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Prikaz slučaja | Case report

The incidence of prolonged stay in ICU due to the development of reperfusion syndrome after carotid endarterectomy – five year analisis from University Clinical Center of Banjaluka

Učestalost produženog boravka u ICU zbog razvoja reperfuzijskog sindroma nakon karotidne endarterektomije – petogodišnji presjek iz UKC Banjaluka

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Descriptors
KAROTID ENDARTERECTOMY;
HEMODYNAMIC INSTABILITY;
CEREBRAL REPERFUSION SYNDROME

SUMMARY. Carotid endarterectomy (CEA) ist the most most frequently performed vascular surgical procedure, and belongs to the type of preventive interventions. Reperfusion syndrome is relatively rare complications of this procedure, but with clinically significant and potentially fatal consequences that can seriously compromise the outcome of treatment after CEA. The focus of this study is on frecuency of development of RS, the factors that favor its occurrence, causes of hemodinamc instability, the modalities of early diagnosis, as well as the possibilities of preventing this complication. The research covered the period from 2018 to 2022 during wich 963 CEA were performed.

Deskriptori
KAROTIDNA ENDARTEREKTOMIJA;
HEMODINAMSKA NESTABILNOST;
CEREBRALNI REPERFUZIJSKI SINDROM

SAŽETAK. Karotidna endarterektomija (CAE) je najčešće izvođeni operativni zahvat vaskularne kirurgije. Spada u niz preventivnih postupaka. Reperfuzijski sindrom je relativno rijetka komplikacija ovog operativnog zahvata, ali s klinički značajnim i potencijalno opasnim posljedicama koje mogu ozbiljno ugroziti ishod liječenja nakon CEA. Fokus ovog rada je na učestalosti razvoja cerebralnog reperfuzijskog sindroma (CRS), čimbenicima koji pogoduju njegovoj pojavi, uzrocima hemodinamske nestabilnosti perioperativno, te modalitetima rane dijagnoze i terapijskog pristupa, kao i mogućnostima prevencije razvoja ove komplikaciju. Istraživanje je obuhvatilo petogodišnje razdoblje (2018–2022) KB Banjaluka u kojem su urađene 963 karotidne endarterektomije.

Introduction

Cerebral reperfusion syndrome (CRS)

Cerebral reperfusion syndrome (CRS) is a relatively rare but potentially life-threatening complication after carotid endarterectomy or carotid stenting. It is defined as focal brain damage that occurred after a revascularization procedure, most often as a result of hyperperfusion. The criteria for diagnosis are as follows:

- Occurrence within 30 days of the operation
- Clinical manifestations such as headache, partial epileptic seizures, motor deficit, disturbance of consciousness (GCS<15) and radiological confirmation (brain edema, hemorrhage)
- Confirmation of hyperperfusion (> 100% of preoperative values) by TCD, SPECT, MRP or systolic pressure values higher than 180 mmHg
- The development of cerebral ischemia, as well as a pharmacological or metabolic cause, is excluded

Data on the frequency of the development of hyperperfusion after CEA in the literature ranges from 0.2 – 19%, while the frequency of CRS is less frequent (1.9% with the development of intracerebral hemorrhage of 0.4%)[1].

Early recognition of the development of CRS is important because it can be successfully treated and stopped at the initial stage. The development of brain edema associated with CRS can be reversible, while the occurrence of intracerebral hemorrhage can have serious consequences for the patient with a mortality rate of over 50%.

Risk factors (Table 1)

Cerebral hyperperfusion syndrome and intracerebral hemorrhage are more common after perioperative hypertension, although they can also occur in normotensive patients after CEA. The clinical picture is similar to hypertensive encephalopathy, and the

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Table 1. The risk factors for development of CRS

Recent ipsilateral stroke
Severe ipsilateral or contralateral carotid disease
Significantly increased cerebral perfusion (*MCA flow velocity or pulsatility*) after establishment of normal flow
Severe postoperative hypertension

mortality rate after hemorrhage can be as high as 67%[2]. The key factor is the loss of local autoregulation, which leads to vasogenic edema of a given hemisphere of the brain, thus essentially a mechanism of ischemia-reperfusion damage to the brain. Edema is reversible and can be treated with medication and strict blood pressure control.

Pathophysiology of the origin of CRS

Autoregulation disorder

Autoregulation of cerebral circulation represents the ability of the brain to maintain a relatively constant blood flow despite changes in perfusion pressure[3]. Autoregulation of circulation is present in many regions of the body and organs, but is particularly developed in the brain due to its need for constant blood flow and water balance. In normotensive adults, cerebral blood flow is maintained at approximately 50 mL/100 g brain tissue per minute, maintaining cerebral perfusion pressure in the range of 60 to 160 mmHg. Below and above these limits, autoregulation is lost and cerebral flow becomes linearly dependent on mean arterial pressure[4]. When cerebral perfusion pressure falls below the lower limit of autoregulation, cerebral ischemia develops. The reduction in flow is compensated by an increase in the extraction of oxygen from the blood[5]. Clinical signs of ischemia are not seen until the drop in perfusion "overcomes" the possibility of increased extraction of oxygen in order to maintain the metabolic needs of the tissue. Reduction of cerebral flow stimulates the release of vasoactive substances from the brain tissue that lead to vasodilation. Possible candidates with a vasoactive role are H+, K+, O2, adenosine and others. Autoregulation of cerebral flow at the upper limits is dependent on arterial smooth muscle constriction in response to elevated perfusion pressure. The importance of autoregulation of cerebral circulation is emphasized by the fact that serious damage to brain tissue occurs when it is lost. For example, in episodes of acute hypertension, when the upper limit of myogenic autoregulation is exceeded, the smooth musculature of brain blood vessels is overcome by high blood pressure, and dilation of blood vessels occurs with the potential danger of blood spilling into the tissue. At the same time, reduced cerebrovascular resistance with increased hydrostatic pressure favors the development of brain edema[6].

Chronic hypertension, microangiopathy and damage to the blood-brain barrier

Chronic hypertension may play an important role in the development of RS after CEA. Long-term untreated hypertension leads to damage to the endothelium of blood vessels, the appearance of microangiopathy and the breakdown of the blood-brain barrier. Studies on animal models offer evidence of extravasation of serum albumin, and activation of the TGFβ signaling pathway, which can initiate the formation of brain parenchyma edema, and "seizure-like" activity of neurons even without the presence of edema. Breakdown of the blood-brain barrier also leads to the extravasation of toxins and free radicals into the brain parenchyma[7].

Baroreceptor dysfunction

Arterial baroreflex is a reflex activity that affects changes in arterial pressure through sympathetic and parasympathetic activity of the cardiovascular system and is detected by baroreceptor bodies located in the carotid sinus and aortic arch. It is responsible for the rapid modulation of arterial pressure, and is damaged in many pathological conditions, such as chronic hypertension, generalized atherosclerosis, diabetes mellitus, cerebrovascular diseases, that is, most of the diseases that accompany patients undergoing endarterectomy. Sudden changes in arterial pressure due to CEA are explained by different theories, such as surgical manipulation, renin angiotensin system alterations, changes in vasopressin concentration or central activity of catecholamines[8]. Certainly, they all contribute a lot to hemodynamic instability, but with one common denominator, the existence of carotid atheroma[9]. Its existence significantly affects cerebral perfusion and cerebrovascular reactivity even in asymptomatic patients. Surgical removal of the plaque leads to additional dysfunction of the already impaired baroreflex activity, and to the appearance of hypertension and hemodynamic instability. This condition can last from a few hours to a few days or weeks. An important fact in baroreceptor dysfunction is the condition of the contralateral circulation, that is, the existence of an atheroma of the opposite side of the carotid artery. Bilateral baroreceptor dysfunction and reduced baroreceptor reserve are usually associated with more pronounced symptoms of hemodynamic instability[10]. In addition to the listed factors, several other factors significantly affect baroreflex activity, primarily chronic hypertension and antihypertensive therapy, age, smoking, diabetes, etc.[11,12].

Effects of cross clamping and shunting on arterial pressure

Clamping of the carotid vessels leads to the expected drop in perfusion often accompanied by a compensa-

tory rise in blood pressure and increased sympathetic activity. The extent of these changes depends on many factors such as the length of clamping, the degree of stenosis and condition of the opposite side, anesthetic and surgical factors, existing comorbidities, etc.

Surgical and anesthetic factors

The eversion technique is accompanied by more frequent postoperative hypertension and more frequent use of vasodilators, and less frequent use of vasoconstrictors postoperatively, compared to the standard technique of longitudinal endarterectomy[13]. The most likely cause is transection or local infiltration of the carotid sinus during eversion endarterectomy, accompanied by more pronounced hemodynamic instability, and the routine use of which no longer recommends[14]. General anesthesia owed its popularity for many years mainly to better conditions for the surgeon and better protection of the brain. In recent years, the popularity of loco-regional anesthesia is increasing again, primarily due to superior neurological monitoring (awake patient) and "cost benefit". Many systematic reviews of the literature have shown no statistically significant differences in outcome in numerous randomized controlled trials comparing OETA and loco-regional anesthesia. The most famous and extensive "GALA Trial" (General anesthesia vs local anesthesia), of over 3,500 subjects from 90 centers, conducted from 2001 to 2007 in Europe, did not show significant differences in one-year survival and the frequency of complications with regard to the type of anesthesia[15].

Preoperative blood pressure control

Blood pressure control in patients undergoing endarterectomy can be complicated for a number of reasons. Postponing surgery until optimal pressure values are reached and the resulting benefits can be canceled out by the numerous risks of postponing surgery. Autoregulation of cerebral flow can be seriously compromised and cerebral flow critically dependent on collateral circulation, especially in chronic hypertensive patients and recent cerebrovascular incidents. The optimal blood pressure target values for such patients have not been established, and the best treatment for such patients may be significantly different compared to other hypertensive patients[16]. Aggressive antihypertensive therapy preoperatively can lead to hypotensive episodes during surgery and potential ischemic episodes[17], and such therapy should be avoided. For people with isolated systolic hypertension, in the absence of clear guidelines and guidelines, it would seem reasonable to maintain systolic pressure (SAP) < 180 mmHg and diastolic pressure (DAP) < 100 mmHg. Blockers of alpha and beta receptors may have a theoretical advantage, and their use also shows a reduction in the incidence of perioperative hypoperfusion[18,19]. The use of blockers of the renin-angiotensin system is more often associated with perioperative hypotension[19]. The generally accepted position of many anesthesiologists and vascular surgeons is to maintain systolic pressure up to 160 mmHg with the continuation of antihypertensive therapy until the day scheduled for surgery, without interruption except in the case of ACE (angiotensin-converting enzyme inhibitor eznima) inhibitors, and the continuation of therapy postoperatively as soon as possible. In any case, the emphasis is on individual optimization of therapy in order to avoid hypotensive episodes in the perioperative period.

Intraoperative blood pressure control

The traditional attitude is intraoperative maintenance of arterial pressure up to 20% higher than initial values. However, these values should be individually adjusted, with monitoring of cerebral circulation, both in patients under general endotracheal anesthesia and in loco-regional anesthesia. If, for example, cerebral perfusion monitoring shows acceptable values despite relative hypotension, it would be justified and reasonable not to insist on raising the arterial pressure. Only intraoperative raising of arterial tension is not without risk, i.e. it can be accompanied by more frequent occurrence of ischemia and myocardial infarction, stroke (hemorrhagic), difficult shunt placement, etc.[20]. Contrary to this, it is definitely recommended to avoid episodes of hypotension, especially in the phase of carotid artery clamping vessels, so that after re-establishment of blood flow, attention should be paid again to hypertensive episodes. The balance in pressure control is certainly influenced by the skill of the surgeon, the surgical technique, the length of the "cross clumping" period, the use of a shunt and many other factors. There is no special evidence of the superiority of any of the medications, taking into account the use of crystalloids, adrenaline, ethylephrine, ephedrine and phenylephrine, which are used in individually adjusted doses, depending on age, the state of the cardiovascular system, and accompanying diseases. The precise effects of vasoactive drugs on cerebral circulation are difficult to predict, because they depend on many factors: systemic pressure, degree of occlusion, baroreceptor condition, collateral circulation, use of shunt, etc.[21].

Postoperative blood pressure control

Postoperative hypertension is a common occurrence after endarterectomy. It is usually of a transient nature, lasts a few hours after the end of the operation and is a consequence of temporarily impaired baroreceptor function. The incidence of serious postoperative hypertension is around 60%, and 40% of these

cases require specific therapy[22,23]. Intraoperative episodes of hypotension with postoperative hypertension may lead to hematoma (3–8% incidence). Hematoma with postoperative edema can cause serious and fatal airway obstruction. In the NASCET study, this mechanism is responsible for the fatal outcomes of endarterectomies that are not directly related to cerebral circulation and brain ischemia[24].

"Timing" for CEA

According to the AHA and ASA (American Heart Association, American Stroke Association) guidelines, the greatest benefit of CEA is if it is performed within two weeks of the occurrence of TIA or ICV. Of course, there is a certain risk for the development of RS if CEA is performed too early in patients with brain infarction or stroke in the beginning and development. In patients with bilateral stenosis, the risk of RS is increased if CEA is performed within three months of the same operation on the opposite side[25].

Prediction, diagnosis and treatment

Transcranial Doppler TCD

TCD is the most commonly used technique for the prediction and diagnosis of RS development perioperatively. Its main advantages are non-invasiveness and results in "real time". This method measures the flow through the MCA (middle cerebri artery) where autoregulation has no effect on the diameter of the MCA. Increase in flow > 100% after "clump off" and 1.5 times higher flow postoperatively have a positive predictive significance for the development of RS.

Cerebral vasoreactivity, i.e. the acetazolamide/CO2 test increases flow by 20–80% in healthy subjects due to vasodilatation. In an ischemic brain, the blood vessels are already dilated, so the expected increase in flow is absent – low cerebral hemodynamic reserve. TCD determined low pressure in the distal part of the internal carotid artery (dICAP < 40 mmHg) is associated with a high predictive value for the development of CRS postoperatively[26,27].

Computed tomography CT

Done immediately after CEA, it often gives a normal result. In the later postoperative period, findings can vary from diffuse edema, changes in the white matter to the occurrence of intracerebral hemorrhage. This diagnostic method has no special predictive value for the development of CRS[28].

Magnetic resonance MR

As a diagnostic method, MR is more sensitive for detecting ischemic changes in the brain, but it is not necessarily better in terms of predicting the development of RS. Pathoanatomical substrates similar to those on CT, edema, zones of infarction or hemorrhage can be seen on the images.

MR perfusion

MR perfusion can show differences in cerebral flow between the cerebral hemispheres. and measuring preoperative values of cerebral blood flow (CBF) can help identify patients at risk for the development of RS. The works of Fukuda et al. showed a significant correlation of preoperatively increased CBF values and the risk of postoperative RS, and the risk is low with normal preoperative values[29].

Single Photon Emission CT (SPECT)

SPECT is a sensitive method that helps in identifying and differentiating ischemic from hyperperfusion areas of the brain. Similarly, TCD can help identify cerebral blood flow reserve (CBF) especially in hyperperfusion that occurs in the first postoperative days. Ogasawara et al give it an advantage over TCD in monitoring middle cerebral artery flow velocity in terms of sensitivity[30].

Therapeutic approaches

Preconditioning with free radical scavengers

Evidence on the use of antioxidants and scavengers of free radicals is limited, and there is currently no clear recommendation on how to use them in clinical practice. According to some studies, the use of edaravone, a lipid peroxidation inhibitor, may reduce the incidence of CRS after CEA (guided by SPECT)[31].

Ischemic Postconditioning (IPCT)

IPCT represents a therapeutic strategy aimed at reducing the frequency and severity of the development of ischemic insult, TIA, and RS after CEA. It is performed by applying cyclic phases (six phases) of clamping and releasing the clamp with the ICA, in periods of 30 seconds, after the reconstruction of the blood vessel after the removal of the plaque. It is a new therapeutic approach, and it requires more extensive clinical trials, and the benefits in the first analyzes show more in the reduction of the frequency of ischemic complications and the development of TIA postoperatively[32].

Use of antiedematous therapy, antihypertensives, anticonvulsants and barbiturates

In the development of brain edema, the use of mannitol and hypertonic solutions of NaCl has its place in the therapeutic sense, although the evidence of benefit in survival as well as long-term prognostic evidence is not strong enough. The use of barbiturates is not recommended routinely, but in patients with severe dis-

turbances of consciousness and respiratory insufficiency, who require controlled mechanical ventilation with induced coma. The use of antiepileptic drugs is not recommended for prophylactic purposes, while in cases of epileptiform attacks it has its place. In antihypertensive therapy, it is recommended to avoid Ca blockers (vasodilator effect), continue ACE inhibitor therapy (more frequent episodes of hypotension), and preference is given to beta blockers (labetolol).

Results

The total number of patients was 963. Table 2 shows the number of patients by year.

The average number of CEAs per year is between 200 and 250 procedures. A certain inconsistency in this matter can be noticed in the table, because the number of elective CEAs was significantly reduced during the Covid pandemic.

Table 2. Total number of patients per calendar year

2018	2019	2020	2021	2022	Ukupno / Total
207	219	75	155	307	963

Table 3. Distribution of patients according to gender and type of anestheia

Pol ispitanika/gender	Anestezija			
	OET/general		BLOK/Block	
	n	%	n	%
Muški/ male	312	57	237	43
Ženski/female	194	47	219	53
Pearson χ^2 test			*p = 0.221*	

Descriptive analysis of patients showed no statistically significant differences in terms of age, gender and type of anesthesia during the five-year period. General endotracheal anesthesia was used in 510 cases, and superficial cervical plexus block in 453 cases (Table 3).

The distribution of patients by gender and type of anesthesia showed no significant statistical differences.

Table 4 shows the age structure of patients according to the type of anesthesia.

Comorbidities

The average ASA score of the patients was III, and the most prevalent diseases in percentage were:

- Chronic myocardiopathy with hypertension 68%
- Arterial hypertension 42%
- Diabetes 40%
- Transient ischemic attack 27%
- Cerebrovascular insult 22%
- Myocardial infarction 20%
- Chronic obstructive pulmonary disease 16%
- Cardiac arrhythmias 12%

Indications for performing an operation

The percentage of symptomatic endarterectomies for the five-year period was 36%. During the Covid pandemic (2020 and 2021), the number of symptomatic CEA was 56% and 68%, respectively.

The duration of the operative procedure

Table 5 shows the average duration of surgery and clamping time according to the type of anesthesia technique, in which no statistically significant difference was noted.

Table 4. Age structure of patients according to type of anesthesia

Starosna dob /Age				
Anestezija Anesthesia	Aritmetička sredina ± standardna devijacija Arithmetic mean ± standard deviation	Medijana (interkvartilni interval) Median (interquartile range)	Minimum – Maksimum Minimum – Maximum	
OET/general	69.75 ± 4.56	69.0 (67.0, 71.5)	61.0 – 80.0	*M-W nez.*
BLOK/block	69.05 ± 5.07	70.0 (66.0, 72.0)	60.0 – 78.0	*p = 0.637*

Table 5. Average duration of surgery and clamping according to the type of anesthesia

	Blok/block (N1=453)			Opšta anestezija/general (N2=510)			p*
	Av/Prosjek ±SD	min	max	Av/prosjek ± SD	min	max	
Vrijeme trajanja operativnog zahvata / Duration of surgery	90 ± 8	69	107	91 ± 8	73	107	**0,488**
Vrijeme trajanja faze klemovanja / Duration of clamping	15 ± 4	6	22	15 ± 3	7	20	**0,971**

* Mann-Whitney test

Table 6. Number of patients by age, length of treatment in ICU and number of complications

Godina/year	2018	2019	2020	2021	2022
Ukupno/total	207	219	75	155	307
Asimptomatske/asimptomatic	168	180	31	99	278
Do 12 h h-din stabilni /bez specifične th Up to 12 hours No therapy	147–71%	181–82%	38–51%	102–65%	277–90%
Do 24 sata h-din nestab. sa th/bez simptoma Up to 24 hours h-din unstabile, No symptoms	48–80%	18–85%	17–45%	41–77%	17–56%
Preko 24 sata h-din nestab.sa th razvojem blažih simpt. Over 24 hours h-dynamic unstabile, mild symptoms	10–83%	2–66%	16–80%	9–75%	10–76%
ICV – koma, indukovana koma, KMV Stroke, induced coma, CMV	2	1	4	3	3
Smrtni ishod (30 dana) Fatal outcome (30 days)	0	0	2	1	1
Ukupno teških komplikacija Total of severe complications	0,96%	0,45%	5,33%	2,58%	0,97%

In the entire study, no statistically significant differences were recorded regarding the percentage of the operated side and the degree of occlusion of the operated side and the opposite side, according to the type of anesthesia (Mann-Whitney test – op side p= 0.429, opposite p = 0.976).

In the entire series, the eversion technique was used (953 patients, 99%), with an average duration of surgery of 90 minutes, and an average length of the carotid blood vessel clamping phase of 16 minutes.

Protective shunt was used 28 times (2.80%). Indications for the use of the shunt were poor neurological response of patients under regional anesthesia (loss of verbal and motor response after "clump on"), and a drop in cerebral oximetry values below critical values (25% of "baseline").

Postoperative monitoring, types and frequency of complications

The total perioperative mortality of the study was 0.41% (within 30 days), the frequency of intracerebral hemorrhage 0.62%, ischemic stroke 0.72%, while the incidence of prolonged stay in the ICU (more than 72 h) with implemented intensive care measures was 1.66%. Postoperative monitoring of 24–72 h had 45 patients (4.67 %) hemodynamically unstable patients with mild symptoms by the CND, and up to 24 hours, hemodynamically unstable patients without symptoms by the CNS 141 patients or 14.64 %. The number of patients without complications whose postoperative monitoring lasted up to 12 hours was 742 or 77%.

Table 6 shows the total number of patients by calendar year, according to the length of stay in the Intensive Care Unit and the number of postoperative complications.

Statistical analysis

The analyzed data are presented tabularly and graphically. Numerical data are presented with arithmetic mean, standard deviation (SD), range (maximum, minimum), median and interquartile range (IQR). Qualitative data are presented in absolute and relative frequencies. The normality of the distribution of all numerical variables was tested using the Shapiro-Wilk test.

The significance of differences between groups for variables with a normal distribution was determined using the Student's t-test and. Variables whose distribution deviates significantly from normal were compared using the Mann-Whitney test. Qualitative data were compared using the $\chi 2$ test and the Pearson $\chi 2$ test.

Data processing was performed using the statistical package IMB SPSS 21.0, and tabular and graphic presentation with MS Office Word 2016 and MS Office Excel 2016.

Discussion

Atherosclerosis is a disease of old age, but which begins to develop relatively early. The clinical manifestations of advanced atherosclerosis appear only in old age. The increase in prevalence with age in men is linear, while in women there is a modulation after the age of fifty when the prevalence in men decreases, which is attributed to the effects of menopause[33].

The average age of all respondents included in the survey is 66.4 years. The largest share of patients in the total number was recorded in the age groups 60–64 years (37%), 65–69 years (21%) and 70–74 years (18%), while the smallest share (3%) was recorded in the age group below 55 years.

In this study, no statistically significant differences were recorded in the age (Mann-Whitney U= 601.5; p=0.897; p>0.05) and gender structure ($\chi 2$=0.543; df=1; p=0.461; p>0, 05), by calendar year, the obtained results are in accordance with the world trends of incidence and prevalence[33,34,35].

All subjects belonged to group II, III and IV according to the ASA classification. A prospective study by Eckstein from 2002[34] analyzed ASA scoring as a predictive factor of perioperative morbidity and mortality, with the conclusion that younger patients with ASA score III or IV have an increased risk of cardiovascular and cerebrovascular complications perioperatively, and patients with ASA score III or IV older people have an increased risk within three weeks of the insult (14.6% : 4.8%), while in patients with ASA score I or II this risk is relatively low (3.4%) even within three weeks of development of insults.

In 57.7% of patients from the total number of cases included in this study, endarterectomy was performed on the right carotid artery. The percentage of occlusion of the operated side ranged from 65% to 90% in all three groups. The degree of occlusion of the opposite side was 0–100%.

According to the available literature, there is no significant statistical difference in the frequency of the operated side, as there is no difference in this study either. Research on the relationship between the thickness of the intima and the media, and the development of the atherosclerotic process (Rosfors, 1998, Ghanashyam, 2008)[36,37] suggest that the thickness of the inner layers of blood vessels is in direct correlation with the speed of development of atherosclerosis at the carotid bifurcation, and that the process develops faster on the left side and in men, but that these results also lose their significance with the age of the studied population.

The average length of the operative procedure of all patients was 97 minutes, and the average length of carotid artery clamping was 17 minutes. The operative technique in both groups was eversion endarterectomy. Recent research suggests that the eversion technique is statistically significantly faster than the conventional technique. *Markovic et al*. in their study from 2008, they found that the clamping time is shorter on average with the eversion technique by more than 5 minutes, while the operative time is shorter by an average of 19 minutes (82 min:101 min)[38]. The advantage of the eversion technique is also that this technique also successfully solves the "kinking" of the internal carotid artery. In contrast, there are studies that suggest a more frequent incidence of postoperative hypertension, as well as reperfusion syndrome when using the eversion technique (Fioriani et al.)[40], the occurrence of which was recorded in one patient in this study.

Anesthesia techniques

Anesthesiological goals in carotid endarterectomy include protection of the brain and heart from ischemic damage, control of heart rate and blood pressure, safe airway, and absence of patient pain. These goals should be met while keeping in mind one goal from the "second plan", no less important, which is to have an alert and cooperative patient (at least at the end of the operation), for the much-needed neurological assessment.

When endarterectomy is performed under regional anesthesia, blood pressure gives higher values on average, especially in the clamping phase[39,40]. In such a situation, cerebral perfusion is better maintained, but the risk of cardiac complications is also higher. Episodes of hypotension, more common in general anesthesia, compromise both cerebral and myocardial circulation, and condition more frequent use of vasopressors, which can have potential negative effects on the myocardium. *Sindelic* in a study from 2004. comparing the hemodynamic parameters in endarterectomy gives preference to regional anesthesia, finding significant pressure changes (fall) after induction into general anesthesia caused by the induction agent thiopental, which was also confirmed by our study[41].

Proponents of GA suggest the ability of barbiturates to act protectively on the central nervous system by reducing O2 consumption (decreasing CMRO2), reducing electrical activity[42].

However, since barbiturates do not affect critical values of cerebral flow, moderate reduction of electrical activity does not offer protection against severe ischemia. Animal studies suggest other possible mechanisms of action of barbiturates: redistribution of regional flow, reduction of intracranial pressure, protection from edema, and inhibition of Ca++ effects, these effects are dose-dependent without a predictable response of the cardiovascular and respiratory systems[44]. Etomidate and propofol offer similar brain protection, without cardiovascular side effects of barbiturates, but there are no clinical, prospective controlled studies that support the theoretical benefits of these anesthetics[43.] The use of volatile anesthetics affects the cardiovascular system (dose-dependent), and leads to a reduction of sympathetic tone, attenuation of baroreflex activity, and a direct effect on the heart and tone blood vessels[44,45.] The use of opiates leads to a weakening of both afferent and efferent sympathetic activity, and the effects of IPPV ventilation can also contribute to hemodynamic instability. The use of nitric oxide increases the plasma concentration of homocysteine and increases the possibility of postoperative myocardial ischemia, and raises CMRO2.

Surgical technique

Sudden changes in pressure and pulse during CEA are caused by surgical manipulation of the sinuses, ac-

tivation of the renin-angiotensin system, increased concentration of vasopressors, or central catecholamine activity. The degree of contralateral stenosis (baroreceptors) contributes to further increase in pressure. In addition to the direct effects of surgery and the degree of stenosis, other factors contribute to baroreflex dysfunction: age, chronic hypertension, effects of antihypertensive therapy, recent stroke or TIA, diabetes (93%)[46].

Clamping itself, and the duration of the clamping period, causes a drop in cerebral flow and a compensatory pressure jump and an increase in sympathetic activity. The degree of pressure jump depends on the previously listed factors.

The surgical technique is one of the more important factors, because the eversion technique takes less time but leads to a higher pressure jump[47].

Eversion carotid endarterectomy involves transection at the level of the carotid bifurcation, removal of arteriosclerotic plaque by twisting the artery and anatomical reimplantation of the internal carotid artery.

Eversion carotid endarterectomy requires a shorter clamping time compared to the standard operative technique. Its advantages are: anatomical reconstruction of the bifurcation, shorter and transversely laid suture line, implantation of foreign material (pach) is not required. In addition, the resection of the elongated carotid artery (kinking, coiling) is much simpler, and all this should prevent complications[38.] *Markovic et al.* in their study from 2008, they found that the clamping time is shorter on average with the eversion technique by more than 5 minutes, while the operative time is shorter by an average of 19 minutes (82 min:101 min)[38.] The effectiveness of carotid endarterectomy in the prevention of stroke in symptomatic and asymptomatic patients has been demonstrated in numerous randomized clinical studies[48], the results of which basically show us that it is a "low risk" procedure with a good long-term benefit for the patient. The frequency and number of these procedures has fluctuated since the 1970s, and has increased significantly since the 1990s thanks to large, randomized, prospective studies. The North American Symptomatic Carotid Endarterectomy Trial (NASCET)[49] and the European Carotid Surgery Trial (ECST)[50] demonstrated a benefit in the form of a reduced risk of stroke of 9% for surgical patients compared to 26% for non-surgical patients over eight years (NASCET), that is, 2.8% for surgical patients versus 16.8% for the medically treated group.

Many indication dilemmas related to the symptomatic group of patients were resolved after the almost simultaneous completion of three large prospective, multicenter, randomized studies – NASCET[49], ECST[50], and VA Trial[51]. dramatically better results in symptomatic patients who underwent surgery compared to those on drug therapy.

According to the world literature, perioperative mortality ranges from 1–2 to 10%, and the accepted perioperative morbidity according to the new guidelines ranges up to 3% for asymptomatic patients, and up to 6% for symptomatic cases (70–90% stenosis)[52.] Two large studies NASCET 49 and ECST 50 provide data on 5.8% and 9.1% of perioperative complications, respectively.

In the conducted study, the total perioperative mortality was 0.41% (within 30 days), while the incidence of prolonged stay in the ICU (more than 72 h) with intensive care measures was 1.66%.

Conclusions and recommendations of the new guidelines

Unlike postoperative hypertension after CEA, the frequency of development of cerebral reperfusion syndrome is a relatively rare complication, especially those accompanied by severe complications. In addition, it is a potentially fatal complication of carotid surgery, which is largely preventable. The prevention strategy includes adequate blood pressure control perioperatively, good timing for performing the operation and the choice of anesthesiological and surgical technique, with a very often individual approach, because the mechanism of RS depends on many factors. Early recognition of symptoms and prompt therapeutic measures are of key importance for the final outcome of treatment.

The guidelines of the European Society of Vascular Surgeons (European Society for Vascular Surgery (ESVS) 2023 – Clinical Practice Guidelines on the Management of Atherosclerotic Carotid and Vertebral Artery Disease) in their "2023 update" regarding blood pressure control do not bring significant news compared to 2018 year. 53

- Recommended antihypertensive therapy for asymptomatic and symptomatic patients Class I Level A
- Hypotensive patients as the first line of measures – administration of volume and plasma expander, and then vasopressor with target systolic pressure > 90 mmHg Class I Level C
- Blood pressure monitoring should be carried out 3–6 h postoperatively in patients undergoing CEA, as well as in patients with stenting procedure Class I Level C
- For hemodynamically unstable patients, after the operative procedure, monitor blood pressure for the first 24 hours Class I Level C
- In the centers that deal with carotid surgery, recommendations for the creation of written protocols for the treatment of postoperative hemodynamically unstable patient Class I Level C

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