Original Article

Outcome of Carotid Stenting in Patients Undergoing Angioplasty

Seifolah Abdi [2], MD; Faramarz Amiri [1], MD; Omid Shafe*[2], MD; Reza Ebrahmi Rad [3], MD; Hamid Fakhreddin [1], MD; Alireza Jebeli [1], MD; Seyed Abdullah Sayadmanesh [1], MD; Moslem Shadmani [1], MD; Ebrahim Ghobadi [1], MD

ABSTRACT

Background: Carotid artery stenosis accounts for 10% of all ischemic strokes. Carotid endarterectomy (CEA) and carotid artery stenting (CAS) are currently the treatment for stroke prevention.

Methods: We sought to compare the efficacy and safety of each treatment in patients with carotid artery stenosis. After treatment, the patients were evaluated regarding their outcomes during the 1st and 6th postprocedural months.

Result: Sixty-nine patients (45 male [65.2%] and 24 female [24.8%]) at a mean age of 63.85 ± 14.17 years were enrolled. In 12 (17.4%) patients, both left and right carotid arteries were stenotic. Neither CEA nor CAS had in-hospital and procedural complications. However, in longer-term follow-up, transient ischemic attack occurred in 2 (2.9%) patients in the CEA group, while significant in-stent restenosis occurred in 2 (2.9%) patients after CAS. Multivariate analysis showed no association between smoking, coronary artery disease, dyslipidemia, hypertension, diabetes mellitus, and age and stent stenosis (P = 0.9, P = 0.9, P = 0.5, P = 0.6, P = 0.8, and P = 0.1, correspondingly).

Conclusions: Both CEA and CAS are approved therapeutic strategies for the treatment of carotid artery stenosis. Low complications and good results can be expected if case selection is done according to the current guidelines. ***(Iranian Heart Journal 2017; 18(1):37-43)***

Keywords: Carotid stenosis, Carotid artery stenting, Carotid endarterectomy

[1] Rajaie Cardiovascular, Medical, and Research Center, Iran University of Medical Sciences, Tehran, I.R. Iran.
[2] Cardiovascular Intervention Research Center, Rajaie Cardiovascular, Medical, and Research Center, Iran University of Medical Sciences, Tehran, I.R. Iran.
[3] Azad Islamic University Complex, Tonekabon Mazandaran, I.R. Iran.

***Corresponding Author:** Omid Shafe, MD; Rajaie Cardiovascular, Medical, and Research Center, Iran University of Medical Sciences, Tehran, I.R. Iran.
E-mail: omid-shafe@hotmail.com **Tel:** 02123922088

Received: October 30, 2016 **Accepted:** February 4, 2017

For the treatment of extracranial carotid artery disease in patients at high risk for adverse events, in 2004, the United States' Food and Drug Administration (FDA) approved the 1st endovascular device system, carotid endarterectomy (CEA), for practice in the country. Meanwhile, carotid artery stenting (CAS) has been performed with increasing numbers in different hospital settings. After the 1st adoption phase in CAS,

there was a noticeable decrease in the rates of adverse outcomes, conceivably related to improved patient selection and increased operator experience. [1] Owing to this accumulating CAS experience, a better understanding of the factors related to the increased risk of adverse outcomes has been possible. During the past 5 years, it has been confirmed that patient-related factors such as age, [2–5] symptom status, [2, 3] timing of symptoms before CAS, [3–5] patient comorbidities, [4, 6, 7] concurrent medications, [2] and smoking history [4] all might influence the outcome. CAS outcomes are also impacted by physician-related factors, including training and experience, as well as hospital volume. [2] Furthermore, these factors are not yet well characterized, while the progression in our understanding of risk predictors and the improvement of outcomes for CAS seem to mirror the experience previously demonstrated for CEA. [8] In the North American Symptomatic Carotid Endarterectomy Trial (NASCET), contralateral occlusion was not excluded, but it resulted in a 30-day risk of stroke and death of 14.3%. Additionally, in the Asymptomatic Carotid Atherosclerosis Study (ACAS), it led to a 2% increase in stroke and death compared with medical therapy. Since the publication of these 2 trials, there has been a broad use of CEA, including in patients with high surgical risks, as a result of the extrapolation of the outcomes of these studies. [9] CEA has been revealed effective as the preventive treatment for symptomatic and asymptomatic diseases. [1–3] CAS was introduced in 1994 and provides another choice of treatment. There are different results of randomized trials comparing CAS with CEA for symptomatic patients. [4–6] The Carotid Revascularization Endarterectomy Versus Stenting Trial (CREST) compared CAS with CEA in both symptomatic and asymptomatic patients. [7]

The aim of the present study was to analyze the outcomes of CEA for physician- or site-related variables associated with differential outcomes for CAS.

METHODS

In this case series, 69 patients who underwent angioplasty between Jun 2013 and June 2015 in our tertiary care center were enrolled. Two methods of treatment are performed for carotid stenosis (CS), namely CEA with surgery or stenting through the femoral artery access. [10] All the patients who underwent carotid stenting were enrolled, and those with intra-arterial coiling and angiography without angioplasty were excluded. A large number of studies have compared these 2 methods. [10] In the present study, all the data on the patients who underwent carotid angioplasty were recorded regarding the presence of neurological and clinical symptoms—whether bilateral or ipsilateral—via Doppler sonography. The success of treatment was evaluated in terms of the patients' recovery and absence of symptoms as well as follow-up outcomes by Doppler sonography. The patients underwent carotid angiography and carotid stenting 1 day after hospitalization, and primary care and laboratory examination were performed. In this study, the patients who were diagnosed with CS via Doppler sonography but did not show considerable stenosis on angiography and had no need for stenting were entirely excluded.

Statistical Analysis

The Mann–Whitney *U*-test was used to measure the relationship between the ordinal and categorical variables. SPSS 18.0 (Chicago, USA) was used for all the statistical analyses. The continuous and categorical variables are presented as means ± standard deviations (SDs) and percentages. The Student *t*-test was utilized to compare the quantitative variables, and the χ^2 test was applied to compare the categorical variables. The 2 groups were compared using the Pearson χ^2 or the Fisher exact test for the

categorical variables. A nonparametric test (Kruskal–Wallis test) was employed to remove the effect of the confounding factors of the variables.

RESULTS

In this study, 69 patients (45 [65.2%] male and 24 [24.8%] female) at a mean age of 63.85 ± 14.17 years were enrolled. The patients were divided into 3 groups: 11 (15.9%) patients who showed occlusion during the accidental assessment of their carotid arteries, 50 (72.2%) patients who were hospitalized due to cerebrovascular accident/transient ischemic attack (CVA/TIA) and were referred due to carotid occlusion, and 8 (11.6%) cases with neurological disorders who were hospitalized due to CS. All the patients' demographic and clinical data are depicted in Table 1. The patients were evaluated regarding their outcomes during the 1st and 6th postprocedural months via Doppler sonography and were administered ASA (80 mg/d) and Plavix (75 mg/d) and then continued on ASA (80 mg/d). Twenty-four (34.8%) cases had single right CS, 23 (33.2%) had left CS, and 12 (17.4%) had left and right stenoses. Two patients had left or right CS concomitant with vertebral, basilar, or subclavian stenosis. Six cases had complete left or right CS without any flow in addition to the severe stenosis of the other side and 2 (2.9%) cases were hospitalized owing to carotid dissection. The prevalence of the patients according the location of their CS is illustrated in Table 2. None of the patients showed periprocedural complications such as stroke, TIA, myocardial infarction, and bleeding. Apropos delayed postoperative complications, 2 (2.9%) cases suffered TIA, but their stent was open; therefore, it does not seem that it was related to the stent. With the exception of 1 case with a pacemaker, all the patients presented with sinus rhythm. As regards stent stenosis, 4 (5.4%) cases had mild stenosis (< 39%), 1 (1.4%) patient had moderate stenosis (40%–69%), 2 (2.9%) cases had severe stenosis (> 70%), and 1 (1.4%) patient had dissection. The stenoses were categorized as moderate to severe. Totally, 3 (4.5%) cases had moderate-to-severe stenosis and 1 (1.4%) case had dissection; nevertheless, none of the cases had CVA or TIA. Typically, the stenosis was unilateral. In 3 (4.3%) patients who underwent angioplasty, new stenosis was seen on the other side.

The patients with severe stent stenosis had a history of CVA, and a significant relation between stent restenosis and previous CVA/TIA was found ($P = 0.3$). There was no association between stent stenosis and the side of stenting ($P = 0.4$). Stenting was performed in the common carotid to the eternal carotid in some of the patients; no significant difference was seen between restenosis and the length of the stent ($P = 0.3$). No significant relationship was also found between hypertension ($P > 0.05$), coronary artery disease ($P = 0.6$), diabetes mellitus ($P = 0.9$), dyslipidemia ($P > 0.05$), and smoking ($P = 0.9$). The result of the multivariate analysis showed no association between coronary artery disease, dyslipidemia, hypertension, diabetes mellitus, and age and CS ($P = 0.9$, $P = 0.9$, $P = 0.5$, $P = 0.6$, $P = 0.8$, and $P = 0.1$, respectively). The relationships between the clinical data and stent stenosis are shown in Table 3.

Table 1. Demographic and baseline clinical data

Variables	N(%)
Male	54(65.2%)
Female	24(34.8%)
No symptoms	11(15.9%)
CVA/TIA	50(72.5%)
Neurological disorder	8(11.6%)
Right side	24(34.8%)
Left side	23(33.3%)
Right and left	12(17.4%)
R/L and vertebral or basilar	2(2.9%)
HTN	18(26.1%)
CAD	10(14.5%)
CS	3(4.3%)

R, Right; L, left; CVA, Cerebrovascular accident; TIA, Transient ischemic attack; HTN, Hypertension; CAD, Coronary artery disease; CS, Carotid stenosis

Iranian Heart Journal; 2017; 18 (1)

Table 2. Complications and clinical data during and after surgery or at follow-up

		N (%)
Stent stenosis	Mild	4(5.8%)
	Moderate	1(1.4%)
	Severe	2(2.9%)
	Dissection	1(1.4%)
Bilateral stent stenosis		1(1.4%)
Unilateral stent stenosis		7(10.1%)
No side		61(88.4%)
stenosis on contralateral side		3(4.3%)
Complications		1(1.4%)

Table 3. The relationship between the clinical and demographic data and stent stenosis

	No Stenosis	Mild Stenosis	Moderate Stenosis	Severe Stenosis	*P*
Male	39	3	1	1	0.8
Female	22	1	0	1	0.8
CVA/TIA	45	3	1	0	0.03
Neurological disorder	6	0	0	2	0.03
No symptoms	10	1	0	0	0.03
Side before stenting					
Right	22	1(1.4%)	0	0	0.4
Left	22	0	0	1(1.4%)	
R+L	9	2(2.9%)	0	1(1.4%)	
R/L+ vertebral of basilar	2(2.9%)	0	0	0	
Stent stenosis, total occlusion	4	0	0	0	
Dissection	61	4	1(1.4%)		

CVA, Cerebrovascular accident; TIA, Transient ischemic attack; R, Right; L, Left
A *P* value < 0.05 was considered the level of significance.

DISCUSSION

The CREST study showed that out of 2000 patients who underwent angioplasty or endarterectomy, 120 cases developed restenosis during 2 years of follow-up. In these patients, hyperlipidemia and diabetes mellitus were the causes of restenosis. The stenosis was mostly seen in the 1st year of follow-up. Another study defined the time interval between the incidence of CVA and the performance of clinical treatment as a variable and suggested that angioplasty be avoided during the acute phase of the disease. Elsewhere, the rate of restenosis in patients with diabetes mellitus and TIA was in line with that in our study. We found no significant relationships between age, diabetes mellitus, and hyperlipidemia, which may be due to our small sample size. [10]

Previous investigations demonstrated that CAS and CEA had comparable outcomes in symptomatic and asymptomatic male and female patients, although there was a lower incidence rate of myocardial infarction directly after CAS and a lower incidence of stroke immediately after CEA. [11, 12] One study reported that its older patients had a better outcome after CEA, while its younger patients had a slightly better outcome following CAS. [13] Consequently, patients' preferences and their age may be important considerations in the choice of treatment for CS. The relationship between advancing age and increasing adverse events after CAS has been highlighted previously [14, 5, 15] and the effect of advancing age on treatment differences, CAS versus CEA, was revealed in the Stent-Protected Angioplasty versus Carotid Endarterectomy (SPACE) trial.

The periprocedural safety outcomes for CAS and CEA are the best stated to date for patients with pre- and postprocedural medical, neurological, ECG, and enzyme evaluations.

An effective credentialing process for the surgeon, rigorous training and credentialing process for the interventionist, and increasing integration of endovascular expertise might be the reflection of these brilliant CREST outcomes. [14] Advanced and supplementary medical therapies that are commonly used may also be an explanation for the favorable outcomes observed after CEA in the CREST study compared with outcomes in previous randomized clinical trials of CEA. [9, 16–19]

Two analyses [16, 17] have confirmed the need for prospective neurological evaluations before and after CEA to best estimate the outcome, with a 3-fold increase in events via neurological assessment compared with outcomes that were otherwise self-reported; this is especially applicable since the NASCET and ACAS trials used such evaluations and constitute the basis for the guidelines of the American Heart Association (AHA). Likewise, it is remarkable that in the original CAPTURE study, [20] CEA adjudication led to the identification of 50% more 30-day adverse outcome events compared with the site-reporting of events alone; thereby approving the importance of both prospective data gathering and the adjudication process in providing full reporting of the outcomes. [9] In the present study, no significant relationship was found between neurological disorders and stent stenosis ($P > 0.05$).

While there continues to be disagreement in some circles regarding the actual definition of high surgical risk, [21, 22] recent randomized data have confirmed the perception vis-à-vis the increase in stroke and death outcomes in a predefined surgical population with both physiological and anatomical surgical risks. [23] Nonetheless, in the 10 years since the publication of the AHA's guidelines, there has not been a similarly rough demonstration of the fulfillment of the guidelines in the high-surgical-risk population undergoing CEA. [9]

CAS, when performed by experienced and skilled interventionists, has patient outcomes comparable to those of CEA performed by experienced and skilled surgeons. During the perioperative period, more incidences of stroke arise after CAS. Younger patients have a considerably better outcome with CAS and older patients have a better outcome with CEA. For the future, both CEA and CAS appear to be suitable tools for preventing stroke. In the present study, the rate of stent stenosis in the patients with CS who were hospitalized with CVA was higher than the other outcome ($P < 0.05$). The results of our study chime in with another investigation that showed that the most significant cause of CS was CVA/TIA. The rate of total occlusion in our study was 5%–7%. Additionally, the rate of postoperative complications was not considerable. It has been suggested that follow-up of the stenosis be continued on the other side of the carotid artery. Six months' or yearly follow-up of the stented side has been recommended.

In the current study, successful flow was achieved by opening the occlusion in the patients with severe stenosis. Nevertheless, complete occlusion and concomitant absence of flow was detected on the other side. No treatment was performed while the other side was reopened, and there was no complication during surgery. Among our study population, the most significant complications were CVA and TIA; however, no myocardial infarction and major and minor bleeding occurred. Our results were in accordance with the outcomes of other studies, although the procedures were different. With regard to the patients' recovery after surgery, almost 97% of the cases recovered well. The remaining few experienced delayed TIA after surgery. Regarding the patients suffering mild and severe stent stenosis, dissection was seen in 1 (1.4%) of the cases. One (1.4%) patient had Takayasu's arteritis and had a different clinical outcome and showed bilateral stenosis. Stent stenosis was mostly seen in the patients who underwent stent implantation due to CVA ($P = 0.03$). Thirteen of the cases with CS had diabetes mellitus; no significant

relationship was, however, found between stent stenosis and diabetes mellitus ($P > 0.05$). These results are not concordant with those previously reported. Two (2.9%) cases were assessed regarding dissection with no significant stenosis.

In the CREST study, smoking was introduced as the main risk factor in patients undergoing endarterectomy. In contrast, in our study, no significant relationship was found between smoking and CS ($P > 0.05$). There was only a significant relationship between the patients with CVA/TIA and restenosis; this finding is consistent with the results of the studies reporting the occurrence of stenosis during the 1st month of evaluation ($P < 0.05$). [10] Among the perioperative complications in our study, there was 1 (1.4%) patient with TIA. In the present study, all the implanted stents were particularly bare-metal ones and the results are similar to those of the previous studies, although the latter investigations had larger populations.

Limitations

The major limitation of the present study is our small sample size, which underscores the essential need for further research with a greater sample size.

ACKNOWLEDGEMENTS

The authors express their gratitude to Dr Mona Heidarali for her assistance in the scientific writing of the manuscript.

Conflict of Interest: There was no conflict of interest. This manuscript was financially supported by a fund awarded by Iran University of Medical Sciences, Tehran, I.R. Iran.

REFERENCES

1. Goldstein LB, Adams R, Alberts MJ, Appel LJ, Brass LM, Bushnell CD, et al. Primary prevention of ischemic stroke: a guideline from the American Heart Association/American Stroke Association Stroke Council: cosponsored by the Atherosclerotic Peripheral Vascular Disease Interdisciplinary Working Group; Cardiovascular Nursing Council; Clinical Cardiology Council; Nutrition, Physical Activity, and Metabolism Council; and the Quality of Care and Outcomes Research Interdisciplinary Working Group: The American Academy of Neurology affirms the value of this guideline. Stroke. 2006; 37:1583–1633.

2. Adams RJ, Albers G, Alberts MJ, Benavente O, Furie K, Goldstein LB, Gorelick P, Halperin J, Harbaugh R, Johnston SC, Katzan I, Kelly-Hayes M, Kenton EJ, Marks M, et al. Update to the AHA/ASA recommendations for the prevention of stroke in patients with stroke and transient ischemic attack. Stroke. 2008;39:1647–1652.

3. Ederle J, Featherstone RL, Brown MM. Percutaneous transluminal angioplasty and stenting for carotid artery stenosis. Cochrane Database Syst Rev. 2007;4: CD000515.

4. Yadav JS, Wholey MH, Kuntz RE, Fayad P, Katzen BT, Mishkel GJ, et al. Protected carotid-artery stenting versus endarterectomy in high-risk patients. N Engl J Med. 2004; 351: 1493–1501.

5. Ringleb PA, Allenberg J, Bruckmann H, Eckstein HH, Fraedrich G, Hartmann M, et al. 30 day results from the SPACE trial of stent-protected angioplasty versus carotid endarterectomy in symptomatic patients: a randomized non-inferiority trial. Lancet. 2006;368:1239 –1247.

6. Mas JL, Chatellier G, Beyssen B, Branchereau A, Moulin T, Becquemin JP, et al. Endarterectomy versus stenting in patients with symptomatic severe carotid stenosis. N Engl J Med. 2006; 355:1660 –1671.

7. Brott TG, Hobson RW II, Howard G, Roubin GS, Clark WM, Brooks W, et al. Stenting versus endarterectomy for treatment of carotid-artery stenosis. N Engl J Med. 2010;363:11–23.

8. Sheffet AJ, Roubin G, Howard G, Howard V, Moore W, Meschia J, Hobson RW II, Brott TG. Design of the Carotid Revascularization

Endarterectomy vs Stenting Trial (CREST). Int J Stroke. 2010; 5:40–46.

9. [No authors listed]. Endarterectomy for asymptomatic carotid artery stenosis. Executive Committee for the Asymptomatic Carotid Atherosclerosis Study. JAMA. 1995; 273:1421–1428.

10. William A. Gray, Seemant Chaturvedi, Patrick Verta. Thirty-Day Outcomes for Carotid Artery Stenting in 6320 Patients From 2 Prospective, Multicenter, High-Surgical-Risk Registries.; (Circ Cardiovasc Intervent. 2009;2:159-166

11. Brajesh K Lal, Kirk W Beach, Gary S Roubin, Helmi L Lutsep, Wesley S Moore, Mahmoud B Malas, et al. Restenosis after carotid artery stenting and endarterectomy: a secondary analysis of CREST, a randomised controlled trial., Lancet Neurol 2012; 11: 755–63

12. Landesberg G, Shatz V, Akopnik I, Wolf YG, Mayer M, Berlatzky Y, et al. Association of cardiac troponin, CK-MB, and postoperative myocardial ischemia with long-term survival after major vascular surgery. J Am Coll Cardiol. 2003;42:1547–1554.

13. van Wijk I, Koudstaal P, Kappelle L, van Gijn J, Gorter J, Algra A, et al. Long-term occurrence of death and cardiovascular events in patients with transient ischaemic attack or minor ischaemic stroke: comparison between arterial and cardiac source of the index event. J Neurol Neurosurg Psychiatry. 2008; 79:895–899

14. Chiam PT, Roubin GS, Iyer SS, Green RM, Soffer DE, Brennan C, et al. Carotid artery stenting in elderly patients: importance of case selection. Catheter Cardiovasc Interv, 2008;72:318 –324.

15. Hopkins LN, Rougin GS, Chakhtoura EY, Gray WA, Ferguson RD, Katzen BT, et al. The Carotid Revascularization Endarterectomy vs Stenting Trial: credentialing of interventionalists and final results of lead-in phase. J Stroke Cerebrovasc Dis. 2010;19: 153–162.

16. Carotid artery stenting compared with endarterectomy in patients with symptomatic carotid stenosis (International Carotid Stenting Study): an interim analysis of a randomised controlled trial. Lancet. 2010; 375: 985–997.

17. Beneficial effect of carotid endarterectomy in symptomatic patients with high-grade carotid stenosis. North American Symptomatic Carotid Endarterectomy Trial Collaborators. N Engl J Med. 1991;325: 445– 453.

18. Barnett HJ, Taylor DW, Eliasziw M, Fox AJ, Ferguson GG, Haynes RB, et al. Benefit of carotid endarterectomy in patients with symptomatic moderate or severe stenosis. North American Symptomatic Carotid Endarterectomy Trial Collaborators. N Engl J Med. 1998;339: 1415–1425.

19. Randomised trial of endarterectomy for recently symptomatic carotid stenosis: final results of the MRC European Carotid Surgery Trial (ECST). Lancet 1998; 351: 1379 –1387.

20. Halliday A, Mansfield A, Marro J, Peto C, Peto R, Potter J, et al. Prevention of disabling and fatal strokes by successful carotid endarterectomy in patients without recent neurological symptoms: randomized controlled trial. Lancet 2004; 363:1491–1502.

21. Gray WA, Yadav JS, Verta P, Scicli A, Fairman R, Wholey M, et al. The CAPTURE registry: results of carotid stenting with embolic protection in the post approval setting. Catheter Cardiovasc Interv. 2007; 69:341–348.

22. Mozes G, Sullivan TM, Torres-Russotto DR, Bower TC, Hoskin TL, Sampaio SM, et al. Carotid endarterectomy in SAPPHIRE-eligible high-risk patients: implications for selecting patients for carotid angioplasty and stenting. J Vasc Surg. 2004; 39:958 –965.

23. Boules TN, Proctor MC, Aref A, Upchurch GR Jr, Stanley JC, Henke PK. Carotid endarterectomy remains the standard of care, even in high-risk surgical patients. Ann Surg. 2005; 241:356 –363.

24. Yadav JS, Wholey MH, Kuntz RE, Fayad P, Katzen BT, Mishkel GJ, et al. Protected carotid-artery stenting versus endarterectomy in high-risk patients. N Engl J Med. 2004; 351:1493–1501.