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SAFETY OF EARLY CAROTID ENDARTERECTOMY

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Abstract

Carotid endarterectomy is indicated in patients with symptomatic stenosis of internal carotid arteries above 50%. The aim of the study was to determine safe time span between neurological symptoms and surgery, and to compare how different periods have changed the rates of complications in three groups of patients.

Patients were divided by period between neurological symptoms and surgery in three groups: first group consisted of patients operated up to 14 days from symptoms, second from day 15 to day 30, and third group consisted of patients operated more than 30 days from neurological symptomatology. All patients underwent surgery at our department from January 2015 to December 2018.

Totally 316 patients were operated at our department during the last four years. Major postoperative complications (stroke, death or myocardial infarct) occurred in 8 patients (2.5%). From the first group, 3 patients suffered postoperative stroke or death (2.36%), in the second group 2 patients (2.2%), and 2 patients (2.04%) in the third group of patients. The difference between the groups was not significant.

Most recurrent strokes occur within two weeks since primary stroke. Timing of carotid endarterectomy overcame several historical stages because of postoperative complications. Safe period for the best benefit of patients had to be found. At our department, we perform carotid endarterectomy within 14 days from symptoms, if the ischemic lesion in the brain is smaller than 2×3cm.

Carotid endarterectomy can be safely performed after the primary stroke, without significant difference in postoperative complications in different groups. The best timing of surgery to prevent recurrent stroke is within two weeks since primary stroke.

Keywords: *carotid endarterectomy, timing, atherosclerosis, symptomatic stenosis, stroke.*

Introduction

Carotid endarterectomy (CEA) is the gold standard of stroke prevention in patients with hemodynamically severe stenosis of the internal carotid artery (ICA). For hemodynamically severe ICA stenosis, stenosis is considered to be over 70% in asymptomatic patients and over 50% in symptomatic patients [*Naylor A et al., 2017*]. However, the risk of vascular stroke is not the same in patients with symptomatic and asymptomatic ICA stenosis. For asymptomatic patients, the annual stroke risk is about 3.2% [*Inzitari M et al., 2011*], with the risk of recurrent stroke in patients with symptomatic ICA stenosis up to 37% [*Rothwell P, 2008; Torma N et al., 2015*]. More than one third of patients with ICA stenosis over 50% will suffer from a second stroke, which may lead to death or disability. However, the time stratification of the risk of secondary brain ischemia after the overcome stroke is not unified. Most follow-up strokes, up to 20%, are within the first two weeks of primary stroke [*Rothwell P, 2008*]. Beside stenosis, quality of atherosclerotid plaque seems to be the important risk factor. There are several biochemical markers, which could help to detect such plaques from blood samples, such as inflammatory vascular markers IL-4, Lp-PLA2. These marks along with ultrasonography could be used to determin quality of atheroscelrotid plaque before surgical procedure. [*Štefanič P et al., 2017*]. Vascular surgeons have been cautious, following initial failures of early carotid endarterectomy, in

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performing CEA recently after stroke. The poor results of early carotid endarterectomy in the 60s and 70s of the past century, along with anxiety from intracranial hemorrhage, led to the fact that the ICA obturation became a contraindication to CEA, and a safe interval between stroke and CEA was established for 4-6 weeks [*Ojemman R et al., 1975*]. Currently, the only exception to this contraindication is a timely closure of ICA, which can be revascularized within 6 hours of symptom formation, with intracranial hemorrhage being excluded by CT screening. ICA closures lasting longer than 6 hours are contraindicated for revascularization because of the high risk of intracranial hemorrhage. At the turn of the millennium, a 6-week interval between stroke and surgery was considered safe. However, several studies at the beginning of our millennium have confirmed that carotid endarterectomy can be safely performed in the first weeks after the stroke [*Sbarigia E et al., 2006; Vikatmaa P et al., 2011*]. The risk of serious complications in these studies was up to 7.3%. Based on these studies and on the NASCET study, recommendations from international societies were accepted that carotid endarterectomy should be performed within 14 days of recent stroke [*Ricotta J et al., 2011; Naylor A et al., 2017*]. Recurrent ischemic events have been associated with delayed carotid endarterectomy (CEA) for patients who present with acute strokes. As such, earlier intervention has been advocated to preserve cerebral function and expedient rehabilitation. In ACS-NSQIP study, a total of 3,427 patients were identified who underwent CEA for acute stroke. The analysis of this study compared differences in 30-day postoperative major adverse clinical events (MACEs) for patients who undergo early (≤7 days) and delayed (>7 days) CEA after acute stroke. There were no differences in postoperative 30-day death, stroke, or MI in early and delayed CEA after an acute stroke. These results substantiate the recommendation for early (<7 days) CEA after acute strokes. [*Blay E et al., 2019*]. The aim of this work is to evaluate the occurrence of serious complications in patients operated at our workplace for symptomatic ICA stenosis over 50% in relation to the time span from a stroke.

MATERIAL AND METHODS

Our study included patients treated for the hemodynamically significant symptomatic ICA stenosis at the Clinic of Vascular Surgery of LF UPJŠ and VÚSCH a.s., Košice from 1.1.2015 to 31.12.2018. Patients who have experienced a stroke or transient ischemic attack (TIA) in the last 180 days have been considered symptomatic. Patients who did not overcome stroke or TIA or experienced it more than 180 days ago were considered asymptomatic and were not included in the study. Hemodynamically severe stenosis of ICA was defined as stenosis above 50%. The degree of stenosis was determined by ultrasound or angiography. Patients who met the endarterectomy indications but were high-risk for surgery, either because of comorbidities or local findings, were referred to carotid stenting (CAS). All patients had a CT or MRI scan performed before surgery to determine the extent of the ischemic lesion. At the size of the ischemic lesion up to 2×3 *cm*, patients were operated after the necessary preparation with an effort to perform surgery within 14 days of an ischemic event. Patients with an ischemic lesion in the brain larger than 2×3 *cm* were operated after a minimum interval of 4-6 weeks from cerebral ischemia. All patients were operated in total anesthesia. Transcranial cerebral oximetry using INVOS ® 5100 C, Somanetics, Medtronic (Minneapolis, USA) was used to monitor cerebral blood flow. The patient had clamps on ICA during surgery, and if saturation on transcranial cerebral oximetry was reduced by more than 20% of baseline, a shunt was introduced into ICA to provide brain perfusion. Patients had either an eversive carotid endarterectomy or a conventional carotid endarterectomy. The selection of the endarterectomy type was left on the surgeon. An eversion carotid endarterectomy was

To overcome it is possible, due to the uniting the knowledge and will of all doctors in the world

performed in the absence of shunt insertion. Conventional endarterectomy with the patch was performed with the need for shunt insertion, or in patients with more severe atherosclerosis of ICA, where conventional endarterectomy allows a better fixation of distal intima. Conventional endarterectomy was performed using a prosthetic patch. In the postoperative period, each patient was examined by an independent neurologist. Stroke, myocardial infarction, or death of the patient was considered a major postoperative complication. Small lesions of the cranial nerves or bleeding requiring a surgical revision were considered as minor postoperative complications. In terms of timing, patients were divided into three groups. The first group consists of patients operated within 14 days of stroke or TIA. The second group patients were operated from 15 days to one month from cerebral ischemia, and 3th group consisted of patients operated from one month from cerebral ischemia. The results were statistically processed using the GraphPad Prism software, where we applied a chi-square test.

Results

Symtomatic stenosis of ICA occurred in 316 patients, who were operated at our department. From them, 209 were men (66.14%), and 107 were women (33.86%). The average age of patients was 66.3 years. A total of 21 patients (6.65%) had a shunt introduced to ICA during the surgery for a decrease in cerebral saturation greater than 20%. An eversion carotid endarterectomy was performed in 285 patients (90.19%) and conventional endarterectomy with the patch in 31 patients (9.81%). Severe complications occurred in our group in eight patients (2.5%), from which there were five cases of stroke (1.6%), two deaths (0.6%) and one myocardial infarction (0.3%). From minor postoperative complications, bleeding occurred in seven cases (2.2%) and cranial nerve lesions in eleven cases (3.5%) (Table 1).

In terms of time span, 127 patients (40.2%) operated within 14 days of stroke or TIA were in the 1st group. There were 91 patients (28.8%) in the second group, and the 3rd group consisted of 98 patients (31%), postoperative stroke or death in a group of patients operated within 14 days (I group) occurred in three cases (2.36%). In the 2nd group (patients operated from 15 days to one month from the stroke) stroke or death occurred in two cases (2.2%), and the 3rd group (more than 30 days from the stroke) stroke or death occurred in two patients (2.04%). The difference between groups was not statistically significant (Table 2).

Table 1

Postoperative complications in our study

Complication	Patients (n=316)	%
Stroke	5	1.6%
Death	2	0.6%
MI	1	0.3%
Stroke + death	7	2.2%
Stroke + death + MI	8	2.5%
Bleeding	7	2.2%
Lesion of cranial nerves	11	3.5%

Note: *MI - myocardial infarct*

Discussion

Current indications for surgeries on carotid arteries vary from its etiological origin and health condition of patients. Most common cause of surgery is stenosis, which can be symptomatic, in patients which had neurological deficits such as stroke or TIA in the past 6 months. Patients with

Table 2

Major postoperative complications (stroke and death) in our study in association with the interval between the stroke and carotid endarterectomy

Interval	No of patients in interval	complications No	%	p
up to 14 days	127 (40.2%)	3	2.36%	NS
15-30 days	91 (28.8%)	2	2.2%	NS
over 30 days	98 (31%)	2	2.04%	NS
total	316 (100%)	7	2.22%	NS

Note: *The result is not significant at p <0.10*

symptomatic stenosis below 50% are not indicated for the surgical procedure. The only exception to 50% of the limit is in the current indications of repeated TIA or strokes in the carotid basin in a patient with symptomatic ICA stenosis below 50%, with other causes of cerebral ischemia being excluded, and this indication should be confirmed by a multidisciplinary consensus [*Kopolovets I et al., 2017; Naylor A et al., 2017*]. These are often patients with an unstable, vulnerable carotid plaque, with such an unstable plaque significantly increasing the risk of stroke [*Sarlon-Bartoli G et al., 2012*]. In the NASCET study alone, the incidence of stroke or death within 30 days of surgery was 5.8% [*Barnett H et al., 1991*]. NASCET results helped establish a generally accepted limit of 6% of major postoperative complications (stroke or death) that the CEA workplace for symptomatic ICA stenosis should meet [*Ricotta J et al., 2011*]. In 2008, Rothwell's analysis of four studies, including the NASCET study, found that up to 37% of patients with symptomatic ICA stenosis over 50% experience another stroke which may have fatal consequences [*Rothwell P, 2008*]. However, in terms of time span, the most recurrent stroke, up to 20%, occurs within two weeks of the first stroke. In the third and fourth weeks, only 10% of other strokes are present, and after the month incidence of the second stroke is only 7%. This means that the greatest risk of another, recurrent stroke is in the first two weeks of primary stroke. Then the risk of another stroke decreases. Rothwell also found that in the NASCET study there was no statistically significant difference in the occurrence of serious complications (death or stroke) after the CEA performed in the first two weeks after primary stroke, compared with carotid endarterectomy performed later. Similar results were also published by Berek P. with co-authors in 2018, where 223 patients after a stroke underwent an early CEA. The percentage of serious post-operative complications occurred in this work up to 2.2% [*Berek P et al., 2018*]. The selection of patients was significant when the author operated only patients with a neurological finding. A preoperative CT scan was also important, with patients with cerebral hemorrhage and ischemic stroke patients being excluded with more than 30% of the media cerebral artery, which corresponds to a lesion of approximately 2x3*cm*.

Study of SPACE, EVA 3S and ICSS [*Eckstein H et al., 2008; Rantner B et al., 2013*] was also interesting in this respect. The analysis of these three studies, comprising 3,433 patients, was focused on early interventions. Patients were divided into three groups in terms of the time interval between primary stroke and surgery. In the first group, patients were operated within 7 days of stroke, in the second group patients were operated on days 8 to 14 from stroke and in the third group patients were operated from 15 to 30 days of stroke. This subanalysis showed that there was no statistically significant difference in the number of serious complications in surgical treatment if CEA was performed within 7 days, from 8-14 days or from 15 to 30 days after primary stroke [*Rantner B et al., 2013*]. Severe complications occurred in a group of patients treated surgically in all three time groups, with a rate up to 4%. Furthermore, this subanalysis confirmed that CEA can be safely performed in the first week after primary stroke, with severe complications occurring within the range of 2.8%.

Our work had similar results, where patients operated within 14 days of primary stroke had a significant postoperative complication (stroke or death) of 2.36%. Patients operated from 15 days to 30 days after primary stroke had severe complications of 2.2%, and patients operated 30 days after primary stroke had severe complications in 2.04% of cases. The difference between groups was not statistically significant. These results and our study confirms that patients with ischemic brain lesion up to 2x3*cm* and with symptomatic ICA stenosis above 50% may be safely operated within 14 days of primary stroke without a higher risk of severe postoperative complications.

Based on the studies mentioned above, indications for a surgical solution for symptomatic ICE stenosis were more or less "crystallized". Relevant specialist societies such as the American Society for Vascular Surgery (SVS) and the European Society for Vascular Surgery (ESVS) recommend using

CEA in patients with symptomatic ICA stenosis over 50%. If possible, the CEA should be done within 14 days of the primary stroke. Serious complications (stroke and death) should occur in less than 6%vof cases [*Ricotta J et al., 2011; Naylor A et al., 2017*]. Contraindication of carotid endarterectomy is the ICA closure, hemiplegia and the patient in the overall bad health conditions. At our workplace, we have good experience with postponing surgery for patients with cerebral ischemia deposits greater than 2×3 *cm* on CT or MRI examinations for 4-6 weeks. The reason is the concern about intracranial hemorrhage in early carotid endarterectomy in patients with large ischemic brain lesions.

One aspect of the case is society's recommendations, the other is an everyday practice. Compliance with the 14-day interval between stroke and surgery requires multidisciplinary collaboration between neurologists, radiodiagnostics, and surgeons. We managed to operate within 14 days of the primary stroke of 40.2% of our patients. In the second group, operations from 15 to 30 days of primary stroke were 28.8% of the patients and 31% of the patients in the group where the stroke and CEA interval was over 30 days. These results are due to the excellent collaboration between neurologists and our workplace. Patients with the atherosclerotic carotid disease are often polymorbid and postoperative complications are common [*Gavornik P et al., 2015*].

The results of the carotid endarterectomy performed in 316 patients also show that our procedure and indications are correct. Severe complications (stroke, death or myocardial infarction) occurred in only 8 cases (2.5%). This result corresponds to the number of complications in the studies mentioned above [*Rantner B et al., 2013*] and also meets the requirements of relevant specialist societies for the occurrence of serious postoperative complications up to 6% in patients with symptomatic stenosis [*Ricotta J et al., 2011; Naylor A et al., 2017*]. Less severe complications occurred in our series: seven post-operative bleeding requiring a surgical revision (2.2%) and eleven cranial nerve lesions (3.5%). These results are similar to the relevant studies, for example, the ICSS study had 5.8% of severe bleedings and 5.2% of cervical nerve lesions [*Ederle J et al., 2010*]. Cervical nerve lesions are reversible in the vast majority of cases, and after several months, the status was corrected to the preoperative state.

There are studies where the interval between stroke and surgery is minimal, just a few days. In 2011 Leseche C. and co-authors published an article on 64 patients with recurrent TIA, crescendo TIA [*Leseche C et al., 2011*]. The mean median from the stroke to surgery was only 5 days. There were no serious postoperative complications in this set. This work demonstrates that patients with crescendo TIA can be safely operated if an ICA obturation is not present and a large ischemic lesion in the brain is not present. The systematic analysis of studies, published by Karkos C. and co-authors in 2009, since 1980 since 2008, has shown that patients who have been operated on repeated TIA, i.e. crescendo TIA, have had serious complications in 5.6% of cases [*Karkos C et al., 2009*].

Based on our experience and also in accordance with the results of extensive studies, we have the following timing of carotid endarterectomy:

1. Within 6 hours of symptoms, we perform surgery in acute ICE obturation. Intracranial hemorrhage should be excluded from CT. For ICE closure, we perform CEA and supplement ICA thrombectomy. The ICA closure lasting over 6 hours is a strict contraindication for the high risk of intracranial hemorrhage.
2. We perform CEA within 24 hours if recurrent TIA is present and ICA stenosis is confirmed to be more than 50% in the symptomatic carotid basin, or severe thrombolytic ICA stenosis. The condition is the absence of cerebral hemorrhage and ischemic deposits less than 2 x 3 *cm* in the CT or MRI of the brain.
3. Within 14 days we perform CEA at symptomatic stenosis of ICA above 50% and ischemic brain lesion less than 2×3 *cm* on CT or MRI.
4. With a 4-6 week interval, we perform CEA in

patients with symptomatic ICA stenosis above 50% and ischemic brain lesion over 2×3 *cm*.

CONCLUSION

Up to 40% of patients with symptomatic ICA stenosis exceeding 50% experience the primary stroke. Carotid endarterectomy is an effective prevention of subsequent strokes. Its timing has historically surpassed several periods. At present, carotid endarterectomy should be performed within 14 days of primary stroke in patients with symptomatic ICA stenosis over 50%. At this time, the risk of recurrent, secondary stroke is highest, and carotid endarterectomy has the highest preventative effect. Studies, as well as our results, confirm that it is safe to perform surgery at this time if the ischemic brain lesion is less than 2×3 *cm*. In the cases of larger stroke, we prefer a 4 to 6 week interval between primary stroke and carotid endarterectomy for fear of intracranial hemorrhage.

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