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The CASSISS Randomized Clinical Trial

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IMPORTANCE Prior randomized trials have generally shown harm or no benefit of stenting added to medical therapy for patients with symptomatic severe intracranial atherosclerotic stenosis, but it remains uncertain as to whether refined patient selection and more experienced surgeons might result in improved outcomes.

OBJECTIVE To compare stenting plus medical therapy vs medical therapy alone in patients with symptomatic severe intracranial atherosclerotic stenosis.

DESIGN, SETTING, AND PARTICIPANTS Multicenter, open-label, randomized, outcome assessor–blinded trial conducted at 8 centers in China. A total of 380 patients with transient ischemic attack or nondisabling, nonperforator (defined as nonbrainstem or non–basal ganglia end artery) territory ischemic stroke attributed to severe intracranial stenosis (70%-99%) and beyond a duration of 3 weeks from the latest ischemic symptom onset were recruited between March 5, 2014, and November 10, 2016, and followed up for 3 years (final follow-up: November 10, 2019).

INTERVENTIONS Medical therapy plus stenting (n = 176) or medical therapy alone (n = 182). Medical therapy included dual-antiplatelet therapy for 90 days (single antiplatelet therapy thereafter) and stroke risk factor control.

MAIN OUTCOMES AND MEASURES The primary outcome was a composite of stroke or death within 30 days or stroke in the qualifying artery territory beyond 30 days through 1 year. There were 5 secondary outcomes, including stroke in the qualifying artery territory at 2 years and 3 years as well as mortality at 3 years.

RESULTS Among 380 patients who were randomized, 358 were confirmed eligible (mean age, 56.3 years; 263 male [73.5%]) and 343 (95.8%) completed the trial. For the stenting plus medical therapy group vs medical therapy alone, no significant difference was found for the primary outcome of risk of stroke or death (8.0% [14/176] vs 7.2% [13/181]; difference, 0.4% [95% CI, −5.0% to 5.9%]; hazard ratio, 1.10 [95% CI, 0.52-2.35]; $P = .82$). Of the 5 prespecified secondary end points, none showed a significant difference including stroke in the qualifying artery territory at 2 years (9.9% [17/171] vs 9.0% [16/178]; difference, 0.7% [95% CI, −5.4% to 6.7%]; hazard ratio, 1.10 [95% CI, 0.56-2.16]; $P = .80$) and 3 years (11.3% [19/168] vs 11.2% [19/170]; difference, −0.2% [95% CI, −7.0% to 6.5%]; hazard ratio, 1.00 [95% CI, 0.53-1.90]; $P > .99$). Mortality at 3 years was 4.4% (7/160) in the stenting plus medical therapy group vs 1.3% (2/159) in the medical therapy alone group (difference, 3.2% [95% CI, −0.5% to 6.9%]; hazard ratio, 3.75 [95% CI, 0.77-18.13]; $P = .08$).

CONCLUSIONS AND RELEVANCE Among patients with transient ischemic attack or ischemic stroke due to symptomatic severe intracranial atherosclerotic stenosis, the addition of percutaneous transluminal angioplasty and stenting to medical therapy, compared with medical therapy alone, resulted in no significant difference in the risk of stroke or death within 30 days or stroke in the qualifying artery territory beyond 30 days through 1 year. The findings do not support the addition of percutaneous transluminal angioplasty and stenting to medical therapy for the treatment of patients with symptomatic severe intracranial atherosclerotic stenosis.

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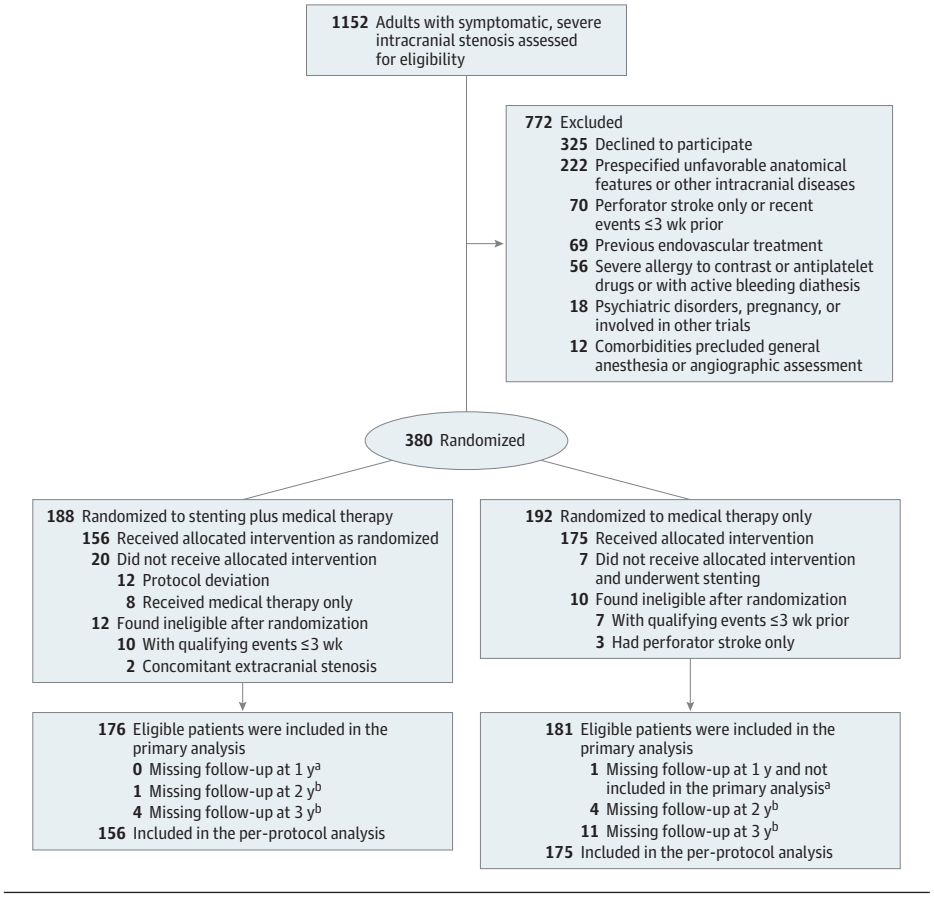
Stroke was the second leading cause of death worldwide and the leading cause of death in China in 2017.[1,2] Intracranial atherosclerotic stenosis accounted for 10% to 15% of ischemic stroke in Western countries,[3] and as much as 46.6% in Asia in 2009.[4] Patients with intracranial atheroscle-

Simple 1:1 randomization without block or stratification was performed. Computer-generated random number by an Interactive Voice Response System (Clinical Soft Company) was used



[a] Primary outcome was assessed up to 1 year.

[b] Time points at which some secondary outcomes were assessed.

considered statistically significant. All analyses were performed with SAS software, version 9.4 (SAS Institute).

Results

From March 4, 2014, to November 10, 2016, 1152 patients were assessed for trial eligibility at 8 study sites. A total of 380 patients signed informed consent and were enrolled and randomly assigned to the stenting (188 patients) and medical (192 patients) groups (**Figure 1**). Of the 380 patients, 22 (12 in the stenting and 10 in the medical therapy alone groups) were confirmed ineligible by central adjudication. The remaining 358 patients (176 in the stenting and 182 in the medical therapy alone groups) were included in the FAS for final analysis. A total of 343 patients (95.8%) completed the trial.

Seven patients assigned to the medical therapy alone group crossed over to stenting procedures. Among patients assigned to stenting, 8 crossed over to medical therapy only and 12 had either an unsuccessful stenting procedure or a procedure that deviated from the protocol (3 received delayed procedures, 2 did not have it due to failed lesion access, 2 were aborted due to total occlusion, 1 received angioplasty alone, and 4 received nonstudy stents). Thus, a total of 331 patients (156 in the stenting and 175 in the medical therapy alone groups) were included in the PPS for secondary analysis.

The baseline characteristics of patients in the FAS were well balanced between the groups (**Table 1**). The mean (SD) age was 56.3 (9.6) years, and 73.5% were male. The median time from the latest event to randomization was 35 days. Among all 358 patients, 194 patients (54.2%) presented with index stroke as a qualifying event. The inferred mechanisms of stroke from the brain imaging were artery-to-artery embolism in 115 patients (59.3%), isolated hypoperfusion in 40 (20.6%), and mixed mechanism in 39 (20.1%) (Table 1). The stroke mechanism distribution was balanced between groups (Table 1; eTable 1 in Supplement 3). The measures of all risk factors were similar in both groups at baseline and during follow-up (eTable 2 and eFigure 1 in Supplement 3).

Proportional hazard assumption was tested and met for the primary outcome and all the secondary outcomes in the Cox regression model. The primary outcome, risk of stroke or death within 30 days or stroke in the qualifying artery territory beyond 30 days through 1 year, was not significantly different (stenting: 8.0% [14/176] vs medical: 7.2% [13/181]; difference, 0.4% [95% CI, −5.0% to 5.9%]; HR, 1.10 [95% CI, 0.52-2.35];

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Characteristic	No. (%) Percutaneous transluminal angioplasty and stenting group (n = 176)	Medical therapy alone group (n = 182)
Age, mean (SD), y	56.7 (9.4)	55.9 (9.8)
Sex		
Male	128 (72.7)	135 (74.2)
Female	48 (27.3)	47 (25.8)
Ethnicity[a]		
Han	172 (97.7)	179 (98.4)
Non-Han	4 (2.3)	3 (1.6)
Medical history[b]		
Hypertension	117 (66.5)	125 (68.7)
Diabetes	57 (32.4)	44 (24.2)
Coronary artery disease	19 (10.8)	19 (10.4)
Lipid disorder	18 (10.2)	21 (11.5)
Peripheral artery disease	0 (0.0)	1 (0.5)
Received antiplatelet therapy prior to latest qualifying event	49 (27.8)	48 (26.4)
Received statin therapy prior to latest qualifying event	19 (10.8)	20 (11.0)
Alcohol history		
Former	25 (14.2)	22 (12.1)
Current	30 (17.0)	32 (17.6)
Smoking history		
Former	39 (22.2)	38 (20.9)
Current	41 (23.3)	50 (27.5)
Qualifying event		
TIA[c]	87 (49.4)	77 (42.3)
Stroke	89 (50.6)	105 (57.7)
Artery-to-artery embolism	57 (64.0)	58 (55.2)
Isolated hemodynamic compromise[d]	18 (20.2)	22 (21.0)
Mixed mechanism	14 (15.7)	25 (23.8)
Time from latest ischemic event to randomization, median (IQR), d	34.5 (27.0-65.5)	36.0 (28.0-68.0)
TIA	33.0 (25.0-52.0)	33.0 (28.0-57.0)
Stroke	38.0 (27.0-75.0)	40.0 (29.0-72.0)
Symptomatic qualifying artery		
Middle cerebral artery (M1)	65 (36.9)	79 (43.4)
Basilar artery	50 (28.4)	52 (28.6)
Intracranial vertebral artery	46 (26.1)	34 (18.7)
Intracranial internal carotid artery	15 (8.5)	17 (9.3)
Stenosis of symptomatic qualifying artery[e]		
% Stenosis, median (IQR)	78.5 (74.1-82.6)	76.6 (73.2-80.9)
Distribution, % stenosis		
70-79	105 (59.7)	130 (71.4)
80-89	65 (36.9)	46 (25.3)
90-99	6 (3.4)	6 (3.3)

(continued)

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Characteristic	No. (%) Percutaneous transluminal angioplasty and stenting group (n = 176)	Medical therapy alone group (n = 182)
NIHSS score, median (IQR)[f]	0.0 (0.0-1.0)	0.0 (0.0-0.0)
mRS score, median (IQR)[g]	0.0 (0.0-1.0)	0.0 (0.0-1.0)

Abbreviations: mRS, modified Rankin Scale; NIHSS, National Institutes of Health Stroke Scale; TIA, transient ischemic attack.

[a] Ethnicity was self-reported.

[b] Medical history was collected at the baseline visit, based on a combination of self-reports from patients, medicated conditions, and laboratory results.

[c] TIA was a clinical diagnosis without imaging.

[d] Isolated hemodynamic compromise refers to strokes with an arterial border zone or "watershed" pattern.

[e] Stenosis was quantified on the basis of a reading of the angiogram by the site interventionist on the criteria of the WASID trial.[18]

[f] NIHSS score ranges from 0 to 42, with higher scores indicating worse neurologic deficits.

[g] mRS score ranges from 0 to 6, with higher scores indicating worse function deficits (0 indicates no deficit and 6 indicates death).

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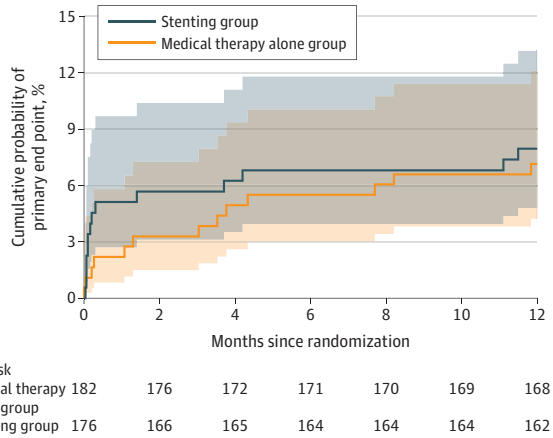

The primary outcome was stroke or death within 30 days after enrollment or stroke in the qualifying artery territory beyond 30 days through 1 year. One patient lost to follow-up within 1 year in the control group was treated as censored data. All other patients were followed up to event or 1 year. $P = .82$ for log-rank testing between the stenting and medical therapy alone groups with center as stratification factor.

$P = .82$) (**Figure 2** and **Table 2**). The per-protocol analysis yielded a similar result (9.0% [14/156] vs 7.4% [13/175]; HR, 1.23 [95% CI, 0.58-2.62]; $P = .59$) (eFigure 2 in Supplement 3).

No significant difference was found between groups for the 2-year risk of stroke in the qualifying artery territory (9.9% [17/171] in the stenting group vs 9.0% [16/178] in the medical therapy alone group; difference, 0.7% [95% CI, −5.4% to 6.7%]; HR, 1.10 [95% CI, 0.56-2.16]; $P = .80$), 3-year risk of stroke in the qualifying artery territory (11.3% [19/168] vs 11.2% [19/170];

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	No./total (%)				
	Percutaneous transluminal angioplasty and stenting group (n = 176)	Medical therapy alone group (n = 181)[a]	Incidence difference, % (95% CI)[b]	Hazard ratio (95% CI)[b]	*P* value[c]
Components of the primary outcome	14/176 (8.0)	13/181 (7.2)	0.4 (−5.0 to 5.9)	1.10 (0.52 to 2.35)	.82
Stroke or death within 30 d after enrollment[d]	9/176 (5.1)[e]	4/181 (2.2)[f]			
Stroke in territory of qualifying artery beyond 30 d through 1 y[d]	5/176 (2.8)	9/181 (5.0)			
Secondary outcomes					
Stroke in the same territory within 2 y	17/171 (9.9)[g]	16/178 (9.0)[h]	0.7 (−5.4 to 6.7)	1.10 (0.56 to 2.16)	.80
Stroke in the same territory within 3 y	19/168 (11.3)[i]	19/170 (11.2)[j]	−0.2 (−7.0 to 6.5)	1.00 (0.53 to 1.90)	>.99
Disabling stroke or death within 3 y	19/168 (11.3)[k]	15/166 (9.0)[l]	2.0 (−4.6 to 8.6)	1.28 (0.65 to 2.52)	.49
Any stroke, TIA, cardiovascular events related to stenting or medical therapy within 3 y	24/169 (14.2)[m]	31/172 (18.0)[n]	−4.1 (−12.0 to 3.7)	0.76 (0.45 to 1.30)	.31
Death within 3 y	7/160 (4.4)[o,p]	2/159 (1.3)[q,r]	3.2 (−0.5 to 6.9)	3.75 (0.77 to 18.13)	.08
Stroke-related death[d]	4/160 (2.5)	2/159 (1.3)			
Nonstroke-related death[d]	3/160 (1.9)	0/159 (0)			

Abbreviation: TIA, transient ischemic attack.

[a] One participant randomized to the medical therapy alone group was not included due to missing outcome data. See Figure 1.

[b] Adjusted for site effect.

[c] Log-rank test adjusted for site effect.

[d] Post hoc analysis.

[e] There were 5 ischemic stroke and 4 hemorrhagic strokes. Of the 4 symptomatic hemorrhagic strokes, 1 was periprocedural subarachnoid hemorrhage immediately after percutaneous transluminal angioplasty and stenting (probably related to guidewire perforation); 1 was periprocedural parenchymal and subdural brain hemorrhage evident immediately after percutaneous transluminal angioplasty and stenting (probably related to guidewire perforation); 1 was cerebellar and occipital hemorrhage that occurred 3 days after percutaneous transluminal angioplasty and stenting (probably related to reperfusion); and 1 was subarachnoid hemorrhage within 24 hours after percutaneous transluminal angioplasty and stenting (probably related to reperfusion). A total of 2 of these hemorrhages were fatal (1 developed massive cerebral infarction and brain hernia, and 1 had parenchymal brain hemorrhage), and 2 were nondisabling (1 cerebellar and occipital hemorrhage and 1 subarachnoid hemorrhage).

[f] There were 4 ischemic strokes and 0 hemorrhagic strokes. Of the 4 ischemic strokes, 2 were disabling, 2 were nondisabling, and none were fatal.

[g] One missing follow-up and 4 died.

[h] Four missing follow-up and 0 died.

[i] Four missing follow-up and 4 died.

[j] Eleven missing follow-up and 1 died.

[k] Eight missing follow-up, including 4 with primary outcomes (but no disabling stroke or death).

[l] Sixteen missing follow-up, including 5 with primary outcomes (but no disabling stroke or death).

[m] Four missing follow-up and 3 died.

[n] Ten missing follow-up and 0 died.

[o] Sixteen missing follow-up, including 12 with primary outcomes.

[p] The causes of death in the percutaneous transluminal angioplasty and stenting group were as follows: brain hemorrhage (n = 2), ischemic stroke (n = 2), sudden cardiac arrest (n = 1), intrahepatic cholangiocarcinoma (n = 1), and aortic artery aneurysm (n = 1).

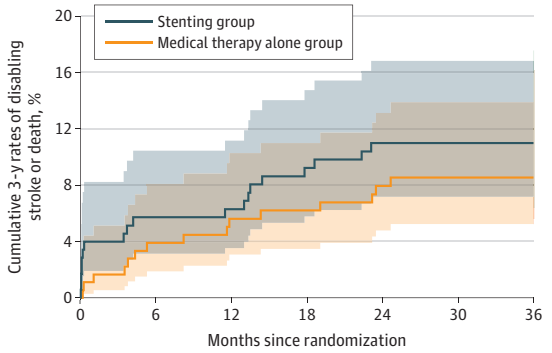
[q] Twenty-three missing follow-up, including 12 with primary outcomes.

[r] The causes of death in the medical management group were as follows: ischemic stroke (n = 1) and brain hemorrhage (n = 1).

difference, −0.2% [95% CI, −7.0% to 6.5%]; HR, 1.00 [95% CI, 0.53-1.90]; $P > .99$) (Table 2), and the cumulative 3-year risk of disabling stroke or death (11.3% [19/168] vs 9.0% [15/166]; difference, 2.0% [95% CI, −4.6% to 8.6%]; HR, 1.28 [95% CI, 0.65-2.52]; $P = .49$) (**Figure**). There was no significant difference in the rate of 3-year risk of death (4.4% [7/160] vs 1.3% [2/159]; difference, 3.2% [95% CI, −0.5% to 6.9%]; HR, 3.75 [95% CI, 0.77-18.13]; $P = .08$) or cumulative 3-year risk of any stroke, TIA, or cardiovascular events (14.2% [24/169] vs18.0% [31/172]; difference, −4.1% [95% CI, −12.0% to 3.7%]; HR, 0.76 [95% CI, 0.45-1.30]; $P = .31$) between the groups (eFigure 3 in Supplement 3).

A post hoc analysis of the primary outcome using a mixed-effects model with center as a random effect yielded an HR of 1.11 (95% CI, 0.52-2.36) (eTable 3 in Supplement 3). Considering the components of the primary outcome, the 30-day rate of stroke or death was 5.1% (9/176) in the stenting group and 2.2% (4/181) in the medical therapy alone group (Table 2). In the stenting group, there were 5 ischemic strokes within 30 days (5 were ultimately disabling, 0 were fatal) and 4 hemorrhagic strokes within 30 days (0 were ultimately disabling, 2 were fatal). In the medical therapy alone group, there were 4 ischemic strokes within 30 days (2 were ultimately disabling, 0 were fatal) and 0 hemorrhagic strokes within 30 days (eTable 4 in Supplement 3). The rate of stroke in the qualifying artery territory beyond 30 days to 1 year was 2.8% (5/176) in the stenting group and 5.0% (9/181) in the medical therapy alone group (Table 2). Subgroup analysis by the qualifying events showed the rate of primary outcome in patients qualified with ischemic stroke was 10.1% (9/89) in the stenting group and 8.6% (9/105) in the medical therapy alone group. For patients qualified with TIA, the rate of primary outcome was 5.7% (5/87) in the stenting group and 5.3% (4/76) in the medical therapy alone group (eTable 5 in Supplement 3).

In the stenting group, 5 patients (2.8%) had disabling stroke, 4 (2.3%) had symptomatic intracranial hemorrhage, and 2 (1.1%) died of stroke within 30 days. In the medical therapy alone group, 2 patients (1.1%) had disabling ischemic stroke within 30 days. At 3 years of follow-up, 4.4% (7/160) and 1.3% (2/159)



No. at risk

Medical therapy alone group	182	170	166	162	159	151	151
Stenting group	176	163	162	155	152	149	149

The median time of observation was 36.0 months (IQR, 36.0-36.0) for the stenting group and 36.0 months (IQR, 36.0-36.0) for the medical therapy alone group. *P* = .49 for log-rank testing between stenting group and medical therapy alone group with center as stratification factor.

patients died in the stenting and medical therapy alone groups, respectively (Table 2).

Discussion

This multicenter, randomized, open-label trial in patients presenting with TIA or nondisabling ischemic stroke and severe intracranial atherosclerotic stenosis demonstrated that the addition of stenting to medical therapy, compared with medical therapy alone, resulted in no significant difference in the risk of subsequent stroke or death within 30 days or stroke in the qualifying artery territory beyond 30 days through 1 year. The results on all prespecified secondary outcomes also showed no significant difference.

Despite efforts to reduce perioperative complication rates by vetting of surgeons and sites and refining patient selection, the findings nonetheless demonstrated no clinical benefit from the addition of stenting to medical therapy for the treatment of patients with symptomatic severe intracranial atherosclerotic stenosis. The results of this study, together with that from previous trials,[11-13] support the recent American Academy of Neurology Practice Advisory regarding stroke prevention in symptomatic large artery intracranial atherosclerosis,[23] which recommends aggressive medical therapy rather than stenting for patients with symptomatic severe intracranial atherosclerotic stenosis.

Compared with previous randomized trials,[11-13] the cumulative 1-year risk of stroke or death in both the stenting and medical therapy alone groups was much lower. The primary reason for the difference is likely attributable to the exclusion of patients with ischemic symptoms within 3 weeks of study enrollment. These patients were likely at the highest risk for 30-day stroke or death. All previous studies enrolled patients without the requirement on the interval between disease onset and enrollment. Other possible reasons include differences in age or ethnicity. The mean age was 56 years in the present study vs 60 years in SAMMPRIS and 62 years in VISSIT. The study populations of SAMMPRIS and VISSIT were predominantly Black and White, and the present study population were mainly Chinese Hans.

The 30-day event rate in the stenting group was much higher in both the SAMMPRIS and VISSIT studies, leading to early stopping in both. In the present study, the 30-day event rate was also numerically higher in the stenting group. While a large portion of the procedural risk reduction observed in the present study may be attributable to patient selection, other factors are likely involved as well. First, the present study selected high-volume clinical sites and used a lead-in phase to credential surgeons and to ensure their experience with stenting. A recent prospective registry in high-volume centers (>100 cases each year) showed similar 30-day rate of stroke or death (4.3%).[14] The association of lower risk of complications with higher-volume centers was also shown in SAMMPRIS,[24] the WEAVE registry,[16] and the National Institutes of Health registry,[25] suggesting the importance of experience in performing intracranial stenting procedures.[26] Differences in periprocedural care could also be a key factor that distinguishes high-volume centers. Second, patient selection also likely decreases periprocedural risk. All patients in the present study underwent MRI or computed tomography at the time of screening, and those with perforator stroke alone without artery-to-artery embolism or distal hypoperfusion were excluded. This exclusion criterion may have reduced the risk of perforator occlusion related to the stenting procedure. The SAMMPRIS trial had 22.8% of patients recruited with perforator stroke only.[27] A post hoc analysis of SAMMPRIS data showed that most periprocedural strokes in the stenting group were perforator strokes (15 of 21).[28,29] Third, timing was also shown to be associated with safety outcomes of stenting.[30] Recent studies have indicated stenting within a time interval of 3 weeks may confer higher procedural risk.[31,32] The present study enrolled patients with a time from most recent event to stenting of more than 3 weeks (median time, 35 days), which was significantly longer than that for SAMMPRIS (median time, 7 days)[11] and VISSIT (median time, 9 days).[12] A higher risk of complication for early stenting might be related to plaque detachment and/or reperfusion injury,[11,25,33] which was less pronounced with extended intervals.

One of the factors in the observed lack of superiority of stenting over medical therapy may be related to the nonnegligible periprocedural complications. The rate of 30-day symptomatic intracranial hemorrhage was numerically higher in the stenting than the medical therapy alone group (2.3% [4/176] vs 0% [0/182]; eTable 4 in Supplement 3). In the stenting group, the risk of hemorrhage may be related to guidewire perforation during the stenting procedure. In addition to the device limitations, the endovascular approach for treatment of intracranial stenosis is technically challenging and involves navigating the tortuous nature of intracranial vasculature and through diseased small vessels that can disturb the atherosclerotic plaque during advancement. Furthermore, periprocedural management (eg, maintaining a goal systolic blood pressure to avoid hyperperfusion after a procedure)[14-16] may also be a target for

future improvement in safety of stenting in intracranial atherosclerotic stenosis because there were 2 reperfusion hemorrhages after the procedure in the stenting group.

Another factor contributing to the lack of observed benefit with stenting was the lower rate of ischemic stroke risk in the medical therapy alone group. During the 3-year follow-up, the rates of the outcome were low in both groups and not significantly different between the 2 groups. These data imply that even if the periprocedural risk in the stenting group could be reduced to as low as the 30-day rate in the medical therapy alone group, stenting still may not provide long-term benefit over medical therapy. As mentioned above, the low event rate in the medical therapy alone group is likely related to a longer time interval after last symptom onset to randomization (median, 35 days in this trial vs 7 days in SAMMPRIS[11] vs 15 days in VISSIT).[12] In 3 studies, most strokes occurred within a relatively short interval after initial onset, with no further ischemic events in the second or third year.[11,19,34] In the MyRIAD (Mechanisms of Early Recurrence in Intracranial Atherosclerotic Disease) study that included patients with symptomatic intracranial atherosclerotic disease (50%-99% stenosis), 5 of 9 same-territory ischemic strokes (55.6%) occurred within the first 6- to 8-week follow-up visit.[34] Previous randomized trials seemed to follow this trend.[11,19,33]

This study has several limitations. First, this trial did not evaluate angioplasty alone or other devices (eg, drug-coated balloon, drug-eluting stent, other self-expandable stents, or a combination) that are currently used off-label to treat patients with intracranial atherosclerotic stenosis.[35-38] Second, this trial applied routine history, the NIHSS and mRS scoring, and brain imaging when necessary to identify a recurrent stroke during follow-up, but didn't use the Questionnaire for Verifying Stroke-Free Status, which may cause potential missing information in follow-up case ascertainment. However, because the study used central independent adjudication, the bias is expected to be small and may affect both groups similarly.

Third, because the study was conducted only in centers in China, its generalizability to other populations outside of China is uncertain. Fourth, the patients were treated from 2014 to 2016, so it is uncertain whether or how the results apply to current stroke care, given the changes in management that have occurred over that time. Fifth, the medical management used in this trial may not have been as aggressive as that used in previous trials and the management in this trial may differ from what is considered standard of care in some countries. Sixth, the enrolled population had a lower risk of events than was anticipated in the power calculations. Therefore, the study findings apply specifically to the study population included in this study and the results may not be applicable to patients with intracranial stenosis with higher risk for events.

Conclusions

Among patients with TIA or ischemic stroke due to symptomatic severe intracranial atherosclerotic stenosis, the addition of percutaneous transluminal angioplasty and stenting to medical therapy, compared with medical therapy alone, resulted in no significant difference in the risk of stroke or death within 30 days or stroke in the qualifying artery territory beyond 30 days through 1 year. The findings do not support the addition of percutaneous transluminal angioplasty and stenting to medical therapy for the treatment of patients with symptomatic severe intracranial atherosclerotic stenosis.

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