

Neurological Outcome of Stenting in Carotid Occlusive Diseases

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Abstract

Background: Carotid artery stenting (CAS) has become widely available and considered as an alternative to carotid endarterectomy.

Objective: To compare CAS under protection device with medical treatment.

Material and Method: Fifty patients were enrolled in these study (30 patients treated with carotid stenting and 20 patients managed medically) with stenosis > 60% with follow up at six months later clinically and radiologically using carotid duplex.

Result: After 6 months 4 (13.4%) patients in CAS group develop TIA while in medically treated group 6 (30%) patients, 1 (3.3%) patient in CAS group develop stroke which was after procedure while 6 (30%) patients in medically treated group develop stroke during follow up within 6 months, 1 (3.3%) patient die in CAS group due to myocardial infarction, while in medically treated group 2 (10%) patients died one of them due to large stroke and the other due to myocardial infarction. There was high significant difference between CAS and medical treated group after 6 months ($p < 0.01$).

Conclusion: CAS under protection device is associated with better outcome than medical treatment.

Introduction

Stroke is estimated to be responsible for 5.5 million deaths worldwide annually. It is now the leading cause of disability in developed countries. Of those affected by first stroke approximately one third die, one third recover and one third are disabled [1].

Keywords

Carotid Artery Stenting;
Medical Treatment;
Neurological Outcome;
Carotid Stenosis.

Stroke risk increase with stenosis severity and plaque morphology. The aim of the treatment of carotid artery stenosis is to prevent neurological complications; this could be achieved by medical treatment, surgical or endovascular interventions [2].

Complications related to CEA which either early or late and Some them are devastating complications that involve the neurological system. These tend to occur early, within the first 30 days after surgery. [3].

Since the inception of carotid angioplasty over two decades ago, techniques and equipment for carotid artery stenting (CAS) have radically improved. Equipment with lower profile (e.g., smaller outer diameter sheaths with large inner lumen, 0.014" system balloon catheters and stent catheters) and targeted to carotid arteries (e.g., emboli protection devices, self-expanding stents) have evolved dramatically, lead-ing to improved technical success and procedural safety of CAS especially for high risk surgical patients with low morbidity and mortality. [4].

Materials and Methods

This prospective study was conducted on fifty patients with carotid stenosis more than 60% between 2011 and 2015 after obtaining a written informed consent from all patients. Thirty patient treated with carotid stenting and twenty patients were managed medically. Exclusion criteria include Major functional impairment (modified Rankin Scale ≥ 3), Significant cognitive impairment. Major stroke within 4 weeks (new neurological event that persisted after 7 days and increased NIH stroke scale score by ≥ 4). Contraindication to acetylsalicylic or dual antiplatelet treatment for 4 weeks. Inability to achieve safe vascular access, Intracranial aneurysm > 2 mm or AVM requiring treatment. Concentric heavy lesion calci-fication, visible thrombus in lesion. Total occlusion and Long subtotal occlusion (string sign).

All patients were subjected to complete history taking, bed side examination including general ex-

aminations, full neurological examinations scales (NIHSS) scale [5] and modified Rankin Scale [6] at 4 points (Before CAS, within 3 days after the procedure, one month, 6 months after the procedure, and when necessary).

Also carotid duplex \pm MRA or CTA (neck vessels) at day zero and after 6 months and laboratory investigations (complete blood count, PT, PTT, liver and renal function tests, random blood sugar, lipid profile and serum uric acid), ECG and trans-thoracic echocardiography.

CAS Procedure

All patients will be treated with acetyl-salicylic acid (150 mg/d) associated with clopidogrel (75 mg/d) for one week or 300 mg clopidogrel at least 24 h before the procedure. the procedures were performed with local anesthesia then percutaneous transfemoral access F8 with heparin to achieve an activated clotting time (ACT) longer than 200-250 sec. and atropine (0.51 mg IV) will be given in order to reduce the bradycardia and hypotension potentially associated with carotid dilation.

All patients will undergo an angiographic examination of the culprit carotid lesion in at least two different real-time projections and an angiographic examination of intracranial circulation in antero-posterior and lateral projection.

The guidewire will be used to cross the carotid-artery stenosis first, and then the filter will be expanded before the stent deployment.

Carotid stenting will be carried out by using self-expandable crush resistant stents (Smart Precise-Cordis or Carotid Wallstent -Boston Scientific).

The pre-dilation balloons will be routinely undersized (artery: balloon ratio = 2:1.5) in order to reduce vessel dissection and/or distal embolization.

Stent placement will be optimized through single or multiple postdilations by using suitably sized balloons based on angiographic quantitative analysis of the vessel.

Procedural success was defined as; to achieve a less than 30% residual diameter stenosis of the treated lesion in at least two matched views on angiography and finally absence of distal embolization.

Medical treated group took double antiplatelet (DAP) group (acetyl-salicylic acid 150 mg/day + clopidogrel 75 mg/day), statins, controlling the associated modifiable atherogenic risk factors and were followed for at least 6 months clinically using NIHSS and MRS and radiological using carotid duplex \pm MRA or CTA.

Statistical Analysis

Data was analyzed on an IBM personal computer, using Statistical Package for Special Science (SPSS) software computer program version 15. Then data described as mean \pm standard deviation (SD) for quantitative (Numerical) variables and as frequency and percentage for qualitative (Categorical) variables. Chi-square test (or Fisher's exact test when appropriate) used for comparison of distribution of qualitative variables among different group.

Results

The study was conducted on 50 patients with mean age \pm standard deviation (66 \pm 7.92). 17 (56.6%) patients in CAS group were male patients while 13 (43.4%) patients were female. In medically treated group 10 (50%) patients were male and 10 (50%) patients were female with no statically difference between male and female ($p > 0.05$). In CAS group 8 (26.8%) patients had Moderate stenosis (50%-69% stenosis), 20 (66.6%) patients had sever stenosis (70%-95% stenosis) and 2 (6.6%) patients had critical stenosis (96%-99% stenosis), while in medically treated group, 7 (35%) patients had moderate stenosis, 11 (55%) patients had sever stenosis and 2 (10%) patients had critical stenosis with no statically difference between CAS and Medically treated group ($p > 0.05$).

Main risk factors include diabetes mellitus that was detected in 21 (70%) patients in CAS and in 14 (70%) patients in medically treated group, hypertension detected in 19 (63.3) patients in CAS and in 12 (60%) patients in medically treated group.

17 (56.6%) patients in CAS group had Coronary artery disease (CAD) while 11 (55%) patients in medically treated group had CAD. AF was detected in 9 (30%) patients in CAS group and in 6 (30%) patients in medically treated group. Dyslipidemia was detected in 22 (73.3%) patients in CAS group and in 14 (70%) patients in medically treated group. 13 (43.3%) patients in CAS group were smokers while 8 (40%) patients in medically treated group. Peripheral vascular disease were detected in 4 (13.3%) patients in CAS group and in 4 (20%) patients in medically treated group. History of Previous stroke in 5 (16.6%) patients in CAS group and in 3 (15%) patients in medically treated group. With no statically difference between CAS and medically treated group ($p > 0.05$). According to disability as regard MRS at presentation in each group, 8 (26.6%) patients in CAS had MRS 0, 22 (73.4) patients had MRS 1-2 and no patients had MRS 3, while in medically treated group 4 (20%) patients had MRS 0, 16 (80%) patients had MRS 1-2 and no patients had MRS 3, with no statically difference between CAS and Medically treated group ($p > 0.05$). As regard NIHSS at presentation, 8 (26.7%) patients in CAS group were normal (NIHSS was 0), 7 (23.3%) patients had mild stroke (NIHSS 1-5), 15 (50%) patients had moderate stroke (NIHSS 6-15) and no patient had moderate to sever (NIHSS 16-25) or sever stroke (NIHSS 26-42), while in medically treated group 4 (20%) patients were normal, 7 (35%) patients had mild stroke, 9 (45%) patients had moderate stroke and no patient had moderate to sever or sever stroke. With no statically difference between CAS and medically treated group ($p > 0.05$). (Table 1, 2 & 3)

Table 1. Age ,sex and degree of stenosis distribution in CAS and medically treated groups.

		CAS	Medical treatment
Medically Treated Groups			
Age mean ± SD		66.24±7.92	
Sex	Male number (%)	17(56.6%)	10(50%)
	Female number (%)	13(43.4%)	10(50%)
Total		30	20
Medically Treated Groups			
Moderate number (%)		8(26.8%)	7(35%)
Sever number (%)		20(66.6%)	11(55%)
Critical number (%)		2(6.6%)	2(10%)

Table 2. Medical history, MRS and NIHSS at presentation.

		CAS	Medical Treatment	Test of Significance
Medical History				
Diabetis mellitus		21(70%)	14(70%)	P >0.05
Hypertension		19(63.3%)	12(60%)	
Coronary artery disease	17(56.6%)	11(55%)	68.75	
AF		9 (30%)	6(30%)	
Dyslipedimia		22(73.3%)	14(70%)	
Smoking		13(43.3%)	8(40%)	
Peripheral vascular disease		4 (13.3%)	4(20%)	
Previous stroke		5(16.6%)	3(15%)	
MRS				
0		8(26.6%)	4(20%)	P <0.05
1-2		22(73.4%)	16(80%)	
NIHSS				
Normal	0	8(26.7%)	4(20%)	P >0.05
MILD	1-5	7(23.3%)	7(35%)	
Moderate	6-15	15(50%)	9(45%)	
Moderate to Sever	16-25	0(0%)	0(0%)	
Sever	26-42	0(0%)	0(0%)	

Table 3. Outcomes after 6 months.

	CAS	Medical Treatment	Test of Significance	
TIA	4(13.4%)	6(30%)	P<0.01	
Stroke	1(3.3%)	6(30%)		
Death	1(3.3%)	2(10%)		
No New Event	24(80%)	6(30%)		
Total		30	20	
MRS				
0	8(26.6%)	4(20%)	P<.0.05	
1-2	21(73.4%)	10(50%)		
3	0(0%)	2(10%)		
4	0(0%)	3(15%)		
5	0(0%)	1(5%)		
6	1(3.3%)	2(10%)		
NIHSS				
Normal	0	8(26.7%)	3(15%)	P>0.05
MILD	1-5	6(20%)	5(25%)	
Moderate	6-15	15(50%)	10(50%)	
Moderate to Sever	16-25	0(0%)	0(0%)	
Sever	26-42	1(3.3%)	2(10%)	

Outcome and correlative analysis

After 6 months 4 (13.4%) patients in CAS group developed TIA, 1 (3.3%) patient developed stroke which was after procedure and 1 (3.3%) patient die due to myocardial infarction while in medically treated group 6 (30%) patients developed TIA, 6 (30%) patients developed stroke and 2 (10%) patients died one of them due to large stroke and the other due to myocardial infarction. There was high significant difference between CAS and medically treated group after 6 months (p<0.01). According to disability as regard MRS after 6 months in each group, In CAS group 8 (26.7%) patients had MRS 0.21 (70%) patients had MRS 1-2 and one (3.3%) patient had MRS 6, while in medically treated group 2 (10%) patients had MRS 0.10 (50%) patients had

MRS 1-2, 2 (10%) patients and MRS 3, 3 (15%) patients had MRS 4, one (5%) patient had MRS 5 and 2 (10) patients had MRS 6. with statically difference between CAS and Medically treated group ($p < 0.05$). As regard NIHSS after 6 months, 8 (26.7%) of patients in CAS group were normal (NIHSS was 0), 6 (20%) of patients had mild stroke (NIHSS 1-5), 15 (50%) patients had moderate stroke, no patient had moderate to sever and one patient (3.3%) had sever stroke, while in medically treated group 3 (15%) patients were normal, 5 (25%) patients had mild stroke. 10 (50%) patients had moderate stroke, no patient had moderate to sever and 2 (10%) had sever stroke with no statically difference between CAS and medically treated group ($p > 0.05$).

Discussion

Atherosclerotic disease of the carotid artery is responsible for 20%-30% of all strokes [7] and significant clinically relevant stenosis $>50\%$ was detected in (2.5%) of the atherosclerotic symptomatic subjects [8].

Patient selection to determine the most appropriate means of carotid stenosis management is a complex one and decision regarding the optimal mode of treatment must be determined on an individual patient by patient basis. [9].

The aim of this study is to assess the value and consequences of extracranial carotid artery stenting immediately and at short term follow-up versus best medical treatment using clinical assessment and carotid Doppler ultrasonography.

In the present study the mean age of patients is (66 ± 7.92 years) which is younger than most studies as (SAPPHIRE) Stenting and angioplasty with protection in patients at high risk for endarterectomy population [10], (EVA-3S) Endarterectomy versus stenting in patients with symptomatic severe carotid stenosis [11], (CAVATAS) Carotid and Vertebral Artery Transluminal Angioplasty Study [12], (SPACE) Stent Protected Angioplasty versus Carotid Endar-

terectomy [13] and the study done by Naylor *et al.*, 1998 (14) in them the mean age by years was 72.6, 69.7, 67, 67.9 and 71 respectively.

The presence of patients with younger age in the current study may be explained by the difference in vascular risk factors between the current study and the other studies, the frequency of diabetes mellitus is more in this study than that in other studies, the frequency of other risk factors as hypercholesterolemia, hypertension, ischemic heart disease and smoking is equal or slightly higher than other studies. This leads to early atherosclerosis and subsequent early occurrence of carotid stenosis in young age [15].

In this study the frequency of carotid stenosis is more common in male than female 54% versus 46%, this finding is congruent with SAPPHIRE [10] study in which the prevalence of male is more than female (62%) [16]. De WEERD *et al.*, 2009 [17] found that Prevalence of moderate stenosis increases with age in both men and women, but men at all ages have the higher prevalence estimates.

Sex difference in carotid stenosis is now widely accepted. Sex hormones seem to play a fundamental protective role in women through widespread actions, affecting endothelial function, lipid homeostasis, and cardiovascular risk factor reduction [18]. Moreover, some authors claim that estrogens might have plaque stabilization properties and effects on inflammatory status [19].

The results of this study showed 0% restenosis rate after 6 months follow up with 0% ipsilateral strokes due to restenosis. These results compare well with results of POWELL *et al.* (2004) [20] who reported 2.7% restenosis rate with 0% stroke after 6 months follow-up. CERNETTI *et al* (2003) [21] reported 3.9% restenosis rate with 0% stroke. MUDRA *et al* (2003) [22] reported 2.4% restenosis rate with 0% stroke. HENRY *et al* (2002) [23] reported 0.6% restenosis rate with 0% stroke after 6 months follow up. GUPTA *et al* (2000) [24] reported 1.9% restenosis rate with 0% stroke after 18 months follow up. Gross

et al (1999) [25] reported 3.7% restenosis rate with 0% stroke. Also the results of the largest multicenter survey to date by *WHOLEY et al* (2003) [26] included over 11,243 patients reported 2.7% restenosis rates after 12 months, 2.6% after 24 months and 2.4% after 36 months, the rate of neurologic events after stent placement was 1.2%, 1.3%, and 1.7% at 1, 2, and 3 years, respectively. All these studies used the $\geq 50\%$ restenosis threshold.

Contrary to results of the present study higher restenosis rates were reported by different studies. *SCHILLINGER et al* (2004) [27] reported 14% restenosis rate with 2% stroke. *BOWSER et al* (2003) [28] reported 15.4% restenosis rate with 0% stroke. *BONALDI et al* (2002) [29] reported 8% restenosis rate with 0% stroke. *CHAKHTOURA et al* (2001) [30] reported 12.2% restenosis rate with 0% stroke. *NEW et al* (2001) [31] reported 7.2% restenosis rate with 0.6% stroke. *GROSCHERL et al* (2005) [32] conducted a systematic analysis of all peer-reviewed studies reporting on the rate of restenosis ($\geq 50\%$) after carotid artery stenting based on duplex ultrasound or angiography that were published between January 1990 and July 2004. They identified 34 studies that reported on a total of 4,185 patients with a follow-up of 3,814 arteries over a median of 13 months (range, 6 to 31 months). The cumulative restenosis rates after 1 and 2 years were 6% and 7.5% in those studies, which used a lower restenosis threshold $\geq 50\%$ to 70%.

This difference can be explained by that all cases included in the current study carotid stenosis due to atherosclerosis while other studies carotid in-stent restenosis occurs mostly in non- atherosclerotic carotid stenosis lesions (radiation induced carotid stenosis and post-endarterectomy restenosis) which have more liability to restenosis.

According to results of the present study and that of previous studies the short-term restenosis rates after CAS is promising, thus there is a need for further research on the long-term durability of CAS procedures which showed a higher restenosis rates.

Finally, there still is the need for identifying specific risk factors for the development of restenosis after CAS. Some studies have identified advanced age [33], female gender [33], hyperglycemia [34], previous treatment with a CEA [35], and increased serum levels of acute-phase reactants [36] as potential risk factors for the development of a restenosis after CAS; however, the definitive role of these factors remains to be elucidated in larger trials. Also, CAS under protection device is associated with better outcome than medical treatment and it appears to be a safe procedure.

Conclusion

CAS under protection device is associated with better outcome than best medical treatment and it appears to be a safe procedure.

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