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The effect of depressive disorder on the clinical presentation of coronary artery disease and five-year survival of patients after myocardial infarction

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ABSTRACT

Aim. To assess the effect of depressive disorder (DD) on the clinical presentation of coronary artery disease (CAD) and five-year survival rate of patients with chronic CAD.

Materials and methods. The study included 79 patients with functional class II–III exertional angina who experienced myocardial infarction more than 6 months before. The patients were divided into two groups: group 1 (n = 45) consisted of patients with CAD and depression and group 2 (n = 34) encompassed patients with CAD without depression. The clinical presentation of CAD was assessed by the results of filling out the angina pectoris self-control diary and exertion tests. The presence and severity of DD were determined using psychometric scales, such as Hospital Anxiety and Depression Scale (HADS) and Beck Depression Inventory (BDI), and verified by the psychiatrist. Information about five-year survival was obtained via telephone interviews with the patients and their relatives.

Results. Patients with CAD and DD were characterized by more frequent episodes of angina pectoris during a week (10 [8; 14] vs 6 [4; 7], p = 0.000004), an increased demand for nitroglycerin (4 [0; 10] tablets vs 0 [0; 4] tablets, p = 0.001), and lower exercise tolerance (50 [25; 75] W vs 75 [50; 75] W (p = 0.06), 350 [250; 400] meters vs 435 [350; 500] meters (p = 0.01) than CAD patients without DD. The five-year survival rate was significantly lower in group 1 than in group 2 (69 [62; 72] vs 71 [68; 72] months (p = 0.04)), 35 (77.8%) vs 32 (94.1%) patients survived. In group 1, a greater number of deaths from cardiovascular accidents (10 (22.2%) vs 2 (5.9%)) was noted (log-rank test, p = 0.03).

Conclusion. In patients with CAD, associated depression results in aggravation of the clinical course of CAD and poor disease prognosis, which requires timely diagnosis and treatment of DD.

Keywords: coronary artery disease, depressive disorders, myocardial infarction, survival, mortality

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

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Conformity with the principles of ethics. All patients signed an informed consent to participate in the study. The study was approved by the Ethics Committee at the Cardiology Research Institute, Tomsk NRMC (Protocol No. 177 of 30.10.2018).

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Влияние депрессивного расстройства на клиническую картину коронарной болезни и пятилетнюю выживаемость больных после перенесенного инфаркта миокарда

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РЕЗЮМЕ

Цель. Оценить влияние депрессивных расстройств (ДР) на клиническую картину коронарной болезни и пятилетнюю выживаемость больных с хронической ишемической болезнью сердца (ИБС).

Материалы и методы. В исследование включены 79 больных со стенокардией напряжения II–III функциональных классов, перенесшие инфаркт миокарда давностью более 6 мес. Сформированы две группы: 1-я – 45 больных ИБС с депрессией и 2-я – 34 больных ИБС без депрессии. Клиническая картина ИБС оценивалась по результатам заполнения дневника самоконтроля стенокардии, по пробам с физической нагрузкой. Наличие и выраженность ДР определялись с помощью психометрических шкал (Госпитальная шкала тревоги и депрессии (HADS) и Шкала депрессии Бека (BDI)) и верифицировался психиатром. Информация о пятилетней выживаемости была получена методом телефонного интервью с пациентами и их родственниками.

Результаты. Больных ИБС с ДР в сравнении с пациентами без ДР чаще беспокоили ангинозные приступы в течение недели (10 [8; 14] vs 6 [4; 7], p = 0,000004), отмечалась большая потребность в приеме нитроглицерина (4 [0; 10] vs 0 [0; 4] таблеток, p = 0,001), более низкая толерантность к физической нагрузке (50 [25; 75] Вт vs 75 [50; 75] Вт (p = 0,06), 350 [250; 400] м vs 435 [350; 500] м (p = 0,01). В первой группе пятилетняя выживаемость была значительно ниже, чем во второй (69 [62; 72] vs 71 [68; 72] мес (p = 0,04)), выжило (35 (77,8%) vs 32 (94,1%), отмечалось большее число летальных исходов от сердечно-сосудистых катастроф (10 (22,2%) vs 2 (5,9%)) (лог-ранг тест p = 0,03).

Заключение. У больных ИБС присоединение депрессии приводит к ухудшению клинического течения коронарной болезни и прогноза, что требует своевременной диагностики и коррекции ДР.

Ключевые слова: ишемическая болезнь сердца, депрессивные расстройства, инфаркт миокарда, выживаемость, летальность

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

Источник финансирования. Авторы заявляют об отсутствии финансирования при проведении исследования.

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INTRODUCTION

Coronary artery disease (CAD) and depressive disorders (DD) have always been of great interest for science. According to the World Health Organization (WHO) forecasts, by 2030, CAD and depression will have become the leading causes of disability and invalidism in high-income countries around the world [1, 2]. Depression itself contributes to the occurrence of CAD; at the same time, it is more often observed

in patients with confirmed cardiovascular diseases [3] and is a strong predictor of a poor disease prognosis [4]. The risk of death in patients with cardiovascular pathology directly depends on the severity of the affective disorder [5–7]. In CAD with comorbid DD, more severe angina pectoris is noted and social functioning of patients is significantly reduced [5]. DD is verified in 40% of patients after acute myocardial infarction, which increases the risk of death by 3–6 times [6].

Studies have shown that less than 30% of patients have psychological complaints, leading to the development of depressive disorders in the future, due to which underdiagnosis of DD and untimely prescription of appropriate therapy for it are noted [9, 10]. Besides, patients with CAD with associated affective disorders show worse compliance with doctor's recommendations on a healthy lifestyle [11] and regular baseline therapy for CAD, which leads to frequent visits to the clinic and hospitalizations [12]. The relevance of studying the comorbidity of CAD and DD is beyond doubt, therefore, the aim of this study was to assess the effect of DD on the clinical presentation of CAD and five-year survival rate of patients with chronic CAD.

MATERIALS AND METHODS

The study included 79 patients with angina pectoris who experienced myocardial infarction more than 6 months before. The patients were divided into two groups: group 1 (n = 45) consisted of patients with exertional angina and depression and group 2 (n = 34) encompassed patients with exertional angina without depression. The diagnosis of DD was made based on the analysis of scales for detecting the presence of DD (Hospital Anxiety and Depression Scale (HADS)) and its severity (Beck Depression Inventory (BDI)). Depressive symptoms were considered elevated with the score of more than 8 on HADS and / or more than 19 on BDI. The final diagnosis was established by the psychiatrist.

Features of the clinical presentation of CAD in patients with depression compared with patients without DD were assessed by the angina pectoris self-control diary (the number of angina pectoris episodes per week, the need for nitroglycerin per week) and by exercise tests (bicycle ergometry, six-minute walk test).To determine the functional class of angina pectoris, we used the classification developed by the Canadian Heart Association (L. Campeau, 1976) and additionally compared it with the results of bicycle ergometry (W). The life expectancy of patients was assessed from the moment of admission to the hospital for 5 years. Information on five-year survival was obtained via telephone interviews with patients and their relatives and the analysis of medical records. Patients who were followed up to a certain endpoint (5 years), as well as patients who dropped out of the follow-up for unknown reasons (contact with them was lost) were considered as censored patients.

The differences were considered statistically significant at $p < 0.05$. For normally distributed quantitative variables, the data were presented as $M \pm SD$, where M is the mean and SD is the standard deviation. In this case, the reliability was checked using the t-test; to compare two dependent samples, Student's t-test was used. For non-normally distributed variables, the data were presented as the median and the interquartile range (Me [Q_1; Q_3]) and described by the Mann – Whitney test. For the analysis of qualitative variables, contingency tables and the $\chi 2$ test were used. Patient survival was assessed using the Kaplan – Meier method and presented graphically; a log-rank test was used to assess the differences.

RESULTS

The groups were comparable by age and sex: in group 1, the average age was 57.3 ± 7.1 years, 41 men and 4 women; in group 2, the average age was 57.5 ± 7.3, 31 men and 3 women ($p > 0.5$). According to the anamnestic data and clinical, laboratory, and instrumental parameters, the patients of groups 1 and 2 did not differ: the duration of myocardial infarction was 30 [6; 96] vs 24 [7; 72] months (p = 0.4), history of hypertension – 108 [24; 180] vs 90 [36; 132] months (p = 0.6), number of smokers – 21 vs 15 people (p = 0.8), percutaneous coronary intervention – 28 vs 27 patients (p = 0.1), body mass index – 28.8 [25.5; 31] vs 28.9 [26; 31] kg / m2 (p = 0.8), ejection fraction – 60.6 ± 10.1 vs 61.2 ± 7.7% (p = 0.1), total cholesterol level – 5.6 ± 1.2 vs 5.5 ± 1.6 mmol / l (p = 0.08). Patients with and without DD also did not differ in the functional class of exertional angina: class II – 29 vs 26 patients (p = 0.2), class III – 16 vs 8 patients (p = 0.2). Patients received baseline treatment for stable angina pectoris and complied with the doctor's recommendations, which made it possible to maintain the target values of heart rate and blood pressure. The average heart rate per day was 64 [61; 67] vs 65 [62; 71] beats per min (p = 0.3), the average daily systolic blood pressure was 120 [110; 130] vs 121 [112; 124] mm Hg (p = 0.9), and the average daily

diastolic blood pressure was 76 mm Hg [70; 82] vs 75 mm Hg [73; 78] (p = 0.7).

When testing for the preliminary diagnosis of depression using HADS and BDI scales, the following results were obtained: HADS – 8 [8; 10] vs 4 [3; 6] points (p = 0.0000001), BDI – 22 [16; 26] vs 15 [14; 19] points in group 1 and group 2, respectively (p = 0.0001). Afterwards, the diagnosis of depression was verified by the psychiatrist.

The groups were comparable in terms of the functional class of angina, however, patients with DD complained of angina pectoris episodes significantly more often (10 [8; 14] vs 6 [4; 7] per week (p = 0.000004) and more often needed nitroglycerin (4 [0; 10] vs 0 [0; 4] tablets) (p = 0.001). Besides, patients with DD performed worse in the six-minute walk test: 350 [250; 400] vs 435 [350; 500] meters (p = 0.01). Bicycle ergometry showed a trend toward significantly lower exercise tolerance in CAD patients with DD compared with CAD patients without DD: 50 [25; 75] vs 75 [50; 75] W (p = 0.06). Therefore, the comorbidity of DD with CAD aggravates the course of the underlying disease.

The information on five-year survival was obtained via telephone interviews with patients and their relatives and the analysis of medical records. After 5 years of follow-up, 67 patients (84.8%) survived, 12 patients (15.1%) died. In the group of patients with CAD with DD, as opposed to CAD patients without depression, significantly fewer patients survived (35 (77.8%) vs 32 people (94.1%)), and more fatal outcomes from cardiovascular events (10 (22.2%) vs 2 (5.9%)) were noted (log-rank test p = 0.03) (Fig. 1).

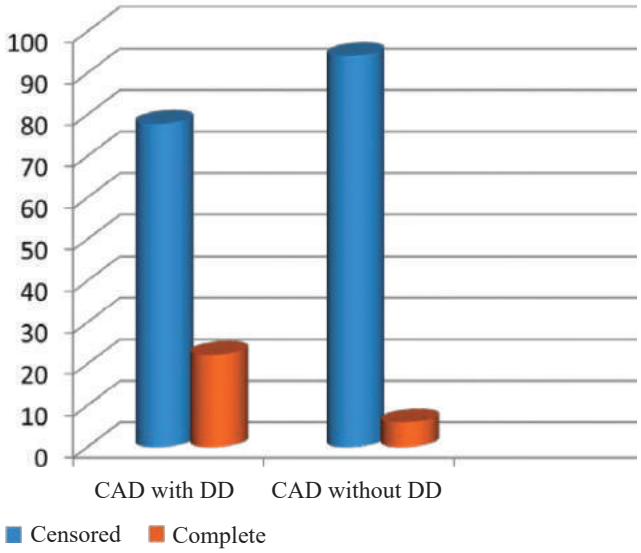

Fig.1. Five-year survival of patients

A significant difference was revealed in the Kaplan – Meier survival analysis; the data are presented in Figure 2. It was found that the survival rate was significantly lower in group 1 than in group 2: 69 [62; 72] vs 71 [68; 72] months (p = 0.04).

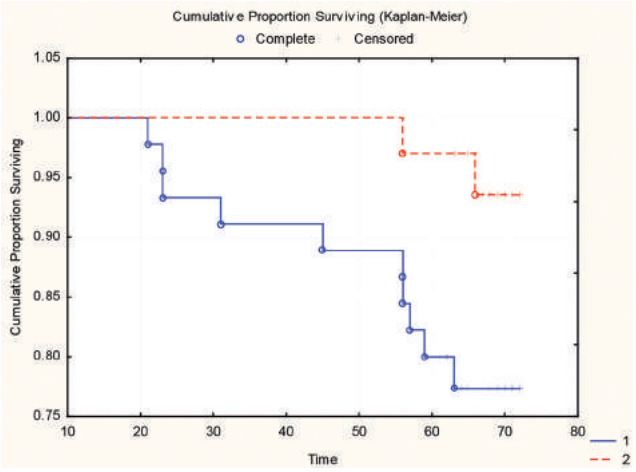

Fig. 2. Kaplan – Meier survival analysis in CAD patients with DD compared with CAD patients without DD

DISCUSSION

According to many large studies (MONICA, Cardiovascular Health Study, INTERHEART, ENRICHD, SADHART), depression can be considered as a predictor of cardiovascular events. Those studies included patients with acute coronary syndrome. We studied the clinical presentation of CAD in patients who experienced myocardial infarction (more than 6 months before) against the background of an affective disorder. Many psychometric scales and tests are currently used for DD screening. We used the most common and standardized questionnaires, such as BDI and HADS [13]. After testing, the patients were consulted by the psychiatrist, and the diagnosis of moderate DD was verified. In both groups, functional class II–III exertional angina was diagnosed, but according to self-control diaries, it was determined that patients with DD more often experienced episodes of angina and needed nitroglycerin. The aggravation of the clinical presentation of CAD in patients with DD was confirmed objectively: during bicycle ergometry, exercise tolerance was decreased, and patients covered a much shorter distance during the six-minute walk test. Similar results on the negative impact of DD on the course of CAD were described in previous studies [5, 14, 15].

Later, when analyzing the five-year survival rate using the Kaplan – Meier method, we found significant differences: the survival rate of CAD patients with

concomitant DD was significantly lower. The increase in mortality in CAD patients with DD is most likely associated with common pathogenetic mechanisms that exacerbate each other. Particularly, stress causes hyperactivation of the sympathetic adrenal system and autonomic dysfunction, which leads to development of life-threatening arrhythmias [16–18]. Moreover, DD results in an increased risk of thrombosis and, consequently, in CAD exacerbation [19]. Behavioral characteristics of patients with mental disorders play a crucial role in the disease prognosis: they do not adhere to a healthy lifestyle and show low compliance with CAD therapy, which significantly reduces their quality of life [14].

Therefore, DD significantly affects cardiovascular diseases: both the clinical course and the disease prognosis. For early detection of DD, according to the results of modern psychometric scales, patients should be timely referred to a psychiatrist for early prescription of antidepressants. Close observation of such patients by a joint team of a cardiologist and a psychiatrist will improve the survival of patients with CAD.

CONCLUSION

The aggravation of the clinical presentation of CAD and poor disease prognosis are typical of patients with CAD with associated depression. Our results confirm the need for timely verification and correction of DD. Affective disorders significantly reduce the long-term survival of patients with CAD.

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