Clinical characteristics, aetiology and occurrence of type 2 acute myocardial infarction

Filip M. Szymański1, Grzegorz Karpiński1, Anna E. Platek1, Franciszek Majstrak2, Anna Hryniewicz-Szymańska³, Marcin Kotkowski1, Bartosz Puchalski1, Krzysztof J. Filipiak1, Grzegorz Opolski1

1Department of Cardiology, Medical University of Warsaw, Poland
2Department of Cardiac Surgery, Medical University of Warsaw, Poland
3Department of Cardiology, Hypertension and Internal Diseases, Medical University of Warsaw, Poland

Abstract

Background: Cardiovascular diseases are the leading cause of death worldwide. One of the most important diseases in this group is myocardial infarction (MI). According to the universal definition developed by the European Society of Cardiology (ESC), MI is divided into five main types based on its cause. Type 2 MI is secondary to ischaemia due to either increased demand or decreased supply of oxygen (for example due to coronary artery spasm, anaemia, arrhythmia, coronary embolism, hypertension, or hypotension).

Aim: To assess the occurrence and aetiology of type 2 acute MI (AMI), and to describe the clinical characteristics and prognosis of study patients.

Methods: Into a retrospective study, we enrolled 2,882 patients in the Cardiology Department with an initial diagnosis of AMI between 2009 and 2012. Diagnosis of AMI was made based on ESC criteria. In all patients, coronary angiography was performed in order to exclude haemodynamically significant coronary lesions.

Results: Among 2,882 patients hospitalised in the described time period, 58 (2%) patients were diagnosed with type 2 AMI. The mean age of the study group was 67.3 ± 13.2 years; and the majority of the study group, 60.3%, were women. Out of them, 23 (39.6%) patients experienced AMI due to coronary artery spasm, 15 (25.9%) due to arrhythmias, 11 (19%) due to severe anaemia, and nine (15.5%) due to hypertension, without significant coronary artery disease. 42 (72.4%) patients, were diagnosed as non-ST-segment elevation MI, 14 (24.1%) as ST-segment elevation MI, and two (3.5%) as AMI in the presence of ventricular paced rhythm. History of classical cardiovascular risk factors including hypertension, diabetes, dyslipidaemia, family history of heart diseases, and smoking was reported in 42 (72.4%), 14 (24.1%), 23 (39.7%), 24 (41.4%), and 16 (27.6%) cases, respectively. All-cause 30-day mortality rate was 5.2%, and six-month was 6.9%.

Conclusions: Type 2 AMI patients were more often female, and they were more often diagnosed as non-ST-segment elevation MI. The prevalence of classical cardiovascular risk factors in this subgroup of patients was very high. The leading cause of AMI was coronary artery spasm.

Key words: acute myocardial infarction type 2, aetiology, prognosis

INTRODUCTION

Cardiovascular (CV) diseases are the number one cause of death globally. Among them, one of the most dangerous is acute myocardial infarction (AMI). According to the universal definition of MI updated in 2012, AMI is divided into five types based on a causative factor [1]. Type 2 covers AMI caused by a primary imbalance between myocardial oxygen supply and/or demand due to coronary artery spasm, anaemia, arrhythmia, coronary embolism, hypertension or hypotension. Diagnosis of type 2 AMI is not always easy to establish, and no broader studies had yet been reported to find how often this diagnosis is made in clinical practice. Patients with this type of AMI are often a heterogeneous group, and there have been very few studies focusing on their characteristics. The
The aim of this study was to assess the occurrence and aetiology of type 2 AMI, and to describe the clinical characteristics and prognosis of study patients.

**METHODS**

**Study design**

We retrospectively analysed medical records of 2,882 consecutive patients who presented to the Emergency Department between 2009 and July 2012 with an initial diagnosis of acute coronary syndrome. Diagnosis of AMI and division into types were made with respect to the universal definition of MI criteria [2]. AMI was diagnosed when there was a rise/fall in cardiac troponin (defined as a value exceeding the 99th percentile of a normal reference population, in at least one measurement), with symptoms or electrocardiography (ECG) patterns specific for ischaemia. ST-elevation MI (STEMI) was diagnosed when ECG showed persistent elevation of ST segment of ≥0.1 mV in two contiguous leads (or ≥0.2 mV² 0.25 mV in men, and ≥0.15 mV in women in V₂-V₃ leads) [3]. Other cases were classified as AMI in the presence of ventricular paced rhythm, or as non-ST-elevation MI (NSTEMI). All patients underwent coronary angiography which was performed in standard projections for different coronary arteries. Digital angiograms were then analysed by two independent, experienced interventional cardiologists. All angiograms were assessed with respect to the TIMI flow scale. Patients had heart wall motion abnormalities (hypo- or akinesis of at least one heart segment) confirmed by a full transthoracic echocardiography. The studies were carried out with Philips iE 33 and 2.5–3.5 MHz transthoracic probe. Data concerning baseline characteristics was collected. Medical records were reviewed for a history of major adverse cardiac and cerebrovascular events, hypertension, diabetes mellitus, dyslipidaemia, smoking, family history of heart disease and other CV risk factors. 30-day and six-month all-cause mortality was analysed. We excluded from the study patients with a final diagnosis of tako-tsubo cardiomyopathy, myocarditis, cardiac amyloidosis/sarcoidosis, pulmonary embolism, and/or patients with previous major surgical operations or trauma (Fig. 1).

**Diagnosis of type 2 AMI**

Type 2 AMI was diagnosed when there were no signs of haemodynamically significant stenosis of atherosclerotic origin in coronary arteries. Aetiology of the infarction (coronary artery spasm, anaemia, arrhythmia, coronary embolism, hypertension, or hypotension) was established based on the medical records, with use of specific objective criteria for the leading mechanisms.

**Statistical analysis**

Continuous data is presented as mean ± standard deviation (SD) and was compared with Mann-Whitney test or Student’s t-test, while categorical variables were compared using either χ² or Fisher exact tests. A p value of less than 0.05 was considered statistically significant, whereas the confidence intervals (CI) were 95%. Statistical analyses were performed using SAS statistical software version 8.02 (SAS Institute, Inc, Cary, NC, USA).

**RESULTS**

Out of 2,882 patients, 58 were diagnosed with type 2 AMI; this counted for 2.0% of the study group. The mean age of type 2 AMI patients was 67.3 ± 13.2 years. The majority of patients (60.3%) were females. The baseline characteristics of the study group are presented in Table 1. The mean body mass index was 27.6 ± 4.5 kg/m², mean heart rate was 81.4 ± 23.6 bpm, and mean systolic and diastolic blood pressure were 135.6 ± 23.2, and 78.1 ± 13.5 mm Hg, respectively. Classical CV risk factors, as well as various co-morbidities, were highly prevalent in our patients. History of hypertension, diabetes, dyslipidaemia, and a family history of heart diseases was reported in 42 (72.4%), 14 (24.1%), 23 (39.7%), and 24 (41.4%) cases, respectively. Out of the study patients, 16 (27.6%) were current smokers and eight (13.8%) had smoked in the past. In the group of patients with type 2 AMI, 34 (58.6%) suffered from chest pain of various intensity, 17 (29.3%) had palpitations, and nine (15.5%) had dyspnoea. Fainting was a manifestation of AMI in eight (13.8%) patients. As for MI itself, the most frequent (72.4%) presentation was NSTEMI. 14 (24.1%) patients had STEMI, and in two (3.4%) cases admission ECG showed ventricular paced rhythm (Table 1).

The most common cause of type 2 AMI in our group of patients was coronary artery spasm (39.6%). Other causes were arrhythmias (25.9%), severe anaemia (19%), and hypertension (15.5%) (Fig. 2).

Biochemical parameters collected on admission showed that mean concentration of first troponin I was 1.6 ± 2.6 μg/L, and creatine kinase-MB (CK-MB) mass concentration was...
Clinical characteristics, aetiology and occurrence of type 2 acute myocardial infarction

14.5 ± 32.05 ng/mL. The highest peak concentration of troponin I was 2.8 ± 3.5 μg/L. The all-cause mortality rate at 30 days was 5.2%, and at six months — 6.9% (Table 1).

**DISCUSSION**

The universal definition of MI is a document of significant scientific and clinical importance. The previous update of the definition released in 2007 was associated with an increase in the number of diagnosed AMI events by one-quarter, and was proven to be predictive of ten-year mortality [2, 4]. The expert consensus not only helped to establish clear end-points for clinical studies, but was also associated with an improvement in the management of patients with AMI, resulting in less myocardial injury, in spite of clinical presentation [1].

Proper medical treatment for AMI, including early reperfusion therapy and antithrombotic medication, is necessary regardless of the AMI mechanism or co-morbidities [5]. Data from all patients who were hospitalised in the Cardiology Department with AMI was analysed. But how many patients with AMI type 2 were misdiagnosed? Are we so willing to diagnose MI in everyday practice, for example in an elderly patient with end-stage renal disease, chest discomfort and an only slightly elevated troponin level? Sometimes, the line between myocardial injury and actual AMI is very subtle. Nevertheless, distinguishing the difference is extremely important, because it affects the patient’s treatment and long-term prognosis. A possible diagnosis of AMI in patients with many co-morbidities cannot be forgotten, even though, as in our study, the troponin levels in these patients may often be only slightly elevated.

A single measurement of troponin at peak, after 24, 48 or 72 h provides information about the heart muscle damage, and consequently its further function [6, 7]. It has been proven that...
it is even possible to establish certain cut-off points for troponin concentration, after which we can with high probability predict that MI will be complicated with subsequent development of congestive heart failure or pulmonary hypertension [8]. Previous studies have shown that, most importantly troponin concentration correlates with patients’ mortality rates [9, 10]. In this study, the mean cardiac troponin I concentration on admission was 1.6 ± 2.6 μg/L, and its mean peak concentration was 2.8 ± 3.5 μg/L in patients with type 2 AMI. These values are quite low compared to a type 1 population, which was also shown in previous studies [11]. This may mean that also the area of heart muscle necrosis was not very big, and consequently suggests that symptoms of ischaemia in this group of patients might not be severe. Type 1 and type 2 can have various clinical manifestations. Patients may present to the emergency department with typical symptoms of ischaemia such as chest, upper extremity, mandibular or epigastric pain, and its equivalents, like dyspnoea, palpitations or fatigue. But many patients do not present any symptoms [12]. In this study, chest pain of various intensity occurred only in 58% of cases. Patients with mild symptoms will have a longer time from pain onset to hospital admission, and consequently longer door-to-reperfusion time. Some patients may even withdraw from medical treatment and experience AMI without any medical service. This will have a negative impact on general outcome, including mortality [13, 14]. Also, silent AMI may be one of the type 2 AMI presentations which is well known to be associated with an increased all-cause mortality [12]. Even though the troponin I concentration was low in our patients, hospitalisation time was long, and similar to the group of patients with AMI type 1.

Most CV diseases can be prevented by properly addressing risk factors such as diabetes, raised blood pressure, raised lipids, tobacco use, unhealthy diet and obesity, physical inactivity, stress, and depression. Unlike in most studies considering AMI patients, type 2 AMI patients were predominantly female. The prevalence of classical CV risk factors in our study group was high. Also novel CV risk factors considering mental health were highly prevalent in this group. Collective data concerning the presence of anxiety disorders, depression or severe emotional stress prior to AMI showed that they were present in more than 25% of our patients. It has been proven that all these factors contribute to the development of further adverse CV events, and worsen the prognosis. It is important to introduce this group of patients to proper CV disease prevention programmes [15].

The leading cause of type 2 AMI in our study was coronary artery spasm. Vasoconstriction of epicardial coronary arteries is often limited to just one segment. The vessel usually occludes or nearly occludes, diminishing blood flow and oxygen supply, consequently leading to signs of ischaemia and MI. Pathomechanisms of the spasm are not yet fully disclosed, but are suggested to be associated with endothelial dysfunction. Constriction of coronary artery wall muscles more often takes place in patients with dyslipidaemia and hypertension, and can be triggered by alcohol withdrawal, exposure to cold, medications, stimulant drugs (e.g. amphetamine, cocaine), or emotional stress [16]. In our study group, hypertension, dyslipidaemia, as well as emotional stress were highly prevalent which confirms findings of the previous studies. Nearly one-fifth of our study group suffered from type 2 AMI due to severe anaemia, which was caused by either intensive, or prolonged haemorrhage, or disorders in haemoglobin production and metabolism pathways. In both cases, it was due to an underlying, often severe, medical condition.

As we have proven, patients with type 2 AMI are a heterogeneous group. On the one hand, in most cases, they probably suffered from AMI of a size smaller than patients with other types. On the other hand, some patients have various, often severe, co-morbidities, and some suffer AMI only due to an isolated coronary artery spasm. Early detection and active management of type 2 AMI is clouded by a number of factors. Firstly, by often non-specific ischaemia symptoms, which may be caused by coronary artery spasm being transient or infarction size being limited. The second important issue is a probable underestimation of the total number of type 2 AMI. Another factor indicating how little focus is put on this group is the fact that there are almost no studies describing it properly.

The results of this study have potentially high clinical implications for physicians. Patients with type 2 AMI should receive standard therapy according to the guidelines for MI.

**Limitations of the study**

There are several limitations to this study. One is that it is based on a relatively small number of patients. In the study we analysed all patients with an AMI diagnosis, but we could not reach those in whom this condition was not diagnosed, mostly due to severe clinical condition, or comorbidities. There is a need for a much larger, prospective analysis, preferably from other centres, to make sure that the same observations are made in other series of patients.

**CONCLUSIONS**

The prevalence of classical CV risk factors in type 2 AMI patients was very high. Patients were more often female and diagnosed as NSTEMI. The outcome is similar to patients with AMI type 1. The leading cause of AMI type 2 was coronary artery spasm.

**Conflict of interest:** none declared

**References**

Clinical characteristics, aetiology and occurrence of type 2 acute myocardial infarction


Zawał serca typu 2: etiologia, częstość występowania i charakterystyka kliniczna pacjentów

Filip M. Szymański1, Grzegorz Karpiński1, Anna E. Platek1, Franciszek Majstrak2, Anna Hrynkiewicz-Szymańska3, Marcin Kotkowski1, Bartosz Puchalski1, Krzysztof J. Filipiak1, Grzegorz Opolski1

1Klinika Kardiologii, Warszawski Uniwersytet Medyczny, Warszawa
2Klinika Kardiochirurgii, Warszawski Uniwersytet Medyczny, Warszawa
3Klinika Kardiologii, Nadciśnienia Tętniczego i Chorób Wewnętrznych, Warszawski Uniwersytet Medyczny, Warszawa

Streszczenie


Cel: Celem badania było ustalenie częstości występowania i etiologii ostrego MI (AMI) typu 2 oraz przedstawienie charakte-rystyki klinicznej, a także ocena rokowania pacjentów dotkniętych tym schorzeniem.


Wyniki: Wśród 2882 pacjentów hospitalizowanych w opisanym okresie u 58 (2%) chorych rozpoznano AMI typu 2. Średni wiek tych pacjentów wynosił 67,3 ± 13,2 roku, a większość badanej grupy stanowiły kobiety (60,3%). Spośród wszystkich badanych pacjentów z AMI typu 2 u 23 (39,6%) osób MI był spowodowany skurczem tętnicy wieńcowej, u 15 (25,9%) nastąpił wskutek wystąpienia zaburzeń rytmu serca, u 11 (19,0%) osób był wywołany ciężką niedokrwistością, natomiast u 9 (15,5%) chorych — wysokim ciśnieniem tętniczym. U żadnego z pacjentów nie stwierdzono występowania istotnych hemodynamicznie zmian miażdży w tętnicach wieńcowych. U większości [42 (72,4%)] pacjentów rozpoznano MI bez uniesienia odcinka ST (NSTEMI), u 14 (24,1%) — MI z uniesieniem odcinka ST, a w 2 (3,5%) przypadkach MI wystąpił u pacjentów ze stałą komorową stymulacją serca. Obecność klasycznych czynników ryzyka chorób układu sercowo-naczyniowego, takich jak nadciśnienie tętnicze, cukrzyca, zaburzenia gospodarki lipidowej, dodatni wywiad rodzinny w kierunku chorób układu krążenia oraz nikotynizm odnotowano, odpowiednio u 42 (72,4%), 14 (24,1%), 23 (39,7%), 24 (41,4%) oraz 16 (27,6%) badanych pacjentów z AMI typu 2. 30-dniowa śmiertelność całkowita w badanej grupie wynosiła 5,2%, natomiast całkowita śmiertelność 6-miesięczna sięgała 6,9%.

Wnioski: Większość pacjentów z AMI typu 2 stanowią kobiety. W analizowanej grupie MI częściej przebiega pod postacią NSTEMI, a częstość występowania klasycznych czynników ryzyka chorób układu sercowo-naczyniowego jest bardzo wysoka. Najczęstszą przyczyną MI typu 2 jest skurcz tętnicy wieńcowej.

Słowa kluczowe: ostry zawał serca typu 2, etiologia, rokowanie

Kardiol Pol 2014; 72, 4: 339–344