

# Early Identification of Patients with the Risk for Postoperative Carotid Restenosis Development

Ines Strenja-Linić<sup>1</sup>, Miljenko Kovačević<sup>3</sup>, Slavica Kovačić<sup>2</sup>, Aldo Ivančić<sup>3</sup> and Berislav Budiselić<sup>2</sup>

<sup>1</sup> Cerebrovascular Department, Neurology Clinic, Rijeka University Hospital, Rijeka, Croatia

<sup>2</sup> Rijeka University Hospital Center, Department of Radiology, Rijeka, Croatia

<sup>3</sup> Rijeka University Hospital Center, Department of Thoracovascular Surgery, Rijeka, Croatia

## ABSTRACT

Multiple randomized trials over the last decade for both symptomatic and asymptomatic carotid stenosis have proven the efficacy of carotid endarterectomy (CEA) in reducing the risk of stroke. The aim of this prospective non-randomizing cohort study was to determine the incidence of carotid arteries restenosis after CEA as well as to ascertain the clinical and etiological characteristics for the development of restenosis. Treatment data from 178 KBC Rijeka patients that had undergone CEA in the period 1. 09. 2005–30. 8. 2009 has been processed. All patients are monitored through our Neurosonology laboratory algorithm – first Doppler ultrasound examination within the first week after CEA and the following after 1, 3, 6 and 12 months. After this time once a year. The average monitoring time was 21 month (1–36 months). In the stated period 27 restenosis was diagnosed (15.16%). Only four of them were symptomatic (14.81%). Patient survival rate is 98% in the first 12 and 92% in the first 36 months. Carotid restenosis is usually asymptomatic. Non-invasive post-operative carotid arteries color Doppler screening is essential in the early identification of patients with the risk for the development of restenosis.

**Key words:** carotid endarterectomy (CEA), carotid arteries restenosis, risk factors, ultrasound screening

## Introduction

Cerebrovascular diseases are one of the leading causes of death in industrial countries but stroke is still a preventable disease. Internal carotid artery stenosis is responsible for a considerable proportion of transient ischemic attacks and strokes. Atherosclerosis is responsible for stenosis formation of extracranial carotid stenosis and also a significant factor in restenosis after endarterectomy. Carotid endarterectomy (CEA) is an effective operation designed to prevent stroke. Multiple randomized trials over the last decade for both symptomatic and asymptomatic carotid stenosis have proven the efficacy of CEA in reducing the risk of stroke<sup>1–4</sup>.

CEA was highly beneficial for patients with 70% or more stenosis without near-occlusion, of some benefit for those with 50–69% stenosis, of no benefit in those with 30–49% stenosis and harmful in patients with less than 30% stenosis<sup>5</sup>. In the largest trial of asymptomatic subjects Asymptomatic Carotid Surgery Trial (ACST), the perioperative risk of stroke or death was 3.1%, and thereafter the 5-year stroke risk was 3.8 vs. 11% for best medi-

cal therapy, i.e. 16 CEA were needed to prevent one stroke in 5 years. In the Asymptomatic Carotid Atherosclerosis Study (ACAS), the perioperative risk of stroke and death was very low, and 83 CEA were needed to prevent one stroke in 2 years<sup>4,6</sup>.

Recurrent carotid stenosis or restenosis is the re-narrowing of the blood vessel after surgical or endovascular revascularization. Stoney and String<sup>7</sup> described two pathologically different types of recurrent carotid stenosis; early restenosis that results from myointimal (neointimal) hyperplasia and late restenosis that results from recurrent atherosclerosis<sup>7–9</sup>. Early restenosis usually occurs after 30 days but before 2 years postoperatively, while late restenosis can be seen 2 years after the operation. Additionally, residual stenosis due to technical failure can cause “restenosis” as well, which can be observed even earlier than 30 days postoperatively. Neointimal hyperplasia appears as smooth, firmly localized thickenings at the site of previous CEA, whereas atherosclerotic le-

sions tend to be irregular, friable, and occasionally ulcerated with a tendency to give rise to symptoms in the carotid territory<sup>9</sup>. Late restenotic lesions contain foam cells, cholesterol deposits, abundant collagen and calcium just like the primary atherosclerotic lesion<sup>10</sup>. Cardiovascular risk factors are the same as the ones for restenosis and include smoking, family history of cardiovascular disease, diabetes mellitus, coronary heart disease and hyperlipidemia<sup>22,23,26,27</sup>. It has recently been shown that newly acquired risk factors after follow-up including hypertension, coronary heart disease, diabetes and peripheral artery disease result in a higher risk for restenosis after CEA. This finding underlines the importance of risk factor management in vascular patients in order to reduce restenosis rates<sup>20</sup>.

Depending on the definition criteria for recurrent carotid stenosis, the length of the follow-up period, and the deviation in the number of patients assigned to these studies, the incidence of restenosis varied widely between 1% and 36%<sup>7,11–13</sup>. According to a review by Frederick et al, the risk of recurrent carotid stenosis was 10% in the first year, 3% in the second year, and 2% thereafter suggesting, that most of these complications occur in the first postoperative year<sup>14,22</sup>. Restenotic lesions are usually less thrombogenic than the primary atherosclerotic plaques, with consequently lower risk of cerebrovascular incidents. While primary atherosclerosis often leads to neurological symptoms as an amaurosis fugax, transient ischemic attack or stroke, restenosis generally appears asymptomatic<sup>15</sup>. When restenosis became significant, re-intervention may also become necessary to avoid the re-occurrence of clinical symptoms. Nowadays, most of the carotid restenotic cases are to be treated by CAS (Carotid artery stenting) instead of a redo CEA<sup>16–18</sup>.

## Patients and Methods

Treatment data from 178 KBC Rijeka patients that had undergone CEA in the period 1. 09. 2005–30. 8. 2009

has been processed. Pre-operative work-up, clinical as well as haemodynamic postoperative follow up has been done in the Cerebrovascular Department and in the Neurosonology Laboratory of the Neurology Clinic, Rijeka University Hospital, Croatia. ALOCA ALFA 10 ultrasound machine and 5–7.5 MHz transducers were used. All patients are monitored through our Neurosonology Laboratory algorithm – first doppler ultrasound examination within the first week after CEA and the following after 1.6 and 12 months. After this time once a year.

The average monitoring time was 21 month (1–36 months). Duplex grading of ICA stenosis was according to previously published criteria<sup>19,21,22,25</sup>. Peak systolic velocities (PSV) within the ICA of 150 to 249 mm/sec and the ratio of PSV of the ICA and common carotid artery (CCA) of 2.0 to 3.9 were quantified as 50 to 69% stenosis. PSV within the ICA greater 250 mm/sec and the ratio of PSV of the ICA and CCA of greater 4 were quantified as 70 to 99% stenosis. In our study carotid restenosis was defined as an above 50% restenosis or occlusion. Digital subtraction carotidography (DSA) or MSCT carotidography was performed in every patient prior to the CEA. Also we perform to all patients CT scan or brain MRI.

Incidences of risk factors for arterial stenosis such as treated hypertension, smoking, treated diabetes, hypercholesterolemia and hyperhomocysteinemia in these two groups were also monitored.

## Results

This study focused on the incidence of carotid artery restenosis based on Duplex studies and confirmed by angiography. In the stated period 27 restenosis of 178 CEA was diagnosed (15.16%). The average monitoring time was 21 month (1–36 months). Patient baseline demographic and distribution of risk factors among the studied patients with carotid restenosis are shown in Table 1. There was no statistical difference between the traditional cardiovascular risk factors between carotid steno-

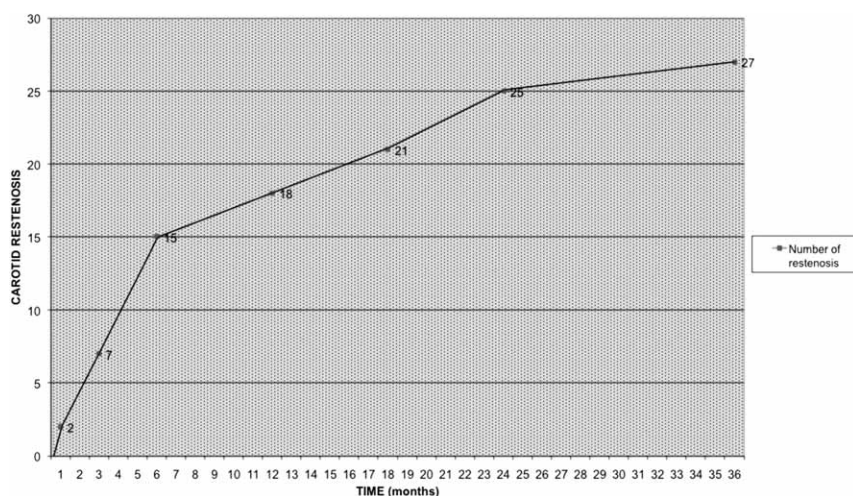


Fig. 1. Carotid restenosis.

**TABLE 1**  
DISTRIBUTION OF RISK FACTORS AMONG THE STUDIED PATIENTS

Variable (N =178)	CEA	Restenosis	p value
Number of patients	178	27	
Mean age (years)	73.3	66.8	
Sex			
Male	102	12	0.2203
Female	76	15	
Overweight (BMI)	103	9	0.0114
PAD	31	9	0.0671
Homocysteine level over 5 mmol/L (N=91)	49	19	0.1823
Stroke or TIA	139	4	0.001
Current tobacco use	75	9	0.4110
Coronary artery disease	61	10	0.8294
Prior stent or surgical bypass graft mellitus	41	8	0.4173
Hypertension	152	23	1
Diabetes mellitus	81	14	0.543
Hyperlipidemia	97	17	0.5336
Chronic renal failure (creatinine >2)	24	4	0.7698
Atrial fibrillation	34	5	1

sis patients after CEA and those patients who developed carotid restenosis, except for overweight patients with increased BMI  $p < 0.05$ . Eighteen patients (66.67%) with restenosis were treated by endovascular procedures – stenting. Considering all restenosis, only four were symptomatic (14.81%) while five were post-operative occlusions (18.52%). Two occlusions occurred within the first week after CEA. Patient survival rate is 98% in the first 12 and 92% in the first 36 months. Over 55.6% of restenosis developed within six months follow-up, 77,8% within 18 months (Figure 1).

All recognized restenosis were in group of early restenosis.

## Discussion and Conclusion

Carotid stenosis or/and its consequences could be prevented. Since the main risk factors for atherosclerosis are well known, prevention can be achieved by lipid-lowering, antihypertensive, antidiabetic therapies, weight control or by omitting smoking and treating other risk

factors. Besides these modifiable factors, some risk factors like age, gender or gene polymorphisms cannot be affected. In contrast, the prevention of recurrent stenosis is not yet fully established. It is probably useful to pay further attention to the classical atherosclerosis risk factors but most important prevention methods is regular ultrasonographic checkup of the carotids – 1 week, 1 months, 3 months, 6 months, 12 months postoperatively, than every 12 months thereafter, should be scheduled regarding, that the incidence of restenosis is highest within the first 18 months after CEA. Routine follow – up and serial monitoring of all patients with carotid after CEA is required, especially in first 18 months because restenosis usually arises early on after surgery and rarely symptomatic.

In case of recurrent carotid stenosis, stent placement is the method of choice according the criteria. In some cases, carotid restenosis can also be treated by repeated endarterectomy. The additional antiplatelet therapy (aspirin, clopidogrel) is essential, especially for the prevention of thrombosis.

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*I. Strenja-Linić*

*Neurology Clinic, Rijeka University Hospital Center, Cambierieva 17/8, 51000 Rijeka, Croatia  
e-mail: medines4@yahoo.com*

## **RANA IDENTIFIKACIJA BOLESNIKA OD POVEĆANOG RIZIKA ZA RAZVOJ POSTOPERATIVNE RESTENOZE KAROTIDNIH ARTERIJA**

### **S A Ž E T A K**

Mnogobrojna randomizirana istraživanja posljednje desetljeće simptomatskih i asimptomatskih karotidnih stenoza dokazale su uspješnost karotidne endarterektomija (KEA) u snižavanju rizika za nastanak moždanog udara. Cilj ove prospektivne nerandomizirane kohortne studije bio je utvrditi incidenciju restenoze karotidnih arterija nakon karotidne endarterektomija (KEA) te procijeniti kliničke karakteristike i etiološke čimbenike za razvoj restenoze. Obradeni su podaci 178 bolesnika liječenih u KBC Rijeka, kojima je učinjena KEA u razdoblju od 1. rujna 2005. do 30. kolovoza 2009. godine. Preoperativna obrada, kliničko te ultrazvučno postoperativno praćenje učinjeno je pri Zavodu za cerebrovaskularne bolesti i Neurosonološkom laboratoriju Klinike za neurologiju KBC Rijeka. Svi bolesnici su praćeni prema algoritmu našeg Neurosonološkog laboratorija – prvi ultrazvučni pregled u prvih tjedan dana nakon KEA te kontrolni nakon 1, 3, 6 i 12 mjeseci. Nakon toga jednom godišnje. Prosječno vrijeme praćenja bilo je 21 mjesec (3–36 mjeseci). U navedenom periodu dijagnosticirano je 27 restenoza (15,16%). Od svih restenoza samo su 4 bile simptomatske (14,81%). Preživljavanje pacijenta je 98 i 92% u 12 i 36 mjeseci. Karotidna restenoza najčešće je asimptomatska. Postoperativno neinvazivno ultrazvučno praćenje karotidnih arterija bitan je čimbenik u ranoj identifikaciji pacijenata s rizikom za razvoj restenoza.