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Gender and age clinical characteristics of patients with acute coronary syndrome

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ABSTRACT

Cardiovascular diseases remain a common cause of morbidity and mortality in populations around the world, varying in incidence by age and gender. Every year, more than 7 million people around the world are diagnosed with acute coronary syndrome, which may be the first clinical manifestation of coronary heart disease. In the ranking of mortality causes in the Russian Federation, diseases of the circulatory system occupy a leading place. The purpose of the review was to analyze the clinical characteristics and spectrum of coronary lesions of patients with acute coronary syndrome depending on age and gender. Thus, according to the results of coronary angiography, young patients with myocardial infarction were rarely accompanied by multivessel or ostial lesions of the coronary arteries, in contrast to the elderly patients. It was revealed that multivessel lesions of the coronary arteries more often characterize males, and singlevessel lesions more often characterize females. It is obvious that the prognosis of patients with acute coronary syndrome will largely depend not only on age and gender, but also on the outcome of the syndrome, the quality and scope of diagnostic and treatment procedures. This is especially important since most patients under 60 years of age are exposed to some form of systematic work load in their field of activity. The influence of polypathy, characteristic of modern cardiac patients, can be expressed to varying degrees depending on the gender and age of the patient with acute coronary syndrome. The article presents data on the short-term and long-term prognosis of patients with acute coronary syndrome, taking into account gender and age periods, including depending on the tactics of their management. Determining the clinical characteristics of patients of different ages allows to take them into account for selecting effective and safe therapy, preventing wave-like atherosclerosis as the main cause of coronary heart disease, thereby improving prognosis and survival.

Keywords: acute coronary syndrome; myocardial infarction; age; gender; forecast.

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Половозрастные клинические характеристики пациентов с острым коронарным синдромом

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АННОТАЦИЯ

Сердечно-сосудистые заболевания остаются частой причиной заболеваемости и смертности населения всего мира, варьируя по частоте в зависимости от возраста и пола. Ежегодно более чем у 7 млн человек в мире диагностируют острый коронарный синдром, который может быть первым клиническим проявлением ишемической болезни сердца. В рейтинге причин смертности населения Российской Федерации болезни системы кровообращения занимают ведущее место. Цель обзора — анализ клинических характеристик, спектра поражений коронарного русла пациентов с острым коронарным синдромом в зависимости от возраста и пола. Так, по результатам коронароангиографии пациентам молодого возраста с инфарктом миокарда редко сопутствовало многососудистое или устьевое поражение коронарных артерий в отличие от пожилых. Выявлено, что многососудистое поражение коронарных артерий чаще характеризует представителей мужского пола, а одножосудистое — женского. Очевидно, что и прогноз пациентов с острым коронарным синдромом в значительной степени будет зависеть не только от возраста и пола, но и от исходов синдрома, качества и объёма диагностических и лечебных процедур. Это особенно важно, так как большинство пациентов моложе 60 лет подвергаются той или иной систематической трудовой нагрузке в своей сфере деятельности. Влияние полипатии, свойственной современному кардиологическому больному, в разной степени может быть выражено в зависимости от пола и возраста пациента с острым коронарным синдромом. В статье приведены данные краткосрочного и отдалённого прогноза пациентов с острым коронарным синдромом с учётом пола и возрастных периодов, в том числе в зависимости от тактики их ведения. Определение клинических характеристик пациентов различного возраста позволяет учитывать их для подбора эффективной и безопасной терапии, профилактики волнообразно протекающего атеросклероза как основной причины ишемической болезни сердца, тем самым улучшая прогноз и выживаемость.

Ключевые слова: острый коронарный синдром; инфаркт миокарда; возраст; пол; прогноз.

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INTRODUCTION

Cardiovascular diseases remain the leading causes of morbidity and mortality worldwide. The 2023 European Society of Cardiology guidelines for the diagnosis and treatment of acute coronary syndrome (ACS) indicate that there were 2.2 million deaths in women and 1.9 million deaths in men [1]. In 2019, 5.8 million new cases of coronary heart disease (CHD) in the 57 European Community member states were reported [1].

Cardiovascular diseases represent a significant proportion of mortality in the Russian population, accounting for 55% of all deaths among the population, including one-third of the deceased who were of working age [2]. Infectious and cardiovascular diseases are common causes of death among individuals aged 20–40 years [3].

Moreover, circulatory system diseases are the leading cause of death in individuals aged >40 years [3]. The increasing mortality trend of the working age population is crucial. Every year, approximately 400,000 people die before reaching retirement age, and >75% of the working age Russians who die are men [3].

Cardiovascular diseases are found to be the primary cause of mortality in Russia, accounting for 46.3% of all deaths, including those in men [2, 3]. In 2018, 52.6% of deaths from circulatory diseases were attributed to CHD, including 6.5% due to myocardial infarction (MI) [2]. Annually, over 7 million individuals worldwide are diagnosed with ACS, which is a common initial clinical manifestation of cardiovascular disease [1, 5].

ACS is a set of clinical signs or symptoms indicative of acute MI or unstable angina [5]. The GRACE registry shows that the mortality rate of patients who have experienced ACS within the past 5 years remains at 20%. This rate is 22% for patients who have undergone non*ST*-elevation MI (NSTEMI), 19% for those who have experienced *ST*-elevation MI (STEMI), and 18% for those who have had unstable angina [5].

A greater proportion of fatal outcomes are observed during hospitalization, specifically in STEMI cases, and after the patient has been discharged from the hospital. This is observed in both NSTEMI (87%) and unstable angina (97%) [5]. The recent trend indicates a shift in the ratio of STEMI to NSTEMI within the overall MI population, with an observed increase in NSTEMI. The trend in recent years shows a change in the STEMI/NSTEMI ratio in the total pool of MI toward an increase in the incidence of NSTEMI. This is partly due to the widespread use of cardiac markers of necrosis and other modern investigative techniques in emergency cardiology [6].

In contrast to STEMI, comorbidities such as diabetes mellitus, hypertension, and obesity are more common in the baseline characteristics of patients with NSTEMI, whereas no significant differences are noted in age [7].

In Russia, the annual registration of ACS averages 520,000 cases, including 36.4% of MI and 63.6% of unstable angina. The 2012 Moscow registry of ACS cases reveals that 28.3% of cases were classified as ST-elevation ACS (STE–ACS). The hospital mortality rate was 12.4% in patients with STE–ACS and 1.9% in patients with nonST-elevation ACS (NSTE–ACS) [8].

A comprehensive search of the PubMed and eLibrary databases was conducted using the following keywords: “acute coronary syndrome,” “acute coronary syndrome in young patients,” “myocardial infarction,” “age,” and “gender.” The search was conducted in Russian and English. The search period spanned the years 2004–2023. Articles containing only summaries or abstracts were excluded. Accordingly, this descriptive review consisted of summarized and systematized data from 51 sources, including actual clinical trials, reports, and systematic reviews.

INCIDENCE OF ACS BY SEX AND AGE

Several studies have shown differences in the incidence of MI in men and women and in different age groups [9]. In men aged 30–39 years, 1 MI case/1,000 was found. In the age group 60–64 years, the incidence increased to 18 cases/1,000 people. ACS and its endovascular treatment in patients aged <35 years is not sufficiently described in the literature. Studies on this topic are limited to the description of clinical cases or analysis of the whole population of young patients with ACS [10–12].

According to the World Health Organization age classification, young age includes people aged 25–44 years [13]. In young patients, the prevalence of MI is five times higher in men than in women. In the middle-aged group, MI is two times less frequent in women than in men. In the elderly and senile, the incidence of MI does not significantly differ by sex [14].

Studies by Yunyun et al. are of clinical interest because they revealed the possibility of premature death and long-term disability in individuals aged <45 years, despite the rarer detection of MI than in older people. Age is recognized as a factor in sex differences in acute CHD mortality worldwide [15]. STEMI is diagnosed more frequently in men than in women [6]. In the age cohort <60 years, ACS is diagnosed 3–4 times more often in men, whereas in the group aged >75 years, it is diagnosed more often in women [16].

A meta-analysis by Lei et al. reported differences in cardiac risk factors between young and older patients with acute MI: smoking [odds ratio (OR): 2.71; 95% confidence interval (CI): 1.87–3.92], family history of CHD (OR: 2.36; 95% CI: 1.22–4.59), obesity (OR: 1.76; 95% CI: 1.13–2.74), and alcohol consumption (OR: 1.76; 95% CI: 1.04–2.97) [17].

The course of MI in individuals aged <45 years has a short ischemic history. For example, the duration of clinical symptoms of angina pectoris in young patients does not exceed several days, and electrocardiographic changes are detected only during the pain syndrome [18]. Patients aged <45 years who are hospitalized with a diagnosis of MI have not been under previous medical supervision [19].

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Ponomarenko et al. studied 474 patients with ACS and found a higher proportion of women in the middle-age and elderly group (45–74 years; n = 175; 42.3%) compared to the young group (25–44 years; n = 299; 13.4%; $p < 0.001$). Patients younger than 45 years were more likely to have MI in the anterior wall (59.5% vs. 36.5%; $p < 0.001$), inferior wall (20% vs. 11.1%; $p = 0.046$), and posterior wall (9.1% vs. 43.7%; $p < 0.001$) of the left ventricle compared to middle-aged and elderly patients [20].

PECULIARITIES OF CORONARY ARTERY LESIONS

Kitulwatte believed that, in young patients, a greater proportion of MI cases develop due to coronary thrombosis than due to atherosclerosis, as is the case in older patients [21]. The coronary angiographic data of young patients with MI showed fewer coronary lesions and multivessel and orifice lesions of the coronary arteries than those of older patients with MI [22, 23]. The coronary arteries are more intact or the lesion is univascular in young individuals than in patients aged >50 years [18]. In young people, univascular lesions of the anterior descending coronary artery predominate [24].

Ponomarenko et al. showed a predominant single-vessel atherosclerotic lesion of the coronary artery in young individuals than in the elderly in 56.5% and 20% of cases, respectively ($p < 0.001$), less frequently two-vessel in 21.4% and 32.6% ($p = 0.01$), and multivessel in 10% and 44.5% ($p < 0.001$). Lesions of the left coronary and circumflex arteries are diagnosed less frequently in the younger than in the older age group (3.1% vs. 9.1%, $p = 0.014$, and 19.9% vs. 48%, $p < 0.001$, respectively) [20].

Yang et al. studied 7,106 individuals aged 18–44 years with ACS and revealed that left main lesions were more common in women (7.3%) than in men (4.1%) ($p < 0.01$); multivessel lesions were more common in men (43.4%) and univessel lesions in women (47.0%); and women were more likely to have small vessel occlusions than men (Killip II–IV) (38.6% vs. 25.6%; $p < 0.05$) [25]. Multifocality of the lesion with involvement of noncoronary vascular basins in the atherosclerotic process is not influenced by sex [26].

The structure of coronary lesions in patients aged <40 years is dominated by pathology of the anterior interventricular artery (56%–80%), less frequently the right coronary artery (15.6%–39%) and circumflex artery (14%–26%). The left main coronary artery was significantly less frequently affected in young patients than in age-matched patients [19]. The incidence of left main coronary artery stenosis in young patients with CHD was 0.9%–2.1% [27].

Ricci et al. reported less coronary artery calcification in young people. The volume of coronary artery lesions calculated on the Syntax scale increased with age by 20.2% in men and 4.1% in women [22].

PROGNOSIS IN PATIENTS WITH ACS DEPENDING ON SEX AND AGE

Registry data indicated sex differences in CHD mortality; however, general patterns of sex- and age-specific mortality remain unclear. According to the meta-analysis by Lunova et al. (20-22), short- and long-term survival from all causes was worse in women with ACS than in men with ACS 3, 28]. Manzo-Silberman et al. (based on data from seven French registries in 2005–2012) reported a threefold increase in in-hospital mortality in women than in men and high incidence of death in women within 12 months after MI [29].

In a retrospective analysis of the US National Inpatient Sample, no sex differences were found in in-hospital mortality for acute MI between the ages of 18 and 45 years [30]. Ten Haaf et al. showed a higher 1-year mortality from ACS in young women than in men in the Netherlands (7.3% vs. 5.6%, $p < 0.001$), and a lower mortality in women aged >71 years than in men [31].

In Russia, the mean values of mortality for each of the acute forms of CHD were significantly higher in men than in women in 2015 ($p < 0.0001$) and 2019 ($p < 0.0001$) [24]. Several studies noted a high post-infarction mortality in young and middle-aged women, which levels off after the age of 60 [32–34].

Despite a significant reduction in cardiovascular mortality in women over the past decades, sex differences in ACS incidence remain poorly understood [30, 35]. Postmortem studies showed sex differences in coronary plaque morphology, with a higher prevalence of erosion in young women and frequent plaque rupture in menopausal women and no increase in prevalence of plaque rupture with aging in men [30, 35].

Significant differences were found in the underlying mechanisms of ACS between different age groups. In women, in contrast to men, the number of plaque ruptures ($p < 0.001$) and vulnerability, such as lipid plaque ($p < 0.001$), thin-capped fibroatheroma ($p = 0.005$), and microstructures, including macrophages, cholesterol crystals, and calcification ($p = 0.026$), tended to increase with age [30, 35].

Women younger than 65 years are characterized by a lower incidence of *Q*-wave MI and a relatively favorable outcome, whereas the proportion of such MI increases with age. In men, the prevalence of *Q*-wave MI as a result of ACS does not change significantly with age [36].

Amsterdam et al. recommended a predominantly invasive ACS treatment, including for patients in older age groups (≥75 years) [37].

Considering that cardiovascular pathology, in addition to mortality, affects the quality of life of elderly and senile patients, it is crucial to understand the characteristics of symptoms and syndromes in elderly patients with ACS owing to the growth of this age group. However, their description in publications and clinical trials is underrepresented [38, 39].

In a study by Lopes et al., data from 367,110 patients aged >65 years who had undergone NSTEMI revealed an elevated

incidence of 1-year mortality with increasing age. The mortality rates were 13.3% for patients aged 65–75 years, 23.0% for those aged 80–84 years, 33.6% for those aged 85–89 years, and 45.5% for those aged ⩾90 years. Moreover, the incidence of repeat hospitalizations within a 1-year period was increased in all age groups, with rates reaching 52.7% (52.0–53.3) in individuals aged 65–79 years, 59.6% (58.4–60.7) in those aged 80–84 years, 59.5% (58.1–60.9) in those aged 85–89 years, and 56.5% (54.6–58.4) in those aged ⩾90 years. The authors employed a continuous modeling of age with mortality, revascularization, and drug therapy, which revealed a 50% increase in the risk of death for every 10-year increase in age (hazard ratio: 1.50; 95% CI: 1.45–1.56; $p < 0.0001$) [40].

A comparative analysis of the short-term prognosis (30 days) of patients aged 75 years (n = 564) and younger patients (n = 1,017) in the multicenter registry Registro Osservazionale Angina Instabile-2 revealed an increased risk of death (6.4% vs. 1.7%), MI (7.1% vs. 5%), and cerebral stroke (1.3% vs. 0.5%) in the older age group. In patients aged ⩾75 years, the independent predictors of mortality were conservative therapy tactics (OR: 2.1; 95% CI: 1.20–4.48) and the development of nonQ-wave MI (OR: 2.27; 95% CI: 1.32–3.93) [41].

The results from Fragmin and Fast Revascularization During Instability in Coronary Artery Disease, Invasive versus Conservative Treatment in Unstable Coronary Syndromes, and Third Randomized Intervention Treatment of Angina trials showed that patients aged 65–74 years with NSTE–ACS have a reduced risk of cardiovascular death or MI with mandatory percutaneous coronary intervention within 5 years (OR: 0. 72; 95% CI: 0.58–0.90) than those aged >75 years (OR: 0.71; 95% CI: 0.55–0.91). The benefit of the mandatory intervention strategy was less pronounced in women than in men ($p < 0.009$) [42].

According to the Treat Angina with Aggrastat and Determine Cost of Therapy with an Invasive or Conservative Strategy –Thrombolysis in Myocardial Infarction–trial, early invasive intervention in patients with NSTE–ACS aged ⩾75 years (n = 2,200) leads to a reduction in the absolute risk of death and MI within 6 months (10.8% vs. 21.6%, $p = 0.016$) and a relative risk reduction of 56% [43].

The pathogenesis and course of MI are age-specific. Knowledge of these peculiarities in young and elderly people is aimed at ACS prevention and prognosis improvement [12].

The negative trends in the lifestyle of young patients, including chronic stress, fatigue, poor nutrition, hypodynamia leading to impaired carbohydrate and lipid metabolism, and obesity, contribute to the "rejuvenation" of cardiovascular diseases [20].

Genetic predisposition is a nonmodifiable risk factor for the development of ACS. A paternal family history of CHD (up to 50 years of age) increases the risk of early-onset ACS by twofold in men and by 70% in women. Moreover, it increases the risk of a fatal outcome by a factor of 1.5 [44]. Notably, in different years of observation and in different countries – members of the European Community –age is a factor determining the trends of sex differences in mortality from acute forms of CHD [45].

Currently, Russian and foreign clinical recommendations lack clearly formulated data on the peculiarities of management tactics for patients of different age and sex [1, 5, 7, 8, 37, 45, 46]. The mortality rate of MI has decreased with the widespread introduction of endovascular treatment [8].

Comorbidities in ACS are relevant, as they significantly influence the clinical presentation and prognosis of patients. Comorbidity is age-related, occurring in 90% of patients aged >65 years [47].

CONCLUSIONS

Prognostic scales have been developed to determine the prognosis of patients with ACS. Myocardial necrosis markers, multivessel coronary lesions, electrocardiographic changes, decreased left ventricular contractility, previous MI, type 2 diabetes mellitus, obesity, decreased glomerular filtration rate, inflammatory markers, and advanced age were the most crucial criteria.

Thus, abnormalities in the clinical course and spectrum of coronary lesions in patients with ACS depend on age and sex.

ADDITIONAL INFORMATION

Authors' contribution. O.V.B.—conceptualization, supervision, writing—review & editing; E.I.M.—investigation, resources, writing—original draft, writing—review & editing; E.V.Kh.—investigation, resources, writing—original draft, writing—review & editing.

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