

Clinical and laboratory assessment of patients with new-onset atrial fibrillation in acute myocardial infarction

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Abstract

Background: New-onset atrial fibrillation (NOAF) is one of the complications of acute myocardial infarction (AMI), and is associated with poor outcome. The aim of the study was clinical and laboratory assessment of patients with NOAF in AMI. **Material and methods:** This is a retrospective, single-centre study of AMI patients with NOAF, who were admitted to Clinical Centre of Cardiology of the University Clinical Centre in Gdańsk, from January 2016 to June 2018. The medical history, echocardiography parameters, AMI localization and infarcted-related artery as well as laboratory parameters at the admission and at the moment of NOAF onset were taken into further analyses. **Results:** From 1155 consecutive AMI patients 103 (8.9%) with NOAF were enrolled into the study. A significant increase in C-reactive protein (CRP) and high-sensitive Troponine I (hsTnI) level, whereas significant decrease in potassium and hemoglobin level was observed at the moment of NOAF in comparison to admission. **Conclusions:** Our study suggests that markers of inflammation (CRP), myocardial necrosis (hsTnI), hemoglobin and serum potassium may be associated with NOAF in the setting on AMI. The aforementioned parameters are generally available and may be used as an inexpensive and rapid way to select patients who are at high risk of developing NOAF.

Keywords: atrial fibrillation • acute myocardial infarction • NOAF

Citation

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Introduction

Atrial fibrillation (AF) is the most common arrhythmia that is characterized by irregular and rapid activation in the atria without P waves in the electrocardio-

gram (ECG). In various countries around the world AF prevalence is estimated at 3% of adults aged 20 years or older [1]. The most significant risk factor for AF is age, although female sex, diabetes mellitus (DM), smoking, body mass index (BMI), alcohol consumption, hyperten-

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sion treatment, systolic blood pressure, heart failure, left ventricular hypertrophy and myocardial infarction also were identified [2]. The CHA₂DS₂-VASc score is used to estimate the risk of stroke in patients with AF and to guide prophylactic treatment. According to this score, patients with AF but without clinical risk factors for stroke do not need antithrombotic therapy, but oral anticoagulation is strongly recommended for patients with ≥ 1 risk factors [3] with a substantial increase in stroke and systemic thromboembolism. Strokes related to AF are associated with higher mortality, greater disability, longer hospital stays, and lower chance of being discharged home than strokes unrelated to AF.

According to the literature, AF coincides in 6-21% patients with acute myocardial infarction (AMI) [4]. It is well known that AF is connected with adverse outcomes in AMI [5]. Moreover, AF is independent risk factor of increased long-term mortality, regardless if AF is a primary or secondary diagnosis during hospitalization [6]. As in the general population, AF in AMI is associated with increased risks of cardiovascular and cerebrovascular complications [7]. Similarly, in patients with AMI advanced age, heart failure, higher BMI, DM, and depression of left ventricular function are the risk factors of AF, but there are still some predictors which are not clearly defined in patients with AMI [2, 4]. Furthermore, there is no scoring system dedicated to assessing the risk of new-onset AF (NOAF) in patients who are having an AMI.

The knowledge about the pathogenesis of AF in the setting of AMI is still evolving. Due to the fact that AF is an independent predictor of mortality after AMI, the aim of our study was to conduct clinical and laboratory assessment of patients with NOAF in AMI and to define predictors of NOAF in the setting of AMI.

Material and methods

This single-centre retrospective study enrolled 103 consecutive patients with NOAF from 1155 patients hospitalized in 4 cardiology units between January 2016 and June 2018 due to AMI. 418 of those patients had ST segment elevation myocardial infarction (STEMI) and 737 had non-ST elevation myocardial infarction (NSTEMI). Data was collected through MedStream Designer (Transition Technologies, Poland) which was fully integrated with the hospital information system. The diagnosis of STEMI was made based on acute chest pain and ST-segment elevation. All of the patients had a 12-lead ECG acquired and interpreted as soon as possible. The diagnosis of NSTEMI was based on the serum markers of myocardial necrosis [8].

Diagnosis of AF, defined as irregular RR intervals and the absence of P waves lasting for ≥ 30 seconds, was based on physician interpretation of ECG. The term

NOAF was applied to any newly diagnosed AF that appeared during the index hospitalization, irrespective of the duration of the arrhythmia. All the patients then had continuous ECG monitoring in the cardiac intensive care unit, afterwards they had 12-lead ECG performed daily during their hospital admission. The exclusion criteria were: < 18 years of age and history of prior AF or atrial flutter.

The medical history (prior MI, revascularization, hypertension, diabetes, smoking), echocardiographic parameters (left ventricular ejection fraction [LVEF], left atrium size [LA], presence of mitral regurgitation [MR]), laboratory parameters (brain natriuretic peptide [BNP], C-Reactive Protein [CRP], high-sensitive Troponin I [hsTnI], creatine kinase muscle-brain, complete blood count, hemoglobin [Hgb], leucocytes, neutrophils, glucose, serum potassium) at the admission and at the moment of NOAF onset were taken into further analyses. The incidence of in-hospital mortality was also taken into consideration.

Coronary angiography and percutaneous coronary angioplasty (PCI) were performed according to standard practice in every patient. Coronary blood flow assessed during PCI was determined according to Thrombolysis in Myocardial Infarction (TIMI) classification. All angiograms were ranked as to the number of diseased major branches of coronary arteries. We classified a coronary artery as 'diseased' if there was any obstructive lesion $\geq 30\%$ of that artery's diameter.

Patients were treated with anti-thrombotic agents, beta-blockers and angiotensin converting enzyme (ACE) inhibitors or angiotensin receptor blockers (ARBs) and cholesterol-lowering agents according to contemporary guidelines [9-10].

The protocol of the study was approved by the local bioethics committee.

Statistical analysis

Continuous data are presented as median (25th-75th percentile), while categorical data are expressed in proportion. We performed the Shapiro-Wilk test to check whether our data were normally distributed. Majority of the analysed parameters did not have a normal distribution, even after logarithmic data transformation. Thus, we selected appropriate statistical analysis methods based on non-parametric tests: comparison of laboratory results upon admission and at the moment of NOAF onset was performed with Wilcoxon matched-pairs test. The statistical analysis was performed using STATISTICA 9.0 (StatSoft, Tulsa OK, USA) package and R 2.15.2 environment.

Results

Table 1. Demographic, clinical and laboratory data of the studied group

	NOAF patients n = 103
Age, years *	72 (64-82)
Male, n (%)	64 (62%)
Hypertension, n (%)	72 (70%)
Diabetes mellitus, n (%)	32 (31%)
Active smoker, n (%)	30 (30%)
Former smoker, n (%)	53 (51%)
BMI, kg/m ²	27 (24-30)
Previous MI/PCI/CABG, n (%)	39 (38%)
Previous ASA, n (%)	46 (45%)
Previous ACEI/ARB, n (%)	53 (51%)
Previous statins, n (%)	40 (39%)
In-hospital death, n (%)	16 (16%)
Hospitalization time, days *	10 (7-18)
Development of NOAF, day *	1 (1-3)
STEMI, n (%)	37 (36%)
NSTEMI, n (%)	66 (64%)
BNP, pg/ml *	371 (168-1064)
Creatinine, mg/ml *	0.96 (0.81-1.31)
Glucose, mg/dl *	153 (121-216)
Total cholesterol, mg/dl *	168 (131-193)
High density lipoprotein, mg/dl *	41 (33-52)
Low density lipoprotein, mg/dl *	94 (71-121)
Triglyceride, mg/dl *	108 (76-145)
C-reactive protein, mg/l *	12.3 (3.3-36.1)
hsTnI, ng/ml *	0.49 (0.07-4.08)
CK-MB, ng/ml *	4.8 (2.2-14.6)
Hemoglobin, g/dl *	13.3 (12.2 - 14.5)
Leukocytes, x10 ⁹ /l *	10.6 (7.9-14.2)
Neutrophil/lymphocyte ratio *	3.8 (2.2-6.0)
K, mmol/l *	4.3 (3.9-4.6)

* data are presented as median (25th-75th percentile)

Abbreviations: MI – myocardial infarction; PCI – percutaneous coronary angioplasty; CABG – coronary artery bypass graft; ASA – acetylsalicylic acid; ACEI – angiotensin converting enzyme inhibitor; ARB – angiotensin receptor blocker, NOAF – new-onset atrial fibrillation; STEMI – ST-segment-elevation myocardial infarction; NSTEMI – non-ST-segment-elevation myocardial infarction; BNP – brain natriuretic peptide; CRP – C-Reactive Protein; hsTnI – high sensitive Troponin I; CK-MB – creatine kinase-muscle/brain; K – serum potassium

After applying the exclusion criteria, the final study cohort comprised a total of 103 patients with AMI, with no prior history of AF and who developed NOAF. From this group more than a half patients had NSTEMI. The overall incidence of NOAF was 8,9% (n=103) of the enrolled study population (n=1155), the mean age was 72 years, and more than a half of group were male. Most of the patients developed the NOAF in the first day of the admission (n=65), 28 patients developed the NOAF between second and fifth day of the index hospitalization, 10 patients developed after the fifth day.

A total of 16 patients died during the analyzed hospital stays: 69% (n=11) died due to cardiologic complications, 2 due to sepsis, 1 due to hemorrhagic stroke and 2 from other reasons. The demographic, clinical data and laboratory results (upon admission) of the studied group are summarized in Table 1.

Table 2. Angiographic and echocardiographic findings

NOAF patients n = 103	
Infarct-related artery in coronary angiography	
LM, n(%)	1 (1%)
LAD, n (%)	23 (22%)
RCA, n (%)	24 (24%)
LCX, n (%)	22 (21%)
Others, n (%)	10 (10%)
Multi-vessel coronary artery disease, n (%)	5 (5%)
TIMI 3	71 (70%)
Echocardiography	
LVEF, %*	42 (33-50)
LA diameter, mm*	41 (37-44)
Mitral regurgitation	
Mild, n (%)	70 (70%)
Moderate, n (%)	25 (24%)
Severe, n (%)	8 (8%)

* data are presented as median (25th-75th percentile)

Abbreviations: LM – left main artery; LAD – left anterior descending artery; RCA – right coronary artery; LCX – left circumflex artery; LVEF – left ventricular ejection fraction

Table 3. Laboratory parameters upon admission and at the moment of NOAF which are statistically significant or borderline

	On admission n = 103	NOAF onset n = 103	P
C-reactive protein, mg/l	12.3 (3.3-36.1)	30.4 (5.7-110.6)	< 0.0001
hsTnI, ng/ml	0.49 (0.07-4.08)	0.86 (0.08-8.29)	< 0.0001
CK-MB, ng/ml	4.8 (2.2-14.6)	25.9 (12.1-97.7)	0.083
Hemoglobin, g/dl	13.3 (12.2-14.5)	12.9 (11.4-14.0)	< 0.0001
Leukocytes, x10 ⁹ /l	10.6 (7.9-14.2)	10.3 (8.1-14.6)	0.164
Neutrophil/lymphocyte ratio	3.8 (2.2-6.0)	7.2 (5.2-10.1)	0.110
K, mmol/l	4.3 (3.9-4.6)	4.1 (3.8-4.5)	< 0.013

* data are presented as median (25th-75th percentile)

Abbreviations: CRP – C-Reactive Protein; hsTnI – high sensitive Troponin I; CK-MB – creatine kinase-muscle/brain; K – serum potassium

The angiographic, echocardiographic characteristics of the studied group are presented in Table 2. All of the laboratory parameters withdrawn on admission and at the moment of NOAF, which are statistically significant (or borderline significant) are presented in Table 3.

Discussion

The major finding of this study is that markers of inflammation (CRP), myocardial necrosis (hsTnI), Hgb and serum potassium may be associated with NOAF in the setting of AMI. These simple, inexpensive parameters could be helpful in identification patients with higher risk of NOAF.

Our results confirm the role of the CRP-AF correlation which was demonstrated in prior studies [11-12]. However, there are still discussions about the role of CRP in the pathogenesis of myocardial infarction [13]. There is also a possibility that patients with AMI are more likely to develop inflammation, which may promote AF. Moreover, neutrophil/lymphocyte ratio, which is also a reflection of systemic inflammatory status, is also described as a predictive factor of NOAF [14]. Our results did not confirm that hypothesis, however our analysis was not restricted to just patients with STEMI as in the previously the aforementioned article.

Zhu et al recently established that hsTnI level is an independent predictor of AF incidents. Our results are similar, however we only claim the association between the increase of hsTnI and outcome of NOAF [15]. We found a similar increase in the level of CK-MB, but it was not statistically significant. In another study, Parashar et al denied the connection between another factor of myocardial necrosis – Troponin T [TnT] and the occurrence of NOAF [12]. However we analyzed the increase of hsTnI level between the hospital admission and day of NOAF, whereas Parashar et al measured the level of TnT only once.

Another predictive factor is the level of hemoglobin. Our study suggests that NOAF onset is associated with a decrease in hemoglobin level. The literature on this subject is inconsistent. For example, Distelmaier *et*

al. demonstrated a statistically significant relationship between elevated levels of Hgb and occurrence of AF after AMI [16]. This might be due to the fact that they compared the level of Hgb between the NOAF after AMI patient group and matched controls [16]. In contrast, we analyzed the changes in Hgb level during the index hospitalization within the patient group only.

Several studies previously investigated the influence of potassium in the development of AF [17-19]. It is a well-known fact, that lower levels of serum potassium were associated with a higher risk of AF. We demonstrated that a decreasing level of serum potassium after AMI may be also the connected with NOAF.

There are a lot of echocardiographic parameters of AF, e.g. the parameters of systolic and diastolic LV function, as well as the LA parameters [20-23]. In our data, the LVEF value was below references range for healthy people. There were no data of LAVI, only LA diameter due to retrospective character of our study. Moreover, the Framingham Heart Study proved that every 5-mm increase in LA diameter increased the occurrence of AF by 39% while the Cardiovascular Health Study showed more than a double-fold increase in the developing NOAF when LA diameter >40 mm [22-23].

It should be noted that there are some limitations of the study. First of all, this was a single-centre retrospective study with a relatively small sample size. We did not analyze the entire hospitalized population with AMI to find the differences between those groups. Moreover, we do not have data on the duration of AF.

Conclusions

Our study suggests that markers of inflammation (CRP), myocardial necrosis (hsTnI), potassium and Hgb may be associated with NOAF in the setting on AMI. The aforementioned parameters are generally available and may be used as an inexpensive and rapid way to select patients who are at a high risk of developing NOAF. Further studies should be performed to design a dedicated scoring system for patients who are at risk of developing NOAF in the setting of AMI.

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