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ATHEROSCLEROSIS OF THE CAROTID AND CORONARY ARTERIES IN ELDERLY PATIENTS WITH ACUTE CORONARY SYNDROME

Aim To study the relationship between severities of the carotid artery injury and the atherosclerotic process in coronary arteries of elderly patients with acute coronary syndrome (ACS). Material and Methods The study included 110 patients aged >75 years. Based on the degree of maximal carotid stenosis according to data of duplex scanning (DS), all patients were divided into group I, (>50% stenosis) and group II (<50% stenosis). Results According to coronary angiographic data, multivessel disease was observed in 63.6% of patients. Patients of group I more frequently had three-vessel coronary artery disease than patients of group II (35.8 and 5.3%, p<0.001). Coronary angiography and DS showed that 82.7% patients (in group II, not all carotid stenoses were hemodynamically significant) had a combined damage of coronary and carotid arteries; carotid artery stenoses of >50% were associated with three-vessel coronary artery disease. A correlation between atherosclerosis of carotid and coronary arteries was found. Considering this correlation, a scale was introduced that suggested the severity of coronary atherosclerosis based on DS of carotid arteries. The score was assigned by assessing the degree of maximal stenoses in carotid arteries. A ROC analysis has determined a threshold score suggestive of the severity of coronary atherosclerosis: score <6, absence of >70% coronary stenosis; score >6, likely presence of >70% coronary stenosis (sensitivity, 70%; specificity, 89%). Conclusion Combined coronary and carotid artery disease was detected in 82.7% of elderly patients with ACS. A correlation between the severity of atherosclerosis in carotid and coronary arteries was found. DS of carotid arteries can be extensively used in evaluation of elderly patients with ACS, which will allow additional stratification of patients at high risk of cerebrovascular and recurrent cardiovascular diseases. Keywords Acute coronary syndrome; carotid arteries; old age; duplex scanning For citations Sagatelyan A.A., Konstantinova E.V., Bogdanova A.A., Svet A.V., Pershina E.S., Pershukov I.V. et al. Atherosclerosis of the carotid and coronary arteries in elderly patients with acute coronary syndrome. Kardiologiia. 2022;62(8):38-44. [Russian: Сагателян А.А., Константинова Е.В., Богданова А.А., Свет А.В., Першина Е.С., Першуков И.В. и др. Атеросклероз каротидных и коронарных артерий у пациентов старческого возраста с острым коронарным синдромом. Кардиология. 2022;62(8):38-44]. For citations Pershukov I.V. E-mail: cardio.ru@gmail.com

Introduction

Atherosclerosis is a generalized and progressive process that can simultaneously affect several vascular systems, i.e., has multifocal nature virtually from the onset [1, 2]. According to previous studies including a cohort of patients with various cardiovascular diseases (CVDs), the incidence of combined coronary and carotid atherosclerosis varies from 20 % to 75 % [1, 2].

It has been shown previously that the cardiovascular risk increased twice in patients with carotid artery stenosis of less than 50 % and 3.1-fold in patients with more than 50 % stenosis [3]. Identification and evaluation of atherosclerotic plaques in carotid arteries

has a significant diagnostic value for the prognosis of CVDs [4]. Duplex scanning (DS) is the most informative and accessible imaging technique [5]. It allows determining signs of plaque instability [6].

According to Savji et al., the combined damage of two different vascular systems, including coronary and carotid circulation, increases with age: by 0.04 % from 40 to 50 years and by 3.6 % from 81 to 90 years [7, 8].

Objective

Study the relationship between the degree of carotid artery disease and the severity of the atherosclerotic process in coronary arteries in senile patients with ACS.



Material and methods

The study was carried out in basis of N. I. Pirogov City Clinical Hospital no. 1. A total of 110 patients with ACS aged 75 years and older were enrolled (43 male patients, median age 81 (79; 85) years). All patients signed the informed consent to participate in the study. The study protocol was approved by the ethics committee of the N. I. Pirogov Russian National Research Medical University (Minutes no.203) and complied with the Declaration of Helsinki. Exclusion criteria were age less than 75 years, absence of ACS, presence of acute cerebrovascular accident.

On day 1 of hospitalization, all patients underwent a standard examination: clinical and biochemical blood tests, electrocardiogram, and echocardiography. Coronary angiography (CAG) was also performed on day 1 of hospitalization through the transradial access. CAG and assessment of the coronary artery lesions were performed using standard techniques, following the ACC/AHA guideline developed in collaboration with the Society for Cardiac Angiography and Interventions [9]. The ACC/AHA/SCAI guideline for coronary angiography are based on the standardized evaluation scores for coronary artery lesions set out in the CASS TIMI, and BARI studies [10-12]. This system provides a nomenclature of 29 most frequently described coronary artery segments [13]. Any lesion of the main trunk of the left coronary artery (LCA) of 50% or more was considered a two-vessel lesion, multivessel diseases also included hemodynamically significant (>70%) stenosis in at least two of the three major coronary arteries [left anterior descending artery (LAD), left circumflex artery (LCX), right coronary artery (RCA)], and/or their main branches. Quantitative coronary analysis was carried out using the software suite of the TOSHIBA Infinix VF angiographic system following the standard analysis procedures [14].

According to the inclusion criteria, all patients had significant coronary artery lesions. Diagnostic coronary angiography was followed by percutaneous coronary intervention, including balloon angioplasty, which ended with mandatory placement of a balloon-expandable stent [15].

Given that CAG followed by stenting was conducted in all patients. We further investigated other coronary arteries, not paying special attention to infarct-related arteries (stented coronary arteries were excluded from further analysis).

On days 2–5, DS of carotid arteries was performed using the Vivid E95 ultrasound system and the 9L transducer. The presence and severity of carotid atherosclerosis and the degree of maximum stenosis

were determined. Extracranial segments of the right and left brachiocephalic arteries were evaluated. The presence of an atherosclerotic plaque was established by the focal vascular thickening by more than 0.5 mm or 50% compared to the surrounding areas [16]. The percentage of stenosis was calculated in the 2D B-mode using the ECST (European Carotid Surgery Trial) method. Depending on the degree of maximum carotid stenosis, all patients were divided into groups: Group I consisted of patients with stenosis of 50% or more, Group II included patients with stenosis of less than 50%.

All patients received standard drug therapy following the clinical guideline: antiplatelet drugs, lipid-lowering drugs, beta-blocker therapy, renin-angiotensin-aldosterone system inhibitors.

Statistical analysis

The statistical analysis of data obtained was performed using Statistica v.10.0. The comparison of qualitative variables was performed using the χ^2 test. Qualitative variables are expressed as the absolute and relative values (n (%)). Quantitative variables were compared between the groups using the Mann -Whitney U-test. The data are presented as the medians and interquartile ranges. The Spearman correlation analysis was used to identify correlations. A regression analysis with the calculation of the odds ratio (OR) and the 95% confidence interval (CI) was used to identify the correlation between the severity of coronary and carotid atherosclerosis. The score was developed based on a ROC analysis with evaluation of sensitivity and specificity, calculation of area under the curve (AUC), and construction of characteristic curves. When testing statistical hypotheses, the intergroup differences was considered significant with p<0.05.

Results

The study included 110 patients of 75 years and older with confirmed ACS were enrolled (Table 1).

According to the Eurasian Association of Cardiology, patients with carotid artery stenosis of 50% or more are classified in the category of very high cardiovascular risk [17]. Group I consisted of 53 patients with ≥50% stenosis (41.5% of male patients), Group II included 57 patients with <50% stenosis (36.8% of male patients). The groups were comparable in terms of sex, age, anamnestic, clinical, and laboratory characteristics. The patient characteristics are presented in Table 2.

Among the 110 senile patients with ACS included in the study, CAG followed by stenting was performed in 100% of cases. Of them, 65 (59%), 35 (32%), and



Table 1. Main characteristics of the included patients

Parameter	Examined patients (n=110)
Age, years	81 (79; 85)
Male, n (%)	43 (39.1)
Patients with DM, n (%)	33 (30)
Patients with AH, n (%)	107 (97.2)
Patients with a history of MI (n=19)	40 (36.4)
Patients with AF, n (%)	47 (42.7)
Patients with STE-ACS, n (%)	51 (46.4)
Patients with chronic HFrEF, n (%)	32 (29.1)
Patients with chronic HFmrEF, n (%)	17 (15.4)
Patients with chronic HFpEF, n (%)	8 (7.3)

The data are presented as Me (25 %; 75 %), the number of patients – n (%). DM, diabetes mellitus; AH, arterial hypertension; MI, myocardial infarction; AF, atrial fibrillation; STE-ACS, ST-segment elevation acute coronary syndrome; HFrEF, heart failure with reduced ejection fraction; HFmrEF, heart failure with mid-range ejection fraction; HFpEF, heart failure with preserved ejection fraction.

Table 2. Comparative characteristics of patients included in Group I and Group II depending on the severity of carotid atherosclerosis

Parameter	Group I (n=53)	Group II (n=57)	p
Age, years	82 (80; 86)	81 (79; 85)	0.468
Male, n (%)	22 (41.5)	21 (36.8)	0.76
Patients with DM, n (%)	17 (32.1)	16 (28.1)	0.803
Patients with AH, n (%)	52 (98.1)	55 (96.5)	1.000
Patients with a history of MI (n=19)	22 (41.5)	18 (31.6)	0.377
Patients with AF, n (%)	23 (43.4)	24 (42.1)	1.000
Patients with STE-ACS, n (%)	24 (45.3)	27 (47.4)	0.978
Patients with chronic HFrEF, n (%)	18 (34)	14 (24.6)	0.382
GFR, mL/min/1.73m ²	53.3 (40.56; 61.64)	53.64 (42.69; 60.83)	0.702
Urea, mmol/L	7.6 (6.1; 10.9)	7.8 (6.3; 9.3)	0.431
Hemoglobin, g/L	128 (116; 141)	132 (114; 143)	0.68
Glucose, mmol/L	5.1 (4.5; 6.1)	5.3 (4.4; 5.8)	0.855
CRP, mg/L	9.25 (2.1; 30.42)	5.6 (0; 14)	0.123
TC, mmol/L	4.4 (3.75; 5.25)	4.5 (3.5; 5.44)	1.000
TG, mmol/L	1.1 (0.86; 1.58)	1.27 (0.99; 1.48)	0.397
LDL cholesterol, mmol/L	2.8 (1.98; 3.49)	2.7 (1.82; 3.92)	0.887
VLDL cholesterol, mmol/L	0.51 (0.4; 0.85)	0.58 (0.45; 0.79)	0.548
HDL, mmol/L	1.2 (1; 1.42)	1.15 (0.94; 1.31)	0.373

The data are presented as Me (25%; 75%), the number of patients – n (%). DM, diabetes mellitus; AH, arterial hypertension; MI, myocardial infarction; AF, atrial fibrillation; STE-ACS, ST-segment elevation acute coronary syndrome; HFrEF, heart failure with reduced ejection fraction; GFR, glomerular filtration rate; CRP, C-reactive protein; TG, triglycerides; LDL, low-density lipoprotein; VLDL, very low-density lipoprotein; HDL, high-density lipoprotein.

10 (9%) patients had hemodynamically significant stenosis of LAD, LCX, and RCA, respectively. Significant LAD stenosis was observed in Group – 75 (35; 95) and Group II – 70 (30; 90) (p=0.781). Among the studied patients, multivessel disease was detected in 70 (63.6%) patients with two-vessel lesions in 30% of cases and three-vessel lesions in 33.6%. CAG showed that three-vessel coronary disease was more frequent in Group I compared to Group II: 56.9% versus 5.3% (p<0.001).

Combined coronary and carotid atherosclerosis was found in 82.7% (in Group II, all carotid artery lesions were not hemodynamically significant according to the criteria for formation of groups). It was more common in Group I that in Group II: 100% and 66.7%, respectively (p<0.001). DS did not detect carotid atherosclerosis in 17.3%.

A regression analysis of the data of the 110 patients with ACS revealed that carotid stenosis of more than 50% was associated with 91% sensitivity and 74% specificity with the presence of three-vessel coronary artery disease (OR=32, 95% CI: 8.8–117; p<0.001).

Since the studied patients were subjected to balloon angioplasty and stenting of the infarct-related artery, we evaluated the severity of the atherosclerotic process in other large epicardial coronary arteries according to the CAG data. It was found that coronary stenosis of >70% (excluding the infarct-related artery) were less common in Group II than in Group I: 19% and 81%, respectively (p<0.001). The severity of carotid and coronary atherosclerosis was found to be correlated. The correlation was more pronounced in Group I: r=0.535, p<0.001; and the correlation in Group II was r=0.19, p=0.038.

Given the obtained correlation and depending on the degree of maximum stenosis of carotid arteries, we introduced a score based on the DS findings (Table 3).

The scoring was based on the degree of maximum stenosis in all carotid arteries: right and left common, internal, and external arteries. Patients without carotid stenosis scored 0; patients with stenosis in at least one of the arteries scored 1, 2, or 3, depending on the degree of maximum stenosis. The minimum total score was 0 and the maximum total score was 18. The mean score among the 110 patients under study was 5.6: 7.8 in Group I and 3.4 in Group II. ROC analysis established a threshold score, which allowed assuming the presence and the severity of atherosclerosis in one of the large epicardial coronary arteries: less than 6 means the probable absence of coronary stenosis of more than 70% and more than 6 corresponded to the



probable presence of coronary stenosis of 70% or more (70% sensitivity and 89% specificity) (Figure 1).

Analysis of the characteristic curve revealed the correlation between the severity of coronary atherosclerosis, i.e., the presence of hemodynamically significant stenosis in one of the large epicardial coronary arteries, and the degree of damage of carotid artery disease. The higher the score obtained using carotid DS and the evaluation of severity of stenosis, the more likely is the presence of hemodynamically significant coronary atherosclerosis in senile patients with ACS.

Discussion

The number of patients with combined carotid and coronary artery disease has increased in recent years [18]. The Russian and foreign literature contains more and more data confirming the correlation between atherosclerotic lesions of these arteries. The relationship between carotid artery stenosis and the cardiovascular risk was shown in a multicenter study including 5,895 patients, and it was found that the presence of more than two carotid plaques was a significant predictor of cardiovascular risk [19].

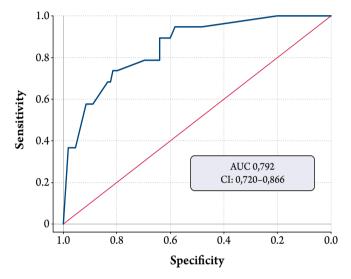
The percentage of combined coronary and carotid artery disease varies significantly. In this work, we studied a specific group of patients: patients of exclusively senile age and with the presence of confirmed ACS. Combined coronary and carotid artery disease was found in 82.7% of the studied patients. A similar percentage of combined coronary and carotid artery lesions was found by Zhu et al. [20]. However, patients with stable CAD and control patients (without CAD) were included in this study, and the mean age of the studied patients was lower. It was shown that patients with coronary artery disease confirmed by CAG had carotid artery atherosclerosis in 80% of cases, and patients with intact coronary arteries had carotid artery disease in only 49% of cases [20]. The obtained data indicate that the percentage of combined coronary and carotid artery disease in younger patients with stable CAD did not differ significantly from senile patients with ACS. Equivalent results were presented by Gavrilova et al., who studied an extensive cohort of patients, including individuals of different age (33-85 years), and combined carotid and coronary artery disease was observed in 74.7% [2]. This study also showed a minor difference in the percentage of combined atherosclerosis in the group of senile patients and the group of younger patients.

It should be noted that, in our study, the main clinical and laboratory characteristics of patients did not differ

Table 3. Score based on carotid DS data

Score	Maximum carotid artery stenosis (%)
0	No stenosis
1	< 50%
2	50-70%
3	> 70%

Figure 1. Characteristic curve in determining the degree of atherosclerosis of large epicardial coronary arteries by evaluating the severity of carotid artery stenosis



CI, confidence interval; AUC, area under the curve.

between Group I (carotid stenosis of 50% or more) and Group II (stenosis of less than 50%).

A correlation was shown between the severity of carotid artery atherosclerosis and the number of coronary arteries involved. According to Song et al., higher degree of carotid stenosis is associated with more coronary arteries involved [21]. The correlation between carotid atherosclerosis and multivessel coronary artery disease was demonstrated, but the age over 80 years was an exclusion criterion in this study [21]. Our findings showed a correlation between the severity of carotid atherosclerosis and the presence of two-vessel and three-vessel coronary artery disease in patients of 75 years and older. Three-vessel coronary artery disease was more frequent in Group I than in Group II: 35.8% and 5.3%, respectively. Moreover, the presence of carotid stenosis of more than 50% was found to be associated with three-vessel coronary artery disease.

The Russian and foreign literature contains data on the correlation between carotid artery disease and the severity of coronary atherosclerosis. Hemodynamically significant coronary stenosis is more common in



patients with more severe carotid atherosclerosis. Wang and He [22] demonstrated that the degree of carotid stenosis was associated with the severity of coronary stenosis. The examination of 231 patients (mean age 60 years) found that 128 patients had more severe coronary stenosis, 79 patients had more severe carotid stenosis; the severity of carotid stenosis was associated with the severity coronary stenosis [22]. In our study, the correlation between the severity of coronary and carotid atherosclerosis was evaluated in senile patients. However, we investigated not only infarct-related arteries but also other coronary arteries due to the available data from the SWEDEHEART study indicating that the risk of recurrent myocardial infarction caused by the coronary artery disease of another location was twice as high as the risk of repeated accidents caused by the lesion of the original infarct-related artery [23]. The data obtained were compared with the severity of carotid atherosclerosis. Our findings showed that coronary stenosis of >70% (excluding the infarct-related artery) were less common in Group II than in Group I: 19% and 81%, respectively. Patients with carotid stenosis of more than 50% were more likely to have coronary stenosis of 70% or more.

We found a correlation between the severity of carotid and coronary atherosclerosis, which was more pronounced in the group of patients with carotid stenosis of 50% or more (r=0.535, p<0.001). A similar correlation was established in a large meta-analysis of 89 studies, but it investigated a vast cohort of patients of different ages, unlike our study, which included exclusively senile patients with confirmed ACS [24].

There are scoring systems that allow evaluating the cardiovascular risk and predicting the development of CVDs, and there are scores that allow assessing the cardiovascular risk by the severity of atherosclerosis of other arteries [25]. Given the presence of the correlation between coronary and carotid atherosclerosis, we also developed the relevant score. Unlike the previously proposed scores, we evaluated only the carotid arteries and the correlation with coronary arterial system; the

degree of maximum carotid stenosis was taken into consideration. The ROC analysis was used to define the threshold score. The score of less than 6 meant the probable absence of severe coronary stenosis, more than 6 corresponded to the probable presence of coronary stenosis of 70% or more.

Limitations

The limitation in this study was a relatively small cohort of patients enrolled in the study in the development of the original score. Thus, further research is needed to confirm the data obtained.

Conclusion

In real-world clinical practice, combined coronary and carotid artery disease occurs in 82.7% of patients with senile ACS, and carotid plaques reducing the lumen by more than 50% were detected in 48%. The main clinical and laboratory characteristics of the patients included in the study and selected depending on the severity of carotid atherosclerosis did not differ.

Multivessel coronary artery disease occurred in 63.6% of patients with senile ACS. The severity of carotid and coronary atherosclerosis was found to be correlated. Moreover, it was found that the degree of carotid stenosis is associated with both the degree of coronary stenosis and the number of coronary arteries involved.

The original score developed in the study may be used to determine the severity of coronary atherosclerosis in senile patients (75 years and older), but further research is necessary to confirm the data obtained.

Thus, carotid DS can be used more widely to examine patients with senile ACS, which will allow the additional stratification of patients at high risk of cerebrovascular and recurrent cardiovascular diseases.

No conflict of interest is reported.

The article was received on 20/04/22

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