Long-term outcomes of total arch replacement using a 4-branched graft

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ABSTRACT

Objective: Our study evaluated the long-term outcomes of total arch replacement using a 4-branched graft.

Methods: From October 1999 to December 2016, 655 patients underwent total arch replacement using a 4-branched graft (pathology in the 655 patients was distributed as 399 no dissection, 149 acute dissection, and 107 chronic dissection). Two hundred nine patients (31.9%) underwent nonelective surgery. Mean follow-up term was 5.0 ± 4.1 years and follow-up rate was 97.1%.

Results: Of 655 patients who underwent total arch replacement using a 4-branched graft, operative mortality occurred in 34 patients (5.2%) and permanent neurologic deficit occurred in 24 patients (3.7%). One hundred ninety late deaths occurred, with 20 aortic event-related deaths. Overall survival was $73.1\% \pm 1.9\%$ at 5 years and $54.8\% \pm 2.7\%$ at 10 years. Multivariate Cox-hazard regression analysis demonstrated that older age, lower estimated glomerular filtration rate, concurrent procedures, permanent neurologic deficit, tracheostomy, and renal failure were significant risk factors for late death. Freedom from repeat operation on the aorta was $98.0\% \pm 0.7\%$ at 5 years and $93.9\% \pm 1.8\%$ at 10 years and freedom from additional aortic operation was $87.2\% \pm 1.5\%$ at 5 years and $77.3\% \pm 2.7\%$ at 10 years. The incidence of pseudoaneurysm was 2.2%.

Conclusions: The long-term outcomes for patients undergoing total arch replacement using 4-branched graft are favorable. However, even in the late phase, periodic follow-up is necessary to address subsequent aorta-related events. (J Thorac Cardiovasc Surg 2019;157:75-85)

Surgical schema of total arch replacement using a 4-branched graft.

Central Message

Total arch replacement using 4-branched graft was a desirable procedure from the long-term perspective. Postoperative complications were significant risk factors for late survival.

Perspective

To improve long-term outcomes following total arch replacement using a 4-branched graft, we have to pay attention to not only postoperative complications but also to late aortic events. Even in the late phase, periodic follow-up is required to prepare for subsequent aortic events.

See Editorial Commentary page 86.

Surgical outcomes for patients undergoing total arch replacement has improved dramatically over the past 2 decades.¹⁻⁴ This achievement has been attributed the development of water-sealed grafts, the evolution of cardiopulmonary bypass technique and equipment, a better understanding of brain protection, and refinement of the surgical procedures.^{5,6} The development of a 4-branched

graft has brought the discussion toward total arch replacements. It has several advantages over the island aortic cuff technique when used to reconstruct arch vessels, and it has been widely used.^{7,8} Hospital mortality after elective total arch replacement was 5.7% in the Japanese Adult Cardiovascular Surgery Database between 2008 and 2013,⁹ and hospital mortality after emergent total arch replacement for acute type A aortic dissection (AADA)

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Abbreviations and Acronyms

AADA	= acute type A aortic dissection
ACP	= antegrade selective cerebral perfusion
CT	= computed tomography
MAAE	= major adverse aortic event
PND	= permanent neurologic deficit
TND	= transient neurologic deficit

was reported to be 10.4% in the Japanese Association for Thoracic Surgery 2012 registry.¹⁰

Endovascular treatment or hybrid treatment have also shown lower early mortality and are considered attractive alternatives to conventional surgery, especially for high-risk patients.¹¹⁻¹³ However, late reintervention is a well-known complication of these procedures.¹⁴ Because the number of patients with aortic arch disease has been increasing steadily in aging societies,¹⁰ surgeons are confronted with complex decisions to determine the optimal strategy for treatment by anticipating long-term outcomes for each patient on top of considering early outcomes. However, there are limited data regarding late outcomes following arch repair even in the context of conventional total arch replacement.

The aim of this study was to evaluate the long-term outcomes of patients undergoing total arch replacement using a 4-branched graft.

PATIENTS AND METHODS

Study Population

From October 1999 to December 2016, 661 patients underwent total arch replacement at our institution. Six patients in whom a 4-branched graft was not used for their arch vessels reconstruction were excluded. Six hundred fifty-five patients were eventually included in this study.

Follow-up data were obtained by clinical visit, telephone, or written correspondence and a common closing date (March 2018) was used. Follow-up data were available for all but 19 patients (2.9%) who were lost within 1 year of their operation. The mean follow-up period was 5.0 ± 4.1 years (range, 0.01-17.9 years). This study protocol was reviewed and approved by our institutional review board. An informed consent waiver was granted due to the design of the study.

Definitions of Clinical Outcomes

Operative mortality was defined as all 30-day mortality and in-hospital mortality, including any deaths occurring after transfer to another hospital or long-term acute-care facility.¹⁵ Permanent neurologic deficits (PNDs) were defined as the presence of deficits that persisted at hospital discharge. Transient neurologic deficits (TNDs) were defined as delayed awakening, transient loss of orientation, slurred language, agitation, poor response to commands, and transient hemiparesis that had recovered by hospital discharge.

Acute dissection was defined as <2 weeks after symptom onset, whereas chronic dissection was defined as >2 weeks after symptom onset. Aorta-related death was defined as death due to aneurysm rupture, aortic dissection, graft infection, and aortic surgery. Repeated aortic operation was defined as surgery on the aorta for graft infection and pseudoaneurysm.

Additional aortic operation was defined as surgery on the aorta for the repair of dilatation of the thoracic and thoracoabdominal aorta. The surgical indication for additional aortic operation was diameter > 50 mm. A major adverse aortic event (MAAE) was defined as aorta-related death; aneurysm rupture; aortic dissection; graft infection; and any subsequent surgery on the aorta, including the entire aorta from aortic root to aortic bifurcation.

The diagnosis of pseudoaneurysm was based on enhanced computed tomography (CT) and CT follow-up was repeated annually as possible. Postoperative CT assessment was performed in 625 patients (95.4%) 3.6 ± 3.7 years after surgery.

Surgical Approach

All 655 patients underwent total arch replacement through median sternotomy, and our surgical strategies evolved over time, as described in our previous series (Video 1).^{4,7} Briefly, since 2002, we have exclusively used antegrade selective cerebral perfusion (ACP) for brain protection, with minimal tympanic temperatures between 20°C and 23°C and minimal rectal temperatures below 30°C. To prevent left recurrent nerve injury, we made a direct circumferential transection from the inner side of the distal end of the aneurysm without longitudinal incision of the aortic arch. We indicated elephant trunk insertion in patients with DeBakey type I acute aortic dissection, and dilated descending or thoracoabdominal aorta because patients did not have atherothrombotic plaque in the descending aorta. After the distal anastomosis, antegrade perfusion of the lower body and rewarming was started. Subsequently, the proximal anastomosis was performed, followed by coronary reperfusion. Finally, the aortic arch was divided to make arch vessel buttons. Three arch vessels were reconstructed individually using a 4-branched graft and 5-0 polypropylene sutures. However, in 13 patients with severe carotid artery stenosis and atherothrombotic plaque, arch vessel reconstruction was prioritized to proximal anastomosis to decrease ACP time.

Statistical Analysis

All continuous variables were expressed as mean $\pm$ standard deviation or median (interquartile range [25th-75th percentile]). Categorical

VIDEO 1. The aortic arch was opened under moderate hypothermic circulatory arrest with antegrade selective cerebral perfusion for brain protection. To prevent left recurrent nerve injury, we made a direct circumferential transection from the inner side of the distal end of the aneurysm without longitudinal incision of the aortic arch. After the distal anastomosis, antegrade perfusion of the lower body and rewarming was started. Subsequently, the proximal anastomosis was performed, followed by coronary reperfusion. Finally, the aortic arch was divided to make arch vessel buttons. Three arch vessels were reconstructed, individually, using a 4-branched graft and 5-0 polypropylene sutures. Video available at: [https://www.jtcvs.org/article/S0022-5223\(18\)32823-X/fulltext](https://www.jtcvs.org/article/S0022-5223(18)32823-X/fulltext).

TABLE 1. Patient characteristics

Variable	Overall (n = 655)	No dissection (n = 399)	Acute dissection (n = 149)	Chronic dissection (n = 107)	P value
Age (y)	70.1 ± 11.9	74.3 ± 8.5	61.5 ± 13.1	66.4 ± 13.6	<.001*
Octogenarian	127 (19.3)	102 (25.6)	11 (7.4)	14 (13.1)	<.001*
Female	190 (29.0)	91 (22.8)	54 (36.2)	45 (42.1)	<.001*
Hypertension	521 (79.5)	333 (83.5)	103 (69.1)	85 (79.4)	.002*
Dyslipidemia	189 (28.9)	144 (36.1)	18 (12.1)	27 (25.2)	<.001*
Diabetes mellitus	83 (12.7)	71 (17.8)	7 (4.7)	5 (4.7)	<.001*
Smoking	399 (60.9)	294 (73.7)	59 (39.6)	46 (43.0)	<.001*
eGFR (mL/min/1.73 m ²)	57.3 ± 22.3	55.0 ± 21.2	62.0 ± 24.1	59.0 ± 22.6	.003*
Chronic lung disease	134 (20.4)	114 (28.6)	2 (1.3)	18 (16.8)	<.001*
Coronary artery disease	174 (26.6)	142 (35.6)	10 (6.7)	22 (20.6)	<.001*
Marfan syndrome	16 (2.4)	0 (0)	7 (4.7)	9 (8.4)	<.001*
Old cerebral infarction	77 (11.8)	50 (12.5)	13 (8.7)	14 (13.1)	.400
Previous thoracic aortic surgery	72 (11.0)	24 (6.0)	7 (4.7)	41 (38.3)	<.001*
Atherothrombotic aorta	46 (7.0)	40 (10.0)	1 (0.7)	5 (4.7)	<.001*
Malperfusion	46 (7.0)	0 (0)	46 (30.9)	0 (0)	<.001*
Brain malperfusion	15 (2.3)	0 (0)	15 (10.1)	0 (0)	<.001*
Shock status	36 (5.5)	12 (3.0)	21 (14.1)	3 (2.8)	<.001*
Cardiac arrest	8 (1.2)	2 (0.5)	6 (4.0)	0 (0)	.004*
Intubated	8 (1.2)	4 (1.0)	3 (2.0)	1 (0.9)	.634
Infection	18 (2.7)	11 (2.8)	0 (0)	7 (6.5)	.002*
Rupture	40 (6.1)	34 (8.5)	2 (1.3)	4 (3.7)	.001*
Elective	446 (68.1)	353 (88.5)	3 (2.0)	90 (84.1)	<.001*
Urgent	38 (5.8)	13 (3.3)	15 (10.1)	10 (9.4)	.003*
Emergent	171 (26.1)	33 (8.3)	131 (87.9)	7 (6.5)	<.001*

Values are presented as mean ± standard deviation or n (%). eGFR, Estimated glomerular filtration rate. * $P < .05$.

variables are expressed as the number and percentage of patients. Data were analyzed by the χ^2 test for categoric variables. Assumption of normality of continuous data was tested with the Shapiro-Wilk test. If assumption of normality was met, continuous variables were compared using the Student t test, whereas the Mann-Whitney U test was used for nonparametric variables. The values of overall late survival, freedom from aorta-related death, freedom from repeated surgery on the aorta, freedom from additional surgeries on the aorta, MAAE-free survival, and freedom from stroke were computed using the Kaplan-Meier methods and was expressed as the rate ± standard error. Death was modeled as a competing risk in freedom from repeated surgery on the aorta, freedom from additional surgeries on the aorta, MAAE-free survival, and freedom from stroke analyses. The comparison of Kaplan-Meier curves was performed using log-rank test. Univariate risk factor analysis of overall survival was performed on the cumulative incidence function using Cox regression and hazard ratio (HR) with 95% confidence interval (CI). $P < .05$ in the univariate analysis was defined for selecting variables for entry into the multivariate regression analysis for overall survival. Comparison of patient survival with the general age- and sex-matched population was performed using the Japanese population life table available from the Japanese Ministry of Health, Labor, and Welfare,¹⁶ according to the methods outlined by Finkelstein and colleagues.¹⁷ All data analyses were performed with JMP software version 11.0 (SAS Institute Inc, Cary, NC).

RESULTS

Patient Characteristics

Preoperative patient characteristics are shown in Table 1. Aortic pathologies were classified into 3 groups: no dissection (n = 399 [60.9%]); acute dissection (n = 149 [22.7%]) including AADA in 143; and chronic dissection (n = 107 [16.3%]) including previous AADA repair in 37, type A dissection in 25, and type B dissection in 45). Mean age was 70.1 ± 11.9 years (no dissection: 74.3 ± 8.5 years, acute dissection: 61.5 ± 13.1 years, and chronic dissection: 66.4 ± 13.6 years) ($P < .001$), and 127 patients (19.4%) were octogenarians/nonagenarians. Regarding preoperative hemodynamic status, patients with shock status—defined as systolic blood pressure <90 mm Hg (n = 37 [5.5%]), cardiac arrest (n = 8 [1.2%]), infection (n = 18 [2.7%]), rupture (n = 40 [6.1%]), and brain malperfusion (n = 15 [2.3%])—were included. Forty-seven patients (7.2%) underwent re sternotomy. Emergent surgery was performed in 171 patients (26.1%), urgent surgery was performed in

TABLE 2. Operative data

Variable	Overall (n = 655)	No dissection (n = 399)	Acute dissection (n = 149)	Chronic dissection (n = 107)	P value
Operative time (min)	424.3 ± 152.7	399.7 ± 141.6	465.5 ± 169.8	459.1 ± 150.3	<.001*
CPB time (min)	193.0 ± 67.6	177.7 ± 56.6	231.9 ± 78.9	197.10 ± 67.3	<.001*
Myocardial ischemic time (min)	92.9 ± 47.1	77.3 ± 33.6	125.5 ± 49.9	105.7 ± 58.2	<.001*
Circulation arrest of lower body (min)	44.0 ± 16.8	40.6 ± 15.4	53.7 ± 17.9	42.9 ± 14.7	<.001*
Antegrade cerebral perfusion	606 (92.5)	370 (92.7)	142 (95.3)	94 (87.9)	.191
Cerebral perfusion time (min)	100.8 ± 39.4	92.7 ± 33.3	126.4 ± 45.1	95.4 ± 37.4	<.001*
Minimal tympanic temperature (°C)	21.0 ± 2.1	21.1 ± 2.1	20.8 ± 1.9	20.8 ± 2.3	.319
Minimal rectal temperature (°C)	25.9 ± 2.2	26.1 ± 2.2	25.6 ± 2.2	25.7 ± 1.8	.031*
Concurrent procedures	235 (35.9)	157 (39.4)	34 (22.8)	44 (41.1)	<.001*
Coronary artery bypass grafting	150 (22.9)	127 (31.8)	7 (4.7)	16 (15.0)	<.001*
Aortic valve replacement	21 (3.2)	15 (3.8)	0 (0)	6 (5.6)	.003*
Aortic root replacement	41 (6.3)	8 (2.0)	14 (9.4)	19 (17.8)	<.001*
Valve-sparing reimplantation	26 (4.0)	3 (0.8)	13 (8.7)	10 (9.4)	<.001*
Mitral valve surgery	6 (0.9)	4 (1.0)	1 (0.7)	1 (0.9)	.932
Elephant trunk insertion	244 (37.2)	50 (12.5)	138 (92.6)	56 (52.3)	<.001*
Frozen elephant trunk	28 (4.3)	3 (0.8)	22 (14.8)	3 (2.8)	.097

Values are presented as mean ± standard deviation or n (%). CPB, Cardiopulmonary bypass. * $P < .05$.

38 patients (5.8%), and 466 patients (68.1%) underwent elective surgery.

Operative Details

Operation-related data are shown in Table 2. The mean cardiopulmonary bypass time was 193.0 ± 67.6 minutes, mean myocardial ischemia time was 92.9 ± 47.1 minutes, mean lower body circulatory arrest time was 44.0 ± 16.8 minutes, and mean cerebral perfusion time was 100.8 ± 39.4 minutes. Concurrent procedures were performed in 235 patients (35.9%) and 150 of those (22.9%) underwent coronary artery bypass grafting. Two hundred forty-three

patients underwent elephant trunk insertion (50 patients in the no dissection group, 138 patients in the acute dissection group, and 55 patients in the chronic dissection group).

Early Outcomes

Early outcomes are shown in Table 3. The overall operative mortality was 5.2% (34 out of 655 patients). The 30-day mortality was 2.7% (18 out of 655 patients). Hospital mortality was 5.2% (34 out of 655 patients). Operative mortality was 3.1% in those undergoing elective surgery (14 out of 446 patients) and 9.6% in those undergoing nonelective surgery (20 out of 209 patients). The cause of

TABLE 3. Early outcomes

Variable	Overall (n = 655)	No dissection (n = 399)	Acute dissection (n = 149)	Chronic dissection (n = 107)	P value
Operative mortality	34 (5.2)	18 (4.5)	14 (9.4)	2 (1.9)	.019*
30-d mortality	18 (2.7)	7 (1.8)	9 (6.0)	2 (1.9)	.038*
Hospital mortality	34 (5.2)	18 (4.5)	14 (9.4)	2 (1.9)	.019*
1-y mortality	77 (12.1)	49 (12.7)	21 (14.5)	7 (6.6)	.111
Permanent neurologic deficit	24 (3.7)	10 (2.5)	13 (8.7)	1 (0.9)	.002*
Transient neurologic deficit	64 (9.8)	38 (9.5)	19 (12.8)	7 (6.5)	.243
Mediastinitis	11 (1.7)	5 (1.3)	5 (3.4)	1 (0.9)	.238
Tracheostomy	51 (7.8)	33 (8.3)	12 (8.1)	6 (5.7)	.661
Hoarseness	96 (14.7)	68 (17.0)	13 (8.7)	15 (14.0)	.038*
Renal failure	40 (6.1)	27 (6.8)	12 (8.1)	1 (1.0)	.014*
Hospital stay (d)	24 (17-35)	23 (17-35)	25 (18-39.8)	25 (18-33)	.244
Discharge to home	499 (80.4)	322 (84.5)	96 (71.1)	81 (77.1)	.003*

Values are presented as n (%). * $P < .05$.

TABLE 4. Cause of late death

Variable	n (%)
Overall	191
Aortic	21 (11.0)
Aneurysm rupture	9
Graft infection	5
Aortic dissection	1
Subsequent aortic surgery	6
Cardiac	17 (8.9)
Cerebrovascular accident	20 (10.5)
Pulmonary	39 (20.4)
Renal	14 (7.3)
Malignancy	33 (17.3)
Gastrointestinal	5 (2.6)
Sepsis	10 (5.2)
Elderly age	9 (4.7)
Trauma	2 (1.0)
Sudden death	5 (2.6)
Unknown	16 (8.4)

death was cerebrovascular accident in 11 patients, sepsis in 6 patients, necrosis of the intestine in 5 patients, pulmonary complications in 9 patients, and hemorrhage in 3 patients.

Regarding postoperative complications, PND and TND occurred in 24 patients (3.7%) and in 64 patients (9.8%), respectively. Mediastinitis occurred in 11 patients (1.7%). Tracheostomy was required in 51 patients (7.8%). New hoarseness occurred in 96 patients (14.7%). Renal failure developed in 40 patients (6.1%).

Late Outcomes

Survival. During the observation period, 191 late deaths occurred, including 21 aorta-related deaths. The causes of late death are summarized in Table 4. Overall survival was $73.1\% \pm 1.9\%$ at 5 years and $54.8\% \pm 2.7\%$ at 10 years (median survival time, 11.3 years) (Figure 1, A). Across the study period, overall survival was $65.9\% \pm 4.2\%$ during the first 6 years (1999-2004), $76.6\% \pm 2.9\%$ during the second 6 years (2005-2010), and $73.6\% \pm 3.4\%$ during the last 6 years (2011-2016) ($P = .597$) (Figure E1). Stratified with aortic pathologies, 5-year survival was significantly lower in the no dissection group (no dissection, $68.6\% \pm 2.6\%$; acute dissection, $81.3\% \pm 3.4\%$; and chronic dissection, $78.0\% \pm 4.4\%$) ($P < .001$) (Figure 1, B), whereas the differences between the healthy population and overall survival were similar across the 3 groups (Figure 1, C-E).

Univariate Cox-hazard regression analysis revealed that older age, lower estimated glomerular filtration rate, chronic lung disease, coronary artery disease, old cerebral infarction, nondissection aneurysm, preoperative cardiac

arrest, ruptured aneurysm, and concurrent procedures were significant risk factors for late death. On the other hand, Marfan syndrome was found to be a significant positive prognostic factor of survival. In addition, PND, tracheostomy, hoarseness, and renal failure were significant risk factors of late death (Table 5).

Multivariate Cox-hazard regression analysis demonstrated that older age (HR, 1.06; 95% CI, 1.04-1.08; $P < .001$), lower estimated glomerular filtration rate (HR, 0.98; 95% CI, 0.97-0.99; $P < .001$), concurrent procedures (HR, 1.41; 95% CI, 1.01-2.11; $P = .043$), PND (HR, 3.31; 95% CI, 1.79-5.79; $P < .001$), tracheostomy (HR, 2.38; 95% CI, 1.53-3.60; $P < .001$), and renal failure (HR, 2.53, 95% CI, 1.57-3.97; $P < .001$) were significant risk factors for late death (Table 5).

Freedom from aorta-related death was $91.5\% \pm 1.2\%$ at 5 years and $90.3\% \pm 1.4\%$ at 10 years (Figure E2, A). Stratified with aortic pathologies, freedom from aorta-related death at 5 years was similar within groups (no dissection, $91.5\% \pm 1.6\%$; acute dissection, $89.9\% \pm 2.5\%$; and chronic dissection, $93.6\% \pm 2.6\%$ [$P = .289$]) (Figure E2, B).

Reoperation. One hundred two patients required reoperation, including 18 repeated aorta operations (2.7%) and 85 additional aorta operations (13.0%). The details of reoperations performed in our patients is shown in Table 6. Freedom from repeated aorta operation was $98.0\% \pm 0.7\%$ at 5 years and $93.9\% \pm 1.8\%$ at 10 years (Figure 2, A). In each pathology group, freedom from repeated aorta operation at 5 years was significantly worse in the acute dissection group (no dissection, $99.4\% \pm 0.4\%$; acute dissection, $93.4\% \pm 2.7\%$; and chronic dissection, $99.0\% \pm 1.0\%$) ($P = .004$) (Figure 2, B). Freedom from additional operations on the aorta was $87.4\% \pm 1.5\%$ at 5 years and $77.1\% \pm 2.7\%$ at 10 years (Figure 2, C). In each pathology group, freedom from additional aortic operation at 5 years was significantly worse in the chronic dissection group (no dissection, $90.2\% \pm 1.8\%$; acute dissection, $89.8\% \pm 3.0\%$; and chronic dissection, $75.5\% \pm 4.6\%$) ($P < .001$) (Figure 2, D). Forty-four additional repairs (53.7%) were performed due to distal residual dissection and included descending aorta replacement ($n = 9$), thoracoabdominal aortic aneurysm repair ($n = 26$), and thoracic endovascular aortic repair ($n = 9$).

Events. MAAE-free survival was $57.7\% \pm 2.2\%$ at 5 years and $36.4\% \pm 2.6\%$ at 10 years (Figure E3, A). Stratified with aortic pathologies, MAAE-free survival at 5 years was similar in the 3 groups (no dissection, $55.9\% \pm 2.5\%$; acute dissection, $63.9\% \pm 4.3\%$; and chronic dissection, $55.9\% \pm 5.2\%$) ($P = .404$) (Figure E3, B). Freedom from stroke was $85.3\% \pm 1.5\%$ at 5 years and $78.9\% \pm 2.3\%$ at 10 years (Figure E3, C) and it was also similar in each aortic pathologies

FIGURE 1. A, Overall survival. B, Overall survival by pathology: non-dissection (blue line), acute dissection (red line), and chronic dissection (green line). Significant differences were found between non-dissection and acute dissection as well as non-dissection and chronic dissection. Overall survival in the Japanese healthy population adjusted for age and sex. C, Non-dissection. D, Acute dissection. E, Chronic dissection.

TABLE 5. Univariate and multivariate analysis of overall survival (Cox hazard analysis)

Variable	Univariate		Multivariate	
	HR (95% CI)	P value	HR (95% CI)	P value
Age (y)	1.07 (1.05-1.08)	<.001*	1.06 (1.04-1.08)	<.001*
Female	1.02 (0.76-1.35)	.891		
Hypertension	0.79 (0.59-1.08)	.133		
Dyslipidemia	0.95 (0.70-1.28)	.752		
Diabetes mellitus	1.03 (0.69-1.49)	.882		
Smoking	0.94 (0.72-1.22)	.625		
eGFR (mL/min/1.73 m ²)	0.97 (0.97-0.98)	<.001*	0.98 (0.97-0.99)	<.001*
Chronic lung disease	1.69 (1.24-2.28)	.001*	1.12 (0.79-1.55)	.519
Coronary artery disease	1.59 (1.20-2.09)	.001*	0.83 (0.56-1.23)	.357
Marfan syndrome	0.34 (0.08-0.90)	.026*	1.44 (0.34-4.20)	.574
Old cerebral infarction	1.69 (1.15-2.41)	.009*	1.31 (0.88-1.90)	.184
Previous thoracic aortic surgery	1.23 (0.83-1.77)	.298		
No dissection	1.80 (1.36-2.42)	<.001*	1.12 (0.79-1.59)	.527
Atherothrombotic aorta	1.60 (0.96-2.49)	.068		
Malperfusion	0.80 (0.43-1.34)	.419		
Shock status	1.22 (0.67-2.01)	.495		
Cardiac arrest	4.35 (1.54-9.52)	.009*	1.78 (0.61-4.13)	.264
Infection	1.35 (0.58-2.67)	.452		
Rupture	2.54 (1.55-3.94)	<.001*	1.52 (0.89-2.45)	.119
Nonelective operation	0.90 (0.67-1.20)	.493		
CPB time (min)	1.00 (1.00-1.00)	.449		
Myocardial ischemic time (min)	1.00 (0.99-1.00)	.058		
Circulation arrest of lower body (min)	1.00 (0.99-1.00)	.423		
Antegrade cerebral perfusion	1.15 (0.76-1.80)	.529		
Cerebral perfusion time (min)	1.00 (1.00-1.00)	.760		
Minimal tympanic temperature (°C)	1.03 (0.97-1.09)	.317		
Minimal rectal temperature (°C)	0.99 (0.92-1.05)	.656		
Concurrent procedures	1.41 (1.08-1.84)	.011*	1.47 (1.01-2.11)	.043*
Permanent neurologic deficit	2.04 (1.26-3.13)	.005*	3.31 (1.79-5.79)	<.001*
Transient neurologic deficit	1.14 (0.72-1.72)	.558		
Mediastinitis	2.19 (0.86-4.51)	.092		
Tracheostomy	4.48 (3.09-6.32)	<.001*	2.38 (1.53-3.60)	<.001*
Hoarseness	1.57 (1.13-2.15)	.008*	1.29 (0.91-1.79)	.146
Renal failure	4.64 (3.02-6.84)	<.001*	2.53 (1.57-3.97)	<.001*

HR, Hazard ratio; CI, confidence interval; eGFR, estimated glomerular filtration rate; CPB, cardiopulmonary bypass. * $P < .05$.

($P = .613$). After discharge, 42 patients were diagnosed with a new stroke based on image assessment.

Apart from 11 patients with postoperative mediastinitis, graft infection occurred in 6 patients (0.9%). Four of those 6 patients underwent surgical repair. One patient underwent ascending aorta replacement at 6.1 years. Two patients underwent descending aorta replacement due to elephant trunk infection at 1.5 and 6.4 years. In addition, 1 patient underwent descending aorta repair for aorto-esophageal fistula due to previous stentgraft. One patient was complicated

with aorto-esophageal fistula in 0.5 years. The patient and family rejected open repair and debridement, and he died 2 months later. The last patient, who experienced graft infection of the Bentall graft in 3.8 years, died from sepsis under medical treatment at another institution.

The overall incidence of pseudoaneurysm was 2.2% (14 out of 625 patients). The incidence of pseudoaneurysm was similar between proximal and distal anastomosis (1.0% and 1.2%, respectively). There were no significant differences in the incidence of pseudoaneurysm across the aortic

TABLE 6. The mode of reoperation

Procedure	n (%)
Repeated operation	18 (2.7)
Root replacement for proximal pseudoaneurysm	5 (0.8)
Ascending Ao replacement for proximal pseudoaneurysm	2 (0.3)
Ascending Ao replacement for graft infection	1 (0.2)
Descending Ao replacement for graft infection	3 (0.5)
TEVAR for distal pseudoaneurysm	4 (0.6)
TEVAR for residual dissection in aortic arch	1 (0.2)
TEVAR for ET kinking	1 (0.2)
TEVAR for AEF	1 (0.2)
Additional operation	85 (13.0)
Root replacement	3 (0.5)
Descending Ao replacement	10 (1.5)
TAAA	38 (5.8)
Extent I	5
Extent II	16
Extent III	14
Extent IV	3
TEVAR	34 (5.2)

Ao, Aorta; TEVAR, thoracic endovascular aortic repair; ET, elephant trunk; AEF, aorto-esophageal fistula; TAAA, thoracoabdominal aortic aneurysm.

pathologies ($P = .864$). No pseudoaneurysm and aneurysmal dilatation in the arch vessel anastomoses were diagnosed during the observation period, and there were no stenosis or occlusion of branch grafts.

DISCUSSION

Although strides have been made to improve early outcomes, the value of long-term outcomes following total arch replacement remains controversial. It has been reported that 5-year survival after total arch replacement was 69.3% to 86.7% in 3.3 to 4.5 years of follow-up, and freedom from reoperation was 86.0% to 97.8% at 5 years.^{12,18-22}

In comparison to our previous report (5-year survival was $79.6\% \pm 3.3\%$ and 10-year survival was $71.2\% \pm 5.0\%$ in 2.4 ± 2.3 years of follow-up, respectively),⁷ our present study shows lower survival rates ($73.1\% \pm 1.9\%$ at 5 years and $54.8\% \pm 2.7\%$ at 10 years). The difference in survival rates between our previous data and the current data can be attributed to our ability to analyze the number and the cause of late deaths more accurately (51 late deaths in our previous report and 190 late deaths in this report) in the longer follow-up period (5.0 ± 4.1 years and 97.1% patients were followed for longer than 1 year). In investigating the causes of death, we demonstrated that >80% of patients died of nonaortic disease in their late phase. However, it is possible that this number was underestimated because patients who died from pneumonia due to dysphagia caused by stroke or hoarseness or senility due to falling down caused by postoperative frail deterioration were not included in aorta-related death.

This study demonstrated that 3 perioperative factors (ie, older age, chronic kidney disease, and concurrent procedures) and 3 postoperative complications (ie, PND, tracheostomy, and renal failure) were significant risk factors for late death. Age and chronic kidney disease could not be altered preoperatively and have broad spectrum. It was difficult to set a definitive cut-off value of each factor. Indeed, we do not determine surgical indication from single variable. Although we previously reported that concomitant coronary artery bypass grafting was not a risk factor for hospital mortality,²³ in the perspective of late survival, less-invasive treatment might be considered in patients who have multiple risk factors to decrease surgical invasion. Preoperative hemodynamic status was not a significant risk factor in multivariate analysis. In serious situations, total arch replacement was a reasonable option from a long-term perspective, given that the patient was in a low-risk group, because in the subgroup analysis of octogenarians/nonagenarians ($n = 127$) emergent surgery was a significant risk factor for late death (HR, 2.05; 95% CI, 1.03-3.80; $P = .042$). Moreover, we also demonstrated that some postoperative complications were significant risk factors for late death. Therefore, to improve late outcomes, cardiothoracic surgeons should aim to not only to prevent late aortic events but also to prevent postoperative complications.

Regarding reoperation, freedom from repeated aortic surgery was significantly lower in patients with acute dissection. The use of gelatin-resorcinol-formaldehyde glue was considered to be the cause of glue necrosis because it was used at our institution from 1999 to 2010.²⁴ The toxic effect caused recurrent dissection and pseudoaneurysm formation at the anastomosis site. Luehr and colleagues²⁵ reported on 1232 patients who underwent elective total arch replacement in several centers, noting that 6 patients (0.4%) required reoperation for pseudoaneurysm in a 4.1-year follow-up period. Our data indicate that 2.2% of patients developed pseudoaneurysm. In addition, graft infection is a serious complication, although the incidence was low (0.9%; 6 out of 655 patients). However, no operative mortality was found in all 4 patients who underwent surgical repair and debridement. As in our previous report,²⁶ aggressive surgical treatment is essential in this cohort. Even in the late phase, periodic follow-up is needed.

Moreover, freedom from additional operations was significantly lower in patients with chronic dissection. As recently reported,^{27,28} total arch replacement with elephant trunk contributes to positive aortic remodeling of the descending aorta in acute dissection. Frozen elephant trunk also had a significant remodeling effect in acute dissection, whereas the effect of positive remodeling is smaller in chronic dissection.²⁹ Oda and colleagues³⁰ reported that the risk of rupture increased with an aortic diameter ≥ 5.0 cm in patients with chronic dissection in the descending or thoracoabdominal aorta. Based on these

FIGURE 2. A, Freedom from repeated aortic operation. B, Freedom from repeated aortic operation by pathology: non-dissection (blue line), acute dissection (red line), and chronic dissection (green line). A significant difference was found between non-dissection and acute dissection. C, Freedom from additional aortic operation. D, Freedom from additional aortic operation by pathology: non-dissection (blue line), acute dissection (red line), and chronic dissection (green line). Significant differences were found between (non-dissection and chronic dissection as well as acute dissection and chronic dissection).

data, it is critical to consider late dilation of the downstream aorta before initial total arch replacement of the aortic arch aneurysm itself. However, the result that only 3 patients (0.5%) required additional aortic root replacement following initial total arch replacement supports our surgical indication of aortic root.

Individual anastomosis of each arch vessel using 4-branched graft could provide a secure anastomosis. The greatest advantage of 4-branched graft over en bloc reconstruction is the ability to transect each vessel at an appropriate cross-section, avoiding atherosclerotic plaques. This strategy contributed to fewer adverse neurologic outcomes in patients with an atherothrombotic aorta from

the perspective of both early and long-term outcomes. Moreover, in this observation period, 1 patient with connective tissue disease who underwent en bloc reconstruction of arch vessels developed cuff dilatation, whereas no pseudoaneurysms or dilation of arch vessels were found in the individual reconstruction group.

Some authors reported that 5-year survival after hybrid repair was 54.3% to 84% in 1.9 to 4.5 years of follow-up, and freedom from reoperation was 80.0% to 91.9% at 5 years.^{11,31-33} These midterm results suggest that hybrid repair has become an alternative option. However, the high incidence of stroke after hybrid treatment is still controversial (2.8%-11.6%)^{21,34} and

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Key Words: aortic arch replacement, total arch replacement, aortic aneurysm, aortic dissection

FIGURE E1. Overall survival according to time from operation over 18 years. The first 6 years (1999-2004) (*red line*), the second 6 years (2005-2010) (*green line*), and the last 6 years (2011-2016) (*blue line*).

FIGURE E2. A, Freedom from aortic-related death. B, Freedom from aortic-related death by pathology: non-dissection (blue line), acute dissection (red line), and chronic dissection (green line).

FIGURE E3. A, Survival without major adverse aortic event (MAAE). B, MAAE-free survival by pathology: non-dissection (blue line), acute dissection (red line), and chronic dissection (green line). C, Freedom from stroke.