ANALYSIS OF THE HISTORY OF THE SEARCH FOR METHODS OF PROTECTING THE BRAIN DURING OPERATIONS ON THE INTERNAL CAROTID ARTERY

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Abstract

The review covers the first studies of the vessels of the brain. The history of the emergence and development of the doctrine of protecting the brain during operations on the carotid arteries is given. Experience has been accumulated in the development of the doctrine of surgical protection of the brain during primary operations on the carotid arteries and compression of the carotid arteries. The analysis of existing and existing methods was carried out. Based on the above analysis, ways of further development of methods of protecting the brain during operations on the carotid arteries are shown.

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Ішкі ұйқы артериясына операция жасау кезінде миды қорғау әдістерін іздеу тарихын талдау

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Түйіндеме

Шолуда ми тамырларының алғашқы зерттеулері қамтылған. Каротид артерияларына операция жасау кезінде миды қорғау туралы ілімнің пайда болуы мен даму тарихы келтірілген. Каротид артерияларына алғашқы операциялар жасау және каротид артерияларын қысу кезінде миды хирургиялық қорғау туралы ілімді дамыту тәжірибесі жинақталған. Қолданыстағы және қолданыстағы әдістерге талдау жасалды. Жоғарыда келтірілген талдау негізінде каротид артерияларындағы операциялар кезінде миды қорғау әдістерін одан әрі дамыту жолдары көрсетілген.

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Анализ истории поиска методов защиты головного мозга при операциях на внутренней сонной артерии

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Аннотация

В обзоре освещены первые исследования сосудов головного мозга. Приведена история зарождения и развития учения о защите головного мозга при операциях на сонных артериях. Обобщен опыт первых операций на сонных артериях и развития учения о хирургической защите головного мозга при пережатии сонных артерий. Проведен анализ существовавших и существующих методов. На основании приведенного анализа, намечены пути дальнейшего развития методов защиты головного мозга при операциях на сонных артериях.

Introduction

The relevance of stroke prevention at the moment is beyond doubt. However, if the actual operation on the carotid arteries is quite well developed, then the question remains unresolved of how to protect the brain from ischemia and the subsequent development of stroke in the perioperative period.

Up to 60% of cerebrovascular complications occur during the intraoperative period. Complications of operations on extracranial arteries include ischemic brain damage (32%), distal arterio-arterial embolism, when the common carotid artery is clamped, as well as haemorrhagic hyper perfusion injuries (29%).[1]

Carotid artery surgery is a relatively young discipline. The first successful endarterectomy was performed on August 7, 1953 by *M. De Bakey*, then a 53-year-old man with transient ischemic attacks.[2,3]

However, it is generally accepted that, approximately 1 year later, an operation was performed that became the impetus for the development of carotid surgery, carried out by *Eastcott H., Pickering G., Rob C. on May 19, 1954,* reporting this in the November issue of «The Lancet».[4] In subsequent years, scientists such as *De Bakey M., Crawford E., Cooley D., Morris G.J. and Wylie E.* had a significant influence on the development of surgery for occlusive-stenotic lesions of the carotid arteries.[2,3]

To date, no one doubts that carotid endarterectomy is an effective method for preventing stroke. The dawn of study occurred in the 90s and the beginning of the 21st century.[5,6,7,8]

The first significant description of the carotid arteries was made by the Swiss physician *Johann Jakob Wepfer* in 1658, who noted the hemispheric blood supply to the brain by the carotid arteries and was the first to document the relationship between changes in the arteries and symptoms of cerebral ischemia. Later, *Thomas Willis* expanded the works of *J.J. Wepfer* and other researchers and in 1664 published a work on cerebral anatomy (Cerebri Anatome) with detailed illustrations by *Christopher Wren*, in which he explained the true significance of the vascular anastomoses of the base of the brain.[9]

Key importance in ensuring the safety of surgery on the carotid arteries is given to preoperative assessment of the state of the circle of Willis and monitoring of cerebral circulation during clamping of the internal carotid artery (ICA). This research was based on the classic works of *Matas R.*, who published his results in 1911. The purpose of the study is to manually clamp the contralateral carotid artery.[10]

An important role is played by angiography, which provides information about the angioarchitecture of the circle of Willis, topical localization, the degree of damage to the brachiocephalic arteries (BCA) and the pathways of collateral circulation of the brain (CBF).[11,12] This can be achieved using various modifications of ultrasound examination, which make it possible to develop new diagnostic criteria for ICA stenosis.[11,12]

Multislice computed tomographic angiography (MSCT AG) is a highly informative method for studying the angioarchitecture of the carotid arteries. Using this method, it is possible to obtain an image of the vessels supplying the brain from the aortic arch along its entire length, to assess the degree of stenosis of the carotid arteries, and to identify lesions of intracranial vessels.[13,14]

When using perfusion computed tomography (PCT) in the preoperative period, it is possible to assess the state of cerebral blood flow and possible risk factors for the development of complications after surgery. The disadvantages of PCT include the need to administer a contrast agent and radiation exposure.[15,16,17,18]

Another method is magnetic resonance angiography (MRA) without the administration of a contrast agent, which can detect narrowing of the lumen of the carotid arteries in both intra- and extracranial sections with sensitivity and specificity of about 93% and 88%, respectively.[17,19,20,21]

There is no consensus on whether it is possible to predict the development of hyper perfusion syndrome in the postoperative period using available technologies for studying changes in cerebral blood flow (ultrasound, CT perfusion, MR perfusion).[13,21]

Rheoencephalography (REG), although the method is considered outdated, has also not lost its clinical significance.[22] An achievement of modern medicine is the assessment of CBF by radioisotope methods, which make it possible to quantitatively and qualitatively characterize regional blood circulation.[23]

Protection of the brain during arrest of blood flow through the internal carotid artery remains extremely important, regardless of the state of the arterial circle at the base of the brain. A situation that arises when it is necessary to operate on pathological tortuosity.

Historically, three directions have developed.

Craniohypothermia

Mechanisms that protect the brain during ischemia are few. *Duffy T.E et.al.* in 1972 obtained evidence that with a lack of oxygen, the oxidative metabolism of the brain is immediately inhibited, which leads to a kind of hypoxic anaesthesia (cited by *Plum F., Posner J.B.).*[24] Subsequently, 3 mechanisms of tissue protection from the damaging effects of lactate were described.[25]. The presence of lactate dehydrogenase isoenzymes has been shown to control tissue lactate levels, leaching lactate into the bloodstream followed by buffering and preparation for metabolic use of lactate. About the possibility of using lactate by the brain, which increases in the blood in small quantities during hypoxia? Lactate takes part in the synthesis of glycogen, as shown by the results of a study in 1964 (cited from *Labori G. 1974*).[26] The ability to biosynthesize glucose (gluconeogenesis) from intermediate metabolites (pyruvate, lactate, amino acids, etc.) has been shown by a number of researchers.[27]

The cause of acute ischemia is a lack of cerebral blood flow. There are several degrees of critical levels of response of brain tissue to this ischemia. Cerebral ischemia is characterized by a decrease in cerebral blood flow to 70-80% of the normal value. At the first level of decrease it is i.e., less than 50-55 ml/100 g of brain tissue/min.[28] At the second level, a decrease in perfusion to 10-15 ml/100 g of brain tissue/min and below leads to rapid and severe cell damage with the formation of an ischemic nucleus, activation of anaerobic glycolysis, increased extraction of lactate from the blood, development of lactic acidosis up to the development of toxic cerebral oedema.[28,29,30,31,32,33,34,35,36]

The third level is the most studied, with destabilization of cell membranes, disruption of ion transport channels, and release of excessively excitatory neurotransmitters.[37]

Along the periphery of the ischemic core, neuronal damage develops much more slowly, due to the supporting system of collaterals, which allows maintaining the level of perfusion above the threshold leading to cell death. This zone contains viable cells with partially preserved integrity of cellular structures, but with reduced functional activity, which makes them maximally vulnerable to pathogenic processes that disrupt their metabolic balance.[35] The cells most sensitive to ischemia are neurons, and to a lesser extent are oligodendrocytes, astrocytes and vascular endothelium.[36,37]

V. Fitch, considering the trigger point of ischemic damage to brain cells as an imbalance between provision and need, makes a simple conclusion about the possibility of influencing this ratio, increasing provision and reducing needs.[38] To improve the supply of the brain, artificial hypertension and hypervolemic hemodilution are proposed, and to reduce the need, artificial hypothermia and pharmacological reduction of the functional activity of the brain are proposed.

Metabolic inhibition in combination with increased oxygen delivery is the basis for the prevention of ischemia. Back in 1969, researchers noticed that an increase in systemic blood pressure (BP) with the normal structure of the circle of *Willis* leads to an increase in cerebral blood flow (CBF) and cerebral perfusion, which is described by the formula CBF = CPP / CVR, where CBF is volumetric blood flow, CPP - cerebral perfusion pressure, CVR-cerebral vascular resistance and, accordingly, improved cerebral oxygenation.[39] The method of artificial hypertension based on these observations has found its place in surgery of the brachycephalic arteries, but its effectiveness is quite questionable, since anatomical studies have shown that a symmetrical and closed circle of *Willis* occurs in only 28% of people. In addition, arterial hypertension as an adaptive reaction of the body in patients with cerebrovascular insufficiency occurs only in 20-30% of cases,[40] due to the lack of a linear relationship between the level of systemic blood pressure (SBP) and CBF due to the phenomenon of autoregulation. By studying the dependence of cerebral oxygenation on cerebral perfusion pressure (CPP), a two-phase nature was revealed. When CPP<70mmHg the relationship between it and oxygen saturation in the jugular vein bulb is linear. This implies the advisability of maintaining cerebral blood flow above the threshold level by stabilizing SBP. For this purpose, in 1997 *Dirden N.M.* recommended inotropic support with norepinephrine and phenylephrine, due to the ability of these drugs to increase SBP without adverse effects on intracranial pressure (ICP).[41]

Intraoperative protection of the brain during temporary occlusion of the internal carotid artery remains a serious aesthetic problem, the solution of which largely determines the success of the operation. The Novosibirsk Research Institute of Circulatory Pathology has accumulated extensive experience in the use of hypothermia in cardiac surgery; it has been proven that moderate hypothermia creates a significantly more favourable effect, since it does not carry side effects associated with hypothermia itself.[41,42]

The decrease in oxygen consumption by brain tissue at 32°C, according to various authors, is 45+5%.[43] Studying the effect of temperature on CBF during artificial circulation, by collecting blood from the radial artery and the bulb of the internal jugular vein (IJV) we came to concluded that a decrease in temperature from 37 to 27°C led to a 64% decrease in brain O2 consumption. The reduction in oxygen consumption rate (CMR) with a decrease in temperature from 37 to 27°C ranges from 50 to 80%.[44] Along with a decrease in oxygen consumption in the brain, there is a decrease in CBF by 5–7% upon cooling by 1°C.[45]

According to modern concepts, hypothermia also increases the latent period of anoxic depolarization, which reduces both the release and excitotoxic effect of excitatory neurotransmitters (glutamate, aspartate, and glycine).[46,47,48]

Experimental evidence suggests that hypothermia may be the most potent technique for providing cerebral protection,[49] but hypothermia administered after ischemia only delays neuronal death.

In summary, it can be stated that the attempt to protect the brain with local hypothermia (covering the head with ice during surgery), which appeared in the 80s of the last centuries, did not become widespread. In 2004, a dissertation for the academic degree of Candidate of Medical Sciences was defended in Novosibirsk. The author points out in the conclusions that craniocerebral cooling reaching a temperature in the nasopharynx of 33-34°C in patients with unilateral and bilateral hemodynamically significant atherosclerotic lesions of the carotid arteries under conditions of multicomponent general anaesthesia makes it possible to safely perform long-term (up to 60 minutes or more) surgical reconstruction of the internal carotid arteries. However, the same conclusions indicate that surgical intervention on the carotid arteries under anaesthetic conditions, including the use of a halogen-containing anaesthetic, like phthorothane up to 1 vol%, sodium thiopental 4-5 mg/kg, ataralgesia and craniocerebral hypothermia is characterized by reliable anti-ischemic protection of the brain during the period of temporary occlusion internal carotid artery. However, phthorothan and sodium thiopental "protect" the brain from ischemic damage, as many researchers point out,[50,51,52] so it is apparently premature to talk about the correctness of the conclusions made in the dissertation work. In 2005, the results were published in a dissertation also for the degree of candidate of medical sciences, the author makes ambiguous conclusions: "The consequence of craniocerebral hypothermia using the external cooling method is tension and ineffectiveness of compensatory mechanisms in the early post-hypothermic period". Although the research work is devoted to the protection of the brain during operations with artificial circulation, this does not change the essence of the conclusions.

It should be noted that now, in carotid artery surgery, the method is practically not used.

To date, two main directions have emerged in protecting the brain during clamping of the ICA: 1. Surgical (placement of a temporary shunt) and 2. Pharmacological protection. If the first one remained practically unchanged, only the indications for installing a temporary shunt were clarified, then the second one is constantly developing and expanding.

Surgical part

Temporary cessation of blood flow through the carotid artery during carotid endarterectomy (CEA) can be prevented by using a temporary shunt. Two studies, including 590 patients, compared the results of CEA with routine bypass and without bypass. Another study of 131 patients compared the results of CEA using a combination of EEG to monitor and measure carotid retrograde pressure with isolated retrograde pressure measurement to determine the need for a temporary shunt.[53,54] There was no statistically significant difference in the incidence of all strokes, ipsilateral strokes, or deaths within 30 days after surgery between patients who routinely used a temporary shunt and those who did not, although the study data were limited. There was also no significant difference in the risk of ipsilateral stroke in patients selected for shunting using EEG combined with retrograde pressure measurements compared with those in the group in which the indication for a temporary shunt was determined using retrograde pressure measurements alone, although the data were also limited.[55] There was no statistically significant difference in the incidence of all strokes, ipsilateral strokes, or deaths within 30 days after surgery in the group of patients with routine use of a temporary shunt and the group with complete refusal to use it.[56] In 2009, the results of studies conducted from 2005 to 2007 were published, the authors concluded that the routine use of an internal shunt is preferable, arguing that cerebral ischemia can also be caused by stenosis of the contralateral carotid artery.[57] In the large ECST study, which included 1729 patients, there was no statistically significant difference in the risk of intraoperative complications associated with the use of a temporary shunt, the use of expansion patches, intraoperative EEG monitoring, or the type of anaesthesia.[58]

Currently, many researchers are evaluating the capabilities of transcranial oximetry in assessing cerebral oxygenation.[59,60,61,62,63]

A decrease in haemoglobin oxygen saturation due to an increase in oxygen extraction from flowing blood is one of the first signs of developing tissue hypoxia and ischemia. Using transcranial oximetry during reconstructive operations on the carotid arteries, we came to the conclusion that this method makes it possible to assess in real time the degree of cerebral ischemia both during test clamping and during the main stage, to make a timely decision on additional methods of protecting the brain, and after completion of the reconstructive stage of the operation, immediately evaluate the effectiveness of revascularization.[60,61,62]

The discussion ended with the Russian Clinical Guidelines, which formulated the following recommendation: Selective use of a temporary shunt. is preferable. To intraoperatively determine the indications for the use of a temporary shunt, one of the following methods should be used: – measurement of retrograde pressure in the ICA, – measurement of blood flow velocity in the middle cerebral artery (MCA) using TCDG monitoring, cerebral oximetry (level of evidence B).[64]

Anaesthesia

Since the mid-1950s, CEA has traditionally been performed under general anaesthesia. Subsequently, since the 1970s, regional anaesthesia (RA) was developed and introduced to provide anaesthetic management for patients at high surgical risk, which became a real alternative for general anaesthesia. Currently, the main directions in the choice of anaesthesia during operations on the carotid arteries are general anaesthesia, regional anaesthesia, as well as combined anaesthesia (CA), which is a combination of them.[65,66,67,68,69]

Research has still not given a clear answer to the question - which of the above methods has undeniable advantages.[70,71,72,73,74] Studies and scientific articles indicate both the advantages and disadvantages of each method of pain relief for CEA.[66,71,75,76]

Regional or general anaesthesia CEA reduces the risk of stroke in people with symptoms of a recent stroke and significant carotid stenosis. However, there is a significant perioperative risk that can be reduced by performing the procedure under local (preferred) or general anaesthesia. The Cochrane review included 6 randomized studies totalling 554 operations, as well as a non-randomized study with 25.662 operations,[77,78,79,80,81] totalling 554 operations and 41 non-randomized studies with 25.662 operations.[82] The methodological quality of non-randomized studies is controversial. Eleven of these studies were prospective, 29 were performed in consecutive series of patients. In nine non-randomized studies, the number of arteries compared to patients was imprecise. A meta-analysis of non-randomized studies found that the use of local anaesthesia was associated with significant reductions in death (35 studies), stroke (31), stroke or death (26), myocardial infarction (22), and pulmonary complications (7 studies) within 30 days of surgery. A meta-analysis of randomized trials found that the use of local anaesthesia is associated with a significant reduction in bleeding within 30 days after surgery, but there is no evidence of a reduction in intraoperative stroke. However, the volume of studies was small to draw a clear conclusion, and in some studies, the results of the analysis obviously supported the chosen treatment method, therefore, they are not suitable for analysis. The GALA (General Anaesthesia vs Local Anaesthesia) study is the largest randomized surgical and anaesthesiology trial, including 3526 patients treated at 95 centres in 24 countries.[83] This double-arm, parallel-group, multicentre randomized controlled trial was designed to determine whether type of anaesthesia affects perioperative all-cause and stroke mortality, short-term quality of life, and stroke-free and heart attack-free outcomes at one year of follow-up.[84]

In 2023, the European Community summarized the results of a comparison between RA and GA,[85] noting that there is still controversy regarding whether CEA should be performed under regional anaesthesia (RA) or general anaesthesia (GA). The General Anaesthesia vs Local Anaesthesia study (n = 3.526) was the largest randomized controlled trial (RCT). There was no difference in the perioperative incidence of death, stroke or myocardial infarction between the GA (4.8%) and RA (4.5%) groups.[83] However, pooled data from five RCTs showed a reduction in the 30-day incidence of stroke/death when performing CEA under RA,[85] while NIBL (New ischemic brain lesion) occurred more often in the GA group (17.1% compared with 6. 7%).[86]

According to the National Surgical Quality Improvement Initiative of the American College of Surgeons, RA is associated with shorter operative and hospital stays, fewer readmissions, fewer cases of postoperative pneumonia, and fewer blood transfusions.[87,88] However, RA was associated with lower patient satisfaction (65% versus 93%) and was less likely to be considered for future treatment (61% versus 97%).[88] In a large meta-analysis (25 observational studies, six RCTs [n = 152.376]), RA was associated with statistically significantly shorter operative time, lower perioperative rates of stroke, cardiac complications, and lower mortality.[89] However, the RCT did not find statistically significant differences in any endpoint.[89] Some authors believe that RCTs have lack of sufficient statistical power.[90]

In a systematic review of 69 studies (n = 10.081), combined deep + superficial cervical plexus block was associated with a statistically significantly higher complication rate.[91]

The ESVS recommendations regarding the management of RA versus GA are the same as those in the SVS guideline and the German-Austrian guideline, stated as follows: The decision regarding the choice of anaesthesia (regional or general) in patients undergoing carotid endarterectomy should be made at the discretion of the surgeon/anaesthesiologist, performing the procedure, taking into account local experience, patient preferences and preferred antiplatelet therapy strategy.[92,93]

Pharmacological protection of the brain in CEA

One of the first works devoted to pharmacological protection of the brain, apparently, is the work of *J. R. Kenyon, A. B. Thomas, D. P. Goodwin,* published in 1972.[94] In a consecutive series of thirty-four total operations in thirty-one patients hospitalized with stenotic lesions of the internal carotid artery, heparin (3 mg per kg body weight), administered systemically and regionally, was the only method of cerebral protection for arterial insufficiency. The arrest of blood flow by carotid artery (CA) varied from 7 to 30.5 minutes (average 15.3 minutes). Ten patients (32%) had more than one lesion. There were no deaths or immediate neurological consequences. Two patients experienced transient ischemic attacks 2 and 5 days after surgery, but they resolved completely within 24 hours and were attributed to technical reasons.

According to most authors, the use of local anaesthetics allows for adequate analgesia in carotid surgery: pain relief is provided either by tissue infiltration or by blocking the cervical plexus along with infusion of small doses of fentanyl or droperidol to achieve sedation.[95,96,97,98,99] The main argument of supporters of regional anaesthesia during CE is the possibility of direct assessment of the functional state of the central nervous system and timely diagnosis of brain ischemia. When the first signs of neurological deficit appear, the generally accepted method of preventing irreversible hypoxia of the brain remains the use of a shunt.[100,101] The relative simplicity and low cost of local anaesthesia and the ability to selectively use an internal shunt are the indisputable advantages of this method of pain relief in carotid surgery.

General anaesthesia (GA) increases the brain's tolerance to hypoxia, reducing its oxygen demand.[102,103] Under anaesthesia, it becomes possible to use techniques that potentiate its antihypoxic effect during the period of carotid reconstruction. For this purpose, phthorothane inhalation, artificial hypertension, infusion of antihypoxants, hyperoxygenation and their combinations are used.

Much work has been devoted to the study of hypercapnia as a method of protecting the brain, but it has been found that adding 2-5% carbon dioxide to an inhaled drug mixture or performing temporary hypoventilation can cause intracerebral steal.[104]

The ability of barbiturates to inhibit the metabolic processes of the brain, in particular, oxygen consumption, is used in carotid surgery: thiopental infusion is carried out immediately before the occlusion stage or during the entire operation; however, the depressive effect of barbituric anaesthesia on haemodynamic makes it necessary to use this method of protecting the brain with caution.

Currently, the main directions in the choice of anaesthesia during operations on the carotid arteries are general anaesthesia, regional anaesthesia, as well as combined anaesthesia (CA), which is a combination of them.[105]

In clinical practice, depending on the specific clinical situation, preferences and capabilities of the medical institution, the choice of anaesthesia is usually determined collectively by a group of specialists (anaesthesiologist, surgeon, neurologist, cardiologist) and agreed with the patient.[106,107]

The share of RA in the overall structure of pain management during CEA ranges from 6 to 74%, in some clinics reaching 99% - such a wide range is largely explained by the preferences of clinics and their technical equipment.[108-110]

The studies carried out still have not given a clear answer to the question - which of the above methods has undeniable advantages.[70-74,111]

The main advantages of GA are immobility of the patient, decreased metabolism of brain cells and its protection during ischemia, adequate control of airway patency, external respiratory function and carbon dioxide concentration, reduced reaction to operational stress.[74,76,112,113] The main disadvantage of GA is the inability to control the patient's neurological status during surgery, which explains the later (only after the end of anaesthesia) detection of neurological deficits and complications.[73] Other disadvantages of GA include hemodynamic instability (intraoperative hypotension or sharp fluctuations in blood pressure; postoperative hypertension), and a higher frequency of use of a temporary intraluminal shunt.[76]

RA does not have many of the problems associated with general anaesthesia.[114,115]

The main advantage of RA is the possibility of constant monitoring of the patient's neurological status throughout the operation and in the early postoperative period, clinical assessment of his cognitive, verbal and motor functions, i.e. so-called dynamic neurological monitoring.[116] In 2016, Lee J. et al. published their experience, operating under RA, 5 minutes before clamping the ICA, the so-called "awake test" was performed, including assessment of the patient's speech, squeezing a rubber ball with the contralateral hand and movement of the big toe of the contralateral foot; the test was repeated immediately after clamping the ICA and then at intervals of 5 minutes throughout the entire cross-clamping period.[117] Dynamic neuromonitoring makes it possible to assess the preservation of higher cortical functions and the adequacy of collateral blood flow during clamping of the ICA, and in the event of the appearance of neurological symptoms, it provides rapid detection of cerebral ischemia.[64,116]

Another important advantage of RA, according to some authors, is the reduction in the frequency of using a temporary internal shunt (TIS), the use of which can be accompanied by cerebral ischemia in approximately 5% of cases. The main causes of ischemic complications are damage to the intimal ICA by the shunt, dissection of the ICA, embolism with fragments of atherosclerotic plaque, thromboembolism, air embolism, shunt occlusion, and the use of a TIS itself can act as a cause of ICA thrombosis in the early postoperative period and lead to late arterial restenosis.[73,118]

AbuRahma A. F. et al., summarizing and analyzing the literature in PubMed and Medline until 2010, calculated that the routine use of TIS during CEA is accompanied by a lower incidence of perioperative stroke (1.4%) than when not using it during surgery (2%).[64,119] *Bellosta R. et al.* (2006) during operations on the ICA using an internal shunt in 99.4% of cases noted a complication rate of less than 2%.[120] *Lobo M. et al.* found that the internal shunt was used significantly less frequently in the group of patients with RA (n=540, TIS in 3%, $p<0.05$) compared to the cohort of patients operated on for GA (n=197, TIS in 14%).[109] The frequency of use of TIS during operations under RA is much lower and ranges from 2.4 to 13%.[119,121-123] Other authors, during operations under GA, recommend installing TIS when the retrograde mean pressure in the ICA is below 40 mmHg.[124]

During operations under RA, the main indication for shunt installation is the appearance of clinical signs of cerebral ischemia.[116,125] However, patients who develop negative neurological symptoms requiring TIS placement have an increased risk of perioperative stroke and death.[124]

Among the disadvantages of RA, a number of authors point out: lack of brain protection during ICA clamping, lack of reliable control over airway patency, external respiratory function and carbon dioxide concentration, the possibility of developing perioperative arterial hypertension, a higher level of operational stress, as well as the forced position of the patient during surgery.[76,112]

Indications for RA are: the presence of an embologenic plaque in the operated ICA, the absence of an ultrasound window for performing Transcranial Doppler Ultrasound, severe damage to the coronary bed, severe stenosis of the aortic and mitral valves, low left ventricular ejection fraction, cardiac rhythm and conduction disturbances, diseases of the respiratory system, patient refusal of general anaesthesia.[126] In addition, according to *Kavakli A. S. et al*, they believe that RA is most indicated in patients with critical contralateral ICA stenosis, when it is especially important to assess the need to install an internal shunt. In 2016, the results of a study were published in which the degree of contralateral ICA stenosis in patients operated under RA and intolerant to ICA clamping, the average degree of artery stenosis was 57.5%. Among patients tolerant to ICA clamping, the degree of contralateral stenosis was on average 27.8%.[107,121]

Contraindications to RA during operations on the carotid arteries are impossibility of verbal contact with the patient, patient inadequacy, contralateral paresis of the phrenic or recurrent nerve, blood coagulation disorders, and patient refusal of RA.[127] *Lee J. et al.* indicate that a high location of carotid artery stenosis (level of the second cervical vertebra) is also a contraindication to RA.[117,118]

According to *Brown D.L.* (2009), bilateral cervical plexus blocks should be avoided, as there is a risk of blocking both phrenic nerves.[59]

It is now generally accepted that in clinical practice it is optimal to use multimodal neuromonitoring (for example, TDU (Transcranial Doppler Ultrasound) + CO (cerebral oximetry) + EEG), which reduces the disadvantages of each method.[125,128] *Kolkert J. L. P. et al.* in 2017 noted that the addition of neuromonitoring modalities increases the cost of anaesthesia and, therefore, average hospital costs. In the isolated group, measurements of retrograde pressure in the ICA and in the TDU + EEG group increased almost 2 times.[124,126]

There are conflicting opinions regarding the need for drug sedation of patients during CEA under RA. According to *Lawrence P. F.,* drug sedation should not be used or used minimally when the patient is restless and agitated, since there is a need for constant monitoring of the patient's neurological status during surgery under RA.[115]

Currently, modern medicine has a limited range of drugs that in clinical practice can prevent ischemic and reperfusion complications. When choosing drugs for neuroprotection, it would be desirable to use mechanisms that not only reduce the intensity of metabolic processes in the brain, but also correct cellular neuronal hypoxia.[129]

Conclusion

Craniocerebral hypothermia, despite its long-term study, is currently not widely used. Indications for the use of an internal shunt have been worked out. Provisions on the choice of anaesthesia have been formulated. The effect of various drugs in cerebral ischemia has been studied. Obviously, there remains a huge direction in the surgery of the carotid arteries, namely pathological tortuosity, in which the use of an internal shunt is not possible, which determines the development of pharmacological protection of the brain.

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