

## Review

# High risk group: the elderly with atypical presentation of acute coronary syndrome

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In accordance with the information from the World Health Organization (WHO), people having reached the age of 65 are called seniors in the most of developed countries of the world. This definition, however, does not apply to African countries. Therefore, the United Nations have not denoted the specific number defining elderly age. Yet, according to the decision of the United Nations, the age of 60 or more years is considered to be consistent with the definition of “advanced age” or “the elderly”. In 2007, the WHO announced that longevity means good health, and the longer age of the world population indicates the fact that the health care system is improving. According to the information from the WHO, in 2007, the number of people over 60 years old all over the world was 650 million. The forecast is that by 2050 the number of such people will total 2 billion. This trend is doubtlessly quite a challenge to the health care systems of the 21<sup>st</sup> century.

So far a unanimous and universal definition of the advanced or elderly age has not been given due to the fact that the exact biomarker for the assessment of senescence does not exist. Physiological age-related changes do not upstart at a certain strictly defined age, as each individual is bound to follow one’s own individual pace of aging. Gerontologists classify this part of population as “young old” (60–74 age group), “old old” (75–85 age group) and “very old” (85+ age group) [1].

WHO experts forecast the increase of death rates caused by coronary heart disease by 120% among women and 137% among men within the next 20 years [2]. Such forecasts are largely based on the expansion of the elderly population within the society. Cardiovascular morbidity and mortality is sharply rising among the elderly over 75 years old. This patient group which represents only 6% of the USA population accounts for 60% of deaths occurring due to sustained myocardial infarctions [3]. Elderly patients (over 75 years old) account for about 30% of patients with acute coronary syndrome [4]. Moreover, the forecast is that by 2030 the number of people over 85 years old in the USA is going to double, and by 2050 – to triple [5].

In 1996, the average life expectancy for Lithuanian men was 64.64 years and 75.89 years for Lithuanian women while according to the statistics from 2009 the average life expectancy for Lithuanian men increased to 67.51 years and to 78.56 years for Lithuanian women [6].

According to the information from the Statistics Lithuania under the Government of Lithuania, in 2005, the number of people over 75 years of age accounted for 6% of the population of Lithuania while in 2010 the rate increased and reached 7.1%. The Statistics Lithuania under the Government of Lithuania announced that in 2009, 46.3% of deaths among men and as much as 65.2% of deaths among women were caused by cardiovascular diseases [7].

Physicians working in intensive cardiology departments note that their patients are mostly seniors suffering not only from heart diseases but also from numerous co-morbidities, the number of which is constantly growing. Therefore, due to the aging population, intensive cardiology

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departments instead of providing treatment for myocardial infarctions and its complications are turning into intensive therapy departments dealing with cardiovascular diseases [8].

It is common knowledge that people over 65 years of age mostly suffer from cardiovascular diseases, arterial hypertension or coronary heart disease. Development of atherosclerotic processes in the coronary blood vessels results in the inadequacy between the demand for and supply with the oxygen. Such processes cause pain in the chest known as angina pectoris. However, one of the characteristics of acute coronary syndrome in the elderly is the fact that it often presents a painless form, i.e. atypical manifestation, or atypically. In 1903, Colbeck suggested the "mechanical" theory of the pain development. According to this theory, pain develops due to the left ventricular wall strain [9]. In 1932, Lewis suggested the "chemical" theory of the pain development. Its essence lies in the fact that during myocardial ischemia chemicals that cause pain are being released. Subsequent studies indicated that adenosine may be one of the mediators causing pain [10]. On the grounds of such findings the "chemical" pain development theory has emerged [11]. Besides the above mentioned theories there also exists a hypothesis of "neurogenic" development of pain which is another interpretation of the pain development [12]. Unfortunately, the mechanism of the pain development is not quite clear yet. Also, there is no unanimous theory explaining the development of pain. There is as yet no competent explanation of the painless myocardial infarction phenomenon. Supposedly, the perception of pain changes with age. The number of co-morbidities such as diabetes is increasing in the elderly [13]. Diabetes causes autonomic neuropathy resulting in pain perception changes which is often the cause of atypical development of myocardial infarction [14].

Typical ischemic pain, so-called angina pectoris is usually defined as strong pressure or compression in the chest, also "burning" and difficulty while breathing. In most cases, the pain is radiating to the left shoulder, neck or arm and lasts a few minutes. The pain may start during physical activity or following a psycho-emotional stress.

The references of the American College of Cardiology and the American Heart Association list the characteristics of the atypical ischemic pain as follows: pain as sharp as a stab of a knife, depending on breathing movements, also cough, discomfort in the lower or middle abdomen, pain in a small spot of the heart apex, pain while moving or palpation of the chest, sustained pain lasting

several hours, very short painful episodes lasting a few seconds, pain radiating to legs [15].

However, acute coronary syndrome (ACS) may present without pain, and then it manifests dyspnoea, profuse diaphoresis, retching, belching, vomiting, syncope, changed behaviour. ACS with atypical pain or no pain is defined as atypical ACS.

In 1995, there were findings of the prospective Reykjavik Study announced on the epidemiology of undiagnosed myocardial infarction, its clinical characteristics and the prognostic significance of angina pectoris. The study included 9,141 men. The patients have been observed for 20 years. It was found that the frequency of cases of undiagnosed myocardial infarction are more frequent having reached the age of 60. There was an interesting finding while comparing survival rates among patients with the diagnosed myocardial infarction and the undiagnosed one – it appeared that the 10-year survival rates did not present any statistical significance [16].

Another extensive prospective study attempting to find out whether there is a link between the symptoms of acute myocardial infarction and the patients' age, gender as well as other usual risk factors was being carried out while examining 1,996 patients arriving to Split hospital with myocardial infarction. This study has been verifying the findings on how the patients' gender and other factors may determine the symptoms of myocardial infarction. According to the findings, the independent risk factors determining atypical (i.e. without pain) development of acute myocardial infarction both for men and women are as follows: lower concentration of CK-MB ( $p < 0.0001$ ), diabetes ( $p < 0.0002$ ), advanced age. Atypical manifestation of myocardial infarction is particularly characteristic to elderly women. The study has established that approximately 34.3% of men and 48.4% of women have dyspnoea, 59.7% of men and 48.1% of women have diaphoresis, 40.9% of men and 57.4% of women have nausea, 17.6% of men and 21% of women are vomiting [17].

The data on 20,881 patients with acute coronary syndrome were being evaluated using the GRACE (the Global Registry of Acute Coronary Events) database. It has been found that 1,763 patients (8.4%) had atypical development of acute coronary syndrome. It was mostly dyspnoea (49.3%), diaphoresis (26.2%), nausea and vomiting (24.3%), syncope or pre-syncope (19.1%). The form of acute coronary syndrome without pain was mostly characteristic to elderly patients, especially elderly women.

The atypical development determined a prolonged time from the symptom onset to arrival

at hospital (3.2 vs 2.9 hours accordingly;  $p < 0.02$ ) [18]. A similar trend has been indicated in NRMI-2 (the National Registry of Myocardial Infarction 2) according to which the atypical development of myocardial infarction results in more than 2 hours' delay before arrival at hospital (7.9 vs 5.3 hours) [19].

Based on the information provided in the GRACE it was found that acute coronary syndrome has not been diagnosed immediately upon arrival at hospital for as many as 23.8% of patients with atypical clinical manifestation. Therefore, the treatment of such patients was less effective, their in-hospital mortality rates were higher than those of patients with typical painful myocardial infarction (13% vs 4.3% accordingly;  $p < 0.0001$ ) [18].

The similar findings are provided in NRMI-2: the in-hospital mortality rate for patients with myocardial infarction without pain and for those with typical myocardial infarction was 23.3% and 9.3% accordingly [19].

Complications during hospitalization (heart failure, cardiogenic shock, renal failure, arrhythmia) were also more common for patients with atypical acute coronary syndrome. The in-hospital mortality rate was as high as 13.0% in the cases of atypical clinical manifestation. In the cases of typical clinical manifestation the in-hospital mortality rate was 4.3%. The statistical reliability of the rates given above is  $p < 0.0001$  [18]. While trying to find out how in-hospital mortality depended on the form of acute coronary syndrome it was established that the mortality rate for patients with atypical form of acute myocardial infarction with ST elevation was 20% (18.7% of atypical symptoms, 6.3% of typical symptoms,  $p < 0.001$ ). The greatest frequency of in-hospital deaths was among patients with anterior ST elevation myocardial infarction (further on referred to as STEMI) in the case of both typical and atypical presentation (23.4% vs 7.4% accordingly;  $p < 0.001$ ). Higher morbidity rates in the cases of all other forms of acute myocardial infarction were prognosticated by their atypical developments [18].

The fact that acute coronary syndrome has been diagnosed with delay upon arrival at hospital for approximately 25% of patients in the GRACE means also a delay in proper treatment. This partly explains the high mortality rates for patients with atypical presentation of STEMI as they require reperfusion treatment most urgently [20].

Based on the information provided in NRMI-2, there were six important factors established related to atypical myocardial infarction presentation: congested heart failure, medical history

of stroke, advanced age, diabetes, female gender, non-white race. The more the above mentioned factors are presented in a patient, the greater the probability of myocardial infarction without pain development, i.e. atypical [19].

It is evident that the information on the characteristics of MI presentation provided in the reference sources is rather ambiguous. Therefore, based on the existent data it is impossible to create guidelines for diagnostics and treatment which could be applied in clinical practice or follow-up of such patients.

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