium surface (cm <sup>2</sup> )	18.000	16.702	0.733	NS
Mean right atrium surface (cm <sup>2</sup> )	8.000	11.283	0.234	NS
Mean Diastolic diameter of right ventricle	23.000	24.764	0.627	NS
Mean Diastolic diameter of left ventricle	48.000	54.146	0.333	NS
<b>Coronary angiography</b>				

Severe coronary artery lesions	1/1	101/328	0.310	NS
Left main coronary artery severe lesion	0/1	12/328	0.963	NS
Left anterior descending artery lesion	1/1	208/328	0.635	NS
Left circumflex coronary artery lesion	1/1	117/327	0.359	NS
Right coronary artery lesion	0/1	139/327	0.576	NS
Two-vessel coronary artery disease	1/1	127/328	0.389	NS
Multi-vessel coronary artery disease	0/1	61/328	0.814	NS
TIMI flow grade 0	0/1	65/328	0.802	NS
<b>Biology</b>				
<b>Hemoglobin</b>	<b>8.800</b>	<b>13.173</b>	<b>0.007</b>	<b>S</b>
<b>Hemoglobin ≤ 9g/dl</b>	<b>1/2</b>	<b>9/460</b>	<b>0.042</b>	<b>S</b>
Average blood glucose	2.060	1.616	0.455	NS
Average blood urea g/l	0.340	0.374	0.852	NS
Average blood creatinine mg/l	13.000	11.827	0.805	NS
High-Sensitivity Troponin ≥ 5 ng/ml	1/1	158/417	0.380	NS
ACS: Acute Coronary Syndrome, ACE inhibitors: Angiotensin-Converting Enzyme inhibitors ARB: Angiotensin Receptor-Blocker, DBP Diastolic Blood Pressure, PAC: Premature Auricular Complexes, PVC : Premature Ventricular Complexes, QTc: Corrected QT interval, SBP: Systolic Blood Pressure.				

Treatment at admission and during hospitalization: Metalyse (Tenecteplase) as fibrinolytics treatment were administered in the two patients (100 %), one patient had presented typical atrial flutter at admission before any therapy, and one patient had presented typical flutter after thrombolysis.

Aspirin, Clopidogrel and Anticoagulants were administered in the two patients (100 %), beta blockers in one patient (50 %), ACE inhibitors in 1 patient (50 %), sympathomimetic agents in one patient (50 %), Atropine in 1 patient (50 %).

**Thrombolysis failure:** the persistence of chest pain and ST segment elevation after thrombolysis was observed in 1 patient.

**Doppler echocardiography** was performed in the man, his left ventricular fraction was 43 % was found in 10 patients (100%), left ventricular hypertrophy in 3 patients (30 %), the area of the left atrium: 18 cm<sup>2</sup>, that of the right atrium: 8 cm<sup>2</sup>, the diastolic diameter of the left ventricle: 48 mm, the diastolic diameter of the right ventricle was 23 mm, the systolic pulmonary blood pressure: 25 mm Hg, presence of inferior wall akinesia and absence of left ventricular hypertrophy.

**Holter ECG** was performed in the man patient; this exam had participated in the recording of atrial flutter, showed its duration and detected Premature Auricular Complexes.

**Evolution and complications:** the woman died 1 hour after admission

**Coronary angiography** was performed in 1 patient, who had severe stenosis of the left anterior descending and circumflex arteries.

**Predictive factors**

According to the univariate study, two variables had a statistically significant association with the occurrence of typical atrial flutter: Right heart failure and hemoglobin level ≤ 9g/dl (Table 2)

**Table 2: Univariate study: variables associated with typical atrial flutter**

Variables	RR	CI 95%	P
Right heart failure	41.45	2.77-620	0.04
Hemoglobin ≤ 9 g/dl	45.2	3.04-672.63	0.04

But after the multivariate analysis using binary logistic regression, one predictive factor was identified: right heart failure (Table 3)

**Table 3 : Predictive factor of typical atrial flutter**

Predictive factor	OR	CI 95%	P
Right heart failure	109	3.9-3265	0.007

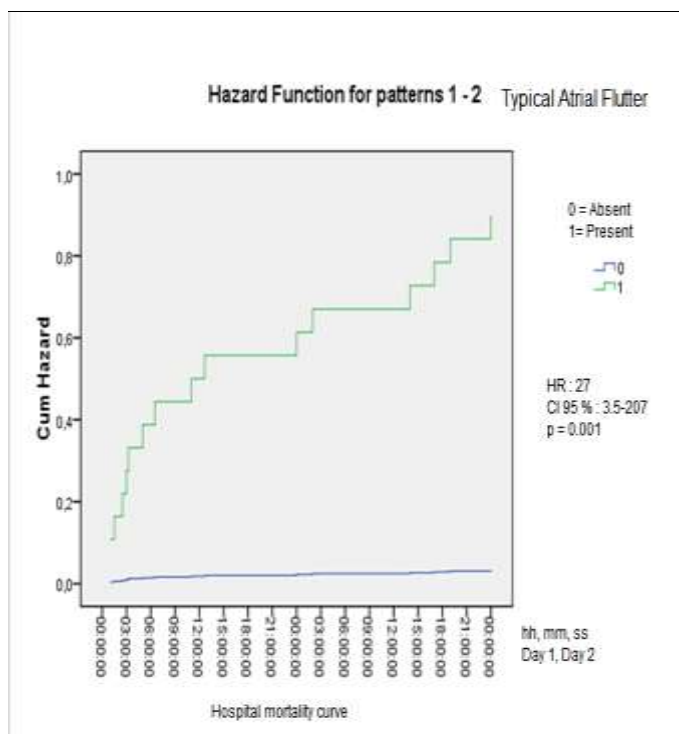
The magnitude of the relationship between atrial flutter and its predictive factor is moderate; the Cramer V coefficient exceeds 0.2. (Table 4)

**Table 4: Magnitude of the relationship between typical atrial flutter and its predictive factor**

Predictive factor of typical atrial flutter	Cramer V coefficient	P
Right heart failure	0.217	0.000

**Mortality**

Hospital mortality (first 48 hours), in the typical atrial flutter group is 50 % while it does not exceed 3.44% in the group without typical atrial flutter, (HR at 27 CI 95% [3.5-207], p = 0.001 (Figure 2)



**Figure 2: Hospital mortality curve (48h) in Typical Atrial Flutter group versus group without Typical Atrial Flutter**

Cox regression was used for univariate and multivariate studies of mortality predictors. According to the univariate study, some factors have a statistically significant association with the occurrence of mortality in the Typical Atrial Flutter group. (Table 5)

Factors	OR	IC95%	P
Female gender	3.2	1.1-8.7	0.023
Age ≥ 65 years	8	2.2-28.4	0.001
Right heart failure	54.9	19.3-156.2	0.000
Cardiogenic shock	195.6	54-702	0.000
Right ventricle acute coronary syndrome	5.6	1.9-16	0.001
Persistence of ST segment elevation	41	14-120	0.000
Persistence of chest pain	25.3	9.2-69.7	0.000
Diastolic blood pressure ≤ 60 mm Hg	3	1-8.5	0.035
Systolic blood pressure ≤ 100 mm Hg	8.4	3-22.9	0.000
Blood creatinine ≥ 17 mg/l	9.5	3-30	0.000
GRACE Score	7	2-25.5	0.002

According to multivariate analysis, right heart failure was identified as predictive factor of mortality. (Table 6)

Predictive factor of mortality in Typical Atrial Flutter group	OR	CI95%	P
Right heart failure	54	19-156	0.000

The strong magnitude of the relationship between mortality and its predictive factor was not significant in Typical Atrial Flutter group. (Table 7)

Predictive factors of mortality in Typical Atrial Flutter group	Cramer V Coefficient	P
Right heart failure	1	0.157

**Discussion**

Typical Atrial Flutter in acute coronary syndrome with ST segment elevation is very rare and much less frequent than atrial fibrillation, so never reported as a separate electrocardiographic entity, but associated with atrial fibrillation.

In the general population the incidence of atrial flutter is about 88/100,000 person-years [1], but its incidence in acute coronary syndrome has never been reported in the literature.

The surface ECG showed “negative saw tooth” flutter waves in inferior leads, it may be recorded on admission or appear during hospitalization, before or after thrombolysis, transient, paroxysmal or persistent; its occurrence complicates the management of the ACS and worsens the prognosis, because atrial flutter with rapid ventricular response may be dangerous and causing hemodynamic instability.

Typical atrial flutter illustrates the mechanism of macro re-entry in the right atrium; it’s a macro re-entrant tachycardia around the tricuspid annulus. [2]

The impulse travels up the atrium septum and then travels inferiorly down the right atrial free wall to re-enter the atrial septum through the cavo tricuspid isthmus. [2]

In ACS the pathophysiological mechanism of atrial flutter is complex and multifactorial, ischemia of the atrial wall or stretching following the increase in intra-atrial pressure constitute the substrate for the installation of this arrhythmia, inflammation, autonomic nervous system, hormonal activation participate in its initiation and perpetuation, thus the alteration of right ventricular function and increased filling pressures, inflammation of the pericardium, hypoxia, hypokalemia, catecholamines, sinus dysfunction, promote the installation of atrial flutter [3].

The diagnosis of persistent typical atrial flutter is usually obvious, but for intermittent and short term episodes the diagnosis may be difficult, so Holter ECG may be useful in those cases.

The incidence of typical atrial flutter in our study was 0.4 % (2 patients), CI 95% [0 %-1%]; this incidence is very low compared to other arrhythmias.

According to our study, right ventricular heart failure was identified as predictive factor of typical atrial flutter, this could be related to right acute coronary syndrome, dilation of right ventricle, and increased filling pressures with dilation of right atrium.

Right atrium wall ischemia and/or necrosis may contribute to occurrence of atrial flutter.

In our study, in-hospital mortality (first 48 hours), in the typical atrial flutter group is about 50 %, with HR at 27, so occurrence

of typical atrial flutter increases in-hospital mortality. The right ventricular heart failure is the predictive factor of mortality, which could be related to hemodynamic instability [4].

### Conclusion

Typical atrial flutter in acute coronary syndrome with ST segment elevation is rare, never reported in the literature. In our study we reported its incidence, predictive factor and also related mortality.

According to our study, its predictive factor is the right ventricular heart failure; the occurrence of typical atrial flutter increases the risk of in-hospital mortality, related to hemodynamic instability.

To our knowledge, incidence and predictive factor of typical atrial flutter was reported for the first time.

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