Sex characteristics of cognitive functions assessed by the MMSE and MoCA scores in patients with coronary artery disease

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Aim. To study the sex characteristics of cognitive functions in a cohort of patients undergoing coronary artery bypass grafting (CABG) by comparing the results of Mini-mental state examination (MMSE) and Montreal Cognitive Assessment (MoCA) scores.

Material and methods. The prospective cohort study included 272 people, including 74 women aged 41 to 82 years, who were admitted to the Research Institute of Complex Issues of Cardiovascular Diseases for CABG surgery. All patients underwent clinical, laboratory, electrophysiological and ultrasound examinations. The Charlson comorbidity index (CCI) was calculated. Assessment of cognitive functions was carried out using the MMSE and MoCA scores. All types of statistical analysis were performed using the STATISTICA 10 program (StatSoft Inc., USA).

Results. It was found that women scheduled for CABG have an older age and a higher CCI score compared to men (p=0,008). According to the MMSE, the likelihood of moderate and severe cognitive impairment in men compared with women was 1,36 times higher (odds ratio (OR), 1,35; 95% confidence interval (CI), 0,79-2,32, Z=1,11, p=0,27). The MoCA scores showed that half of the male (49%) and female (50%) participants had severe cognitive impairment. The likelihood of moderate and severe cognitive impairment in men compared with women was 1,33 times higher (OR, 1,33; 95% CI, 0,68-2,59, Z=0,841, p=0,40). According to subtests of the MoCA, men were better in naming (p=0,002), abstraction (p=0,005), and women outperformed men in verbal fluency (p=0,04). Regression analysis revealed that the most significant negative predictors for cognitive status as measured by the MMSE and MoCA scores for men and women were age and CCI.

Conclusion. Women scheduled for CABG, having the worst clinical and demographic indicators, are comparable with men in cognitive status using the MMSE score. The MoCA score shows sex differences in naming, abstraction, and verbal fluency domains and revealed a higher percentage of severe cognitive disorders (up to 50%) compared to the MMSE score (7-9%). In male and female candidates for CABG, age and comorbidities are negatively associated with cognitive status.

Keywords: sex characteristics, cognitive status, MMSE and MoCA scores, coronary artery bypass grafting.

Relationships and Activities: none.

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Currently, the leading reason of cognitive decline in patients with cardiovascular diseases (CVD) is not considered to be the processes of natural aging and a number of socio-demographic factors, including a low educational level, but CVD itself, which, together with the above factors and the neurodegeneration processes, can lead to complete cognitive degradation [1, 2]. It was noted that in patients with CVD, atrophic processes in the brain are uneven. First of all, changes are observed in the prefrontal cortex, while here a drop in cerebral blood flow is also observed [3]. A characteristic feature of cognitive deficits in CVD is a decrease in executive control, action planning, and working memory [3, 4]. It takes on crucial significance for the cohort of patients requiring surgical myocardial revascularization due to the fact that already existing cognitive deficits can progress in the postoperative period. This, in turn, can negatively affect the operation results and the quality of life, making it difficult to rehabilitate patients. Therefore, it is important to assess the cognitive status of patients even before intervention.

Recent studies have confirmed the presence of gender differences in the clinical course of coronary artery disease and adherence to therapy [5]. The gender imbalance among candidates for coronary surgery at the age of 45-70 years is also described [6, 7]. The specific gender differences in cognitive functions were found in healthy individuals, as well as in patients with a cardiovascular profile [1, 8, 9].

Therefore, it is believed that the gender differences play an important role in pathological changes in cognitive functions associated with CVD. According to the literature data, cognitive decline in normal and vascular aging begins earlier in men [2]. In case of vascular form of pathological aging, this process occurs more intensively than in relatively healthy elderly people. The study of verbal fluency test indicators revealed a greater depletion of this ability in men at the end of the 3-minute test at a young age and an reverse trend in the older age group, possibly due to the stronger influence of CVD at a relatively young age on cognitive functions. Similar changes in cognitive functions have been described in patients with hypertension [10]. There is an opinion that the vascular factor does not qualitatively change the nature of age factor influence, but, as a rule, shifts the same patterns as in healthy people to a lower cognitive level [1].

A fairly large number of neuropsychological scales are currently used to assess cognitive status [11, 12]. However, the Mini-mental state examination (MMSE) scale is the most commonly used tool with high validity, verified by many studies [11, 13, 14]. The MMSE tests abilities such as orientation, attention, short- and long-term memory, language and ability to perform simple written and oral tasks [15]. Another tool is the Montreal Cognitive Assessment Scale, or the Montreal Cognitive Assessment Scale (MoCA), which assess cognitive abilities such as concentration, counting, orientation, memory, language, as well as visual-spatial skills, executive functions, and abstract thinking that are not studied under the MMSE scale [16]. It was found that MoCA has an advantage in detecting pre-dement cognitive impairment, especially mild cognitive impairment (MCI), compared to MMSE [17-19]. A possible explanation for MoCA superiority is that the subtests of this scale are more difficult to perform than similar MMSE subtests. Consequently, MoCA may be more sensitive to detect milder cognitive impairments [20]. Comparing the results of two most commonly used MMSE and MoCA scales can provide additional data on general state of cognitive status of such a complex patient category as candidates for coronary surgery, as well as about its gender characteristics. Due to the fact that the structure of MMSE and MoCA screening scales is slightly different, the gender factor can make corrections to the effectiveness of these two scales, which is of significant methodological importance.

Thus, taking all the foregoing into account, the goal of this work was to study the gender characteristics of cognitive functions in a cohort of patients requiring coronary artery bypass graft (CABG), when comparing the results of two cognitive screening scales — MMSE and MoCA.

Material and methods

Patients. The prospective cohort study involved 272 people (74 of them women), aged 41 to 82 years, who were admitted to the Federal State Budgetary Scientific Institution of the Research Institute of Complex Problems of CVD. The study was conducted in accordance with the Helsinki Declaration of 1964, and was approved by the Ethics Committee of the Institute. The patient enrollment was carried out after signing a voluntary informed consent. The enrollment criteria were as follows: planned CABG, age 40 and older, ability to adequately complete the tasks included in MMSE and MoCA.

All patients underwent a standard preoperative examination, including clinical and laboratory, electrophysiological and ultrasound methods of examination. Based on the obtained clinical and anamnestic data, the Charlson comorbidity index was calculated according to the standard method [21]. It is a point system for assessing the age and presence of certain concomitant diseases, such as diabetes mellitus, chronic obstructive pulmonary

Clinical and anamnestic characteristics of male and female patients proposed for CABG

Indicator	Men (n=198)	Women (n=74)	p
Age, years, M±SD	63,2±7,56	66,3±7,02	0,002
Education level, n (%) secondary and dual, higher education	158 (80) 40 (20)	54 (73) 20 (27)	0,28
Body mass index, M±SD	28,5±4,06	30,7±3,75	0,0001
Charlson comorbidity index	3,6±1,10	4,0±1,25	0,008
Left ventricular ejection fraction	56,4±11,72	61,1±9,54	0,002
FC of angina pectoris, n (%) 0-I II III	60 (30) 107 (54) 31 (16)	11 (15) 47 (63,5) 16 (21,5)	0,03
CHF (NYHA FC), n (%) 0-I II III	59 (30) 126 (63,5) 13 (6,5)	15 (20) 51 (69) 8 (11)	0,19
Post-infarction cardiosclerosis, n (%)	125 (63)	38 (51)	0,07
Type 2 diabetes mellitus, n (%)	40 (20)	26 (35)	0,01
Carotid artery stenosis, n (%) no <50% >50%	90 (46) 60 (30) 48 (24)	35 (47) 25 (34) 14 (19)	0,63
Anamnesis of acute disorders of cerebral circulation, n (%)	17 (9)	4 (5)	0,38

Abbreviations: FC — functional class, CHF — chronic heart failure.

**Indicators of individual subtests of the MMSE scale
in the groups of men and women planned for CABG**

Subtest	Men (n=198)	Women (n=74)	p
Time knowledge	4,9±0,27	5,0±0,16	0,14
Location knowledge	5,0±0,19	4,9±0,28	0,33
Perception (remember and repeat 3 words)	3,00±0,00	3,0±0,23	0,10
Concentration and counting (consecutive subtraction by 7)	4,3±1,18	4,4±1,18	0,65
Memory	2,1±0,87	1,9±0,79	0,24
Speech: "Show the pen and watch, ask — how does is called?"	1,99±0,07	1,97±0,16	0,12
Speech: "There are no ifs, and or buts about it" — repeat the sentence	0,3±0,51	0,4±0,48	0,51
Speech: Executing a 3-step command	2,97±0,15	3,0±0,00	0,17
Reading: Close your eyes	1,0±0,00	0,99±0,11	0,10
Reading: Write a sentence	0,97±0,17	0,97±0,16	0,88
Reading: Draw a picture	0,4±0,49	0,4±0,49	0,91

diseases, peripheral vascular disease, systemic connective tissue diseases, cerebral circulatory disorders, oncopathology, immunodeficiency, etc.

Neuropsychological study. The cognitive function state assessment was performed using screening neuropsychological scales-MMSE and MoCA. According to the MMSE scale (from 0 to 30), the sum of points equal to or greater than 28 indicates a normal state of cognitive functions, 27-24 points — MCI syndrome, <24 points — severe cognitive impairment (dementia). According to the MoCA scale (also from 0 to 30), a score above 26 points indicates no cognitive impairment, a score of 24-26 points indicates MCI, and a score below 24 points indicates severe cognitive impairment.

Statistical analysis. All types of statistical analysis of the obtained data were performed according to the program STATISTICA 10 (StatSoft, Inc.,

Table 3

**Indicators of individual subtests of the MoCA scale
in the groups of men and women proposed for CABG**

| Subtest	Men (n=198)	Women (n=4)	p
Drawing a polyline	0,53±0,50	0,46±0,50	0,31
Copy (cube)	0,44±0,49	0,49±0,50	0,55
Drawing a clock	2,41±0,81	2,21±0,92	0,09
Naming objects	2,98±0,12	2,87±0,44	0,002
Naming of numbers, in direct order	0,84±0,36	0,86±0,35	0,72
Naming of numbers in reverse order	0,83±0,38	0,81±0,40	0,68
Tapping test	0,80±0,44	0,75±0,44	0,40
Sequential subtraction by 7	2,75±0,60	2,69±0,68	0,49
Repetition of sentences	1,15±0,66	1,19±0,64	0,60
Verbal fluency	0,39±0,49	0,53±0,50	0,04
Abstract thinking	1,49±0,65	1,24±0,68	0,005
Delayed recall	1,96±1,47	2,22±1,46	0,19
Orientation	5,93±0,33	5,93±0,31	0,97
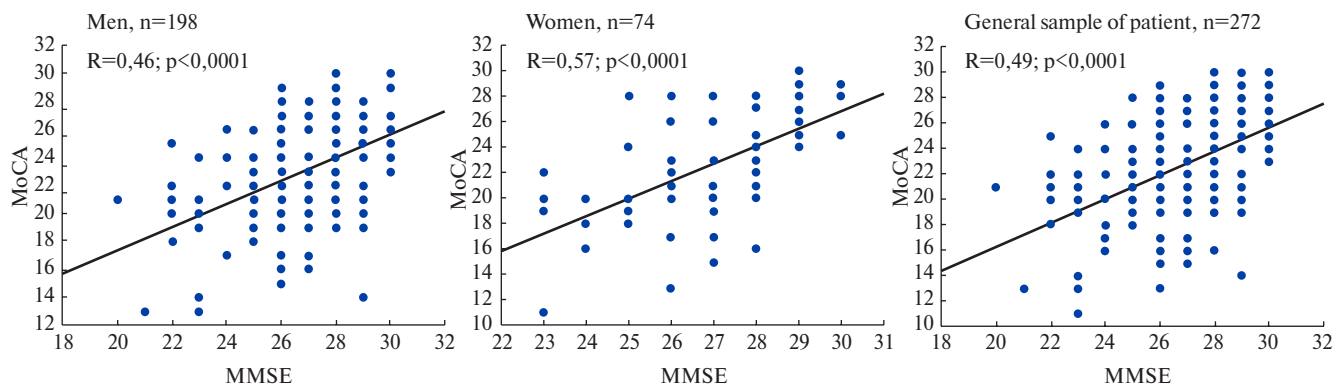
Figure 1. The results of correlation analysis between the MMSE and MoCA scores in the general sample of patients and separately for the groups of male and female patients proposed for CABG.

USA). The distribution normality for quantitative clinical and anamnestic indicators and indicators of cognitive status was assessed using the Kolmogorov-Smirnov test, most of the data had a normal or close to normal data distribution. Consequently, the comparison of indicators was carried out using the t-test for independent samples. "P<0,05" was considered statistically significant. The data is presented as averages and standard deviation.

Results

The clinical and anamnestic characteristics of the examined patients are given in Table 1. It is worth noting that the male patients had a younger age at the time of examination, a lower body mass index and a lower ejection fraction. There was a close to statistically significant trend towards a greater number of men who had a history of myocardial infarction. At the same time, women in 85% of cases had II-III functional class of angina pectoris, while in men such indicators were observed in 70% of patients. There were no statistically significant differences between men and women in the functional class of heart failure according to NYHA, as well as in the number of moderate and severe carotid artery stenoses, the number of people with a history of acute cerebral circulatory disorders. Women were more likely to have type 2 diabetes. Accordingly, the Charlson comorbidity index in women was statistically significantly higher than in men. The samples of men and women were comparable in educational status: the majority of the examined had secondary or specialized secondary education (80% and 73%, respectively).

Neuropsychological indicators. According to the MMSE scale, in the group of men, 46% (92 patients) did not have cognitive impairment, the MCI frequency was 45% (89 patients), and dementia —

Table 4

The main parameters of regression models and predictors of cognitive status according to the MMSE and MoCA scale in patients proposed for CABG

Predictor	Beta	t	p
MMSE			
Men			
$F_{(2,196)}=4,0$; $p<0,02$; $R^2=0,04$			
Age	-0,16	-1,49	0,14
Charlson comorbidity index	-0,11	-1,05	0,30
Women			
$F_{(3,70)}=5,03$; $p<0,004$; $R^2=0,18$			
Charlson comorbidity index	-0,29	-1,98	0,05
Number of training years	0,18	1,52	0,13
Age	-0,17	-1,11	0,27
MoCA			
Men			
$F_{(2,196)}=6,27$; $p<0,0025$; $R^2=0,07$			
Age	-0,28	-3,33	0,001
Number of training years	-0,11	-1,29	0,20
Women			
$F_{(3,70)}=5,31$; $p<0,003$; $R^2=0,20$			
Age	-0,33	-2,18	0,03
Number of training years	0,17	1,41	0,16
Charlson comorbidity index	-0,16	-1,05	0,30

9% (17 people). In women, the absence of cognitive deficits was noted in 54% (40 people), in 39% (29 people) — MCI was observed, dementia — in 7% of cases (5 patients). The significance of intergroup differences according to the χ^2 criterion was — $F_{(1;272)}=1,27$; $p=0,53$. Men were 1,36 times more likely to have moderate to severe cognitive disorders than women, but this effect was not statistically significant (odds ratio (OR) =1,35; 95% confidence interval (CI): 0,79-2,32, Z=1,11, p=0,27).

The analysis of individual subtests of the MMSE scale did not reveal statistically significant differences between the groups of men and women (Table 2). Women were slightly more time-oriented, perceived information better, performed a 3-stage command, while men had slightly better delayed reproduction rates, were more successful at naming items, but these differences were only at the trend level.

The indicator study of the MoCA neuropsychological scale revealed that the absence of cognitive impairment was observed in 17% of men (n=34) and 22% of women (n=16). The MCI syndrome was observed in 34% of men (n=67) and 28% of women (n=21), and half of the male (49%,

n=97) and (50%, n=37) female participants had severe cognitive impairment. The significance of intergroup differences according to the χ^2 criterion was — $F_{(1;272)}=1,34$; $p=0,51$. As for the MMSE scale, men were 1,33 times more likely to have moderate to severe cognitive disorders than women, but this effect was not statistically significant (OR =1,33; 95% CI: 0,68-2,59, Z=0,841, p=0,40).

A comparison of the performance of the MoCA scale subtests revealed differences between the groups of men and women in terms of "Naming objects", "Abstract thinking" and "Verbal fluency" (Table 3).

It was found that men were more successful at naming objects and had higher rates of abstract thinking, while women had an advantage in the verbal fluency test.

The analysis of correlations between the MMSE and MoCA total score indicators both in the general group of examined patients and separately in the groups of men and women demonstrated statistically significant positive relationships (Figure 1).

As can be seen in the figure, higher MoCA scores corresponded to higher MMSE scores in all the examined groups.

Further, a regression analysis was performed separately for men and women. In some models, the dependent variable was the total score according to the MMSE scale, in others — according to the MoCA scale. Age, learning duration in years, Charlson comorbidity index, body mass index, and left ventricular ejection fraction were considered as independent predictors of cognitive status in all statistical models. The correlation coefficients between the indicators selected as independent predictors were <0,7, which make it possible to state that there is no multicollinearity between them.

For the dependent variables — the total score according to the MMSE and MoCA scales, statistically significant models were obtained (Table 4). However, statistical significance test for the regression equations with the selected predictors demonstrated that the equations are statistically significant in general, but the weighted coefficient of determination (R^2) indicate a low overall quality of the obtained models.

It was found that age and the Charlson comorbidity index were predictors of the cognitive status determined by the MMSE scale in men. Older age and higher values of the comorbidity index were associated with a low level of cognitive function, but the relationship was not statistically significant. In women, the Charlson comorbidity index was also the only statistically significant negative predictor for this method of determining basic cognitive status.

The selected predictors for the cognitive status determined by the MoCA scale had a slightly greater predictive ability. For both men and women, age was a statistically significant negative predictor. Older patients proposed for CABG have poorer cognitive status.

Discussion

As the study results shown, male and female patients who need in CABG, despite the greater clinical severity and older age in women, have the comparable cognitive status. Only certain subtests of the MoCA scale, such as "Naming objects", "Abstract Thinking" and "Verbal Fluency", revealed statistically significant gender differences. Men had higher scores in abstract thinking and semantic memory, while women had an advantage in the verbal fluency test. The data obtained in this study are consistent with previous studies on healthy individuals, where women were more successful in verbal cognitive tests and men-in figurative-spatial and abstract tasks [22, 23]. Thus, the presence of severe CVD does not change the gender profile of intellectual abilities. However, only the use of the MoHS scale allowed to reveal gender differences, which suggests its more pronounced sensitivity to cognitive deficits in men and women.

However, special consideration should be given to the fact that older women with more pronounced comorbidity retain a cognitive level comparable to men. Psychophysiological studies have shown that equal success in performing a number of cognitive tasks by healthy men and women is ensured by different strategies [24-26]. According to one hypothesis, women use the resources of the left and right hemispheres more flexibly in information processing, which leads to better verbal skills, while figurative-spatial information is processed worse in them due to competition with verbal signals in the right hemisphere [22, 27]. The men's advantage in figurative-spatial abilities is associated with a greater specialization of the hemispheres, i.e., the performance of speech functions at the expense of the left hemisphere, and figurative-spatial — right [24, 28]. At the same time, a feature of brain damage in CVD is the predominant left hemisphere involvement in the pathological process [4, 29]. Left-hemisphere strokes were found to be associated with an increased risk of vascular cognitive impairment [4, 30]. It was found that the functional significance of left hemisphere damage is higher compared to damage to the right brain [29]. Taking all the foregoing into account, it can be expected that women's cognitive status is more resistant to factors connected with vascular brain damage, given the smaller hemisphere specialization and the possibility

of using right-hemisphere strategies to solve left-hemisphere problems. However, this issue requires additional study.

It is also paying attention that the basic cognitive status determination according to the MoCA scale revealed more cases of severe cognitive disorders (~50% in both men and women) as compared to testing according to the MMSE scale (7-9% in the male and female samples). Given the significant positive correlations between the two scales, it can be expected that the MoCA scale additionally reveals the deficit of those functions that the MMSE scale does not take into account (figurative-spatial, executive functions, abstract thinking). It was previously emphasized that the MoCA scale assess more cognitive domains and contains tasks that are considered more complex by the subjects than similar MMSE tests [31]. The MMSE scale proved itself to be good as a screening tool that is widely used in studies of various brain pathologies [32], but is now increasingly criticized regarding the possibility of detecting cognitive deficits in early stages of brain pathology [33].

The detection in the present study of a high percentage of severe cognitive impairment (~50%) in both men and women may be of crucial significance for patients undergoing direct myocardial revascularization, and in the postoperative period may be associated with the progression of cognitive deficits, a violation of the normal course of the CABG recovery period in this category of patients with coronary artery disease. Therefore, in preparation for surgery and in the postoperative CABG period, these patients need additional preventive and rehabilitative services, as well as possible changes in the surgical tactics of patient management.

At the same time, in this specific sample of patients-candidates for cardiac surgery, it was confirmed that age and comorbid diseases are the most significant clinical and demographic factors connected with lower cognitive status in both men and women, and the cognitive reserve, indirectly measured by the length of training years, resists the deterioration of intellectual abilities. It has been demonstrated that a high level of cognitive reserve is a protective factor, creating opportunities for "successful" mental aging [34].

Understanding gender characteristics when examining the cognitive functions of cardiac surgery patients is important for many reasons. First, vascular cognitive impairment is a very common and progressive condition with time or perioperative risk factors. Secondly, since gender differences in cognitive functions in healthy individuals are in existence, it is possible to assume their preservation during the CVD development, and their study will

reveal what has a protective effect for people of different sexes or makes them vulnerable. This will contribute to the development of new therapeutic and rehabilitative approaches. Third, vascular cognitive disorders develop inseparably and in parallel with the aging process in conditions of reduced levels of sex hormones. How reduced endocrine function of the gonads affects the brains of men and women, as well as how the use of hormone replacement therapy changes the brain vulnerability to the development of vascular cognitive deficits, are relevant issues, and obtaining strong evidence in this field will have serious clinical consequences for future personalized medicine.

Conclusion

Female patients, candidates for CABG, with worse clinical and demographic indicators, including a higher Charlson comorbidity index and older age, have a comparable cognitive status with men when assessed according to the MMSE scale. However, the assessment of basic cognitive status using the MoCA scale showed gender differences in the subtests "Naming objects", "Abstract thinking" and "Verbal fluency". Using the MoCA scale, up to 50% of severe cognitive disorders are detected in male and female patients, which is significantly higher than the MMSE score (7-9%), which allows to give it preference for assessing the cognitive status of this category of cardiac surgery patients. Age and comorbid diseases are the most significant clinical and demographic factors connected with lower cognitive status in both men and women, and a high level of education is a protective factor.

Relationships and Activities: none.

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