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ORIGINAL RESEARCH

Basilar Artery Stent Angioplasty for Symptomatic Intracranial Athero-Occlusive Disease: Complications and Late Midterm Clinical Outcomes

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BACKGROUND AND PURPOSE: After an initial series of basilar artery stent angioplasty indicated a high technical success rate and minimal morbidity, subsequent reports suggested significant procedural risks. We retrospectively reviewed our experience with basilar artery stent placement to assess complications and clinical outcomes.

MATERIALS AND METHODS: Ten consecutive patients with symptomatic intracranial athero-occlusive disease underwent stent placement of the basilar artery at our institution (1999–2003). We collected clinical data by chart review and determined outcomes (modified Rankin Scale [mRS]) by telephone interview. Angiographic data were analyzed by 2 blinded investigators. Clinical and angiographic variables were tested for correlation with outcome and complications using the Pearson correlation test.

RESULTS: Of 10 patients (mean follow-up time, 31 months), 4 patients suffered 6 ischemic complications that were immediate in 1, early delayed (<2 weeks) in 4, and late delayed (>2 weeks) in 1. Complications included basilar artery rupture in 1 patient, access site complications in 1 patient, and other non-neurologic complications in 5. Symptomatic restenosis occurred in 1 patient. Outcomes (mRS) were excellent (0–2) in 5 patients, good (3) in 4, and poor (4–6) in 1 patient, who died. Ischemic complications were associated with lesion lumen ≤0.5 mm and lesion angulation >45° ($P < .05$). Less favorable clinical outcomes were associated with few ischemic complications and the presence of fewer than 2 patent vertebral arteries ($P < .05$).

CONCLUSIONS: Despite a significant incidence of ischemic and nonischemic complications after basilar artery stent placement, most patients in this small series achieved freedom from vertebrobasilar ischemia and good to excellent clinical outcomes at late midterm follow-up (12–46 months). Ischemic complications usually had an early delayed presentation and procedural risks correlated with lesion characteristics.

The risk of fatal or disabling stroke in symptomatic intracranial athero-occlusive disease involving the vertebrobasilar circulation is high.[1,2] In patients with symptomatic intracranial atherosclerosis, single-agent antiplatelet therapy with aspirin or anticoagulation with warfarin is associated with a 2-year ischemic stroke rate of 17%–20%.[3] Although surgical bypass is a well-known treatment option for intracranial vertebrobasilar atherosclerosis, reported morbidity and mortality rates are high.[4,5] Several authors have demonstrated the feasibility of basilar artery stent revascularization using current microcatheter and stent technology.[6-10] Clinical outcomes and complication rates remain poorly understood because of limited collective experience. Recent studies suggest that the risk of procedure-related stroke is significant.[10-12] Although short-term clinical outcomes after basilar artery stent placement have been reported previously, midterm clinical outcome data are lacking.[4,9,11]

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We retrospectively reviewed our experience with patients who underwent basilar artery stent angioplasty to determine the frequency of ischemic stroke complications, the frequency and nature of nonischemic complications, and clinical outcomes. We also analyzed dependent variables for correlation with these end points including patient-related variables, technique-related variables, perioperative antithrombotic therapy, anatomic characteristics, and lesion characteristics, including the Mori classification.[8,13] We further analyzed the effect of ischemic and nonischemic complications on clinical outcomes.

Materials and Methods

This retrospective study was performed under a protocol approved by the local Institutional Review Board (IRB) in accordance with National Institutes of Health guidelines (IRB ID 606-2003). We reviewed all consecutive cases of basilar artery stent angioplasty performed for athero-occlusive disease at our Atlanta institution from March 1999 through March 2003. All procedures were performed on a Philips Integris biplane neuroangiography unit (Philips Medical Systems, Andover, Mass) by fellowship-trained interventional neuroradiologists (2) or neurosurgeons (1).

Clinical Data

Clinical data were obtained by retrospective chart review, including patient- and technique-related variables, perioperative antithrombotic therapy, and complications. Operator experience was consid-

ered a technique-related variable because we differentiated cases performed early (March 1999–July 2001) from those performed later (August 2001–March 2003). Technical success was defined as successful delivery of a stent to the target lesion with less than 50% residual stenosis. The timetable for administration of antithrombotic drugs in relation to stent placement was assessed in each patient. When available, intraoperative activated clotting times (ACTs) were evaluated.

Ischemic complications were assessed for temporal relationship to stent placement, background antithrombotic therapy, presentation, affected anatomy on brain imaging, acute therapy, maintenance therapy, and findings of diagnostic conventional angiography. When available, catheter angiograms were reviewed.

Angiographic Data

Anatomic characteristics, lesion characteristics, residual stenosis after stent placement, major branch artery jailing, and causes of ischemic stroke complications were evaluated by analysis of digital subtraction angiograms (DSA). Consensus agreement was reached by 2 fellowship-trained interventional neuroradiologists (T.A.A. and F.C.T.); neither radiologist was a primary operator for any of the stent placement procedures.

Pretreatment stenosis, prestent lesion lumen, residual stenosis, and lesion length were calculated electronically using EZ Vision software on an EZ Vision workstation (Philips Medical Systems). Stenoses were based on the normal basilar artery lumen (consensus judgment by T.A.A. and F.C.T.) as the denominator. Lumen and length of the lesion were measured using the distance between proximal and distal stent markers as an internal calibration standard. When measurements were made on pretreatment DSA, a retroanalysis was performed using a shared marker vessel as a calibration standard to bridge pretreatment and posttreatment DSA. Pretreatment stenosis, prestent lesion lumen, and residual stenosis were determined in the projection that demonstrated the most severe pretreatment luminal narrowing. Lesion ulceration was considered present if luminal contours were markedly irregular with overhanging margins.

Lesion angle was determined by tracing the central linear axes of the basilar artery on the proximal and distal sides of each lesion; the angle between the 2 axes was measured with a protractor in the projection that demonstrated the most severe angulation. Lesion length was determined in the projection that maximally elongated the lesion.

Lesion location was designated as distal if the craniocaudal center of the lesion was at or distal to the craniocaudal median of the basilar artery or proximal if the lesion did not meet these criteria. For the evaluation of vertebral artery and basilar branch artery pathology, stenosis was considered severe if ≥50%, moderate if 21%–49%, and mild if ≤20%.

Outcome Data

Outcome data, including modified Rankin scores (mRS), were obtained by telephone interview of each patient. Interval events/changes occurred after stent placement and discharge from the hospital. Any event requiring hospitalization or a change in antithrombotic medication was considered clinically significant; details of clinically significant interval events were obtained by chart review. Clinical outcomes were defined as excellent (mRS 0–2), good (mRS 3), or poor (mRS 4–6).

Statistical Analysis

The Pearson correlation test identified statistically significant associations of clinical and angiographic variables (Table 1) with mRS, clinical outcome (excellent, good, or poor), and complications (ischemic and nonischemic). Analysis of variance determined statistically significant associations of mRS and clinical outcome with procedure-related complications (ischemic stroke, intracranial hemorrhage, access site complications, symptomatic restenosis) and non–procedure-related complications (cardiac events, pulmonary events, infectious complications, hematologic complications).

Table 1: Summary of dependent variables in 10 consecutive patients who underwent basilar artery stenting for symptomatic athero-occlusive disease

Variables
Patient-related variables
Age >70 years
Sex
Pre-existing history of diabetes
Pre-existing history of significant heart disease
Indication for stenting
Rate of onset of index event (abrupt vs progressive)
Recent failed balloon angioplasty
Preoperative acute/subacute infarction
Technique-related variables
Experience (procedure performed 1999–2000 versus 2001–2003)
Primary stenting (versus pre-dilation of target lesion with angioplasty balloon)
More than one stent implanted
Type of anesthesia (general versus conscious sedation)
Major branch artery jailed by stent construct
Residual stenosis <20%
Perioperative antithrombotic therapy
Preloaded with clopidogrel before procedure
Intraoperative anticoagulation with documented activated clotting times ≥250 seconds
Intraoperative IIb/IIIa inhibitors
Postoperative IIb/IIIa inhibitors ≥12 hours
Postoperative anticoagulation with heparin and/or warfarin for ≥48 hours
Postoperative maintenance therapy with dual antiplatelet agents
Anatomic characteristics
Lesion location
Lesion extension across basilar artery branch ostia
Number of patent vertebral arteries contributing to basilar circulation
At least moderate stenosis affecting 2 or more major basilar artery branches
At least 1 posterior communicating artery giving collateral flow to the basilar artery
Lesion characteristics
Mori classification
Pretreatment stenosis ≥80%
Lesion ulceration
Prestent lesion lumen ≤0.5 mm
Lesion length >10 mm
Lesion angle >45°

Results

Patient-Related Variables

Between March 1999 and March 2003, 2 women and 8 men ranging in age from 50 to 83 years underwent basilar artery stent placement for athero-occlusive disease at our institution (Table 2). Hypertension was the most common comorbidity, affecting 90% of patients. The indications for stent placement were refractory symptoms of vertebrobasilar ischemia despite medical therapy for the presenting index event (patients 1–7) or clinical factors (eg, chronic gait instability) that made patients 8–10 poor candidates for long-term anticoagulation. The onset of index symptoms was abrupt in 6 patients and

Table 2: Patient demographics and clinical presentation

No.	Age/Sex	Medical Comorbidities	Presenting Symptoms	Background Treatment at Presentation	Initial Treatment for Presenting Index Event	Acute Infarcts on Prestent Brain MRI
1	68/F	Hypertension, hypothyroidism	Hemi-numbness, hemiparesis, dysarthria	None	Heparin	Bilateral cerebellar, left parieto-occipital lobe
2	80/M	Hypertension, NIDDM, paroxysmal atrial fibrillation, ischemic coronary artery disease	Vertigo, ataxia	Aspirin 81 mg/day, warfarin (INR 2.17 seconds)	Heparin	None
3	76/M	Hypertension, tobacco abuse, dyslipidemia	Vertigo, drop attacks/syncope, ataxia, dysarthria, blurred vision	Clopidogrel	Warfarin	None
4	57/M	Hypertension, ischemic coronary artery disease	Hemiparesis, hemi-numbness	Clopidogrel, aspirin 325 mg/day	tPA, heparin, abciximab	None
5	83/F	Hypertension, ischemic coronary artery disease, congestive heart failure, hypothyroidism	Dysarthria, hemiparesis	Warfarin (INR unknown)	Heparin, aspirin 325 mg/day	None
6	50/M	NIDDM, dyslipidemia, tobacco and alcohol abuse	Hemiparesis, vertigo, dysarthria, ataxia	Clopidogrel, aspirin 325 mg/day × 3 months after balloon angioplasty of Mori B lesion (70% stenosis with 25% residual stenosis)	Heparin	No prestent brain MRI
7	61/M	Hypertension, NIDDM, alcohol abuse	Homonymous hemianopsia, drop attacks/syncope	Aspirin 325 mg/day × 4 months after acute thrombotic occlusion of basilar artery, 1 month after balloon angioplasty of Mori C lesion (90% stenosis with 50% residual stenosis)	Heparin	None.
8	72/M	Hypertension, IDDM, dyslipidemia, paroxysmal atrial fibrillation, COPD, hypothyroidism, alcohol abuse, ischemic coronary artery disease	Vertigo, dysarthria, ataxia	Clopidogrel, aspirin 325 mg/day	Heparin	Left cerebellar
9	69/M	Ischemic coronary artery disease, hypertension	Dysarthria, hemiplegia	None	Clopidogrel, aspirin 325 mg/day	Left hemi-pontine
10	67/M	Hypertension	Hemi-numbness, hemiparesis	Aspirin (dose unknown)	Warfarin, aspirin 325 mg/day	None

Note:—MRI indicates MR imaging; NIDDM, non–insulin-dependent diabetes mellitus; IDDM, insulin-dependent diabetes mellitus; COPD, chronic obstructive pulmonary disease; INR, international normalized ratio; sec, seconds; tPA, tissue plasminogen activator.

progressive in patients 2, 3, 6, and 8. Medical therapies administered to treat the presenting index symptoms are listed in Table 2. All 10 cases were performed with the intention to stent. There were no "bail out" procedures to salvage failed balloon angioplasties. Only patient 6 did not undergo a prestent brain MR imaging; this patient had no clinical evidence of stroke before and during the first 3 days after stent placement. Three patients had MR imaging-proved acute strokes at the time they presented for stent placement.

Two patients underwent balloon angioplasty of the basilar artery 3–5 months before stent placement (Table 2). Patient 7 underwent balloon angioplasty for a Mori type C lesion (90% stenosis) 5 months before stent placement. This resulted in 50% residual stenosis that occluded 1 month after angioplasty, subsequently recanalized, and became symptomatic while the patient was taking aspirin. Patient 6 underwent balloon angioplasty for a Mori type B lesion (70% stenosis) 3 months before stent placement that resulted in 25% residual stenosis, which subsequently became symptomatic while the patient was taking clopidogrel (Plavix) and aspirin.

Technique-Related Variables

Patients 1–5 and 7 underwent treatment between March 1999 and July 2001 and patients 6 and 8–10 underwent treatment

Table 3: Characteristics of basilar artery lesions in 10 patients with symptomatic athero-occlusive disease

Patient No.	Lesion Length (mm)	Angulation (°)	Morphology	No. Patent Vertebral Arteries	Mori Class	Ulceration	Prestent Lesion Lumen (mm)	Stenosis of Luminal Diameter (%)	Residual Stenosis after Stenting (%)
1	9.2	0	Concentric	2	B	Ulcerated	0.6	77.0	22.8
2	9.0	80	Concentric	2	B	Smooth	0.2	81.9	14.5
3	10.0	60	Eccentric	2	B	Smooth	1.2	70.5	28.8
4	6.8	45	Eccentric	2	A	Ulcerated	0.6	81.0	40.4
5	4.7	0	Concentric	1	A	Smooth	0.1	92.9	7.4
6	31.0	45	Concentric	1	C	Smooth	0.4	84.0	21.7
7	25.7	0	Eccentric	2	C	Smooth	0.2	95.0	43.0
8	7.0	0	Eccentric	2	B	Ulcerated	0.5	67.2	32.0
9	5.6	55	Concentric	2	B	Smooth	0.4	79.0	0
10	7.4	60	Concentric	2	B	Smooth	0.6	78.8	10

between August 2001 and March 2003. Patients 1 and 3 were treated under conscious sedation, and the remaining received general endotracheal anesthesia.

Except for patient 6, all patients underwent anticoagulation with heparin intraoperatively. Intraoperative ACTs were above 250 seconds in patients 3, 7, 9, and 10 and were not recorded in patients 1, 4, and 8. During the procedure, patient 10 did not receive IIb/IIIa inhibitors, patient 7 received tirofiban (Aggrastat), and the remaining patients received abciximab (ReoPro).

Technical success was achieved in all 10 patients. Arterial access was transfemoral in 9 patients and transbrachial in 1 patient. The basilar artery lesion was predilated with an over-the-wire angioplasty balloon before stent placement in all patients except 9 and 10. Nine procedures were performed using only balloon-mounted coronary stents that included the PRIMO (Boston Scientific, Natick, Mass), Tristar (Guidant, Indianapolis, Ind), GFX^{AVE}, S670 ^{AVE}, S7 ^{AVE} (Advanced Vascular Engineering; Medtronic, Santa Clara, Calif), and Sonic Hepacoat (Cordis, Miami Lakes, Fla). Patient 6 received a self-expanding Magic Wallstent (Boston Scientific) in addition to balloon-mounted coronary stents. Treatment included 1 stent in 7 patients (patients 1, 3–5, 8–10), 2 stents in patient 7, 3 stents in patient 2, and 4 stents in patient 6. The anterior inferior cerebellar artery (AICA) was jailed bilaterally in all patients except 4, 9, and 10; a posterior inferior cerebellar artery was jailed in patient 2.

Perioperative Antithrombotic Therapy

Preoperative antiplatelet therapy included aspirin and clopidogrel in 4 patients (patients 6, 8–10), clopidogrel only in patients 1 and 3, aspirin only in patients 5 and 7, and clopidogrel and abciximab in patient 4. Patient 2 was not given antiplatelet agents before treatment. Preoperative anticoagulation with heparin was administered to 6 patients (patients 1–3, 5–7). Patient 4 was given intravenous tissue plasminogen activator for acute stroke preoperatively.

Postoperative antiplatelet therapy included clopidogrel and aspirin in 6 patients (patients 1, 2, 5, 6, 8, 9), clopidogrel only in patient 3, and dipyridamole/aspirin (Aggrenox) only in patient 7. Patients 4 and 10 did not receive postoperative antiplatelet therapy. Anticoagulative agents were administered postoperatively for 24 hours in patients 2 and 4, for 48 hours in patients 1 and 7, and for 6 days in patient 8. All patients, except patients 1 and 7, who received postoperative anticoagulation therapy, were continued on warfarin after heparin was discontinued.

Anatomic Characteristics

Basilar artery stenosis was proximal in 7 (patients 1–5, 8, 9) and distal in patients 6, 7, and 10. Patients 1, 8, and 10 did not have athero-occlusive disease of the vertebral arteries. Intracranial vertebral artery stenosis was severe and bilateral in patient 2; severe and unilateral in patients 3, 5 and 9; and mild and unilateral in patients 7 and 4. In patients 5 and 6, one vertebral artery was occluded. In patient 5, the left vertebral artery was occluded, and the right vertebral artery was affected by tandem stenoses involving its origin and intradural segment.

No basilar branch artery pathologic lesions were demonstrated angiographically in patients 4, 5, 8, and 10. Moderate to severe stenosis of the AICA was bilateral in patients 7 and 9 and unilateral in patients 1–3. Patient 6 had occlusion of the left AICA and severe stenosis of the right AICA. Moderate stenosis was found in a posterior cerebral artery in patients 2, 3, and 7 and in a superior cerebellar artery in patient 2. Five (patients 3–5, 7, 10) had no demonstrable posterior communicating artery (PcomA), 3 (patients 1, 2, 9) had bilateral PcomAs, and 2 (patients 6 and 8) had unilateral PcomAs.

Lesion Characteristics

Mori classification of the basilar artery lesion was A in 2 patients, B in 6 patients, and C in 2 patients (Table 3). Mean measurements included pretreatment stenosis of 80.7%, prestent lesion lumen of 0.5 mm, lesion length of 11.6 mm, and lesion angle of 34.5°.

Ischemic and Nonischemic Complications

Within the first 30 days after basilar artery stent placement, 6 ischemic stroke complications affected patients 5–8 (Table 4). The postoperative course was complicated by multiple discrete strokes in patient 6 and a single stroke in 3 patients, including one that was fatal (patient 5).

Six patients (patients 2, 3, 5, 8–10) suffered nonischemic complications. Acute myocardial infarction occurred in patient 5 and supraventricular tachycardias occurred in patients 2, 5 and 8. Pulmonary complications included atelectasis (patient 5), pneumonia (patient 10), aspiration pneumonitis (patient 8), and pulmonary embolism (patient 9). The postoperative course was complicated by urosepsis in patients 5 and 8

Table 4: Ischemic complications of basilar artery stenting

Patient No.	Time of Onset Relative to Stenting	Anti-Thrombotic Medications at Time of Ictus	Clinical Presentation	Acute Infarcts (Imaging Modality)	Catheter Angiography	Acute Treatment	Maintenance Therapy
5	Immediate	Abciximab	Deep coma; after withdrawal of support, patient died on poststent day 10	Right cerebellum and anterior pons (CT)	Not performed	Not applicable	Not applicable
6	Day 4	Clopidogrel, aspirin*	Vertigo, ataxia	Left cerebellum (MRI)	No acute abnormality	Heparin, clopidogrel, aspirin × 8 days	Clopidogrel, aspirin
	Day 12	Clopidogrel, aspirin	Hemiparesis	Left middle cerebellar peduncle (MRI)	No acute abnormality	Heparin, tirofiban × 4 days	Enoxaparin, warfarin, aspirin
	Day 17	Aspirin, enoxaparin, warfarin (INR = 2.03 seconds)	Dysarthria, hemiplegia	Left pons (MRI)	Not performed	Heparin, tirofiban × 7 days	Enoxaparin, warfarin, aspirin
7	Day 2	Tirofiban	Ophthalmoplegia, dysarthria, hemiplegia	Right pons (MRI)	Stent thrombosis	Endovascular mechanical thrombectomy and tirofiban × 2 days	Warfarin, tirofiban
8	Day 1	Abciximab	Hemiplegia, respiratory failure	Right pons (MRI)	No acute abnormality	Heparin × 6 days.	Warfarin, clopidogrel, aspirin

Note:—INR indicates international normalized ratio; MRI, MR imaging; *, when aspirin is indicated, 325 mg/day.

and catheter sepsis in patients 8 and 10. Patient 10 suffered from symptomatic anemia requiring blood transfusion.

In patient 10, the basilar artery ruptured during stent deployment when the carrier balloon was inflated to nominal pressure (10 atmospheres). The resulting hemorrhage was controlled by tamponade with a 4 × 15 mm HyperForm balloon occlusion catheter (ev3, Irvine, Calif) and reversal of anticoagulation with protamine. Postoperative hydrocephalus was managed by external ventricular drainage, and refractory intracranial hypertension was treated with osmolar therapy (hypertonic saline and mannitol), hypothermia, and pentobarbital coma. With no MR imaging evidence of brain ischemia, the patient was ultimately discharged to an inpatient rehabilitation facility, where he recovered and achieved an excellent outcome.

In patient 3, an attempted closure of a brachial arteriotomy with a Perclose device (Abbott Vascular Devices, Redwood City, Calif) was unsuccessful, resulting in a pseudoaneurysm that required immediate postoperative surgical repair. This patient subsequently developed chronic disabling median neuropathy.

Clinical Outcomes

One procedure-related death (patient 5) occurred because of a large pontocerebellar infarction (Table 5). There were no poor clinical outcomes in surviving patients. Three patients had clinically significant interval events, including patient 3, who developed symptomatic restenosis. Patients 3 and 6 quit smoking at the time of their stent placement procedure.

Of 9 surviving patients (mean follow-up time, 31 months), 3 patients (patients 1, 2, 9) reported no symptoms at last follow-up and 5 (patients 4–8, 10) reported persistent fixed neurologic deficits that were stable or improving, consistent with the sequelae of completed ischemic strokes. Patient 3 complained of chronic fluctuating gait instability and positional vertigo.

Statistical Analysis

Ischemic complications were significantly associated with prestent lesion lumen ≤0.5 mm and lesion angle >45° ($P < .05$). Recent failed balloon angioplasty and lesion length >10 mm approached significance for association with ischemic complications ($P < .06$). Nonischemic complications had no significant associations. The mRS score ($P < .05$) and clinical outcome ($P < .001$) were significantly associated with ischemic complications. Fewer than 2 patent vertebral arteries contributing to the basilar artery circulation was significantly associated with the mRS score ($P < .05$).

Discussion

Clinical Outcome after Stent Revascularization of the Basilar Artery

Late midterm clinical follow-up (12–46 months) in a cohort of patients with symptomatic basilar artery atherosclerosis treated by stent placement is presented here for the first time. In our experience, most patients had good to excellent clinical outcomes and were free of vertebrobasilar ischemia (as defined by progressive or fluctuating symptoms) at 2–3 years after stent placement despite a significant incidence of isch-

Table 5: Clinical outcomes in 10 patients after basilar artery stenting for symptomatic athero-occlusive disease

Patient No.	Follow-Up (months)	mRS	Persistent Symptoms	Clinically Significant Interval Events	Maintenance Medical Therapy at Last Follow-Up
1	44	0			Clopidogrel, aspirin, atorvastatin
2	46	0		4 hospitalizations for gastrointestinal hemorrhage secondary to excessive anticoagulation	Warfarin, aspirin
3	45	3	Chronic imbalance, positional dizzy spells, dominant hand disability related to access site complication	MRI 44 months poststent performed to assess recurrent vertigo, diplopia, and gait ataxia while on clopidogrel showed no new infarcts. Angiogram showed 50% concentric stenosis just proximal to stent. Symptoms stabilized on heparin and remained stable on warfarin.	Warfarin, clopidogrel, simvastatin
4	39	2	Fixed difficulties with fine motor control		Warfarin, aspirin, simvastatin
5	10 days	6	NA	NA	NA
6	29	3	Fixed gait ataxia, vertigo, dysarthria, dysphagia		Aspirin, warfarin, simvastatin
7	38	3	Fixed left hemiparesis, diplopia		Warfarin
8	18	3	Fixed left hemiparesis, dysphagia	Major myocardial infarction 30 days after discharge from stent hospitalization. Treated by coronary artery bypass grafting surgery and automated implantable cardiac defibrillator	Warfarin, lovastatin
9	12	0			Clopidogrel, aspirin, simvastatin
10	8	2	Fixed gait ataxia, dysarthria, dysphagia		Aspirin, fenofibrate

Note:—mRS indicates modified Rankin score; MRI, magnetic resonance imaging, NA, not applicable.

emic and nonischemic procedure-related complications. Our results echo those reported by Levy et al[12] who found good to excellent short-term outcomes despite a high initial mortality. Our symptomatic restenosis rate of 11% is similar to that reported by the Stenting of Symptomatic Atherosclerotic Lesions in the Vertebral or Intracranial Arteries (SSYLVIA) trial, where the rate of symptomatic restenosis for all intracranial lesions at 6 months was approximately 15%.[10]

Correlates of clinical outcome in our study included ischemic complications and the number of vertebral arteries contributing to the basilar artery circulation. Our results confirm that optimizing clinical outcome depends on the prevention of ischemic complications. One possible reason for the significance of vertebral artery anatomy is that spasm around the guide catheter in the instrumented vertebral artery limits basilar artery circulation to the noninstrumented vertebral artery. Poor perfusion of the basilar artery and local thrombus promoted by stasis increase the risk of ischemic brain injury, more so in patients who do not have the benefit of a functional contralateral vertebral artery.

Predictors of Procedural Risk

Although the Mori classification did not correlate with stroke complications in our series, 2 components of the Mori scale did: lesion angle >45° was significant, and lesion length >10 mm approached significance. These findings emphasize that technical difficulty relates to the risk of ischemic complications. Mori et al have shown that technical difficulty in intracranial stent placement depends on a number of angiographic features incorporated into the Mori scale.[8,13] On the basis of the Mori scale, most cases in our series were of intermediate difficulty (6 Mori B, 2 Mori A, and 2 Mori C).

We found that prestent lesion lumen ≤0.5 mm was associated with ischemic complications. This association may reflect the larger burden of embolic debris released when stents are advanced through a small-caliber lumen or redistribution of a larger plaque mass over the surface area incorporating perforator ostia. Other mechanisms may have been operant because most stroke complications in our patients presented in a delayed manner. Redistributed plaque may not immediately occlude perforator ostia but may encroach sufficiently to disturb local hemodynamics, thus enhancing platelet aggregation and thrombus formation. As subsequent downgrading of the antithrombotic drug regimen may push the rate of platelet aggregation toward the threshold for occlusion of perforator ostia, there may be a rationale to extend the period of anticoagulation in patients with critical luminal narrowing.

Although a smaller posttreatment lumen caliber may translate into less complete stent expansion and crowding of struts over perforator ostia, residual stenosis did not correlate with stroke risk in our series. In theory, a larger posttreatment lumen caliber should also decrease the need for anticoagulation and improve long-term patency rates. Marks et al, who advocated balloon angioplasty without stent placement for the treatment of intracranial atherosclerosis, emphasized that only a small change in lumen caliber is necessary to affect a large increase in flow.[14] Theoretic advantages of primary stent placement over balloon angioplasty alone are both a reduction of complications resulting from acute vessel dissection and a reduction in the rate of restenosis.[7] Proponents of balloon angioplasty alone have reported long-term results with a 5-year stroke-free survival of 85% when procedural complications are excluded[14]; they also suggest that procedural risks are lower than for primary stent placement. A recent series has

reported the peri-procedural risk of stroke or death after intracranial vertebrobasilar angioplasty of less than 10%[14]; however, others have found the risk to be as high as 28%.[15]

Ischemic complications did not significantly correlate with perioperative antithrombotic therapy; however, all but one stroke occurred on antiplatelet drugs alone (no anticoagulation). The one stroke that occurred in the setting of anticoagulation (patient 6) presented on day 17 (late delayed stroke)—a time when the effects of intimal hyperplasia could be operant. Because most stroke complications were early delayed, there may be a rationale to extend postoperative anticoagulation to 2 weeks, at which time patients would be managed with antiplatelet agents only.

Although ischemic complications did not correlate with clopidogrel preloading or postoperative dual antiplatelet therapy in our series, our small number of cases may have precluded detection of such an association. We could not assess the adequacy of perioperative platelet inhibition in the current series because platelet function assays were not obtained. In clinical practice and future studies, routine implementation of platelet function assays may help to prevent thromboembolic strokes that are the consequence of inadequate platelet inhibition secondary to insufficient dosing or patient resistance.[16]

Lack of Correlation between Technical Success and Procedural Complications

Our experience with basilar artery stent placement reveals a significant risk of periprocedural ischemic stroke that is consistent with other recently reported experiences.[12] Although the technical success rate was 100% in our series, 4 patients suffered stroke complications. Our findings are similar to a series of 11 cases reported by Levy et al in which 4 patients died, 2 from basilar or vertebral artery rupture, and 2 from pontine stroke.[12] In that series, patients with poor outcomes had Mori B and C lesions. In the SSYLVIA trial, 2 of 17 (12%) patients who underwent basilar artery stent placement suffered stroke within 30 days[10]; this relatively low stroke rate may have been related to the lesion characteristics of the patients selected for treatment in whom mean pretreatment stenosis was only 69.9%. Mori classifications were not reported.

Timing of Ischemic Complications and Theoretic Mechanisms

Acute intraoperative strokes that manifest immediately after stent placement may be the result of a "snow plowing" effect, thromboembolism, acute occlusion of perforator ostia by stent struts, or in situ thrombus.[17] One such stroke was encountered in our series. Early delayed strokes that develop within the first few days after stent placement may be related to in-stent thrombus, occlusion of perforator ostia, or thromboembolism.

Early delayed strokes represented most stroke complications in our series (4 of 6). Patient 7 demonstrated stent thrombosis and the other 3 (patients 5, 6, and 8) with early delayed strokes had no associated angiographic evidence of in-stent/intra-arterial thrombus, flow-limiting dissection, or branch artery occlusion. In each case, the stented basilar artery was widely patent. The pons was affected in 4 events, a middle cerebellar peduncle was affected in 1 event, and a cerebellar hemisphere was affected in 2 events. The results suggest that most early delayed strokes are related to small thromboemboli and perforator occlusions.

Late delayed strokes ($\geq$2 weeks after stent placement) may be related to all of the above in addition to another potential mechanism caused by intimal hyperplasia within and around perforator ostia. In nonhuman primate models of postangioplasty restenosis, marked intimal thickening occurs between 14 and 28 days later.[18] Side branch occlusion resulting from in-stent restenosis has been reported in the coronary circulation.[19] In our series, only one late delayed stroke occurred, suggesting that if this phenomenon occurs after basilar artery stent placement, it does not account for most procedure-related strokes.

Conclusions

Despite technically satisfactory results, ischemic and nonischemic complications are common in patients who undergo basilar artery stent angioplasty. Lesion characteristics that predict technical difficulty, including prestent lumen diameter and lesion angle, also predict ischemic complications. Longer and more aggressive anticoagulation regimens may be beneficial because most ischemic complications have an early delayed presentation and affect patients unprotected by anticoagulation. Clinical outcomes correlate with ischemic complications and vertebrobasilar anatomy. Despite a significant complication rate, most of our patients experienced good to excellent clinical outcomes and were free of vertebrobasilar ischemia at late midterm follow-up. In consideration of these findings and the malignant natural history of symptomatic intracranial vertebrobasilar athero-occlusive disease, stent angioplasty may be a reasonably good treatment option for patients with technically favorable lesions, especially in those with medically refractory symptoms. Although we do not believe that our data should influence a change in the indications for basilar artery stent placement, our experience provides a basis on which patients and referring physicians can be informed about procedure-related risks. Whether the long-term risk-to-benefit ratio of stent placement will compare favorably to best medical therapy in all or select patients with symptomatic basilar artery atherosclerosis will need to be assessed in randomized clinical trials.

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References

1. WASID Study Group. The **Warfarin-Aspirin Symptomatic Intracranial Disease Study G. Prognosis of patients with symptomatic vertebral or basilar artery stenosis.** *Stroke* 1998;29:1389–92
2. Thijs V, Albers G. **Symptomatic intracranial atherosclerosis: outcome of patients who fail antithrombotic therapy.** *Neurology* 2000;55:490–97
3. Chimowitz MI, Lynn MJ, Howlett-Smith H, et al. **Warfarin-aspirin Symptomatic Intracranial Disease Trial Investigators: Comparison of warfarin and aspirin for symptomatic intracranial arterial stenosis.** *New Engl J Med* 2005;352:1305–16
4. Hopkins L, Martin N, Hadley M, et al. **Vertebrobasilar insufficiency. Part 2. Microsurgical treatment of intracranial vertebrobasilar disease.** *J Neurosurg* 1987;66:662–74
5. Spetzler R, Hadley M, Martin N, et al. **Vertebrobasilar insufficiency. Part 1:**

Microsurgical treatment of extracranial vertebrobasilar disease. *J Neurosurg* 1987;66:648–61
6. Lylyk P, Cohen J, Ceratto R, et al. **Angioplasty and stent placement in intracranial atherosclerotic stenoses and dissections.** *AJNR Am J Neuroradiol* 2002;23:430–36
7. Malek A, Higashida R, Halbach V, et al. **Tandem intracranial stent deployment for treatment of an iatrogenic, flow-limiting, basilar artery dissection: Technical case report.** *Neurosurgery* 1999;45:919–24
8. Mori T, Kazita K, Chokyu K, et al. **Short-term arteriographic and clinical outcome after cerebral angioplasty and stenting for intracranial vertebrobasilar and carotid atherosclerotic occlusive disease.** *AJNR Am J Neuroradiol* 2000;21:249–54
9. Phatouros C, Higashida R, Malek A, et al. **Endovascular stenting of an acutely thrombosed basilar artery: technical case report and review of the literature.** *Neurosurgery* 1999;44:667–73
10. SSYLVIA Study Investigators. **Stenting of Symptomatic Atherosclerotic Lesions in the Vertebral or Intracranial Arteries (SSYLVIA): study results.** *Stroke* 2004;35:1388–92
11. Levy E, Hanel R, Boulos A, et al. **Comparison of periprocedure complications resulting from direct stent placement compared with those due to conventional and staged stent placement in the basilar artery.** *J Neurosurg* 2003;99:653–60
12. Levy E, Horowitz M, Koebbe C, et al. **Transluminal stent-assisted angioplasty of the intracranial vertebrobasilar system for medically refractory, posterior circulation ischemia: early results.** *Neurosurgery* 2001;48:1215–23
13. Mori T, Fukuoka M, Kazita K, et al. **Follow up study after intracranial percutaneous transluminal cerebral balloon angioplasty.** *AJNR Am J Neuroradiol* 1998;19:1525–33
14. Marks MP, Marcellus ML, Do HM, et al. **Intracranial angioplasty without stenting for symptomatic atherosclerotic stenosis: long term follow up.** *AJNR Am J Neuroradiol* 2005;26:525–30
15. Gress DR, Smith WS, Dowd CF, et al. **Angioplasty for intracranial symptomatic vertebrobasilar ischemia.** *Neurosurgery* 2002;51:23–29
16. Piedade PR, Gagliardi RJ, Damiani IT, et al. [**Platelet aggregation test: application in the control of antiplatelet aggregation in the secondary prevention of stroke**]**.** *Arq Neuropsiquiatr* 2003;61:764–67
17. Lopes DK, Ringer AJ, Boulos AS, et al. **Fate of branch arteries after intracranial stenting.** *Neurosurgery* 2003;52:1275–79
18. Cho G, Lee C, Hong M, et al. **Effects of stent design on side branch occlusion after coronary stent placement.** *Catheter Cardiovasc Interv* 2001;52:18–23
19. Geary R, Williams J, Golden D, et al. **Time course of cellular proliferation, intimal hyperplasia, and remodeling following angioplasty in monkeys with established atherosclerosis. A nonhuman primate model of restenosis.** *Arterioscler Thromb Vasc Biol* 1996;16:34–43