Carotid angioplasty and stenting is safe and effective for treatment of recurrent stenosis after eversion endarterectomy

Djordje Radak, MD, PhD,[a,b] Slobodan Tanaskovic, MD,[a] Dragan Sagic, MD, PhD,[b,c] Zelimir Antonic, MD,[c] Srdjan Babic, MD, PhD,[a] Petar Popov, MD, PhD,[a,b] Predrag Matic, MD,[a] and **Zoran Rancic, MD, PhD,[d]**
Belgrade, Serbia; and Zurich, Switzerland

Objective: **This study was conducted to determine the efficiency and long-term durability of percutaneous transluminal angioplasty and carotid artery stenting in carotid restenosis (CR) treatment after eversion endarterectomy, with emphasis on variables that could influence the outcome.**
Methods: **We analyzed 319 patients (220 asymptomatic and 99 symptomatic) who underwent carotid angioplasty from 2002 until 2012 for CR that occurred after eversion endarterectomy. During this period, 7993 eversion endarterectomies were done for significant carotid artery stenosis. Significant CR was detected by ultrasound examination and confirmed by digital subtraction angiography or multidetector computed tomography angiography. After angioplasty (with or without stenting), color duplex ultrasound imaging was done after 1 month, 6 months, 1 year, and annually thereafter. End points encompassed myocardial infarction, stroke, and cardiovascular death (fatal myocardial infarction, fatal cardiac failure, fatal stroke), and also puncture site hematoma and recurrent restenosis. Primary end points were analyzed as early results (≤30 days after the procedure), and secondary end points were long-term results (>30 days). Variables and risk factors influencing the early-term and long-term results were also analyzed. Median follow-up was 49.8 ± 22.8 months (range, 17-121 months).**
Results: **All but one procedure ended with a technical success (99.7%). In the early postoperative period, transient ischemic attack occurred in 2.8% of the patients and stroke in 1.6%, followed by one lethal outcome (0.3%). Stent thrombosis occurred in one patient (0.3%) several hours after the angioplasty, followed by urgent surgery and graft interposition. In the long-term follow-up, there were no transient ischemic attacks or strokes, non-neurologic mortality was 3.13%, and the recurrent restenosis rate was 4.4%. The rate of non-neurologic outcomes during the follow-up was significantly higher in asymptomatic patients than in symptomatic patients (4.54% vs 0%; $P = .034$). The statically highest rate of transient ischemic attack was verified in patients in whom Precise (Cordis Corporation, New Brunswick, NJ) stents was used (12.2%) and a Spider Fx (Covidien, Dublin, Ireland) cerebral protection device (12.5%) was used. Female gender, coronary artery disease, plaque calcifications, and smoking history were associated with an adverse outcome after angioplasty.**
Conclusions: **Carotid artery stenting is safe and reliable procedure for CR after eversion endarterectomy treatment, with low rate of postprocedural complications. Type of stent and cerebral embolic protection device may influence the rate of postprocedural neurologic ischemic events. (J Vasc Surg 2014;60:645-51.)**

Carotid endarterectomy (CEA) is an effective and reliable procedure for stroke prevention in symptomatic and asymptomatic patients with severe carotid stenosis.[1,2] However, one of the major complications that occurs and thereby influences early and late neurologic ischemic events is carotid restenosis (CR). The reported incidence of symptomatic restenosis after CEA ranges from 0.6% to 3.6%, and the reported incidence of asymptomatic restenosis is 8.8% to 19%.[3-5] Most authors agree that symptomatic CR necessitates intervention, but the issue of asymptomatic CR treatment remains controversial.[6]

The therapeutic options for CR are percutaneous transluminal angioplasty (PTA), with or without carotid artery stenting (CAS), and repeated open surgical treatment. Some authors have reported satisfactory results of redo surgery, but the surgery still has a higher rate of postoperative complications compared with surgery for primary atherosclerotic lesions.[7-10] PTA is considered to be a less invasive procedure for CR treatment, with low rate of postprocedural stroke and mortality.[11-14] In most of these studies, however, the number of treated patients has been too low and follow-up has been limited.

The aim of the present study was to determine the early results and long-term durability of carotid PTA in CR treatment after eversion CEA (eCEA), with an emphasis on the predictive value of variables that could influence the outcome.

From the Vascular Surgery Clinic, "Dedinje" Cardiovascular Institute, Belgrade[a]; the Faculty of Medicine, University of Belgrade, Belgrade[b]; the Department for Diagnostic and Interventional Radiology, "Dedinje" Cardiovascular Institute, Belgrade[c]; and the Clinic for Cardiovascular Surgery, University Hospital Zurich, Zurich.[d]
This manuscript was partially supported by grant No. 41002 funded by the Ministry of Science, Republic of Serbia.
Author conflict of interest: none.
Reprint requests: Slobodan Tanaskovic, MD, "Dedinje" Cardiovascular Institute, Vascular Surgery Clinic, Heroja Milana Tepica 1 St, 11000 Belgrade, Serbia (e-mail: drslobex@yahoo.com or drslobex@gmail.com).
The editors and reviewers of this article have no relevant financial relationships to disclose per the JVS policy that requires reviewers to decline review of any manuscript for which they may have a conflict of interest.
0741-5214/$36.00

http://dx.doi.org/10.1016/j.jvs.2014.03.288

METHODS

The current study is a retrospective review of prospectively collected data at the University Vascular Surgery Clinic in Belgrade, Serbia. From 2002 until 2012, 319 patients received carotid PTA for significant CR. During this period, 7993 eCEAs were performed for significant carotid stenosis, for a significant restenosis treated patient rate of 3.99% (319 patients). The Ethics Committee of the institution approved this study, and all patients provided written informed consent.

CR occurred in all patients after eCEA. The technique of eCEA is described in detail elsewhere.[15] During the follow-up after treatment, all patients underwent color duplex examination using an Alfa10 color duplex system (Aloka Co Ltd, Tokyo, Japan) at 1 month, after 6 months, and then annually thereafter.

The ultrasound criteria to determine CR were (1) peak systolic velocity >215 cm/s, corresponding to >50% restenosis, and (2) peak systolic velocity >275 cm/s, corresponding to >70% restenosis.[16] Carotid artery restenosis was considered significant in symptomatic patients if a diameter reduction of >50% was detected and was considered significant in asymptomatic patients with a >85% reduction. Apart from the hemodynamic characteristics, color duplex ultrasound assessed the morphology of the plaque, including quality of the plaque and surface irregularity and ulceration. Patients with residual restenosis were not included in the study.

The patients with CR after the initial CEA were considered symptomatic if they experienced transient ischemic attack (TIA), stroke, or amaurosis fugax ≤6 months before the ultrasound assessment and clinical admission.

In all patients for whom the ultrasound imaging detected significant CR, the lesions were additionally evaluated with digital subtraction angiography (Siemens, Erlangen, Germany) from 2002 to 2005 and with multidetector computed tomography (CT) angiography (Lightspeed VCT; GE Healthcare, Milwaukee, Wisc) from 2005 to 2012.

CT was necessary to identify any aortic arch and supraaortic branch pathologies and for treatment planning. All patients were examined by the institution's attending neurologist, and brain CT was performed before or upon admission and after the angioplasty in patients with postprocedural neurologic ischemic events.

Endovascular technique and procedural management. The indication for treatment was made interdisciplinarily with consensus among a vascular surgeon, interventional radiologist, and neurologist. Acetylsalicylic acid (100 mg/d) and clopidogrel (75 mg/d) or ticlopidine (250 mg twice daily) were administered ≥3 days before the intervention to prevent thrombosis and embolic complications. Patients who were immobile after the procedure (stroke, puncture site hematoma, etc) were administered low-molecular-weight heparin at a thrombosis prophylaxis dose. After primary eCEA, 90.9% of the patients received statins on discharge, 91.6% received acetylsalicylic acid (100 mg/d), and 27.6% received clopidogrel (75 mg/d) when specified. All patients received statins and dual-antiplatelet therapy after CAS.

The PTA and stenting were performed according to our standardized operating procedure. All procedures were performed under local anesthesia. The femoral artery was the most commonly used access site, but if indicated, the radial or brachial artery was used as well. After heparin (100 IU/kg) administration, the access artery was punctured, the sheath was introduced, and the guidewire was passed through the aorta into the arch. A carotid angiogram was performed, and if the position was appropriate, we continued with the procedure.

For the common carotid artery access, a 6F or 7F sheath was placed, and the guidewire was passed through the area of carotid narrowing. Embolic protection device was then introduced to prevent debris and embolic complications. The type of embolic protection device used depended on anatomical characteristics, plaque embolic potentials, and localization and degree of the stenosis. If very tight stenosis was to be treated, coronary balloons were used for predilation; otherwise, direct stenting was done with self-expanding stents, followed by balloon angioplasty of the appropriate size. The balloon sized ranged from 5 × 15 mm to 8 × 30 mm, with the most commonly used size being 6 × 20 mm. After the procedure, the protection device, guidewires, and the sheath were removed, followed by puncture site aftercare. The activated clotting time was measured after the procedure to evaluate the optimal time of arterial sheath removal and hemostasis.

The type of embolic protection device used depended on the anatomical characteristics, plaque embolic potentials, and localization and degree of the stenosis. The most frequently used protection device was a FilterWire (Boston Scientific, Natick, Mass) in 151 patients (47.3%), followed by an Angiogard Rx (Cordis Corp, New Brunswick, NJ) in 127 (39.8%), a Spider Fx (Covidien, Dublin, Ireland) in 40 (12.5%), and an Emboshield (Abbot Vascular, Temecula, Calif) in one (0.31%).

The most frequently used stent was a Carotid Wallstent (Boston Scientific), in 158 patients (49.5%), followed by a Protégé Rx (Covidien), in 76 (23.8%), and a Precise Rx (Cordis Corp), in 49 (15.4%). The most rarely used stents were the Crystallo Ideale (Medtronic, Minn), in 16 patients (5.01%), and the Xact (Abbot Vascular), in two patients (0.62%). The most frequently used balloons were Cordis Aqua and Amia (Johnson & Johnson, New Brunswick, NJ), followed by Ultrasoft and Gazelle (Boston Scientific).

Follow-up protocol and primary and secondary end points. Follow-up after the procedure was identical for all patients: clinical control by the attending surgeon and color duplex ultrasound imaging at 1 month, 6 months, 1 year, and annually thereafter.

The end points for the current study encompassed mayor adverse cardiovascular events, including myocardial infarction (MI), stroke, and cardiovascular death (fatal MI,

fatal cardiac failure, and fatal stroke), and also puncture site hematoma and recurrent restenosis.

The primary end points of the study were analyzed as early results. Results >30 days after the procedure and secondary end points were analyzed as long-term results. Median follow-up was 49.8 ± 22.8 months (range, 17-121 months). If significant recurrent restenosis (>50% symptomatic patients; >85% asymptomatic patients) was registered, multidetector CT angiography was performed for repeated angioplasty assessment.

All variables and risk factors that could predict the outcome were analyzed as well: (1) demographics (age and gender), (2) atherosclerosis risk factors (hypertension, dyslipidemia, smoking, and family history), (3) diabetes mellitus, (4) coronary disease, (5) contralateral carotid occlusion, (6) peripheral occlusive arterial disease, (7) time of CR occurrence after eCEA, defined as early (≤2 years) or late (>2 years); (8) previous TIA and stroke, (9) plaque characteristics (degree of stenosis, quality, embolic potential, calcifications, length and localization), (10) predilatation, and (11) type of stent and embolic protection devices used.

Statistical analysis. The normality of the data distribution was tested using the Kolmogorov-Smirnov test. Numeric variables were described using the arithmetic mean and standard deviation. The χ^2 test or Fisher exact test was used to test the significance of differences in the frequency distribution among the categories. To analyze the current level of measurement of the variables, we applied the Mann-Whitney test.

The Kaplan-Meier method was used for survival assessment. Cox univariate and multivariate analyses were performed to assess predictors of survival. Control covariates (age, gender, type of stent and protection device, risk factors) were also analyzed using the multivariate Cox regression model. The Breslow (generalized Wilcoxon) method was used for evaluation of the differences in the survival between the categories of patients. The minimum accepted level of significance of the first order error was 0.05. Data were statistically analyzed using SPSS 19.0 software (SPSS/IBM Corp, Armonk, NY).

RESULTS

The overall patient demographic characteristics are reported in Table I. Restenotic plaque characteristics are reported in Table II. The average time of the occurrence of restenosis was 4.07 ± 3.96 years (range, 6 months-17 years). In 57.7% of patients, intimal hyperplasia was the main reason for restenosis occurrence. Plaques consisting of intimal hyperplasia occurred earlier after primary surgery (3.54 ± 3.46 years) than atherosclerotic lesions (4.78 ± 4.26 years; $P = .048$).

The femoral artery was the access site in 93.4% of the patients, whereas the radial or brachial artery was used in 6.6% because of severe aortoiliac occlusive disease (4.7%), previous aortic bifemoral bypass graft (1.2%), or abdominal aortic aneurysm (0.6%).

Early results. All but one procedure ended with a technical success (99.69%), which was defined as the deployment of the carotid stent or balloon angioplasty alone. Six patients required multiple stents because of complicated lesions. PTA was performed in 12 patients without stent placement. Predilation was performed in 62 patients (19.4%), whereas postdilation was performed in 222 (69.6%).

In the early postoperative period, TIA occurred in 2.8% of the patients and stroke in 1.6%, followed by one death of a neurologic cause (0.3%; Table III). The most common stent-related complication was arterial spasm (1.9%), which resolved spontaneously in all cases.

In one patient (0.3%), stent thrombosis occurred 2 hours after the angioplasty. The patient presented with contralateral weakness, and emergency CT angiography revealed stent thrombosis. The patient underwent urgent

Table I. Patients' demographic and preoperative characteristics

Variables[a]	*Patients (N = 319)*
Gender	
Male	191 (71)
Female	128 (29)
Age, years	64.99 ± 7.87
Arterial hypertension	301 (94.4)
Hyperlipidemia	284 (89.02)
Smoking history	212 (66.5)
Diabetes mellitus	114 (35.7)
Heredity	162 (50.8)
Coronary artery disease	112 (35.1)
Previous MI	34 (10.6)
Previous CABG	27 (8.5)
Symptomatic patients	99 (31.03)
Asymptomatic patients	220 (68.96)
Contralateral ICA occlusion	19 (5.6)
Peripheral vascular disease	87 (27.3)

CABG, Coronary artery bypass grafting; *ICA,* internal carotid artery; *MI,* myocardial infarction; *TIA,* transient ischemic attack.
[a]Continuous data are shown as mean ± standard deviation and categoric data as number (%).

Table II. Occurrence and characteristics of carotid restenosis (*CR*) lesion

Variables[a]	*Patients (N = 319)*
Average time of CR occurrence, years	4.07 ± 3.96
Intimal hyperplasia	184 (57.7)
Novel atherosclerotic lesions	135 (42.3)
Plaque characteristic	
Stable	291 (91.2)
Ulcerated with embolic potential[b]	28 (8.8)
Calcified	39 (12.2)
Proximal CCA lesion only	26 (8.2)
Bifurcation and ICA origin	247 (77.4)
Diffuse CCA and ICA origin	46 (14.4)
Short lesion (≤15 mm)	238 (74.6)
Long lesion (>15 mm)	81 (25.4)

CCA, Common carotid artery; *ICA,* internal carotid artery.
[a]Continuous data are shown as mean ± standard deviation and categoric data as number (%).
[b]Plaque with ulcerated surface, echolucent.

Table III. Early postprocedural results (≤30 days)

Variable	*Patients (N = 319), No. (%)*
Residual stenosis (20%-30%)	7 (2.2)
Dissection of CCA	2 (0.6)
Spasm	6 (1.9)
Stent thrombosis	1 (0.3)
Conversion to open surgery	1 (0.3)
Hematoma/hemorrhage	7 (2.2)
TIA	9 (2.8)
Stroke	5 (1.6)
Mortality	
Neurologic	1 (0.3)
Non-neurologic	0

CCA, Common carotid artery; *TIA*, transient ischemic attack.

Table IV. Long-term results after angioplasty and carotid artery stenting (CAS) for carotid restenosis (CR) after eversion carotid endarterectomy (eCEA)

Long-term results	*Patients (N = 319), No. (%)*
RR	14 (4.4)
Treatment for RR	
Re-PTA	11 (3.4)
Redo surgery	3 (0.9)
Mortality	
Neurologic	0
Non-neurologic	10 (3.13)
Coronary angioplasty	32 (10.0)
Fatal MI	2 (0.6)
Peripheral angioplasty[a]	41 (12.9)

MI, Myocardial infarction; *PTA*, percutaneous transluminal angioplasty; *RR*, recurrent restenosis.
[a]Aortoiliac, femoropopliteal, distal crural.

surgery with Dacron (DuPont, Wilmington, Del) graft interposition. Brain CT performed after the surgery revealed ipsilateral acute ischemia; still, this patient completely recovered due to emergency surgery and fast revascularization.

Puncture site hematoma was verified in 2.2% of the patients, and 1.3% of these were surgically treated. Three patients (0.94%) were operated on for femoral access hematoma, and one patient (0.31%) for hematoma after brachial artery puncture. In two patients (0.6%), common carotid artery dissection was noted and was resolved by additional angioplasty and stenting.

Long-term results. No TIAs or strokes were verified during the follow-up, and non-neurologic mortality was 3.13% (Table IV). Two patients died after fatal MIs (0.6%), 1 after cardiac surgery (0.3%), 1 (0.3%) after multi-organ failure due to malignancy, and 7 lethal outcomes occurred due to an unknown cause. Recurrent restenosis occurred in 14 patients (4.4%). Repeated balloon angioplasty was performed in 12 patients, and graft interposition was performed in two patients because of extensive and calcified lesions. All procedures were uneventful.

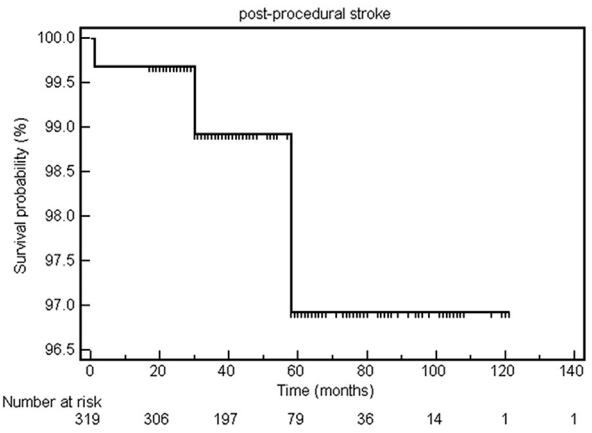

Fig 1. Kaplan-Meier curve shows survival rate after stroke following carotid angioplasty for recurrent stenosis. The standard error of survival after stroke was 0.0031 at 1 month, 0.0062 at 30 months, and 0.0153 at 58 months.

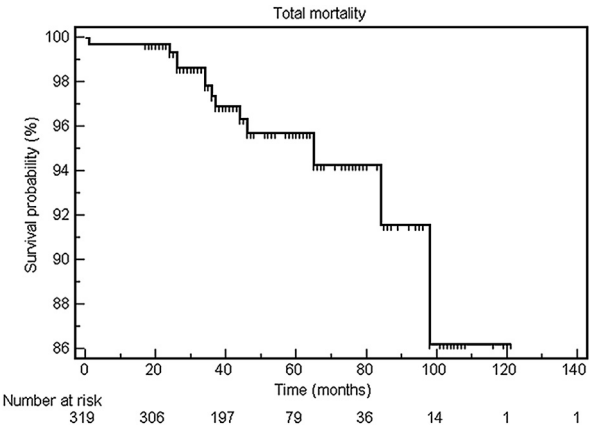

Fig 2. Kaplan-Meier curve shows overall mortality after carotid angioplasty for recurrent stenosis. The standard error of overall survival rate was 0.0031 at 1 month, 0.0047 at 26 months, 0.0074 at 34 months, 0.0087 at 36 months, 0.0098 at 37 months, 0.0113 at 44 months, 0.0129 at 46 months, 0.0191 at 65 months, 0.0326 at 84 months, and 0.0609 after 98 months.

The survival rate after stroke was 0.997 ± 0.0031 after 1 year and 0.969 ± 0.0153, both after 5 and 10 years (Fig 1). Estimated mean was 116.939 ± 1.376 months (95% confidence interval, 114.242-119.636 months). Overall mortality was also assessed by Kaplan-Meier method (Fig 2). The survival rate was 0.997 ± 0.0031 after 1 year, 0.949 ± 0.0191 after 5 years, and 0.868 ± 0.0609 after 10 years. Estimated mean survival time was 114.816 ± 2.018 months (95% confidence interval, 110.861-118.770 months).

Symptomatic vs asymptomatic CR. As reported in Table I, 99 of 319 patients (31.03%) were symptomatic and 220 (68.96%) were asymptomatic before CAS for recurrent stenosis. Before carotid angioplasty and stenting,

90 patients had a previous stroke, 11 had previous TIA, and 2 had both TIA and stroke. Patients with nonhemispheric symptoms (vertigo, dizziness, walking, and instability) were considered asymptomatic.

Preprocedural characteristics. Men comprised 69.7% of the asymptomatic group vs 55.5% of the symptomatic group, whereas women were 44.5% of the asymptomatic group and 30.3% of the symptomatic group ($P = .016$). Patients with a smoking history were more common in the symptomatic group than in the asymptomatic group (76.8% vs 62.4%; $P = .012$) group, as was contralateral internal carotid artery occlusion (10.1% vs 4.1%, $P = .036$).

Significant differences were observed when ischemic symptoms were assessed by the degree of restenosis. As expected, ulcerated plaques were more likely to be symptomatic than plaques that occurred as a result of intimal hyperplasia without ulcerations ($P = .005$).

Postprocedural results. When symptomatic and asymptomatic patients were compared by postprocedural results, no significant differences were found in any of the evaluated outcomes except for non-neurologic mortality (MI, cardiac morbidity, malignancy and sudden death of unknown cause) during the follow-up period (4.54% in asymptomatic group vs 0% in symptomatic group, $P = .034$; Table V). A Kaplan-Meier curve describing the mortality between the two groups is shown in Fig 3. All lethal outcomes were noted in asymptomatic patients, with a survival rate of 0.995 ± 0.0045 after 1 year, 0.918 ± 0.0316 after 5 years, and 0.730 ± 0.128 after 10 years.

Variables influencing carotid angioplasty outcome. The predictive value of different factors regarding outcome after carotid angioplasty for restenosis is presented in Table VI. Smoking history was highly predictive for postprocedural TIA occurrence (all nine patients with TIA were smokers), nonsmokers had a higher incidence for non-neurologic mortality during the follow-up period (nine vs two patients). Coronary artery disease was an important predictor for non-neurologic mortality during the follow-up period as well as for recurrent restenosis occurrence.

Female gender was associated with a higher incidence of non-neurologic mortality during the follow-up period, whereas plaque calcifications were a significant predictor of recurrent restenosis occurrence. Carotid angioplasty was performed at the bifurcation level in 10 of 14 patients (71.4%) with recurrent restenosis.

The type of the stent and embolic protection device used significantly strongly predicted neurologic outcome after the procedure. When the type of the stent was analyzed, postprocedural TIA was most frequent in patients who received a Precise stent (six of 49 [12.2%]), whereas the lowest incidence (0%) was noted in the 76 patients who received a Protégé stent. When we examined embolic protection device influence on outcome, the highest statistical incidence of postprocedural TIA was noted in patients in whom a Spider Fx device was used (five of 40 patients [12.5%]), whereas no postprocedural neurologic ischemic events occurred in the 150 patients in the FilterWire group.

Table V. Postprocedural results in symptomatic and asymptomatic patients

Postprocedural result	*Asymptomatic patients (n= 220), No. (%)*	*Symptomatic patients (n = 99), No. (%)*	P
Spasm	3 (1.3)	3 (3.03)	NS
Stent thrombosis	1 (0.45)	…	NS
Hematoma/ hemorrhage	7 (3.18)	…	NS
TIA	4 (1.8)	5 (5.05)	NS
Stroke	3 (1.3)	2 (2.02)	NS
Early mortality (<30 days)			
Neurologic	1 (0.45)	0	NS
Non-neurologic	0	0	…
Late mortality	0	0	…
Neurologic	…	…	…
Non-neurologic	10 (4.54)	0	.034

NS, Nonsignificant; *TIA,* transient ischemic attack.

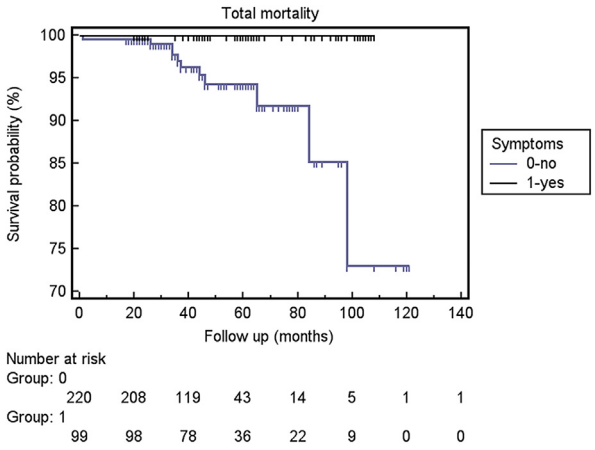

Fig 3. Kaplan-Meier curve shows mortality in symptomatic (*black line*) vs asymptomatic (*blue line*) patients after carotid angioplasty for recurrent stenosis. The standard error of survival rate in asymptomatic patients was 0.0045 at 1 month, 0.0046 at 26 months, 0.0112 at 34 months, 0.0133 at 36 months, 0.0153 at 37 months, 0.0177 at 44 months, 0.0205 at 46 months, 0.0316 at 65 months, 0.0696 at 84 months, and 0.1280 after 98 months (>10%).

DISCUSSION

CR is one of the major complications that follow carotid surgery.[17,18] CR appears in two different forms: early, caused by neointimal hyperplasia within the first 24 months after CEA, and late (the result of new atherosclerotic lesions), which occurs >2 years after CEA.[3,19]

Two modalities are recommended for the treatment of CR after CEA: CAS and redo surgery. Opponents of open redo surgery for CR highlight the increased risk of cranial nerve injury and postoperative morbidity due to recurrent tissue trauma.[20-23] Proponents of CAS report that CAS is safe and reliable for CR treatment.[11,24]

Table VI. Distribution of evaluated variables and their predictive value

Evaluated variable	*Evaluated outcome*	*Predictive value*	P
Smoking history	Postprocedural TIA	Significant	.032
Stent postdilatation	Postprocedural stroke	Significant	.031
Female gender	Non-neurologic mortality during the follow-up	Significant	.025
Smoking history	Non-neurologic mortality during the follow-up	High	.012
Coronary artery disease	Non-neurologic mortality during the follow-up	High	.015
Coronary artery disease	Recurrent restenosis	Extremely high	.007
Site of restenotic plaque	Recurrent restenosis	Extremely high	.009
Restenotic plaque calcification	Recurrent restenosis	Extremely high	.003
Type of stent	Postprocedural TIA	Significant	.033
Type of cerebral protection device	Postprocedural TIA	High	.001

TIA, Transient ischemic attack.

Because of the controversy and conflicting opinions concerning CR treatment, numerous studies have compared CAS and redo surgical treatment.[16,19,25] These studies registered a similar outcome after CAS and redo CEA, but CAS was still associated with a higher recurrent restenosis rate during the follow-up, whereas redo surgery had a higher incidence of cranial nerve injury.[16,19,25]

In the present study, the results of carotid angioplasty were analyzed in patients with CR that occurred exclusively after eCEA. No previously published studies have analyzed only post-eCEA restenosis treated by PTA, with or without stenting. The results of the present study revealed that CAS is a safe and reliable procedure for CR treatment, with a low rate of early and long-term post-procedural complications. De Borst et al[11] reported a 3.5% incidence of early TIA and no strokes or deaths in patients with CAS for restenosis, whereas significant recurrent restenosis was verified in 19% of their patients. Despite a longer follow-up, our study indicated better long-term results with a lower incidence of recurrent restenosis with a similar rate of early complications.

In our study, symptomatic patients were more likely to be males and smokers in whom contralateral internal carotid artery occlusion was more commonly observed. Despite the lower incidence of preprocedural ischemic symptoms compared with symptomatic patients, asymptomatic patients had higher mortality rate (4.54% vs 0%). This could be because there were more asymptomatic patients (69% vs 31%) who were also significantly older (65.92 ± 7.8 years vs 62.92 ± 7.67 years; $P = .002$). Similarly as in the studies published so far,[11,14,26] most of the patients in our study were asymptomatic (69%); still, the follow-up in the present study was significantly longer (range, 17-121 months). That no lethal outcomes were verified in symptomatic patients might seem surprising; however, the overall mortality rate was 3.13%, making the results of the present study appropriate and authentic.

In addition to the early-term and long-term results, our study highlights the importance of the procedural technical details during the CAS that influence postprocedural outcome. The highest rate of TIA was verified in patients in whom a Precise stent (6 of 49 patients [12.2%]) and in those in whom a Spider Fx cerebral protection device (5 of 40 patients [12.5%]) was used.

These facts are of great importance, especially when taking into consideration that in a significantly greater number of patients, a Carotid Wallstent was used with a lower rate of postprocedural ischemic events (3 of 158 [1.9%]). Similarly, a FilterWire cerebral protection device was used in 150 patients, and no postprocedural complications were observed. As for other predictors, coronary artery disease and plaque calcifications had a strong impact on the recurrent restenosis rate, whereas female gender and coronary artery disease influenced the higher incidence of non-neurologic lethal outcome during the follow-up period.

One important finding is that the present study confirms plaque calcification as a strong predictive factor for recurrent restenosis occurrence. Smoking history was associated with higher rate of postprocedural TIA but a lower rate of non-neurologic mortality during the follow-up period as well.

Thus, far no study has published similar results on the effect of stent and cerebral protection device selection on neurologic outcome after CAS in patients with CR. The results of the present study might provide important directions in future interventions to reduce the incidence of postprocedural neurologic complications.

When the present results were compared with our previously reported results for surgical treatment of CR,[10] a higher incidence of early postprocedural complications was noted after surgical treatment than after CAS (TIA: 7.6% vs 2.8%; stroke: 3.8% vs 1.6%; cranial nerve injury: 7.6% vs 0%).

According to our experience, we recommend carotid angioplasty and stenting as the first treatment modality in patients with significant carotid artery restenosis after eCEA. However, if carotid angioplasty is not possible, redo surgery is the preferable treatment option. This is our algorithm for the treatment of patients with CR after eCEA.

Limitations. This report compared many different materials used for PTA and CAS. Although the study was retrospective with prospectively collected data and involved small numbers of complications and materials, the variation between the variables, when significant, might be of clinical relevance. Furthermore, open repair was the preferable

treatment option in the first years of the study, and has currently has almost been completely replaced by CAS.

We included patients treated only with balloon angioplasty without stenting as well those treated with CAS. The reason for that choice was to present "real-world" treatment for restenosis after eCEA.

Keeping in mind that there is no common agreed upon protocol to assess the restenotic carotid plaque after CEA, we used standard ultrasound characteristics for primary atherosclerotic lesions, especially in the patients treated by CEA in the beginning of last decade of the last century. Our ultrasound criteria for restenosis diagnosis proved to be reliable, as we demonstrated that ultrasound imaging had a specificity of 97.7%, sensitivity of 100%, a positive-predictive value of 98.4% and a negative-predictive value of 100% compared with CT angiography.[27]

CONCLUSIONS

CAS is a safe and reliable procedure for CR treatment after eCEA, with a low rate of postprocedural complications. Female gender, coronary artery disease, plaque calcifications, and smoking history are associated with adverse outcome after CAS. The type of stent and cerebral embolic protection device and their selection during the stenting may influence the rate of postprocedural neurologic ischemic events.

AUTHOR CONTRIBUTIONS

Conception and design: DR, ST, DS, ZA, ZR
Analysis and interpretation: DR, SA, SB, PP, PM, ZR
Data collection: DR, ST, SB, ZR
Writing the article: DR, ST, SG, ZR
Critical revision of the article: DR, ZA, PP, PM, SB, ZR
Final approval of the article: DR, ST, DG, ZA, PP, SB, PM, ZR
Statistical analysis: DR, ST, SB, PP
Obtained funding: DR
Overall responsibility: DR

REFERENCES

1. European Carotid Surgery Trialists Group. MRC European carotid surgery trial: interim result for symptomatic patients with severe (70-99%) or with mild (0-29%) carotid stenosis. Lancet 1991;337:1235-43.
2. Executive Committee for ACAS Study. Endarterectomy for asymptomatic carotid artery stenosis. JAMA 1995;273:1243-421.
3. Carballo RE, Towne JB, Seabrook GR, Freischlag JA, Cambria RA. An outcome analysis of carotid endarterectomy: the incidence and natural history of recurrent stenosis. J Vasc Surg 1996;23:749-54.
4. Roederer CO, Langlois YE, Jagar KA, Primozich JF, Beach KW, Phillips DJ, et al. The natural history of carotid artery disease in asymptomatic patients with cervical bruits. Stroke 1984;15:605-13.
5. Frericks H, Kievit J, van Baalen JM, van Bockel JH. Carotid recurrent stenosis and risk of ipsilateral stroke: a systematic review of the literature. Stroke 1998;29:244-50.
6. O'Donnell TF Jr, Rodriquez AA, Fortunato JE, Welch HJ, Mackey WC. Management of recurrent carotid stenosis: should asymptomatic lesions be treated surgically? J Vasc Surg 1996;24:207-12.
7. Hobson RW 2nd, Goldstein JE, Jamil Z, Lee BC, Padberg FI Jr, Hanna AK, et al. Carotid restenosis: operative and endovascular management. J Vasc Surg 1999;29:228-35.
8. Aburahma AF, Jennings TG, Wulu JT, Tarahji L, Robinson PA. Redo carotid endarterectomy versus primary carotid endarterectomy. Stroke 2001;32:2787-92.
9. Meyer FB, Piepgras DG, Fode NC. Surgical treatment of recurrent carotid artery stenosis. J Neurosurg 1994;80:781-7.
10. Radak D, Davidovic L, Tanaskovic S, Koncar I, Babic S, Kostic D, et al. Surgical treatment of carotid restenosis after eversion endarterectomy—Serbian bicentric prospective study. Ann Vasc Surg 2012;26:783-9.
11. Borst De, Ackerstaff R, de Vries JP, vd Pavoordt ED, Vos JA, Overtoom TT, et al. Carotid angioplasty and stenting for post-endarterectomy stenosis: long-term follow-up. J Vasc Surg 2007;45:118-23.
12. Vitek JJ, Roubin GS, New G, Al-Mubarak N, Iyer SS. Carotid angioplasty with stenting in post-carotid endarterectomy restenosis. J Invasive Cardiol 2001;13:123-5.
13. Lanzino GL, Mericle RA, Lopes DK, Wakhloo AK, Guiterman LR, Hopkins LN. Percutaneous transluminal angioplasty and stent placement for recurrent carotid stenosis. J Neurosurg 1999;90:688-94.
14. McDonnell CO, Legge D, Twomey E, Kavanagh EG, Dundon S, O'Donohoe MK, et al. Carotid artery angioplasty for restenosis following endarterectomy. Eur J Vasc Endovasc Surg 2004;27:163-6.
15. Radak D, Tanasković S, Matić P, Babić S, Aleksić N, Ilijevski N. Eversion carotid endarterectomy—our experience after 20 years of carotid surgery and 9897 carotid endarterectomy procedures. Ann Vasc Surg 2012;26:924-8.
16. AbuRahma AF, Abu-Halimah S, Hass SM, Nanjundappa A, Stone PA, Mousa A, et al. Carotid artery stenting outcomes are equivalent to carotid endarterectomy outcomes for patients with post-carotid endarterectomy stenosis. J Vasc Surg 2010;52:1180-7.
17. Moore WS, Kempezinski RF, Nelson JJ, Toole JF. Recurrent carotid stenosis. Stroke 1998;29:2018-25.
18. Johnson CA, Tollefson DF, Olsen SB, Andersen CH, McKee-Johnson J. The natural history of early recurrent carotid artery stenosis. Am J Surg 1999;177:433-636.
19. AbuRahma AF, Bates MC, Stone PA, Wulu JT. Comparative study of operative treatment and percutaneous transluminal angioplasty/stenting for recurrent carotid disease. J Vasc Surg 2001;34:831-8.
20. Cho JS, Pandurangi K, Conrad MF, Shepard AS, Carr JA, Nypaver TJ, et al. Safety and durability of redo carotid operation: an 11-year experience. J Vasc Surg 2004;39:155-61.
21. Chakhtoura EY, Hobson RW 2nd, Goldstein J, Simonian GT, Lal BK, Haser PB, et al. In-stent restenosis after carotid angioplasty-stenting: incidence and management. J Vasc Surg 2001;33:220-6; discussion: 225-6.
22. Zhou W, Lin PH, Bush RL, Peden EK, Guerrero MA, Kougias P, et al. Management of in-stent restenosis after carotid artery stenting in high-risk patients. J Vasc Surg 2006;43:305-12.
23. O'Hara PJ, Hertzer NR, Karafa MT, Mascha EJ, Krajewski LP, Even EG. Reoperation for recurrent carotid stenosis: early results and late outcome in 199 patients. J Vasc Surg 2001;34:5-12.
24. New G, Roubin GS, Iyer SS, Vitek JJ, Wholey MH, Diethrich EB, et al. Safety, efficacy, and durability of carotid artery stenting for restenosis following carotid endarterectomy: a multicenter study. J Endovasc Ther 2000;7:345-52.
25. Bowser AN, Bandyk DF, Evans A, Novotney M, Leo F, Back MR, et al. Outcome of carotid stent-assisted angioplasty versus open surgical repair of recurrent carotid stenosis. J Vasc Surg 2003;38:432-8.
26. Vos JA, de Borst GJ, Overtoom TT, de Vries JP, van de Pavoordt ED, Zanen P, et al. Antonius Carotid Endarterectomy, Angioplasty, and Stenting Study Group. Carotid angioplasty and stenting: treatment of post carotid endarterectomy restenosis is at least as safe as primary stenosis treatment. J Vasc Surg 2009;50:755-61.
27. Aleksic N, Tanaskovic S, Radak S, Mitrasinovic A, Kolar J, Babic S, et al. Color duplex sonography in the detection of internal carotid artery restenosis after carotid endarterectomy: comparison with computed tomographic angiography. J Ultrasound Med 2011;30:1677-82.

Submitted Feb 26, 2014; accepted Mar 27, 2014.