Update in Carotid Disease

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Abstract: This review of the literature analyzes publications over the past five years on various problems associated with carotid endarterectomy: 1. Is the eversion or classical technique of surgery with plastic repair of the reconstruction area with a patch more effective? 2. Carotid endarterectomy or carotid angioplasty with stenting is more optimal? 3. When should brain revascularization be performed after the development of ischemic stroke? 4. Should a temporary shunt be used to protect the brain during carotid endarterectomy? 5. How to prevent and treat different types of intraoperative ischemic strokes? 6. What tactics of treatment of patients with combined lesions of the carotid and coronary arteries is more effective? 7. What are the causes and methods of elimination of restenosis of the internal carotid artery known? 8. Is carotid endarterectomy safe in old age? (Curr Probl Cardiol 2023;48:101676.)

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Introduction

The history of carotid endarterectomy lasts more than half a century.[1-5] Today, this is the most numerous open operation on the arterial bed, both in Russia and abroad.[6,7] The current guidelines set strict standards for the performance of this intervention.[6,7] However, for a number of problems, the "scales" still do not find their balance.[6,7]

The purpose of this literature review was to analyze domestic and foreign publications over the past 5 years on the 3 most discussed issues of carotid surgery.

Classic or Eversion Technique?

Eversion and classical carotid endarterectomy with patch repair of the reconstruction zone are the most popular and studied surgical techniques.[6-8] The first involves cutting off the internal carotid artery at the mouth, followed by endarterectomy by eversion and its implantation in its original place.[6-8] The second is performed using a longitudinal arteriotomy of the common carotid artery with a transition to the internal carotid artery, open endarterectomy and patch implantation.[4,6-8] The pros and cons of both methods are well-known.[4,6-8] Eversion carotid endarterectomy does not always guarantee reliable fixation of the intima or atherosclerotic plaque behind the endarterectomy zone. As a result, thrombosis of the internal carotid artery may develop after the start of blood flow.[9-13] The classical operation, in turn, in addition to requiring additional costs for the purchase of patches, differs in that after implantation of the latter, the lumen of the common carotid artery and the internal carotid artery expands.[14-16] This, in turn, leads to the development of turbulent blood flow, the risk of parietal thrombosis, neointima hyperplasia, and subsequent restenosis.[14-16] In addition to everything, the reaction of the body to a synthetic or biological patch can occur according to the type of "rejection" (conflict "donor-recipient").[16] This trend will be accompanied by an enhanced inflammatory response, which will make a significant contribution to the development of vessel lumen loss.[16] Despite the above facts, a comparative analysis of the 2 techniques of carotid endarterectomy has been in the trend of interest of vascular surgeons in all years.

Bokeria L.A. et al. analyzed the treatment of 60 patients from 2009 to 2015. The authors concluded that restenosis of the internal carotid artery in the late postoperative period is most often diagnosed after classical surgery.[9]

In the publication of Dudanov I.P. et al. a lower-risk of complications after eversion carotid endarterectomy was also confirmed.[10] The study

included 122 patients, among whom plasty of the reconstruction zone with a patch was implemented in 30 cases. After classical carotid endarterectomy during 3 years of follow-up, the total number of complications reached 33.3%. Among them, in 2 cases, thrombosis of the internal carotid artery was diagnosed, in 2 others – restenosis of the internal carotid artery, in 1 - myocardial infarction. After the eversion technique, the combined endpoint reached 9.8%, and restenosis of the reconstruction zone was visualized in 1 patient.[10]

Grinev K.M. et al. analyzed their own experience of performing various techniques of carotid endarterectomy for 25 years.[11] In the long-term follow-up period, hemodynamically significant restenosis of the internal carotid artery was observed only in 5.6% of cases after patch implantation. The authors concluded that the eversion type of operation is the most preferable.[11]

In the study of Kazantsev A.N. et al., devoted to the results of different types of carotid endarterectomy in the same patient with bilateral stenosis of the internal carotid artery, the following conclusions were drawn. Both techniques showed comparable quality of treatment. However, an increase in the number of restenoses persisted after patch implantation: 17.3% versus 9.3%.[12] In another work Kazantsev A.N. et al. analyzed the results of 1493 classical and 637 eversion CEE after 48.8 ± 19.6 months. After patch implantation, restenosis (4.2% vs 2.1%, $P = 0.02$) and thrombosis/occlusion of the reconstruction zone (5.2% vs 5.3%, $P = 0.01$) were more often visualized.[13]

A high-risk of restenosis of the internal carotid artery in the implementation of classical carotid endarterectomy was also determined by Darwish N.A.M.A. et al. The authors came to the conclusion that the eversion technique should be the operation of choice.[17]

Gavrilenko A.V. et al. conducted a meta-analysis of existing studies on this topic.[18] One thousand seven hundred eighteen eversion and 1954 classic carotid endarterectomy were included. The authors found that the development of restenosis of the internal carotid artery ($P = 0.006$) and in-hospital/remote ischemic stroke ($P = 0.005/P = 0.000$) is most often observed after plasty of the reconstruction zone with a patch.[18]

The largest Russian study comparing 2 techniques of carotid endarterectomy was conducted under the leadership of Belov Yu.V.[19] The multicenter study included 25,106 patients operated on between February 1, 2006 and September 1, 2021. In the long-term follow-up period (124.7 ± 53.8 months), death from all causes ($P < 0.0001$), death from ischemic stroke by ischemic type ($P < 0.0001$), nonfatal ischemic stroke ($P < 0.0001$) 0.0001), restenosis of the internal carotid artery ($P < 0.0001$)

was most often diagnosed after classical surgery with patch repair of the reconstruction zone.[19]

Thus, in Russia, most studies favor the eversion technique of surgery. But what are the trends around the world?

One of the questions about the high-risk of restenosis of the internal carotid artery after classical carotid endarterectomy was the type of patch. However, numerous studies have shown that the nature of the latter does not affect the immediate and long-term outcomes of operations. In a publication by Leonore F.T. et al. compared 168 outcomes of carotid endarterectomy with the use of a xenopericardial patch and 174 synthetic outcomes.[20] The frequency of hemodynamically significant restenosis on the 301st day of observation was 5.16% and 4.11% ($P = 0.55$), respectively.[20]

In a meta-analysis of randomized trials by Texakalidis P. et al. analyzed the results of the use of synthetic, autovenous, and biological patches in 3234 patients.[21] Risk of 30-day stroke (RR, 1.00; 95% CI, 0.45-2.19; I 2 = 0%), transient ischemic attack (RR, 1.14; 95% CI, 0.41-3.19; I 2 = 0%), myocardial infarction (RR, 0.75; 95% CI, 0.14-3.97; I 2 = 0%), death (RR, 0.53; 95% CI, 0.21-1.34; I 2 = 0%), wound infection (RR, 1.84; 95% CI, 0.43-7.81; I 2 = 0%), carotid thrombosis (RR, 1.47; 95% CI, 0.44-4.97; I 2 = 0%) and long-term stroke (RR, 2.33; 95% CI: 0.76-7.10; I 2 = 0%), death (RR, 1.09; 95% CI, 0.65-1.83; I 2 = 0%), restenosis more than 50% (RR, 0.48; 95% CI, 0.19-1.20; I 2 = 0%) was similar between the groups of synthetic and venous patches.[21] Comparison of the results of the use of biological and synthetic patches also did not give statistically significant differences in terms of 30-day stroke (RR, 1.44; 95% CI, 0.19-10.79; I 2 = 12.7%), transient ischemic attack (RR, 1.05; 95% CI, 0.11-10.27; I 2 = 0%) and death (RR, 4.01; 95% CI, 0.46-34.85; I 2 = 0%).[21]

Despite the fact that the nature of the patch does not affect the outcome of carotid endarterectomy, there is an evidence of one important disadvantage of such an operation. This is an infection of the reconstruction zone with the formation of an aneurysm.[22-25] In such a situation, it is necessary to repeat the intervention with resection of the latter, secondary surgical debridement, and subsequent replacement of the internal carotid artery.[22-25] Failure to comply with these measures may lead to the development of angiosepsis and arrosive bleeding.[22-25] Thus, having studied this side of the issue, the main focus of the scientific community was also aimed at comparing the outcomes of classical and eversion surgical techniques.

In a large meta-analysis of Paraskevas K.I. et al. included the results of 16,249 eversion and 33,251 classical carotid endarterectomies.[26] The eversion technique was associated with significant reductions in 30-day mortality (RR, 0.46; $P < 0.0001$), stroke (RR, 0.58; $P < 0.0001$), stroke death (OR, 0.52; $P < 0$ .0001), death from stroke or myocardial infarction (OR, 0.50; $P < 0.0001$), and late restenosis of the internal carotid artery (OR, 0.49; $P = 0.032$) compared with patch repair of the reconstruction area.[26]

In a study by Chen G.Z. et al. 211 eversion and 230 classical carotid endarterectomies were analyzed.[27] The authors showed that the frequency of restenosis of the internal carotid artery and deaths in the long-term follow-up period did not differ significantly ($P = 0.86$ and $P = 0.17$, respectively).[27]

Maguire S.C. et al. presented the results of 114 classical and 90 eversion carotid endarterectomies.[28] Within 7 years, the authors did not obtain statistically significant differences in the frequency of complications between the samples.[28] However, it was noted that the time of operation and clamping of the internal carotid artery was significantly less when implementing the eversion technique, which reduces the risk of intraoperative stroke.[28]

Dakour-Aridi H. et al. conducted an analysis of data from the Vascular Quality Initiative registry, including 30-day and 1-year results of 12,050 eversion and 83,676 classic carotid endarterectomies.[29] Although there was no statistical difference in the incidence of restenosis of the internal carotid artery, the authors found that the eversion technique was associated with a lower rate of stroke and death at 30 days (OR, 0.72, 95% CI, 0.54-0 .95, $P = 0.02$) and after 1 year (RR, 0.75, 95% CI, 0.58−0.97, $P = 0.03$).[29]

In the work of Cheng S.F. et al., the authors compared the results of 3 types of carotid endarterectomy: group 1 (n = 511) with patch plasty; group 2 (n = 232) − primary suture; group 3 (n = 47) − eversion.[30] The cumulative rates of restenosis ≥ 50% at 1 year were 18.9%, 26.1%, and 17.7%, respectively, and at 5 years, 25.9%, 37.2%, and 30.0%, respectively. There was no difference in risk between the eversion and classical carotid endarterectomy groups (OR, 0.90, 95% CI, 0.45-1.81; $P = 0.77$).[30] Primary closure had a higher risk of restenosis than the classical technique (OR, 1.45, 95% CI, 1.06-1.98; $P = 0.019$). Cumulative restenosis rates ≥ 70% did not differ between primary closure and patch repair (12.1% vs 7.1%, OR, 1.59, 95% CI: 0.88-2.89; $P = 0.12$), and between patch repair and eversion endarterectomy (4.7%, heart rate 0.45, 95% CI, 0.06-3.35; $P = 0.44$).[30]

Meyer A. et al. compared the results of 585 carotid endarterectomies with patch application and 274 eversion carotid endarterectomies.[31] There was no difference in the frequency of postoperative complications.[31]

Lazarides M.K. et al. performed a large meta-analysis (4440 patients) evaluating the outcomes of various carotid endarterectomy techniques: 431 eversion, 973 autovenous patch, 948 PTFE patch, 828 dacron patch, 828 xenopericardial patch, and 258 polyurethane patch.[22] After eversion carotid endarterectomy, a statistically lower number of 30-day postoperative strokes, deaths, and restenosis of the internal carotid artery was recorded in the long-term follow-up period.[22]

Thus, both the Russian and foreign medical communities still do not come to a common denominator as to which carotid endarterectomy technique is the most optimal. However, the results of large multicenter studies and meta-analyses confidently demonstrate that the classical technique with patch repair of the reconstruction area is associated with the highest risk of restenosis of the internal carotid artery in the late postoperative period. However, additional prospective, randomized studies are required to finally resolve the issue of identifying the best method of cerebral revascularization in the presence of hemodynamically significant stenosis of the internal carotid artery.

Carotid Endarterectomy or Carotid Angioplasty With Stenting?

According to the current Russian recommendations, carotid endarterectomy is the operation of choice in the presence of hemodynamically significant stenosis of the internal carotid artery.[6] However, with the development of endovascular technologies, carotid angioplasty with stenting has become an alternative option for revascularization.[32,33]

Speaking of symptomatic patients, the latter may be preferable to open intervention when there is a high surgical risk of carotid endarterectomy.[6] Implementation of carotid angioplasty with stenting is also possible in asymptomatic patients, but only in medical institutions with high operational activity and the level of complications corresponding to the existing "quality standards."[6]

However, according to the 2017 European Society for Vascular Surgery Guidelines, carotid endarterectomy remains the "gold standard for revascularization" (Class IIa; Level of Evidence: B).[7,34] However, in some cases, carotid angioplasty with stenting may be considered as the procedure of choice (Class IIb; Level of Evidence: B) in the presence of

one or more clinical/imaging characteristics that may be associated with an increased risk of late ipsilateral stroke (heart attack). Brain of embolic origin, a history of contralateral stroke, etc.) provided that the perioperative stroke/mortality rate is <3%, and the patient's life expectancy is >5 years.[7,34]

Against this background, friction between vascular and endovascular surgeons over the effectiveness of one or another correction method does not subside. Constant improvement of interventional technologies, modernization of stents and drug supply, in some cases, allow us to think about the position of carotid endarterectomy as an operation of choice.

Stolyarov D.P. et al. in their publication demonstrated the outcomes of 132 carotid endarterectomies and 137 carotid angioplasties with stenting. No lethal outcomes were recorded. There were no differences in the incidence of stroke (1.5% and 4.5%, respectively, $P = 0.13$). Damage to the cranial nerves was diagnosed only during carotid endarterectomy (7.6%, $P = 0.001$).[35]

Khafizov T.N. et al. analyzed the immediate results of 353 carotid endarterectomies and 242 carotid angioplasties with stenting. The frequency of postoperative strokes in group 1 reached 2.3%, in group 2%-3.7%.[36] The authors concluded that both methods have comparable efficacy and safety.[36]

Cui L. et al. conducted a meta-analysis of 5 randomized clinical trials including 3901 patients.[37] The authors found that the risk of any stroke during the periprocedural period was significantly lower in patients undergoing carotid endarterectomy (RR, 0.53; 95% CI, 0.29-0.96).[37]

Bokeria L.A. et al. analyzed the results of treatment of 256 patients. Depending on the type of operation, 3 groups were formed: 1 - eversion carotid endarterectomy, 2 - classical carotid endarterectomy, 3 - carotid angioplasty with stenting.[38] Restenosis of the internal carotid artery in 1 reached 2.1%, in 2%-4.3%, in 3%-1.6%. The findings of the study demonstrated that patch implantation is the least preferred method of reconstruction, while eversion carotid endarterectomy and carotid angioplasty with stenting showed comparable safety and efficacy.[38]

Bazylev V.V. et al. analyzed the results of 522 carotid angioplasties with stenting and 386 carotid endarterectomies. The incidence of stroke in both groups was comparable (1.7% and 1.04%, respectively, $P = 0.5$).[39] There were no lethal outcomes and hemorrhagic transformations.[39]

Batchelder A.J. et al. conducted a systematic review and meta-analysis of 20 randomized clinical trials. The 30-day mortality/stroke rate was significantly higher after carotid angioplasty with stenting in seven studies

with 3467 asymptomatic patients (RR, 1.64, 95% CI, 1.02-2.64) and in 10 studies with 5797 symptomatic patients. Patients (RR, 1.71, 95% CI, 1.38-2.11).[40] The frequency of restenoses was the highest after carotid angioplasty with stenting and reached 10%. Also, after carotid angioplasty with stenting, the maximum number of ischemic strokes was recorded (23% vs 9%).[40]

Brott T.G. et al. analyzed the long-term results of carotid endarterectomy and carotid angioplasty with stenting in a sample of 4775 patients.[41] The authors proved that the frequency of complications and restenosis of the internal carotid artery in both cohorts did not differ during 12 years of follow-up.[41]

Chernyavsky M.A. et al. in their study, they studied the annual outcomes of 232 carotid angioplasties with stenting, 90 classic carotid endarterectomies, and 142 eversion ones.[42] Despite the fact that the results were comparable, the authors noted a greater increase in the number of adverse cardiovascular events and restenoses after patch implantation.[42]

In a study by Bracale U.M. et al. compared 2-year results of carotid endarterectomy (n = 86) and carotid angioplasty with stenting (n = 33) with a 2-layer microlattice stent in a retrospective format.[43] The highest number of deaths was recorded after the endovascular procedure ($P = 0.03$). No statistically significant differences were found for other types of complications.[43]

Matsumura J.S. et al. conducted an analysis of 2 large randomized clinical trials, including the results of treatment of 2544 asymptomatic patients.[44] The authors found that the development of myocardial infarction is more typical for patients who underwent carotid endarterectomy (0.6% vs 1.7%, $P = 0.01$). No statistical difference was obtained for other complications.[44]

In a study by Qureshi AI et al. studied the incidence of restenosis 10 years after carotid angioplasty with stenting and carotid endarterectomy.[45] No statistically significant differences were found. The mean survival without revascularization was 8.2 ± 0.1 years and 8.0 ± 0.1 years, respectively (logarithmic test $P = 0.0823$).[45]

Speaking about the choice between carotid angioplasty with stenting and carotid endarterectomy, Vinogradov R.A. proposed focusing on the severity of calcification of the internal carotid artery.[46] So, with the degree of the latter up to 30%, stenting is recommended, from 31% to 70% – stenting or carotid endarterectomy, and more than 70% – only carotid endarterectomy. The author explains this approach by the fact that severe calcification of the internal carotid artery can prevent the full deployment of the stent.[46] Its implantation under these conditions will be

characterized by the presence of residual stenosis, the risk of distal embolism and arterial dissection.[46]

I would like to pay special attention to the importance of the factor of calcification of the carotid arteries. Carotid calcification is a well-known marker of atherosclerosis and is associated with high morbidity and mortality. It is now believed that vascular calcification is an active, enzymatically regulated process, including dystrophic calcification and early endothelial dysfunction.[47-51] This induces a pathogenic inflammatory response leading to the deposition of calcium phosphate as microcalcifications, leading to the formation of atherosclerotic plaques, which eventually become unstable.[47-51] If inflammation ceases, hydroxyapatite crystals begin to form, resulting in macrocalcifications that help maintain plaque stability.[47-51] Since carotid calcification may be asymptomatic, it is critical to detect it early with diagnostic imaging. The assessment of carotid calcification is calculated using computed tomographic angiography, which is a confirmatory test that allows studying the composition of the atherosclerotic plaque and calculating the assessment of carotid calcification.[47-51]

Returning to the choice between stenting and carotid endarterectomy, it must be remembered that the latter is most often performed according to the eversion or classical technique with patch repair of the reconstruction area.[52-54] Summarizing the above studies, it is important to note that in the overwhelming majority of cases, the authors compare the total cohort of open surgeries with the endovascular technique. However, this is not true. As noted in the previous section of this article, patch implantation is most often associated with an increased risk of restenosis of the internal carotid artery due to dilatation of the reconstruction zone and arterial lumen with deformation of the physical properties of the blood flow.[15,16,19,55]

Against this background, in the study by Raptis A. et al. presented the results of computer 3D modeling of the reconstruction zone after classical carotid endarterectomy and stenting.[56] The authors showed that as a result of open intervention, there is indeed a large dilatation of the arterial lumen, its tortuosity and curvature, which aggravates all the physical characteristics of the blood flow and is combined with a greater risk of restenosis compared to stenting.[56] Therefore, an interventional intervention is preferable to a patch.

Of particular interest are the results of carotid endarterectomy and stenting in asymptomatic patients over 75 years of age. On the one hand, according to the recommendations, endovascular revascularization cannot be the operation of choice in this situation.[6] On the other hand, the

high surgical risk suggests that the implementation of carotid endarterectomy will be characterized by a high-risk of postoperative adverse cardiovascular events.[6,57] Publications demonstrating the results of carotid endarterectomy in small patient populations tend to suggest that open surgery is safe for elderly patients.[58,59] However, the only Russian multicenter study showed that death ($P = 0.037$), myocardial infarction ($P = 0.0006$), ischemic stroke ($P = 0.03$), and wound revision due to bleeding ($P < 0.0001$) most often are diagnosed in patients older than 75 years.[60] In this situation, the question of the advisability of stenting in the older age group is particularly acute.

Mutaev M.M. et al. analyzed the results of 52 carotid endarterectomies and 17 stents in patients older than 80 years. Ischemic strokes and deaths were not recorded. Both methods have shown their safety and efficacy.[61]

Hammar K. et al. demonstrated the outcomes of carotid endarterectomy and stenting in 7589 patients with a mean age of 72 ± 8 years.[62] They proved that the category of patients older than 80 years was characterized by an increased risk of stroke after stenting relative to open revascularization (RR 3.2; 95% CI, 2.03-5.03).[62]

Mehta A. et al. conducted an analysis of carotid endarterectomy stenting in a sample of 33,115 patients. The authors found that stenting had a higher-risk of both 30-day stroke/death (RR 1.78; 95% CI, 1.10-2.89) and 1-year stroke/death (RR, 1.85; 95% CI, 1.35-2.54) in patients older than 80 years.[63]

Thus, there is no consensus on the effectiveness of one or another method of brain revascularization. This pattern applies to all characteristics of patients with precerebral atherosclerosis, regardless of age, symptomatic/asymptomatic and severity of comorbid background. Some studies demonstrate the benefits of carotid endarterectomy, others show the benefits of stenting and vice versa. Ultimately, the choice in favor of one or another method of correction should be personalized, based on the stratification of the risk of complications and the experience of the medical institution.

Carotid Endarterectomy in the Acute Period of Stroke

According to current recommendations, the presence of hemodynamically significant symptomatic carotid stenosis is an indication for cerebral revascularization.[6,7] At the same time, carotid endaretrectomy or carotid angioplasty with stenting in this situation can be implemented if it is a "minor" stroke without concomitant severe neurological deficit.[6,7]

Reconstructive intervention is allowed in the acute period of stroke.[64-68] Tarasov R.S. et al. presented the outcomes of 145 carotid endarterectomies performed in the acute period of stroke. Among the complications, 1 ischemic stroke was recorded. Myocardial infarctions and lethal outcomes were not observed.[69]

Roussopoulou A. et al. compared the results of carotid endarterectomy in 2 groups of patients: 1 - within 0-2 days after the development of ischemic stroke (n = 63) and 2 - within 3-14 days (n = 248). The 30-day incidence of stroke in the samples did not differ (7.9% vs 4.4%, $P = 0.333$).[70] At the same time, the median duration of hospitalization was shorter for urgent carotid endarterectomy (6 days (interquartile range 4-6) versus 10 days (interquartile range 7-14); $P < 0.001$).[70]

In the work of Kazantsev A.N. et al. outcomes of carotid endarterectomy depending on the stroke period were presented: acute (up to 28 days, n = 493), early recovery (up to 6 months, n = 481), late recovery (up to 2 years, n = 115).[71] The smallest number of complications was recorded in the acute and late recovery periods of ischemic stroke.[71]

Borghese O. et al. presented the outcomes of 72 carotid endarterectomies performed in the acute period of stroke.[72] There were no hospital strokes, myocardial infarctions, or deaths. The combined end point (death/stroke/myocardial infarction) was 5.5% at 30 days postoperatively.[72] The neurological deficit on the National Institute of Health Stroke Scale (NIHSS) regressed by more than 2 points in 47.2% of cases.[72]

Chisci E. et al. analyzed the results of carotid endarterectomy at different times after the manifestation of a neurological event.[73] They concluded that the best results of revascularization are achieved in the acute period of stroke.[73]

Zakirzhanov N.R. et al. presented a publication describing the outcomes of 32 carotid endarterectomies up to 72 hours after stroke.[74] The comparison group was a sample of 48 patients operated on 4-14 days after the formation of a neurological event. In the study sample, 2 hemorrhagic transformations were recorded, in one case with a fatal outcome.[74] A new ischemic stroke was diagnosed in 1 case in the comparison group. The authors concluded that emergency carotid endarterectomy is safe and effective.[74]

Summarizing the presented data, it should be noted that one of the problems that hinders surgeons from implementing active surgical treatment in an urgent mode is the risk of hemorrhagic transformation of the ischemic focus. On the one hand, the latter can develop against the background of hyperperfusion syndrome after the start of blood flow.[75-77] On

the other hand, a number of authors have proven that damage to the carotid glomus during carotid endarterectomy can lead to its formation, which will be accompanied by unstable hemodynamics and a tendency to hypertension.[77] In their study, they analyzed the results of 214 glomus-sparing (group 1), 145 classical (group 2), and 158 eversion (group 3) carotid endarterectomies.[77] The results of the work demonstrated that the implementation of glomus-sparing carotid endarterectomy is not accompanied by the development of any adverse cardiovascular events.[77]

Thus, the results of operations in the acute periods of stroke most often demonstrate optimal results. Although there is still no consensus on this matter. Against this background, the works devoted to stenting of the carotid artery under these conditions are of interest.

Ermolaeva T.V. et al. demonstrated that in a sample of 30 patients after stenting, it was not accompanied by the development of any adverse cardiovascular events.[78] At the same time, there was a significant regression of neurological symptoms.[78]

Limaye K. et al. compared the outcomes of stenting in the first hour after the development of a stroke (n = 39) and the acute (n = 58) period of ischemic stroke.[79] In the first one, the predominance of all postoperative complications was observed (15.3% vs 3.4%, $P = 0.05$)[79]. The frequency of restenosis in both groups reached comparable values after 13.7 months of follow-up (8.1% vs 9.1%, $P = 0.8$).[79]

Kazantsev A.N. et al. presented the results of 312 carotid artery stentings in the most acute period of stroke.[80] In the hospital follow-up period, 1.92% of deaths, 1.6% of myocardial infarctions, 1.6% of non-fatal strokes, 2.2% of asymptomatic strokes, 0.64% of hemorrhagic transformations, and 0.32% of internal thrombosis were detected. -ney of the carotid artery.[80] In view of the fact that the presented data corresponded to the limits of the incidence of stroke and deaths, which were established by the current recommendations, the authors came to the conclusion about the effectiveness and safety of carotid artery stenting in the urgent mode.[80]

Thus, studies on carotid angioplasty with stenting in the acute period of ischemic stroke also demonstrate a lack of certainty about the efficacy and safety of this revascularization strategy in these conditions.

It should be noted that today there is a tendency for the predominance of publications devoted to isolated results of carotid endarterectomy stenting. Along with this, there are not enough works comparing the results of the implementation of both methods.

Khripun A.I. et al. analyzed the results of both methods of treatment in the period from 2 to 7 days after the development of ischemic stroke.[81]

No complications were recorded in the postoperative period.[81] The authors specified that the success of revascularization was associated with the absence of severe neurological deficit (no more than 3 points on the Rankin scale) and the size of the ischemic focus in the brain no more than 4 cm.[81]

Altman D.A. et al. presented the results of 32 carotid endarterectomies and 20 carotid angioplasties with stenting within a period of several hours to 2 weeks from the onset of stroke.[82] Both groups received 1 postoperative ischemic stroke. No other complications were recorded.[82]

In 2021, the first multicenter Russian study was published, studying the results of carotid angioplasty with stenting (group 1, n = 312) and carotid endarterectomy (group 2, n = 357) in the urgent mode.[83] The inclusion criterion was the presence of a mild neurological deficit (from 3 to 8 points according to the NIHSS scale) and an ischemic focus in the brain, not exceeding a diameter of 2.5 cm.[83] Statistically significant differences were obtained in the frequency of hemorrhagic transformations (0.64% vs 3.6%, $P = 0.001$) and "silent" hemorrhagic transformations (0% vs 7.3%, $P = 0.001$).[83] The authors concluded that carotid endarterectomy in the most acute period of stroke is associated with the development of complications in every fifth patient, and carotid angioplasty with stenting is the most optimal method of revascularization.[83]

Cui C.L. et al. analyzed the results of stenting and carotid endarterectomy at different times from the onset of stroke in 18,643 patients.[84] The highest rates of deaths + stroke were recorded after carotid angioplasty with stenting.[84]

Discussing the problem of emergency carotid endarterectomy, one cannot fail to mention the new circumstances that turned the world of modern medicine over 2 years ago. We are talking about patients with COVID-19. As is known, the SARS-CoV-2 virus is capable of causing coagulopathy and endotheliitis.[85-87] Both processes lead to thrombotic complications of various localization and destabilization of the atherosclerotic plaque.[85-87] Since the current Russian and foreign recommendations were created long before the start of the pandemic, there was no consensus and rules for providing primary vascular care to this cohort of patients.[6,7] However, in case of symptomatic non-occlusive thrombosis of the internal carotid artery against the background of a novel coronavirus infection (NCI), existing indications for carotid endarterectomy can be used if there is no severe neurological deficit and extensive ischemic focus in the brain.[88] However, despite the fact that thrombosis of the internal carotid artery under conditions of COVID-19 can be observed in

a quarter of cases, there is a lack of publications on emergency surgery for this condition.[89]

The world literature provides only a few cases of carotid endretrectomy in the most acute period of stroke against the background of thrombosis of the internal carotid artery in patients with NCI.[89-93] As a rule, publications report a successful outcome of revascularization if there is no severe course of COVID-19 and local anesthesia is used.[89-93] According to the authors, the refusal of general anesthesia with the transition to artificial lung ventilation prevents the development of pulmonary barotrauma, which ensures a favorable prognosis of the postoperative period.[89-93]

In Russia, according to the electronic library elibrary.ru, there are only 3 publications devoted to this problem. In the first, the authors under the guidance of Kazantsev A.N. report a successful carotid endarterectomy in a patient with local occlusive thrombosis of the internal carotid artery in the presence of an unstable plaque and retrograde filling of the artery.[88] The optimal outcome of revascularization, according to surgeons, was associated with the use of local anesthesia and the installation of 2 drains, which contribute to the prevention of hemorrhagic complications in conditions of virus-induced coagulopathy.[88]

In another publication, the authors analyzed the results of treatment of 43 patients of this profile, comparing them with the outcomes of 89 carotid endarterectomies in the pre-Covid period.[89] The groups were comparable in terms of the frequency of all cardiovascular events. However, in the cohort with COVID-19, a hematoma in the intervention area developed more often (11.6% vs 1.1%, $P = 0.02$).[94] The authors concluded that carotid endarterectomy is effective and safe in the acute period of stroke against the background of thrombosis of the internal carotid artery under conditions of COVID-19.[94]

The third publication on this topic analyzed the results of operations for extended atherosclerotic lesions of the internal carotid artery and parietal thrombosis in 49 patients with a positive PCR test for the presence of SARS-CoV-2.[95] No complications were recorded in the postoperative period. Neurological deficit on the NIHSS scale) regressed from 10.5 ± 3.5 points to 6.5 ± 1.5; $P = 0.001$. The authors confirmed the effectiveness of this treatment strategy.[95]

Summarizing the data of the presented section, it should be noted that certainty regarding the use of carotid endrterectomy and stenting of the carotid artery in the urgent mode has not yet been achieved. It also remains unclear which of the 2 methods of revascularization is the most optimal. In this regard, the approach to choosing a treatment strategy for

this cohort of patients can only be personalized and selected by a multidisciplinary council based on the experience of the institution and current recommendations.

Carotid Endarterectomy and Temporary Shunt

The debate about the need to install a temporary shunt in certain conditions during carotid endarterectomy has never subsided. On the one hand, it is indisputable that contralateral occlusion of the internal carotid artery, contralateral Steel syndrome, occlusion of the vertebral arteries, open structure of the circle of Willis can objectively reduce the compensatory mechanisms of hemocirculatory hemostasis at the cerebral level. On the other hand, the current recommendations do not consider these conditions as an undeniable indication for the installation of a temporary shunt during clamping of the internal carotid artery. As for the severity of contralateral stenosis of the internal carotid artery, existing studies suggest that even the subocclusion factor does not worsen the results of carotid endarterectomy in relation to 60%-70% of lesions.[96-98] However, in these studies, in the presence of 90%-99% stenosis of the internal carotid artery, the authors more often resorted to the use of a temporary shunt.[96-98] In this situation, the current recommendations also do not give any comments. According to the recommendation, the only indication for the placement of a temporary shunt may be a decrease in retrograde pressure in the internal carotid artery or cerebral oximetry when the internal carotid artery is clamped. But besides the fact that this conclusion has a low level of evidence (Evidence class B), the recommendations do not provide strict boundaries that allow us to state the need for a temporary shunt. Thus, it is not clear how much retrograde pressure should decrease – by 20%, 50%, 80%? The same uncertainty exists in the parameters of oximetry. Ultimately, each institution relies only on its local experience, establishing internal protocols and indications for the placement of a temporary shunt. The existing reality has led to the fact that a temporary shunt can be used both selectively and routinely, and generally refuse to use it. And until the recommendations provide guidelines with an absolute level of evidence, the community of practicing vascular surgeons will be divided into two camps of supporters and opponents of a temporary shunt. And both sides are right.

In the study of Gavrilenko A.V. et al. a temporary shunt was used selectively in 24 patients based on changes in intraoperative electroencephalography. Complications were not recorded. The authors concluded that the selective use of a temporary shunt mitigates the negative effect of

cerebral hemodynamic insufficiency caused by contralateral occlusion/subocclusion of the internal carotid artery.[99] However, in a more recent study based on a treatment analysis of 156 patients, the authors demonstrated that placement of a temporary shunt was a predictor of stroke and internal carotid thrombosis ($P = 0.00011$), refuting their conclusions about the safety of this brain protection measure.[100] Zholkovsky A.V. et al. indicated that in the general sample where a temporary shunt is not used, the incidence of stroke can be as high as 20%. Analyzing their experience of 40 operations, the authors did not receive a single perioperative stroke.[101] Mikhailov I.V. et al. presented the results of classic carotid endarterectomy with a temporary shunt in 167 patients. There were no intraoperative strokes or deaths.[102] In the work of the same authors, published two years later, the sample of patients increased to 325. No intraoperative strokes were detected. On day 3 after surgery, 1 ischemic stroke was diagnosed, and on days 5 and 7, 2 deaths (due to the development of hemorrhagic stroke).[103] However, it cannot be stated with complete certainty that the timing of the development of adverse cerebral events corresponded to those indicated. In view of the fact that multispiral computed tomography of the brain was performed only after the development of a stroke, these events could be the outcome of the formation of "silent" strokes in the brain as a result of embolization against the background of a temporary shunt. In addition, the authors indicated that both patients tended to hypertension throughout the entire postoperative period, which could cause hyperperfusion syndrome with the development of hemorrhagic transformation of asymptomatic ischemic stroke.[103] Against this background, Ignatiev I.M. et al. In his study, he demonstrated the data of intraoperative electroencephalography, according to which, among 9 patients who underwent the installation of a temporary shunt, multiple microembolic signals were recorded. According to magnetic resonance imaging, these patients were diagnosed with "silent" foci of lacunar cerebral infarctions. In those patients in whom a temporary shunt was not installed, only in a third of cases were single microembolic signals recorded without signs of "silent" strokes. Thus, the authors proved that the installation of a temporary shunt is associated with a high risk of distal embolism, with subsequent structural changes in the brain substance.[104] According to the literature, the frequency of "silent" strokes can significantly exceed the number of symptomatic strokes after carotid endarterectomy. As a rule, this condition requires, first of all, the control of postoperative hypertension to prevent the development of hemorrhagic transformation and cerebral edema.[105,106] Given these facts, it is necessary to revise the current recommendations for the

postoperative management of this cohort of patients with the introduction of mandatory brain computed tomography to detect asymptomatic pathological conditions.

Returning to the question of choosing a method for assessing cerebral hemodynamics compensation under conditions of clamping of the internal carotid artery, it should be emphasized that the recommendations also do not give a complete answer to which method is more effective − measurement of retrograde pressure in the internal carotid artery or cerebral oximetry. In the study of Kamenskaya O.V. et al. an analysis of the outcomes of 469 carotid endarterectomies was given. Among them, as a result of low retrograde pressure in the internal carotid artery, the installation of a temporary shunt was required in 16% of patients. However, thanks to the determination of the optimal indicators of cerebral oximetry, their number was reduced to 3%. Thus, it can be emphasized that cerebral oximetry is a less sensitive method for assessing cerebral hemodynamics relative to invasive assessment.[107] Later Kamenskaya O.V. et al. under the leadership of Kuzhuget R.A. found that only a synchronous decrease in cerebral oximetry by 40% and retrograde pressure below 40 mm Hg. from the systemic may be the main criterion for the installation of a temporary shunt. This tactic leads to a decrease in the incidence of perioperative stroke from 2.6% to 0.8%.[108] In another article, this group of authors, led by Karpenko A.A. proved that clamping the internal carotid artery for any period of time leads to a significant increase in markers of ischemic brain injury (NSE, S-100). At the same time, none of the methods (measurement of retrograde pressure of the internal carotid artery, cerebral oximetry) can predict the development of intraoperative stroke, which makes their use uninformative.[109] Thus, the conclusion suggests itself that the installation of a temporary shunt must be performed by everyone. Development of ischemic stroke is impossible to predict. However, in their latest work from 2017, this team of authors proved that the main predictor of stroke development is the use of a temporary shunt ($P < 0.00001$), which immediately crossed out the previous conclusion.[110] In the study of Lysenko A.V. et al. presented the results of CEA in the group with temporary bypass (n = 15) and in the group without temporary bypass (n = 55).[111] In the first, no complications were recorded, while in the second, 1.5% (n = 1) of cases developed a stroke. In this study, the decision to install a temporary bypass was made based on the results of transcranial Doppler sonography (50% reduction in mean blood flow velocity in the ipsilateral middle cerebral artery). In a patient who had a stroke, monitoring parameters after clamping the internal carotid artery remained within the normal range. Thus, it was

demonstrated that this technique for assessing collateral blood flow did not show the necessary effectiveness for preventing the development of ischemic complications.[111] Thus, summarizing the presented layer of domestic works, none of the methods for measuring the compensatory capabilities of collateral blood flow can predict the development of intraoperative stroke during cross-clamping of the internal carotid artery. The preventive use of a temporary shunt is not safe due to the high risk of embolization and the development of "silent" strokes. At the same time, the installation of a temporary shunt is the only way to maintain homeostasis of cerebral hemodynamics in order to reduce the likelihood of ischemic stroke. We find ourselves in a vicious circle, a safe way out of which does not exist today.

Let us dwell separately on the analysis of world studies. Rocha-Neves JM performed 79 carotid endarterectomies. A temporary shunt was required in 31.6% (n = 25) of cases. There was no intergroup difference in the incidence of stroke ($P = 0.3$) and hemorrhagic transformations ($P = 0.3$).[112] In a study by Sihotsky V et al. carotid endrterectomy was performed in 654 patients. Among them, in 11.4%, a temporary shunt was installed with a decrease in brain oximetry parameters. The stroke + death rate in the group with a temporary bypass was 2.7%, in the group without a temporary bypass it was 2.1% ($P = 0.7$).[113]

Levin SR et al. analyzed the results of 5683 carotid endarterectomies. The patients were divided into 3 groups: the use of a temporary shunt for all; according to indications; deliberate refusal of a temporary shunt. There was no intergroup difference in the incidence of stroke ($P = 0.457$).[114] Piazza M et al. proposed to perform the installation of a temporary shunt "with a dela," only after removal of the atherosclerotic plaque. This approach reduced the risks of distal embolization. In a sample of 1745 patients, stroke developed in 0.4% (n = 6) of cases, transient ischemic attack – 0.2% (n = 4). This method has been recognized as safe and effective.[115] Perini P et al. in their study, 138 patients were divided into 2 groups: group 1 - patients with a history of stroke against the background of an unstable atherosclerotic plaque; Group 2 - a patient with a history of hemodynamic stroke. All patients underwent carotid endrterectomy with a temporary shunt. In group 1, 7.8% (n = 7) of new ischemic strokes were detected, in group 2%-0%. The authors concluded that routine placement of a temporary shunt is safe only in the absence of unstable atherosclerotic plaque and is necessary in patients with a hemodynamic type of stroke.[116] The Cho JW study examined the outcome of carotid endarterectomy under selective temporary shunting (44.4% [n = 20]). The mortality rate was 2.2%, 20% had a transient

ischemic attack. Thus, despite the presence of indications for the installation of a temporary shunt, this procedure is combined with a high probability of adverse postoperative ischemic events.[117]

Analyzing possible options for determining the adequacy of cerebral perfusion after clamping the internal carotid artery, most foreign authors prefer cerebral oximetry.[118] Balaji A found that 41.6% of patients undergoing carotid endarterectomy require a temporary shunt due to a decrease in cerebral oximetry.[119] Lee J et al. proposed to use simultaneously both the measurement of retrograde pressure in the internal carotid artery and cerebral oximetry. In their study, they showed the effectiveness of this approach.[120] The same conclusions were confirmed by Chang JW et al. Nevertheless, among 50 cases of surgery with the installation of a temporary shunt with a decrease in retrograde pressure in the internal carotid artery and cerebral oximetry, 3 patients (6%) had a new ischemic stroke.[121] Tyagi SC et al. studied the results of carotid endarterectomy without the use of a temporary shunt in patients in 2 groups: group 1 - the level of retrograde pressure in the internal carotid artery is below 50% of the systemic one; Group 2 is higher. Most patients with a history of stroke were concentrated in group 1. Among them, a high frequency of postoperative strokes was determined relative to group 2 patients ($P = 0.017$). Thus, the authors proved the preventive role of measurement of retrograde pressure in the internal carotid artery in establishing indications for the use of a temporary shunt.[122]

In search of an ideal approach to assessing the compensatory capabilities of collateral blood flow, Makovec M et al. came to conclusions similar to the study by A.A. Karpenko.[123] The main point was that the measurement of retrograde pressure in the internal carotid artery and cerebral oximetry have a low sensitivity to intraoperative cerebral ischemia. Therefore, the only most reliable option for assessing cerebral tolerance to blood flow insufficiency was the measurement of the concentration of the S100B marker. An increase in the level of this protein in the blood serum by 22.5% after clamping the internal carotid artery correlates with a high risk of intraoperative stroke. However, this method cannot be used routinely, because requires a long period of time to obtain S100B concentration results. Under conditions of clamping of the internal carotid artery, this possibility is very limited.[123] Banga PV et al. presented the results of carotid endarterectomy in patients with an open circle of Willis (n = 492) who did not intentionally use a temporary bypass. In this analysis, the open circle of Willis was an independent predictor of perioperative stroke (OR, 11.12; 95% CI, 3.57-35.87; $P = 0.001$). Thus, it has been demonstrated

that, along with the measurement of retrograde pressure in the internal carotid artery and cerebral oximetry, the consistency of the circle of Willis has an additional value in setting indications for the use of a temporary shunt.[124]

Summarizing the research results, it should be noted that there is no certainty in the routine/selective use of a temporary shunt or deliberate refusal of it today.[125-129] On the one hand, the installation of a temporary shunt is associated with the risk of embolization and ischemic stroke, on the other hand, not using a temporary shunt can lead to cerebral blood flow insufficiency and subsequent adverse events.[130,131] However, according to some authors, the use of a temporary shunt may be justified in the presence of an ipsilateral hemodynamic stroke, as well as in conditions of an open circle of Willis.[126,132] Thus, due to the lack of certainty in current recommendations, those who apply a temporary bypass selectively, those who use a temporary bypass routinely, and those who refuse to use a temporary bypass will be right.[1]

There is also no universal way to determine the adequacy of cerebral hemodynamics after clamping the internal carotid artery. Either they have low sensitivity (measurement of retrograde pressure in the internal carotid artery, cerebral oximetry), or against the background of 100% accuracy, a long period of time is performed (determination of the concentration of the S100B marker).[133,134] Some authors prefer a combination of the 2 methods (measurement of retrograde pressure in the internal carotid artery + cerebral oximetry), but other studies refute the effectiveness of this type of monitoring.[130,131] Thus, no certainty has been achieved in this area either.

The only way out of this situation is to perform carotid endarterectomy strictly according to the recommendations. Returning to the latter, it must be emphasized that a temporary shunt should be used only selectively, and to establish indications for its use, one of the following types of measurement of brain tolerance to ischemia should be used: the level of retrograde pressure in the internal carotid artery, cerebral oximetry. It is this postulate that, although not the highest, has a "Level of Evidence B." Options such as intentional refusal to install a temporary shunt or its routine use do not have any level of evidence, and therefore cannot be considered as strategies of choice. Priority in their favor will indicate a refusal to comply with the main postulates of national recommendations for the management of patients with diseases of the brachiocephalic arteries.

Types, Causes and Methods of Treatment of Strokes That Developed During Carotid Endarterectom

Currently, the mechanisms of rare forms of stroke, which do not exceed one percent, are of the greatest interest. So hemorrhagic stroke can develop due to systemic inflammation or activation of the normal hemostatic pathway. In addition, this mechanism may be more intense among patients who did not stop taking anticoagulants during preparation for surgery. The most common cause of hemorrhagic stroke is the syndrome of "luxury perfusion" of the brain after carotid endarterectomy.[135-137] Anesthesia itself rarely causes this condition, since most anesthetics most often induce hypotension.[138-142] Under these conditions, the state of the cerebrovascular reserve is a key factor, especially when postoperative hypertension persists for several hours.[143-147] In patients with impaired cerebral circulation, compensatory vasodilation already exists in the affected vascular areas, usually located in deeper structures: basal ganglia, thalamus, pons, cerebellum. Thus, the probable development of hyperperfusion syndrome in these areas will be accompanied by a serious neurological deficit and an unfavorable prognosis.

However, a fine line must be observed between hyperperfusion and hypoperfusion of the brain. The mechanism of the latter is reduced either to insufficient drug-induced hypertension during ipsilateral clamping of the carotid arteries, which reduces compensatory blood circulation in the cerebral hemisphere; or hypoperfusion can be induced by damage to the carotid sinus at the stage of isolation of the carotid bifurcation or during the period of eversion endarterectomy. Traumatization of the glomus leads to severe bradycardia and hypotension, in some cases ending in asystole.[142] Two large retrospective patient database studies are known to investigate the relationship between intraoperative blood pressure and postoperative stroke. Bijker et al showed an association between intraoperative hypotension up to 70% of baseline blood pressure and a high risk of stroke.[143] Other authors have demonstrated an association between carotid glomus injury and intraoperative hypotension, as well as postoperative hypertension. Thus, by using glomus-sparing carotid endarterectomy, we avoid trauma to the carotid sinus, which can cause either ischemic stroke during surgery or hemorrhagic stroke in the early postoperative period.[142]

Another important nuance in the development of perioperative stroke is the duration of the previous stroke. It is still not clear how soon after a stroke a carotid endarterectomy should be performed. A number of studies come to the conclusion that carotid endarterectomy is necessary and

safe for patients with occlusive-stenotic lesions of the carotid arteries in the acute period of a stroke, if the ischemic focus does not exceed one and a half centimeters in diameter. In a similar study by Gertler, only 2.7% of patients had deterioration in neurological deficit, in the Leseche study, no adverse outcomes were found.[135-137] So, in 81% of patients, a complete recovery of the neurological status was observed, and 19% had a residual deficit. In a meta-analysis of 47 carotid surgery studies published between 1980 and 2008. Rerkasem did not find any additional risk for carotid endartercatomy in the acute phase of stroke compared with patients without stroke.[136] However, there are data on less favorable results of urgent carotid endarterectomy in neurologically unstable patients. Karkos in his meta-analysis reported 16.9% of cases of perioperative stroke and 20% of deaths in this sample of patients,[135,138] Crescendo demonstrated 6.5% of recurrent strokes and 9% of deaths.[135] Bond and Halm found that carotid endarterectomy performed in the acute period of stroke was superior to carotid endarterectomy 30 days after stroke in terms of the combined stroke + death rate by 11.2%.[135,139] In one of the latest foreign studies, new data were published on the timing of carotid endartercatomy after a stroke.[137] This analysis demonstrated a direct relationship between elective carotid endarterectomy within 6-9 months after stroke and an increased risk of perioperative mortality. The authors included a large number of operations that were performed less than 6 months after stroke, with a subsequent increase in statistical power to determine the effect of the timing of intervention on the development of stroke, which was not demonstrated in previous studies.[138,139] In the end, the authors came to the conclusion that the most optimal time interval between stroke and carotid endarterectomy, associated with the lowest risk of developing the latter, is a period not exceeding 6 months.[137]

Hyperglycemia makes a special contribution to the development of intraoperative stroke. Moreover, this condition is observed not only in patients with diabetes mellitus, but also in patients with a normal glycemic profile, as a reaction to the administration of solutions containing dextrose, catecholamines, and steroids.[130] Cerebral ischemia during clamping of the carotid arteries provokes the release of lactate against the background of anaerobic metabolism, which worsens intracellular acidosis. Hyperglycemia results in greater substrate availability with a consequent increase in lactate production. Acidosis as a consequence inhibits glycolysis and protein synthesis. And hyperglycemia accelerates the release of excitotoxic amino acids (glutamate and aspartate), which are mediators of the cerebral ischemic cascade. Thus, hyperglycemia

enhances the effects of cerebral ischemia and, as a result, increases the risk of early complications.[131]

A significant role in the induction of stroke is assigned to cerebral hypoxia. There are 2 mechanisms for the development of the latter: (1) Intraoperative blood loss causing anemic syndrome; (2) The awakening of the patient after general anesthesia, when, against the background of the cessation of the action of muscle relaxants, there is an incomplete restoration of voluntary breathing, which threatens with a short-term decrease in saturation.[131,132] It must also be remembered that the vast majority of patients undergoing carotid endarterectomy are hypertensive. One of the popular drugs intended for this group of patients are β2-blockers, which also reduce cerebral vasodilation and worsen hypoxic changes in the brain against the background of all of the above factors, which is also demonstrated by a number of works.[131,133,134] Thus, the results of the Mashour study with co-authors forced many to rethink the approach to the use of this group of drugs. In a retrospective study of 57218 patients, the authors found a three-fold (95% CI, 1.4-7.8; $P = 0.003$) uncontrolled increased risk of perioperative stroke in patients treated with metoprolol. Previously, there was a lack of data associated with the risk of perioperative stroke associated with the use of specific β-blockers and their dosage regimens.[144]

Thus, for patients who are assigned an increased risk of developing intraoperative stroke, it is necessary to use various methods of neuromonitoring, such as electroencephalography and determination of somatosensory potential, which can detect the presence of cerebral ischemia.[140,141] However, electroencephalography can provide faster and more sensitive detection of the latter. An addition to the above can be the assessment of regional brain oxygenation (rSO2), where the oxygenation of the brain tissue is measured by means of infrared spectroscopy.[140,141]

It is known that approximately 85%-95% of all strokes occur at least 24 hours after carotid endarterectomy.[144] Given this important time window, continued clinical vigilance along with timely neurological consultation are of paramount importance for the successful diagnosis and treatment of postoperative stroke. Neuroimaging should be conducted in parallel with a multidisciplinary discussion of each individual patient and accompanied by the use of interventional neuroradiology and anesthesiology as needed. Rapid evaluation and diagnosis of stroke should be sought, as hospital-acquired stroke may be associated with more adverse outcomes compared to community-based stroke.[144] Timely and optimal treatment is crucial for this group of patients with a high risk of complications.

Treatment of postoperative stroke remains a source of ongoing discussion. According to the AHA/ASA guidelines, patients who have undergone carotid endarterectomy may be candidates for intravenous fibrinolysis after a thorough risk-benefit analysis of the procedure.[144] This principle suggests that selective intra-arterial thrombolysis can be justified only in a select group of patients with a low risk of systemic bleeding. With regard to blood pressure control in patients after carotid endarterectomy, the AHA/ASA guidelines allow persistent hypertension up to 220/120 mm Hg unless patients are candidates for thrombolytic reperfusion and do not have severe comorbid disease (aortic dissection, acute myocardial infarction, etc.). If there are indications for thrombolysis, the maximum allowed blood pressure values do not exceed 185/110 mm Hg.[144]

Combined Damage to the Carotid Arteries and the Coronary Bed

The first and most important direction is the choice of revascularization strategy in patients with simultaneous atherosclerotic lesions of the internal carotid artery and coronary bed. In a large Russian study, which included more than 300 patients, 4 treatment tactics were analyzed, including staged operations (coronary bypass grafting, carotid endarterectomy in various sequences), simultaneous and hybrid interventions (percutaneous coronary intervention + carotid endarterectomy).[145-149] The authors came to the conclusion that there can be no single universal optimal strategy for revascularization, since patients with multifocal atherosclerosis are completely disparate among themselves. The choice of treatment method should be only personalized.[150-154] And then, under the guidance of Kazantsev A.N., a unique program was developed based on a complex mathematical analysis of the predictors of the development of certain cardiovascular complications after each of the 4 revascularization strategies.[155-159] This development made it possible to determine the probability of formation of postoperative adverse events, creating opportunities for personalized determination of treatment tactics associated with the lowest risk of developing the latter.[160-164]

A separate sub-direction of this study was associated with the development of a hybrid form of revascularization, which had not been performed anywhere else in the world before (simultaneous carotid endrterectomy with percutaneous coronary intervention).[165-169] The authors described in detail the entire scheme of surgical treatment, developed a method for hemostasis and wound drainage after intervention on

the internal carotid artery.[170-174] The patient during hybrid revascularization was subjected to aggressive anticoagulant and antiplatelet therapy, which was accompanied by high wound bleeding, as well as the risk of developing acute hematoma of the intervention area.[172,175,176] The use of local hemostasis, as well as a key factor – double drainage, made it possible to significantly reduce the incidence of all hemorrhagic complications in this cohort of patients, which made this tactic a safe form of treatment.[172,175,176] Its introduction into practice made it possible to abandon traumatic coronary bypass surgery, which not only reduced postoperative mortality, but also significantly reduced the period of rehabilitation of patients.[172,175,176] The study of hospital and long-term results of the hybrid operation proved its high efficiency.

Restenosis of the ICA: Computer Modeling, Genetics

Analyzing hospital and long-term results of carotid endarterectomy, as well as predictors of adverse cardiovascular events, a group of Russian authors came to a number of interesting conclusions.[177-181] In particular, one of the important provisions demonstrated a high incidence of restenosis of the internal carotid artery after the classical technique of surgery with plasty of the reconstruction zone with a patch.[182] Studying histological preparations of a removed substrate narrowing the lumen of an artery, it was found that neointimal hyperplasia, which does not depend on dyslipidemia, diabetes mellitus, smoking, etc., plays a fundamental role in this process.[183]. Later, on the basis of computer modeling of the properties of hemodynamics in the carotid bifurcation, the team of authors led by Kazantsev A.N. proved for the first time in Russia that patch implantation leads to expansion of the carotid bulb.[184-188] This, in turn, causes a turbulent pattern of blood flow, with mural thrombosis and congestion zones, which is a trigger for future changes and restenosis of the internal carotid artery.[184-188] Therefore, classical carotid endarterectomy is an unsafe type of operation.[184–188] Subsequently, long-term outcomes of ipsilateral classical surgery and contralateral eversion surgery were demonstrated in the same patient.[189,190] Thus, there was an equal amount of all biochemical, physical, genetic factors capable of causing restenosis. The study showed that after the classical technique of surgery with plastic reconstruction of the reconstruction zone with a patch, a greater number of verified cases of loss of the vessel lumen was observed, which confirmed the unsafety of this method of revascularization.[189,190]

However, cases of restenosis have also been observed after the eversion intervention technique.[191,192] But they, as a rule, were diagnosed in

a later period of observation (more than 2 years).[191-193] Genetic studies have shown that the DNA contained in an atherosclerotic plaque removed from the carotid artery has strict sequences that occur only when restenosis develops.[194-198] Thus, the direct hereditary nature of this phenomenon was proved.[199-203]

But with the development of medical technologies, carotid angioplasty with stenting has become an alternative to carotid endrterectomy, and in some cases a significant competitor.[204] To date, the results of stenting have been studied, demonstrating a high-rate of complications in the long-term follow-up period associated with stent fracture and restenosis.[204-206] In general, the number of adverse cardiovascular events reached the equivalent values of the classical operation, but was much inferior to the eversion technique.[204] Thus, eversion surgery may be the only safe operation of choice for patients with hemodynamically significant stenoses of the internal carotid arteries.

Ways to Eliminate Restenosis of the Internal Carotid Artery

The development of hemodynamically significant restenosis after carotid endarterectomy and carotid angioplasty with stenting is always accompanied by the risk of ischemic stroke.[207-209] Therefore, the choice of treatment tactics for these patients plays a key role in the prevention of this complication. It is known that restenosis after stenting is successfully eliminated by performing carotid endarterectomy with stent removal.[205,206] The most common cause of restenosis in these conditions was stent fracture or progressive atherosclerotic plaque growth through its cells.[205,206] Therefore, a radical operation made it possible to remove both the foreign body (stent) and the substrate (plaque) with an optimal result of the operation. If we were talking about restenosis after carotid endarterectomy, then the most preferred option for reconstruction was carotid angioplasty with stenting.[207] After all, repeated carotid endrterectomy in these conditions is performed with the release of arteries from scar tissue, which is associated with a risk of bleeding and traumatization of the cranial nerves.[207,210,211] However, in some cases where there are absolute contraindications to stenting (renal failure with high creatinine levels, allergy to contrast agent, etc.), the operation of choice is repeated carotid endarterectomy.[210,211] One of the studies demonstrated a high incidence of hypoglossal neuropathy after repeated carotid endarterectomy, which was accompanied by a decrease in the quality of life of the patient and was not always characterized by regression of symptoms.[210]

Under these conditions, to eliminate this complication, a new eversion carotid endarterectomy with transposition of the internal carotid artery over the hypoglossal nerve was developed.[212,213] Thus, if a patient developed restenosis and there was a need to perform a second carotid endarterectomy, then the nerve was located under the internal carotid artery, which excluded its trauma during arterial exposure.[212,213] Ultimately, the issue of hypoglossal neuropathy was completely eliminated.[212,213]

Optimal Age for Carotid Endarterectomy

Characterizing patients with multifocal atherosclerosis, numerous works have repeatedly mentioned that these patients most often have an aggravated comorbid background and an age exceeding 60 years.[214-216] Through small single-centre studies, teams of authors have demonstrated that age over 75 years does not affect the incidence of postoperative complications.[217-219] Although it is logical that it is in this cohort of patients that the maximum number of cases of multivessel coronary lesions, atrial fibrillation, diabetes mellitus, chronic renal failure, etc. should be concentrated. In August 2021, a breakthrough multicenter (8 medical institutions in St. Petersburg, Krasnodar, Kemerovo) study on this issue was published.[200] For 12 years, the results of 7248 operations on the internal carotid artery were analyzed. Of these, in 712 cases, carotid endarterectomy was performed in patients older than 75 years.[220] Among them, mortality reached 1%, myocardial infarction - 2%, ischemic stroke - 1.7%. Thus, the combined endpoint was 4.6% ($P < 0.0001$).[220] For the first time in Russia, it was proved that carotid endarterectomy in old age is an unsafe method of brain revascularization.[220] In this regard, the authors came to the conclusion that a more justified type of reconstruction in patients over 75 years of age may be stenting, which is not combined with high trauma and the need to clamp the internal carotid artery.[220]

Conclusion

Only indications and contraindications for carotid endarterectomy are known. Most of the questions related to this operation remain unanswered.

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