Multicenter Analysis of Stenting in Symptomatic Intracranial Atherosclerosis

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BACKGROUND: Stenting for symptomatic intracranial atherosclerotic disease is a therapeutic option in patients in whom medical therapy fails.

OBJECTIVE: To determine the periprocedural complication rates and mid-term restenosis rates in patients treated with balloon-expandable stents (BESs) compared with self-expanding stents (SESs).

METHODS: A retrospective review of consecutive patients treated with intracranial stents at 5 institutions was performed. Predictors of 30-day stroke and death as well as mid-term restenosis rates were analyzed.

RESULTS: A total of 670 lesions were treated in 637 patients with a mean age of 57 ± 13 years. A total of 454 lesions (68%) were treated with BESs and 216 lesions (32%) with SESs. The overall 30-day periprocedural complication rate was 6.1%, without any difference noted between the 2 groups. Patients treated within 24 hours of the index event were significantly more likely to have experienced a periprocedural complication (odds ratio [OR], 4.0; 95% confidence interval [CI]: 1.7-6.7; $P < .007$), whereas focal lesions were less likely to have a complication (OR, 0.31; 95% CI: 0.13-0.72; $P < .001$). Midterm restenosis was less likely in patients with a lower percentage of posttreatment stenosis (OR, 0.97; 95% CI: 0.95-0.99; $P < .006$), which was more common in BES-treated patients and focal concentric lesions (OR, 0.33; 95% CI: 0.23-0.55; $P < .0001$).

CONCLUSION: BESs have periprocedural complication rates similar to those of SESs. Less posttreatment stenosis was associated with lower rates of mid-term restenosis. Future randomized trials comparing BESs and SESs may help to identify the stent type that is safest and most durable.

KEY WORDS: Angioplasty, Intracranial stenosis, Intracranial stenting, Ischemic stroke, Stent

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Intracranial atherosclerotic disease (ICAD) has been implicated as the etiology of ischemic stroke in 10% of patients in the United States and in as many as 33% in China.[1,2] Recent studies have shown that patients with symptomatic lesions with more than 70% luminal narrowing and with the event occurring within 2 weeks appear to have a 23% risk of subsequent events at 1 year despite receiving adequate antiplatelet or anticoagulation therapy.[3] Endovascular treatments offer potential treatment strategies for patients with symptomatic ICAD. Balloon angioplasty offers a deliverable technology with lower cost, but with the potential for plaque dissection and vessel recoil leading to restenosis.[4,5] Bare metal balloon-expandable stents (BESs) have been used but may be difficult to deliver through the carotid siphon because of the stiffness of the catheter. With recent advances in guide catheter technology, deliverability has improved for BESs. These stents allow for increase in luminal gain compared with angioplasty alone or self-expanding stents (SESs) and thus may be associated with lower restenosis rates.[6] Drug-eluting BESs have a deliverability profile similar to that of bare metal stents and may offer lower rates of restenosis,[7] but reports from the coronary vessels do suggest concerns for delayed thrombosis, particularly with premature discontinuation of clopidogrel and in patients with diabetes.[8] The Wingspan

ABBREVIATIONS: BES, balloon-expandable stent; **CI,** confidence interval; **ICAD,** intracranial atherosclerotic disease; **SES,** self-expanding stent; **TCD,** transcranial Doppler; **TIA,** transient ischemic attack

stent (Boston Scientific, Natick, Massachusetts) is an SES that is flexible and allows for a high rate of delivery to the target lesion.[9] However, there have been concerns with regard to restenosis and the clinical consequences associated with this device.[10] Given the varied experiences reported in the literature, we sought to compare periprocedural complications and restenosis differences in patients treated with BESs and SESs in high-volume centers that perform these procedures.

PATIENTS AND METHODS

This is a study of intracranial stenting culled from 5 institutions. Consecutive patients from the Cleveland Clinic Foundation, Medical College of Wisconsin, University of Louisville Medical Center, and University of Pittsburgh Medical Center were retrospectively reviewed from 2007 to 2009. Consecutive patients from Tiantan Hospital in Beijing, China, were prospectively collected in a database from 2005 to 2007. Patients after 2007 from Tiantan Hospital are being enrolled in a prospective Wingspan registry in China and thus were not analyzed. All patients treated with endovascular therapy for symptomatic intracranial occlusive disease were included in this study after approval from each respective institutional review board. Each center has extensive clinical experience with the placement of intracranial stents for atherosclerosis. Patients who presented with acute arterial occlusion treated with stents were excluded. Additionally, patients treated with primary intent for angioplasty alone (ie, not stent failures) were not included in this study.

Data were collected with regard to demographics, clinical history, type of stent used, periprocedural complications, timing of treatment, radiographic studies performed, type of treatment used, treatment failures, and follow-up imaging to assess for restenosis. The following types and number of BESs were deployed: Vision (N = 94), Mini-Vision (N = 165), Penta (N = 12) (Abbott Vascular, Abbott Park, Illinois), Taxus, Express 2 (N = 20) (Boston Scientific), Cypher (N = 3) (Cordis Corporation, Miami Lakes, Florida), S70 (N = 30), Driver (N = 94) (Medtronic, Santa Rosa, California), Apollo (N = 29) (MicroPort Medical, Shanghai, China), and BiodivYsio (N = 7) (Biocompatibles, San Jose, California). The Wingspan stent (Boston Scientific) was the only SES used. Angiograms were reviewed to determine the lesion type based on the previously described Mori classification,[11] stenosis before treatment, and stenosis after treatment blinded to the clinical history. Severity of stenosis was measured using the formula $\{[1 - (D_{stenosis}/D_{normal})]\} \times 100$, as previously described.[12] $D_{stenosis}$ was defined as the diameter of the maximum stenosis and D_{normal} as the vessel diameter of a straight segment proximal to the stenosis.

Different institutional protocols were used to assess for restenosis in follow-up imaging. If transcranial Doppler (TCD) was used, each patient underwent ultrasonography before treatment, the day after treatment, and then at 3 and 6 months. The following values were considered significant for restenosis based on TCD criteria: a mean velocity of greater than 160 cm/s in the middle cerebral artery, greater than 120 cm/s in the internal carotid artery, and greater than 100 cm/s for the basilar or vertebral artery. Additionally, the TCD velocities were compared with the pretreatment and posttreatment values. If TCD velocities showed progression on follow-up studies or if clinical symptoms correlating with the ipsilateral side developed in the patient, catheter angiography was performed to confirm the degree of narrowing. When computed tomography angiography was used, if the entire stented segment and proximal and distal portions were visualized without evidence of narrowing, patients were designated as exhibiting no evidence of restenosis. If there was poor visualization of the stented segment or the distal portion appeared tapered, a catheter angiogram was obtained to better define the degree of narrowing. When catheter angiography was used, the method described for pretreatment angiography was used. If the narrowing was greater than 50%, this was considered a restenosis. We analyzed patients who had studies within the 3- to 6-month time frame to assess for mid-term restenosis.

Procedure

All patients were pretreated with aspirin and either ticlopidine or clopidogrel for at least 3 days before the procedure. If the procedure was emergent, then a loading dose of clopidogrel was given based on institutional protocol, but a minimum of 450 mg was administered if the procedure was to be done within 4 hours. The patients were placed under general anesthesia or conscious sedation based on institutional protocol. A 6-French guide catheter was placed in the ipsilateral target vessel to access the intracranial lesion. In patients with more tortuous anatomy, a long sheath was placed in conjunction with the guide catheter. All patients were given systemic intravenous heparin to achieve an activated clotting time of 225 to 300 seconds during the procedure. A microcatheter and microwire were used to traverse the lesion under road-mapping guidance. The microcatheter was removed over an exchange length .014-inch microwire. For SES placement, a balloon was navigated over the microwire and placed across the stenosis. The balloon was also inflated slowly over 30 to 60 seconds to nominal pressure to 10% less than the measured luminal diameter. An SES was placed over the microwire and deployed across the lesion with at least 2 mm of the stent on each side of the lesion covering normal segments of the vessel. If a BES was placed, this was navigated over the microwire and positioned across the lesion with inflation over 30 to 60 seconds to nominal pressure. The stent was sized to 10% less than the measured luminal diameter. After stent deployment, the blood pressure was reduced to less than 130/80 mm Hg, and the patients were monitored over a 24-hour period. If any neurologic change occurred, appropriate imaging was performed with computed tomography or magnetic resonance imaging scans of the brain. Patients were maintained on dual antiplatelet therapy (aspirin and either ticlopidine or clopidogrel) for at least 3 months postprocedure.

Statistics

A univariate analysis was performed using the Fisher exact test for categorical variables and the Student *t* test for continuous variables to compare SESs and BESs. A similar univariate analysis was then performed to determine predictors of periprocedural stroke and mid-term restenosis. A binary logistic regression was then constructed with variables with a P value $<.20$ to determine independent associations with the use of BESs, periprocedural stroke, and mid-term restenosis in follow-up imaging. Analysis was performed using SPSS version 10.0 (SPSS Inc, Chicago, Illinois).

RESULTS

A total of 670 lesions were treated in 637 patients with a mean age of 57 $\pm$ 13 years, of whom 222 (32%) were women. The distribution of stent placement was as follows: middle cerebral artery, 270 (40%); posterior circulation, 263 (39%); and intracranial internal carotid artery, 137 (21%). The ethnic distribution was as follows: white, 323 (48%); Asian, 269 (40%); African

American, 71 (11%); and Hispanic, 7 (1%). A total of 454 lesions (68%) were treated with BESs and 216 lesions (32%) with SESs. Of the BESs implanted, 23 (5%) were drug-eluting stents. Table 1 summarizes the univariate analysis comparing SESs with BESs. Mori A lesions were more frequent in the SES group, and post-procedure residual stenosis was lower in the BES group. In binary logistic regression modeling, the use of BESs was associated with a significantly lower percentage of stenosis after the procedure (odds ratio [OR], 0.91; 95% confidence interval [CI]: 0.89-0.93; $P < .0001$), whereas Mori A lesions were more common in the SES group (OR, 1.95; 95% CI: 1.31-2.88; $P < .001$).

There were an additional 38 lesions in which a stent could not be delivered, and these patients were not included in the analysis because the patients were either treated with angioplasty alone or medical therapy. A BES could not be placed in 35 lesions and an SES could not be placed in 3 lesions. Thus, the technical failure rate for delivery of a BES was 35 of 489 lesions (7.1%) and 3 of 219 lesions (1.4%) for an SES ($P < .001$).

The 30-day periprocedural stroke or death resulted in 41 procedures (6.1%), with 31 ischemic strokes, and 8 hemorrhagic strokes, and 2 deaths not related to the stroke complication (aspiration pneumonia and sepsis). There were an additional 4 deaths caused by the complications of the periprocedural stroke; thus, a total of 6 patients (0.94%) died. Of the 31 ischemic strokes, perforator strokes occurred in 20 procedures (2.98%), whereas distal embolic strokes occurred in 11 procedures (1.64%). The majority of complications occurred within the first 24 hours of the procedure (n = 35, 5.2%). There was no difference in periprocedural stroke complications between the BES group and SES group (6.0% vs 6.4%, respectively). Only 1 procedure (4.3%) with a drug-eluting stent resulted in a periprocedural complication. Table 2 summarizes the univariate predictors of 30-day stroke and death in patients successfully treated with stents. Patients treated urgently or acutely with a complex lesion (Mori B or C) involving the middle cerebral artery and a higher percentage of stenosis pretreatment appeared to have a higher risk of stroke. In contrast, ischemic or hemorrhagic stroke complications were less likely to develop in patients with intracranial internal carotid artery lesions. In binary logistic regression modeling, patients treated within 24 hours were at significantly higher risk of periprocedural stroke or death (OR, 4.0; 95% CI: 1.7-6.7; $P < .001$), whereas Mori type A lesions were safer to treat (OR, 0.31; 95% CI: 0.13-0.72; $P < .007$).

Follow-up imaging performed between 3 and 6 months (mid-term) to assess for restenosis was available for 485 stents (72%). Drug-eluting stents were not analyzed for overall restenosis, but of the 23 placed, only 2 (8.6%) showed mid-term restenosis. A total of 54 (11%) patients presented with a transient ischemic attack (TIA) or stroke when the mid-term restenosis was detected. The method of imaging used to detect restenosis was catheter angiography in 334 patients (69%), computed tomography angiography in 43 patients (9%), and TCD in 108 patients (22%). Overall, patients with a BES had a significantly lower restenosis rate at 20% (60 of 295 lesions) compared with 28% (53 of 190 lesions) for SES ($P < .02$). When comparing patients assessed with catheter angiography for restenosis, BESs were noted to have 20% (47 of 230) compared with 30% (31 of 104) for SESs ($P < .01$). The mean stenosis posttreatment with SESs

TABLE 1. Univariate Analysis Comparing Patients Treated With Balloon-Expandable Stents or Self-Expanding Stents[a]

Variable	Balloon-Expandable Stent (N = 454), No. (%)	Self-Expanding Stent (N = 216), No. (%)	*P* Value
Demographics			
Age, y ± SD	58 ± 15	59 ± 12	.41
Female	146 (32)	76 (35)	.32
Diabetes mellitus	149 (33)	72 (33)	.77
Hypertension	312 (69)	149 (69)	.85
Index event stroke	222 (49)	95 (44)	.15
Location of lesion			
Basilar artery	112 (25)	53 (25)	.84
Vertebral artery	71 (16)	29 (13)	.57
Middle cerebral artery	185 (41)	85 (39)	.69
Internal carotid artery	86 (19)	49 (23)	.09
Stent procedure			
Acute (<24 h)	37 (8)	23 (11)	.08
Urgent (<2 wk)	147 (32)	73 (34)	.21
Elective (>2 wk)	270 (59)	120 (55)	.11
Mori type A lesion	147 (32)	95 (44)	.003
Pretreatment stenosis, mean ± SD	78 ± 12	80 ± 13	.11
Posttreatment stenosis, mean ± SD	12 ± 11	24 ± 11	.001
Periprocedural stroke	27 (6)	14 (6)	.46

[a]SD, standard deviation.

TABLE 2. Univariate Predictors of a Periprocedural Stroke or Death[a]

Variable	No Periprocedural Event (N = 629), No. (%)	Periprocedural Stroke/Death (N = 41), No. (%)	*P* Value
Demographics			
Age, y, ± SD	57 ± 13	59 ± 15	.37
Female	209 (32)	13 (32)	.72
Diabetes mellitus	206 (33)	15 (37)	.37
Hypertension	435 (69)	26 (63)	.25
Index event stroke	299 (48)	18 (43)	.38
Location of lesion			
Basilar artery	155 (25)	12 (29)	.28
Vertebral artery	94 (15)	4 (10)	.25
Middle cerebral artery	248 (39)	22 (54)	.05
Internal carotid artery	132 (21)	3 (7)	.02
Stent procedure			
Acute (<24 h)	49 (8)	11 (27)	.001
Urgent (<2 wk)	211 (34)	9 (22)	.04
Elective (>2 wk)	369 (59)	21 (51)	.32
Mori type A lesion	235 (37)	7 (17)	.005
Pretreatment stenosis, mean ± SD	78 ± 12	81 ± 10	.04
Posttreatment stenosis, mean ± SD	16 ± 12	16 ± 13	.79

[a]SD, standard deviation.

was 24 ± 11% compared with 12 ± 11% ($P < .01$) for BESs. Table 3 summarizes the predictors of restenosis after stent implantation. In patients with lower posttreatment stenosis and Mori A lesions, restenosis was less likely to develop. The use of a BES had a significant interaction with posttreatment stenosis and thus was not included in the multivariate model for prediction of restenosis. Patients in whom a BES was implanted were more likely to have a lower stenosis posttreatment, which correlated with lower restenosis rates. Table 4 summarizes the independent predictors of the development of restenosis. Patients

TABLE 3. Univariate Predictors of In-Stent Restenosis at Midterm 3- to 6-Month Follow-up[a]

Variable	No Restenosis (N = 372), No. (%)	Restenosis (N = 113), No. (%)	*P* Value
Demographics			
Age, y, ± SD	59 ± 13	58 ± 13	.47
Female	143 (38)	46 (41)	.72
Diabetes mellitus	137 (37)	38 (34)	.31
Hypertension	260 (70)	85 (75)	.18
Coronary artery disease	99 (27)	29 (26)	.46
Index event stroke	188 (51)	61 (54)	.30
Location of lesion			
Posterior circulation	143 (38)	43 (38)	.52
Middle cerebral artery	143 (38)	47 (42)	.32
Internal carotid artery	84 (23)	22 (19)	.29
Stent procedure			
Balloon-expandable stent	235 (63)	60 (53)	.02
Acute (<24 h)	44 (12)	12 (11)	.44
Urgent (<2 wk)	138 (37)	45 (40)	.34
Elective (>2 wk)	191 (51)	56 (50)	.41
Mori type A lesion	165 (44)	25 (22)	.0001
Pretreatment stenosis, mean ± SD	79 ± 12	79 ± 11	.57
Posttreatment stenosis, mean ± SD	15 ± 11	20 ± 14	.002

[a]SD, standard deviation.

TABLE 4. Independent Predictors of the Development of Mid-Term In-Stent Restenosis[a]

Variable	Odds Ratio	95% CI	*P* Value
Mori A lesion	0.33	0.21–0.55	.0001
Poststent stenosis	0.97	0.95–0.99	.006

[a]CI, confidence interval.

with lower poststent stenosis were protected from restenosis, whereas patients with Mori B or C lesions were at a significantly higher risk of the development of restenosis.

When comparing patients treated in China with those in the United States, there were no differences in periprocedural stroke rates (6.1% vs 6.2%, respectively) or overall restenosis rates (25% vs 22%, respectively). Moreover, when we performed an analysis to determine whether ethnicity was linked to periprocedural stroke or restenosis, no statistical differences were found.

DISCUSSION

This report demonstrates that treatment of intracranial atheromatous lesions with BESs has periprocedural complication rates similar to those of SESs. Increased luminal gain and a lower posttreatment stenosis were associated with a lower restenosis rate in the mid-term. Additionally, patients treated within 24 hours of presenting symptom onset with a Mori type B or C lesion were at a higher risk of periprocedural stroke.

The SES technology offers the advantage of easier stent delivery in the setting of tortuous intracranial anatomy. Unfortunately, there are concerns with regard to restenosis that may lead to further neurologic events and repeat procedures with their inherent complications. The proposed mechanism for this may relate to the sustained force of the stent on the artery leading to neovascularization and thus aggressive neointimal hyperplasia.[13] In a 4-center registry, the 30 day periprocedural complication rate was 6.1% for stroke or death in 82 treated lesions.[14] A follow-up study was performed by the same group of 84 patients with angiographic imaging to assess for mid-term restenosis at an average of 5.9 months. The rate of restenosis or complete thrombosis was 35%. Eight of the 29 patients (27%) with restenosis or occlusion presented with stroke or TIA. Thus, the mid-term rate of stroke or TIA was noted to be nearly 16% in patients treated with the Wingspan stent system.[10] Moreover, 15 of the 29 patients underwent repeat treatment with angioplasty or stenting, and reperfusion hemorrhage developed in 1 patient.[10] Similarly, the National Institutes of Health registry of 129 patients showed a 14% rate of stroke or death before 30 days or ipsilateral stroke at 6 months.[15] Although SESs are promising with regard to deliverability, there is concern about restenosis because it does not appear to be a benign entity based on these studies. Our current study highlights that 11% of patients with restenosis presented with neurologic symptoms. Additionally, the current study shows that although there was a higher rate of the inability to deliver a BES, the restenosis rates were lower in patients in whom a BES was successfully placed.

There have been concerns about the use of BESs because of the risk of stroke from the procedure as well as the difficulty with navigability. A recent systematic review assessed 31 studies in the literature with reports of intracranial stenting.[6] A total of 906 patients were treated with BESs and 271 with SESs. There was no statistical difference in periprocedural complications between the BES and SES groups (9.5% vs 7.7%, respectively), but the posttreatment residual stenosis was significantly lower in the BES group (11% vs 29%). Additionally, there was a significantly higher proportion of patients with restenosis in the SES group compared with the BES-treated patients.[6] Our current study confirms similar periprocedural complication rates between BES and SES, although BES is associated with a lower midterm restenosis rate.

The Mori classification has been proposed as a method of assessing plaque characteristics before treatment with a stent. Mori A lesions are concentric and less than 5 mm in length, whereas type B lesions are eccentric lesions 5 to 10 mm in length, and type C lesions are longer than 10 mm with excessive tortuosity associated with them.[11] We did not include any patients with total occlusions in our study. The association of higher complication rates with the type of lesion is important for operators to recognize. This is likely attributed to the fact that longer lesions are more likely to span perforator branches that may be occluded at the time of stent placement. Moreover, eccentric lesions may be more friable, and distal embolization may occur with this type of lesion. Also, eccentric lesions may be more prone to vessel dissection or perforation with angioplasty. Mori B and C lesions are also longer, and placement of a stent across longer lesions has been correlated with in-stent restenosis in the coronary arteries.[16] The current study assessed angiographic high-risk features, but future trials may assess the technique of spin-echo magnetic resonance imaging[17]with contrast or intravascular ultrasound.[18] These techniques may help to assess the vulnerability of a plaque and features that may deem the lesion to be at higher risk to treat.

Patients treated within 24 hours of their stroke or TIA were more likely to have a periprocedural complication. These patients were treated because of crescendo TIAs or progression of their clinical symptoms, and they also represent a more clinically unstable group of patients to treat medically. Previous studies have confirmed that endovascular treatment closer to the index event is associated with higher rates of periprocedural strokes.[19,20] Moreover, placement of a stent in a coronary vessel in the acute setting is associated with poor vessel healing and higher levels of fibrin deposition and inflammation, leading to more thrombotic complications as well as restenosis.[21] The highest rate of recurrence also appears to occur within the first 2 weeks of the index event,[3] thus making the clinical decision regarding treatment selection difficult. A second mechanism may be related to the dosing and timing of administration of clopidogrel relative to

stent implantation. A loading dose of 600 mg has been shown to enhance platelet inhibition compared with 300 mg within 4 hours of stent implantation in the coronary arteries. There is a limit to oral absorption, and thus doses greater than 600 mg may not yield additional inhibition.[22] Each center administered 450 mg or more of clopidogrel when performing an emergent stent placement, but unfortunately we do not have precise timing of dosing, and, thus, this may represent a possible explanation for higher stroke rates in patients treated emergently.

There are several limitations to the current study because of its retrospective design. The first limitation is that there were different methodologies used for detecting restenosis based on institutional protocols, and a significant proportion of patients did not undergo follow-up imaging. Additionally, there were imbalances, with fewer available follow-up data for BES-treated patients. The SONIA (Stroke Outcomes and Neuroimaging of Intracranial Atherosclerosis) trial showed that TCD has a good negative predictive value for detecting a moderate to severe stenosis in intracranial atherosclerosis.[23] We used the thresholds for TCD from this study, but it is possible that we underestimated the restenosis rates by not performing catheter angiography on each patient. Patients in whom TCD was performed were followed sequentially for changes in mean flow velocities compared with baseline. A second potential limitation is that the cohorts were from different time periods in which these patients were treated in centers in the United States and China. It is not likely that there have been significant improvements in techniques leading to differences in periprocedural complications given that the results are similar to those of other published studies conducted during similar time frames. A third limitation is that images were not reviewed by a central core laboratory because of the retrospective nature of the study. Last, we do not have consistent longer term follow-up data with which to determine the durability of the treatment. Nonetheless, the study offers insight into the complication rates and mid-term restenosis rates associated with both stent platforms. Stent design may affect clinical outcomes in the future and should be addressed in future ongoing prospective clinical trials.

Disclosures

Dr Zaidat is a consultant to and serves on the Scientific Advisory Board of Boston Scientific. Dr Jovin is a consultant to and serves on the Scientific Advisory Board of Concentric Medical, EV3, Coaxia, and Neurointerventions. Dr Gupta is consultant to and serves on the Scientific Advisory Board of CoAxia, Codman Corporation, and Concentric Medical; is a consultant to and serves on the Data Monitoring Board of Rapid Medical; and serves on the Data Safety and Monitoring Board of Reverse Medical. The other authors have no personal financial or institutional interest in any of the drugs, materials, or devices described in this article.

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COMMENTS

In their study, Jiang et al compared the procedural complication rates and the restenosis rates for the endovascular treatment of intracranial arterial stenoses with either balloon-expandable stents (BESs) or self-expanding stents (SESs). About two-thirds of the 670 stenoses were treated with BESs. As expected, the technical failure rate (ie, the inability to deliver the stent) was 7.1% for BESs and only 1.4% for SESs. The incidence of stroke and death within 30 days after the procedure was 6% and 6.4% for BESs and SESs, respectively. The recurrence rate (digital subtraction angiography based) was 20% for BESs and 30% for SESs. All these results are completely within the range of what could be considered as ''common sense.'' This and the fact that these data are based on a large series of 637 patients justifies the publication.

The study has gained unexpected additional impact since April 11, 2011, when the National Institute of Neurological Disorders and Stroke (NINDS) released a ''Clinical Alert.'' The SAMMPRIS (Stenting and Aggressive Medical Management for Preventing Recurrent Stroke in Intracranial Stenosis) study was a prospective, randomized multicenter trial comparing aggressive medical management alone with aggressive medical management plus angioplasty combined with stenting (Gateway/Wingspan) in patients with symptomatic high-grade intracranial stenosis. All patients were enrolled within 30 days after a transient ischemic attack or nondisabling stroke. Between November 2008 and April 2011, 451 patients had been enrolled at 50 US centers. Interim analysis of the data showed that 14% of patients in the angioplasty/stent arm and 5.8% of patients treated with medical therapy alone experienced a stroke or died within 30 days after enrollment.

A morbidity/mortality rate of 14% after stent-percutaneous transluminal angioplasty of an intracranial stenosis is an irritating observation and more than twice the 6% reported by Jiang et al. This 6% morbidity/mortality rate is in line with those reported in several others publications and probably represents a rate that can be considered as a realistic perspective for both patients and relatives. There is plenty of space for speculations about what went wrong with SAMMPRIS. The method (Gateway/Wingspan) has issues, but they are mainly related to the mid- and long-term results and the occurrence of in-stent restenoses and certainly not to safety aspects of the procedure itself. What remains is a simple alternative: the wrong patients were enrolled or unsuitable centers participated or a combination thereof. We completely disagree with the conclusion of the NINDS authors that ''the trial data currently available indicate that aggressive medical management alone is superior to angioplasty combined with stenting in patients with recent symptoms and high grade intracranial arterial stenosis.'' To us, these data show that a stroke and death rate of 14% for the endovascular treatment of intracranial arterial stenoses is absolutely unacceptable. The medical treatment of these patients requires a limited level of skills and experience (and still yields a 5.8% rate of stroke or death within 30 days!). The endovascular treatment, however, should only be offered by selected and highly specialized centers. These patients carry a variety of vascular and nonvascular risks, and the procedure from access to withdrawal can present difficulties in a quite unexpected way. The endovascular treatment of severe and symptomatic intracranial stenosis is superior to any known medical regimen in terms of safety and efficacy, but the interventional institutions should control and understand their morbidity/mortality margins. Many of these topics are properly addressed by Jiang et al, who were able to show good results in a so-called real-world setting.

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The role of stent design in the risk and efficacy of intracranial stenting remains unknown. Before the US Food and Drug Administration humanitarian use device (HUD) approval of the self-expanding Wingspan stent in 2005, coronary BES were used off-label by neurointerventionalists for intracranial stenting (IS). Although the majority of centers in the United States shifted to using the approved Wingspan stent after 2005, the reports of high in-stent restenosis rates (ISRs) have led to a few centers shifting back to using coronary BESs and sometimes coronary drug-eluting stents in the hope of achieving lower ISRs. Such a shift is based on very little scientific evidence. In this article, Jiang et al report the largest case series to date comparing BESs and SESs for patients with medically refractory symptomatic intracranial stenosis. They must be commended for studying 637 consecutive cases and 670 lesions from 5 centers and recruiting a center from China that has large volume of BES use. The feasibility of placing SESs was significantly higher compared with BES, but once the stent was placed, the 30-day stroke and death rate was not significantly different between the 2 stents (6.1% vs 6.4%, BESs vs SESs). The mid-term ISR with BESs was 20%, significantly lower than the 28% seen with SESs. The authors took care to analyze that this difference in restenosis rate between the 2 stents results from the lower post-stenting residual stenosis with the BES. IS done within 24 hours of presentation and long and eccentric lesion morphology were associated with a higher 30-day stroke and death rate. The results are tempting to draw definitive conclusions aligned with previous assumptions regarding the effects of intracranial stent design, but several limitations of the study make them only hypothesis generating. Not only was the study retrospective and there was no uniform protocol for preprocedure antiplatelet therapy and stenting technique, but also there was also no verification of the restenosis rates by a central laboratory. Of course, the more important outcome endpoint of long-term recurrent stroke and death rate was not addressed by this study. However, the study does suggest an effect of stent design on mid-term ISR and shows the need for more systematic and prospective comparisons of intracranial stent design to achieve the best long-term outcomes.

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