

Original Article

Technical factors affecting outcomes following endovascular treatment of posterior circulation atherosclerotic lesions

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Abstract

Background: Atherosclerotic disease of the vertebrobasilar system causes significant morbidity and mortality. All lesions require aggressive medical management, but the role of endovascular interventions remains unsettled. This study examines such endovascular interventions for vertebrobasilar atherosclerosis.

Methods: Retrospective review was performed of prospectively maintained procedure logs at three hospitals with comprehensive neurointerventional services. Patients with angiographically-proven stenosis undergoing elective stent placement were selected for analysis of demographic factors, lesion characteristics, and treatment details. Multivariate analysis was performed to evaluate for associations with ischemic stroke, death, and functional status as measured by modified Rankin scale at multiple intervals.

Results: One hundred and twenty-three lesions were treated in 110 patients. A total of 43 (58.1%) lesions caused stroke, while 66 (89.2%) caused transient ischemic attacks (TIAs). Forty lesions (32.5%) were at the vertebral origin; 97 (60.2%) were intracranial. A total of 112 (91.1%) were treated successfully. 4 (3.3%) of 10 (8.1%) procedural complications were symptomatic. Intracranial lesions were associated with death at 1 and 2 years (OR 24.91, $P < 0.001$) and mRS >2 at last contact (OR 12.83, $P < 0.001$). Stenting treatment with conjunctive angioplasty had lower rates of death (OR 0.303, $P = 0.046$) and mRS >2 at last contact (OR 0.234, $P = 0.018$) when angioplasty was performed with a device other than that packaged with the stent.

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Conclusion: Endovascular treatment of vertebrobasilar atherosclerosis can be performed safely, particularly for vertebral origin lesions. Higher rates of technical failure and complication may be acceptable for certain intracranial lesions due to their refractory nature and the morbidity caused by such lesions. Treatment should be tailored to features of each individual lesion.

Key Words: Angioplasty, atherosclerosis, ischemic stroke, stenting

INTRODUCTION

Atherosclerosis of the vertebrobasilar system accounts for a significant portion of ischemic strokes. The optimal role for endovascular therapies remains uncertain, particularly with respect to intracranial disease, in light of poorer outcomes of the stenting cohort in the SAMMPRIS trial.^[13] However, robust registries and years of experience prior to that trial reported technical feasibility and good postoperative outcomes for such lesions, and no other viable treatment options exist for medically refractory lesions in the posterior circulation.^[12,16,20,28,34,42,43,56] The effect of patient comorbidities and symptom types on outcomes following endovascular treatment of anterior circulation intracranial atherosclerosis and intra- and extracranial posterior circulation atherosclerosis has been reported elsewhere.^[2-4] To augment our understanding of these procedures performed in the vertebrobasilar system, technical considerations are herein reported.

MATERIALS AND METHODS

Under IRB-approved protocols, medical records were retrospectively reviewed by searching prospectively maintained procedure databases at a large academic medical center and two affiliated hospitals, all with high volume comprehensive neurointerventional services. All patients with stenosis of the vertebral or basilar arteries were identified. From this group, patients undergoing elective angioplasty or stent deployment were selected. Patients with luminal narrowing due to disease processes other than atherosclerosis were excluded. Patients in whom an intervention was attempted but unsuccessful were included in an intention to treat analysis.

Information was gathered according to the guidelines of the Standards Committee of the Society for NeuroInterventional Surgery for investigations of endovascular treatment of intracranial atherosclerotic disease.^[28] Presenting symptoms were noted. Dates of intervention and anesthesia type were recorded. Lesions were classified by vessel and most distal segment treated. Lesions at the vertebral artery origin were considered separately from lesions in the V1 segment of the vertebral artery not involving the origin. Lesion features and technical success were recorded according to those reported by the primary interventionalist, if available. When not explicitly

stated, these data were assessed by investigators conducting data review. The degree of stenosis was determined using the Warfarin-Aspirin Symptomatic Intracranial Disease Trial (WASID) technique.^[14,28,48] Stenosis length was measured, presence of tandem stenosis was noted, and Mori classification was assigned.^[38] Device type, model, and size were noted, as was the indicated deployment site for stents used. Stents in turn were classified as primarily designed for intracranial, coronary, biliary, or peripheral/renal vascular use. Post-treatment stenosis was measured in the same fashion as measurement prior to deployment. Technical success was defined as residual stenosis <50% without procedural complication.^[28] Any procedural complications were noted, as well as means taken to treat them, if applicable, and whether or not such complications were symptomatic.

Timing and type of clinical and imaging follow up were determined by the primary interventionalist; no uniform protocol existed between practitioners. The most recent date of contact was determined for long-term follow up. For those patients with available records, the Social Security death index was queried to screen for deaths among patients lost to follow up.^[44] Endpoints evaluated were ischemic stroke, intraparenchymal hemorrhage, death, or other adverse event related to treatment at thirty days, ninety days, one year, two years, and point of last contact. Point of last contact was also considered with exclusion of those patients not contacted following discharge from the intervention. Functional status was also assessed at these time points with mRS. Recursive partitioning analysis was performed to evaluate for temporal changes in outcomes and for any inflection points to include in univariate analysis performed with Chi-square tests and multivariate logistic regression analysis. Additionally, outcomes were investigated before and after key trials that altered clinical management of cervicocerebral atherosclerosis at our institution, WASID (1998), SPARCL (2006), and SAMMPRIS (2011). Kaplan-Meier curves were constructed to compare outcomes between lesion locations. All statistical tests were performed using IBM SPSS version 22 (IBM, Armonk, NY).^[17]

RESULTS

One hundred and twenty-three lesions in 110 patients were treated between August 1998 and August 2013

and met inclusion criteria. Patient demographics, lesion characteristics, and treatment features are summarized in Table 1. Technical success was achieved in 112 (91.1%) procedures; 48 (98.0%) procedures were successful in extracranial locations. A total of 10 (8.1%) procedural complications occurred, all in the intracranial posterior circulation, of which 4 (3.3%) were symptomatic. Complications are summarized in Table 2. Mean follow-up time was 873 days (standard deviation, 1078; median, 419). Summary clinical follow-up data are provided in Table 3.

Table 1: Lesion and treatment characteristics

	Extracranial 49 Lesions 46 Patients	Intracranial 74 Lesions 64 Patients	Total 123 Lesions 110 Patients
Age (Years)	60.2±9.25	63.9±11.3	62.4±10.7
Male Gender	30 (61.2%)	63 (85.1%)	93 (75.6%)
Presenting Symptom			
Stroke	14 (28.6%)	29 (39.2%)	43 (58.1%)
TIA	24 (49.0%)	42 (56.8%)	66 (89.2%)
None	11 (22.4%)	3 (4.1%)	13 (17.6%)
Artery			
Vertebral	49 (100%)	38 (51.4%)	87 (70.7%)
Origin	40 (81.6%)	-	40 (32.5%)
V1	5 (10.2%)	-	5 (6.8%)
V2	2 (4.1%)	-	2 (1.6%)
V3	2 (4.1%)	-	2 (1.6%)
V4	-	38 (51.4%)	38 (30.9%)
Dominant vertebral artery	22 (44.9%)	24 (63.2%)	46 (37.4%)
Basilar	-	36 (48.6%)	36 (29.3%)
Proximal	-	9 (12.2%)	9 (7.3%)
Mid	-	23 (31.1%)	23 (18.7%)
Distal	-	4 (5.4%)	4 (3.3%)
Lesion characteristics			
Stenosis (%)	81.5±11.6	81.7±12.1	81.6±11.9
Lesion Length (mm)	6.6±2.5	8.4±3.6	7.7±3.3
Mori Classification			
A	16 (32.7%)	11 (14.9%)	26 (21.1%)
B	29 (59.2%)	43 (58.1%)	72 (58.5%)
C	4 (8.2%)	20 (27.0%)	24 (19.5%)
Tandem stenoses	26 (53.1%)	47 (63.5%)	73 (59.3%)
Treatment characteristics			
Treatment Type			
Angioplasty Alone	2 (4.1%)	12 (16.2%)	16 (13.0%)
Stent Deployment	47 (95.9%)	62 (83.8%)	109 (88.6%)
Intracranial (Wingspan)	0 (0.0%)	6 (9.7%)	6 (5.5%)
Coronary	19 (40.4%)	56 (90.3%)	75 (68.6%)
Biliary	25 (53.2%)	0 (0.0%)	25 (22.9%)
Peripheral/renal vascular	3 (6.4%)	0 (0.0%)	3 (2.8%)
Technical success	48 (98.0%)	63 (85.1%)	112 (91.1%)
Procedural complication	0 (0.0%)	10 (13.5%)	10 (8.1%)
Symptomatic procedural complication	0 (0.0%)	4 (5.4%)	4 (3.3%)

Results of univariate analysis are summarized in Supplemental Tables 1–14. Factors associated with adverse outcomes in this analysis included male gender, intracranial lesions, lesions distal to the vertebral origin, tandem lesions, angioplasty performed in addition to stenting, deployment of a drug-eluting stent, use of general anesthesia during intervention, and technical failure.

Temporal inflection points reflecting changes in outcomes identified by recursive partitioning are summarized in Table 4. Recursive partitioning analysis yielded no significant findings for other continuous variables. Bivariate analysis of outcomes according to the release of SPARCL demonstrated fewer deaths at 1 year (OR 4.7, $P = 0.043$), 2 years (OR 4.7, $P = 0.043$), and last follow up (OR 15.7, $P < 0.001$); fewer strokes at last follow up (OR 6.0, $P = 0.022$); and fewer patients with disability or death at last follow up (OR 16.9, $P < 0.001$) after the publication. No statistically significant effects were noted before and after publication of WASID or SAMMPRIS.

In multivariate analysis, statistical significance persisted for the association of intracranial lesion location with death at 1 year (OR, 24.91; 95% CI, 2.746–226.0; $P < 0.001$), death at 2 years (OR, 24.91; 95% CI, 2.746–226.0; $P < 0.001$), and mRS >2 at last contact (OR, 12.83, 95% CI, 2.567–641.0; $P < 0.001$). When stent deployment was performed, statistically significant inverse relationships were noted between use of an angioplasty balloon other than that packaged with a stent with death at last contact (OR, 0.303; 95% CI, 0.094–0.979; $P = 0.046$) and mRS >2 at last contact (OR, 0.234; 95% CI 0.070–0.780; $P = 0.018$).

DISCUSSION

In the United States, intracranial atherosclerosis causes 10–15% of ischemic strokes, and is the etiology of up to half of stroke in populations outside of the U.S.^[10,27,28,32,47,53–55] Additionally, extracranial atherosclerosis frequently causes ischemic symptoms. Disease in the posterior circulation is of particular concern due to the severity of symptoms resulting from ischemia of structures supplied by these vessels. Medical and endovascular treatments exist for atherosclerotic disease, although most treatment paradigms now favor the former for intracranial disease following results of the SAMMPRIS trial.^[15] Endovascular treatments for extracranial atherosclerosis of the posterior circulation have not been as rigorously investigated as intracranial disease and have fallen out of favor at many centers. Many interventionalists believe endovascular treatment remains appropriate for certain lesions, although this remains controversial. This study investigates technical factors that affect outcomes following endovascular treatment in a large cohort of posterior circulation lesions.

Table 2: Procedural complications

Age	Gender	Presenting symptoms	Location	Stenosis (%)	Length (mm)	Mori	Complication	Treatment	Outcome
Elderly	M	TIA	V4	80	9	B	Dissection	Observation	Rehab Transfer Day 5, mRS 4
Elderly	M	TIA	V4	85	7	B	Dissection	Observation	Discharged Asymptomatic
Elderly	M	TIA	Proximal basilar	80	4	A	Dissection	Observation	Discharged Asymptomatic
Elderly	M	TIA	Distal basilar	99	8	B	Dissection	Observation	Discharged Asymptomatic
Middle aged	M	Stroke	V4	70	8	B	Dissection	Stent	Discharged Home Day 22, mRS 2
Elderly	M	TIA	V4	80	12	C	Extravasation	EVD	Died Day 1
Elderly	M	TIA	Mid basilar	90	20	C	Thrombosis	Thrombolysis, Stent	Died Day 9
Middle aged	F	TIA	V4	90	13	C	Extravasation	Observation	Discharged Asymptomatic
Middle aged	M	Stroke	V4	100	11	C	Extravasation	Observation	SNF Transfer Day 7
Middle aged	M	Stroke	V4	80	10	C	Extravasation, Occlusive Vasospasm	Observation	Discharged Home Day 7, mRS 2

Table 3: Clinical follow-up

	Extracranial	Intracranial	Total
Mean follow-up	799±925	922±1172	873±1078
Median follow-up	445	406	419
30-day follow-up (n=27)	(n=27)	(n=20)	(n=47)
TIA	0 (0.0%)	0 (0.0%)	0 (0.0%)
Stroke	0 (0.0%)	0 (0.0%)	0 (0.0%)
mRS >2	0 (0.0%)	3 (15.0%)	0 (0.0%)
Death	0 (0.0%)	0 (0.0%)	0 (0.0%)
90-day follow-up (n=14)	(n=14)	(n=10)	(n=24)
TIA	1 (7.1%)	0 (0.0%)	1 (4.2%)
Stroke	0 (0.0%)	0 (0.0%)	0 (0.0%)
mRS >2	0 (0.0%)	3 (30.0%)	3 (12.5%)
Death	0 (0.0%)	0 (0.0%)	0 (0.0%)
Last contact (n=49)	(n=49)	(n=74)	(n=123)
TIA	4 (8.2%)	10 (13%)	14 (11.4%)
Stroke	3 (6.1%)	8 (10.8%)	11 (8.9%)
mRS >2	3 (6.1%)	18 (24.3%)	21 (17.1%)
Death	3 (6.1%)	17 (23.0%)	20 (16.3%)

Twenty-five to forty percent of ischemic strokes are in the posterior circulation.^[7,9,16,52] The vertebral artery origin is the most common site of stenosis in the posterior circulation, as 20% of posterior circulation strokes occur in the setting of ostial stenosis, and 25% of patients with posterior circulation transient ischemic attacks (TIAs) or strokes have atherosclerotic lesions in the vertebral and/or basilar arteries.^[11,16,25,37,45] Such lesions often cause progressive symptoms, and patients with TIAs with extracranial vertebral disease carry a 30% risk of stroke within 5 years.^[18,29-31,50] Furthermore, 10–15% annual recurrence risk for strokes in this territory are more than tripled with concomitant underlying stenosis.^[1,5,11,23,39,45] While medical management is the first line treatment for atherosclerosis, appropriate treatments are needed for refractory disease.

Surgical treatments for posterior circulation atherosclerosis have shown no benefit or are prohibitively morbid.^[28] Angioplasty has been successfully performed in the intracranial and extracranial circulation, but many practitioners opt instead for concomitant stent deployment due to concerns for the recurrent stenosis or flow-limiting dissection with the angioplasty.^[28,35,36,42] To be considered an option for treating such disease, endovascular therapies must be acceptably safe. The overall success rate over 90% and symptomatic complication rate below 3% in this current series suggest acceptable safety does exist for these procedures when performed by experienced operators with meticulous technique. The interventionalist has several factors to consider when choosing stent type and model to perform revascularization. To date, the Wingspan stent system that includes the Gateway angioplasty balloon catheter is the only device with FDA approval for deployment in the intracranial circulation. However, following the results of the SAMMPRIS trial, use of this device has fallen dramatically. With self-expanding stents such as Wingspan, there is increased radial force compared to balloon-mounted stents.^[49] This continuous force against the vessel wall increases neovascularization and may lead to restenosis from neointimal hyperplasia.^[22,49] Balloon-mounted stents involve the risks inherent in angioplasty that lead to higher risk for complication, while their initial technical success rates may meet or exceed those of self-expanding stents.^[28,35,36,42,46,49] The reduced radial force these stents generate makes them less desirable for vessels subject to anatomic compression, which is important to consider in the high extracranial vertebral artery. In order to realize the benefit of lower complication rates of self-expanding stents while improving long term patency, drug-eluting stents have also been used.^[6,24,28,41] However, the promise of drug-eluting stents, realized elsewhere in the body,

Table 4: Temporal effects on outcomes

Outcome	df	n	χ^2	P
Death at 1 Year 57.1% before June 2002 2.0% after June 2002	1	72	30.61	<0.001
Death at 2 Years 57.1% before June 2002 2.0% after June 2002	1	72	30.61	<0.001
Death at Last Contact 37.0% before August 2004 3.7% after August 2004	1	136	25.815	<0.001
mRS >2 at 90 Days 8.3% before July 2008 75.0% after July 2008	1	20	9.38	0.020
mRS >2 at Last Contact 38.9% before August 2004 4.3% August 2004 to June 2011 46.2% after June 2011	2	136	25.875	<0.001
Same or Improved mRS 57.4% before August 2004 92.7% after August 2004	1	136	24.15	<0.001
mRS >2 at last contact (seen after discharge) 57.1% before September 2001 16.1% September 2001 to July 2005 2.3% July 2005 to April 2011 40.0% after April 2011	3	106	28.24	<0.001

has not been borne out in the neurointerventional literature and current series showed association of these devices with higher stroke rates at one and two years.^[3,28,41]

Technical failure was associated with poor outcomes regardless the stent type (balloon-mounted vs. self-expanding, biliary vs. coronary vs. intracranial). Additionally, the need to consider treatment of these lesions on a case-by-case basis is reflected in the multiple device types operators preferred over many years. Attempts to simplify and generalize devices belie the importance of planning each treatment individually to best fit lesion characteristics. This is suggested by the improved outcomes when using an angioplasty balloon other than that packaged with a stent, a statistically significant relationship that persisted in multivariate analysis.

In addition to selecting the proper devices, understanding the inherent risks of different lesions is important. Intracranial lesion location was a strong predictor of poor outcomes, with statistical significance in the multivariate models for association with death at one year and two years, as well as mRS>2 at last contact. Success rates were lower for these lesions compared to extracranial disease (85.1% vs. 98.0%, respectively), and all procedural complications in the current analysis occurred during treatment of intracranial lesions. Additionally, presence

of tandem stenoses was predictive of adverse events in univariate analysis. Such outcomes, which are concordant with findings elsewhere, should be taken into account when considering endovascular treatment of intracranial posterior circulation atherosclerosis.^[3,8,19,21,40] However, given the above-described progressive, medically refractory disease involved, such intervention may be indicated, particularly when considering the morbidity of infarction in portions of the brain served by the posterior circulation.

Whereas endovascular treatment of intracranial lesions carries inherent risks, such treatment of extracranial disease, particularly at the vertebral artery origin, is relatively safe. Prior studies have demonstrated high rates of technical success and few procedural complications.^[16,26,33,51] Technical success was achieved in all 40 ostial interventions in the current study without complications.

Endovascular device technology continues to advance, as does medical management. This study found that better outcomes occurred following publication of the SPARCL trial, after which time statin treatment for cervicocerebral atherosclerosis became standard at our medical center. Indeed, we have previously reported the beneficial impact of statin treatment on our cohort of patients treated with angioplasty or stenting.^[3,4] Interestingly, no additional temporal differences were identified, including the publication dates for both WASID and SAMMPRIS. Endovascular treatments declined in number dramatically following publication of the SAMMPRIS results, with 5 of the 123 treatments occurring after September 2011. Among temporal inflection points identified by recursive partitioning analysis summarized in Table 4, none occurred at times of major changes in management of ICAD in our practice.

Given the above findings and discussion, endovascular treatment of atherosclerosis in the posterior circulation can be achieved with high levels of technical success and good outcomes. However, further investigation is needed considering limitations of this current study, most of which are due to retrospective design and selection bias inherent in studying only patients for whom treatment was elected. Lack of prospectively developed follow-up protocols limited data capture within early post-procedure periods and the similarly limited assessment of follow up imaging. Additionally, this study reflects over sixteen years of interventions and includes patients treated with methods formerly considered appropriate but not currently standard of care. As such, adverse technical events might be lower for interventions performed with contemporary techniques and equipment.

CONCLUSION

Endovascular treatment of atherosclerosis of the vertebrobasilar system can be performed with high rates

of technical success and few complications. This is particularly true for lesions of the extracranial vertebral arteries, for which endovascular treatment should be sought for lesions refractory to medical management. Higher rates of failure and complication may be acceptable for intracranial lesions refractory to medical care due to the poor natural history prognosis of such lesions and the morbidity inherent to infarctions in this territory.

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Conflicts of interest

There are no conflicts of interest.

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Supplemental Table 1: Predictors of procedural complication

Feature	df	n	χ^2	P
Intracranial Location	1	123	7.21	0.005
Location Distal to Ostium	1	123	5.25	0.016
Balloon Included with Stent	1	123	5.55	0.024

Supplemental Table 2: Predictors of TIA at last contact

Feature	df	n	χ^2	P
Male Gender	1	123	5.10	0.015
Tandem Lesions	1	123	4.55	0.028

Supplemental Table 3: Predictors of TIA at last contact beyond discharge

Feature	df	n	χ^2	P
Tandem Lesions	1	97	4.03	0.039

Supplemental Table 4: Predictors of stroke at 1 year

Feature	df	n	χ^2	P
Drug Eluting Stent	1	62	7.95	0.043

Supplemental Table 5: Predictors of stroke at 2 years

Feature	df	n	χ^2	P
Drug-Eluting Stent	1	47	10.58	0.027

Supplemental Table 6: Predictors of stroke at last contact

Feature	df	n	χ^2	P
Tandem Lesions	1	123	4.99	0.022
General Anesthesia	1	123	4.81	0.021
Balloon Included with Stent	1	123	4.08	0.048

Supplemental Table 7: Predictors of stroke at last contact beyond discharge

Feature	df	n	χ^2	P
General Anesthesia	1	97	4.31	0.030

Supplemental Table 8: Predictors of death at 1 Year

Feature	df	n	χ^2	P
General Anesthesia	1	66	6.07	0.009
Intracranial Location	1	66	7.39	0.006
Location Distal to Ostium	1	66	4.79	0.025
Technical Failure	1	66	5.56	0.048

Supplemental Table 9: Predictors of death at 2 Years

Feature	df	n	χ^2	P
General Anesthesia	1	66	6.07	0.009
Intracranial Location	1	66	7.39	0.006
Location Distal to Ostium	1	66	4.79	0.025
Technical Failure	1	66	5.56	0.048

Supplemental Table 10: Predictors of death at last contact

Feature	df	n	χ^2	P
Male Gender	1	123	4.87	0.019
General Anesthesia	1	123	9.50	0.001
Intracranial Location	1	123	6.15	0.010
Tandem Lesions	1	123	6.51	0.008
Balloon Included with Stent	1	123	12.18	0.001
Technical Failure	1	123	6.30	0.026

Supplemental Table 11: Predictors of mRS ≥ 3 at 30 days

Feature	df	n	χ^2	P
Technical Failure	1	33	19.39	0.007

Supplemental Table 12: Predictors of mRS ≥ 3 at last contact

Feature	df	n	χ^2	P
Male Gender	1	123	5.29	0.014
General Anesthesia	1	123	10.07	<0.001
Intracranial Location	1	123	6.90	0.007
Location Distal to Ostium	1	123	3.84	0.039
Tandem Lesions	1	123	4.90	0.022
Balloon Included with Stent	1	123	14.01	<0.001
Technical Failure	1	123	5.68	0.032

Supplemental Table 13: Predictors of mRS ≥ 3 at last contact beyond discharge

Feature	df	n	χ^2	P
General Anesthesia	1	97	7.67	0.002
Intracranial Location	1	97	4.70	0.025
Tandem Lesions	1	97	5.17	0.018
Balloon Included with Stent	1	97	8.76	0.004

Supplemental Table 14: Predictors of retreatment

Feature	df	n	χ^2	P
General Anesthesia	1	123	7.34	0.012