ORIGINAL ARTICLE

Complications of Angioplasty and Stenting of Cervicocerebral Arteries in Iran

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ABSTRACT

Angioplasty and stenting of the cervicocerebral arteries is a novel treatment for atherosclerotic stenosis, which has periprocedural complications. Data were collected prospectively from 2007 to 2009 in a multicenter cohort of patients undergoing interventions for cervicocerebral stenosis. Retrospective assessment of the 2003–2006 archives of the same interventionists and a review of their published work is the second part of this national survey. In 592 extracranial internal carotid artery angioplasty and stenting procedures in 581 patients (73% male; mean age, 63.4 ± 7 years), transient ischemic attack, stroke, intracerebral hemorrhage, and death occurred in 1.7%, 1.7%, 0.34%, and 1.52%, respectively. In 114 extracranial vertebral artery angioplasty and stenting procedures in 110 patients (68% male; mean age, 65.3 ± 6 years), transient ischemic attack and stroke each developed in 1 (0.92%) patient, but there was no intracerebral hemorrhage or death. In 70 intracranial angioplasty and stenting procedures in 67 patients (76% male; mean age, 68.5 ± 8 years), transient ischemic attack, stroke, intracerebral hemorrhage, and death were observed in 1.4%, 8.6%, 1.4%, and 2.9%, respectively. The frequency of periprocedural complications in angioplasty and stenting of cervicocerebral arteries by our neurointerventionists was similar to that in developed countries.

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KEYWORDS: Angioplasty, Balloon, Carotid Stenosis, Cerebral Arterial Diseases, Drug-Eluting Stents, Stents

INTRODUCTION

Ongoing assessment of stenting techniques for neck and brain arteries requires accurate determination of stent performance and procedural risk to define acceptable complication rates for each group of patients. There should be concern when performing endovascular manipulation in a vessel with diffuse atherosclerosis, because of the risk of dislodging plaque.[1] There are numerous cardiovascular, neurologic, and systemic complications that might result from cervicocerebral angioplasty and stenting. It is important to understand the scenarios in which additional efforts may be beneficial to patients, and when misdirected efforts may expose them to greater danger.[1] Intra- and periprocedural embolic neurologic complications may arise from the stent lattice if there is inadequate anticoagulation and antiplatelet therapy.[2] During instrumentation of an artery, a dissection flap may be created, leading to embolus formation and seeding. Case series have been reported of embolic complications occurring at the time

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of stent placement, which benefitted technically and clinically from directed intracranial thrombolytic therapy, and by pursuing the clot intracranially for microcatheter-based treatment.[3] Many of these embolic complications are due to atherosclerotic rather than thrombotic emboli. Procedural complications also include reperfusion injury. The chronic response to hypoperfusion could induce maximal vasodilation through autoregulation.[1] This may be dangerous if the protective vasoconstrictive reflex is blunted or temporarily lost, because when the stenotic lesion is opened, the pressure in the downstream circulation increases, permitting leakage into the arterial and capillary beds.[3] This could cause brain edema and intracerebral hemorrhage. Angioplasty and stenting for symptomatic intracranial atherosclerosis remains an investigational procedure. This is the first comprehensive assessment of the results of our neurointerventionists.

Patients and Methods

This multicenter study involved a mixed cohort of patients undergoing procedures performed by 9 interventionists working in 5 university hospitals and 7 private hospitals. Data were collected prospectively in a national data bank from 2007 to 2009. These interventionists used similar techniques, patient selection criteria, and methods for recording complications. Retrospective assessment of the neurointerventional archives of these operators from 2003 to 2006, and a review of their published articles, is the second part of this national survey of cervicocerebral arterial angioplasty and stenting. When analyzing the retrospective data, 44% of cases were omitted due to variations in technique, protocol, selection of patients, or recording of complications. All of the angioplasty and stenting procedures were carried out under local anesthesia. The research project was approved by the ethics committees of the involved hospitals, and written informed consent was obtained from the patients or their first-degree relatives.

Four neurointerventionsts only performed angioplasty and stenting of extracranial ICA in patients with symptomatic $>70\%$ carotid stenosis and other 4 neurointerventionists performed the procedure in patients with symptomatic $>50\%$ extracranial ICA stenosis or asymptomatic $>70\%$ extracranial ICA stenosis. The number of procedures in patients with symptomatic stenosis undertaken by each interventionist is listed in Table 1. Exclusion criteria included: allergy to aspirin, clopidogrel, or angiographic contrast medium; angiographic appearance of fresh thrombus at the lesion site; and arterial total occlusion or a long pre-occlusive lesion (string sign).[4] After deployment of a distal protection device in all patients, a self-expanding mesh stent was implanted. Balloon pre-dilation was undertaken in tight or sub-occlusive arterial stenoses, using coronary balloons. Stent placement was optimized by post-dilation using suitably sized balloons. Technical success was defined as the ability to access the carotid artery and stent the lesion with $<30\%$ residual stenosis.[5] Patients underwent laboratory measurements of platelets, hematocrit, and coagulation profile before the procedure. Those taking warfarin on a long-term basis discontinued it for 3 days, and a repeat coagulation profile was performed on the morning of the procedure.[6] Aspirin 325 mg per day and clopidogrel 75 mg per day were started 5 days before the procedure. Heparin 70–100 $IU \cdot kg^{-1}$ was given just before the procedure to achieve an activated clotting time >250 sec.[5] Patients were discharged on a regimen of aspirin indefinitely and clopidogrel for 1 month.[6] Hospital stay was usually 1–2 days. Neurologic examinations, including the National Institutes of Health Stroke Scale, were performed before and at 1 and 30 days after the procedure.[4] Postprocedure brain computed tomography was carried out in patients with documented neurologic complications.[5] Procedure-related complications from the start of the intervention through 30 days of follow-up were recorded. Mild hyperperfusion syndrome was defined

Table 1. **Complications of angioplasty and stenting of extracranial internal carotid arteries**

Interventionist	No. of Procedures	Success	Symptomatic Stenosis	TIA	Stroke	Mild HS	Seizure	Bradycardia	ATN	ICH	Death
Karimi	81	96%	63%	0	2	1	3	17	1	0	0
Ghorbani	80	94%	92%	2	1	1	3	0	0	1	1*
Edraki	300	95%	100%	5	2	7	5	1	0	0	3†
Kojuri-Ostovan[5]	41	96%	100%	2	1	12	0	8	0	1	1‡
Haji-Zeinali/ Kazemi-Saleh[4]	38	95%	20%	0	2	0	0	0	0	0	4§
Shabestrai	52	96%	100%	1	2	0	0	0	0	0	0
Total	592	95%	89%	10	10	21	11	26	1	2	9

*Due to ICH and MHS. †One due to stroke, 2 due to acute myocardial infarction. ‡Due to ICH and HS. §Due to acute myocardial infarction. ATN = acute tubular necrosis, ICH = intracerebral hemorrhage, HS = hyperperfusion syndrome, TIA = transient ischemic attack.

as headache, nausea, hallucination, or disorientation occurring within 24 h postprocedure.[1] The single and cumulative complication rates were calculated as the number of complications divided by the total number of successful procedures.

For angioplasty and stenting of the extracranial vertebral artery (VA), the pre- and postprocedural management was similar to that for extracranial ICA. A distal protection device was introduced through the lesion and deployed in the distal cervical segment of the VA.[7] Drug-eluting coronary stents were used. Angioplasty and stenting of extracranial VA was performed in patients with $>70\%$ VA stenosis, usually with symptomatic stenosis, as shown in Table 2. The primary technical endpoint of the study was the ability to traverse, deploy, and retrieve the distal protection device, and deploy the stent with $<30\%$ residual stenosis.[7] The primary clinical endpoint was the 30-day composite occurrence of stroke and death.

Pre- and postprocedural management and endpoint assessment of intracranial angioplasty and stenting were similar to those for extracranial VA endovascular interventions.[8] Intracranial procedures were performed in patients with symptomatic intracranial artery stenosis $>50\%$. Pre-dilatation of selected intracranial arterial stenoses was undertaken, and a drug-eluting coronary stent was advanced over the guidewire to cover the stenosed segment and deployed, followed by post-dilatation balloon inflation.[8]

Results

There were 581 patients (73% male) with a mean age 63.4 ± 7 years who underwent 592 extracranial ICA interventions; the procedure success rate was 95%. Transient ischemic attack (TIA), stroke, intracerebral hemorrhage (ICH), and death occurred in 1.7%, 1.7%, 0.34%, and 1.52% of extracranial ICA procedures, respectively. Mild hyperperfusion syndrome, seizure, bradycardia, and acute tubular necrosis (due to sensitivity to contrast medium) developed in 3.55%, 1.86%, 4.39%, and 0.17% of extracranial ICA procedures, respectively; the composite stroke and death rate was 3.2% (19/592). Table 1 lists the complications arising from extracranial ICA procedures.

There were 114 extracranial VA procedures in 110 patients (68% male) with a mean age 65.3 ± 6 years. Procedure success was calculated as 99% for extracranial VA interventions. TIA and stroke developed in 1 (0.92%) patient each, and mild hyperperfusion syndrome was seen in 3 (2.7%) patients during procedure; ICH and death did not occur in these patients. Table 2 shows the complications resulting from extracranial VA procedures.

Seventy intracranial artery stents were delivered in 67 patients (76% male) with a mean age 68.5 ± 8 years. TIA and stroke were observed in 1.4% and 8.6% of intracranial artery procedures, respectively. ICH due to hyperperfusion syndrome, death, and mild hyperperfusion syndrome resulted from 1.4%, 2.8%, and 11.4% of

Table 2. **Complications of angioplasty and stenting of extracranial vertebral arteries**

Interventionist	No. of Procedures	Success	Symptomatic Stenosis	TIA	Stroke	Mild HS
Edraki	70	99%	100%	1	0	0
Ghorbani	17	100%	55%	0	1	0
Kojuri-Ostovan	18	100%	100%	0	0	3
Shabestrai	7	100%	100%	0	0	0
Karimi	2	100%	50%	0	0	0
Total	114	99%	92%	1	1	3

HS = hyperperfusion syndrome, TIA = transient ischemic attack.

Table 3. **Localization of 70 angioplasty and stenting of intracranial arteries**

Interventionist	Number of procedures	Intracranial ICA	MCA	ACA	PCA	Vertebral	Basilar
Ghorbani	16	1	4	–	–	5	6
Karimi	2	1	1	–	–	–	–
Edraki	29	15	3	1	–	6	4
Kojuri-Ostovam	21	8	–	1	–	4	8
Sanatgar-Ghasemi[13]	2	–	–	–	–	–	2
Total	70	25	8	2	–	15	20

Table 4. **Complications of angioplasty and stenting of intracranial arteries**

Interventionist	Success	Stenosis	TIA	Stroke	Mild HS	ICH	Death
Ghorbani	100%	100%	1	0	0	0	0
Karimi	100%	100%	0	3	0	0	0
Edraki	96%	100%	0	3*	0	0	1†
Kojury-Ostovan	95%	100%	0	0	8	1	1‡
Sanaatgar-Ghasemi[13]	100%	100%	0	0	0	0	0
Total	97%	100%	1	6	8	1	2

*2 middle cerebral and 1 basilar artery intervention. †Due to stent thrombosis in basilar artery and stroke. ‡Due to ICH and HS. ICH = intracerebral hemorrhage, HS = hyperperfusion syndrome, TIA = transient ischemic attack.

intracranial procedures, respectively. Table 3 lists the sites of 70 intracranial interventions, and complications are given in Table 4.

Discussion

A meta-analysis of 10 clinical trials (3,580 patients) comparing the primary outcome of 30-day stroke or death after ICA angioplasty and stenting vs. carotid endarterectomy (CEA), showed that patients who underwent angioplasty and stenting has a higher risk of stroke and death (risk ratio = 1.30).[9] Subgroup analysis of trials enrolling only symptomatic patients showed a higher relative risk of 30-day stroke and death for angioplasty and stenting of extracranial ICA (risk ratio = 1.63).[9] Qureshi and colleagues[10] analyzed 5 randomized trials (1,154 patients: 577 randomized to CEA and 577 to angioplasty and stenting); the composite endpoint of 1-month stroke or death was not significantly different between groups (relative risk = 1.3, $p = 0.5$). Lower rates of myocardial infarction and cranial nerve injury were observed with the endovascular intervention compared to CEA.[10] Thirty-day outcomes of 1,450 ICA angioplasty and stenting procedures were compared to 3,259 CEA operations performed in the USA:[11] for angioplasty and stenting, the combined rate of death, stroke, and myocardial infarction was 7.1% in symptomatic patients, and 4.6% in asymptomatic patients; for CEA, the death, stroke, and myocardial infarction rate was 3.7% in symptomatic patients, and 1.9% in asymptomatic patients ($p = 0.05$). Thus the current evidence does not support a change in CEA as the treatment of choice for suitable carotid artery stenoses.

Haj-Zaeinali and colleagues[4] and Kojuri and colleagues[5] pioneered external ICA stenting in Iran. The cumulative stroke and death rate of 3.2% for extracranial ICA procedures by our neurointerventionists is better than that of other studies.[11] Assessment of CEA in the national neurovascular centers showed a combined stroke and death rate of 6.4% for CEA performed by our vascular surgeons. Therefore, extracranial ICA angioplasty and stenting is a good alternative to CEA in Iran. Complications of stenting the extracranial VA are reported to be less than those for extracranial ICA in Germany.[12] Our combined stroke and death rate of < 1% is similar to the German result.[12] The first report of intracranial angioplasty and stenting in Iran involved 2 cases of basilar artery stenosis treated by Ghasemi and colleagues.[13] Careful patient selection, meticulous periprocedural care, and skillful neurointerventionists are essential for performing intracranial artery stenting with an acceptable risk.[14] Studies have suggested that intracranial stenosis ≥ 50% with the following characteristics may be considered for angioplasty and stenting: recurrent transient ischemic attacks or ischemic stroke within 180 days, refractoriness to antithrombotic therapy, and relevant cerebral hypoperfusion or a border-zone infarct in the corresponding territory.[14] Contraindications to intracranial artery angioplasty include vasculitis, moyamoya disease, intracranial hemorrhage within 6 weeks, platelet count < 100,000, international normalized ratio > 1.5, bleeding diathesis, or patient contraindications to antithrombotic therapy or contrast medium.[14] Patients with recent cerebral ischemic symptoms attributed to intracranial stenosis ≥ 70% and associated with perfusion failure, may benefit most from this procedure.[14]

Recently, based on the results of the European Wingspan pilot study, the US Federal Drug Administration approved the Wingspan stent for treatment of patients with symptomatic intracranial stenosis ≥ 50% and refractory to medical treatment.[15] Perioperative complications of intracranial artery stenting remain of prime concern because they may offset the potential benefit of the procedure. Jiang and colleagues[16] reported 20 complications (stroke, ICH, and death) in 169 (11.8%) patients who underwent balloon-expandable stenting for symptomatic intracranial stenosis. Hyperperfusion and vessel perforation are the main causes of ICH after intracranial stenting. Currently, aggressive systemic blood pressure control is the best way to prevent and treat hyperperfusion syndrome.[14] Compared to VA interventions, basilar artery stenting is associated with a higher risk of stroke, related to its greater number of

perforators.[7] A review of 6 multicenter prospective studies of angioplasty in 1,011 cases of intracranial atherosclerosis revealed 30-day combined stroke and death rates of 4.5%–6.6%.[14] In 21 intracranial interventions performed by Gupta and colleagues[17] in New York, each patient had failed maximal medical therapy and was thought to be at high risk of an imminent stroke; ICH, disabling ischemic stroke, and death occurred in 17%, 11%, and 14%, respectively. Nahser and colleagues[18] reported 1 periprocedural TIA and 1 stroke in 20 patients with intracranial vertebrobasilar stenosis who underwent successful angioplasty (procedural complication rate: 10%). Another study evaluated the technical efficacy of drug-eluting stents in 15 patients with intracranial atherosclerosis in either the carotid or vertebrobasilar territories.[3] Technical success was achieved in 94%, with 1 stroke/death after 1 month.[3] A report of 37 intracranial angioplasties without stenting for symptomatic atherosclerotic stenosis revealed a periprocedural stroke and death rate of 8.3%.[14]

Based on these clinical trials, sufficient evidence now exists to recommend that intracranial angioplasty with or without stenting should be offered to symptomatic patients with intracranial stenosis and failed medical therapy.[14] The overall stroke and death rate of 10% for intracranial angioplasty and stenting performed by our neurointerventionists is similar to that of other studies.[14,18] Patient benefit from cervicocerebral angioplasty and stenting is critically dependent on a low periprocedural stroke and death rate; therefore, the procedures should be performed by an experienced neurointerventionist.

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