УДК 616.132.2-089.86-037:616.12-005.4-03
https://doi.org/10.20538/1682-0363-2022-1-152-161

Comorbidity of coronary artery disease and its significance in predicting the results of coronary artery bypass grafting

Rublev V.Yu.[1], Geltser B.I.[1], Sergeev E.A.[1], Kotelnikov V.N.[1], Karpov R.S.[2]

[1] *Far Eastern Federal University (FEFU)*
6, Sukhanova Str., Vladivostok, 690091, Russian Federation

[2] *Cardiology Research Institute, Tomsk National Research Medical Center (NRMC), Russian Academy of Sciences*
111a, Kievskaya Str., Tomsk, 634012, Russian Federation

ABSTRACT

The review presents an analysis of the scientific literature on comorbidity of coronary artery disease (CAD) and assessment of its impact on the results of coronary artery bypass grafting (CABG). Arterial hypertension (AH), chronic obstructive pulmonary disease (COPD), metabolic syndrome (MS), and diabetes mellitus (DM) have been shown to be the most common comorbidities in CAD patients. Clinical manifestations of cardiovascular comorbidities also include atrial fibrillation, acute cerebral ischemia, atherosclerosis of carotid and lower limb arteries, and chronic heart failure.

Concomitant COPD doubles the risk of postoperative complications after CABG and reduces the 10-year survival rate in patients to 30%. In CAD patients with MS, the risk of postoperative mortality increases by 1.4 times, and the 5-year survival rate decreases by 3 times. Diabetes significantly worsens the long-term survival of patients after CABG and is an independent predictor of acute cardiovascular events after revascularization in the long term. The presence of various comorbidities in CAD patients requires a personalized approach to managing the risks of adverse outcomes after CABG and introduction of modern artificial intelligence (AI) technologies into clinical practice, which significantly increase the accuracy of prognosis.

Keywords: comorbidity, coronary artery disease, coronary artery bypass grafting, prognosis

Conflict of interest. The authors declare the absence of obvious or potential conflicts of interest related to the publication of this article.

Source of financing. The study was carried out within the RFBR grants No. 19-29-01077 and No. 18-29-03131.

Conformity with the principles of ethics. The study was approved by the local Ethics Committee at Far Eastern Federal University (Protocol No. 12 of 15.11.2017).

For citation: Rublev V.Yu., Geltser B.I., Sergeev E.A., Kotelnikov V.N., Karpov R.S. Comorbidity of coronary artery disease and its significance in predicting the results of coronary artery bypass grafting. *Bulletin of Siberian Medicine.* 2022;21(1):152–161. https://doi.org/10.20538/1682-0363-2022-1-152-161.

✉ *Kotelnikov Vladimir N.,* 671235@mail.ru

Коморбидность ишемической болезни сердца и ее значение в прогнозировании результатов аортокоронарного шунтирования

Рублев В.Ю.[1], Гельцер Б.И.[1], Сергеев Е.А.[1], Котельников В.Н.[1], Карпов Р.С.[2]

[1] *Дальневосточный федеральный университет (ДВФУ)*
Россия, 690091, г. Владивосток, ул. Суханова, 8

[2] *Научно-исследовательский институт (НИИ) кардиологии, Томский национальный исследовательский медицинский центр (НИМЦ) Российской академии наук*
Россия, 634012, г. Томск, ул. Киевская, 111а

РЕЗЮМЕ

Представлен анализ научной литературы по проблеме коморбидности ишемической болезни сердца (ИБС) и оценке ее влияния на результаты аортокоронарного шунтирования (АКШ). Показано, что наиболее частыми вариантами коморбидной патологии у больных ИБС являются артериальная гипертензия (АГ), хроническая обструктивная болезнь легких (ХОБЛ), метаболический синдром (МС) и сахарный диабет (СД). Сердечно-сосудистая коморбидность помимо АГ проявляется также фибрилляцией предсердий, острой церебральной ишемией, атеросклерозом сонных артерий и артерий нижних конечностей, хронической сердечной недостаточностью.

Респираторная коморбидность, представленная ХОБЛ, увеличивает риск послеоперационных осложнений АКШ в 2 раза, а 10-летняя выживаемость этих больных снижается до 30%. У больных ИБС с МС риск послеоперационной летальности увеличивается в 1,4 раза, а 5-летняя выживаемость снижается в 3 раза. СД существенно ухудшает долгосрочную выживаемость больных после АКШ и является независимым предиктором острых сердечно-сосудистых событий в отдаленный период после реваскуляризации. Наличие различных вариантов коморбидности у больных ИБС требует персонифицированного подхода к управлению рисками неблагоприятных исходов АКШ и внедрения в клиническую практику современных технологий искусственного интеллекта, повышающих точность прогнозирования.

Ключевые слова: коморбидность, ишемическая болезнь сердца, аортокоронарное шунтирование, прогнозирование

Конфликт интересов. Авторы декларируют отсутствие явных и потенциальных конфликтов интересов, связанных с публикацией настоящей статьи.

Источник финансирования. Работа выполнена при поддержке грантов РФФИ в рамках научных проектов № 18-29-03131, № 19-29-01077.

Соответствие принципам этики. Исследование одобрено локальным этическим комитетом ДВФУ (протокол № 12 от 15.11.2017).

Для цитирования: Рублев В.Ю., Гельцер Б.И., Сергеев Е.А., Котельников В.Н., Карпов Р.С. Коморбидность ишемической болезни сердца и ее значение в прогнозировании результатов аортокоронарного шунтирования. *Бюллетень сибирской медицины.* 2022;21(1):152–161. https://doi.org/10.20538/1682-0363-2022-1-152-161.

INTRODUCTION

Currently, comorbidity is understood as coexistence of two or more diseases, regardless of their intensity, which are pathogenetically interconnected or coincide in time for one patient [1]. Comorbidity has been proven to be associated with adverse disease outcomes, an increased risk of adverse effects of drug therapy, and a significant increase in treatment costs. One of the main reasons for the growth of concomitant conditions is increased life expectancy in developed countries. Thus, more than 50% of people aged over 60 years have at least three concomitant diseases, and the proportion of patients from older age groups with five or more comorbid pathologies is constantly increasing [2]. Comorbidity of coronary artery disease (CAD) with other pathologies significantly aggravates its clinical course and reduces the effectiveness of therapy and survival prognosis after myocardial revascularization. Therefore, the problem of comorbidity in such groups of patients is of special interest [3].

Today, coronary artery bypass grafting (CABG) is one of the most common types of surgical treatment for CAD, which restores coronary blood flow and increases the quality and expectancy of patients' life. Evaluation of its long-term results is the subject of numerous studies. Thus, the accumulated clinical experience indicates that CABG does not fully prevent progressive or recurrent myocardial ischemia (MI). It has been proven, in particular, that within 2–3 years after CABG, recurrent angina pectoris develops in 3.5–7.2% of patients, and by the fifth year, their number increases up to 17–36% [4].

The frequency and timing of angina pectoris recurrence are determined by the clinical features of CAD before myocardial revascularization, surgical risk factors, the presence or absence of postinfarction cardiosclerosis, the prevalence and localization of coronary artery (CA) stenosis, and the presence and intensity of concomitant pathology [5–9]. In the multicenter study conducted by the US Society of Thoracic Surgeons, factors that most commonly appear as the main causes of rehospitalization for patients after CABG were identified. These included: chronic obstructive pulmonary disease (COPD) (odds ratio (OR) 1.81), cerebrovascular disease (OR 1.56), diabetes mellitus (DM) (OR 1.44), and chronic heart failure (CHF) (OR 2.21).

It was shown that one year after CABG, in patients of older age groups with comorbidities, behavioral risk factors affecting their quality of life and disease outcome were more likely to persist (smoking, irregular intake of medications, non-compliance with diet, sedentary lifestyle, etc.) [10,11]. According to the results of the national study in Iceland, it was found that 5-year survival for patients after CABG was 89.9%, and the most significant predictors of mortality were concomitant conditions, such as COPD, chronic renal failure, and diabetes [12]. Another study found that significant predictors of long-term mortality (7 years after CABG) are cerebrovascular diseases, significant peripheral arterial disease, COPD, CHF, and ventricular arrhythmias [13].

According to the data from the Russian Cardiac Surgery Center registry, 10-year survival rate for patients after CABG was 76.4%, and comorbidities, such as DM, COPD, and ischemic stroke (IS) were among the factors that significantly influenced survival [14]. A number of studies have shown that negative CABG prognosis is also associated with the presence of left ventricular (LV) aneurysms, low ejection fraction (EF), small CA diameter, and the use of vein grafts [4, 8, 12, 14]. The quantity and intensity of concomitant pathology for CAD patients is associated with certain gender differences: women are more likely to have hypertension, diabetes, thyroid pathology, bronchial asthma (BA), and varicose veins, while men more commonly have hypertension, lower extremity artery stenosis, COPD, and urolithiasis.

It was noted that the presence of comorbidities in CAD patients planning to undergo CABG is generally a rule, not an exception, which requires an optimal strategy for personalized therapy for comorbidities in preoperative period, as well as adherence to recommendations on their examination and treatment in the postoperative period. In addition, understanding the clinical and pathophysiological features of various types of comorbidities, as well as common biological patterns of non-random co-occurrence of diseases (syntropic diseases) should provide higher efficiency of risk management for adverse outcomes upon surgical myocardial revascularization. In such cases, interdisciplinary interaction of specialists, including the information technology field, is particularly relevant, making it possible to evaluate a wider range of predictors characterizing the postoperative period and long-term consequences of CABG prognosis. However, the problem of CAD comorbidity with account of its typological features, including cardiovascular, respiratory, metabolic, and other clinical variants of the disease, has not been fully resolved and requires further study.

COMORBIDITIES OF CAD WITH OTHER CARDIOVASCULAR DISEASES

As a rule, pathologies of the coronary, cerebral, and peripheral arteries develop simultaneously due the same pathophysiological mechanisms of atherosclerotic lesion formation in the vascular pool. For example, a combination of carotid artery atherosclerosis and CA occlusion occurs in 74.7–92.4% of patients. The most common clinical variant of associated vascular comorbidity in CAD is arterial hypertension (AH), which, according to various sources, can be seen in 64–81.2% of CAD patients [15–17]. In younger groups of patients (up to 50 years of age), this combination is found in around 45% of cases, while in patients over 70 years, it is observed in 85% of cases. The combination of these pathologies leads to an increase in LV stiffness due to its hypertrophy, which worsens the clinical prospects in patients after myocardial revascularization [18]. According to 3-year follow-up, in the absence of AH treatment, the frequency of LV hypertrophy (LVH) in patients with CAD increased from 57 up to 77%, and the number of cases with diastolic and systolic dysfunction of both ventricles increased drastically [19].

In other studies, LVH was registered in 11.8–59% of patients with CAD. The clinical significance of LVH lies primarily in the fact that it is an independent and strong predictor of cardiovascular mortality: its presence doubles the risk of death for CAD patients [18]. In CAD with comorbid AH, increased LV myocardial mass has greater prognostic value in terms of mortality than a degree of blood pressure (BP) increase and other risk factors, except age, with the worst prognosis occurring for patients with concentric LVH [19]. That happens due reduction of the number of resistance microvessels per unit of myocardial tissue during LVH, which in turn accelerates coronary remodeling, reduces its vasodilation potential, and increases intracardiac vascular resistance. In addition, these changes contribute to the development of perivascular fibrosis, which also limits the coronary flow reserve and increases myocardial oxygen demand.

A combination of AH, LVH, and CAD significantly increases CA stiffness and worsens the prognosis in both diseases [20]. At the same time, it was shown that for CAD patients with LVH, a combination of CABG and surgical LV reconstruction to reduce its volume did not lead to a decrease in the severity of cardiac symptoms, exercise tolerance, hospitalization rates, and mortality [21]. In patients with CAD associated with AH, 3–5 years after CABG, relapses of angina pectoris, coronary atherosclerosis progression, and vein graft stenosis were noted significantly more often than in patients with effective control. These changes were closely related with the degree and time index of the average daily systolic and diastolic blood pressure, as well as with the insufficient degree of its nighttime drop.

A frequent combination of CAD, AH, and carotid artery atherosclerosis determines a high risk of IS in such patients. Thus, CAD was diagnosed in 74% of patients with IS [22]. In other studies, the combination of CAD and IS was recorded in 30–60% of cases [23]. According to various authors, hemodynamically significant carotid artery stenosis was found in 2.8–17% of CABG patients. It was also shown that around 28–40% of patients after carotid endarterectomy are diagnosed with concomitant CA lesion [24]. For patients with a history of transient ischemic attack or IS, the risk of recurrent acute ischemic stroke in the perioperative period increases up to 8.5%. At the same time, the risk of death for patients after simultaneous CABG and endarterectomy is around 10–12% [23, 24].

In the postoperative period, paroxysmal atrial fibrillation (PAF) develops in 30–50% of patients who underwent CABG with cardiopulmonary bypass (CPB) and less frequently – in off-pump CABG, which increases the risk of embolic complications by 4 times and the risk of sudden cardiac death by 3 times [25]. Higher incidence of atrial fibrillation (AF) is associated with older age, male sex, prolonged mechanical ventilation, multifocal atherosclerosis, COPD, left atrial enlargement, valvular lesions, episodes of AF before surgery, diabetes, and obesity.

Pathogenetic features of postoperative AF are determined by the presence of new triggers associated with cardiac surgery and CPB: impaired blood ionic composition, atrial edema, compliment activation and expression of proinflammatory cytokines, increased sympathetic activity, oxidative stress, and pericardial effusion. It was also established that the presence of even a single episode of PAF in the postoperative period acts as an independent risk factor for development of a persistent form of the disease (risk ratio (RR) 4.99). Long-term comorbidity of CAD and AF in the preoperative period exacerbates ischemic myocardial damage and aggravates patient's hemodynamic status. AF episodes before CABG dramatically increase the risk of sudden cardiac death in the postoperative period (9 vs. 2%), ischemic cerebrovascular events (7 vs. 2%), and development of end-stage CHF (18 vs. 7%) [26]. To prevent such complications, various options for simultaneous surgical treatment of paroxysmal and persistent AF during CABG have been developed, which contributes to restoration and stabilization of sinus rhythm in a significant number of patients and improves the structural, functional, and electrophysiological characteristics of the myocardium [27].

Chronic critical lower extremity ischemia combined with CAD is observed in 37–78% of patients [28]. Combined atherosclerotic damage to the lower extremity arteries and branches of the aortic arch and abdominal aorta occurs in almost half of CAD patients [24]. For such patients, the risk of IS and MI in the early postoperative period after CABG reaches 12% (against 3.8% in the general population) [22, 23]. Depending on the number of damaged arteries, the risk of postoperative vascular events increases by 1.64–10.5 times compared with isolated coronary artery disease. Independent predictors of overall and cardiovascular mortality after CABG were determined for patients with multifocal atherosclerosis, which include the presence of clinical manifestations of lower limb ischemia (OR 3.6) and a decrease in the ankle-brachial index without clinical manifestations (OR 2.4). The 3-year cardiovascular mortality after CABG in patients with multifocal atherosclerosis is 18.5% vs. 11.2% in the general population of CAD patients [29].

In the European epidemiological study of patients with CAD, functional class (FC) III–IV CHF was detected in 5 and 0.6% of CAD patients, respectively [30]. It was proven that chronic impairment of coronary circulation leads to structural changes in cardiomyocytes and a decrease in myocardial contractility due to ischemic cardiomyopathy formation. On the other hand, limitation of LV contractility contributes to development of arterial hypoxemia, increases myocardial oxygen demand, and aggravates the clinical course of CAD. It was established that in CAD patients with CHF, surgical myocardial revascularization is more preferable than percutaneous coronary intervention. According to meta-analysis data, patients with left ventricular ejection fraction (LVEF) ≤ 35% after CABG show operative mortality of around 50% and 5-year survival of up to 73% [13, 24]. In patients with normal ejection fraction (EF), the same parameters are 2 and 83.8%, respectively. Therefore, AH with LVH, CHF, AF, atherosclerotic stenoses of carotid and peripheral arteries, and episodes of acute ischemic stroke should be attributed to the most frequent and dangerous manifestations of cardiovascular comorbidity in CAD patients. The effectiveness of CABG in such cases depends on the effectiveness of risk stratification in the preoperative period, as well as on personalized programs for preparation for surgery and postoperative rehabilitation for such patients.

COMORBIDITY OF CAD WITH CHRONIC OBSTRUCTIVE PULMONARY DISEASE

According to numerous studies, COPD prevalence in the Russian Federation is around 15.3% in the general population and 21.8% among people with respiratory symptoms. At the same time, mortality from COPD ranks 4th around the world. COPD is classified as a multisystem disease, the most important extrapulmonary manifestation of which is damage to the cardiovascular system. Large epidemiological studies demonstrate that the leading cause of mortality for COPD patients is cardiovascular pathology, which is recorded in at least 50% of these patients [31]. It has been shown that every 10% decrease in forced expiratory volume in 1 second (FEV1) increases the risk of cardiovascular mortality by 28% and non-fatal coronary events by 20% [32].

The key mechanisms of cardiovascular comorbidity in COPD are chronic systemic inflammation, arterial hypoxemia and tissue hypoxia, oxidative stress and degradation of the extracellular matrix, which accelerate atherogenesis and are involved in the pathogenesis of intracardiac, central, and pulmonary hemodynamic disorders and myocardial contractile dysfunction. A number of authors point to certain difficulties in diagnosing CAD in COPD patients due the fact that in the clinical presentation of the concomitant pathology, signs of dyspnea due to respiratory failure prevail instead of the coronary syndrome [33, 34].

One of the factors contributing to the atypical course of CAD in patients with COPD is chronic arterial hypoxemia, which increases the pain threshold. This explains, in particular, that painless forms of myocardial ischemia are more common for patients with COPD, they are recorded in 66.7–84.4% of cases. According to results of various studies, atypical localization of chest pain is recorded much more often in patients with comorbidity, than in individuals with isolated CAD [35, 36].

In patients with CAD against the background of COPD, a more severe course of angina pectoris and CHF is also observed. In addition, in CAD patients with comorbidity, the severity of bronchial obstruction is significantly higher than in patients with isolated COPD. The main mechanisms of mutual aggravation of these diseases include augmented pulmonary shunt both due to ventilation – perfusion mismatch characteristic of COPD and alveolar shunt against the background of left ventricular failure and diffusion disorders associated with ischemic cardiomyopathy. It should be noted that progression of CAD and COPD during their comorbidity is characterized by commonality of some links in their pathogenesis. In particular, formation of secondary pulmonary hypertension increases the load on the right heart and left atrium, limiting the coronary flow reserve, which increases MI in both ventricles and contributes to progression of coronary and pulmonary heart disease [37].

It is believed that a severe course of COPD reduces traditional clinical and functional manifestations of CAD [33]. In these situations, more careful monitoring of physiological functions in the dynamics of the disease is required. In addition, according to various authors, the frequency of the established COPD diagnosis in patients with CAD referred for CABG ranges from 6.7 up to 14% [36]. However, spirometry for all patients before CABG makes it possible to diagnose obstructive disorders in more than a third of all cases. Thus, in real clinical practice, the problem of cardiorespiratory comorbidity in patients with CAD is underestimated due COPD underdiagnosis. The SYNTAX II scoring scale has been proven to be a useful tool for optimizing the choice of surgical revascularization and predicting 4-year survival outcomes among patients with complex CAD forms, which include associated COPD. It was shown that risks of complications during the hospital stay in patients with cardiorespiratory comorbidity double [35]. Other studies identified an increase in the risk of mortality in patients with COPD after CABG by 1.4–1.8 times compared with the control group (27.2 vs.14.5%) [34]. According to the results of the Spanish Registry, the 10-year survival rate for patients with CAD and concomitant COPD after CABG is 30% [33].

A number of studies indicate a predictive role of individual parameters of lung ventilation function in assessing early and long-term CABG consequences in patients with COPD. In particular, FEV1 has been shown to be an informative predictor of 5-year survival in COPD patients who underwent CABG [33]. According to other data, FEV1 less than 60% of the expected value is an unfavorable prognostic factor for postoperative respiratory complications and long-term results of revascularization [36].

The predictive value of forced vital capacity in assessing the risk of developing hospital-acquired pneumonia, atelectasis, and postoperative wound infections and increasing the duration of mechanical ventilation after surgery and reintubation was also shown. One of the factors aggravating respiratory failure and increasing the risk of cardiovascular complications in COPD patients in the postoperative period is respiratory muscle dysfunction, which timely diagnosis and correction at the preoperative stage can reduce the risk of postoperative complications. It has been shown that prehabilitation of COPD patients with respiratory simulators and modern methods of bronchodilator therapy significantly improves postoperative period prognosis and respiratory function recovery rate [33].

COMORBIDITY OF CAD WITH METABOLIC SYNDROME

Metabolic syndrome (MS) is defined as a complex of endocrine and metabolic disorders associated with insulin resistance. A detailed study of its development mechanisms is of great clinical importance, since this syndrome is reversible and amenable to therapeutic control. In the “classic” variant of MS, it is characterized by abdominal obesity, dyslipidemia, impaired carbohydrate metabolism, and hypertension, which determines its high atherogenic potential. Thus, the incidence of CAD in people with MS increases by 2.9–4.2 times and mortality rate – by 2.6–3 times. After CABG, the presence of MS is recorded in 55.4% of women and 41.3% of men [38]. In patients with MS, the incidence of life-threatening cardiovascular diseases increases by almost 4 times [39].

The importance of individual MS components and their combinations in the development of coronary artery atherosclerosis, LVH, LV diastolic dysfunction, AF, and other variants of cardiovascular comorbidity has been proven [39, 40]. According to individual studies, a complete MS cluster is formed within at least 10 years, and its multicomponent variants are characterized by severe comorbidity [41, 42].

Development of acute cardiovascular events after CABG in patients with MS is significantly more frequent, and a number of authors indicate a significant increase in mortality in such groups (2.4 vs. 0.9%) [42]. According to the American Society of Thoracic Surgeons, the presence of MS increases the risk of postoperative mortality by 1.4 times [43]. In MS, the risk of developing respiratory complications and postoperative wound increases by 2.5 times, and thorough correction of carbohydrate metabolism in the perioperative period reduces it by 2 times. Another study confirmed a significant association of MS with wound infections and pulmonary complications (OR 6.64), cardiac arrhythmias (OR 5.47), prolonged mechanical ventilation (OR 5.47), and almost a 3-fold increase in the risk of postoperative mortality after CABG, compared with the control group (3.1 vs. 1.1%) [42, 43]. In CAD patients with MS, CA lesions are usually more diffuse and distal, which in some cases limits the use of endovascular revascularization. This explains the advantage of CABG with arterial bypasses compared with percutaneous coronary intervention for such patients. In CAD patients with MS over 65 years, surgical myocardial revascularization increases the 10-year survival rate by almost 50% [39].

Besides, it has been shown that with coronary artery occlusion in patients with MS, the degree of collateral circulation development is lower, and the clinical course of atherosclerosis is more aggressive with an increased risk of developing various complications. A high risk of adverse cardiac events, shunt obstruction or new coronary artery damage within 2–5 years after CABG correlates with triglyceride and blood glucose levels. It has been shown that in MS patients with high triglyceride levels and elevated (>8.6%) levels of glycosylated hemoglobin in the preoperative period, mortality after CABG increases by 4 times [44]. In case of CAD with concomitant MS in the long-term period after revascularization, the incidence of CHF increases by 46%. According to the Scottish registry, after CABG, patients with a body mass index (BMI) of 27.5–30 kg / m^2 had a decrease in the 5-year mortality rate by 41% compared with patients whose BMI was more than 30 kg / m^2 [12]. These data support the hypothesis on atherogenic and inflammatory activity of visceral adipose tissue in patients with MS. Thus, according to the results of a five-year cohort study, patients with MS after CABG, distributed according to the presence or absence of obesity, significantly differed in terms of early postoperative complications (30.26 vs. 20.75%, OR 2.04) and five-year mortality (11.84 vs. 3.74%, OR 4.65) [45].

COMORBIDITY OF CAD WITH DIABETES MELLITUS

Based on the WHO data, the number of patients with diabetes mellitus (DM) is steadily growing and now accounts for about 2.1% of the population, while DM contribution to the overall mortality by 2030 will reach 3.3%. According to the DECODE study, DM prevalence increases with age, regardless of gender, and the lifetime risk of morbidity is 30–40%. DM prevalence among CAD patients planning to undergo surgical treatment is about 35% [46, 47].

DM is one of the leading pathogenetic factors for development and progression of circulatory disorders, and the risk of cardiovascular mortality in patients with CAD and associated DM increases by 2 times in males and by 4 times in females [48]. In particular, it has been shown that mortality in patients with acute coronary syndrome and DM is 2–3 times higher than in patients with normal carbohydrate metabolism [49]. In case of CAD and DM comorbidity, coronary artery atherosclerosis is more diffuse, with frequent involvement of the epicardial ST segment and an increased tendency to restenosis and shunt obstruction [44]. A number of studies have noted an increase in mortality during CABG in patients with DM (3 vs. 1%) [39, 42, 44]. Other studies have shown that immediate CABG outcomes in patients with DM may not differ compared with patients without DM [45]. Thus, according to a retrospective analysis of 4,508 bimammary CABG surgeries, the presence of DM did not affect the overall hospital mortality, but was associated with wound infection and postoperative bleeding. In a similar study, the presence of DM did not increase the risk of mortality and cardiovascular and other hospital-acquired complications, with the exception of renal dysfunction [50, 51]. However, the clinical prospects of long-term CABG results for patients with DM are not so optimistic. Thus, patient's 1-, 5-, 10-, and 20- year survival after CABG with and without DM was 94 vs. 94%, 80 vs. 84%, 56 vs. 66%, and 20 vs. 32%, respectively [52].

DM significantly impairs long-term survival after surgical revascularization, being an independent predictor of acute cardiovascular events [41,48]. Moreover, in patients with type 2 diabetes receiving insulin therapy, IS, MI or sudden cardiac death were significantly more likely to develop both during the short-term (30 days) and medium-term follow-up (1 year) – OR 1.66 and 1.50, respectively [53]. For patients with type 1 diabetes, according to the SWEDEHEART registry, the risk of mortality after CABG increased by more than 2 times compared with the general population (OR 2.04) [54].

The 5-year mortality after CABG in patients with DM was 6 times higher than in the control group (12.1 and 2.1%, respectively). In the structure of 5-year mortality in patients with DM after CABG, acute heart failure prevails, usually associated with MI [52]. The long-term prognosis is also affected by the presence of prediabetes detected in the preoperative stage. Thus, after CABG, the risk of acute cardiovascular events for such patients is significantly higher (OR 1.40), which proves the importance of an active approach to DM detection [50]. The results of 6-year survival after off-pump CABG in patients with DM differ significantly from the results after CABG with CPB and reach 69.9 and 54.7%, respectively [54].

CONCLUSION

Thus, literature data indicate that the presence of certain types of comorbidities in patients with CAD is the most important prognostic factor characterizing the expectancy and quality of life after CABG. The most frequent and unfavorable concomitant pathologies include cardiovascular, respiratory, and metabolic comorbidities, the clinical manifestations of which have a significant impact on the effectiveness of surgical myocardial revascularization. The presence of concomitant pathology in CAD patients requires personalized approaches to peri- and postoperative management, as well as development of automated programs for predicting complications and long-term consequences of surgical treatment, taking into account individual risk factors. In addition, introduction of modern artificial intelligence technologies into clinical practice will significantly improve the accuracy of CABG outcome prediction and optimize treatment costs.

REFERENCES

1. Shirinsky V.S., Shirinsky I.V. Comorbid diseases as an important problem of clinical medicine. *Siberian Medical Journal*. 2014;29(1):7–12 (in Russ.). DOI: 10.29001/2073-8552-2014-29-1-7-12.
2. Sumin A.N., Korok E.V., Shcheglova A.V., Barabash O.L. Comorbidities in patients with ischemic heart disease: gender differences. *Rational Pharmacotherapy in Cardiology.* 2017;13 (5):622–629 (in Russ.). DOI: 10.20996/1819-6446-2017-13-5-622-629.
3. Bokeriya L.A., Aronov D.M. et al. Russian clinical guidelines. Coronary artery bypass grafting in patients with ischemic heart disease: rehabilitation and secondary prevention. *Cardiosomatics.* 2016;7(3–4):5–71 (in Russ.).
4. Cherniavsky A.M., Yefremova O.S., Ruzmatov T.M., Efendiev E.U. Predictors of remote mortality of CAD patients with severe left ventricular dysfunction. *Circulation Pathology and Cardiac Surgery*. 2015;19(2):49–54 (in Russ.). DOI:10.21688/1681-3472-2015-2-49-54.
5. Zubarevich A., Kadyraliev B., Arutyunyan V. et al. On-pump versus off-pump coronary artery bypass surgery for multi-vessel coronary revascularization. *J. Thorac. Dis*. 2020;12(10):5639–5646. DOI: 10.21037/jtd-20-1284.
6. Selcuk E., Cevirme D., Bugra O. Prognostic value of coronary dominance in patients undergoing elective coronary artery bypass surgery. *Braz. J. Cardiovasc. Surg*. 2020;35(4):452–458. DOI: 10.21470/1678-9741-2019-0079.
7. Liu M.-J., Chen Ch.-F., Gao X.-F., Liu X.-H., Xu Y.-Zh. In-hospital outcomes of chronic total occlusion percutaneous coronary intervention in patients with and without prior coronary artery bypass graft: A systematic review and meta analysis. *Medicine (Baltimore*). 2020; 99(23):e19977. DOI: 10.1097/MD.0000000000019977.
8. Antonopoulos A.S., Odutayo A., Oikonomou E.K., Trivella M., Petrou M., Collins G.S. et al. Development of a risk score for early saphenous vein graft failure: An individual patient data meta-analysis. *J. Thorac. Cardiovasc. Surg*. 2020;160(1):116–127.e4. DOI: 10.1016/j.jtcvs.2019.07.086.
9. Barabash O.L., Pomeshkina S.A., Kondrikova N.V., Trubnikova O.V. The problems of implementation of rehabilitation programs after coronary bypass grafting in Russia. *Cardiology and Cardiovascular Surgery.* 2017;10(4):8–12 (in Russ.). DOI: 10.17116/kardio20171048-12.
10. Lancey R., Kurlansky P., Argenziano M. et al. Uniform standards do not apply to readmission following coronary artery bypass surgery: A multi-institutional study. *J. Thorac. Cardiovasc. Surg.* 2015;149(3):850–857.e1. DOI: 10.1016/j.jtcvs.2014.08.059.
11. D'Agostino R.S., Jacobs J.P., Bedhwar V., Fernandez F.G., Paone G., Wormuth D.W. et al. The society of thoracic surgeons adult cardiac surgery database: 2018 update on outcomes and quality. *Ann. Thorac. Surg*. 2018;105(1):15–23. DOI: 10.1016/j.athoracsur.2017.10.035.
12. Johannesdottir H., Arnadottir L.O., Adalsteinsson J.A. et al. Favourable long-term outcome after coronary artery bypass grafting in a nationwide cohort. *Scandin. Cardiovasc. J*. 2017;51(6):327–333. DOI: 10.1080/14017431.2017.1364418.
13. Wu C., Camacho F.T., Zhao S., Wechsler A.S., Culliford A.T., Lahey S.G. et al. Long-term mortality of coronary artery bypass graft surgery and stenting with drug-eluting stents. *Ann. Thorac. Surg.* 2013;95(4):1297–1305. DOI: 10.1016/j.athoracsur.2012.11.073.
14. Efros L.A., Samorodskaya I.V. Survival and working ability in men after coronary bypass surgery (analysis of registry data). *Clinical Medicine*. 2013;91(5):27–31 (in Russ.).
15. Oganov R.G. Vascular comorbidity: general approaches to prevention and treatment. *Rational Pharmacotherapy in Cardiology*. 2015;11(1):4–7 (in Russ.).
16. Ostroumova O.D., Kochetkov A.I., Guseva T.F. Blood pressure variability in hypertension associated with coronary heart disease: prognostic value and management approaches. *Arterial Hypertension*. 2018;24(2):246–256 (in Russ.). DOI: 10.18705/1607-419X-2018-24-2-246-256.
17. Chazova I.E. Arterial hypertension in the light of current recommendations. *Therapeutic Archives*. 2018;90(9):4–7 (in Russ.). DOI: 10.26442/terarkh20189094-7.
18. Komissarova S.M., Zakharova E.Y., Sevruk T.V., Ustinova I.B., Krasko O.V. Predictive value of the global longitudinal strain in hypertrophic cardiomyopathy patients. *Russian Journal of Cardiology*. 2018;154(2):7–12 (in Russ.). DOI: 10.15829/1560-4071-2018-2-7-12.
19. Luan L., Hao H., Li S. A review of studies of quality of life for chinese-speaking patients with ischemic heart disease. *Value in Health Regional Issues*. 2018;15:82–90. DOI: 10.1016/j.vhri.2017.08.013.
20. Sasonko M.I., Atkov O.Y., Gurfinkel Y.I. Relationship between left ventricular hypertrophy and remodeling of capillary network in hypertensive patients. *Arterial Hypertension*. 2014;20(5):433–441 (in Russ.). DOI: 10.18705/1607-419X-2014-20-5-433-441.
21. Bokeriya L.A., Nikonov S.F., Bandeliani N.G., Cheishvili Z.M., Krymov K.V. Effectiveness and influence of a multifactorial approach to the treatment of patients with coronary heart disease after isolated coronary bypass and its combination with geometric reconstruction of the left ventricle on the quality of life and hospitalizations. *Annals of Arrhythmology*. 2012.8(4):43–54 (in Russ.).
22. Filimonova P.A., Volkova L.I., Alasheev A.M. et al. In-hospital stroke in patients after cardiac surgery or invasive interventions. *Neurology, Neuropsychiatry, Psychosomatics*. 2017;9(4):38–45 (in Russ.). DOI: 10.14412/2074-2711-2017-4-38-45.
23. Chichkova M.A., Kozlova O.S., Orlov F.V. Features of the combination of myocardial infarction and acute stroke. *Astrakhan Medical Journal*. 2016;11(1):55–63 (in Russ.).
24. Naylor A.R., Ricco J-B., de Borst G.J. et al. Editor's Choice – management of atherosclerotic carotid and verte-

bral artery disease: 2017 clinical practice guidelines of the European Society for Vascular Surgery (ESVS). *Eur. J. Vasc. Endovasc. Surg*. 2017;55(1):3–81. DOI: 10.1016/j.ejvs.2017.06.021.
25. Konstantino Y., Yovel D.Z., Friger M.D., Sahar G., Knyazer B., Amit J. Postoperative atrial fibrillation following coronary artery bypass graft surgery predicts long-term atrial fibrillation and stroke. *IMAJ.* 2016;18(12):744–748.
26. Butt J.H., Xian Y., Peterson E.D., Olsen P.S., Rorth R., Gundlund A. et al. Long-term thromboembolic risk in patients with postoperative atrial fibrillation after coronary artery bypass graft surgery and patients with nonvalvular atrial fibrillation. *JAMA Cardiol*. 2018;3(5):417–424. DOI: 10.1001/jamacardio.2018.0405.
27. Dynamics of structural and functional electrophysiological parameters of the heart in patients with paroxysmal atrial fibrillation after aortic-coronary bypass grafting simultaneous with radiofrequency ablation of pulmonary vein ostium. *Russian Journal of Cardiology*. 2014;12:19–24 (in Russ.). DOI: 10.15829/1560-4071-2014-12-19-24.
28. Sumin A.N., Kosova M.A., Medvedeva Y.D., Shcheglova A.V., Makarov S.A., Artamonova G.V., et al. Outpatient follow-up of patients with lower extremity atherosclerosis from a cardiologist's point of view. *Russian Journal of Cardiology*. 2016;(12):58–63 (in Russ.). DOI: 10.15829/1560-4071-2016-12-9-15.
29. Hannan E.L, Zhong Y., Wu Ch., Jacobs A.K., Stamato N.J., Sharma S. et al. Comparison of 3-year outcomes for coronary artery bypass graft surgery and drug-eluting stents: does sex matter? *Ann. Thorac. Surg*. 2015;100(6):2227–2236. DOI: 10.1016/j.athoracsur.2015.05.103.
30. Townsend N., Wilson L., Bhatnagar P., Wickramasinghe K., Rayner M., Nichols M. Cardiovascular disease in Europe: epidemiological update 2016. *Eur. Heart J.* 2016;37(42):3232–3245. DOI: 10.1093/eurheartj/ehw334.
31. Geltser B.I., Kurpatov I.G., Kotelnikov V.N., Zayats Yu.V.. Chronic obstructive pulmonary disease and cerebrovascular diseases: functional and clinical aspects of comorbidity. *Therapeutic Archives*. 2018;90(3):81–88 (in Russ.). DOI: 10.26442/terarkh201890381-88.
32. Lopukhova V.A. Analysis of the structure of adult Kursk region population incidence during hospitalization for cardiovascular disease. *International Journal of Applied and Fundamental Research.* 2017;6-2:233–237 (in Russ.).
33. Campo G., Pavasini R., Malagu M., Mascetti S., Biscaglia S., Ceconi C. et al. Chronic obstructive pulmonary disease and ischemic heart disease comorbidity: overview of mechanisms and clinical management. Cardiovascular Drugs Therapy. 2015;29(2):147–157. DOI: 10.1007/s10557-014-6569-y.
34. Didenko D, Rasputina L., Mostovoy Y., Cherepii N. Comorbidity in patients with IHD - the prevalence of COPD. *Eur. Respir. J.* 2016;48:PA1119. DOI: 10.1183/13993003.congress-2016.PA1119.
35. Kurniawan E., Ding F.H., Zhang Q., Yang Kh-H., Hu J., Shen W-F. et al. Predictive value of SYNTAX score II for clinical outcomes in octogenarian undergoing percutaneous coronary intervention. *Journal of Geriatric Cardiology*. 2016;13(9):733–739. DOI: 10.11909/j.issn.1671-5411.2016.09.014.
36. Melikulov A.A., Merzlyakov V.Yu., Klyuchnikov I.V., Mamedova S.K., Baychurin R.K., Ahmedova M.F. Short-term results of coronary artery bypass grafting in patients older than 70 years with multi-vessel coronary lesions. *Creative Cardiology*. 2017;11(3):212–221 (in Russ.). DOI: 10.24022/1997-3187-2017-11-3-212-221.
37. De Miguel-Díez J., Jiménez-García R., Hernández-Barrera V., Carrasco-Garrido P., Bueno H., Puente-Maestu L. et al. Time trends in coronary revascularization procedures among people with COPD: analysis of the Spanish national hospital discharge data (2001–2011). *International Journal of Chronic Obstructive Pulmonary Disease.* 2015;10:2285–2294. DOI: 10.2147/COPD.S92614.
38. Akhmedzhanov N.M., Butrova S.A., Dedov I.I., et al. Consensus of Russian experts on the problem of metabolic syndrome in the Russian Federation: definition, diagnostic criteria, primary prevention and treatment. *Cardiovascular Therapy and Prevention*. 2010;9(5):4–11 (in Russ.).
39. Garvey T.W., Mechanick J.I., Bret E.M., Garber A.G., Hurley D.L., Jastreboff A.M. et al. American Association of Clinical Endocrinologists and American College of Endocrinology Clinical Practice Guidelines for comprehensive medical care of patients with obesity. *Endocrine Practice.* 2016;22(3):1–203. DOI: 10.4158/EP161365.GL.
40. Druzhilov M.A., Beteleva Y.E., Khein I.V., Kuznetsova T.Yu. The "extra-media" thickness of carotid arteries as a novel marker of perivascular visceral adipose tissue: accent on the association with vascular remodeling parameters. *Russian Journal of Cardiology*. 2016;(4):25–29 (in Russ.). DOI: 10.15829/1560-4071-2016-4-25-29.
41. Chugunova Y.V., Chumakova G.A., Ermolin P.A., Baranov A.S. The influence of visceral obesity on cognition in patients after coronary artery bypass surgery. *Russian Journal of Cardiology*. 2016;(4):19–24 (in Russ.). DOI: 10.15829/1560-4071-2016-4-19-24.
42. Raza S., Sabik J.F., Ainkaran P., Blaskstone E.H. Coronary artery bypass grafting in diabetics: a growing healthcare cost crisis. *J. Thorac. Cardiovasc. Surg*. 2015;150(2):304–302.e2. DOI: 10.1016/j.jtcvs.2015.03.041.
43. Tennyson C., Lee R., Attia R. Is there a role for HbA1c in predicting mortality and morbidity outcomes after coronary artery bypassgraft surgery? Interac. Cardiovasc. Thorac. Surg. 2014;17(6):1000–1008. DOI: 10.1093/icvts/ivt351.
44. Ryden L., Grant P.J., Berne C. et al. ESC Guidelines on diabetes, pre-diabetes, and cardiovascular diseases developed in collaboration with the EASD: the Task Force on diabetes, pre-diabetes, and cardiovascular diseases of the European Society of Cardiology (ESC) and developed in collaboration with the European Association for the Study of Diabetes (EASD). *Eur. Heart J.* 2013;34(39):3035–3087. DOI: 10.1093/eurheartj/eht10.
45. Ugurchieva P.O., Didigova R.T., Ugurchieva Z.O., Mamedov M.N. Five-year prognosis in patients with coronary heart disease and comorbidities: data from multicenter study in the Ingushetia republic. *Russian Journal of Cardiology*. 2018;23(3):17–22 (in Russ.). DOI: 10.15829/1560-4071-2018-3-17-22.
46. Roffi M., Patrono C., Collet J.P. et al. 2015 ESC Guidelines

for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation: Task Force for the Management of Acute Coronary Syndromes in Patients Presenting without Persistent ST-Segment Elevation of the European Society of Cardiology (ESC). *Eur. Heart J.* 2016;37(3):67–315. DOI: 10.1093/eurheartj/ehv320.

47. O'Donoghue M.L., Vaidya A., Afsal R. et al. An invasive or conservative strategy in patients with diabetes mellitus and non–ST-segment elevation acute coronary syndromes. *JACC.* 2012;60(2):106–111. DOI:10.1016/j.jacc.2012.02.059.
48. Puzyrev V.P. Genetic basics of comorbidity in humans. *Genetics*. 2015;51(4):191–502 (in Russ.). DOI: 10.7868/S0016675815040098.
49. Moursi I., Fakharany K.A. Prognosis of diabetic coronary artery bypass graft surgery patients. *Journal of the Egyptian Society of Cardio-Thoracic Surgery*. 2017;25(4):294–300. DOI: 10.1016/j.jescts.2017.08.007.
50. Gatti G., Dell'Angela L., Maschietto L. et al. The impact of diabetes on early outcomes after routine bilateral internal thoracic artery grafting. *Heart Lung and Circulation*. 2016;25(8):862–869. DOI: 10.1016/j.hlc.2016.02.009.
51. Munnee K., Bundhun P.K., Quan H. et al. Comparing the clinical outcomes between insulin-treated and non-insulin-treated patients with type 2 diabetes mellitus after coronary artery bypass surgery: a systematic review and meta-analysis. *Medicine (Baltimore*). 2016;95(10):e3006. DOI: 10.1097/MD.0000000000003006.
52. Dalen M., Ivert T., Holzmann M.J. et al. Coronary Artery Bypass Grafting in Patients 50 Years or Younger A Swedish Nationwide Cohort Study. *Circulation*. 2015;131(20):1748–1754. DOI: 10.1161/CIRCULATIONAHA.114.014335.
53. Holzmann M.J., Rathsman B., Eliasson B. et al. Long-term prognosis in patients with type 1 and 2 diabetes mellitus after coronary artery bypass grafting. *JACC*. 2015;65(16):1644–1652. DOI: 10.1016/j.jacc.2015.02.052.
54. Sigaev I.Yu., Keren M.A., Yarbekov R.R., et al. Off-pump coronary artery bypass surgery in patients with diabetes: early and long-term results. *Annals of Surgery*. 2016;21(1-2):99–105 (in Russ.). DOI: 10.18821/1560-9502-2016-21-1-99-105.

Authors information

Rublev Vladislav Yu. – Post-Graduate Student, School of Biomedicine, FEFU, Vladivostok, Russian Federation.

Geltser Boris I. – Dr. Sci. (Med.), Professor, Corresponding Member of the RAS, Director of the Department of Clinical Medicine, School of Biomedicine, FEFU, Vladivostok., Russian Federation, http://orcid.org/ 0000-0002-9250-557X

Sergeev Evgeniy A. – Anesthetist, Resuscitationist, Post-Graduate Student, School of Biomedicine, FEFU, Vladivostok, Russian Federation, https://orcid.org/0000-0002-2176-7070

Kotelnikov Vladimir N. – Dr. Sci. (Med.), Professor, Department of Clinical Medicine, School of Biomedicine, FEFU, Vladivostok., Russian Federation, https://orcid.org/0000-0001-5830-1322

Karpov Rostislav S. – Dr. Sci. (Med.), Professor, Academician of the RAS, Research Supervisor, Cardiology Research Institute, Tomsk NRMC, Tomsk, Russian Federation, https://orcid.org/0000-0002-7011-4316

(✉) **Kotelnikov Vladimir N.** – 671235@mail.ru

Received 26.01.2021;
approved after peer review 17.02.2021;
accepted 25.05.2021