

Prevalence of Musculoskeletal Disorders in Patients with Coronary Artery Disease

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Aim. To study the prevalence of musculoskeletal disorders in patients with stable coronary artery disease (CAD).

Material and methods. Patients with stable CAD (n=387) were included in the study. The subjects were admitted to the hospital for planned myocardial revascularization (ages of 50-82). The median age was 65 [59;69] years. Most of the sample consisted of males – 283 (73.1%). 323 (83.5%) patients had arterial hypertension (AH), 57.1% – history of myocardial infarction, and a quarter of the patients had type 2 diabetes mellitus (DM). The study of musculoskeletal system included the identification of sarcopenia in accordance with The European Working Group on Sarcopenia in Older People (EWGSOP, 2019); verification of osteopenia/osteoporosis according to the WHO criteria (2008); diagnosing osteosarcopenia in case of sarcopenia and osteopenia/osteoporosis coexistence.

Results. At the initial screening of sarcopenia in accordance with EWGSOP, clinical signs (according to the Strength, assistance with walking, rising from a chair, climbing stairs, and falls (SARC-F) questionnaire) were detected in 41.3% of cases, but further examination (dynamometry, quantitative assessment of skeletal muscle) confirmed this diagnosis only in 19.9% of patients with CAD. Among the examined patients with CAD a low T-score according to DEXA was found in 53 (13.7%) of cases, and osteopenia was diagnosed 10 times more often than osteoporosis (90.6% vs. 9.4%). Furthermore, due to combination of low bone density (osteopenia/osteoporosis) and reduced muscle mass and strength (sarcopenia), osteosarcopenia was verified in one patient. Thus, the study revealed the prevalence of particular types of musculoskeletal disorders in 105 (27.1%) patients with stable CAD. The most common type of musculoskeletal disorder was sarcopenia – 52 cases (13.4%); osteopenia/osteoporosis was detected in 28 patients (7.2%), osteosarcopenia in 25 (6.5%). The most pronounced clinical manifestation of sarcopenia and osteopenia/osteoporosis, reflected by a higher score on the SARC-F questionnaire, low handgrip strength, small area of muscle tissue, low musculoskeletal index, as well as low values of bone mineral density, were observed in patients with osteosarcopenia. Patients with osteopenia/osteoporosis did not differ significantly from patients without musculoskeletal conditions in most parameters, with the exception of the T-score, the average SARC-F score, and muscle strength in men. The conducted correlation analysis revealed not only the relationship between the parameters of musculoskeletal function, but also their association with age, duration of AH, CAD, and type 2 DM.

Conclusion. Several types of musculoskeletal disorders were found in a third of patients with CAD. Sarcopenia was revealed to be the most frequent type of musculoskeletal disorder.

Keywords: coronary artery disease, coronary artery bypass grafting, musculoskeletal disorder, osteopenia, osteoporosis, sarcopenia, osteosarcopenia.

For citation: Bazdyrev E.D., Terentyeva N.A., Krivoschapova K. E., Masenko V.L., Wegner E.A., Kokov A.N., Pomeschkina S.A., Barbarash O. L. Prevalence of Musculoskeletal Disorders in Patients with Coronary Artery Disease. *Rational Pharmacotherapy in Cardiology* 2021;17(3):369-375. DOI:10.20996/1819-6446-2021-06-03.

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Received: 02.04.2021

Accepted: 06.04.2021

Introduction

Population aging is becoming an increasingly serious social problem around the world. According to the World Health Organization, the proportion of older people in many countries (including China) will exceed 30% by 2050 [1]. This demographic shift will entail many challenges, including an increase in the economic burden due not only to an increase in the number of chronic diseases, but also to disability and mortality. The exponential growth of the elderly population increases interest in research on age-associated diseases around the world [2-6].

Progressive loss of function, decreased fertility and increased mortality are fundamental biological aging processes inherent in most cellular systems. Aging is naturally associated with a change in the musculoskeletal status, manifested by a decrease in bone mineral density and muscle mass, and leads to age-associated diseases and syndromes. Musculoskeletal disorders include well-studied osteopenia/osteoporosis, sarcopenia, and a new syndrome, osteosarcopenia [2, 3]. Osteosarcopenia combines low bone density (osteopenia/osteoporosis) and reduced muscle mass and strength (sarcopenia) [3]. In the scientific literature, the prevalence of sarcopenia, osteopenia and osteoporosis in cardiac patients is widely discussed, while there are very few works devoted to the combination of these conditions (osteosarcopenia). This problem is considered in patients with diseases of the circulatory system solely from the standpoint of the risk of falling, bone fractures and associated hospitalization and prognosis [3-5]. Studies devoted to the diagnosis of the musculoskeletal status disorders in patients with coronary heart disease, assessment of the clinical status, as well as the importance of these data in the prognosis of early and long-term cardiac surgery, are rare, which served as a prerequisite for this work. The aging trends of the population and, consequently, an increase in the number of elderly people, a high multimorbid background in patients with coronary heart disease indicate the obvious relevance of this study, the aim of which was to analyze the prevalence of various variants of musculoskeletal status disorders in patients with stable coronary heart disease.

Material and methods

The study included 387 patients with stable coronary artery disease who were admitted for planned myocardial revascularization at the Research Institute for Complex Issues of Cardiovascular Diseases. Patients signed an informed consent of the established form,

approved by the local ethics committee of the Research Institute for Complex Issues of Cardiovascular Diseases, Protocol №12 dated December 27, 2019. The sample of patients was formed simultaneously in a continuous order after excluding persons with a history of diseases of the neuromuscular system, as well as patients who had been receiving corticosteroid drugs, antidepressants, cytostatics, barbiturates, or muscle relaxants for a long time. The main inclusion criteria were: age over 50 years, stable coronary artery disease, planned myocardial revascularization.

The study included patients aged 50-82 years. Most of the sample consisted of men (Table 1). Almost all patients included in the study had arterial hypertension (AH), half of the patients had a previous myocardial infarction, a quarter of the patients had a history of type 2 diabetes mellitus. Clinical and anamnestic characteristics of patients with coronary artery disease are presented in Table 1.

Currently, there are no national guidelines for verifying osteosarcopenia. Within the framework of this work, by analogy with the studies of foreign colleagues [2-5], the diagnostic algorithm included the verification of sarcopenia in accordance with the EWGSOP criteria (2019) [7] and osteopenic syndrome (osteopenia/osteoporosis) according to the WHO criteria (2008) for postmenopausal women and men over 50 years old [8]. Osteosarcopenia was diagnosed in the presence of a combination of sarcopenia with osteopenia/osteoporosis [2-5].

Screening for sarcopenia was performed using the SARC-F questionnaire in accordance with the above diagnostic algorithm. Muscle strength was assessed when clinical signs of sarcopenia were detected (≥ 4 scores on this scale). Dynamometry was performed using an electronic medical dynamometer DMER-120 (JSC Tves, Russia). The compressive force of the hand was measured twice on each hand, and the best result was recorded. According to the EWGSOP recommendations, the criterion for reduction in strength is considered to be less than 27 kg for men and less than 16 kg for women. The final stage in the diagnosis of sarcopenia in patients with reduced muscle strength according to the results of dynamometry included a quantitative assessment of skeletal muscles.

The quantitative assessment of muscle tissue was performed on a Somatom Sensation 64 multispiral computed tomograph (Siemens, Germany). The contours of all muscles, including the paravertebral muscles, the iliocostal muscles, the external oblique muscles of the abdomen, the quadratus dorsi, and the

Table 1. Clinical and anamnestic characteristics of patients with coronary artery disease

Indicator	Value
Men/Women, n (%)	283 (73.1) / 104 (26.9)
Age, years	65 [59;69]
Body mass index, kg/m ²	29.3 [26.6; 32]
Arterial hypertension, n (%)	323 (83.5)
Duration of arterial hypertension, years	10 [5.0; 16.5]
Functional class of angina	2.0 [1.0; 2.0]
Duration of coronary artery disease, years	2 [1.0; 5.0]
History of myocardial infarction, n (%)	221 (57.1)
Heart rhythm disturbances, n (%)	38 (9.8)
Type 2 diabetes mellitus, n (%)	98 (25.3)
Duration of type 2 diabetes mellitus, years	5 [1.0; 10.0]
History of acute cerebrovascular accident, n (%)	36 (9.3)
Data are presented as Me [25%; 75%], unless otherwise indicated	

psoas major muscle, were manually outlined at the level of the distal edge of the L3 vertebral body. The range of attenuation for isolated muscle tissue release was limited to values from –29 to +150 HU, which allowed us to selectively calculate the muscle tissue area at the studied level. Subsequently, on the basis of the obtained values of the muscle tissue area, the musculoskeletal index (cm²/m²) was calculated, which is the value of the muscle tissue area normalized to the square of the patient's growth rate. The threshold value of the musculoskeletal index, below which the state of muscle tissue is assessed as sarcopenia, was 52.4 cm²/m² for men and 38.5 cm²/m² for women [9]. It has been shown that a decrease in the volume of musculoskeletal mass at this level correlates with a decrease in total skeletal muscle [10].

«The gold standard» for assessing osteopenic syndrome (osteopenia/osteoporosis) is Dual-Energy X-Ray Absorptiometry (DEXA). This method is used to measure bone mineral density (BMD, g/cm²) in the lumbar spine and proximal femur. Bone density is defined as the density value measured in grams per square centimeter at the level of the L1-L4 vertebrae or the femoral neck with automatic T and Z tests. Only the T-test was assessed, taking into account the age of the studied patients (over 50 years). This criterion corresponds to the number of standard deviations by which the bone density differs from its mean in young healthy people of the same gender and ethnicity. The indicator is used for menopausal women and men over 50 years of age. WHO sets values for the T-score, which define osteopenia and osteoporosis. The indicator of the T-test from –1.0 and above corresponds to the norm; osteoporosis is

diagnosed with a T-test of –2.5 or lower, and osteopenia is diagnosed if this indicator is in the range from –1.0 to –2.5 [8].

Statistical analysis

Statistical analysis of the data was carried out using the Statistica 6.1 software package (StatSoft Inc., USA). The distribution of the data was assessed using the Shapiro-Wilk test. The distribution of all quantitative data was different from the normal value. Qualitative indicators are presented as frequencies (n, %), quantitative indicators are presented by central trends and dispersion: median (Me) and interquartile range [25%; 75%]. Comparison of three or more independent groups was carried out using the Kruskal-Wallis rank analysis of variations. Assessment of differences in relative magnitudes was determined using a 2×2 contingency table analysis. The hypotheses were tested using the Pearson χ^2 test. The two-sided Fisher's exact test with Yates' correction was applied for a small number of observations. The analysis of relationships between features was assessed using the Spearman's rank correlation coefficient. Correlations were considered statistically significant at $p \leq 0.05$.

Results

The SARC-F questionnaire was surveyed at the primary screening for sarcopenia. Clinical signs of sarcopenia were verified in 160 (41.3%) patients with coronary artery disease. The second screening step determined muscle strength by performing dynamometry. A decrease in muscle strength was found in 110 (68.7%) among 160 patients. The final stage of sarcopenia verification consisted in a quantitative assessment of muscle tissue, according to the results of which sarcopenia was diagnosed only in 77 (19.9%) patients.

The results of dual energy X-ray absorptiometry were analyzed to assess the prevalence of osteopenic syndrome, including the presence of osteopenia and osteoporosis. Decreased T-test was found in 53 (13.7%) of 387 patients included in the study; of them osteoporosis was diagnosed in 5 (9.4%), osteopenia was revealed in 48 (90.6%).

Thus, sarcopenia was diagnosed in one fifth of patients with coronary artery disease over 50 years of age who were admitted for planned myocardial revascularization. Violation of the architectonics and bone density was found in 13.7% of patients. Osteopenia was diagnosed 10 times more often than osteoporosis (90.6% vs 9.4%).

The patient was assigned to the group of osteosarcopenia in the presence of diagnosed sarcopenia in combination with osteopenia/osteoporosis [2-5]. Thus, the group of patients with impaired musculoskeletal status included 105 (27.1%) patients with coronary artery disease. Isolated sarcopenia was found in 52 (49.5%) patients, isolated osteopenic syndrome (osteopenia/osteoporosis) was revealed in 28 (26.7%), osteosarcopenia was diagnosed in 25 (23.8%) patients. Comparative analysis of the parameters characterizing the musculoskeletal status in patients with coronary artery disease is presented in Table 2.

Patients of all analyzed groups were characterized by overweight or obesity, assessed according to the body mass index (BMI). The highest values of the indicator were recorded in patients with isolated osteopenic syndrome (group II) and persons without musculoskeletal status disorders (group IV). The average BMI values corresponded to the 1st degree obesity. The mean BMI values in patients with isolated sarcopenia (group I) and osteosarcopenia (group III) were lower and corresponded to the overweight parameters.

The most pronounced clinical manifestations of sarcopenia and osteopenic syndrome, which is reflected in a higher score on the SARC-F questionnaire, such as a lower handshake force, a smaller area of muscle tissue, as well as the minimum indicator characterizing the minimum bone density, were noted in patients of group III (with osteosarcopenia). Patients

with isolated osteopenic syndrome (group II) didn't differ from patients without signs of impaired musculoskeletal status (group IV). The exceptions were the T-test, the average score according to the SARC-F questionnaire, and muscle strength in men.

Correlation analysis revealed a relationship between indicators assessing the state of musculoskeletal status and clinical and anamnestic status. The age of the patients had a multidirectional relationship with muscle area ($r = -0.569$; $p = 0.021$) and muscle strength ($r = -0.735$; $p = 0.000$), as well as with the musculoskeletal index ($r = -0.627$; $p = 0.002$). A unidirectional relationship between the hand compression force and muscle area was revealed ($r = 0.58$; $p = 0.000$). BMI had a positive correlation with muscle area ($r = 0.54$; $p = 0.005$) and musculoskeletal index ($r = 0.62$; $p = 0.00$) and a negative correlation with the SARC-F score ($r = 0.97$; $p = 0.021$). In addition, a positive relationship was found between the average score on the SARC-F questionnaire and the duration of arterial hypertension ($r = 0.68$; $p = 0.019$), coronary artery disease ($r = 0.97$; $p = 0.021$) and type 2 diabetes mellitus ($r = 0.84$; $p = 0.053$).

Thus, the performed correlation analysis showed not only the relationship between the parameters characterizing the musculoskeletal function, but also their association with age, duration of arterial hypertension, coronary artery disease and type 2 diabetes mellitus.

Table 2. Comparative characteristics of patients with coronary artery disease, depending on the type of the musculoskeletal status disorders (n = 387)

Clinical and anamnestic factor	Group I (isolated sarcopenia)	Group II (isolated osteopenic syndrome)	Group III (osteosarcopenia)	Group IV (without musculoskeletal status disorder)
Group size, n (%)	52 (13.4)	28 (7.2)	25 (6.5)	282 (72.9)
Body mass index, kg/m ²	27 [25;30]**†	30.4 [26.6;32.5]†	28 [25.1;30]*	30 [27;32.6]
Score according to SARC-F	5 [5;6]****††††	0 [0;1]****††	6 [5;6]***	2 [0;1]
T-test (femoral neck), units	-0.2 [-0.4;0.3]****††††	-1.3 [-1.65;-0.95]*	-1.4 [-1.8;-1.2]***	-0.2 [-0.7;0.6]
Muscle area, cm ²	140.9 [128.2;154.5]****†	143.9 [105.1;163.9]†	112 [101.7;143.3]**	161.5 [122;174.3]
Dynamometry				
Men, kg	26 [25;26]****††††	31 [29;35]**†††	26 [26;26]***	30 [28;34]
Women, kg	15 [12;14]**†	19.5 [17.5;30]†††	15 [11;15]***	20 [18;30]
Skeletal muscle index				
Men, cm ² /m ²	47.9 [43.7;50.2]****††	56.4 [54.3;59.6]†††	45.4 [40.3;50.6]***	56.8 [54;60.6]
Women, cm ² /m ²	37.03 [35;37.2]****††††	41.75 [40;45.2]†	33.2 [32.3;34.2]*	42.3 [40.3;43.6]
Data are presented as Me [25%; 75%], unless otherwise indicated				
* - $p < 0.05$, ** - $p < 0.01$, *** - $p < 0.001$ compared to group 4; † - $p < 0.05$, †† - $p < 0.01$, ††† - $p < 0.001$ compared to group 3; ‡ - $p < 0.05$, ‡† - $p < 0.01$, ‡†† - $p < 0.001$ compared to group 2.				

Discussion

Musculoskeletal disorders are detected in 27.1% of patients with stable coronary artery disease at the age of 65 [59; 69] years. The most common form of musculoskeletal disorders is isolated sarcopenia (13.4% of cases); isolated osteopenic syndrome (osteopenia/osteoporosis) was detected in 7.2% of patients, osteosarcopenia was detected in 6.5%.

According to various estimates, sarcopenia develops in 5-13% of people aged 60-70 years and in 50% aged 80 years and older, which is consistent with our data (13.4%). In Asia, the prevalence of sarcopenia varies from 4.1% to 11.5% among the general elderly population [11, 12], in Poland this indicator is 12.6% [12], in India this indicator is up to 17.5% [12], while in Brazil this indicator ranges from 5 to 50% [13]. According to Russian studies, this pathology occurs in 37% of patients aged 66-80 years [14]. Several scientists have demonstrated the adverse effects of sarcopenia in patients with various diseases of the cardiovascular system. In a study by N. Zhang et al. [15] sarcopenia was diagnosed in 78 (22.6%) among 345 elderly patients (mean age 74 years) hospitalized with stable coronary artery disease and acute coronary syndrome. At the same time, patients with sarcopenia significantly more often unplannedly sought medical help than people without sarcopenia (34.2 versus 21.8%; $p = 0.036$). The most common causes were angina pectoris/myocardial infarction and infectious diseases. In addition, the survival rate in patients with sarcopenia was significantly lower than in patients without sarcopenia ($\chi^2=4.102$; $p=0.043$). Patients with chronic heart failure suffered from sarcopenia 20% more often compared with healthy people of the same age [16]. Moreover, M. Hajahmadi et al. showed an even higher prevalence of the disease: in 47% of young patients (<55 years) suffering from dilated cardiomyopathy [17].

Isolated osteopenia has received few studies, while the problem of osteoporosis is widely covered. Despite this, several publications have demonstrated that the majority of patients with fractures had bone mineral density in the range of diagnostics of osteopenia, which allows us to conclude that the population with osteopenia is higher than with osteoporosis [18, 19]. During the present study, 7.2% of patients admitted for surgical treatment of coronary artery disease had diagnostic criteria for osteopenic syndrome (osteopenia/osteoporosis), and osteopenia was practically diagnosed 10 times more often than osteoporosis (90.6 and 9.4% of cases, respectively).

The prevalence of osteopenic syndrome in the presented work doesn't correlate with the data of other researchers (a lower incidence has been demonstrated). This is probably due to the fact that we analyzed not only the prevalence of osteopenic syndrome, but also other variants of the musculoskeletal status disorders, and we also included patients of both sexes.

For example, the study by R. Xu et al. [19] included 122 postmenopausal women with coronary artery disease (mean age 64.31 ± 4.71 years); osteoporosis was diagnosed in 19.6% of patients and osteopenia was diagnosed twice as often (41.8% of cases). However, logistic regression analysis showed an association between osteoporosis/osteopenia and more severe coronary artery disease [odds ratio was 2.51, 95% confidence interval (CI) was 1.153-5.657; $p = 0.003$]. International data on the prevalence of osteoporosis are highly controversial. In the BEST (Bone Evaluation Study) study, osteoporosis in patients over 50 years old was detected in 24% of women and 6% of men. These rates are close to 50% in women over 75 years old [20]. In the NHANES (National Health And Nutrition Examination Survey) study, the prevalence of osteoporosis in the general population in the age group from 70 to 79 years was 16.4%, and in the age group 80 years and older, the prevalence of osteoporosis reached 26.2% [21]. In a study that included men in Taiwan aged 70 ± 9.3 years, the prevalence of osteoporosis was 9.7% [22]. At the same time, a study in the United States demonstrated a prevalence of osteoporosis of up to 24% in a similar age group (65 to 99 years) [23]. In the domestic scientific medical literature, the study of the association of osteoporosis and cardiovascular diseases is also widely presented. Studies previously conducted at the Research Institute for Complex Issues of Cardiovascular Diseases demonstrated osteopenic syndrome in 71.6% of patients with angiographically confirmed coronary artery disease, while more severe coronary lesions were characteristic of patients with osteoporosis ($p = 0.029$) [24]. In another study, three-vessel coronary artery disease was detected in 46.1% of patients as a result of an assessment of a group of men with coronary artery disease and the presence of clinically confirmed osteoporosis, while a high gradation of coronary artery disease severity according to the SYNTAX scale was detected in 17.6% of patients, and severe calcification of the coronary arteries were detected in 57.8% [25]. A recent study determined that osteopenic syndrome was most often recorded

in patients with a combination of coronary artery disease and arterial hypertension – 63.7% of cases (of which 38.9% had osteoporosis, 24.8% had osteopenia). In the control group of patients (without signs of coronary artery disease), only osteopenia was found – 26.8% of cases [26].

Loss of muscle mass and decreased bone density are often associated with older adults; some studies have demonstrated a close relationship between osteoporosis and sarcopenia, that is, osteosarcopenia [27]. In a sample of 590 postmenopausal Finnish women, patients with sarcopenia had a 12.9-fold higher risk of osteoporosis compared with women without sarcopenia (95% CI was 3.1-53.5) [4]. Sarcopenia showed a five-fold higher risk of osteoporosis among 232 older adults (95% CI was 1.16-19.41). Two subsequent cross-sectional [28, 29] and one longitudinal [30] studies have shown that osteoporosis increases the risk of sarcopenia and vice versa. A study that included 3334 elderly participants showed that patients with probable and confirmed sarcopenia (compared with no sarcopenia) had lower bone mineral density [31]. As you can see, a bi-directional link exists between osteoporosis and sarcopenia, which leads to the development of osteosarcopenia. According to B.R. Nielsen et al. (2018) [27] and N. Fahimfar and colleagues (2019) [32], the prevalence of osteosarcopenia increases with age: from 14.3-16.4% (60-64 years) to 32-59.4% (≥ 75 years) in men, from 20.3-25.5% (60-64 years) to 48.3-82.6% (≥ 75 years) in women. According to the results of this study, osteosarcopenia was detected in 6.5% of patients over 50 years old with coronary artery disease admitted for myocardial revascularization, and this group of patients accounted for almost a quarter (23.8%) of all patients with musculoskeletal disorders.

Comparative analysis of the attributes of musculoskeletal status demonstrated that patients with osteosarcopenia had the worst parameters characterizing musculoskeletal function, and patients with isolated osteopenic syndrome had practically no differences in comparison with participants without signs of impaired musculoskeletal status. In addition, the correlation analysis revealed not only a natural relationship between the diagnostic components of the musculoskeletal status disorders and age, but also the duration of the course of diseases such as arterial hy-

pertension, coronary artery disease and type 2 diabetes mellitus, which probably indicates a close relationship with dysfunction of the musculoskeletal system.

The revealed relationships are consistent with the data of other works [33-35]. For example, according to a study in China, patients with type 2 diabetes mellitus have a 1.56 times higher risk of sarcopenia than healthy people. A Korean researcher reported that the risk of losing muscle mass is increased by 2-4 times in patients with type 2 diabetes. The authors suggest that, on the one hand, insulin stimulates protein synthesis, and its insufficient secretion or insulin resistance leads to insufficient synthesis and increased breakdown of muscle protein, which can lead to the development of sarcopenia [34]. On the other hand, persistent hyperglycemia causes accumulation of AGEs (advanced glycation end products) in muscle and cartilage, resulting in muscle stiffness and dysfunction [35]. In addition, AGEs promote inflammation and dysfunction of endothelial cells in skeletal muscle microcirculation through AGEs receptors, which leads to sarcopenia [33]. Also, patients with coronary artery disease [36] and patients with type 2 diabetes mellitus [33] showed a higher level of proinflammatory cytokines, which in turn have a negative effect on both muscle mass and its function.

Conclusion

The results of this study allowed us to conclude that almost a third (27.1%) of patients with coronary artery disease admitted for planned myocardial revascularization had various variants of musculoskeletal status disorders. Most of the patients suffered from isolated sarcopenia (13.4%), and isolated osteopenic syndrome (7.2%) and osteosarcopenia (6.5%) were verified twice less frequently.

Relationships and Activities: none.

Financing. The study was supported by Federal State Budgetary Institution of Higher Education “Kemerovo State University” (Contract №1327/2020/223, under the Agreement №075-15-2020-766 made as of 14th of December, 2020, entitled “Patient-centered care for patients with coronary artery disease and osteosarcopenia who underwent coronary artery bypass graft surgery”).

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