Recent advancements of total aortic arch replacement

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Objective: Recent advancements in total aortic arch replacement achieved by our approach were presented.

Methods: From January 2002 to December 2010, 321 consecutive patients (mean age 69.8 ± 13.3 years) underwent total arch replacement through a median sternotomy at our institute. Aortic dissection was present in 94 (28.3%) patients and shaggy aorta in 36 (11.2%), with emergency/urgent surgery required in 106 (33.0%). Our current approach included the following: (1) meticulous selection of arterial cannulation site and type of arterial cannula; (2) antegrade selective cerebral perfusion; (3) maintenance of minimal tympanic temperature between 20°C and 23°C; (4) early rewarming just after distal anastomosis; (5) after 2004, bolus injection of 100 mg of sivelestat sodium hydrate into the pump circuit at the initiation of cardiopulmonary bypass; (6) after 2006, maintaining fluid balance below 1000 mL during cardiopulmonary bypass.

Results: Overall hospital mortality was 4.4% (14/321) and was 1.9% (4/215) in elective cases. Permanent neurologic deficit occurred in 4.4% (14/321) of patients and in 2.8% (6/215) of elective cases. Prolonged ventilation was necessary in 53 (16.5%), with a significant reduction after 2006 (22.8% vs 12.6%; $P = .02$). Multivariate analysis demonstrated that risk factors for hospital mortality were octogenarian (odds ratio, 4.32; $P = .03$), brain malperfusion (odds ratio, 21.2; $P = .001$) and cardiopulmonary bypass time (odds ratio, 1.01; $P = .04$). Survival at 3 and 5 years after surgery was $82.4\% \pm 2.5\%$ and $78.5\% \pm 3.1\%$, respectively.

Conclusions: Our current approach for total aortic arch replacement was associated with low hospital mortality and morbidities and with favorable long-term outcome. (J Thorac Cardiovasc Surg 2012;144:139-45)

Surgical techniques, perioperative care, and sealing grafts in the field of aortic arch surgery have improved dramatically over the past decade. Consequently, recent literature has described improved outcomes in hospital mortality, with rates of 5% or lower cited,¹⁻³ whereas in the past figures in the range of 10% were reported. It becomes imperative to devise not only surgical techniques, but also preoperative accurate imaging for aortic disease, and to monitor brain perfusion, fluid balance during cardiopulmonary bypass (CPB), and pharmacologic interventions for pulmonary protection, which may lead to further improvement in short- and long-term outcomes in the treatment of aortic arch disease.

The purpose of this retrospective study is to describe our surgical approach for total aortic arch replacement (TAR) and the satisfactory outcomes experienced at our institute.

PATIENTS AND METHODS

This study was approved by our institutional review board, and the need for individual consent was waived.

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Patient Profiles (Table 1)

From January 2002 to December 2010, 321 consecutive patients with a mean age of 69.8 ± 13.3 years who underwent TAR through a median sternotomy were retrospectively investigated. There were 66 (20.6%) octogenarians in the series. The type of aortic disease was aortic dissection in 94 (28.3%) including acute type A dissection in 61 (19.0%) and Marfan syndrome in 11 (3.4%). "Shaggy aorta" in the aortic arch was observed in 36 (11.2%). "Shaggy aorta" was defined as very extensive atheromatous disease with diffuse ulcers associated with soft, loosely held debris and a paucity of actual thrombus; the term was advocated by Hollier and associates.⁴ Accordingly, when fragile and spiculated atheroma more than 5 mm in thickness was confirmed by both computed tomography and visual inspection in the aortic arch except the aneurysm itself, the arch pathologic condition was defined as shaggy aorta in the current study. Surgery was performed on an emergency/urgent basis in 106 (33.0%) patients. Other conditions included a history of cerebral infarction in 32 (10.0%) patients, 72 (22.4%) with coronary artery disease, 23 (7.2%) with chronic obstructive pulmonary disease, and 25 (7.8%) with chronic kidney disease (creatinine ≥ 2.0 mg/dL).

Current Surgical Approach

Our current approach since 2002 has been (1) meticulous selection of arterial cannulation site and type of arterial cannula; (2) antegrade selective cerebral perfusion (SCP) for cerebral protection; (3) whole body hypothermia with minimal tympanic temperatures between 20°C and 23°C, and minimal rectal temperatures below 30°C; (4) early rewarming after distal anastomosis with antegrade SCP flow adjustment while monitoring brain oxygenation by near-infrared spectroscopy (NIRS); (5) after 2004, bolus injection of 100 mg of sivelestat sodium hydrate (ONO-5046) into the pump circuit at the initiation of CPB⁵; and (6) after 2006, maintaining strict fluid balance below 1000 mL by the extracorporeal ultrafiltration method during CPB, with the expectation of more rapid pulmonary functional recovery. This overall approach has been applied for all cases since 2006.

Patients were placed in the supine position and the diodes of NIRS were attached on the foreheads bilaterally. For NIRS we used INVOS 5100C (Somanetics, Troy, Mich), which provides continuous regional cerebral

Abbreviations and Acronyms

CA	=	circulatory arrest
CPB	=	cardiopulmonary bypass
NIRS	=	near-infrared spectroscopy
OR	=	odds ratio
PND	=	permanent neurologic deficit
rSO ₂	=	regional cerebral oxygen saturation
SCP	=	selective cerebral perfusion
TAR	=	total aortic arch replacement
TND	=	transient neurologic deficit

oxygen saturation (rSO₂). The rSO₂ readings are expressed as an index, measuring differences from an unknown baseline.

Figure 1, A to H, shows a diagrammatic representation of the TAR procedure. CPB was established with bicaval drainage and the ascending aortic perfusion in the majority of cases (n = 244, 76.0%, Table 1, Figure 1, B). The left side of the ventricle was vented through the right upper pulmonary vein. Femoral artery cannulation was applied (n = 54, 16.8%, Table 1), particularly in patients with aortic dissection. The selection of aortic cannulas depended on the aortic disease, with the site being determined by the findings of a preoperative computed tomographic and intraoperative epiaortic echographic scan. If the ascending aorta/aortic arch was highly diseased, a 24F Dispersion arterial cannula (Duraflo II; Edwards Lifesciences LLC, Irvine, Calif) was inserted near the aortic root with perfusion toward the aortic valve (n = 46, 14.3%). All patients received 100 mg of betamethasone sodium phosphate, and, after 2004, 100 mg of sivelestat sodium hydrate was added to the pump circuit at the initiation of CPB. After the tympanic temperature had dropped to 20°C to 23°C with rectal temperature below 30°C, the aortic arch aneurysm was opened (Figure 1, C) and antegrade SCP initiated. A 14F or 16F balloon-tipped cannula was inserted from inside the aorta into the brachiocephalic artery, and 12F cannulas were positioned in the left common carotid and left subclavian arteries. Avoiding cerebral embolism was particularly important in SCP cannulation. If the ostia of the arch vessels were severely atherosclerotic, arteriotomy of the arch vessels was extended from the diseased ostium to a relatively clear distal part and then cannulas were placed in position under direct vision. Antegrade SCP flow was maintained at 10 to 12 mL · kg⁻¹ · min⁻¹ using an independent roller pump, and balloon tip pressure was maintained between 30 and 40 mm Hg. The distal aortic arch or the descending aorta was transected from inside the aorta to avoid injury to the recurrent nerve during circulatory arrest (CA) of the lower part of the body (Figure 1, D). A sealed quadrifurcated Dacron graft or Triplex vascular graft (Terumo Corporation, Tokyo, Japan) was used. The open distal aortic anastomosis was performed using a 4-0 polypropylene suture with external Teflon felt reinforcement (Figure 1, E). An elephant trunk installation technique into the descending aorta was used for patients with acute type A dissection. After completion of the distal anastomosis, the lower body circulation was reinstituted through a branch graft and the tympanic/rectal temperature was rewarmed to 33°C (Figure 1, F) and maintained at this level during the following procedures. Coincident with rewarming, antegrade SCP flow was gradually increased while maintaining the baseline values of rSO₂. However, antegrade SCP flow was limited below 1200 mL/min to prevent brain edema. The proximal anastomosis was then accomplished, followed by coronary reperfusion (Figure 1, G). Aortic arch vessels were reconstructed with a 5-0 polypropylene suture. If patients also had carotid artery or intracranial artery stenosis/occlusion, reconstruction was performed before rewarming. After 2006, fluid balance during CPB was strictly controlled and kept below 1000 mL by the extracorporeal ultrafiltration method (CAPIOX hemoconcentrator HC11, Terumo

Cardiovascular Systems, Division of Terumo Corporation, Tokyo, Japan). Other concurrent procedures are shown in Table 1.

Definition of Neurologic Deficits

“Permanent neurologic dysfunction” was defined as the presence of deficits that persisted at discharge and were caused by the intraoperative procedure. “Transient dysfunction” was defined as transient loss of orientation, slurred language, agitation, or poor response to commands. Neurologic dysfunction caused by preoperative brain malperfusion associated with acute type A dissection, deep shock status, and postoperative atrial fibrillation was excluded from this category.

Statistical Analysis

Data were processed using Stat View J-5.0 software (SAS Institute, Inc, Cary, NC). Continuous values are expressed as the mean ± standard deviation. Data were analyzed by the χ^2 test for categorical variables. Stepwise logistic regression analysis was performed to identify the risk factors for hospital mortality, permanent neurologic deficit (PND), and transient neurologic deficit (TND). Clinically relevant variables with $P < .05$ on univariate analysis were incorporated into the multivariate models. Survival and freedom from aorta-related death were assessed by the Kaplan-Meier method. Differences were considered statistically significant at $P < .05$.

RESULTS

Average CPB time, myocardial ischemic time, lower body CA time, SCP time, and minimum tympanic and rectal temperatures were 190.3 ± 70.4 minutes, 91.3 ± 51.4 minutes, 42.4 ± 27.8 minutes, 97.3 ± 31.4 minutes, 21.4°C ± 1.7°C, and 25.7°C ± 2.3°C, respectively. Fluid balance during CPB was 938.2 ± 1541.7 mL, but after 2006 the balance was strictly controlled below 1000 mL and values decreased significantly from 1311.0 ± 1463.8 mL before 2006 to 712.5 ± 1551.6 mL ($P = .001$) afterward.

Overall hospital mortality was 4.4% (14/320) and in elective cases, 1.9% (4/215). Figure 2 provides annual figures for number of cases and hospital mortality. The cause of death in all cases was as follows: central nervous system in 5 patients (4 with preoperative brain malperfusion and 1 with preoperative deep shock), sepsis in 3, gastrointestinal tract necrosis in 3, pulmonary related in 2, and hemorrhage in 1. The cause of death in elective cases was gastrointestinal tract necrosis in 2, sepsis in 1, and pulmonary related in 1. Table 2 shows the univariate and multivariate analysis for in-hospital mortality. Multivariate analysis demonstrated that risk factors for hospital mortality were octogenarian (odds ratio [OR], 4.32; $P = .03$), brain malperfusion (OR, 21.2; $P = .001$), and CPB time (OR, 1.01; $P = .04$).

A PND occurred in 14 (4.4%) patients after surgery and in 6 (2.8%) patients operated on electively. An additional 5 patients had a neurologic deficit preoperatively, caused by brain malperfusion in 4 and by deep shock status in 1, resulting from left main trunk malperfusion associated with acute type A aortic dissection. Two patients had stroke secondary to postoperative atrial fibrillation. Table 3 shows the univariate analysis for PND. Univariate analysis failed to identify a risk factor for PND. A TND occurred in 21 (6.5%) patients after surgery and in 19 (8.8%) patients operated on

TABLE 1. Patient profiles

Variables	No.	%
No. of patients	321	
Age (y), mean $\pm$ SD	69.8 $\pm$ 13.3	
Octogenarian	66	20.6
Male gender	234	72.9
Aortic disease		
Dissection	94	28.3
Acute type A dissection	61	19.0
Brain malperfusion	8	2.5
Nondissection	227	70.7
Shaggy aorta	36	11.2
Marfan syndrome	11	3.4
Emergency/urgent	106	33.0
Rupture	26	8.1
Shock	9	2.8
Diabetes mellitus	37	11.5
Old cerebral infarction	32	10.0
Coronary artery disease	72	22.4
Left ventricular EF ($\leq 40\%$)	11	3.4
Chronic obstructive pulmonary disease	23	7.2
Chronic kidney disease (Cr ≥ 2.0)	25	7.8
EuroSCORE	8.2 $\pm$ 2.6	
Concurrent procedure	122	38.0
Coronary artery bypass grafting	72	22.4
Aortic root replacement (valve-sparing)	12	3.7
Aortic root replacement (Bentall)	4	1.2
Aortic valve replacement	5	1.6
Mitral valve repair	3	0.9
Maze procedure	8	2.5
Abdominal aortic replacement	4	1.2
Cannulation sites/type for CPB		
Ascending aorta/arch	244	76.0
Femoral artery	54	16.8
Axillary artery	3	0.9
Femoral artery + axillary artery	8	2.5
Ascending aorta + femoral artery	10	3.1
24F Dispersion cannula	138	43.0

SD, Standard deviation; EF, ejection fraction; Cr, creatinine; CPB, cardiopulmonary bypass.

electively. Table 4 shows the univariate and multivariate analysis for TND. Multivariate analysis demonstrated that risk factors for TND were the aortic pathologic condition of shaggy aorta (OR, 3.73; $P = .018$) and low left ventricular ejection fraction ($\leq 40\%$) (OR, 4.90; $P = .05$).

Additional postoperative complications are shown in Table 5. Mean mechanical ventilation time was 26.5 $\pm$ 46.4 hours. As for respiratory complications, 53 (16.5%) patients required prolonged mechanical ventilation (≥ 48 hours). The incidence was 22.8% before and 12.6% after 2006 with a significant difference ($P = .02$).

Follow-up was completed in 94.1% of patients, and the mean follow-up period was 2.3 $\pm$ 2.2 years. Figure 3 shows overall long-term survival assessed by the Kaplan-Meier method. Survival at 3 and 5 years after surgery was 82.4% $\pm$ 2.5% and 78.5% $\pm$ 3.1%, respectively.

Figure 4 shows freedom from aorta-related death assessed by the Kaplan-Meier method. There were 4 patients who died of aorta-related events during follow-up. Causes of death were rupture of the penetrating atherosclerotic ulcer in the descending aorta 1 year after TAR, rupture of thoracoabdominal aortic aneurysm 3 years after TAR, sudden death with hemoptysis, which presumably was caused by aortopulmonary fistula, and sudden death of unknown reason 4 months after TAR. The freedom from aorta-related death at 3 and 5 years after surgery was 97.9% $\pm$ 1.1% and 97.9% $\pm$ 1.1%, respectively.

DISCUSSION

The major findings of this study were that a standardized approach for TAR since 2002 at our institute has resulted in a low hospital mortality and morbidity with a favorable long-term survival and freedom from aorta-related death. Details are spelled out in the "Current Surgical Approach" section.

The selection of an arterial cannulation site and type of cannula are important in preventing atheroembolic events, particularly neurologic complications. The efficacy of various kinds of arterial cannulation sites has been reported. Strauch,⁶ Ogino,² and their associates reported that SCP with right axillary artery perfusion had a protective effect against stroke. When severe atherosclerotic changes are observed in the orifice of the brachiocephalic artery or on the posterior wall of the ascending aorta,⁷ perfusion through the axillary artery should be performed with caution. In most instances, we selected the ascending aorta as an arterial cannulation site after inspection of the epiaortic echographic scan. Grooters and colleagues⁸ described the advantages of arterial perfusion toward the aortic valve. In an experimental study, Fukuda and coworkers⁹ confirmed that directing the cannula tip of the Dispersion cannula toward the aortic root generated slower and less turbulent flow in the transverse arch of the glass models of both healthy and aneurysmal aortic arches. We often experienced that the atherosclerotic change was less frequent just distal to the sinotubular junction. Accordingly, when we noted the presence of severe atheroma in the ascending aorta/aortic arch, we selected the 24F Dispersion cannula and inserted it into the ascending aorta near the aortic root with perfusion toward the aortic valve. That was a major reason that we seldom selected the right axillary artery perfusion. We could completely avoid PND in patients with shaggy aorta by this approach. We believe the approach may have contributed to the low incidence of neurologic complications that we observed (PND, 4.4%; TND, 6.6%), although univariate and multivariate analysis failed to identify the use of a Dispersion cannula as one of the risk reduction factors for PND or TND. In patients with acute type A dissection, a femoral artery cannulation was mainly applied. Inasmuch as the approach is one of the main providers of malperfusion syndrome, we have recently applied an ascending aortic

FIGURE 1. Surgical procedure. A, Aortic arch exposure. B, Aortic cannulation. C, Aortic arch is opened under circulatory arrest at 20°C to 23°C (tympanic temperature). D, Antegrade selective cerebral perfusion from inside the aortic arch with trimming of the descending aorta. E, Distal anastomosis under circulatory arrest of the lower part of the body. F, Lower body reperfusion through the branch graft and early rewarming while monitoring of near-infrared spectroscopy, followed by proximal anastomosis. G, Coronary reperfusion and arch vessel reconstruction, preceded by repair without rewarming of stenosis/occlusion lesions of carotid or intracranial arteries. H, Discontinuation of cardiopulmonary bypass and completion of total arch replacement.

cannulation¹⁰ using a Seldinger method. That was another reason for scarcity of the right axillary artery perfusion.

Some risk factors for stroke in connection with aortic surgery have been identified.

Aortic disease has not been included in the preoperative risk stratification system such as EuroSCORE but is apparently one of the risk factors for adverse neurologic outcomes. Our group previously reported that severity of the aortic arch atheroma grades has been identified as another risk factor for adverse neurologic outcomes.¹¹ Shaggy aorta

has extensive friable and soft atheromatous lesions.⁴ Amarenco and colleagues¹² indicated a strong, independent association between atherosclerotic disease of the aortic arch and the risk of ischemic stroke, particularly with thick plaque (≥ 4 mm). There were 36 patients with shaggy aorta in this study. None of 36 patients had PND and 10 (27.8%) of 36 patients had TND. Multivariate analysis demonstrated that shaggy aorta was a risk factor for TND but not for PND. We believe that meticulous selection of cannulation site and type of cannula based on the preoperative and intraoperative accurate imaging for aortic disease and complete exclusion of the diseased aorta contributed to avoid PND even in cases of shaggy aorta.

Contemporary strategies for brain protection are deep hypothermic arrest with or without retrograde cerebral perfusion¹³ or SCP.¹⁴ Although deep hypothermic arrest with or without retrograde cerebral perfusion does not require an additional circuit for the brain perfusion, the safety margin is limited to 40 to 60 minutes.^{3,15} A prospective comparative study by one of the coauthors¹⁶ confirmed that SCP significantly reduced the prevalence of temporary neurologic dysfunction compared with retrograde cerebral perfusion. Since then, we have consistently selected SCP under deep hypothermia for brain protection.

The temperature of hypothermic CA during the distal anastomosis is particularly crucial for protecting vital

FIGURE 2. Number of cases and hospital mortality. Solid line depicts the number of cases of total arch replacement and bar graphs the overall hospital mortality.

TABLE 2. Risk factors for hospital mortality identified by univariate and multivariate analysis

Variables	Univariate		Multivariate	
	OR (95% CI)	P value	OR (95% CI)	P value
Octogenarian	3.09 (1.03-9.23)	.04	4.32 (1.19-15.7)	.03
Male gender	0.65 (0.21-2.02)	.46		
Dissection	1.87 (0.63-5.54)	.26		
Brain malperfusion	30.3 (6.61-138.9)	<.0001	21.2 (3.47-130.1)	.001
Shaggy aorta	1.34 (0.29-6.24)	.71		
Emergency/urgent	5.50 (1.68-18.0)	.005	2.31 (0.56-9.55)	.25
Rupture	1.97 (0.42-9.30)	.39		
Shock	2.88 (0.33-24.7)	.34		
Diabetes mellitus	0.58 (0.07-4.56)	.60		
Old cerebral infarction	2.61 (0.69-9.91)	.16		
Coronary artery disease	2.74 (0.92-8.17)	.07		
Low LVEF ($\leq 40\%$)	2.29 (0.27-19.2)	.44		
COPD	2.27 (0.48-10.8)	.30		
CKD	2.06 (0.43-9.76)	.36		
Concurrent procedure	1.23 (0.42-3.63)	.71		
CPB time	1.01 (1.00-1.01)	.006	1.01 (1.00-1.01)	.04
Tympanic temperature	0.81 (0.57-1.14)	.81		
Fluid balance during CPB	1.0 (1.0-1.0)	.95		

OR, Odds ratio; CI, confidence interval; LVEF, left ventricular ejection fraction; COPD, chronic obstructive pulmonary disease; CKD, chronic kidney disease (creatinine ≥ 2.0); CPB, cardiopulmonary bypass.

organs. Inasmuch as the primary goal of core cooling is to achieve a brain temperature compatible with the maximum suppression of metabolism, the lowest temperature that can be safely achieved is optimal for brain protection. On the other hand, deep hypothermia tends to be associated with coagulopathy, which is to be avoided. Apart from the deep hypothermic CA with or without retrograde cerebral perfusion, the optimal temperature in the setting of antegrade SCP seems to be between 20°C and 28°C.^{1,17,18} Minatoya and associates¹⁸ reported that the temperature during hypothermic CA could be safely increased to 28°C with a high SCP flow rate and that the incidence of neurologic events was not increased with significant reduction of CA and SCP time. Inasmuch as we have focused more on the issue of organ protection, we set tympanic temperature between 20°C and 23°C, resulting in optimal CA and SCP times (42.4 ± 27.8 and 97.3 ± 31.4 minutes, respectively). As for the rectal temperature, we aimed it below 30°C just before CA. One of our patients whose rectal temperature before CA was in excess of 30°C had entire colon necrosis, presumably because of calcified stenosis of the mesenteric artery with poor visceral circulation.

TABLE 3. Risk factors for PND identified by univariate analysis

Variables	Univariate	
	OR (95% CI)	P value
Octogenarian	1.06 (0.29-3.90)	.93
Male gender	1.38 (0.38-5.07)	.63
Dissection	1.87 (0.63-5.53)	.16
Emergency/urgent	2.84 (0.96-8.42)	.06
Rupture	3.37 (0.88-12.9)	.08
Shock	2.99 (0.34-26.4)	.32
Diabetes mellitus	0.58 (0.07-4.56)	.58
Old cerebral infarction	1.54 (0.33-7.21)	.58
Coronary artery disease	1.41 (0.43-4.62)	.57
CKD	2.06 (0.43-9.76)	.36
Concurrent procedure	1.23 (0.42-3.63)	.71
CPB time	1.004 (1.00-1.01)	.25
SCP time	1.01 (1.00-1.02)	.11
Tympanic temperature	1.06 (0.79-1.42)	.70
Fluid balance during CPB	1.0 (1.0-1.0)	.14
Use of 24F Dispersion cannula	0.72 (0.24-2.22)	.58

Variables of shaggy aorta, shock status, low left ventricular ejection fraction, and COPD were not tested because PND did not occur in cases with the factors. PND, Permanent neurologic deficit; OR, odds ratio; CI, confidence interval; CKD, chronic kidney disease (creatinine ≥ 2.0); CPB, cardiopulmonary bypass; SCP, selective cerebral perfusion.

Subsequently, we have always kept rectal temperatures below 30°C, without further such complications.

To minimize CPB time, we start rewarming as soon as the distal anastomosis is completed, with concurrent antegrade distal reperfusion to the lower part of the body through the prosthetic graft branch. Monitoring brain oxygenation during rewarming is particularly important because the brain becomes metabolically hyperactive with progressive oxygen desaturation as a result of the uncoupling of the linear relationship between brain blood flow and temperature. NIRS has been used to monitor rSO₂ in several clinical settings. Olsson and Thelin¹⁹ reported the efficacy on NIRS as a noninvasive cerebral saturation trend monitor in antegrade SCP. Baseline values are highly variable between patients, with mean stable rSO₂ levels ranging from 45% to 90%, making it essential to follow trends in oxygen saturation changes rather than absolute values. We increased SCP flow from 10 to 15 mL $\cdot$ min⁻¹ $\cdot$ m⁻² to maintain preoperative values of NIRS; however, the total flow was always maintained below 1200 mL/min to avoid brain edema.

The use of CPB is invariably associated with fluid overload followed by fluid extravasation from the circulation to the interstitial space, which occasionally leads to organ dysfunction, particularly in the lungs. The main causes of CPB-related edema are the occurrence of systemic inflammatory responses and hemodilution. Strategies to reduce the inflammatory response have chiefly focused on the pharmacologic approaches. Steroids are often used as anti-inflammatory agents and may lessen complement activation by causing in vitro inhibition of C3 and C5 convertase.²⁰ However, there are few reports that demonstrate clinically

TABLE 4. Risk factors for TND identified by univariate and multivariate analysis

Variables	Univariate		Multivariate	
	OR (95% CI)	P value	OR (95% CI)	P value
Octogenarian	1.22 (0.43-3.47)	.70		
Male gender	2.33 (0.67-8.12)	.18		
Dissection	0.11 (0.02-0.84)	.04	0.48 (0.05-5.00)	.54
Shaggy aorta	9.58 (3.72-24.7)	<.0001	3.73 (1.26-11.1)	.018
Emergency/urgent	0.20 (0.05-0.87)	.04	0.73 (0.13-4.09)	.72
Rupture	0.55 (0.07-4.27)	.57		
Diabetes mellitus	0.80 (0.18-3.57)	.77		
Old cerebral infarction	1.56 (0.43-5.61)	.50		
Coronary artery disease	4.31 (1.75-10.6)	.002	2.36 (0.45-12.3)	.31
Low LVEF ($\leq 40\%$)	9.85 (2.63-37.0)	.0007	4.90 (1.00-23.9)	.05
COPD	4.90 (1.61-14.9)	.05	2.04 (0.54-7.75)	.30
CKD	3.13 (0.96-10.1)	.05		
Concurrent procedure	2.83 (1.14-7.05)	.03	0.80 (0.15-4.20)	.79
CPB time	1.00 (1.00-1.01)	.27		
SCP time	0.99 (0.98-1.01)	.45		
Tympanic temperature	0.89 (0.68-1.16)	.77		
Use of 24F Dispersion cannula	6.29 (0.24-2.22)	.001	2.49 (0.71-8.76)	.16

A variable of shock status was not tested because permanent neurologic deficit did not occur in cases associated with shock. *TND*, Transient neurologic deficit; *OR*, odds ratio; *CI*, confidence interval; *LVEF*, left ventricular ejection fraction; *CPD*, chronic obstructive pulmonary disease; *CKD*, chronic kidney disease (creatinine ≥ 2.0); *CPB*, cardiopulmonary bypass; *SCP*, selective cerebral perfusion.

significant in vivo effects of these agents.²¹ Neutrophil activation and sequestration, by facilitating secretion of neutrophil elastase, may also cause pulmonary dysfunction. Sivelestat sodium hydrate is a synthetic low-molecular-weight specific neutrophil elastase inhibitor.²² We have used 100 mg of sivelestat into the pump circuit at the

TABLE 5. Additional postoperative complications

Variables	No (%)
Paraplegia	3 (0.9)
Temporary	1 (0.3)
Permanent	2 (0.6)
Paraparesis	1 (0.3)
Temporary	1 (0.3)
Mediastinitis	7 (2.4)
Mean mechanical ventilation time (h)	26.5 $\pm$ 46.4
Prolonged ventilation (≥ 48 h)	53 (16.5)
Prolonged ventilation after 2006	25 (12.6)*
Renal failure	10 (3.1)
Gastrointestinal tract	8 (2.5)
Bleeding	6 (1.9)
Necrosis	2 (0.6)

**P* = .02 versus before 2006.

FIGURE 3. Survival curve. Survival at 3 and 5 years after surgery was $82.4\% \pm 2.5\%$ and $78.5\% \pm 3.1\%$, respectively.

initiation of CPB with attenuation of postoperative pulmonary dysfunction as assessed from respiratory and oxygenation indices, and with earlier tracheal extubation.⁵ As regards hemodilution, a highly positive fluid balance during CPB is associated with adverse outcomes such as increases in the requirement for blood transfusion and in-hospital mortality.²³ Inasmuch as lungs are particularly susceptible to fluid overload, pulmonary dysfunction may occur and result in prolonged postoperative mechanical ventilatory support.²⁴ Therefore, maintaining fluid balance as close to physiologic as possible is crucial. Oliver and associates²⁵ reported that control of fluid balance by hemofiltration facilitated earlier tracheal extubation after normothermic CPB, although no mechanism was elucidated to account for this result. The literature reported that hemofiltration during CPB resulted in 27 mL/kg²⁶ of ultrafiltrate with 1.18 ± 1.99 L of fluid balance. Beginning in 2006, we

FIGURE 4. Freedom from aorta-related death. Freedom from aorta-related death 3 and 5 years after surgery was $97.9\% \pm 1.1\%$ and $97.9\% \pm 1.1\%$, respectively.

also sought to achieve a 1-L fluid balance and noted a significant decrease from 1311.0 ± 1463.8 mL before 2006 to 712.5 ± 1551.6 mL ($P = .001$) afterward, as well a reduction in the percentage of patients requiring prolonged ventilation from 22.8% to 12.6% ($P = .02$). Inasmuch as optimal fluid balance during CPB under deep hypothermia remains unknown, further investigation of this issue will be required.

Previous reports have demonstrated improved outcomes both in mortality and in the incidence of permanent stroke resulting from various kinds of multimodal approaches.^{1,2,17,27} Recent reports have indicated that results of conventional aortic arch surgery even in octogenarians is improving.²⁸ In the current study, overall hospital mortality was satisfactory but that in octogenarian was 9.1% (6/66) and the status was identified as a risk factor for hospital mortality (OR, 4.32; $P = .03$). However, our evolving procedures provided the drastic improvement in octogenarians with a significant reduction in hospital mortality over the 5 years (14.2% before 2006 vs 2.6% after 2006, $P = .03$). We can expect further advancements in the era of the aged society. Although the underlying specific reasons for the recent improvement in outcomes from use of standardized approaches remain unclear, there is evidence at our institute that strict water balance during CPB may be one of the important factors.

Finally, the long-term outcome was satisfactory, particularly in the freedom from aorta-related death, which confirmed that TAR was evolving treatment with better durability.

LIMITATIONS

This is a retrospective study from a single center. Although the favorable outcomes we observed appeared to be the result of our standardized surgical approach for TAR, further prospective studies are required to validate this process and identify those factors that contribute most strongly to this outcome.

CONCLUSIONS

Our approach for TAR has contributed to low hospital mortality and morbidities and with favorable long-term outcome.

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