## ORIGINAL ARTICLE

# Aborted myocardial infarction in patients with ST-segment elevation myocardial infarction treated with mechanical reperfusion

Łukasz Konarski<sup>1</sup>, Marcin Debiński<sup>1</sup>, Aleksandra Kolarczyk-Haczyk<sup>1</sup>, Michał Jelonek<sup>1</sup>, Marek Kondys<sup>1</sup>, Paweł Buszman<sup>2</sup>

3rd Department of Invasive Cardiology, Angiology, and Electrophysiology, American Heart of Poland, Dabrowa Górnicza, Poland

Department of Epidemiology, Medical University of Silesia, Katowice, Poland

## **KEY WORDS**

infarction,

necrosis.

ST-segment elevation

myocardial infarction

### ABSTRACT

BACKGROUND Aborted myocardial infarction (abMI) is a type of acute coronary syndrome in which patients treated with reperfusion avoid the great burden of necrosis. Yet, no definition of abMI in patients undergoing primary percutaneous coronary intervention (pPCI) has been proposed so far.

**AIMS** This study aimed to identify patients with abMI and compare them with the remaining patients with ST-segment elevation myocardial infarction (STEMI).

**METHODS** It was a retrospective study of 1693 consecutive patients with STEMI treated with pPCI. The median (IQR) follow-up was 3.45 (1.45–5.09) years. Aborted MI was diagnosed if ST-segment elevation was reduced by more than 50%, no new abnormal Q waves were observed, the maximal level of creatine kinase MB did not reach a value 5-fold higher than the upper limit of normal (below 125 U/l), and there was successful reperfusion defined as the Thrombolysis in Myocardial Infarction score of 3 after PCI.

**RESULTS** Using our definition, abMI was diagnosed in 176 cases (10.4%). Compared with the remaining patients with STEMI, those with abMI were younger (mean [SD] age, 61.8 [11.5] vs 64.4 [11.6] years; P = 0.005) and were more frequent smokers (48.9% vs 36.7%; P = 0.002). They had greater left ventricular ejection fraction (median [interguartile range (IQR)], 49% [40%–55%] vs 55% [51%–60.5%]; P <0.001), were discharged earlier from the hospital (hospitalization time, median [IQR], 73 [60–90.5] hours vs 87 [69-98] hours; P <0.001), and had a lower mortality rate at 1 month and long-term follow-up (2.27% vs 8%; *P* = 0.006 and 10.8% vs 23.9%; *P* < 0.001, respectively).

**CONCLUSIONS** Patients with abMI had better short- and long-term outcomes than other patients with STEMI. Some negative cardiovascular factors such as smoking were more often observed in the abMI group.

#### Correspondence to:

Łukasz Konarski, MD, 3rd Department of Invasive Cardiology, Angiology, and Electrophysiology, American Heart of Poland, ul. Szpitalna 13, 41-300 Dąbrowa Górnicza, Poland, phone: +48 32 758 66 01, email: konarskilukasz10@gmail.com Received: May 18, 2020. **Revision accepted:** October 11, 2020. Published online: October 16, 2020. Kardiol Pol. 2021; 79 (1): 39-45 doi:10.33963/KP.15650 Copyright by the Author(s), 2021

**INTRODUCTION** ST-segment elevation myocardial infarction (STEMI) is still the most dramatic manifestation of acute coronary syndrome (ACS). Despite the great progress in the treatment of ACS with mechanical reperfusion, it remains the most frequent cause of death and heart failure in Poland and worldwide.<sup>1,2</sup> Time from symptom onset to successful reperfusion has been regarded as the main factor contributing to survival and development of heart failure in patients with MI.<sup>3,4</sup> A subgroup of patients treated in optimal conditions with a rapid reperfusion strategy may avoid necrosis of the

myocardium. Aborted MI (abMI) has already been characterized in previous papers.<sup>5-8</sup> Yet, there has been no standardized definition of abMI so far. In our opinion, the standard definition of abMI should be based on successful reperfusion, a low level of necrosis biomarkers, and absence of myocardial necrosis on electrocardiography and echocardiography, and reference to the universal definition of MI.<sup>9</sup> Based on our previous experience, we proposed the definition of this condition elsewhere.<sup>8</sup> In this study, abMI was diagnosed if ST-segment elevation was reduced by more than 50% following

aborted myocardial atherosclerosis. percutaneous coronary intervention,

#### WHAT'S NEW?

Although primary percutaneous coronary intervention (pPCI) is the main method of reperfusion therapy in patients with ST-segment elevation myocardial infarction (STEMI), there is still no universal definition of aborted myocardial infarction (abMI) in this setting. In this study, considering our own experience, we validated the previously proposed definition based on clinical features and outcomes. Using the new definition of abMI, we could better predict patients' clinical outcomes and prognosis. Additionally, we confirmed that early discharge from a ward (within 48 to 72 hours) is feasible and safe in that group of patients. We believe that those findings may influence therapeutic decisions, clinical outcomes, and economic issues in a long-term perspective. Unexpectedly, some risk factors such as smoking were more frequently observed in patients with abMI.

> revascularization, no new abnormal Q waves were noted, the maximal level of creatine kinase MB (CK-MB) did not reach a value 5-fold higher than the upper limit of normal (CK-MB level <125 U/l), and there was successful reperfusion defined as Thrombolysis in Myocardial Infarction (TIMI) flow grade 3 after percutaneous coronary intervention (PCI).

> **METHODS** It was a single-center retrospective study of patients with STEMI treated with mechanical reperfusion between 2011 and 2016 in the 3rd Department of Invasive Cardiology, Angiology, and Electrophysiology of American Heart of Poland in Dąbrowa Górnicza, Poland. The study population included 1693 consecutive patients with STEMI who were treated with mechanical reperfusion. None of the patients was treated with thrombolysis. Patients without lesions in coronary arteries or with lesions defined as chronic total occlusion were excluded from the study. Also, patients referred for coronary artery bypass grafting were not included in this study.

> ST-segment elevation myocardial infarction was diagnosed if ST-segment elevation greater than 0.1 mV was present in at least 2 contiguous leads other than  $V_2$  through  $V_3$ . Cutoff points for leads  $V_2$  through  $V_3$  were higher than or equal to 0.15 mV in women, higher than or equal to 0.2 mV in men aged 40 years and older, or higher than or equal to 0.25 mV in men younger than 40 years of age.<sup>9</sup> Other criteria for MI such as chest pain and a confirmed infarct-related lesion in the coronary artery were also met. Patients with acute MI and new left bundle-branch block were excluded from the study.

On admission, 12-lead electrocardiography and physical examination were performed, a medical history was taken, and blood samples were obtained before the index procedure. Follow-up electrocardiography was conducted right after index PCI and on every next day. Echocardiographic assessment was performed on admission to the coronary care unit. Control laboratory tests were carried out the day after the procedure and during next days until CK-MB levels normalized. The study patients were divided into 2 groups: the abMI group and the nonabMI group of the remaining patients with STE-MI. The definition of abMI, based on the normalization of ST-segment elevation, presence of a new Q wave, and elevation of CK-MB levels, was presented elsewhere.<sup>8</sup> Following that definition, abMI was diagnosed in 176 study patients (10.4%).

Follow-up data were collected by contacting patients or their families by phone. If no contact was established or an attempt failed, data on mortality were obtained from the Civil Registry Office. Additional data were gathered from medical records. A total of 1691 patients (99.9%) were followed up.

Statistical analysis Statistical analysis was performed using the MedCalc Software, version 18.5 (MedCalc, Ostend, Belgium). Categorical variables were expressed as numbers and percentages of patients, whereas continuous data, as mean (SD) or median (interquartile range [IQR]). Normality of distribution was evaluated by the Shapiro–Wilk test. The  $\chi^2$  test was used to compare categorical variables between the study groups. To compare continuous variables, the t test or the Mann–Whitney test were applied. The Kaplan–Meier curves were used to estimate survival in both groups. Survival curves were compared with the log-rank test. Cox proportional hazard regression was used to analyze the effect of risk factors on short- and long-term survival. A P value less than 0.05 was considered significant.

The study complied with the Declaration of Helsinki. Due to the retrospective design of the study, no ethics committee approval was required.

**RESULTS Baseline characteristics** The baseline characteristics and clinical features of the study groups are presented in TABLE 1. Patients in the abMI group were younger (mean [SD] age, 61.8 [11.5] vs 64.4 [11.6] years; *P* = 0.005) and were more frequent smokers (48.9% vs 36.7%; P = 0.002) than those from the non-abMI group. Differences between other risk factors such as male sex, hypertension, diabetes, hyperlipidemia, and obesity were nonsignificant. Other comorbidities that contribute to the development of coronary artery disease were also included in the baseline characteristics of patients, but only chronic kidney disease was more frequently observed in the non-abMI group (6.2% vs 12.5%; P < 0.014).

In terms of clinical features, the median (IQR) peak CK-MB level reached higher values in the non-abMI group compared with

#### TABLE 1 Baseline characteristics and clinical features of the study patients

Baseline characteristics and comorbidities	abMI group (n = 176)	Non-abMI group (n = 1517)	P value
Age, y, mean (SD)	61.8 (11.5)	64.4 (11.6)	0.005
Male sex	121 (68.7)	1030 (67.9)	0.88
Hypertension	112 (63.6)	972 (64.1)	0.9
Diabetes	31 (17.6)	357 (23.5)	0.07
Hyperlipidemia	61 (34.6)	585 (38.6)	0.31
Obesity	32 (18.1)	265 (17.5)	0.81
Smoking status	86 (48.9)	557 (36.7)	0.002
Peripheral artery disease	7 (3.9)	91 (5.9)	0.27
COPD	4 (2.2	51 (3.7)	0.44
Atrial fibrillation	11 (6.2)	130 (8.6)	0.29
Prior CABG	2 (1.1)	33 (2.2)	0.35
Chronic kidney disease	11 (6.2)	190 (12.5)	0.014
Creatinine, mg/dl, median (IQR)	0.87 (0.74–0.96)	0.85 (0.72–1.05)	0.54
Maximum CK-MB, U/l, median (IQR)	49.1 (31.9–74.5)	133 (67.6–224.8)	<0.001
Aspirin	176 (100)	1490 (98.2)	0.07
P2Y12 inhibitors at discharge	176 (100) 1473 (97.1)		0.022
Time delay, h, median (IQR)	4.6 (2.35–7.65)	3.8 (2–7)	0.065
Hospitalization time, h, median (IQR)	73 (60–90.5)	87 (69–98)	<0.001
Short hospitalization (<72 h)	77 (43.7)	270 (17.8)	<0.001
LVEF, %, median (IQR)	55 (51–60.5)	49 (40–55)	<0.001

Data are presented as number (percentage) of patients unless otherwise indicated.

Abbreviations: abMI, aborted myocardial infarction; CABG, coronary artery bypass grafting; CK-MB, creatine kinase MB; COPD, chronic obstructive pulmonary disease; IQR, interquartile range; LVEF, left ventricular ejection fraction

## TABLE 2 Hospitalization course and outcomes

Characteristics	abMI (n = 176)	Non-abMI (n = 1517)	<i>P</i> value
Killip–Kimball class IV	5 (2.8)	154 (10.1)	0.002
Cardiac arrest	7 (3.9)	118 (7.8)	0.06
IABP	0	10 (0.6)	0.28
Stroke / TIA	0	8 (0.6)	0.33
Major bleeding	0	7 (0.4)	0.36
Acute kidney injury	3 (1.7)	108 (7.1)	0.006
In-hospital death	3 (1.7)	70 (4.6)	0.11

Data are presented as number (percentage) of patients.

Abbreviations: IABP, intra-aortic balloon pump; TIA, transient ischemic attack; others, see TABLE 1

the abMI group (133 [67.6–224.8] U/l vs 49.1 [31.9–74.5] U/l; P <0.001). Treatment with P2Y12 inhibitors was used in all patients with abMI and 97.2% of the patients from the non-abMI group (P <0.022). Compared with the non-abMI patients, those with abMI were hospitalized shorter (median [IQR] hospital stay, 73 [60– 90.5] hours vs 87 [69–98] hours; P <0.001) and also more frequently discharged from the ward earlier than 72 hours after admission (43.7% vs 17.8%; P < 0.001). Median (IQR) time from symptom onset to reperfusion was 4.6 (2.35– 7.65) hours in the abMI group compared with 3.8 (2–7) hours in the non-abMI group (P = 0.065). The difference in time delay between both study groups did not reach statistical significance.

#### TABLE 3 Angiographic data of the study patients

Parameter	abMI (n = 176)	Non-abMI (n = 1517)	<i>P</i> value
TIMI 0 / 1 before PCI	133 (75.6)	1266 (83.5)	0.014
TIMI 2/3 before PCI	43 (24.4)	251 (16.5)	0.012
TIMI 3 after PCI	176 (100)	1448 (95.4)	0.007
MVD	66 (37.5)	717 (47.3)	<0.001

Data are presented as number (percentage) of patients.

Abbreviations: MVD, multivessel disease; PCI, percutaneous coronary intervention; TIMI, Thrombolysis in Myocardial Infarction; others, see TABLE 1



**FIGURE 1** Mortality in the study patients with aborted myocardial infarction and the remaining patients with ST-segment elevation myocardial infarction Abbreviations: see TABLE 1



**FIGURE 2** Kaplan–Meier curves for mortality in the study patients with aborted myocardial infarction and the remaining patients with ST-segment elevation myocardial infarction Abbreviations: see TABLE 1

Median (IQR) left ventricular ejection fraction (LVEF) measured by echocardiography was higher in the abMI group than in the non--abMI group (55% [51%–60.5%) vs 49% [40%– 55%]; P <0.001).

Cardiogenic shock (Killip–Kimball class IV) was more frequently diagnosed in the non-abMI group (2.8% vs 10.1%; P < 0.002). Furthermore, a lower rate of acute kidney injury was noted in patients with abMI (1.7% vs 7.1%; P < 0.006). We did not observe any differences in other analyzed outcomes such as cardiac arrest, use of an intra-aortic balloon pump, stroke, bleeding, and in-hospital mortality (TABLE 2).

#### Coronary artery blood flow and time de-

lav The TIMI scale was used for the assessment of coronary artery blood flow before and after PCI. Partial or normal blood flow (TIMI flow grade of 2/3) was more often observed in the infarct-related artery before PCI in the abMI group (24.4% vs 16.5%; *P* = 0.012). By the adopted definition, all patients with abMI had TIMI flow grade 3 after PCI, while the same grade was reached in 95.4% of the patients in the non-abMI group (P = 0.007). In terms of angiographic findings, a significantly higher rate of multivessel coronary disease was noted in patients without abMI than in those with abMI (47.3% vs 37.5%; P <0.001). Time delay defined as a median (IQR) time between symptom onset and the beginning of PCI did not significantly differ between both study groups (4.6 [2.35-7.65] hours vs 3.8 [2-7] hours; P = 0.065) (TABLE 3).

**Early and long-term outcomes** In patients with abMI, a significantly lower rate of mortality was observed at 30 days, 1 year, and long-term follow-up (FIGURE 1). The Kaplan–Meier curves were used to determine patient survival. During a median (IQR) long-term follow-up of 3.45 (1.45–5.09) years, mortality in the abMI group reached 10.8% and was significantly lower than in the non-abMI group (24.03%; P < 0.001) (FIGURE 2).

**Multivariable analysis** Cox proportional hazard regression was used to determine what factors influenced survival. Those deemed significant in univariate analysis were included in the multivariate model. Presence of abMI in patients with STEMI was an independent factor in the Cox proportional hazard regression model. At 30-day follow-up, patients with abMI were at lower risk of death, but this observation did not reach statistical significance (hazard ratio, 0.39; 95% CI, 0.14–1.07; P = 0.07). At long-term follow-up, abMI was an independent factor that decreased the mortality risk (hazard ratio, 0.47; 95% CI, 0.3–0.75; P = 0.001) (TABLES 4 and 5).

Factor	Univariate Cox regression analysis			Multivariate Cox regression analysis		
	P value	HR	95% CI	P value	HR	95% CI
Age over 75 y	0.002	1.85	1.27–2.72	0.31	1.25	0.81–1.9
Male sex	0.014	0.64	0.45-0.91	0.07	0.71	0.49-1.02
Hypertension	0.016	0.65	0.46-0.92	0.005	0.59	0.41-0.85
Diabetes	<0.001	2.51	1.77-3.57	0.001	1.88	1.29-2.75
Hyperlipidemia	0.45	0.87	0.6–1.25	-	-	-
Obesity	0.16	1.35	0.89-2.05	-	-	-
Chronic kidney disease	0.32	0.91	0.76-1.09	-	-	-
Smoking status	<0.001	0.42	0.27-0.64	0.12	0.68	0.43–1.1
Atrial fibrillation	0.62	1.16	0.64-2.09	-	-	-
Previous CABG	0.8	1.16	0.3719-3.63	-	-	-
abMI	0.011	0.28	0.1-0.74	0.07	0.39	0.14–1.07
Aspirin	<0.001	0.06	0.04-0.1	<0.001	0.2	0.08-0.46
P2Y12 inhibitors	<0.001	0.09	0.06-0.14	0.009	0.35	0.16-0.76
Glycoprotein IIb / IIIa inhibitors	0.014	0.62	0.42-0.91	0.12	0.74	0.5–1.09
Bleeding	0.046	4.13	1.03–16.6	0.22	2.44	0.58-10.22
Stroke / TIA	0.08	3.52	0.88–14.15	-	-	-
Acute kidney injury	<0.001	3.01	1.89-4.79	<0.001	2.55	1.54-4.22

## TABLE 4 Cox proportional hazards regression model for 30-day mortality

Abbreviations: HR, hazard ratio; others, see TABLES 1 and 2

Factor	Univariate Cox regression analysis		Multivariate Cox regression analysis			
	P value	HR	95% CI	P value	HR	95% CI
Age over 75 y	<0.001	2.21	1.77–2.75	<0.001	1.64	1.29–2.1
Male sex	0.23	1.08	0.71–1.08	-	-	-
Hypertension	0.32	1.1	0.73–1.1	-	-	-
Diabetes	<0.001	2.01	1.3-2.01	0.016	1.32	1.05–1.65
Hyperlipidemia	0.74	1.27	0.84-1.27	-	-	-
Obesity	0.68	1.37	0.81–1.37	_	_	-
Chronic kidney disease	0.26	1.05	0.83-1.05	_	_	-
Smoking status	<0.001	0.72	0.47-0.72	0.21	0.86	0.67–1.09
Atrial fibrillation	<0.001	2.37	1.3–2.37	0.08	1.32	0.96–1.81
Previous CABG	0.92	1.94	0.48–1.94	-	-	-
abMI	<0.001	0.66	0.26-0.66	0.001	0.47	0.3-0.75
Aspirin	<0.001	0.2	0.08-0.2	<0.001	0.29	0.14-0.6
P2Y12 inhibitors	<0.001	0.24	0.11-0.24	0.011	0.43	0.23-0.82
Glycoprotein IIb / IIIa inhibitors	<0.001	0.85	0.56-0.85	0.005	0.73	0.59-0.91
Bleeding	0.48	6.6	0.41-6.6	-	-	-
Stroke / TIA	0.18	6.75	0.7-6.75	-	-	-
Acute kidney injury	< 0.001	3.65	1.99–3.65	<0.001	2.18	1.59-2.98

## TABLE 5 Cox proportional hazard regression model for total mortality

Abbreviations: see TABLES 1, 2, and 4

**DISCUSSION** In our study, STEMI patients diagnosed with abMI had better prognosis at both short- and long-term follow-up compared with other patients with STEMI (the non-abMI group).

The concept of abMI was originally described in several trials, based on fibrinolysis as the primary or exclusive method of reperfusion.<sup>5-7</sup> Currently, with a well-developed network of catheterization laboratories, fibrinolysis is rarely used as a method of reperfusion therapy. Therefore, in this study, we analyzed only the data of patients in whom reperfusion was achieved by pPCI and adopted our new definition of abMI.<sup>8</sup> The study definition was developed based on the old definition of abMI following thrombolysis and the new universal definition of MI.<sup>9</sup>

Pyda et al<sup>10</sup> and Prech et al<sup>11</sup> defined abMI as an increase in the CK-MB level lower than a value 2-fold higher than the upper limit of normal and proved better results of interventional treatment of abMI based on electrocardiographic, angiographic, and echocardiographic parameters. They also demonstrated a less extensive inflammatory response in patients with abMI, but no difference in long-term outcomes was seen between the defined groups.<sup>10</sup> Therefore, that definition had a limited value for the prediction of long-term survival.

In a study by Lee et al,<sup>12</sup> patients with abMI, defined as a 2-fold elevation of CK and CK-MB levels and ST-segment normalization above 50% within 2 hours, had normalized myocardial perfusion in the region of ischemia, as visualized by serial magnetic resonance imaging. In that study, patients with a history of myocardial infarction were excluded.<sup>12</sup> Also, that study provided only data on radiological assessment and lack clinical implementation.<sup>12</sup>

By our definition of abMI, the upper limit of the CK-MB level could not be 5-fold higher than normal. Thus, patients with abMI had a lower median (IQR) CK-MB level than others (49.1 [31.9-74.5] U/l vs 133 [67.6-224.8] U/l; *P* <0.001). In our view, CK-MB might be a useful parameter for monitoring patients with suspected abMI because of its dynamic changes in ACS treated with mechanical reperfusion and it could be one of the factors influencing the decision about shortening the hospitalization.<sup>8,13</sup> Vasile et al<sup>14</sup> demonstrated that if we use high-sensitive troponin in patients with STEMI to detect cases of abMI, the frequency of abMI is zero. Therefore, this marker of MI might not be as good as CK-MB.

In our study, the baseline characteristics of both study groups differed in terms of cardiovascular risk factors, treatment, as well as shortand long-term outcomes. Patients with abMI were more often smokers and were younger than the rest of the study cohort. In contrast, there were no differences in the prevalence of other typical cardiovascular factors such as hypertension, hyperlipidemia, diabetes, and obesity. Of note is the smoker's paradox, which has been described in numerous papers<sup>15-19</sup> and associated with inconsistent results of analysis. In the GUSTO-I (Global Utilization of Streptokinase and TPA for Occluded Coronary Arteries) trial, smokers admitted to the hospital with ACS and treated with thrombolytics had a significantly lower rate of in-hospital and 30-day mortality than nonsmokers.<sup>18</sup> Ramotowski et al<sup>19</sup> summarized the influence of smoking on cardiovascular disease development and the smoker's paradox. They hypothesized that hemostasis in smokers is modified, including changes in endothelial function, platetet activation, and fibrinolysis. It was also reported that smokers may have less severe stenoses than nonsmokers. Yet, the probable mechanism of preconditioning the heart for ischemia by smoking cigarettes has not been unambiguously proven.

In our study, on echocardiography, patients with abMI had significantly higher LVEF, which was most likely caused by the absence of the large area of myocardial necrosis. Multivessel coronary disease, defined as a significant stenosis in at least 2 coronary arteries, was rarely diagnosed in patients with abMI. More advanced coronary artery disease in patients without abMI might be associated with their older age and a higher prevalence of diabetes; however, statistical significance was not reached in that case.

Vessel patency on admission, evaluated with the TIMI scale, showed a significantly higher TIMI flow grade 2/3 in the target vessel in the abMI group than in the non-abMI group (24.4% vs 16.5%; *P* = 0.012). Also, patients with abMI had a higher rate of successful reperfusion defined by TIMI flow grade 3 after PCI (100% vs 95.4%; *P* = 0.007). Therefore, those observations may suggest that the patency of the infarct-related vessel before PCI, and not time delay, might be a predictor of abMI occurrence in patients with STEMI treated with pPCI. Prech et al<sup>11</sup> also suggested that TIMI flow grade equal to or higher than 2 in the infarct-related artery before PCI might represent a predictor of abMI. Polańska-Skrzypczyk et al<sup>20</sup> documented that succesful PCI regarded as TIMI flow grade 3, and not TIMI flow grade 2, improves the prognosis of patients with STEMI at long--term follow-up. The above observations may be related to myocardial preconditioning, which limits the infarct size and improves the outcomes of patients with abMI.<sup>21,22</sup> Also, a better viability of the heart muscle reflected in greater LVEF in patients with abMI might be associated with the so-called stunned myocardium that recovers after angioplasty.

Considering time delay, unexpectedly, we did not observe any significant difference between both study groups (median [IQR], 4.6 [2.35–7.65] vs 3.8 [2–7] hours; P = 0.065). However, in this retrospective study, information about time delay was obtained from medical records collected by the emergency medical service personnel, and not directly from the patient. The data did not include details such as the type of chest pain (intermittent or persistent).

Another finding coming from this study showed that patients with abMI were discharged home earlier than non-abMI patients. The median (IQR) time of hospitalization was 73 (60–90.5) vs 87 (69–98) hours (P <0.001). Also, patients with abMI more often met the criteria for short hospitalization defined as discharge within 72 hours of hospitalization. A tendency to reduce hospitalization time after ACS is being observed worldwide. Previous trials confirmed the shortening of hospital stay is feasible and safe.<sup>23,24</sup> This particularly pertains to patients with low-risk STEMI treated with successful reperfusion, the majority of whom meets the criteria for abMI. The economic aspect of early discharge from a ward is also of importance, as numerous resources can be saved in a long--term perspective.

**Conclusions** Patients meeting the new criteria for abMI have a better prognosis at shortand long-term follow-up. Unexpectedly, smoking as a cardiovascular factor was more often observed in patients with abMI.

#### **ARTICLE INFORMATION**

#### CONFLICT OF INTEREST None declared.

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