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Surgical Results of the Carotid Occlusion Surgery Study

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Abstract

Object—The Carotid Occlusion Surgery Study (COSS) was conducted to determine if STA-MCA bypass, when added to best medical therapy, would reduce subsequent ipsilateral stroke in patients with complete ICA occlusion and an elevated OEF in the cerebral hemisphere distal to the carotid occlusion. A recent publication reported the methodology of COSS in detail and briefly outlined the major findings of the trial.[29] The surgical results of COSS are described in detail in this report.

Methods—The Carotid Occlusion Surgery Study (COSS) was a parallel group, prospective, 1:1 randomized, open-label, blinded-adjudication treatment trial. Participants with angiographic confirmed complete occlusion of the ICA causing either a transient ischemic attack (TIA) or ischemic stroke within 120 days and hemodynamic cerebral ischemia demonstrated by an increased oxygen extraction fraction (OEF) measured by positron emission tomography (PET)

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were randomized to either surgical or medical treatment. The surgical patients underwent a STA-MCA cortical branch anastomosis. One hundred and ninety-five patients were randomized: 97 to the surgical group and 98 to the medical group.

Results—In the intention-to-treat analysis, the two-year rates of the primary endpoint were 0.210 for the surgical group and 0.227 for the medical group (p=0.78, log rank). Fourteen (15%) of the 93 patients who had an STA-MCA arterial bypass had an endpoint ipsilateral hemispheric stroke in the 30 day peri-operative period, 12 within two days. The STA-MCA arterial bypass patency rate was 98% at the 30 day post-operative visit and 96% at the last follow-up examination. STA-MCA arterial bypass markedly improved, although it did not normalize, the level of elevated OEF in the symptomatic cerebral hemisphere. Five operated patients and one non-operated patient in the surgical group had an endpoint ipsilateral hemispheric stroke after the 30 day peri-operative period. No baseline characteristics or intra-operative variables were identified that permitted the identification of those who would experience a procedure related stroke.

Conclusions—In spite of excellent bypass graft patency and improved cerebral hemodynamics, STA-MCA anastomosis did not provide an overall benefit on ipsilateral two-year stroke recurrence, mainly due to a much better than expected stroke recurrence rate (22.7%) in the medical group in the trial, but also because of a significant peri-operative stroke rate (15%).

Keywords

symptomatic occluded internal carotid artery; superficial temporal artery-middle cerebral artery anastomosis; impaired cerebral hemodynamics; oxygen extraction fraction; randomized trial

Introduction

Complete occlusion of the internal carotid artery (ICA) by atherosclerotic disease causes approximately 15-25% of ischemic strokes in the carotid artery distribution. Patients treated with medical therapy have a risk of recurrent stroke of 7-10% per year for all stroke and 5-8% per year for ipsilateral ischemic stroke during the first two years following ICA occlusion. [17,18,20,21] ICA occlusion causes an estimated 61,000 first-ever strokes per year in the United States[1,6,22,26,37,39] an incidence more than twice the annual occurrence of ruptured intracranial aneurysms.[5] Superficial temporal artery-middle cerebral artery (STA-MCA) anastomosis was developed to improve hemodynamics distal to an occluded artery.[12,38,41] The International Study of Extracranial-to-Intracranial Arterial Anastomosis (STA-MCA bypass trial) tested the usefulness of STA-MCA bypass surgery as a prophylaxis against stroke.[13] STA-MCA bypass was not effective in preventing subsequent stroke as compared to best medical therapy in any group of patients, including the 808 patients with symptomatic complete occlusion of the ICA. Based on the results of this trial, extracranial-intracranial (EC-IC) arterial bypass was generally abandoned as a treatment for symptomatic complete ICA occlusion. Following the trial, several groups criticized the results on multiple grounds[2,8,36] (Ausman-1986, Day-1986, Sundt-1987), , including the inability to identify and separately analyze a subgroup of patients with impaired cerebral hemodynamics due to occlusive cerebrovascular disease in whom surgical revascularization might be more beneficial.[8]

Since then, advances in neuroimaging have made it possible to determine the hemodynamic effects of ICA occlusion in individual patients.[9,17,20,40] The strongest evidence for an association between cerebral hemodynamic impairment and stroke was provided by the St. Louis Carotid Occlusion Study (STLCOS).[17] This blinded prospective study found that severe hemodynamic failure, manifested by an elevated oxygen extraction fraction (OEF) in the cerebral hemisphere distal to a complete ICA occlusion, was an independent predictor of subsequent stroke in symptomatic medically treated patients. STA-MCA arterial bypass surgery has been shown to improve cerebral hemodynamics distal to an occluded ICA .[4,15,16,27,28,33]

The Carotid Occlusion Surgery Study (COSS) was a parallel group, prospective, 1:1 randomized, open-label, blinded-adjudication treatment trial designed to test the hypothesis that STA-MCA anastomosis, when combined with best medical therapy, could reduce by 40 per cent the subsequent occurrence of ipsilateral ischemic stroke at two years in patients with recent symptomatic ICA occlusion and ipsilateral increased OEF measured by positron emission tomography (PET). The trial design and analysis and primary results have been previously reported.[29] The primary endpoint point in the surgical group was (1) all stroke and death from surgery through 30 days post-operatively plus (2) ipsilateral hemispheric ischemic stroke within two years. The primary endpoint in the non-surgical group was (1) all stroke and death from randomization through 30 days plus (2) ipsilateral hemispheric ischemic stroke within two years. All primary endpoints were ipsilateral ischemic strokes. Based on an intent-to-treat analysis, two-year rates for ipsilateral ischemic stroke were 21.0% (95% CI, 12.8% to 29.2%; 20 events) for the 97 participants in the surgical group and 22.7% (95% CI, 13.9% to 31.6%; 20 events) for the 98 participants in the nonsurgical group (p=0.78, z-test); difference = 1.7% (95% CI, -10.4% to 13.8%).[29]

METHODS

Surgical Procedure

The EC-IC arterial bypass procedure used in the COSS trial was a standard STA-MCA cortical branch anastomosis.[11,25,30,41] If the STA was not suitable for anastomosis to the MCA, the occipital artery (OA) could be used in place of the STA. All surgical patients were placed on 81 mg or 325 mg of aspirin daily prior to the bypass procedure. All other peri-operative issues, such as anticonvulsants, antibiotics, choice of anesthetic agents, intraoperative hemodynamic monitoring and peri-operative fluid loading were left to the discretion of the operating surgeon. The STA-MCA cortical branch anastomosis was done using the best STA branch and the best MCA cortical branch. Only one anastomosis was done. Patients with an “unsuitable” STA (diameter < 1 mm) were excluded from the study. Details of the surgical technique used for the STAMCA anastomosis, such as using running or interrupted 10-0 prolene or nylon sutures, a straight or elliptical incision in the MCA cortical branch, and preparation of the STA graft, were left to the discretion of the operating surgeon. During and immediately following the surgical procedure, data concerning anesthesia techniques, intraoperative blood pressures (BP), cerebral monitoring and technical aspects of the bypass procedure was recorded and saved for analysis. Following surgery, all patients were left on 81 mg or 325 mg of aspirin for at least 30 days. Thereafter,

when deemed appropriate by their neurosurgeon, patients were returned to the anti-thrombotic treatment preferred by their physicians. Doppler ultrasound examination was used to determine post-operative STA-MCA bypass patency at follow-up visits.

Surgical Certification

Surgeons were certified for the study by: (1) attending an initial training workshop in St. Louis where videotape instruction and surgical practice of microvascular anastomosis was done on frozen cadaver heads and live rat carotid arteries, or (2) demonstrating at least 80% bypass graft patency and less than or equal to 10% stroke and death at one month in at least 10 consecutive STA-MCA bypass surgeries. Provisional certification was issued for those with less than 10 STA-MCA bypass cases available for review to perform a STA-MCA bypass operation on a patient enrolled in the trial under the observation of the principal neurosurgical investigator for the trial or a designated neurosurgeon with extensive STAMCA bypass experience.

Further Cerebrovascular Procedures

Both the non-surgical and surgical patients were prohibited from undergoing any additional surgical procedures following the STA-MCA arterial bypass that might alter cerebral hemodynamics or affect stroke risk, except for carotid endarterectomy performed for the development of symptomatic contralateral stenosis of the internal carotid artery.

Statistics

Categorical variables are displayed as counts and p-values are taken for generalized Fisher's exact tests. Continuous variables are displayed as means and standard deviations. Comparisons between groups used t-tests when the normality assumptions were valid. In three cases the normality assumption was not valid and the p-value was derived from a Wilcoxon rank sum test. These instances were noted in the tables.

Results

Thirty different surgeons performed 92 STA-MCA bypasses and 1 OA-MCA bypass at a median 6 days (interquartile range (IQR) 1-13) days following randomization to the surgical group. Four participants randomized to the surgical group did not undergo surgery. No strokes occurred during the time between randomization and surgery. The bypass patency rate was excellent, with a 98% patency rate (88/90 patients with patency data) at the 30 day post-operative visit. One patient died in the peri-operative period and graft patency data was not recorded in two other patients at the 30 day follow-up visit. At the last follow-up visit that assessed STA-MCA arterial bypass patency (mean 605 (±270 SD) days, range 28-1596 days), the graft patency rate was 96% (86/90 patients with patency data). The mean OEF ratio in the surgical group improved from 1.258 at baseline to 1.109 at the 30-60 day post-operative repeat PET scan (data from 87 participants). In a previous study, the upper limit of the OEF ratio calculated by similar methods in 18 normal subjects was 1.062.[17] Twenty-nine per cent (25/87) of the post-operative COSS PET scans were within the normal range.

Fourteen (15%) of the 93 patients who had a STA-MCA arterial bypass had an endpoint ipsilateral hemispheric stroke in the 30 day peri-operative period. Twelve of the 14 peri-operative ipsilateral hemispheric strokes occurred within the first 2 days following surgery. The other two occurred at 5 and 15 days after surgery. The occurrence of 2 strokes more than 2 days after surgery, but within 30 days, was identical to that observed in the non-surgical group of 98 patients who had 2 ipsilateral strokes within 30 days of randomization.

Of the 14 strokes occurring within the 30 day peri-operative period, two were disabling at last follow-up (Barthel index > 12) and one was fatal. The patient who died in the post-operative period had two ipsilateral strokes on the day of surgery, a vertebrobasilar artery distribution stroke on the first postoperative day (POD) and died on POD 4. The bypass was felt to be patent during the surgical procedure. Another patient had a post-operative ipsilateral stroke on the day of surgery. This bypass was also thought to be patent during the procedure, but the graft was occluded at the 30 day follow-up visit. The bypass was not patent at the completion of surgery in a third patient. This patient had an ipsilateral stroke on POD 1. Thus, the STA-MCA bypass was patent at the 30 day follow-up visit in 11 of the 14 patients who had an ipsilateral hemispheric stroke in the 30 day post-operative period. The bypass was patent at last follow-up in the two patients who had a disabling ipsilateral hemispheric stroke in the peri-operative period. In 2 of the patients who had an ipsilateral hemispheric stroke in the 30 day peri-operative period other serious adverse events occurred during this time period (Table 1). One of the patients with a peri-operative ipsilateral hemispheric stroke also had an episode of hypoglycemia on POD 2, a deep venous thrombosis (DVT) on POD 6, an episode of atrial fibrillation/flutter on POD 9, a pulmonary embolus on POD 9, and a non-fatal cardiac tamponade on POD 14. A second patient with a peri-operative ipsilateral hemispheric stroke was found to have a small asymptomatic subdural hematoma and significant anemia on POD 3.

Twelve additional patients who did not have a 30 day peri-operative stroke had serious adverse events reported in the peri-operative period. (Table 1) Among these events were TIA's that occurred in 4 patients on POD 1, 7, 8 and 9 respectively. Three of these TIA's were reported as ipsilateral hemispheric strokes by the clinical sites, but they were later adjudicated as TIA's. Two of the 12 patients had a subdural hematoma (POD 21 and 26). The subdural hematoma found on POD 26 required surgical drainage. This patient also had a post-operative ipsilateral hemispheric stroke on POD 52. Other events in these 12 patients included a significant myocardial infarction on POD 0, severe respiratory distress on POD 0, one wound infection, one episode of severe hypotension, and a seizure in 2 patients.

The surgical certification method and the 30-day post-op stroke rate in the 30 surgeons who operated in COSS are outlined in Table 2. Fifteen of the 30 surgeons in the trial were certified by attending the initial training workshop. They performed 64 STA-MCA arterial bypasses in the trial with 11 (17 %) peri-operative ipsilateral strokes. Thirteen surgeons were certified by submitting data on 10 or more consecutive STA-MCA arterial bypasses that met the criteria listed above. In the trial they performed 24 STA-MCA arterial bypasses with 3 (13 %) peri-operative ipsilateral strokes. Only 2 surgeons in the trial had provisional certification, and they performed 5 STA-MCA arterial bypasses with no peri-operative strokes. Thus, there was no significant difference in the method of surgical certification for

the trial and the incidence of peri-operative strokes (p= .91). Seventeen of the 30 surgeons in the trial provided self-reported data for 292 EC-IC arterial bypasses for the grant submission to the National Institutes of Health for funds to conduct the study. Twenty-seven (9.2%) of these 292 patients had a stroke or died in the 30 day post-operative period. The same 17 surgeons in the COSS trial performed 72 STA-MCA arterial bypasses with 8 (11.1 %) patients having an ipsilateral stroke in the peri-operative period, which was not significantly different from their pre-COSS experience (p=.655).

Since the peri-operative stroke rate negated any net benefit of the bypass surgery, we sought to identify factors that would predict peri-operative stroke occurrence. We performed this analyses for the 12 strokes that occurred within two days, since these were the most likely to be directly related to surgery, and the additional two strokes within 30 days of surgery were the same number as occurred in the non-surgical group within 30 days of randomization. Even though this type of analysis is hazardous because of the increase in false positive rate due to the large number of variables analyzed, we found no baseline or intra-operative variables that were different at the .05 level between those who experienced a stroke within two days of surgery and those who did not (Tables 3, 4A and 4B).

Five operated patients had an endpoint ipsilateral hemispheric stroke after the 30 day peri-operative period. (One non-operated patient had an endpoint ipsilateral hemispheric stroke within the two-year follow-up period). In all five of these operated patients, the STA-MCA bypass was documented as patent following the surgical procedure and prior to the stroke. In 4 of these patients, the bypass was documented as still patent following the stroke. There was no information recorded about bypass patency following the stroke in the other patient. Thus, in the 19 patients who had a primary endpoint ipsilateral hemispheric stroke after surgery, the bypass was documented as patent in 15 of the patients following the stroke. Two additional patients who underwent successful STA-MCA bypasses had strokes in the cerebral hemisphere contralateral to the symptomatic occluded carotid artery. Both patients had less than 50% stenosis of the contralateral carotid artery at the time of randomization, and their bypasses were patent at the last follow-up. In one patient, the stroke occurred on POD 556, and the other patient had contralateral hemispheric strokes on POD 279 and POD 608.

Eliminating the 12 surgical patients who had peri-operative strokes within 2 days of surgery from the analysis, but retaining the two who had strokes between 2 and 30 days because these were identical in number to those occurring in the non-surgical group within 30 days of randomization, the rate of recurrent stroke for the remaining 81 patients in the surgical group was 9.0% compared to 22.7% in the non-surgical group.

Discussion

Prior to the start of the trial, there was concern that problems might be encountered during the study with STA-MCA bypass graft patency rates, as the procedure had not be done for patients with cerebral ischemia by most vascular neurosurgeons after the results of the STA-MCA bypass trial were published in 1985. However, the STA-MCA arterial graft patency rates seen in the COSS trial of 96-98% were similar to the results obtained in the STA-MCA

bypass trial and other reported patient series. In the STA-MCA Bypass Trial, repeat cerebral angiography was carried out at a median time of 32 days post-op in 92% of the 652 STA-MCA bypass trial patients who had a bypass procedure, and 96% of these patients had a patent STA-MCA anastomosis.[13] In a report of 415 STA-MCA anastomoses performed at a single institution over an eight year period, a graft patency rate of 99% was achieved. Cerebral angiography was used to assess graft patency in the first 260 patients and Doppler velocity flow probe examination was performed in the remaining patients in this study.[35] The same investigators found a 96% graft patency rate confirmed by cerebral angiography in a separate analysis of 163 of these patients who had a STA-MCA anastomosis performed for cerebral ischemic symptoms due to complete internal carotid artery occlusion.[19] Other case series of STA-MCA bypasses have reported graft patency rates of 90-96%.[7,23,32,34,42]

A literature review in 1978 of multiple case series reported an average permanent neurological morbidity of 2.4% and an average operative mortality of 4.3% in 376 STA-MCA bypass procedures.[32] There was an “other morbidity” of 13.6% in these patients. Other series of 100 to 415 patients from the same era of STA-MCA bypass surgery reported peri-operative stroke rates of 2-3.6% and peri-operative mortality rates of 1.2-3%.[7,31,42] A peri-operative mortality of 2.1%, a permanent neurological impairment rate of 6.4% and a morbidity rate of 25.5% was found in a more recent series of 47 patient undergoing STA-MCA bypass for cerebral ischemia symptoms[34], while no operative mortality and a 3% peri-operative stroke rate was reported in a contemporary study of 73 similar patients.[23]. However, in the multicenter, randomized STA-MCA bypass trial, 81 (12.2%) strokes in 663 surgical patients occurred between randomization and 30 days post-op using an intent-to-treat analysis of the surgical data. Sixteen of the peri-operative strokes occurred in patients randomized to surgery, but prior to a STA-MCA bypass procedure. The actual (on-treatment) peri-operative stroke rate in this trial was 65 (9.8%) peri-operative strokes in 652 STA-MCA bypass procedures, including 20 (3%) major strokes, with 4 (0.6%) of these strokes having a fatal outcome.[3,13]

There was a substantial occurrence of peri-operative non-stroke serious adverse events in COSS, including 2 patients who also had a peri-operative stroke and an additional 12 who did not. The rate of peri-operative non-stroke serious adverse events in COSS was similar to the occurrence of these events in previously published series of STA-MCA bypasses. Most of the reports of morbidities associated with STA-MCA bypass surgery have focused on ischemic neurologic deficits and have not listed other non-stroke peri-operative morbidity rates. However, a review in 1978 of 376 STA-MCA bypass procedures reported a peri-operative “other morbidity” (non-cerebral ischemic) rate of 13.6%.[32] Seven (2%) of 400 patients[7], 12 (3%) of 415 patients[35], and 3 (6%) of 47 patients[34] undergoing a STA-MCA bypass had a post-operative subdural hematoma/subdural hygroma requiring surgical drainage or subdural-peritoneal shunting. Scalp necrosis around the skin incision developed in 7%[31] and 1.3%[7] of patients in two series of STA-MCA bypasses. A pulmonary embolus occurred in 4 (6%) of 70 patients after a STA-MCA bypass.[31].

In the EC-IC arterial bypass data submitted prior to the COSS trial, many of the EC-IC bypass procedures were not STA-MCA bypasses. Some of the EC-IC bypasses were high flow extracranial carotid artery-MCA anastomoses utilizing a saphenous vein graft or a

radial artery graft. Many of these self-reported procedures were done in patients undergoing either deliberate ICA or MCA occlusion for intracranial aneurysm treatment, intracranial tumor resection, or cerebral ischemia caused by moya-moya disease. Also, the majority of the patients were younger than the patients in the COSS trial. Inexperience with the STA-MCA bypass procedure might account for the higher rate of peri-operative strokes seen in the COSS trial. However, the surgeons in COSS who provided the pre-trial data had similar results in COSS. Furthermore, the 30 day postoperative stroke of 15% in the COSS trial was not statistically different from the 9.8% peri-operative stroke rate seen performed in the STA-MCA bypass trial (p=0.136, Chi-square). An extensive analysis of multiple baseline characteristics and intra-operative variables did not demonstrate factors that would definitely identify patients with an increased risk of procedure related stroke.

Conclusions

The COSS trial confirmed that severe impairment of cerebral hemodynamics is an important risk factor for subsequent stroke in patients with symptomatic complete occlusion of the ICA. The study also confirmed the accuracy of PET measurements of OEF in identifying those patients with an occluded ICA at high risk for recurrent stroke due to poor collateral circulation.[29] In the trial, STA-MCA arterial bypass markedly improved, although it did not normalize, the level of elevated OEF in the symptomatic cerebral hemisphere. After the second post-operative day, the rate of recurrent ipsilateral stroke for the remainder of the two-year follow-up period was only 9%. However, in spite of excellent bypass graft patency and improved cerebral hemodynamics, STA-MCA anastomosis did not provide an overall benefit on ipsilateral two-year stroke recurrence, mainly due to a much better than expected stroke recurrence rate (22.7%) in the medical group in the trial, but also because of a significant peri-operative stroke rate of 15%. These findings again confirm the hazard of relying on even the most carefully studied historical controls and re-affirm the necessity of performing randomized controlled trials to establish clinical efficacy.

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Abbreviations used in the paper

BP	blood pressure
COSS	Carotid Occlusion Surgery Study

EC-IC	extracranial-intracranial
ICA	internal carotid artery
IQR	interquartile range
MCA	middle cerebral artery
NIHSS	National Institutes of Health Stroke Scale
OEF	oxygen extraction fraction
PET	positron emission tomography
OA	occipital artery
OA-MCA	occipital artery-middle cerebral artery
POD	post-operative day
SS-QoL	Stroke Specific Quality of Life
STA	superficial temporal artery
STA-MCA	superficial temporal artery-middle cerebral artery
STA-MCA bypass trial	The International Study of Extracranial-to-Intracranial Arterial Anastomosis
STLCOS	St. Louis Carotid Occlusion Study
TIA	transient ischemic attack

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Table 1

Peri-operative (30 Day) Non-stroke Serious Adverse Events

Event	Number Of Events	Post-op Day
TIA	4	1,7,8,9
Subdural hematoma	3	3,21,26
Wound infection	1	25
Myocardial infarction	1	0
Respiratory distress	1	0
Seizure	2	2,3
DVT	1	6
Pulmonary embolus	1	9
Atrial fibrillation/flutter	1	9
Cardiac tamponade	1	14
Severe hypotension	1	19
Hypoglycemia	1	2
Severe anemia	1	3

Table 2

Surgical Certification and 30 Day Post-operative Stroke Rate

Method of Certification	Number of Surgeons	Number of Peri-operative Strokes
Initial Workshop Attendance	15	11/64 (17%)
Submission 10 Consecutive Cases	13	3/24 (13%)
Provisional certification	2	0/5 (0%)

Table 3

Comparison of Baseline Characteristics Between Those Who Did and Did Not Experience A Stroke Within Two Days After Surgery

	Perioperative Stroke Within 2 days		
	No	**Yes**	***P* value**
Number	81	12	
Age (mean (SD), years)	57.8 (9.3)	61.1(7.6)	0.245[2]
Gender			0.999[1]
Male (66)	57	9	
Female (27)	24	3	
Race			0.599[1]
White (84)	72	12	
Other (9)	9	0	
Hypertension, No. (%)			0.696[1]
No (18)	15	3	
Yes (75)	66	9	
Atrial Fibrillation, No. (%)			0.999[1]
No (92)	80	12	
Yes (1)	1	0	
Hyperlipidemia			0.999[1]
No (16)	14	2	
Yes (77)	67	10	
Diabetes mellitus			0.717[1]
No (73)	64	9	
Yes (20)	17	3	
Cigarette smoking			0.329[1]
Never (7)	6	1	
Former (54)	45	9	
Current (32)	30	2	
Previous Myocardial Infarction			0.117[1]
No (83)	74	9	
Yes (10)	7	3	
Previous Stroke			0.138[1]

	Perioperative Stroke Within 2 days		
	No	**Yes**	***P* value**
No (48)	44	4	
Yes (43)	36	7	
Unknown (2)	1	1	
Entry Event Type			0.130[1]
TIA (42)	34	8	
Stroke (51)	47	4	
Entry Event Side			0.348[1]
Right (54)	49	5	
Left (39)	32	7	
Entry Event to Randomization, mean(SD), days	73.8(38.5)	53.1(27.5)	0.093[3]
Randomization to Surgery, mean(SD), days	10.7(13.3)	7.3(6.7)	0.735[3]
Contralateral Carotid Stenosis (%)			0.999[1]
<50 (75)	65	10	
50-69 (11)	10	1	
≥70 (7)	6	1	
Modified Barthel Scale (mean (SD))	19.2(1.9)	20.0(0.0)	0.113[3]
Modified Rankin Score (mean (SD))	1.4(1.1)	1.1(0.9)	0.375[3]
NIHSS (mean (SD))	1.8(2.2)	1.4(1.9)	0.642[3]
SSQoL (summary) (mean (SD))	3.7(0.9)	4.1(0.8)	0.146[2]
Systolic Blood Pressure (mean (SD), mm Hg)	132.3(14.8)	132.3(18.2)	0.948[2]
Diastolic Blood Pressure (mean (SD), mm Hg	77.0(10.4)	72.4(10.8)	0.163[2]
PET OEF Ratio (mean(SD))	1.25(0.13)	1.29(0.18)	0.381[2]
Collateral Circulation (number of angiographic Collaterals)			0.475[1]
0 (10)	9	1	
1 (34)	31	3	
2 (42)	36	6	
3 (7)	5	2	
Hematocrit (mean (SD))	41.2(4.8)	38.8(3.2)	0.099[2]

[1] Fisher's Exact Test

[2] t-test

[3] Wilcoxon Rank Sum test

Table 4A

Comparison of Intra-operative Data Between Those Who Did and Did Not Experience A Stroke Within Two Days After Surgery

	Stroke No	Stroke Yes	Total No. of Subjects	*P* value*
Anesthesia				
Nitrous oxide				
No	48	9	57	0.357
Yes	33	3	36	
Halothane				
No	78	12	90	0.999
Yes	3	0	3	
Enflurane				
No	80	12	92	0.999
Yes	1	0	1	
Isoflurane				
No	49	7	56	0.999
Yes	32	5	37	
Narcotic				
No	10	2	12	0.651
Yes	71	10	81	
Relaxant				
No	11	3	14	0.382
Yes	70	9	79	
Barbiturates				
No	53	8	61	0.999
Yes	28	4	32	
Propofol				
No	35	2	27	0.498
Yes	56	10	66	
Other general anesthesia				
No	28	4	32	0.999
Yes	53	8	61	
Local anesthesia				
No	67	10	77	0.999
Yes	13	2	15	
Side of surgery				
Right	49	5	54	0.348
Left	32	7	39	
Heparin during MCA occlusion				
No	69	9	78	0.403

	Stroke No	Stroke Yes	Total No. of Subjects	*P* value*
Yes	12	3	15	
Cerebral monitoring				
No	49	6	55	0.504
Yes	32	6	38	
EEG				
No	1	1	2	0.295
Yes	31	5	36	
Change during MCA occlusion				
No	28	5	33	0.999
Yes	3	0	3	
Evoked potentials				
No	18	3	21	0.999
Yes	14	3	17	
Change during MCA occlusion				
No	13	3	16	0.999
Yes	1	0	1	
Type of anastomosis				
Interrupted				
No	21	1	22	0.282
Yes	60	11	71	
Running				
No	67	12	79	0.202
Yes	14	0	14	
Interrupted and running				
Yes	70	11	81	0.999
No	11	1	12	
Suture type				
Nylon	54	8	62	0.999
Prolene	27	4	31	
Suture size				
9-0	21	3	24	0.999
10-0	60	9	69	
Intraoperative bypass graft patency assessment				
Doppler	58	8	66	0.566
Angiography	19	4	23	
Other	1	0	1	
Anastomosis Patent in OR				
No	0	1	1	0.133
Yes	76	13	89	

	Stroke No	Stroke Yes	Total No. of Subjects	*P* value*
No data	3		3	

* ***P* values** - Fisher's exact test

Table 4B

Comparison of Intra-operative Data Between Those Who Did and Did Not Experience A Stroke Within Two Days After Surgery (Continued)

	Stroke	Number	Mean	SD	Minimum	Maximum	*P* value*
Average systolic BP during surgery *(mm Hg)*	No	81	132.8	17.8	98	199	0.264
	Yes	12	138.9	15.3	118	160	
Average diastolic BP during surgery *(mm Hg)*	No	81	66.3	9.7	40	90	0.864
	Yes	12	65.8	9.2	52	80	
Lowest systolic BP during surgery *(mm Hg)*	No	81	102.1	18.3	68	177	0.064
	Yes	12	112.6	15.8	95	145	
Lowest diastolic BP during surgery *(mm Hg)*	No	81	54.3	11.0	30	98	0.1186
	Yes	12	58.8	9.7	40	78	
Duration of lowest BP during surgery *(minutes)*	No	79	8.3	9.9	0	54	0.807
	Yes	12	7.6	5.6	1	20	
Duration of MCA occlusion *(minutes)*	No	78	45.4	24.2	15	123	0.182
	Yes	11	55.9	25.3	26	99	
Average systolic BP during MCA occlusion *(mm Hg)*	No	78	136.2	20.9	95	190	0.572
	Yes	11	140	20.7	106	175	
Average diastolic BP During MCA occlusion *(mm Hg)*	No	78	67.5	11.4	40	100	0.561
	Yes	11	69.7	15.3	55	110	
Heparin dose	No	12	2500.8	2032.7	10	7500	0.704
	Yes	3	3000	1732.1	2000	5000	
Protamine dose	Not used						
Diameter of STA *(mm)*	No	79	1.6	0.7	1	4	0.178
	Yes	12	1.9	0.5	1	3	
Diameter of MCA cortical branch *(mm)*	No	79	1.5	0.6	1	3	0.105
	Yes	12	1.8	0.5	1	3	

* ***P* values** - t-tests