Supplemental Online Content

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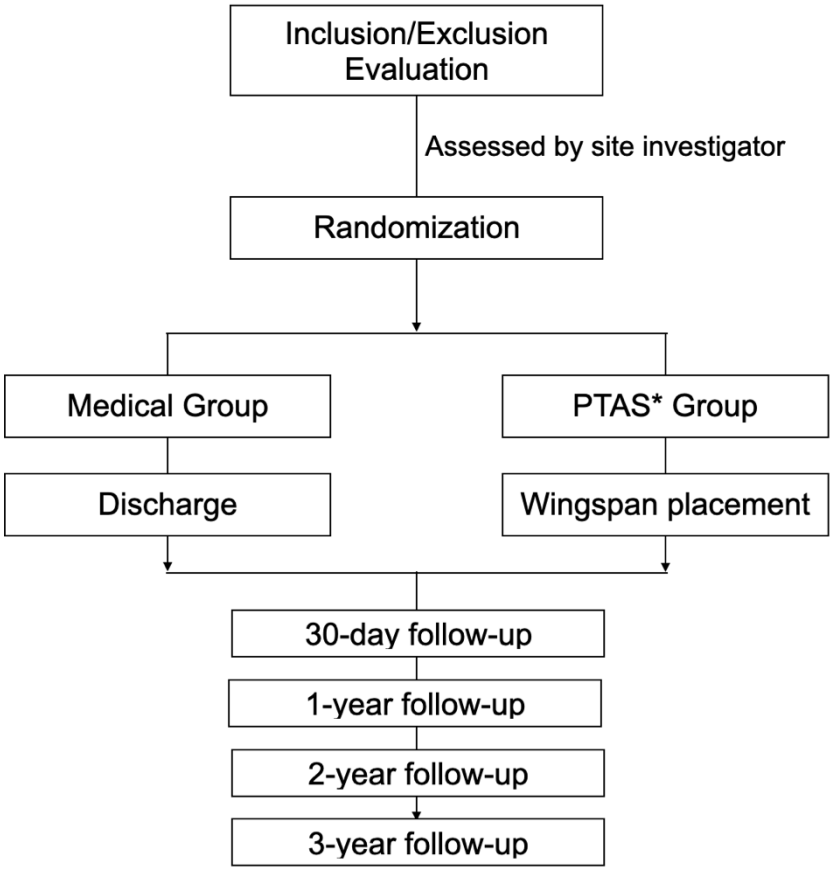
This supplemental material has been provided by the authors to give readers additional information about their work.

1. eMethods

1.1 Study Overview

1.1.1 Flow Chart



*PTAS, percutaneous transluminal angioplasty and stenting

1.1.2 Follow-up Schedule

	In-hospital			Follow-up (Paper-based CRF)			
	Baseline	Procedure	Discharge	30-day	1-year	2-year	3-year
ICF	×						
In-/Exclusion criteria	×						
Demographics	×						
Medical history	×						
Physical exam	×			×	×	×	×
Neurological status							
NIHSS	×	×	×	×	×	×	×
mRS	×	×	×	×	×	×	×
Barthel Index	×	×	×	×	×	×	×
Lab test	×				×	×	×
Neuro-imaging							
CT/MRI (DWI)	×				×	×	×
TCD/CTA/MRA	×				×	×	×
CTP/PWI	×	×			×	×	×
DSA	×	×			×	×	×
Medication	×			×	×	×	×
AE/SAE		×	×	×	×	×	×

1.2 Inclusion Criteria[1]

1. Eligible patients aged between 30 and 80 years; intracranial arterial stenosis related to the following non-atherosclerotic factors will be not be considered: arterial dissection, moya-moya disease; vasculitic disease; herpes zoster, varicella zoster or other viral vasculopathy; neurosyphilis; any other intracranial infection; any intracranial stenosis associated with cerebrospinal fluid pleocytosis; radiation-induced vasculopathy; fibromuscular dysplasia; sickle cell disease; neurofibromatosis; benign angiopathy of central nervous system; postpartum angiopathy; suspected vasospastic process, and suspected recanalized embolus;
2. Symptomatic intracranial stenosis: presented with transient ischemic stroke (TIA) or stroke within the past 12 months attributed to 70%-99% stenosis of a major intracranial artery (ICA, MCA [M1], vertebral artery, or basilar artery [BA]);

3. Degree of stenosis: 70%–99%; stenosis degree must be confirmed by catheter angiography for enrollment in the trial;
4. Remote infarctions on MRI scan, which can be accounted for by the occlusion of the terminal cortical branches or hemodynamic compromise (perforator occlusion excluded). Infarction due to perforators occlusion is defined as basal ganglia or brainstem/thalamus infarction related with M1 or BA stenosis;
5. Expected ability to deliver the stent to the lesion;
6. All the patients should be performed with stenting beyond a duration of three weeks from the latest ischemic symptom onset;
7. No recent infarctions identified on MRI (indicated as high signals on DWI series) upon enrollment;
8. No massive cerebral infarction (>1/2 MCA territory), intracranial hemorrhage, epidural or sub-dural hemorrhage, and intracranial brain tumor on CT or MRI scan;
9. mRS scale score of <=2;
10. Target vessel reference diameter must be measured to be 2.00 mm to 4.50 mm; target area of stenosis is <=14 mm in length;
11. No childbearing potential or has a negative pregnancy test within the past one week prior to study procedure; female patients had normal menses in the last 18 months;
12. Patient is willing and able to return for all follow-up visits required by the protocol;
13. Patients understand the purpose and requirements of the study and have signed informed consent form.

1.3 Exclusion criteria[1]

1. Refractory to general anesthesia; not able to be overcome by pre-treatment with medical therapy
2. Any condition that precludes proper angiographic assessment
3. Tandem extracranial or intracranial stenosis (70%–99%) or occlusion that is proximal or distal to the target intracranial lesion
4. Bilateral intracranial VA stenosis of 70%–99% and uncertainty about which lesion is symptomatic (for example, if patient has pon, midbrain, temporal and occipital symptoms)

5. Presence of a previously placed intravascular stent or graft in the ipsilateral distribution within 30 days
6. Previous treatment of target lesion with a stent, angioplasty, or other mechanical device, or plan to perform staged angioplasty followed by stenting of target lesion
7. Severe vascular tortuosity or anatomy that would preclude the safe introduction of a guiding catheter, guiding sheath or stent placement
8. Plan to perform concomitant angioplasty or stenting of an extracranial vessel tandem to an ipsilateral intracranial stenosis
9. Presence of intraluminal thrombus proximal to or at the target lesion
10. Any aneurysm proximal to or distal to intracranial stenotic artery
11. Intracranial tumors or any intracranial vascular malformations
12. Computed tomographic or angiographic evidence of severe calcification at target lesion
13. Thrombolytic therapy within 24 hours before enrollment
14. Evolving stroke or progressive neurologic signs within 24 hours before enrollment
15. Stroke of sufficient size (>5 cm on CT or MRI) to place patient at risk of hemorrhagic transformation during the procedure; hemorrhagic transformation of an ischemic stroke within the past 15 days
16. Previous spontaneous intracerebral (parenchymal) or other intracranial (subarachnoid, subdural, or epidural) hemorrhage within 30 days
17. Untreated chronic subdural hematoma >5 mm in thickness
18. Other cardiac sources of emboli such as left ventricular aneurysms, intracardiac filling defect, cardiomyopathy, aortic or mitral prosthetic heart valve, calcified aortic stenosis, endocarditis, mitral stenosis, atrial septal defect, atrial septal aneurysm, left atrial myxoma
19. Myocardial infarction within previous 30 days
20. Chronic atrial fibrillation; any episode of paroxysmal atrial fibrillation within the past six months, or history of paroxysmal atrial fibrillation requiring chronic anticoagulation
21. Intolerance or allergic reaction to any of the medical therapy, including aspirin, clopidogrel, heparin, and local or general anesthetics
22. History of life-threatening allergy to contrast medium. If not life threatening and can be effectively pre-treated, patient can be enrolled at physicians' discretion

23. Recent gastrointestinal bleed that would interfere with antiplatelet therapy
24. Active bleeding diathesis or coagulopathy; active peptic ulcer disease, major systemic hemorrhage within 30 days, active bleeding diathesis, platelets count <125,000, hematocrit <30, Hgb <10 g/dl, uncorrected INR >1.5, bleeding time >1 minute beyond upper limit normal, or heparin-associated thrombocytopenia that increases the risk of bleeding, uncontrolled severe hypertension (systolic BP>180mm hg or diastolic BP>115mm hg), severe liver impairment (AST or 25. ALT >3 times normal, cirrhosis), creatinine >265.2 mmol/l (unless on dialysis). Major surgery (including open femoral, aortic, or carotid surgery) within previous 30 days or planned in the next 90 days after enrollment
25. Indication for warfarin or heparin beyond enrollment (exceptions allowed for use of systemic heparin during stenting procedure or subcutaneous heparin for deep venous thrombosis prophylaxis while hospitalized)
26. Inability to understand and cooperate with study procedures or sign informed consent
27. Severe dementia or psychiatric problems that prevent the patients from following an outpatient program reliably
28. Pregnancy or of childbearing potential and unwilling to use contraception for the duration of this study
29. Actively participating in another drug or device trial that has not completed the required protocol follow-up period

1.4 Lead-in Phase Prior To the Randomized Trial

1.4.1 Background of the Lead-in Phase Trial

The US Food and Drug Administration in March 2012 announced that the Wingspan stent system (Stryker Neurovascular, Fremont, CA, USA) continues to remain an option for patients with recurrent stroke despite medical management who have not had any new stroke symptoms within 7 days of stenting. The decision was based on review of the SAMMPRIS trial and the clinical study data supporting humanitarian device exemption approval data, supplemented by the opinions of an advisory panel of experts. The manufacturer, Stryker Neurovascular, was also required to enhance its physician training program for the Wingspan stent. Another expert panel concluded that the SAMMPRIS trial data support modification but not discontinuation of the use of intracranial angioplasty and/or stent placement for intracranial stenosis.

The panel further recommended proceeding with another clinical trial with appropriate modifications in design based on lessons learned from the SAMMPRIS trial to avoid unnecessary elimination of a potentially beneficial treatment in appropriately selected patients. On the basis of the above-mentioned considerations, a multicenter prospective single-arm trial with independent outcome assessment was undertaken to determine whether such modifications will result in lower rates of periprocedural 1-month stroke and/or death in patients treated with intracranial stent placement.[2]

1.4.2 Design, Methods and Outcome of the Lead-in Phase Trial[2]

The study enrolled patients with recent transient ischemic attack or minor ischemic stroke (excluding patients with perforator ischemic events only and with shorter time interval from the latest ischemic events) related to high-grade (70%-99% in severity) stenosis of a major intracranial artery. Patients were treated by using angioplasty and self-expanding stents 3 weeks after the index ischemic event at 1 of the 10 high-volume centers in China. A neurologist independently assessed the occurrence of any stroke and/or death within 1 month after the procedure.

A total of 100 consecutive patients were recruited. The target lesions were located in the middle cerebral artery (M1) (n=38, 38%), intracranial internal carotid artery (n=17, 17%), intradural vertebral artery (n=18, 18%), and basilar artery (n=27, 27%). The technical success rate of stent deployment with residual stenosis of <50% was 100%. The overall 1-month stroke and/or death rate was 2% (95% confidence interval, 0.2%-7.0%). Two ischemic strokes occurred in the pontine region (perforator distribution) in patients following angioplasty and stent placement for basilar artery stenosis. The results of this prospective multicenter study demonstrated that modifications in patient selection and procedural aspects can substantially reduce the 1-month stroke and/or death rate following intracranial stent placement. We were thus encouraged to perform a randomized trial to reappraise the role of intracranial stenting with Wingspan for selected patients in high-volume centers.

1.5 Randomized trial: Site Selection and Monitoring

Prior to the randomized trial, a lead-in phase was performed to determine center eligibility. This aimed to test the credentialing of the operators and participating centers. From July 2013 to March 2014, 10 candidate sites (academic tertiary hospitals) were involved in a competitive registration study of recruiting a combined total of 100 consecutive patients.[2] These patients received balloon-angioplasty followed by stenting using the Wingspan system at each site. Stenting experience, perioperative

complications, and the volume of stenting cases was assessed for each site. Of the 10 sites, 2 sites were excluded and the remaining 8 were finally involved in the randomized trial. The included sites met the following criteria: 1) at least five cases were performed by each primary operator during the lead-in phase; 2) annual volume of intracranial PTAS procedures was more than 30 for the past three years with a proven track record; and 3) according to the records of the past three years 30-day rate of stroke or death after PTAS in the territory of the qualifying artery was lower than 15%.

After each clinical site began to enroll patients, the clinical research associate (CRA) conducted the first monitoring visit to ensure the study protocol was being followed correctly. Within the first year of the study, the CRAs performed random visits at each site (at least twice), where they surveyed for protocol deviations and checked the informed consent forms for all participants. During visits, CRAs ensured paper-based-entry data in the CRF were accurate and verifiable. They also monitored the inpatient, outpatient and follow-up medical records as well as imaging materials of all the subjects and archived all the important documents.

1.6 Patient Selection

Based on the design of the SAMMPRIS trial, the present trial was refined and modernized. Patients were selected at enrollment based on the following considerations: 1) Patients who had an ischemic stroke within the last three weeks were not included because of concern of potential hemorrhagic transformation after PTAS; 2) No recent infarction on MR (indicated as high signal on diffusion weighted imaging with apparent diffusion coefficient correlate); 3) Territorial ischemic stroke greater than anatomical perforator occlusion. Sites were not authorized to recruit cases until they finished the central clinical investigator training program. At each investigational site, the local treating teams always comprised at least a neurologist, a neurosurgeon, a neuroradiologist, and a research coordinator. The local treating team conducted enrollment after they reviewed the qualification of each patient.[1]

1.7 Clinical Investigator Training

The principal site launched the clinical investigation training program, which ensured the trial followed established good clinical trial practice (GCP) guidelines and study protocol. This program had multiple presentation sessions, which covered trial management from planning to close-out, institutional compliance, informed consent,

study conduct, documentation, reporting requirements, and management systems. Also, the training program had established specific topics including intracranial stent placement technique with the Wingspan system, imaging evaluation, and clinical outcome assessment. The central training program followed immediately after the initiation of the launch meeting. At each investigational site, the trial coordinators conducted biannual visits to provide on-site training and recommendations to increase efficiency and assess conduct.

Study Initiation and Investigator Training

1.8 Treatment procedure for percutaneous angioplasty and stenting

Patients randomized to stenting were be placed on DAPT (aspirin, 100 mg daily and clopidogrel 75 mg daily) for 3-5 consecutive days before the procedure. No loading dose was allowed. The study protocol requires that the PTAS procedure is typically performed under general anesthesia by a credentialed interventionist who should be the primary operator. The procedure is typically performed via a transfemorally-placed 6F-long sheath or guiding catheter. The stenotic lesion is primarily crossed with a standard 0.014'' microcatheter microwire system under high magnification fluoroscopic roadmap control. Once across the lesion, the microcatheter is exchanged over a 300-cm, 0.014'' microwire for a Gateway balloon catheter. After angioplasty, the balloon catheter is exchanged for a Wingspan stent delivery system and the self-expanding Wingspan stent is deployed across the stenosis. If the residual stenosis after implanting the Wingspan stent is >50%, the study protocol allows for postdilation with a balloon catheter. The protocol required frequent measurements of blood pressure during the procedure and at least 1 measurement every half an hour during the next 24 hours while the patient is monitored. Patients were continued on aspirin, 100 mg daily, and clopidogrel, 75 mg daily, for the next 90 days and subsequently on aspirin or clopidogrel alone. Risk factor control should be applied thereafter.

Risk factor control is based on the AHA/ASA guidelines[3, 4] and the SAMMPRIS[5] trial protocol. Medical management of risk factors consisted of normalizing low-density lipoprotein (LDL-C) (statins, target LDL-C <2.58 mmol/l [100 mg/dl]), hypertension (systolic pressure <140 mmHg and a diastolic pressure <90 mmHg), glucose derangement (in diabetic patients, hemoglobin A1c [HbA1c] will checked at enrollment and during each clinical visit with a target level of <6.5%), and lifestyle modification. Intensive management of risk factors was applicable to all the included patients (e.g., hypertension, lipid disorder, diabetes mellitus, overweight, obesity, physical inactivity, and cigarette smoking).

1.9 Assessments of the clinical outcome

The site investigators were not authorized to review the clinical outcome until they finished the central or on-site training program. They then determined clinical status at each follow-up visit, supervised the assessment of all the treatment outcomes, and completed the CRF documentation during the follow-up of 3 years. For assessment of mRS, Barthel Index and NIHSS, paper-based CRF was used.

If the primary/secondary outcomes were suspected to have occurred, site investigators were required to follow-up with patients by an in-person or telephone

interview and to fill out the CRF. Additional key neuro-images (CT or MR scans) were collected as adjunct evidence for outcome classification of ischemic or hemorrhagic stroke. Definitions:

- Stroke is defined as the rapid loss of brain function due to disturbance in the blood supply to the brain that persists beyond 24 hours. This can be due to ischemia or hemorrhage;
- Ischemic stroke is further defined as a new focal neurological deficit of sudden onset lasting at least 24 hours that is not associated with a hemorrhage on brain CT or MRI;
- Hemorrhagic stroke is defined as parenchymal, subarachnoid, or intraventricular hemorrhage detected by CT or MRI that is associated with new neurological signs or symptoms lasting >24 hours or a seizure.

Outcome assessments were sent to an independent Outcome Committee. The committee was composed of experienced neurologists who were not involved in the study, blinded to the treatment assignment. All outcomes were adjudicated by the outcome committee, and a consensus was reached by a third clinician in the case of discrepancies.

1.10 Assessments of the imaging outcome

An independent imaging core lab, IsCore Image CoreLab (ICIC, http://imagecorelabcn.com/), was established with the aim of facilitating central reading by clinicians and integrating medical imaging at the baseline control visit and each subsequent visit. IsCore Image Corelab was comprises an experienced expert team of neurologists, neurosurgeons and neuroradiologists all of whom assessed the radiological imaging. In order to reduce reader variability, all the members in the ICIC were trained by an expert team (Prof. Shenmao Li, and Prof. Xiaobo Zhang) prior to official reading. All imaging was read by two interdependent reader groups and a consensus was reached by a third senior reader when discrepancies were identified.

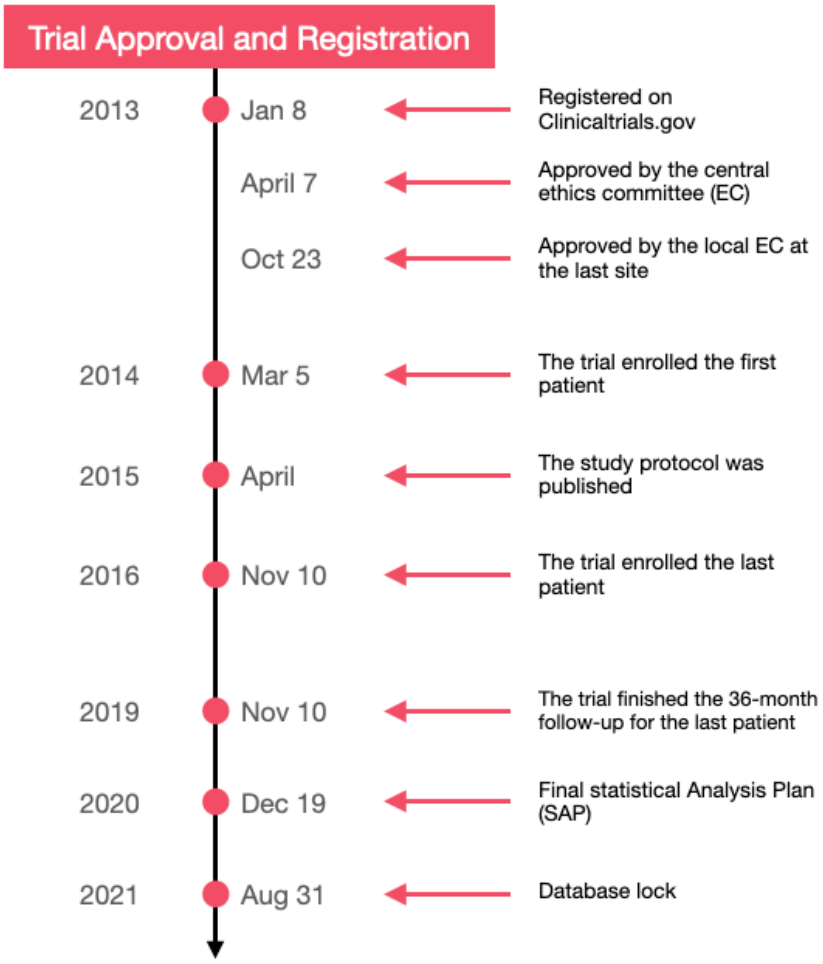
The ICIC demonstrated and analyzed the initial imaging (location, degree of stenosis, lesion length, ischemic pathophysiology), procedural imaging (pre- and post-procedural imaging), immediate and delayed imaging (new ischemia on diffusion-weighted imaging, or hemorrhage on CT), and follow-up imaging (outcome imaging adjudicated on MRA, CTA or angiography). Continuous variables, including the degree of stenosis, target vessel reference diameter and length, were recorded as the mean of the two readers. Discrepancy in reading of categorical variables was resolved by a third senior reader.

Conventional catheter angiography was used to quantitate the pre- and post-procedural severity of stenosis by using the Warfarin-Aspirin Symptomatic Intracranial Disease Study criterion.[6] Among patients with ischemic stroke as a qualifying event, ischemic pathophysiology was defined by infarct pattern of the baseline MRI-DWI and CTA/CT. Practically, stroke mechanisms were classified as: 1) perforator stroke or parent artery atherosclerosis occluding a perforator, 2) artery-to-artery embolism, 3) hypoperfusion, and 4) mixed mechanisms based on the Chinese ischemic stroke sub-classification.[7, 8] Perforator strokes due to perforator occlusion were defined as basal ganglia or brain stem/thalamus infarction related to middle cerebral artery or basilar artery stenosis. After central reading, those patients with perforator stroke only on baseline infarct pattern, or had recent infarctions identified on MRI (indicated as high signal on DWI) at enrollment were excluded due to ineligibility, and the remaining included for intention-to-treat analysis. The ICIC reviewed all the series and captured key images after procedures in order to defined procedure-related complications.

1.11 Trial Approval and Registration

This trial was registered on Clinicaltrials.gov on Jan 8, 2013 and was approved by the Ethics Committee (EC) of Xuanwu Hospital on April 7, 2013. The trial did not enroll patients until it was approved by the local ethics committee at each participating site. The last site approved the trial on Oct 23, 2013. The trial enrolled the first patient on Mar 5, 2014. The initial study protocol was published in April, 2015 in *Interventional Neuroradiology*.[1] The last patient was assessed and enrolled on November 10, 2016. The final statistical analysis plan was completed on December 19, 2020.

Timepoint of the Trial Approval and Registration



1.12 eReferences

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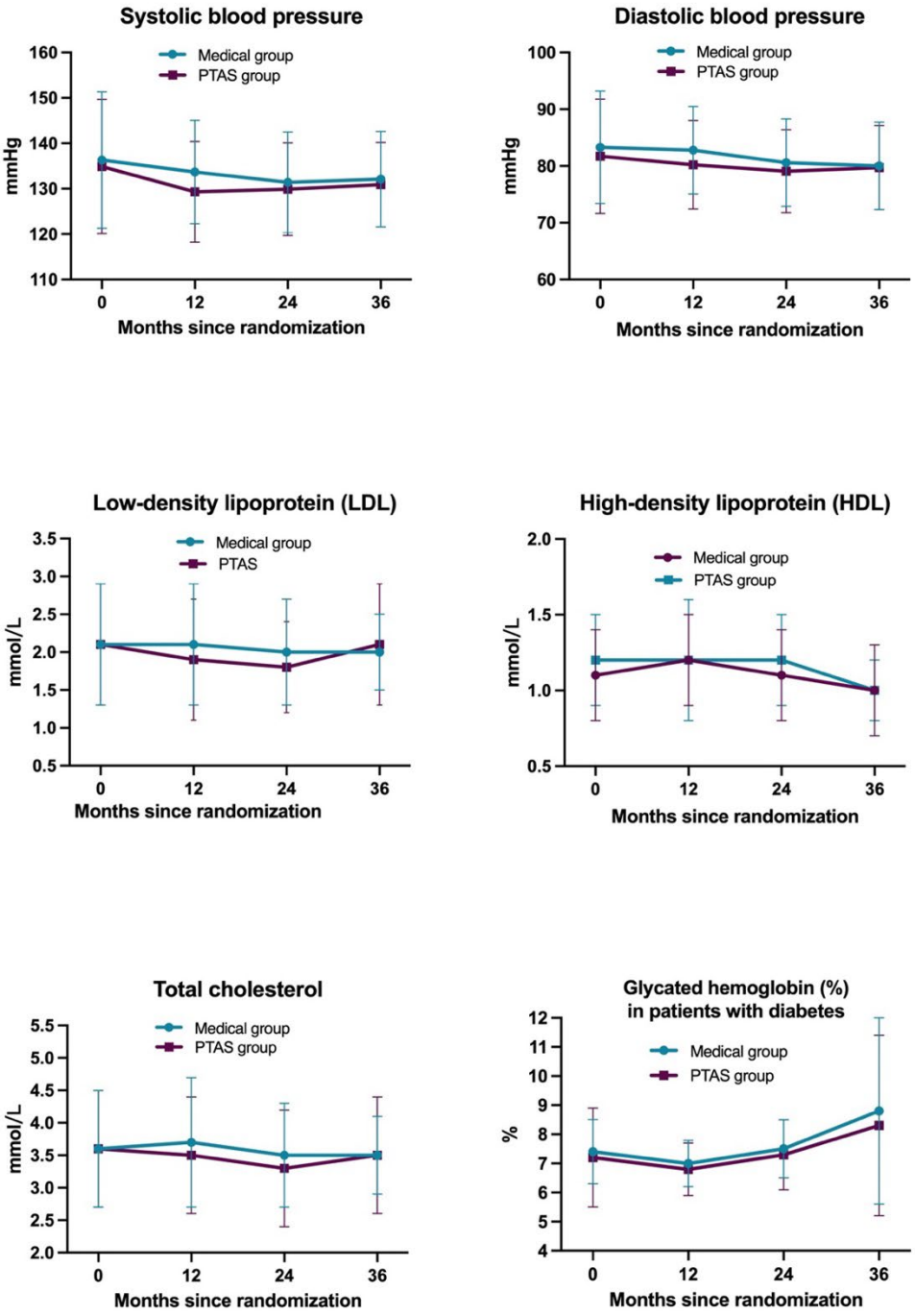
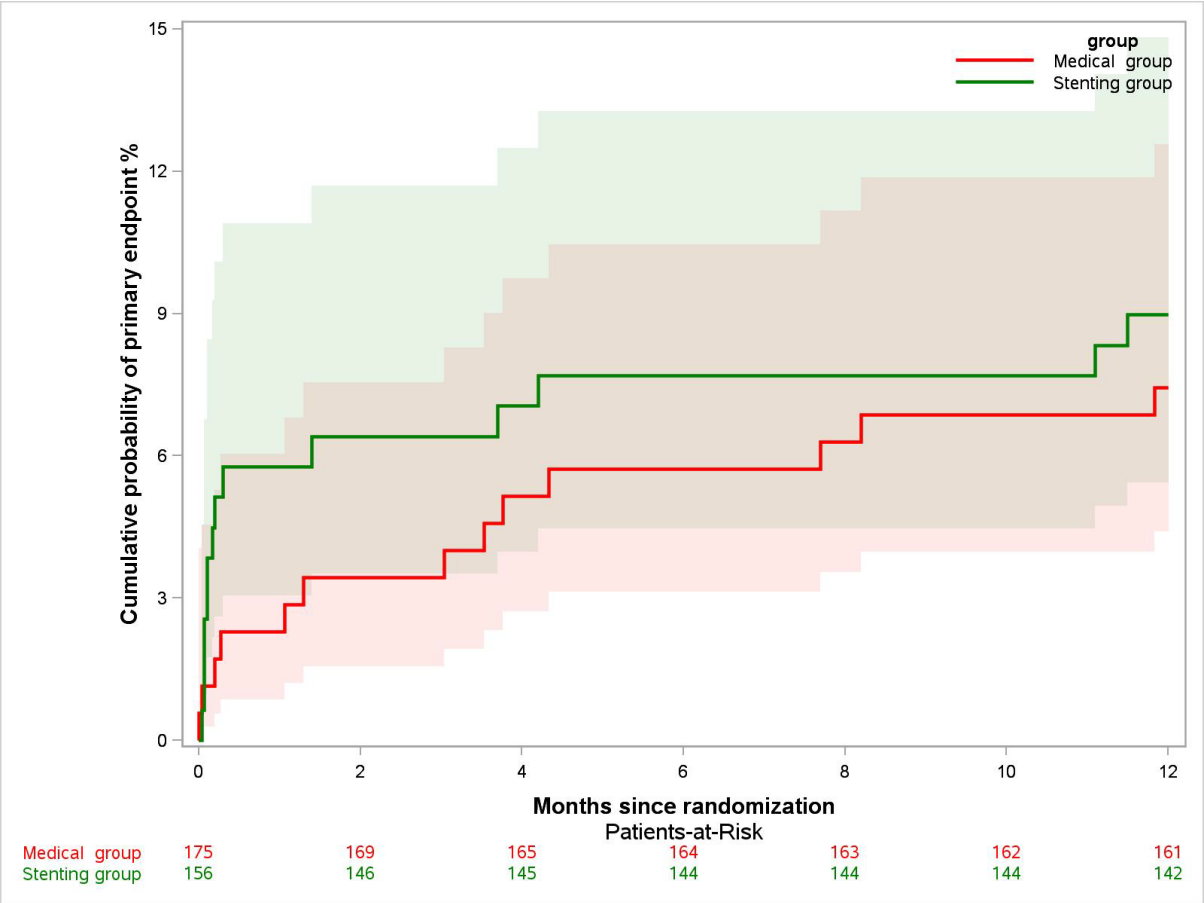
2. eFigures

eFigure 1. Three-year time trends of risk factor control in medical and stenting group*

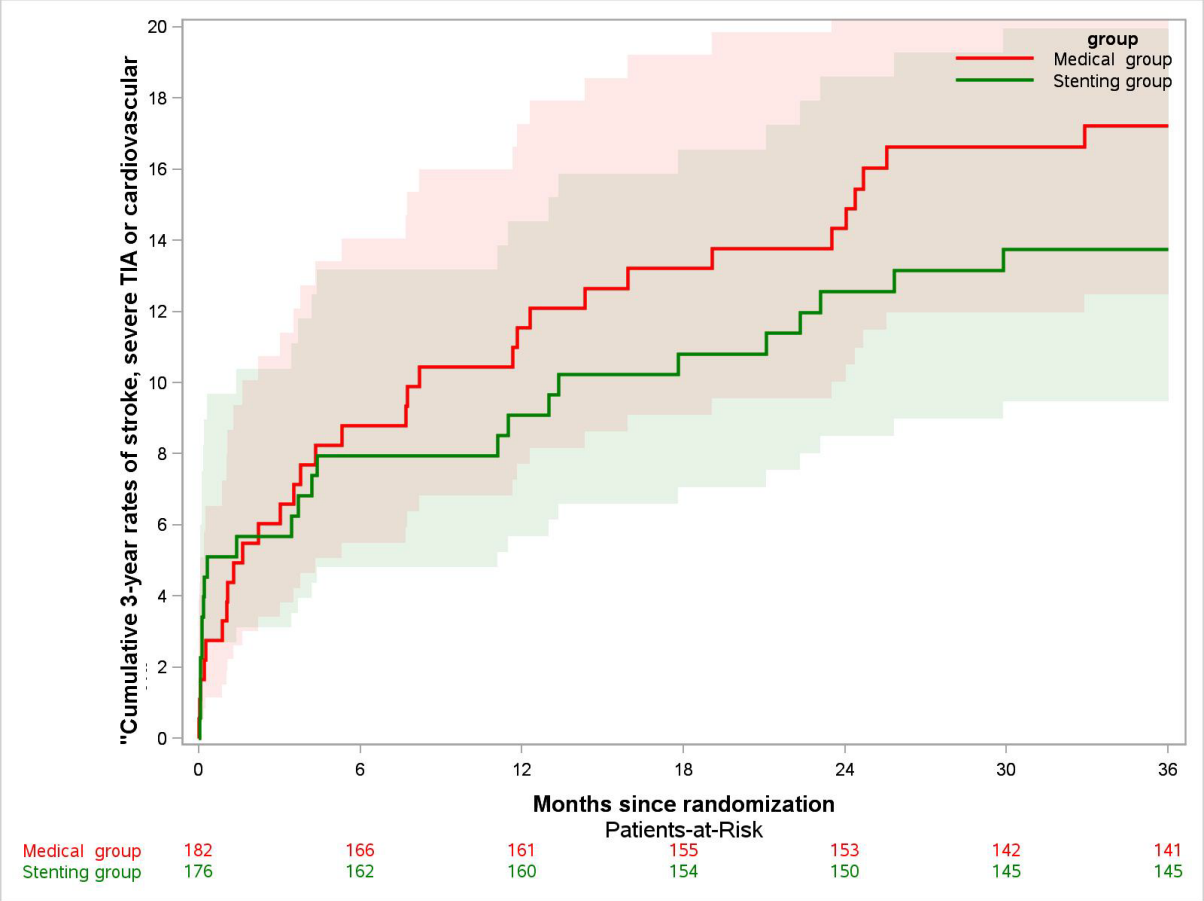


* Values used in this figure were mean plus standard deviation.

eFigure 2. Primary outcome: Kaplan–Meier Curves for the Cumulative Probability of the Primary End Point, According to Treatment Assignment (per-protocol analysis)



eFigure 3. Secondary outcome: Kaplan–Meier Curves for the cumulative 3-year rate of any stroke, TIA, or cardiovascular events, According to Treatment Assignment (Full analysis set population)



3. eTables

eTable 1. Baseline infarcts patterns among patients with qualifying event as stroke: anterior vs posterior circulation

	All	Medical group	Stenting group	P value
Anterior circulation, no. (%)	100 (100.0)	60 (100.0)	40 (100.0)	0.70
Artery-to-artery embolism	21 (21.0)	13 (21.7)	8 (20.0)	
Hemodynamic compromise	40 (40.0)	22 (36.7)	18 (45.0)	
Mixed mechanism	39 (39.0)	25 (41.7)	14 (35.0)	
Posterior circulation, no. (%)	94 (100.0)	45 (100.0)	49 (100.0)	---
Artery-to-artery embolism	94 (100.0)	45 (100.0)	49 (100.0)	
Hemodynamic compromise	0 (0.0)	0 (0.0)	0 (0.0)	
Mixed mechanism	0 (0.0)	0 (0.0)	0 (0.0)	

eTable 2. Measures of Risk Factors at Baseline and Each Visit Within 3-Year Follow-up[a]

The measures of risk factors at baseline and each visit during the 3-year follow-up were summarized. Throughout the trial at various stages, we detected no statistically between-group differences over time with respect to the actual values of the risk factors, except for minor comparisons (described in the footnote).

	Medical group (N=182)				Stenting group (N=176)			
	Baseline	1-year	2-year	3-year	Baseline	1-year	2-year	3-year
Blood pressure (mmHg)								
No. Patients evaluated	n=182	n=179	n=170	n=162	n=176	n=168	n=165	n=157
Systolic, median (IQR)	136.0±21.0	130.0±14.0	130.0±10.0	130.0±12.0	134.5±17.0	130.0±11.5	130.0±16.0	130.0±11.0
Diastolic, median (IQR)	80.0±12.0	80.0±11.0	80.0±9.0	80.0±10.0	80.0±15.0	80.0±9.0	80.0±9.0	80.0±9.0
Lipids (mmol/L)								
No. Patients evaluated	n=177	n=53	n=42	n=26	n=168	n=55	n=57	n=30
LDL cholesterol, median (IQR)	2.0±0.9	2.1±1.1[b]	2.0±0.9	1.9±0.8	2.0±1.0	1.8±0.8[c]	1.7±0.8	2.1±1.3
HDL cholesterol, median (IQR)	1.1±0.4	1.2±0.4	1.1±0.4	1.0±0.4	1.1±0.4	1.2±0.4[d]	1.1±0.4	1.0±0.3
Total cholesterol, median (IQR)	3.5±1.3	3.7±1.4	3.3±1.4	3.5±1.0	3.5±1.3	3.2±0.9	3.2±0.9	3.3±1.4

a Plus-minus values are means ±SD. To convert the values for cholesterol to milligrams per deciliter (mg/dl), multiplied by 38.67. PTAS denotes percutaneous transluminal angioplasty and stenting. Diabetes was defined according to the 2010 criteria of the American Diabetes Association. The difference in systolic blood pressure at 1-year follow-up between the two groups was significant (P=0.01). The difference in diastolic blood pressure at 1-year follow-up between the two groups was significant (P=0.006). The difference in serum triglyceride at 1-year follow-up between the groups was significant (P=0.04). Other comparisons were not significant.

b Number of patients evaluated was 51.

c Number of patients evaluated was 53.

d Number of patients evaluated was 53.

Triglyceride, median (IQR)	1.4±0.9	1.3±0.7	1.2±0.9	1.6±0.7	1.4±0.8	1.1±0.6	1.3±0.6	1.3±0.7
Glycated hemoglobin (%)								
No. Patients evaluated	n=115	n=35	n=26	n=17	n=114	n=41	n=38	n=24
Value, median (IQR)	5.8±1.0	5.7±0.9	5.8±1.2	5.6±0.9	5.9±1.3	5.8±0.8	6.1±1.4	6.3±1.7
Glycated hemoglobin (%) in patients with diabetes								
No. Patients evaluated	n=32	n=8	n=5	n=3	n=43	n=12	n=15	n=11
Value, mean (SD)	7.4±1.1	7.0±0.8	7.5±1.0	8.8±3.2	7.2±1.7	6.8±0.9	7.3±1.2	8.3±3.1
Serum C-reactive protein								
No. Patients evaluated	n=128	n=24	n=26	n=15	n=122	n=32	n=39	n=20
Value, median (IQR)	1.8±3.8	1.8±1.9	0.5±1.4	1.0±1.0	1.6±3.8	1.1±3.2	0.5±1.4	1.0±1.7
Lifestyle[e]								
No. Patients evaluated	n=182			n=65	n=176			n=65
Current smoker (%)	27.5			24.6	23.3			27.7
Body-mass index[f]								
No. Patients evaluated	n=182			n=56	n=176			n=60
Value, mean (SD)	26.0±3.2			26.5±3.6	25.5±2.8			25.9±2.6

e Part of the value was evaluated beyond the follow-up of 3 years.
f The body-mass index is the weight in kilograms divided by the square of the height in meters. Part of the value was evaluated beyond the follow-up of 3 years.

eTable 3. Post Hoc Analysis of Primary and Secondary Outcomes

	Hazard ratio (95%CI)[a,b]
Primary outcomes	1.11 (0.52 to 2.36)
Stroke or death within 30 d after enrollment[b]	
Stroke in territory of qualifying artery beyond 30 d through 1 y[b]	
Secondary outcomes	
Stroke in the same territory within 2 y	1.10 (0.55 to 2.18)
Stroke in the same territory within 3 y	1.02 (0.54 to 1.94)
Disabling stroke or death within 3 y	1.31 (0.66 to 2.58)
Any stroke, TIA, cardiovascular events related to stenting or medical therapy within 3 y	0.78 (0.46 to 1.33)
Death within 3 y	3.64 (0.76 to 17.54)
Stroke-related death[b]	
Non-stroke-related death[b]	

[a]Post hoc analysis.

[b]With site as a random effect in mixed-effects Cox proportional risk model.

eTable 4. Adverse Events Analysis (Full Analysis Set population)

	Stenting group (N=176)	Medical group (N=182)
Stroke or death within 30 days after enrollment	No./total (%)	No./total (%)
Stroke		
Disabling stroke	5/176 (2.8)	2/181 (1.1)
Symptomatic intracranial hemorrhage	4/176 (2.3)	0
Death		
Stroke-related death	2/176 (1.1)	0
Non-stroke-related death	0	0
Stroke in territory of qualifying artery beyond 30 days through 1 year		
Stroke		
Disabling stroke	3/176 (1.7)	6/181 (3.3)
Symptomatic intracranial hemorrhage	1/176 (0.6)	0
Death		
Stroke-related death	0	0
Non-stroke-related death	0	0
Death rate within a follow-up of 3 years	7/160 (4.4)	2/159 (1.3)

eTable 5. Subgroup Analysis of Primary and Secondary Outcomes by the qualifying events (TIA versus Ischemic Stroke).

	Stenting group (N=176), No./total (%)	Medical group (N=182), No./total (%)	Hazard ratio (95%CI) [a]	P value [b]
Ischemic stroke				
Primary outcome	9/89 (10.1)	9/105 (8.6)	1.17 (0.46-3.00)	0.76
Secondary outcomes				
2-year rate of the same-territory stroke	11/86 (12.8)	12/102 (11.8)	1.12 (0.48-2.58)	0.83
3-year rate of the same-territory stroke	12/85 (14.1)	15/99 (15.2)	0.91 (0.41-2.01)	0.79
Disabling stroke or death after enrollment through 3 years	13/85 (15.3)	11/96 (11.5)	1.38 (0.61-3.13)	0.47
TIA				
Primary outcome	5/87(5.7)	4/76 (5.3)	1.13 (0.30-4.21)	0.91
Secondary outcomes				
2-year rate of the same-territory stroke	6/85 (7.1)	4/76 (5.3)	1.35 (0.37-4.88)	0.69
3-year rate of the same-territory stroke	7/83 (8.4)	4/71 (5.6)	1.57 (0.45-5.51)	0.51
Disabling stroke or death after enrollment through 3 years	6/83 (7.2)	4/70 (5.7)	1.38 (0.39-4.92)	0.64

Abbreviations: TIA, transient ischemic attack.
a. Adjusted for site effect
b. Log rank test adjusted for site effect.