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Multifocal Atherosclerosis: The Clinical Course and Surgical Treatment of Combined Atherosclerotic Lesions of the Carotid and Main Arteries of the Lower Extremities

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Abstract: Cardiovascular disease (CVD) has been for many years the major cause of deaths in the World. In Europe, despite recent decreases in mortality rates in many countries, CVD is still responsible for about half (46%) of all deaths. Atherosclerosis is a chronic progressive disease which can affect any vascular bed (coronary, cerebrovascular, visceral, peripheral arterial) as a single disease but can also occurs in more than one territory as polyvascular disease. Presence of atherosclerotic disease in one vascular bed frequently indicates an increased risk for its presence in another. The prevalence of polyvascular disease varies from 6% to 71%, depend on the population in whom the study was performed as well as on the study design. Polyvascular disease patients have the worse higher risk profile and worse prognosis than patients with disease in single arterial territory and an improvement in detection and consequent treatment of these patients have been claimed as necessary. The most difficult choice of treatment tactics is the group of patients with peripheral artery disease and concomitant atherosclerotic lesions of other arterial beds. According to a population study conducted in the United States among 3.6 million healthy volunteers based on ultrasound screening, the detection of two or more arterial regions increases with age from 0.04% at 40-50 years, to 3.6% at 80-90 years. At the same time, the results of treatment and prognosis in these patients are much worse than in those with isolated lesions of only one vascular beds.

Keywords: Multifocal Atherosclerosis, Ischemic Heart Disease, Carotid Stenosis, Claudication, Carotid Artery Stenosis

1. Introduction

Atherosclerosis, being a chronic disease, occurs as a result of a violation of protein and lipid metabolism, is characterized by damage to the arteries and leads to disorders of the organ or general circulation [1, 2]. The main features of atherosclerosis are constant progression and multiplicity of lesions of the main arteries of different bads. Peripheral arterial disease (PAD) are one of the clinical manifestations of atherosclerosis and occur in the 60-90 age group in 10-18% of the population with symptoms of intermittent claudication (IC) in every third patient with PAD [3, 4]. Another clinically significant manifestation of atherosclerosis is cerebrovascular disease (CVD), which leads to the development of severe neurological disorders - cerebral infarction (CI) and transient ischemic attack (TIA). The incidence of cerebral infarction in the European Union is 0.2% of the total population and is about 1.4 million cases per year [5, 6]. One third of cases of CI and TIA are caused by lesions of the extracranial sections of the brachiocephalic arteries (BCA), most often carotid artery stenosis (CAS). In the Republic of Belarus, about 30 thousand cases of cerebral infarction are registered annually, and two thirds of them are primary diseases [7, 8]. More than 100 thousand patients in the Republic of Belarus have IC symptoms. Atherosclerotic lesion of the lower extremities evolves into critical lower limb ischemia (CLLI) in 20-70% of patients and ranges from 500 to 1000 new cases per year per million population [9, 10]. The incidence of CAS ≥70% in patients with PAD is 14% [11, 12]. Thus, at present, there are about 14 thousand patients in Belarus with symptomatic PAD and hemodynamically significant stenosis of the carotid arteries. The choice of the optimal treatment tactics in this group of patients is associated with significant difficulties due to the

determination of the priority of revascularization of one or another bad and the unfavorable outcome of the course of the disease, the frequency of which is 21.14% [13, 14]. Making a decision in the case of an isolated severe symptomatic lesion of the carotid arteries seems to be the least difficult task, since the algorithm for its solution is well developed and is effective in the overwhelming majority of cases. Interventions on the carotid arteries - carotid endarterectomy (CEE) and carotid stenting (CS) - are some of the most radical measures for the secondary prevention of IMH and TIA. At the same time, reconstructive surgeries in patients with PAD can reduce the number of amputations and associated disability and mortality [15].

2. Purpose

To analyze the results of surgical treatment of patients depending on the degree atherosclerotic lesion of carotid arteries and arteries of the lower extremities.

3. Material and Methods

The study was a two-center retrospective cohort without a comparison group. In 2015-2019, in the department of vascular surgery of the 4 City Clinical Hospital named after N. E. Savchenko and Republican Scientific and Practical Centre «Cardiology», 180 patients with concomitant atherosclerotic lesions of the carotid arteries and arteries of the lower extremities were treated. Surgical interventions in patients with CVD and PAD were performed by angiosurgeons on the basis of two Minsk healthcare institutions. Preoperative examination included taking anamnesis (including obtaining information about previously performed operations on various arterial regions), identifying clinical symptoms and signs of multifocal atherosclerotic lesions, ultrasound duplex scanning of the brachiocephalic arteries (BCA) and main arteries of the lower extremities (MAC) with determination of the ankle-brachial index (ABI), echocardiography, abdominal aortography, angiography of BCA or CT angiography of BCA.

The indication for BCA angiography was the presence of significant CAS with the possibility of endovascular treatment, previously established according to BCA ultrasound data, in patients with CLI and severe concomitant pathology. CT angiography of BCA was performed in patients with occlusion or subocclusion of the carotid artery and critical stenosis of the contralateral carotid artery. Patients with coronary artery disease, who by echocardiography zones of hypokinesis or reduced ejection fraction were identified, coronary angiography was performed. Control examinations of patients were performed before discharge from the hospital (10±2 days) and one month after discharge from the hospital. The criteria for enrolling patients in the study were as follows: age over 40 years, the presence of CAS (symptomatic or asymptomatic) requiring surgical treatmen. Symptomatic patients were patients who had TIA or transient monocular blindness and had a history of CI in the past 6 months.

The patients were informed about the nature of the disease, the stages and technique of performing surgical interventions, possible complications and side effects of the operations. The exclusion criteria from the study were isolated lesion of one arterial bad, postoperative restenosis of the ICA, bilateral occlusion of the CA.

Statistical analysis of the data obtained was performed on a personal computer using the Statistica 10.0 program (StatSoftInc., USA, license no. AXXR012E839529FA). The normal distribution of features was assessed using the Shapiro-Wilk method. In the case of a normal distribution, the data are presented M ± m, where M is the arithmetic mean, m is the error of the arithmetic mean. If the data did not follow the normal distribution, they were presented as Me (25%-75%), where Me is the median, and 25% -75% is the 25th and 75th percentiles. The analysis of the statistical significance of intergroup differences in quantitative traits that do not correspond to the law of normal distribution was determined using the Mann-Whitney U-test. When comparing qualitative features, the Pearson $\chi 2$ test was used. The results were considered statistically significant at $p < 0.05$.

Table 1. *Characteristics of clinical groups.*

Parameters	Group 1 (n = 37) symptomatic patients with CAS ≥ 70% and chronic leg ischaemia 2B	Group 2 (n=42) symptomatic patients with CAS ≥ 70% and chronic leg ischaemia 3-4	Group 3 (n=51) asymptomatic patients with CAS ≥ 70% and chronic leg ischaemia 2B	Group 4 (n=50) asymptomatic patients with CAS ≥ 70% and chronic leg ischaemia 3-4	P-величина
Average age (years)	67 +/- 7	63 +/- 4	65 +/- 3,3	68+/- 3,3	0,12
Male	30	43	41	43	0,41
Female	7	5	10	7	0,58
Average duration of illness (year)	5+/-1,2	8+/- 2,2	4+/-1,2	6+/-1,2	0,13
Smoking%	65%	85%	55%	75%	0,81
BMI, кg/м2	31+/-4	28+/-5	27+/-5	29+/-3	0,06
LD, mmol / l	3,8+/-0,9	4,8+/-1,2	3,2+/-1,1	3,7+/-1,1	0,74
CRP, mg / l	6,7+/-1,2	16,7+/-2,2	5,7+/-1,2	9,7+/-1,3	0,99
ejection fraction,%	63+/-7,2	53+/-8,2	59+/-10,2	55+/-10,2	0,37
ABI	0,76+/-0,05	0,43+/-0,14	0,76+/-0,18	0,46+/-0,18	0,97
Average CAS,%	78+/-4,3	82+/-7,8	72+/-2,3	73+/-1,3	0,27
MAX linear velocity in the zone of CA stenosis, cm / s	298+/-25	368+/-67	229+/-17	246+/-25	0,68
Angiography of BCA, %	14	25	9	8	0,99
coronarography, %	37	52	12	13	0,23
CT BCA, %	25	35	15	14	0,26

Note. The groups did not differ statistically for all signs, p> 0.05

Table 2. *Concomitant pathology.*

Concomitant pathology	Group 1	Group 2	Group 3	Group 4	P-value
Ischemic heart disease (IHD),%	56	79	43	61	0,45
Arterial hypertension (AH),%	100	100	100	100	0,56
Myocardial infarction (MI),%	14	23	10	12	0,69
Atrial fibrillation (AF),%	6	11	4	9	0,11
TIA,%	70	55	0	0	0,51
Cerebral infarction (CI),%	30	45	0	0	0,28
Diabet mellitus (DM),%	9	21	5	16	0,56
chronic kidney disease,%	2	6	3	5	0,12

Note. The groups did not differ statistically for all signs, p> 0.05

3.1. Description and Characteristics of Clinical Groups

The patients were retrospectively divided into clinical groups by the nature of atherosclerotic lesions of BCA and MALE. The first group: symptomatic patients with CAS ≥ 70% and grade 2B *(Fontaine classification of chronic leg ischaemia)*. The second group included symptomatic patients with CAS ≥ 70% and grade 3-4 (patients with CLI). The third group: asymptomatic patients with CAS≥ 70% and grade 2B. The fourth group consisted of asymptomatic patients with CAS ≥ 70% and grade 3-4.

3.2. Surgical Tactics

Depending on the results of examinations in clinical groups, various types of interventions were used on the main arteries. The type of operation, the sequence of interventions were determined by a council of doctors based on an assessment of the clinical picture of the disease, determination of the most prognostically unfavorable vascular zone, and study of preoperative examination data.

Based on these criteria, a surgical approach was chosen in all four groups, which included the following tactics of surgical treatment: 1. staged operations (the first stage of carotid endarterectomy (CE), the second - revascularization surgery on the arteries of the lower extremities (RSALE); 2. reversed staged operation (the first stage of the RSALE, the second - CEE; 3. simultaneous operations (CEE + RSALE). The choice of surgical tactics and stages of interventions was based on an assessment of the risk of developing symptoms of cerebrovascular accident and violations of the quality of life due to intermittent claudication, the risk of developing CLI (Table 3).

Table 3. *Types of surgical interventions.*

Interventions	Group 1 (n=37)	Group 2 (n=42)	Group 3 (n=51)	Group 4 (n=50)	ALL (n=180)
1 stage – CEE 2 stage – RSALE	22	21	17	10	68
1 stage - RSALE 2 stage – CEE	4	7	16	33	60
One-staged (CEE+RSALE)	11	14	20	7	52

4. Results and Discussion

When assessing the initial status of patients in clinical groups, the following results were obtained. There were no significant differences in age and gender between all clinical groups (p <0.05). The duration of the disease is significantly higher in 2 and 4 clinical groups, groups of patients with grade 3 and grade 4. There were also more smoking patients in the indicated groups. BMI was significantly higher in group 1. Elevated LDL levels were noted in all groups. CRP was increased in all groups and was maximally increased in groups 2 and 4, which was associated with the manifestation of CLI.

There was a moderate decrease in EF in all clinical groups with a minimum value in group 2. The most significant decrease in ABI was noted in groups 2 and 4, as a marker of the presence of CLI. ICA stenosis, as well as linear velocity, had a maximum value in groups of symptomatic patients - 1 and 2. Angiography of BCA was performed from 2% to 5% of patients in each group with a small value in group 2.

The largest number of CTAs was performed on patients in group 2 of 35 studies, the smallest in group 4, only 14 studies. Coronography was required for 52% of the 2nd group (the highest value) and 12% of the patients of the 3rd group (the lowest number).

The maximum number of comorbidities was found in patients of the 2nd clinical group. Thus, arterial hypertension in 100%, myocardial infarction in 23%, AF was noted in 11%, neurological disorders of TIA and CI in 55% and 45%, respectively. Diabetes mellitus, as a concomitant factor aggravating the course of atherosclerosis, was detected in 21% of patients, CKD in 6%. The most compensated group of patients was clinical group 3, where the incidence of concomitant pathology was minimal among all groups: AH in 100%, MI in 23%, AF in 11%, neurological disorders (TIA and CI) were not detected. Diabetes mellitus, as a concomitant factor aggravating the course of atherosclerosis, was identified in 5% of patients, CKD in 3%.

Postoperative results were assessed in terms of

neurological complications (TIA, CI); adverse clinical outcomes with the limb (amputation and / or thrombosis requiring re-intervention); general adverse outcomes (MI, death). The immediate results of the intervention were evaluated - up to 30 days.

Table 4. *30-day results of surgical treatment of 180 patients.*

Complications (30 day)	Group 1 (n=37)	Group 2 (n=42)	Group 3 (n=51)	Group 4 (n=50)	P-value
TIA	1	2	0	1	0,56
CI	0	2	0	0	0,64
Trombosis	2	3	1	3	0,18
MI	0	1	0	1	0,07
Death	0	3	0	1	0,88

Note. There was no statistical significance for complications between single-stage and staged interventions ($p > 0.05$).

The immediate results of treatment in all groups were assessed one day after surgery based on the clinical picture. If necessary, instrumental and laboratory research methods were used. Thus, all patients with suspected TIA or CI underwent ultrasonography of BCA, the patient was examined by a neurologist. If MI was suspected, the patient was tested for highly sensitive troponins, an EKG was performed, and a cardiologist's examination was performed. In case of postoperative thrombosis in the area of reconstruction of the arteries of the lower extremities, we performed ultrasound diagnostic of lower limb arteries. The largest number of unfavorable outcomes in the early postoperative period was observed in the 2nd clinical group. Moreover, in patients who underwent simultaneous surgery, fewer neurological events were recorded than in patients of the same group who underwent staged operations. The number of adverse outcomes with a limb was the highest in 2 and 4 clinical groups. The smallest number of complications was noted in group 3. Early postoperative mortality was noted in groups 2 and 4 and amounted to 1.8% and 1.2%, respectively.

A month later, 176 patients (97%) were examined. The postoperative examination included an objective examination, ultrasound diagnostic of lower limb arteries and BCA. In this period of observation, the tendencies that arose in the clinical groups immediately after the operation remained.

5. Conclusion

Patients with grade 3 and grade 4 and BCA lesions have the longest history of the disease, pronounced concomitant pathology, among them there are more smokers.

CRP and LDL values exceed normal values in all patients with multifocal lesions, and had a maximum value in patients with aggressive manifestation of atherosclerosis - symptomatic patients with CLI.

Active surgical tactics in relation to the correction of clinically manifested arterial regions is justified and allows preventing adverse outcomes in most patients.

In the immediate postoperative period, combined operations do not lead to an increase in the number of heart attacks and strokes in comparison with staged interventions.

A more sophisticated tool is needed to assess the likelihood of unfavorable outcomes in asymptomatic patients.

The worst treatment results were observed in the groups of patients with CLI, which is a mandatory predictor of an unfavorable outcome of treatment.

Conflict of Interest

There is no conflict of interest.

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