The impact of carotid or intracranial atherosclerosis on perioperative stroke in patients undergoing open aortic arch surgery

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ABSTRACT

Objectives: This study aimed to clarify the impact of carotid or intracranial atherosclerosis on perioperative stroke in patients undergoing open aortic arch surgery.

Methods: Between 2008 and 2015, 200 consecutive patients underwent elective aortic arch surgery with selective antegrade cerebral perfusion and moderate hypothermic circulatory arrest. Nonselective screening for carotid or intracranial atherosclerosis was performed using carotid ultrasonography or magnetic resonance angiography. Carotid or intracranial atherosclerosis was classified as below moderate (0%-49% stenosis), moderate (50%-69%), or severe (70%-100%). In patients with moderate or severe stenosis, cerebral hemodynamics were evaluated using single-photon emission computed tomography with acetazolamide.

Results: None of the 37 patients undergoing preoperative single-photon emission computed tomography with acetazolamide had impaired cerebral hemodynamics. In-hospital mortality rate was 3.5% (7/200). Postoperative neurologic morbidity included permanent stroke in 8 patients (4.0%) and transient neurologic deficits in 27 patients (14%). Permanent stroke occurred in 3 of 159 patients (1.9%) with below moderate stenosis and 5 of 41 patients (12.2%) with moderate or severe stenosis ($P = .008$). Seven of 8 patients (87.5%) with stroke experienced multiple atherothrombotic embolizations, and 1 patient experienced a stroke of unknown cause. In multivariate analysis, previous cerebrovascular accident (odds ratio, 5.0; 95% confidence interval, 2.07-12.42; $P = .0004$) and shaggy aorta (odds ratio, 4.2; 95% confidence interval, 1.58-10.98; $P = .0045$) were significant determinants of neurologic morbidity.

Conclusions: Embolism was the major cause of permanent stroke in our patient population. Preoperative craniocervical and aortic screening may aid in modifying the operative strategy to reduce the occurrence of stroke. (J Thorac Cardiovasc Surg 2017;153:1045-53)

Brain hemodynamics in the right hemisphere of patients with craniocervical atherosclerosis.

Central Message

Our findings suggest that carotid or intracranial atherosclerosis rarely affects the incidence of hemodynamic ischemic stroke during OAAS.

Perspective

Few reports are available on the reliability of brain perfusion SPECT with acetazolamide to assess cerebral hemodynamics during OAAS. Our findings suggest that craniocervical atherosclerosis rarely affects the incidence of hemodynamic ischemic stroke during surgery and that the cause of perioperative stroke is predominantly embolic.

See Editorial Commentary page 1054.

Stroke remains a devastating complication after cardiac surgery, with an incidence as high as 1% to 5%.¹ Moreover, perioperative stroke is approximately 4 times more common in open aortic arch surgery (OAAS) than in coronary

artery bypass grafting or valve surgery.² Perioperative stroke in cardiovascular surgery is attributed to multiple causes, including embolism due to aortic manipulation or the sandblasting effect of flow through the aortic cannula against the aortic root, systemic inflammatory response to cardiopulmonary bypass (CPB), and hypoperfusion arising from significant carotid artery disease.³

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Abbreviations and Acronyms

CIAD	= carotid or intracranial artery disease
CPB	= cardiopulmonary bypass
HCA	= hypothermic circulatory arrest
MRA	= magnetic resonance angiography
OAAS	= open aortic arch surgery
PND	= permanent neurologic deficit
RCP	= retrograde cerebral perfusion
SACP	= selective antegrade cerebral perfusion
SPECT	= single-photon emission computed tomography
TND	= transient neurologic deficit

Internal carotid artery stenosis of 50% or greater and 70% or greater occurs in 17% and 3.6% of patients undergoing aortic aneurysm reconstruction, respectively.⁴ However, the incidence of carotid disease in patients with thoracic aortic aneurysm remains unclear. Moreover, whether the presence of carotid or cerebral artery atherosclerosis affects the risk of perioperative stroke in patients undergoing OAAS remains poorly understood.

Cerebral blood flow is maintained over a wide range of cerebral pressures via cerebral autoregulation.⁵ However, impaired hemodynamic cerebral autoregulation in patients with atherosclerotic internal carotid artery or major intracranial artery occlusive disease is a risk factor for ischemic stroke.⁶ Cerebral hemodynamics are evaluated in physiologic states (ie, pulsatile flow, normothermia, and nonhemodilution) using brain perfusion single-photon emission computed tomography (SPECT) with acetazolamide or positron emission tomography. Nevertheless, little is known regarding the accuracy of cerebral hemodynamic analysis with these devices under nonphysiologic conditions that occur during OAAS (nonpulsatile flow, moderate hypothermia, selective cerebral perfusion, hypotension, and hemodilution). Previously, we revealed that in brain perfusion, SPECT with acetazolamide in obstructive carotid or intracranial artery disease (CIAD) had a negligible impact on the occurrence of hemodynamic ischemic stroke during elective cardiovascular surgery without selective cerebral perfusion.⁷ In the present study, we aimed to clarify whether obstructive CIAD is associated with the occurrence of perioperative stroke in OAAS.

MATERIALS AND METHODS**Study Population**

This study was approved by the National Hospital Organization Kyushu Medical Center Institutional Review Board, and the need for individual consent was waived. Between October 2008 and October 2015, 332 consecutive patients underwent thoracic aortic surgery at our institute. From this cohort, we reviewed 200 patients undergoing elective OAAS with selective cerebral perfusion.

Preoperative Screening of Carotid and Intracranial Cerebral Arteries

Details regarding the preoperative screening of the carotid and intracranial cerebral arteries have been published.⁷ Briefly, carotid ultrasonography or magnetic resonance angiography (MRA) was performed in all 200 patients scheduled to undergo elective OAAS. During carotid ultrasonography screening, the degree of stenosis was calculated on the basis of methods outlined in the European Carotid Surgery Trial.⁸ Meanwhile, the degree of stenosis determined with MRA was calculated using the North American Symptomatic Carotid Endarterectomy Trial criteria.⁹ The calculated percent of stenosis was classified as mild (30%-49%), moderate (50%-69%), severe (70%-99%), or occlusion.¹⁰

Cerebral hemodynamics were evaluated using brain perfusion SPECT with acetazolamide in patients with moderate stenosis, severe stenosis, or occlusion of the major arteries. The E.CAM SPECT apparatus (2-head SPECT system; Siemens, Erlangen, Germany) was used with ^{99m}Tc-ethyl cysteinate dimer as a tracer. By using brain perfusion SPECT with acetazolamide, resting regional cerebral blood flow and regional cerebrovascular reactivity were measured to evaluate cerebrovascular reserve capacity. Regional cerebrovascular reactivity was expressed according to the following equation: [(regional cerebral blood flow after acetazolamide challenge test – resting regional cerebral blood flow)/resting regional cerebral blood flow] × 100 (%). The lower limits of regional cerebral blood flow and regional cerebrovascular reactivity using brain perfusion SPECT were defined as 34 mL/100 g/min and 10%, respectively.⁷ Impaired cerebral perfusion reserve was defined as resting regional cerebral blood flow 34 mL/100 g/min or less with cerebrovascular reactivity of 10% or less. In patients with impaired cerebral perfusion reserve, prophylactic carotid or cerebrovascular intervention for CIAD was taken into consideration to prevent hemodynamic ischemic stroke during OAAS.

Surgical Procedures

Patients received propofol, fentanyl, and sevoflurane for anesthesia and rocuronium for skeletal muscle relaxation. The right radial artery and unilateral femoral artery were cannulated for continuous blood pressure monitoring. In extended aortic arch replacement, patients were intubated with a double-lumen endotracheal tube and the distal anastomosis was performed under single-lung anesthesia. A transesophageal echocardiographic probe was used for confirmation of the diagnosis and assessment of cardiac function. The INVOS Cerebral Oximeter (Somanetics Corp, Troy, Mich) was attached on the forehead bilaterally to estimate intraoperative cerebral ischemia and cerebral oxygen desaturation during surgery. To avoid and reduce macroembolization, epiaortic ultrasonography of the ascending aorta was performed for all patients.

Arterial perfusion sites were bilateral axillary arteries and unilateral femoral artery in 161 patients (80%), bilateral axillary arteries in 5 patients (3%), unilateral axillary artery (right/left: 18/1) and unilateral femoral artery in 19 patients (9%), right axillary artery in 13 patients (7%), right axillary artery and ascending aortic artery in 1 patient (0.5%), and ascending aortic artery in 1 patient (0.5%). By using the axillary artery or femoral artery for arterial inflow, an 8-mm Hemashield Gold vascular graft (Maedox Medicals, Inc, Oakland, NJ) was interposed to perform systemic perfusion from CPB. In most instances, axillary inflow in addition to a graft was used to reduce perioperative stroke.¹¹ Moreover, we preferred to use multiple arterial inflow sites to reduce the likelihood of perioperative stroke from embolic material by decreasing turbulent flow during CPB.^{12,13}

After CPB was established with bicaval drainage, left ventricular venting and systemic cooling were initiated. The order of anastomosis of the ascending aorta or descending aorta was based on the surgeon's choice (proximal anastomosis first, n = 164; distal anastomosis first, n = 36). Adjunctive brain protection was performed via selective antegrade cerebral perfusion (SACP). As for a single-stage extended aortic arch repair, the L-incision approach¹⁴ or combined median sternotomy and left posterior thoracotomy was applied for total arch replacement.

Proximal anastomosis first. After the heart was arrested with antegrade or retrograde cardioplegia, correction of the ascending aorta with or without the aortic root was undertaken, including any other required correction. After gradual cooling and when rectal temperature was approximately 25°C to 28°C, circulatory arrest of the lower body and SACP were performed. Open distal anastomosis was performed during moderate hypothermic circulatory arrest (HCA) and SACP. During total arch replacement, an open distal anastomosis was completed using the elephant trunk technique. In most instances, cerebral perfusion was achieved by cannulation of the left common carotid artery and inflow via synthetic grafts of the bilateral axillary arteries. In patients without axillary artery inflow, cerebral perfusion was achieved by selective cannulation of the brachiocephalic artery, left common carotid artery, and left subclavian artery. The SACP was maintained at a perfusion rate of 10 mL/kg/min and controlled at 40 to 70 mm Hg by regulating the arterial perfusion flow for brain protection. After systemic reperfusion, reconstruction of arch vessels in patients undergoing partial or total arch replacement was performed during rewarming. Isolated anastomoses of arch vessels with respective graft branches were performed at the National Hospital Organization Kyushu Medical Center. After the repair was completed, the patient was warmed to 36°C (rectal temperature) and weaned from CPB. Cardiac de-airing was carefully performed with transesophageal echocardiography before termination of CPB.

Distal anastomosis first. After gradual cooling and when rectal temperature was approximately 25°C to 28°C, lower body circulatory arrest and SACP were performed. The heart was arrested with retrograde cardioplegia or selective antegrade cardioplegia. In patients undergoing concomitant heart surgery, heart procedures were performed during core cooling. Open distal anastomosis with the elephant trunk technique was performed with moderate HCA and SACP. After establishment of the distal anastomosis, lower body reperfusion was initiated through the femoral artery plus graft or 1 branch of the graft that was used for distal anastomosis. Proximal anastomosis of the graft was then completed, followed by coronary and systemic reperfusion. In patients undergoing partial arch replacement or total arch replacement, the aortic arch vessels were reconstructed. CPB weaning was performed in the same manner as previously mentioned.

Definition of Clinical Parameters

CIAD was defined as moderate stenosis, severe stenosis, or occlusion of the carotid or intracranial cerebral artery. Permanent neurologic deficit (PND) was defined as the presence of deficits including stroke or spinal cord ischemia that persisted at discharge. Moreover, PND was classified into permanent stroke versus paraplegia or paraparesis. On the other hand, transient neurologic deficit (TND) was defined as the occurrence of postoperative confusion, agitation, delirium, and prolonged obtundation without any new structural abnormality observed on imaging.¹⁵ Neurologic morbidity was defined as the occurrence of permanent stroke or TND. Shaggy aorta was defined as a fragile and speculated atheroma measuring at least 4 mm by enhanced computed tomography or epiaortic echocardiography in the ascending aorta or the arch, excluding the aneurysm itself.^{16,17} Partial arch replacement was defined as anastomosis of the brachiocephalic artery with the thoracic aortic surgical procedure. Meanwhile, total arch replacement was defined as the anastomosis of supra-aortic vessels (brachiocephalic artery, left common carotid artery, and left subclavian artery) with the thoracic aortic surgical procedure.

Statistical Analysis

Data were analyzed using the statistical analysis system software JMP 12.0.1 (SAS Institute Inc, Cary, NC). Categorical variables are expressed as frequencies and percentages, and continuous variables are expressed as means $\pm$ standard deviations. Pearson's chi-square test or Fisher exact test was used to compare categorical variables. On the basis of methods

previously described by Blackstone,¹⁸ we used logistic regression analysis to determine risk factors associated with in-hospital mortality, permanent stroke, and neurologic morbidity. Categorical variables associated with at least 5 events and continuous variables were selected to investigate risk factors of respective surgical outcomes (Table 1). For in-hospital mortality and permanent stroke, univariate analysis alone was performed because of insufficient outcome events. For neurologic morbidity, 4 variables selected in ascending order of univariate *P* value were entered into the multivariate analysis. Predictive accuracy of our multivariate models was assessed using the concordance index *c*.

RESULTS

Preoperative Screening for Carotid or Intracranial Artery Disease, Patient Characteristics, and Surgical Data

Table 1 reports patient characteristics and surgical data. After preoperative screening, 41 patients (21%) were diagnosed with CIAD: 21 (51%) with moderate ipsilateral stenosis (common carotid artery [*n* = 2], internal carotid artery [*n* = 18], and middle cerebral artery [*n* = 1]); 6 (14%) with moderate bilateral stenosis (bilateral internal carotid artery [*n* = 4] and ipsilateral internal carotid artery + contralateral common carotid artery [*n* = 2]); 8 (20%) with severe ipsilateral stenosis or occlusion (internal carotid artery [*n* = 7] and vertebral artery [*n* = 1]); 2 (5%) with severe ipsilateral stenosis and moderate contralateral stenosis (bilateral internal carotid artery [*n* = 2]); and 4 (10%) with severe bilateral stenosis or occlusion (bilateral middle cerebral artery [*n* = 1], bilateral internal carotid artery [*n* = 1], ipsilateral internal carotid artery + contralateral common carotid artery [*n* = 1], and ipsilateral internal carotid artery + contralateral posterior cerebral artery [*n* = 1]). Of 41 patients with CIAD, 37 (moderate stenosis [*n* = 23] and severe stenosis or occlusion [*n* = 14]) underwent preoperative brain perfusion SPECT with acetazolamide. Brain perfusion SPECT without acetazolamide was conducted in 2 patients whose resting regional cerebral blood flow values (mL/100 g/min) were 50/48 (right/left) and 51/51, respectively. The other 2 patients did not undergo brain perfusion SPECT because of the decision of the attending physician. No patient with CIAD was diagnosed with impaired cerebral perfusion reserve on brain perfusion SPECT with or without acetazolamide challenge (Figure 1).

The causes of thoracic aortic aneurysm were atherosclerotic aneurysm (*n* = 139), chronic dissection (*n* = 49), annuloaortic ectasia (*n* = 10), and aortitis (*n* = 2). A total of 184 patients (92%) underwent ascending aorta or aortic arch replacement through a median sternotomy. Meanwhile, 16 patients (8%) underwent extended aortic arch replacement via L-incision (*n* = 15) or combined median sternotomy and left posterior lateral thoracotomy (*n* = 1). Extensions of thoracic aortic surgery included ascending aortic replacement (including hemiarch replacement) in 31 patients (16%), partial arch replacement in 16 patients (8%), and total arch replacement in 153 patients (76%).

TABLE 1. Descriptive characteristics of the cohort, surgical data, and surgical outcomes

Variables	Overall (n = 200)	In-hospital mortality (n = 7)	Permanent stroke (n = 8)	Neurologic morbidity (n = 35)
Age (SD), y*	71 (12)			
Male (%)*	132 (66)	6	7	28
Obesity (BMI >26 kg/m ²) (%)*	26 (13)	1	1	5
Diabetes mellitus (%)*	26 (13)	1	2	4
Chronic renal dysfunction (serum creatinine ≥2.0 mg/dL) (%)*	10 (5)	1	1	2
COPD (FEV1.0% < 60% or drug use of prednisolone) (%)*	40 (20)	1	3	12
Previous cerebrovascular accident (%)*	42 (21)	3	4	16
CIAD (%)*	41 (21)	2	5	13
Peripheral arterial disease (ankle brachial index ≤0.8) (%)*	39 (20)	2	2	10
Shaggy aorta (%)*	37 (19)	3	6	16
Type of aneurysm (%)				
Atherosclerotic (%)*	139 (70)	4	6	27
Chronic aortic dissection (%)	49 (25)	3	0	5
AAE + AR (%)	10 (5)	0	2	3
Aortitis (%)	2 (1)	0	0	0
Previous cardiac surgery via median sternotomy (%)*	7 (4)	0	0	1
Total arch replacement (%)*	153 (76)	7	6	29
Partial arch replacement (%)	16 (8)	0	0	1
Ascending aortic replacement (including hemiarch replacement) (%)	31 (16)	0	2	5
Concomitant procedures (%)*	68 (34)	2	5	12
Aortic root repair (%)	18 (9)	0	2	1
CABG (%)	38 (19)	2	3	10
Valve surgery (%)	19 (10)	0	0	1
Extended aortic repair through L-incision or combined median sternotomy and left posterior lateral thoracotomy (%)*	16 (8)	1	4	9
Frozen elephant trunk technique (%)*	9 (5)	1	1	3
CPB time (SD), min*	275 (56)			
Coronary ischemic time (SD), min*	88 (49)			
HCA time (SD), min*	65 (21)			
SACP time (SD), min*	136 (56)			
Lowest rectal temperature (SD), °C*	26 (1)			
Operation time (SD), min*	614 (120)			

Data represent mean ± standard deviation or number (percentage). *SD*, Standard deviation; *BMI*, body mass index; *COPD*, chronic obstructive pulmonary disease; *FEV_{1.0}%*, forced expiratory volume 1 second percent; *CIAD*, carotid or intracranial artery disease; *AAE*, annuloaortic ectasia; *AR*, aortic valve regurgitation; *CABG*, coronary artery bypass grafting; *CPB*, cardiopulmonary bypass; *HCA*, hypothermic circulatory arrest; *SACP*, selective antegrade cerebral perfusion. *Represent variables used to determine risk factors of in-hospital mortality, permanent stroke, or neurologic morbidity.

Moreover, concomitant procedures included composite graft replacement (Bentall procedure) in 18 patients (9%), coronary artery bypass grafting in 38 patients (19%), and valve surgery in 19 patients (10%). Nine patients (5%) underwent total arch replacement with frozen elephant trunk procedures.

Shaggy aorta was present in 37 patients (19%). A total of 19 patients (51%) with shaggy aorta had CIAD ($P < .0001$), and 11 patients (30%) with shaggy aorta underwent total arch replacement through an L-incision or combined median sternotomy and left posterior lateral thoracotomy ($P < .0001$).

Operative Results

Table 2 reports the operative outcomes. In-hospital mortality rate was 3.5% ($n = 7$). The causes of death included multiple organ failure in 2 patients, perioperative myocardial infarction in 2 patients, systemic atheromatous embolization

in 1 patient, mesenteric ischemia in 1 patient, and unknown cause in 1 patient. The overall incidence of PND and TND was 5.5% ($n = 11$) and 14% ($n = 27$), respectively. Moreover, the overall incidence of permanent stroke and paraplegia or paraparesis was 4.0% ($n = 8$) and 2.0% ($n = 4$), respectively. A total of 7 (88%) of 8 patients with permanent stroke had multiple atherothrombotic embolizations, and the cause was unknown in the remaining patient (Table 3). Three (37.5%) of 8 patients with permanent stroke died during the postoperative hospital stay, compared with 4 (2.1%) of 192 patients without stroke ($P = .0008$).

Determinants of In-Hospital Mortality, Permanent Stroke, and Neurologic Morbidity

Tables 4 and 5 list the risk factors of in-hospital mortality and permanent stroke determined by univariate analysis.

FIGURE 1. Resting regional cerebral blood flow and regional cerebral vascular reactivity using brain perfusion SPECT with acetazolamide in patients with CIAD: right hemisphere (A) and left hemisphere (B). Red and blue rhombi indicate patients with and without permanent stroke. Dashed vertical and horizontal lines indicate lower limits (34 mL/100 g/min and 10%) of normal regional cerebral blood flow and regional cerebral vascular reactivity, respectively. rCVR, Regional cerebral vascular reactivity; rCBF, regional cerebral blood flow.

Multivariate analysis indicated that previous cerebrovascular accident and shaggy aorta were risk factors for neurologic morbidity (Table 6).

DISCUSSION

The major findings of the present study were as follows: (1) All patients with CIAD undergoing preoperative brain perfusion SPECT with acetazolamide were diagnosed with normal cerebral perfusion reserve; (2) no patient experienced hemodynamic ischemic stroke during OAAS; and (3) previous cerebrovascular accident and shaggy aorta were crucial determinants of neurologic morbidity in multivariate analysis.

Cerebral autoregulation plays a vital role in maintaining adequate cerebral blood flow in response to changes in cerebral perfusion pressure.⁵ However, impaired cerebral perfusion reserve, as indicated by increased oxygen extraction (ie, misery perfusion), carries a high risk of hemodynamic ischemic stroke in patients with steno-occlusive carotid or intracranial arteries.⁶ Imaging studies, including brain perfusion SPECT, positron emission tomography, and magnetic resonance imaging, have been used to assess of cerebral hemodynamics.¹⁹ Among them, brain perfusion SPECT with acetazolamide is widely used because it can evaluate cerebrovascular reactivity and cerebral perfusion, and it is highly sensitive for the detection of flow abnormalities.²⁰ Previously, we reported that brain perfusion SPECT

with acetazolamide can be used to screen patients at high risk of subsequent hemodynamic ischemic stroke under nonphysiologic conditions (ie, nonpulsatile flow, mild hypothermia, hypotension, and hemodilution) that occur during CPB, as well as during physiologic conditions (ie, pulsatile flow, normothermia, and nonhemodilution).⁷ However, to the best of our knowledge, there are no reports concerning the accuracy of brain perfusion SPECT with acetazolamide in patients undergoing OAAS using nonpulsatile CPB with moderate HCA and SACP.

To date, many experimental and clinical studies have investigated brain protection and safe parameters for the optimization of cerebral autoregulation during OAAS, including optimum perfusion pressure, flow, temperature, pH, hematocrit, and cannulation site.^{21,22} Neri and colleagues²¹ showed that in 65 patients undergoing elective aortic arch surgery with deep HCA, SACP was superior to retrograde cerebral perfusion (RCP) or deep HCA without adjuncts for the preservation of postoperative cerebral autoregulation. Moreover, Spielvogel and colleagues²² suggested guidelines for SACP based on data from experimental and clinical studies. However, how obstructive CIAD negatively affects the technical refinements and safe parameters for brain protection in OAAS remains poorly understood. In the present study, we report for the first time that obstructive CIAD is rarely associated with the occurrence of hemodynamic ischemic stroke in OAAS or conventional cardiac surgery and that brain perfusion SPECT can screen patients at high risk of hemodynamic ischemic stroke during OAAS.

Carotid ultrasonography and MRA can be used to assess anatomic vascular lesions, and brain perfusion SPECT with acetazolamide can be used to quantitatively evaluate cerebral perfusion reserve. Urbanski and colleagues²³ showed that all functional assessments using transcranial Doppler ultrasonography during unilateral cerebral perfusion in aortic arch surgery were normal, regardless of morphologic abnormalities of the circle of Willis observed by cranial computed tomographic angiography. These

TABLE 2. Operative outcomes

Variables	n overall = 200
In-hospital mortality (%)	7 (3.5)
PND (%)	11 (5.5)
Permanent stroke	8 (4.0)
Paraplegia or paraparesis	4 (2.0)
TND (%)	27 (14)
Perioperative myocardial infarction (%)	3 (1.5)
Acute renal failure requiring hemofiltration (%)	17 (8.5)
Reexploration for bleeding (%)	8 (4.0)

Data represent number (percentage). PND, Permanent neurologic deficit; TND, transient neurologic deficit.

TABLE 3. Patients with stroke: Preoperative and intraoperative characteristics and surgical results

Case	Age/sex	CIAD/stenosis	Type of aneurysm	Surgical approach	Surgery	Frozen ET technique	Cause	Site of stroke	Outcome
1	66 y/M	Right ICA/moderate	Atherosclerotic Shaggy aorta	MS through L-incision	TAR	N	E	Right cerebellum and occipital lobe, bilateral frontal lobe	Alive
2	87 y/M	N	Atherosclerotic Shaggy aorta	MS	TAR	Y	Unknown	Unknown	Dead
3	82 y/M	Left ICA/moderate	Atherosclerotic Shaggy aorta	MS through L-incision	TAR	N	E	Right frontal and parietal and occipital lobe, left parietal lobe	Dead
4	48 y/M	N	AAE, AR	MS	ARR	N	E	Right basal ganglia and cerebral cortex	Alive
5	76 y/M	Bilateral ICA/severe and moderate	Atherosclerotic Shaggy aorta	MS through L-incision	TAR	N	E	Right occipital lobe, bilateral frontal and parietal and cerebellar lobe, Pons, bilateral thalamus, T6-9	Alive
6	71 y/M	Left MCA/severe	Atherosclerotic Shaggy aorta	MS	TAR	N	E	Left frontal and parietal lobe, bilateral cerebellar lobe	Dead
7	69 y/M	N	AAE, AR	MS	ARR	N	E	Left frontal and parietal lobe, right temporal lobe	Alive
8	71 y/F	Bilateral ICA/severe and moderate	Atherosclerotic Shaggy aorta	MS through L-incision	TAR	N	E	Bilateral temporal and occipital and cerebellar lobe, left frontal lobe	Alive

Case 2: The patient was comatose after surgery. Continuous hemodialysis was initiated because of deterioration of renal function on day 2. After 6 hours of continuous hemodialysis, blood pressure rapidly decreased and the patient developed grand mal seizures. There were no findings of cardiac tamponade or circulatory collapse due to postoperative hemorrhage. Unfortunately, he died of unknown cause despite high-quality cardiopulmonary resuscitation. *CIAD*, Carotid or intracranial artery disease; *ET*, elephant trunk; *Y*, yes; *M*, male; *ICA*, internal carotid artery; *MS*, median sternotomy; *TAR*, total arch replacement; *N*, none; *E*, embolic; *AAE*, annuloaortic ectasia; *AR*, aortic valve regurgitation; *ARR*, aortic root repair; *T6-9*, 6th to 9th thoracic vertebrae; *MCA*, middle cerebral artery; *F*, female.

findings are highly compatible with results of the present study. Anatomic evaluation, such as carotid ultrasonography or MRA, can never evaluate cerebral perfusion reserve. Understandably, given the impaired cerebral perfusion reserve (ie, misery perfusion) in patients with obstructive CIAD, prophylactic carotid or cerebral intervention should be performed before OAAS.

The mechanisms underlying the development of ischemic stroke after cardiovascular surgery are multifactorial. Okada and colleagues²⁴ showed that 11 (5.8%) of 188 patients undergoing partial or total arch replacement with deep HCA and SACP developed intraoperative stroke. The primary cause of stroke was embolic in 8 patients (4.3%) (multiple: 5; solitary: 3) and ischemic in 4 patients (2.1%).²⁴ These

findings are comparable to the postsurgical outcomes reported in the current article. In the present study, patients with CIAD had significantly more advanced aortic atherosclerosis than those without. Moreover, shaggy aorta was identified as a significant determinant of neurologic morbidity in both univariate and multivariate analyses, and all permanent strokes were due to multiple atherothrombotic emboli. Therefore, these findings suggest that CIAD is a surrogate marker of advanced atherosclerosis. Ulcerated plaques in the carotid artery or severe aortic atherothrombosis are potential embolic sources for ischemic stroke. Particularly, when SACP is used for brain protection, an ulcerated carotid plaque can lead to embolic events. Therefore, the preoperative anatomic evaluation of atherosclerotic vessels using ultrasonography or MRA also is highly useful for the prevention of ischemic stroke in OAAS.

TNDs are subtle and diffuse global injuries undetectable by conventional imaging methods. The occurrence of TND in the present study appears high compared with other reported results, which range from 1.5% to 9.3%.²⁵⁻²⁷ Our incidence of TND might be overestimated because the judgment is based on medical records alone. It should be noted that significant variation exists in the definition and assessment of TND, which may confound these findings. TND is believed to be related to the adequacy and type of cerebral protection during the period of

TABLE 4. Risk factors for in-hospital mortality in univariate analysis

Variables	Univariate	
	OR (95% CI)	P value
Age	0.9 (0.79-0.99)	.03
Male	3.2 (0.5-60.89)	.23
CPB time (min)	0.98 (0.97-0.99)	.02
Coronary ischemic time (min)	0.99 (0.98-1.01)	.56
HCA time (min)	0.97 (0.94-0.99)	.04
SACP time (min)	0.98 (0.97-0.99)	.03
Lowest rectal temperature (°C)	1.2 (0.73-2.18)	.45
Operation time (min)	0.996 (0.99-1.00)	.22

OR, Odds ratio; CI, confidence interval; CPB, cardiopulmonary bypass; HCA, hypothermic circulatory arrest; SACP, selective antegrade cerebral perfusion.

TABLE 5. Risk factors for permanent stroke in univariate analysis

Variables	Univariate	
	OR (95% CI)	P value
Age	1.0 (0.93-1.05)	.89
Male	3.8 (0.65-70.89)	.16
CIAD	7.2 (1.70-36.52)	.008
Shaggy aorta	15.6 (3.41-109.72)	.0003
Type of aneurysm (atherosclerotic)	1.3 (0.30-9.26)	.73
Total arch replacement	0.9 (0.20-6.41)	.92
Concomitant heart procedures	3.4 (0.81-17.06)	.09
CPB time (min)	0.98 (0.97-0.99)	.006
Coronary ischemic time (min)	0.99 (0.98-1.01)	.29
HCA time (min)	1.0 (0.97-1.04)	.83
SACP time (min)	0.99 (0.98-1.01)	.45
Lowest rectal temperature (°C)	1.3 (0.81-2.33)	.27
Operation time (min)	0.99 (0.99-1.00)	.15

OR, Odds ratio; CI, confidence interval; CIAD, carotid or intracranial artery disease; CPB, cardiopulmonary bypass; HCA, hypothermic circulatory arrest; SACP, selective antegrade cerebral perfusion.

circulatory arrest.^{11,15,28} Hagl and colleagues²⁸ reported a higher rate of TND with RCP than with SACP in a group of 91 patients who required a cerebral protection time between 40 and 80 minutes. Furthermore, RCP resulted in no reduction of TNDs compared with deep HCA alone. However, total cerebral protection time in OAAS exceeding 80 minutes, even with SACP, increased the occurrence of TNDs.²⁸ In the seminal study by Svensson and colleagues,²⁹ the importance of evaluating postoperative neurologic function using both brain imaging and neurocognitive testing was reported in a randomized trial

comparing SACP and RCP during HCA. Neurocognitive decline without changes in brain imaging or clinical neurologic events may be due to microembolization from the diseased aorta or CIAD. Preoperative craniocervical and aortic screening combined with careful antiembolic procedures during surgery are important for reducing the occurrence of stroke.

As for arterial cannulation, the axillary artery not only provides antegrade arterial perfusion during CPB but also allows for continuous antegrade cerebral perfusion during HCA, minimizing global cerebral ischemia. Bilateral axillary artery perfusion especially has positive effects on the maintenance of uniform circulation in both hemispheres in cases of incomplete circle of Willis, avoidance of spinal cord ischemia, and prevention of arterial complications associated with insufficient unilateral perfusion in patients with small physiques.^{30,31} Because of decreases in the velocity of each inflow site and thus a reduced risk of detachment of atherosclerotic debris,^{12,13} bilateral axillary artery plus unilateral femoral artery perfusion through side grafts is our standard perfusion approach in OAAS. During OAAS in patients with shaggy aorta, the flow rate from the femoral artery is adjusted by a clamp forceps to avoid retrograde atheromatous embolization from the descending thoracic aorta. We believe that the anastomosis of prosthetic grafts in sites far from the diseased aorta or arch vessels and meticulous de-airing are crucially important to avoid neurologic morbidity (Video 1).

Japanese guidelines have imposed strict criteria on using brain perfusion SPECT with acetazolamide because of

TABLE 6. Risk factors for neurologic morbidity in univariate and multivariate analyses

Variables	Univariate		Multivariate: c-index 0.80	
	OR (95% CI)	P value	OR (95% CI)	P value
Age	0.96 (0.93-0.99)	.044		
Male	2.3 (1.01-6.12)	.046		
Obesity	1.1 (0.36-3.07)	.81		
COPD	2.6 (1.11-5.67)	.03		
Previous cerebrovascular accident	4.5 (2.04-9.93)	.0002	5.0 (2.07-12.42)	.0004
CIAD	2.9 (1.28-6.38)	.01		
Peripheral arterial disease	1.9 (0.79-4.25)	.15		
Shaggy aorta	5.8 (2.57-13.06)	<.0001	4.2 (1.58-10.98)	.0045
Type of aneurysm (atherosclerotic)	1.6 (0.71-3.98)	.27		
Total arch replacement	1.6 (0.66-4.50)	.32		
Concomitant heart procedures	1.0 (0.46-2.16)	.97		
Extended aortic repair through L-incision or combined median sternotomy and left posterior lateral thoracotomy	7.8 (2.69-23.67)	.0002	3.1 (0.76-12.20)	.11
CPB time (min)	0.99 (0.98-0.99)	.003	0.99 (0.99-1.00)	.17
Coronary ischemic time (min)	0.99 (0.99-1.00)	.81		
HCA time (min)	0.98 (0.97-1.00)	.06		
SACP time (min)	0.99 (0.98-0.99)	.004		
Lowest rectal temperature (°C)	1.01 (0.79-1.31)	.91		
Operation time (min)	0.99 (0.99-0.99)	.02		

OR, Odds ratio; CI, confidence interval; COPD, chronic obstructive pulmonary disease; CIAD, carotid or intracranial artery disease; CPB, cardiopulmonary bypass; HCA, hypothermic circulatory arrest; SACP, selective antegrade cerebral perfusion.

VIDEO 1. This video shows our standard procedure in a case of total arch replacement using multiple arterial perfusion approach. Video available at: [http://www.jtcvsonline.org/article/S0022-5223\(17\)30016-8/addons](http://www.jtcvsonline.org/article/S0022-5223(17)30016-8/addons).

severe complications. In light of the aforementioned data and our previous findings,⁷ patients with severe CIAD currently undergo brain perfusion SPECT with acetazolamide at the National Hospital Organization Kyushu Medical Center, on the basis of the judgment of the neurologists.

Study Limitations

First, it was a retrospective study from a single center. Moreover, the study is statistically limited because of the small number of patients enrolled. Second, we did not clarify what values below the lower limit in brain perfusion SPECT with acetazolamide are predictive of perioperative hemodynamic ischemic stroke during OAAS. Further studies are needed to document the reliability of preoperative intensive screening as a tool to predict perioperative hemodynamic ischemic stroke during OAAS.

CONCLUSIONS

Preoperative intensive screening of CIAD is a useful step to identify patients at higher risk of hemodynamic ischemic stroke. Advanced systemic atherosclerosis may be a crucial determinant of perioperative stroke due to atherothrombotic embolization. Antiembolic measures during surgery are essential to prevent perioperative stroke.

Conflict of Interest Statement

Authors have nothing to disclose with regard to commercial support.

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- Key Words:** open aortic arch surgery, carotid or intracranial atherosclerosis, perioperative stroke, craniocervical screening, SPECT with acetazolamide

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