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Safety and Efficacy of Balloon Mounted Stent in the Treatment of Symptomatic Intracranial Atherosclerotic Disease: A Multicenter Experience

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Abstract

Background

Randomized clinical trials failed to prove safety and efficacy of endovascular treatment for symptomatic intracranial atherosclerotic disease(sICAD) over medical management. A recent study using self-expandable stent showed acceptable lower rates of periprocedural complications. We aimed to study the safety and efficacy of balloon mounted stent(BMS) in the treatment of sICAD.

Methods

Prospectively maintained databases from 15 neuroendovascular centers between 2010-2020 were reviewed. Patients were included if they had severe symptomatic intracranial stenosis in the target artery, failed medical management, and underwent intracranial stenting with BMS after 24-hours of the qualifying event. The primary outcome was the occurrence of stroke and mortality within 72-hours after the procedure. Secondary outcomes were the occurrence of stroke, transient ischemic attacks(TIA), and mortality on long-term follow-up.

Results

A total of 232 patients were eligible for the analysis(median age;62.8 years and 34.1%females). The intracranial stenotic lesions were located in the anterior circulation in 135(58.2%) cases. Recurrent stroke was the qualifying event in 165(71.1%) while recurrent TIA was identified in 67(28.9%) cases. The median time from the qualifying event to stenting was 5[2-20.75] days. Strokes were reported in 13(5.6%) patients within 72-hours of the procedure; 9(3.9%) ischemic and 4(1.7%) hemorrhagic and mortality in 2(0.9%) cases. Among 189 patients with median follow-up time 6[3-14.5] months, 12(6.3%) had TIA, and 7(3.7%) had strokes. Three patients (1.6%) died from causes not related to stroke.

Conclusion

Our study has shown that BMS may be a safe and effective treatment for medically refractory sICAD. Additional prospective randomized clinical trials are warranted.

Introduction

Intracranial atherosclerotic disease (ICAD) is one of the most common causes of acute ischemic stroke worldwide. Its prevalence differs according to the ethnic background with Asian, Hispanic, and Black populations having the highest disease burden.[1-3] The SAMMPRIS (Stenting and Aggressive Medical Management for Preventing Recurrent Stroke in Intracranial Stenosis) [4] and VISSIT (Vitesse Intracranial Stent Study for Ischemic Stroke Therapy) [5] randomized clinical trials, demonstrated that optimal medical management alone (in the form of dual antiplatelet therapy (DAPT), risk factor mitigation, and lifestyle changes) was superior to angioplasty and stenting plus medical management in the treatment of symptomatic ICAD. Recently, the WEAVE (Wingspan Stent System Post Market Surveillance) and WOVEN (Wingspan One-year Vascular Events and Neurologic outcomes) studies have demonstrated low rates of periprocedural complications (2.6%) and recurrent stroke on long term follow-up (8.5%), following angioplasty and stenting of symptomatic ICAD using the self-expanding Wingspan stent system in selected patients treated by experienced neurointerventionalists.[6 7]

Balloon-mounted stents (BMS) may reduce procedural complications by avoiding the risks related to over-the-wire exchange, which represent one of the most technically demanding maneuvers associated with the use of self-expandable stents (SES). Also, BMS have higher radial force leading to an optimal luminal dilatation, especially in those with calcified lesions. Finally the use of BMS may be associated with lower rates of in-stent restenosis (ISR) compared to SES.[8] However, BMS navigation is challenging due to its stiff nature especially in the elderly with tortuous anatomy as well as in more distal lesions.

In the present study we aimed to identify the safety and early outcomes for the use of BMS in the treatment of symptomatic ICAD.

Methods

The data that support the findings of this study are available from the corresponding author on reasonable request. This study has been approved by each local Institutional Review Board.

Patient selection

Prospectively maintained neuroendovascular databases from 15 comprehensive stroke centers through 2010 to 2020 were merged and the compiled data was analyzed. Patients were included if they had symptomatic intracranial stenosis (≥70%) in the target artery, failed medical management "defined as recurrent transient ischemic attacks (TIA) or stroke on DAPT and statin therapy", had baseline modified Rankin Scale (mRS) ≤3, and underwent intracranial stenting with BMS after 24 hours of the qualifying event. Patients with large vessel occlusion strokes with underlying ICAD who underwent intracranial stenting were excluded from the study.

Endovascular Procedure

The decision to pursue endovascular treatment was based on a multidisciplinary discussion between vascular neurologists and neurointerventionists at each center. The choice of the arterial access, as well as the anesthesia modality, was depending on the operator's preference and site of the lesion. According to the time of the procedure from the qualifying event, the majority of cases were loaded with a dose of 325 mg of acetylsalicylic acid (ASA) daily and 75 mg of clopidogrel at least 3-5 days before stenting. Platelet function was assessed by P2Y12 reaction units (PRU) test with a target of 60-200; if it was above 200, a loading dose (180 mg) of ticagrelor was given then the patient was started on ticagrelor 90 mg BID and ASA 81 mg daily and discontinued clopidogrel. If the procedure was performed less than 3 days after the qualifying event or PRU did not reach the target, an intravenous bolus of tirofiban (8.0 µg/kg) was administered after arterial

puncture followed by a maintenance dose (0.10 µg/kg/min) for 24 hours. During the intervention, all patients were heparinized to activated clotting time from 200 to 250s or 250-300s according to the local protocol at each center. Angiographic examination of the targeted vessel was performed to assess the vessel diameter adjacent to the stenosis and the diameter and length of the stenosis for proper selection of the stent size. The degree of percent stenosis was determined by the neurointerventionalist at each center as follows: percent stenosis = [(1-(Dstenosis/Dnormal)] × 100, where Dstenosis defined as the diameter of the artery at the site of the most severe stenosis and Dnormal as the diameter of the proximal normal artery.[9] Under a road map, the vessel distal to the stenosis was catheterized with a microwire; in cases of near occlusion of the targeted vessel or operator's discretion a pre-dilatation with a balloon was performed, then the balloon was exchanged for the BMS system "which was navigated distally to the lesion with the aid of the proximal support of the distal access catheter" and the stent was deployed. After deflation and withdrawal of the balloon catheter, a final DSA run was carried out to confirm stent deployment at the targeted stenosis and to exclude complications. After the procedure in addition to management of stroke risk factors, patients either received DAPT for 3 months then ASA 325 mg daily indefinitely or continue on DAPT based on the treating center protocol. Two types of BMS (Drug Eluting Stent; DES and Bare Metal Stent) have been used in the study **(Supplemental Table 1. Online Data Supplement)**. The choice between both stents was based on operator's preference and device availability.

Outcome Measures

The primary outcome was the occurrence of stroke (ischemic/hemorrhage) and mortality within 72 hours of the procedure. Stroke was defined as the occurrence of sudden neurological deterioration, was independently assessed clinically by a vascular neurologist, with the

radiological confirmation through a head CT (for hemorrhages) or brain positive DWI (for ischemia). Secondary outcomes included the occurrence of ipsilateral stroke (ischemic/hemorrhage), TIA and mortality on long term follow-up. Also, secondary outcomes included rates of procedural failure defined as failure to deploy the stent at the target artery.

Sensitivity analysis

Anterior and posterior circulation symptomatic ICAD were compared in terms of patient demographics, stroke-related risk factors, and outcome measures.

Subgroup analysis

We aimed to identify the early outcomes including any stroke (ischemic/hemorrhagic) and death within 72 hours after the stenting in a subgroup of patients fulfilling criteria for the WEAVE trial as following: age range from 22 to 80 years old, symptomatic intracranial stenosis of 70% to 99% in an artery 2 mm or larger, and ≥8 days after the qualifying event.[6]

Statistical Analysis

Categorical variables were expressed as frequencies and percentages. After normality testing through Shapiro–Wilk, continuous variables were expressed as mean ± SD for parametric and as median [interquartile range] for non-parametric variables. Comparison of continuous variables was made with the Mann-Whitney U test or Student t-test as appropriate. Categorical variables were compared using Pearson X^2 or Fisher exact as appropriate. Multivariable regression analyses were performed to identify the predictors of the occurrence of stroke (ischemic/hemorrhage) and mortality within 72 hours of the procedure, variables that were sought to be associated with the outcome (age, site of target artery (anterior vs. posterior circulation), degree of pretreatment

stenosis, time from event to treatment and treating center) were included in the model. Similarly, the following variables (age, DM, site of target artery (anterior vs. posterior circulation), degree of pretreatment stenosis, time from event to treatment and time to follow-up imaging) were forced in a regression model to identify predictors of ISR. The models' goodness of fit was assessed using the Hosmer-Lemeshow test. Significance was set at $p<0.05$, and all p values were 2-sided. Statistical analyses were performed using SPSS 26 software (IBM® Armonk, NY, USA).

Results

A total of 232 patients were eligible for the analysis. Mean±SD age was 62.8±12.6 years, 79 (34.1%) were females, 114 (49.1%) were white. Regarding stroke-related risk factors, 203 (87.5%) had hypertension, 137 (56.6%) had diabetes mellitus, 163 (70.3%) had hyperlipidemia and 65 (28%) were current smokers during the presentation. Symptomatic intracranial stenotic lesions were located in anterior circulation in 135 (58.2%) of patients **(Supplemental Figure 1. Online Data Supplement)** and in posterior circulation in 97 (41.8%) of patients **(Figure) and (Supplemental Figure 2. Online Data Supplement)**. DES was used in 144 (62.1%) of patients whereas Bare Metal Stent was used in 88 (37.9%) of patients. Recurrent stroke was the qualifying event in 165 (71.1%) while recurrent transient ischemic attacks (TIA) were identified in 67 (28.9%) of cases. The median time from the qualifying event to stenting was 5 [2-21] days and the median degree of percent stenosis was 80% [72-90]. Patients demographics and clinical characteristics are demonstrated in **(Table 1)**.

Table 1. Demographic and clinical characteristics

All patient n (%)	**N=232**
Age, years mean±SD	62.8±12.6
Female	79 (34.1)

Ethnic background	
White	114 (49.1)
AA	32 (13.8)
Hispanic	38 (16.4)
Asian	7 (3)
Other/unknown	41 (17.7)
Hypertension	203 (87.5)
Diabetes mellitus	137 (56.6)
Hyperlipidemia	163 (70.3)
Current cigarette smoking	65 (28)
Stenosis location	
Anterior circulation:	135 (58.2)
Supraclinoid-ICA	33 (14.2)
Cavernous-ICA	14 (6)
Petrous-ICA	21 (9.1)
Middle cerebral artery	
M1-segment	63 (27.2)
M2-segment	4 (1.7)
Posterior circulation:	97 (41.8)
Vertebral artery V4-segment	60 (25.9)
Basilar artery	35 (15.1)
Posterior cerebral artery	2 (0.9)
Qualifying event	
Recurrent stroke	165 (71.1)
Recurrent TIA	67 (28.9)
Time from last event to stenting, days median [IQR]	5 [2-20.75]
Degree of stenosis (%) median [IQR]	80 [72-90]
Residual stenosis post-stenting (%) median [IQR]	0 [0-10]

Abbreviations; AA: African American, ICA: internal carotid artery, TIA: transient ischemic attack

Early and late outcome

Procedural complications occurred in 2 cases (dissection in one case that led to brain stem infarction and locked-in syndrome, and perforation of posterior communicating artery aneurysm in the other case that led to subarachnoid hemorrhage and patient death). Within 72 hours post

stenting, stroke was reported in 13 (5.6%) patients including 9 (3.9%) ipsilateral ischemic events (resulting in 6 (2.6%) permanent and 3 (1.3%) temporary neurological deficits) and 4 (1.7%) hemorrhagic strokes. Early outcomes are shown in **(Table 2)**. There were no reported cases of procedural failure. On multivariable analysis, older age was an independent predictor of early events within 72 hours post stenting (OR 1.097, 95%CI 1.003-1.200], p=0.04) **(Supplemental Table 2. Online Data Supplement)**.

Table 2. Procedural outcome and follow-up

Early Outcome n (%)	**N=232**
Procedural complications	2 (0.9)
Perforation	1
Dissection	1
Stroke within 72 hours of the procedure	13 (5.6)
Ischemic stroke	9 (3.9)
Temporary	3 (1.3)
Permanent	6 (2.6)
Hemorrhagic stroke	4 (1.7)
Death on discharge	2 (0.9) (1 brain stem infarction/ 1 SAH)
Late Outcome n (%)	**N=189**
Time to clinical follow-up, months median [IQR]	6 [3-14.5]
Clinical Follow up	
TIA	12 (6.3)
Ischemic/hemorrhagic strokes	7 (3.7)
Death	3 (1.6) (1 metastatic cancer, 2 ESRD)
Follow up Imaging	N=133 (DSA=83, CTA=41, MRA=9)
In-stent stenosis	33 (24.8)
- Symptomatic:	15 (11.3)
Retreatment	11 (5 stenting/ 6 angioplasty)
- Asymptomatic	18 (13.5)

Abbreviations; TIA: transient ischemic attack, ESRD: end-stage renal disease, DSA: digital subtraction angiography, CTA: computed tomography angiography, MRA: magnetic resonance angiography

A total of 189 patients had a follow-up with a median [IQR] time of 6 [3-14.5] months in whom transient ischemic attacks and ipsilateral strokes (ischemic/hemorrhagic) were reported in 12 (6.3%) and 7 (3.7%), respectively. Three patients (1.6%) died from non-stroke related complications. On follow-up imaging of 133 patients (70 DES and 63 Bare Metal Stent), in-stent restenosis (ISR) was identified in 33 (24.8%) patients [15/70 (21.5%) DES and 18/63 (28.6%) Bare Metal Stent]. Symptomatic ISR was reported in 15 (11.3%) patients [7/70 (10%) DES and 8/63 (12.7%) Bare Metal Stent] out of which 11 were treated **(Supplemental Figure 3(A&B). Online Data Supplement)**. There were no independent predictors of ISR, only a trend in younger patients (OR 0.958, 95%CI [0.912-1.007], p=0.09). However, the results could be biased by lost follow up in ~ 43% of patients **(Supplemental Table 2. Online Data Supplement)**. Late clinical and imaging follow-up are illustrated in **(Table 2)**.

Anterior vs. posterior circulation

Patients with anterior circulation symptomatic ICAD (n=135) were significantly younger (60±13.1 vs. 66.8±10.7, p<0.001), had a higher proportion of females (42.2% vs. 22.7%, p=0.002), lower proportion of whites and African Americans, and higher proportion of Hispanic as compared to those with posterior circulation symptomatic ICAD (n=97). In addition, there was a trend toward a higher proportion of diabetes mellitus in the anterior circulation group (63.7% vs. 52.6%, p=0.09). There were no differences in terms of early and long-term follow-up among both groups **(Table 3)**.

Outcomes in WEAVE trial eligible subgroup

A total of 67 patients met the inclusion criteria of the WEAVE trial.[6] The mean age was 63.4±11.7 years, 21 (31.3%) were females, 39 (58.2%) had anterior circulation symptomatic ICAD, and the

median [IQR] time from qualifying event to stenting was 30 [15-60] days. One patient (1.5%) had a temporary neurological deficit due to an ischemic stroke that occurred within 72 hours post-stenting. There were no other reported procedural complications.

Table 3. Demographic and clinical characteristics among anterior and posterior circulation

	Anterior circulation N=135	Posterior circulation N=97	P value
Demographic and clinical characteristics n (%)			
Age	60±13.1	66.8±10.7	**<0.001**
Female	57 (42.2)	22 (22.7)	**0.002**
Ethnic background White AA Hispanic Asian Other/unknown	 61 (45.2) 22 (16.3) 30 (22.2) 2 (1.5) 20 (14.8)	 53 (54.6) 10 (10.3) 8 (8.2) 5 (5.2) 21 (21.6)	 **0.01**
Hypertension	115 (85.2)	88 (90.7)	0.21
Diabetes mellitus	86 (63.7)	51 (52.6)	0.09
Hyperlipidemia	90 (66.7)	73 (75.3)	0.16
Current cigarette smoking	37 (27.4)	28 (28.9)	0.81
Time from the last event to stenting, days median [IQR]	5 [3-16.25]	7 [2-24]	0.55
Degree of stenosis (%) median [IQR]	80 [72-90]	80 [72-90]	0.39
Residual stenosis post-stenting (%) median [IQR]	0 [0-0]	0 [0-10]	0.10
Early outcome n (%)			
Procedural complications	1	1	>0.99
Stroke within 72 hours of the procedure Ischemic stroke Temporary Permeant Hemorrhagic stroke	8 (5.9) 0 3 4	6 (6.2) 3 3 0	0.93
Death on discharge	1	1	>0.99
Late outcome n (%)			
Clinical Follow up TIA Ischemic/hemorrhagic strokes Death	N=110 7 (6.4) 8 3	N=79 5 (6.3) 2 0	 0.99 0.20 0.27
Follow up Imaging In-stent stenosis - Symptomatic:	N=75 19	N=58 14	 0.87

Retreatment	11 8 (4 stenting / 4 angioplasty)	4 3 (1 stenting/ 2 angioplasty)	0.18
- Asymptomatic	8	10	0.27

Abbreviations; AA: African American, TIA: transient ischemic attack, IQR: interquartile range

Discussion

The present study found lower rates of periprocedural stroke (5.6%) compared to the SAMMPRIS (14.7%) and VISSIT (24.1%) trials. Likewise, cumulative rates of strokes on long term follow-up (9.3%) were lower compared to SAMMPRIS trial (12.2% in the medical treatment arm and 20% in the stent arm). In addition, cumulative rates of TIA and strokes on long term follow-up (15.6%) were lower compared to VISSIT trial (36.2%).[4 5] Our results are similar to a recent study that evaluated the Acclino flex stent (Acandis GmbH, Pforzheim, Germany), a self-expanding stent that can be delivered through a low profile balloon microcatheter (NeuroSpeed, Acandis GmbH, Pforzheim, Germany) without wire exchange maneuvers. In that study, the periprocedural stroke rate was 6.5% at discharge.[10]

The SAMMPRIS and VISSIT trials reported lower 30-day rates of stroke or death in their medical treatment arm, 5.8% and 9.4% respectively.[4 5] However, in real-world practice higher rates of recurrent stroke within 30 days have been reported (20.2%), even in those treated with aggressive medical treatment consisting of DAPT and high dose statin similar to the SAMMPRIS trial.[11] The higher rates of disabling or fatal stroke within 30 days in the endovascular arm of both trials were mainly due to periprocedural complications. For instance, 16 patients (7.1%) in the stenting group in the SAMMPRIS trial had a disabling or fatal stroke due to periprocedural complications as compared with 4 patients (1.8%) in the medical group. Therefore, if the periprocedural

complication rates can be kept low, the long-term outcomes in patients undergoing angioplasty and stenting may be comparable or superior to medical management alone.

The risk of periprocedural complications may be related to the time interval from the qualifying event to stenting where early intervention in the presence of unstable plaque could increase the risk of plaque disruption and subsequent stroke in the affected territory. Also, the infarcted area is likely more susceptible to reperfusion hemorrhage soon after the event. It has been reported that patients with symptomatic ICAD treated within 24 hours of presenting symptom onset were at a higher risk of periprocedural stroke.[12] To mitigate this effect WEAVE trial included patients with more than 7 days of the ischemic event and found a low periprocedural stroke and death rate of (2.6%) within 72 hours post-stenting. In the present study, the periprocedural rate of stroke was (1.5%) in a subgroup of patients who met the inclusion criteria of the WEAVE trial.

Notably, studies have shown that most early recurrent events occur in the first few days after the initial event.[13 14] The SAMMPRIS trial enrolled patients with a median time of 7 days from the qualifying event and recurrence may already have occurred before enrollment contributing to the observed lower rates of stroke and TIA in the medical arm. In the present study, we enrolled patients after 24 hours of the qualifying event without bypassing the period of highest risk of recurrence. The best timing for endovascular treatment is still questionable since those with early recurrence may be the exactly the ones who would benefit the most from an early intervention. Interestingly, the results of acute stenting for acute stroke patients in the setting of tandem

occlusions or after failed thrombectomy have not shown any significant increase in the risk of cerebral hemorrhage. [15-20]

One disadvantage of the SES is over-the-wire exchange after angioplasty which may result in an increased risk of hemorrhagic and embolic stroke from dissection or wire perforation. In addition to the antiproliferative drug deliverability of some of the BMS (DES), BMS allows for an increase in luminal gain compared with angioplasty alone or SES which reduces the rates of restenosis.[8] In the current study, the rate of ISR (24.8%) was comparable to a recent study that evaluated the balloon mounted Apollo stent (MicroPort NeuroTech, Shanghai, China) in the treatment of symptomatic ICAD where the rate of ISR was (23.4%). However, we reported higher rates of symptomatic ISR (11.3% vs. 3.1%) which could be explained by the longer duration of follow-up of our study in which about 25% of patients had follow-up imaging >14.5 months after procedure compared with 12 months in the Apollo stent study. In addition, the Apollo stent study reported that only 64 patients had follow-up imaging and only about half of the patients with recurrent stroke had available follow-up images (4/9).[21] Moreover, the relatively early intervention in our study from the initial event may have increased the risk of ISR as some studies showed that stent deployment in the acute setting is associated with poor vessel healing and higher levels of fibrin deposition and inflammation, leading to more ISR.[22] Similar rates of ISR have been reported in the Acclino flex stent study as well where follow-up digital subtraction angiography revealed ISR in 25% (15/60) of patients in whom 11.6% (7/60) underwent percutaneous transluminal angioplasty.[10] The WOVEN trial reported (6.9%) symptomatic ISR within 1-year follow-up. The mechanism and best treatment of ISR necessitate further studies since the majority of non-procedural cerebral infarctions in SAMMPRIS at 3 years follow-up were most likely due to ISR.[23]

Previous studies demonstrated the periprocedural stroke rates are significantly higher in the treatment of perforator-bearing arteries in the posterior circulation [24] and middle cerebral artery (because of occlusion of lenticulostriate perforators).[4] In fact, the present study reported comparable rates of early and long-term outcomes among anterior and posterior circulation symptomatic ICAD treated with BMS. In addition, 40.8% of the patients stented in the WEAVE trial had middle cerebral artery lesions that did not show increased rates of stroke due to perforator occlusion.[6]

The present study has the typical limitations inherited to a retrospective design. It only included patients who underwent endovascular treatment lacking a control group. Moreover, we did not consider lesion characteristics like the length in determining the early and late outcome measures as it has been studied that lesions with Mori type C are more prone to procedural complications and ISR.[21] There was no well-defined protocol for follow-up imaging and there was no imaging core laboratory adjudication. Additionally, there was no cut-off degree to define ISR. The present study did not consider the different mechanisms of stroke either in the inclusion or in the outcome. Finally, deployment of BMS requires comparable vessel diameter in the stent landing zones (i.e. proximal and distal to the stenosis) compared to SES and this requirement may have created a bias.

Conclusions

In patients with symptomatic ICAD, angioplasty and stenting using BMS may be a safe and effective treatment option. Additional prospective randomized clinical trials are warranted.

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Contributors MHM: Study conception, design of the work, statistical analysis, interpretation of data, drafting of the manuscript. RGN: Study conception, interpretation of data, critical revision of manuscript. AEH: Study conception, design of the work, critical revision of the manuscript, other co-authors: interpretation of data, critical revision of manuscript

Data Sharing Anonymized data from the study are available upon reasonable request to the corresponding author.

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Figure Legend

Figure. Digital subtraction angiography shows stenosis of the left vertebrobasilar junction (arrow) anterior posterior (A) and lateral (B) views. (C&D) Intracranial navigation of the Rebel balloon mounted stent 3 mm x 12 mm (arrow) to the target lesion anterior posterior view subtracted (C) and unsubtracted (D) images. Anterior posterior (E) and lateral (F) views demonstrates successful deployment of the stent with resolution of the stenosis (arrow).

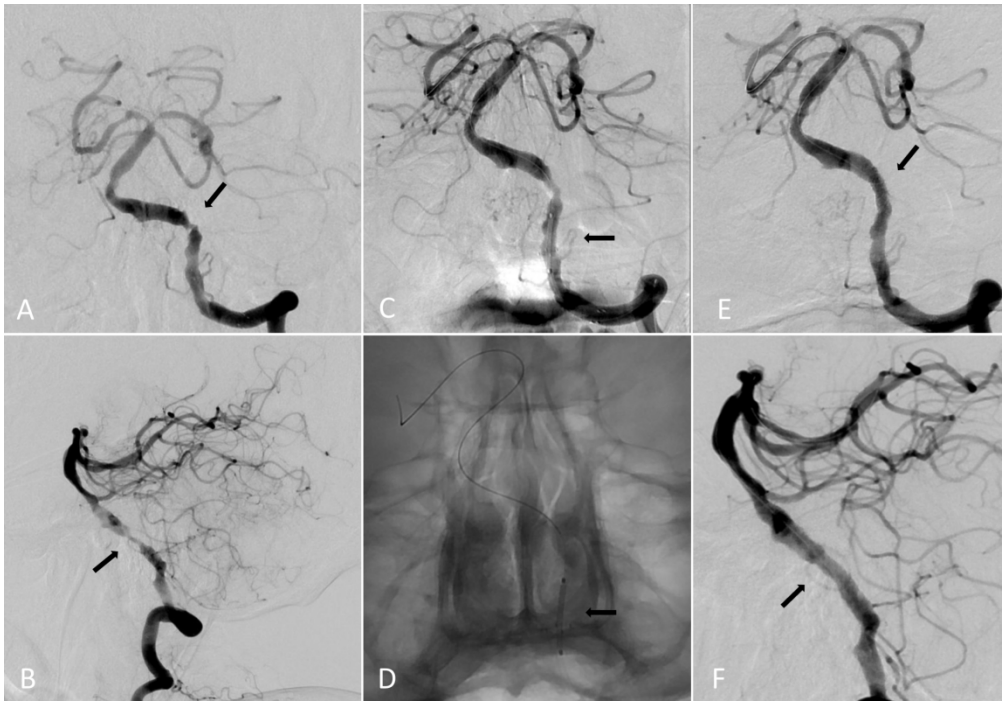


Figure. Digital subtraction angiography shows stenosis of the left vertebrobasilar junction (arrow) anterior posterior (A) and lateral (B) views. (C&D) Intracranial navigation of the Rebel balloon mounted stent 3 mm x 12 mm (arrow) to the target lesion anterior posterior view subtracted (C) and unsubtracted (D) images. Anterior posterior (E) and lateral (F) views demonstrates successful deployment of the stent with resolution of the stenosis (arrow).

200x139mm (300 x 300 DPI)

Supplemental Data

Supplemental Table 1. Balloon mounted stent used in the study

Stent	Sizes	Type
Vision Stent (Abbott Vascular, USA)	3.0*12 mm/3.0*8 mm/3.5*12 mm/4.0*12 mm	Bare Metal
Mini Vision Stent (Abbott Vascular, USA)	2*8mm/2.25*8 mm/ 3.0*8 mm	Bare Metal
Multi-Link Vision (Abbott Vascular, USA)	2*8mm/2.5*8mm/2.5*12mm/2.75*12mm/2.75*8mm / 3x8mm/3*12mm/3.5*8mm/3.5*12mm/ 3.5*18mm	Bare Metal
Micro-Driver Stent (Medtronic, USA)	2.25*8 mm	Bare Metal
VeriFLEX Liberté Stent	3*16mm	Bare Metal
Rebel Stent (Boston Scientific, USA)	2.25*8 mm/2.5*8 mm/ 2.5*12 mm/ 2.5*16 mm/ 3*8 mm/3.5*12 mm	Bare Metal
Resolute Integrity (Medtronic, USA)	2.25*8mm/ 2.25*12 mm/ 2.5*8 mm/ 2.5*14mm/ 3.5* 15 mm	Zotarolimus Eluting
Endeavor Stent (Medtronic, USA)	3.0*12 mm	Zotarolimus Eluting
Resolute Onyx (Medtronic, USA)	2*8mm/ 2*12mm/ 2.5*8mm/ 2.5*12mm/ 3*8mm/ 3*12mm/ 3.5*12mm/ 4*12mm/ 4*18mm/ 5*26mm	Zotarolimus Eluting
Xience Sierra Stent (Abbott Vascular, USA)	3*15 mm/ 2.25*12mm	Everolimus Eluting
Xience Alpine Stent (Abbott Vascular, USA)	2.5*15mm	Everolimus Eluting
Synergy Stent (Boston Scientific, USA)	3*12 mm	Everolimus Eluting
Promus PREMIER Stent (Boston Scientific, USA)	2.75*8 mm/ 3.5 * 12 mm	Everolimus Eluting
Taxus Express Stent (Boston Scientific, USA)	3.5*16 mm	Paclitaxel Eluting
EluNIR Stent (Medinol, USA)	2.5*8mm/ 2.5*12 mm/ 3*8 mm/ 3*20 m	Ridaforolimus Eluting

Supplemental Table 2. Predictors of stroke (ischemic/hemorrhagic) and mortality within 72 hours of the procedure

	OR	95%CI	P value
Age	1.097	1.003-1.200	**0.04**
Time from event to treatment	0.972	0.906-1.041	0.41
Degree of pretreatment stenosis	0.973	0.887-1.068	0.57
Anterior circulation symptomatic ICAD	3.536	0.262-47.689	0.34

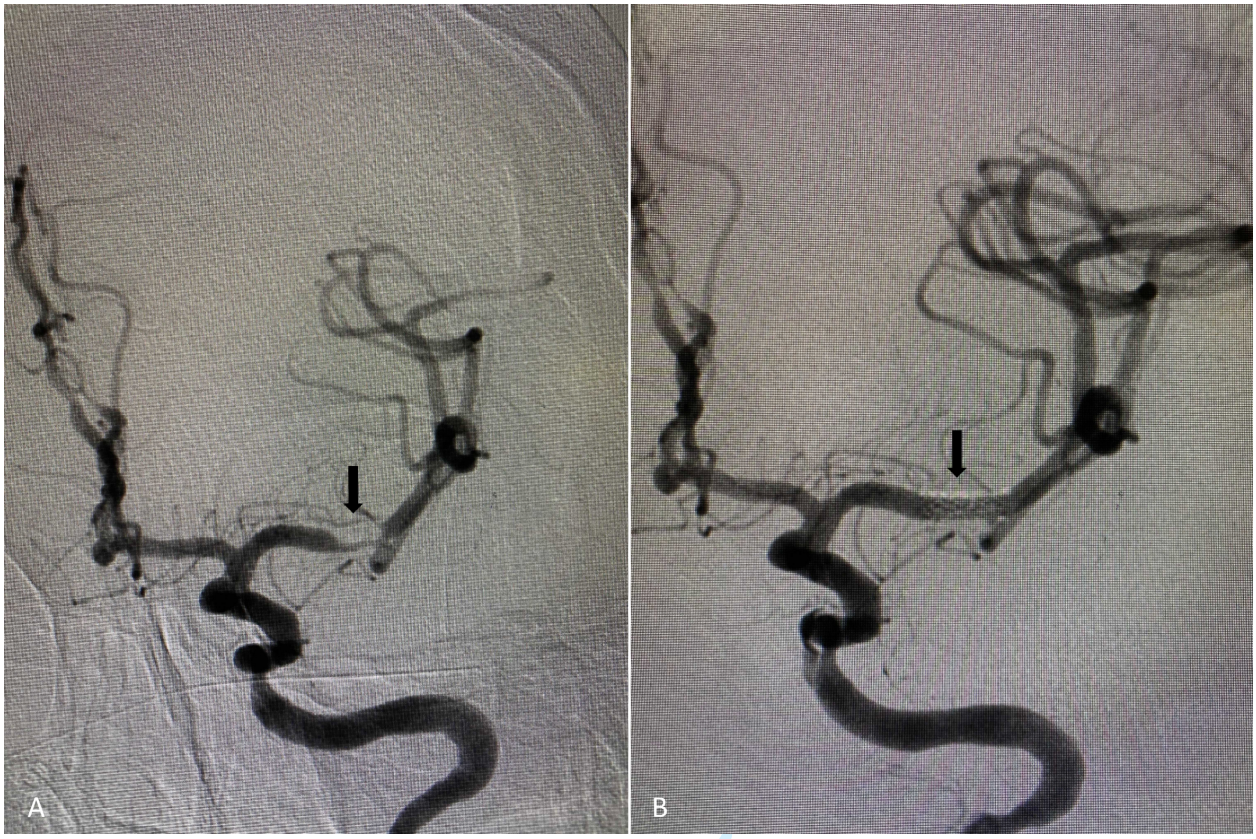
Note. The treatment center was added to the regression model
Abbreviations; OR: odd ratio, CI: confidence interval, ICAD: intracranial atherosclerotic disease.

Supplemental Table 3. Predictors of in-stent restenosis

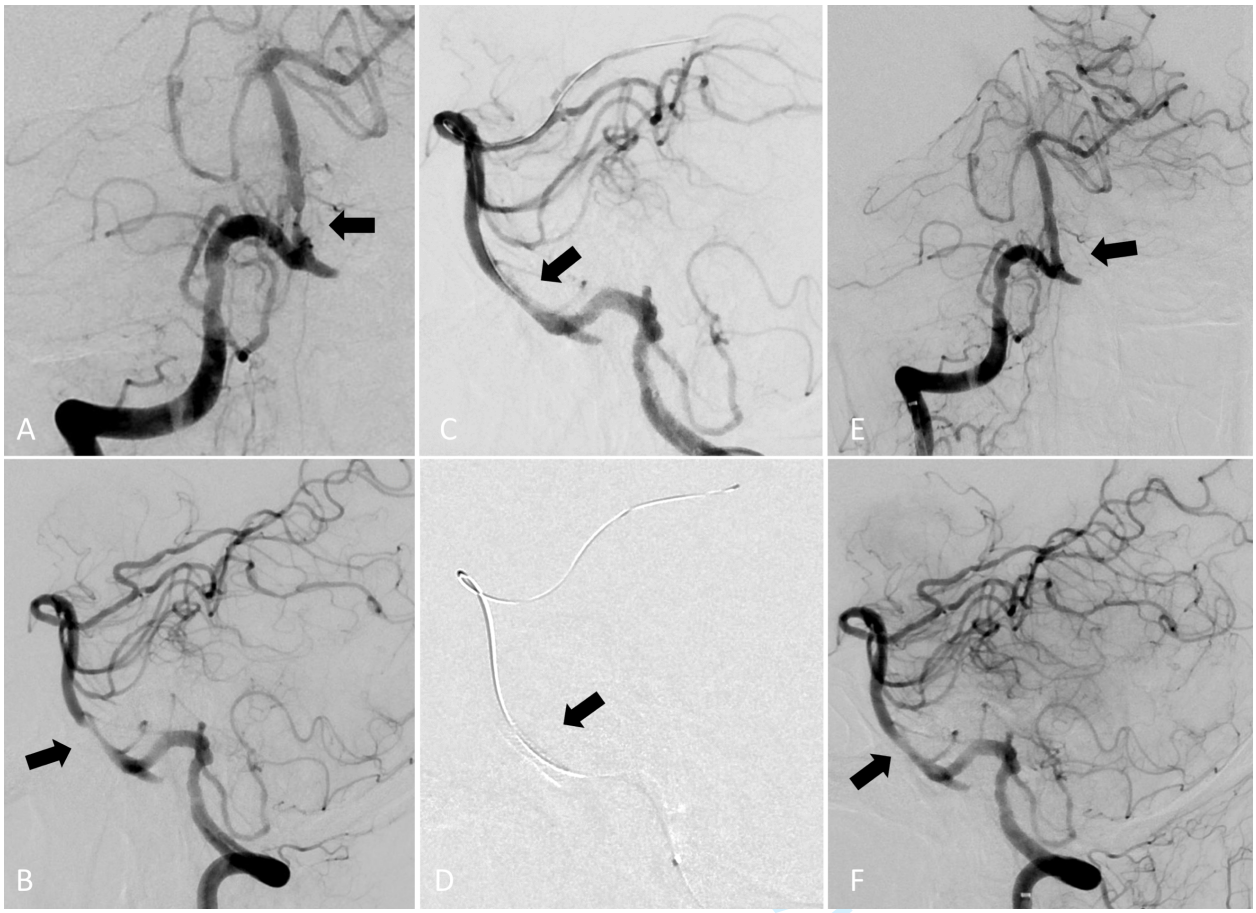
	OR	95%CI	P value
Age	0.958	0.912-1.007	0.09
Diabetes mellitus	1.452	0.451-4.674	0.532
Time from event to treatment	1.010	0.997-1.023	0.14
Degree of pretreatment stenosis	0.997	0.944-1.053	0.91
Timing of follow-up imaging	0.990	0.949-1.033	0.66
Anterior circulation symptomatic ICAD	0.432	0.131-1.422	0.17

Abbreviations; OR: odd ratio, CI: confidence interval, ICAD: intracranial atherosclerotic disease.

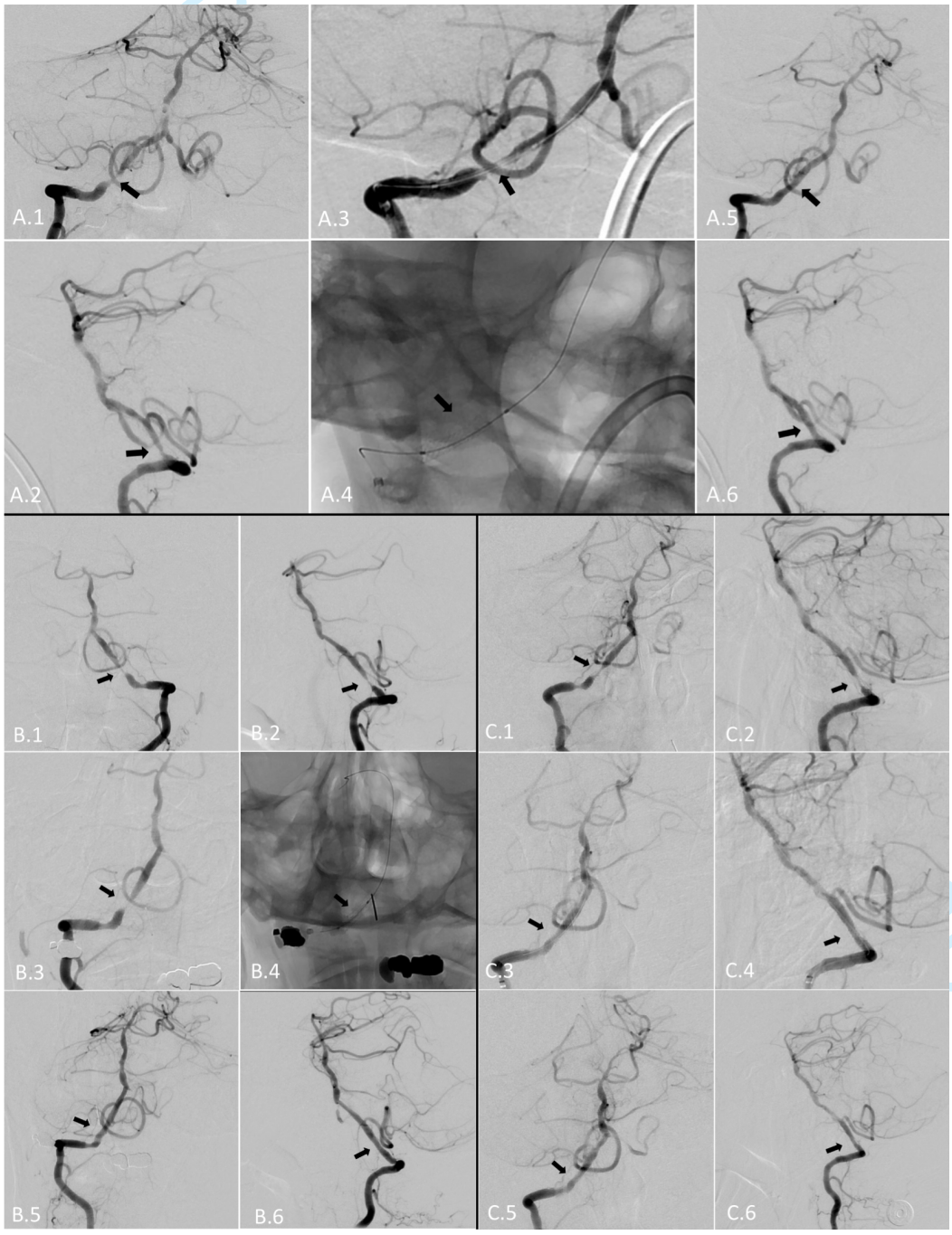
Supplemental Figure 1. (A) Anterior posterior digital subtraction angiography illustrates left distal middle cerebral artery stenosis (arrow). (B) shows successful deployment of Resolute onyx stent (2mm x 8mm) with resolution of the stenosis (arrow).



Supplemental Figure 2. Digital subtraction angiography anterior posterior (A) and lateral (B) views illustrates basilar artery stenosis (arrow). (C&D) shows successful deployment of Rebel balloon mounted stent (2.5mm x 12mm) (arrow) with resolution of the stenosis (E&F).



Supplemental Figure 3A. Digital subtraction angiography (DSA) shows stenosis of the right intracranial vertebral artery (arrow) anterior posterior (A.1) and lateral (A.2) views. Intracranial navigation of the Rebel balloon mounted stent 4.5 mm x 16 mm (arrow) to the target lesion subtracted (A.3) and unsubtracted (A.4) images. (A.5) anterior posterior and lateral (A.6) views demonstrates successful deployment of the stent with resolution of the stenosis (arrow). Three months follow up shows in stent restenosis (arrow) (B.1,B.2&B.3). Successful Intracranial balloon angioplasty (B4) with resolution of restenosis (B.5&B.6). At seven months follow up demonstrates recurrent in stent restenosis (arrow) (C.1&C.2). Successful Intracranial balloon angioplasty (C.3&C.4) with resolution of restenosis (C.5&C.6)



Supplemental Figure 3B. Follow up digital subtraction angiography at 13 months demonstrates patent stent without in stent restenosis anterior posterior (A&B) and lateral (C&D) views.