Carotid Artery Stenting in High Risk Patients - results of first twelve patients at Shifa International Hospital, Islamabad, Pakistan

Ismail A. Khatri[1], Syed Mumtaz A. Shah[2], Atif Rana[3], Faika Usman[4], Arsalan Ahmad[5], Waqas Ahmed[6]
Section of Neurology[1,4,5], Section of Cardiology[2,6], Department of Radiology[3], Shifa International Hospital, Islamabad.

Abstract

Objective: Carotid artery stenting (CAS) is emerging as an alternative procedure to carotid endarterectomy. It is mostly performed in patients with high surgical risk. Many centers in Pakistan have started CAS. We present results of 1st twelve patients who underwent carotid artery stenting at Shifa International Hospital, Islamabad.

Methods: Our carotid intervention team is comprised of a vascular neurologist, interventional cardiologist and interventional radiologist. Based on high risk criteria/patient choice, patients are recruited for CAS. Carotid artery stenting using standard technique with embolic protection device is performed.

Results: Twelve carotid artery stenting procedures were done between August 2006 and March 2008. One patient had TIA before stent deployment and was excluded from final analysis. Of the other 11 patients, ten were males, with mean age of 68.2 ± 11.3 years (median age 71). Ten were symptomatic; one asymptomatic with complete occlusion of contralateral internal carotid artery. High-risk criteria were present in all: complete contralateral occlusion (2 patients); age greater than 70 years (7 patients); severe coronary artery disease (7 patients) and previous ipsilateral endarterectomy (1 patient). The stenosis ranged between 60-95%. Embolic protection device was used in nine (82%). Five (46%) patients developed hypotension requiring intravenous vasopressors. One of them developed persistent hypotension despite maximum pressor support and died. None developed neurological deterioration, acute renal failure, or haematomas/ pseudoaneurysm formation. One-year follow-up is available on two patients with patent stent and no neurological events.

Conclusion: Hypotension is a common and potentially lethal complication of carotid artery stenting. Our results suggest that a multidisciplinary team approach with availability of specialized care can provide results comparable to internationally acceptable outcomes (JPMA 58:370;2008).

Introduction

Approximately 20% of all ischaemic strokes and transient ischaemic attacks (TIA's) are due to atherosclerotic stenosis of internal carotid artery (ICA) that is close to the carotid bifurcation.[1] Carotid Endarterectomy (CEA) has been used for a long time for revascularization of stenosed carotid arteries. Carotid Artery Stenting (CAS) is emerging as a less invasive alternative to CEA for prevention of stroke. In a recent meta-analysis, the 30-day stroke and death rates associated with CAS and CEA were not significantly different, however, lower rates of myocardial infarction (MI) and cranial nerve injuries were observed with CAS.[2] The results of a very large registry concluded that CAS was safe in patients with severe stenosis and high surgical risk, with best outcomes in younger patients.[3] The primary candidates of carotid artery stenting are patients with serious co-morbid medical or anatomical conditions that increase the risk of open surgical procedures or general anaesthesia. Several trials are underway comparing the safety and efficacy of CAS and CEA. We are presenting the results of first twelve patients done at our center.

Patients and Methods

This is a prospective, non-randomized case series of carotid artery stenting procedures performed between August 2006 and March 2008 in Shifa International Hospital, Islamabad, Pakistan, a tertiary care, multi-specialty 500 bed private teaching hospital. We are maintaining a prospective registry of all patients undergoing carotid artery stenting at our hospital. A carotid intervention team has been established which comprises of a vascular neurologist, interventional cardiologist and interventional radiologist.

Subject Selection: The initial diagnosis of carotid stenosis is made on carotid Doppler scan. CT scan brain or MRI brain is done to exclude any other cause of patient's symptoms. The carotid intervention team jointly assesses the patient before selecting for CAS. An informed written consent is obtained from all patients/families. Based on high risk criteria[4] or patient choice, patients are recruited for CAS. The high surgical risk criteria include advanced age, cardiac and pulmonary disease, prior neck irradiation or radical surgery, restenosis after CEA, contralateral carotid occlusion, high lesion behind the mandible and low lesion that would require thoracic exposure.[4] The major exclusion criteria include complete occlusion of the target vessel, expected inability to deliver a balloon or stent to the target lesion for reasons such as excessive tortuosity or calcification, angioplasty or stenting procedure within the past 48 hours, intracranial tumour or arteriovenous malformation, stroke in past 14 days, and severe disability as a result of stroke or dementia (Table 1).

Methods: Baseline investigations including complete blood count (CBC), serum creatinine, electrolytes, blood sugar level, liver function tests, fasting lipid profile, PT and APTT were done. All patients were given aspirin 75 or 150 mg/day and clopidogrel 75 mg/day for four weeks prior to carotid stenting. Oral antihypertensive and oral hypoglycemics were withheld on the day of procedure. All procedures were done through femoral approach under local anaesthesia. Intra-procedure administration of single dose of unfractionated Heparin at 100 units/kg intravenous (IV) was used in all patients. Four vessel cerebral angiogram was performed to confirm the extent of stenosis in target vessel and to exclude significant disease in the rest of the circulation. Pre-dilatation, use of embolic protection device (EPD), stent deployment and post-dilatation were done according to the international procedure guidelines [4]. Varying with individual cases, carotid stenting was performed either directly without pre-dilatation or pre-dilatation was done prior to EPD. IV atropine 0.5-1mg was given prior to post-stent balloon dilatation. All patients underwent clinical assessment by a neurologist before, during and after the procedure including NIHSS scoring before and after the procedure. The patients stayed in the intensive care unit for forty eight hours. The CBC was repeated after 24 hours and the creatinine level was repeated after 48 hours. We defined significant drop in haemoglobin as more than 2 gm/dL decrease from pre-procedure level, and significant rise in creatinine was defined as > 1.3 mg/dL increase from pre-procedure level. A post-procedure carotid Doppler scan was done. All patients were advised to continue aspirin indefinitely after the procedure and clopidogrel 75 mg/day was given for at least three months. Follow up visits and serial Doppler scans were planned at one, three, six months and one year.

Results

A total of twelve carotid artery stenting procedures were done. One patient developed TIA before the deployment of EPD or stent and was excluded from final analysis. She had a small stroke one year later when she had poorly controlled hypertension.

The demographic and clinical features of the other eleven patients are summarized in Table 2. Youngest patient was 47 years old, and oldest was 81 years old. All of them fulfilled one or the other high risk criteria defined in table 1. The degree of carotid artery stenosis in treated vessels ranged from 60-95%. On the untreated side, two (18%) patients had complete occlusion of carotid artery and three (27%) had stenosis range between 70-90%.

Table 1. Inclusion and exclusion criteria.

Inclusion criteria
Adults >18 years
Both sexes
Symptomatic stenosis >50%
Asymptomatic stenosis >70%
High surgical risk
* advance age
* cardiac and pulmonary disease
* prior neck irradiation or radical surgery
* restenosis after CEA
* contralateral carotid occlusion
* high lesion behind the mandible
* low lesion that would require thoracic exposure
Exclusion Criteria
Complete occlusion of the target vessel
Expected inability to deliver a balloon or stents to the target lesion for reasons such as excessive tortuosity or calcification
Angioplasty or stenting procedure within the past 48 hours
Intracranial tumor or arteriovenous malformation
Severely disabled as a result of stroke or dementia
Stroke, TIA or amaurosis fugax within the past 14 days

Table 2. Demographic and Clinical Features.

	No./Description	Percentage (%)
Demographic features		
Age (in years)		
Mean age	68.2 ± 11.3	
Median age	71	
Gender Male: Female	10:1	
Clinical features and stroke risk factors		
Hypertension	9	82
Diabetes mellitus	8	73
Diet controlled	1	
Oral hypoglycemics	6	
Insulin use	1	
Coronary artery disease	7	64
Prior CABG	1	9
Ejection Fraction <35	2	18
Smoking	7	64
Dyslipidemia	6	55
CRF	0	0
Previous Stroke	9	82
Previous TIA	2	18
Previous CEA	2	18
Ipsilateral	1	
Contralateral	1	
Features of treated carotid arteries		
Symptomatic: Asymptomatic	10:1	
Right: Left	9:2	
Degree of Stenosis		
50-59 %	0	-
60-79 %	2	18
= 80%	9	82

Table 3. Intra- and post-procedure complications.

Intra-procedure complications	No. (%)	Post-procedure complications	No. (%)
Hypotension	5 (46%)	Hypotension	5 (46%)
Bradycardia	0	Bradycardia	1 (9%)
TIA	1 (9%)	Renal Failure	0
Pulmonary Oedema	1 (9%)	Neurological Deterioration	0
Seizure	1 (9%)	Drop in hemoglobin >2gm/dL	3 (27%)
Distal vasospasm after stent deployment	1 (9%)	Death	1 (9%)

Technical success rate of stent deployment was 100%. A summary of intra- and post-procedure complications is given in Table 3. Five (46%) patients had intra-procedure hypotension that was managed with IV vasopressor support of whom one died despite full pressor support. The fall in blood pressure resulted in prolongation of stay in ICU by 3 to 10 days (mean stay 5.6 ± 1.75 days). Three patients (27%) had a fall in haemoglobin of > 2 gm/dL, which could be partly due to blood loss during the procedure and the dilutional effect after IV fluid administration. None of our patients developed increase in creatinine at 48 hours. Ten patients (91%) were discharged home with no worsening in their neurological status.

Immediate post-procedure Doppler (<1 week) was available in six patients that showed patent stents in all. Doppler scan at six months was available for 2 patients and at 1 year for one patient with no in-stent stenosis. Clinical follow-up at one month was available on 7 patients, at three months on 5 patients, at six months on 4 patients, at one year on 2 patients. By the end of one year, no patient had recurrent neurological event. One patient had a TIA at 14 months after discontinuing antiplatelet agents for a dental procedure.

Discussion

Stroke is the third most common cause of mortality.[5] Occlusion of the extracranial circulation accounts for 8% to 29% of all strokes world wide and upto 30% of strokes in USA.[6] The percentage of significant carotid artery stenosis is considered lower in the Asian population. A recent data revealed that only 9.2% Thai population had significant carotid stenosis.[7] The prevalence of more than 50% ICA stenosis was low in Taiwanese patients (8%) with first hemispheric ischaemic stroke.[8] In comparison, a recently published paper from Pakistan showed higher percentage (21%) of significant carotid atherosclerosis in acute ischaemic stroke patients.[9]

The first randomized trial that compared CAS with distal protection device to CEA was the SAPPHIRE trial. This trial showed that CAS with embolic protection device (EPD) was not inferior to CEA in the prevention of stroke,

death or myocardial infarction (MI) among patients for whom surgery posed an increased risk.[10] Another trial conducted on high risk patients was ARCHeR. At 1 year, incidence of major stroke and death was 2.5% in ARCHeR II (with EPD) and 3.8% in ARCHeR I (without EPD).[11] The preliminary data of another ongoing trial to answer the question of safety and efficacy of CAS as compared to CEA in low risk asymptomatic patients suggests that for low risk young patients, CAS carries a low risk of stroke.[12] The one year results of CaRESS phase I non-randomized clinical trial showed that 30-day and 1-year risk of death, stroke or MI with CAS is equivalent to that with CEA in symptomatic and asymptomatic patients.[13]

Some trials have questioned the safety of CAS. The results from EVA-3S trial showed that in patients with symptomatic carotid stenosis of 60% or more, the rate of death and stroke at 1 and 6 months were lower with endarterectomy than stenting[14], while results from SPACE trial failed to prove non-inferiority of carotid artery stenting compared with carotid endarterectomy for the peri-procedural complication rate at 30 days.[15] However, significant difference in methodologies may account for these variable results. The primary candidates for CAS are patients with high surgical risk due to co-morbid conditions or anatomical problems.[4] All our patients fulfilled one or the other high surgical risk criteria.

The peri-procedural and post-procedural results of our patients are comparable to most available literature. However, the patients included in our series are all high risk and except for SAPPHIRE, the results cannot be directly compared. One of our patients had a TIA before stent deployment and the procedure was aborted. In rest of the eleven patients the technical success rate of stent deployment was 100%. Pre-dilatation was performed in 7 (64%) patients; the rest were directly stented. EPD was used in 9 (82%) patients. It was not used in our first two patients due to non-availability. The carotid artery lesions are known to contain friable, ulcerated and thrombotic material and release of such material in the form of emboli into the circulation is the major disadvantage of CAS.[16] A vast data from several trials, series and registries have confirmed that embolic complications decrease significantly when EPD is employed. There is an expert consensus that supports the use of an EPD in all CAS procedures.[17]

We performed stenting in symptomatic vessels only except for one case where the symptomatic vessel was completely occluded and the asymptomatic vessel had 80% stenosis. The revascularization of asymptomatic carotid artery is still a subject of debate. A recent editorial on asymptomatic carotid stenting suggested that stenting in patients with asymptomatic 80-99% stenosis is favoured based on the natural history of preocclusive lesions in other vascular compartments.[18]

The most common complication seen was intra- and post-procedure hypotension in 5 patients (45%). Haemodynamic instability is one of the documented complications of CAS. CAS implies instrumentation of the carotid bulb, so baroreceptor dysfunction may provoke haemodynamic instability.[19] Different studies report from 10-42% cases requiring medical treatment for carotid sinus reactions (CSR) including hypotension, hypertension, and bradycardia. Several factors have been studied and predicted as the reason for these complications. These include advance age (>78 years), low ejection fraction (EF) (< 25%), presence of fibrous plaques and ratio between pre- and post-stenting diameters of internal carotid artery.[19,20] A study conducted in Japan introduced a scoring system for predicting prolonged hypotension in patients undergoing CAS that included factors such as the distance from carotid bifurcation to maximum stenotic lesion (< or = 10mm), type of stenosis (eccentric), plaque morphological features (echogenic), and calcification at carotid bifurcation. The score was determined by adding one point for each of these factors. Three points or more on this score strongly suggested a high risk of prolonged hypotension.[21] Among the 5 patients requiring IV pressor support in our series, only one patient (20%) was > 78 years old. None of these patients had EF of < 25%. Three out of 5 (60%) patients had > 80% stenosis at the time of stent deployment, whereas those who did not develop hypotension all had = 80% stenosis. Among the 5 patients who had hypotension, 4 had carotid stenting on the right side (80%), and among the 7 who did not develop hypotension, 5 had stenting on the right side (71%). This suggests that our patients who developed hypotension had no specific predictors; however, we did not look specifically at the morphology and type of stenosis in patients who developed hypotension. Transient bradycardia occurred in only one patient (9%). A recent paper from Italy also reported hypotension and bradycardia in 10% of patients with neurological sequlae in one patient.[19] Uddin et al. in their paper from Karachi reported transient hypotension in 5/18 and transient bradycardia in 5/18 procedures.[22]

One of the limitations of our study is the high loss to follow-up. Only 2 patients had clinical follow-up at one year. None of our patients had symptomatic neurological event at one year, but soon after that one patient became non-compliant with medications and had neurological event which emphasizes the importance of concomitant aggressive medical therapy.

Conclusions

Hypotension requiring vasopressor support was the most commonly observed side effect in our series with one mortality attributable to hypotension. No clear predictors of hypotension were identified in our series. Apart from hypotension, no other serious complications were seen and the results of these patients are comparable with acceptable standards in high risk group. As most patients with carotid disease have concomitant coronary artery disease, we suggest a multidisciplinary team approach of neurologists, interventional radiologists, and interventional cardiologists for optimal patient selection and outcome.

Disclosures and Conflicts of Interest

This paper was presented in part in the 15th Annual Meeting of Pakistan Society of Neurology, April 5 and 6, 2008, in Peshawar, as platform presentation.

All the authors have nothing to disclose.

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