Risk factors for impaired neurological outcome after thoracic aortic surgery

Till J. Demal[1#], Franziska W. Sitzmann[1#], Lennart Bax[1], Yskert von Kodolitsch[2], Jens Brickwedel[1], Johanna Konertz[1], Daniel M. Gaekel[1], Ahmed J. Sadeq[1], Tilo Kölbel[2], Eik Vettorazzi[3], Hermann Reichenspurner[1], Christian Detter[1]

[1]Department of Cardiovascular Surgery, German Aortic Center Hamburg, University Heart Center Hamburg, Hamburg, Germany; [2]Department of Vascular Medicine, German Aortic Center Hamburg, University Heart Center Hamburg, Hamburg, Germany; [3]Department of Medical Biometry and Epidemiology, University Hospital Eppendorf, Hamburg, Germany

Contributions: (I) Conception and design: TJ Demal, C Detter; (II) Administrative support: None; (III) Provision of study materials or patients: H Reichenspurner, C Detter, J Brickwedel, T Kölbel; (IV) Collection and assembly of data: FW Sitzmann, TJ Demal, L Bax, J Konertz, DM Gaekel, AJ Sadeq; (V) Data analysis and interpretation: FW Sitzmann, TJ Demal, E Vettorazzi, Y von Kodolitsch, C Detter; (VI) Manuscript writing: All authors; (VII) Final approval of manuscript: All authors.

[#]These authors contributed equally to this work.

Correspondence to: Franziska W. Sitzmann; Prof. Dr. Christian Detter, MD. Department of Cardiovascular Surgery, German Aortic Center Hamburg, University Heart Center Hamburg, Martinistraße 52, D-20246 Hamburg, Germany. Email: franzi.sitzmann@gmail.com; detter@uke.de.

Background: We aimed to identify risk factors for an impaired postoperative neurological outcome after thoracic aortic surgery.

Methods: Data from all patients undergoing thoracic aortic surgery between 2010 and 2020 at our institution were collected and analyzed retrospectively. Logistic regression analysis was used to identify independent risk factors for permanent postoperative neurological deficit (ND) (stroke), which was defined as a ND lasting at least seven days.

Results: Thoracic aortic surgery was performed in 1,334 patients. Of these, 286 (21.4%) underwent emergency surgery. The mean EuroSCORE II was 8.6±10.1. A perioperative stroke occurred in 94 patients (7.0%). Of all strokes, 62.8% (n=59) were considered of embolic and 24.5% (n=23) of hemodynamic origin. In elective procedures, stroke rates ranged from 0.5% after valve-sparing root replacement to 8.1% after arch surgery. Adjusted logistic regression identified advanced age [>70 years; odds ratio (OR), 1.83; P=0.009], acute type A dissection (ATAD) (OR, 1.69; P=0.0495), aortic arch surgery (OR, 3.24; P<0.001), concomitant coronary artery bypass grafting (CABG) (OR, 2.19; P=0.005), and high extracorporeal circulation (ECC) time (>230 min; OR, 1.70; P=0.034) as independent risk factors for all strokes. Secondary endpoint analyses revealed that risk factors for hemodynamic stroke were arch surgery, advanced age (>70 years), atherosclerosis, and ATAD. Risk factors for embolic stroke were arch surgery, concomitant CABG and preoperative cerebral malperfusion.

Conclusions: Identified independent risk factors for all strokes were advanced age, ATAD, arch surgery, concomitant CABG, and high ECC time. Hemodynamic and embolic strokes show distinct risk profiles.

Keywords: Thoracic aortic surgery; stroke; risk factors; acute type A dissection (ATAD); aortic arch surgery

Introduction

Although surgical techniques and outcome in thoracic aortic surgery have improved over the last decade, stroke remains a common complication with rates around 15% (1). Previously described risk factors for postoperative stroke include female gender (2), emergency surgery (3), preoperative malperfusion syndrome (4,5), total arch replacement (1), increased cardiopulmonary bypass (1,2,6), and circulatory arrest time (3). Postoperative stroke can substantially affect patient's quality of life and is associated with further complications, like renal or multi-organ failure, prolonged ventilation (5), longer duration of hospitalization (7), and mortality (3,4,8). Identification of unknown and verification of known risk factors in a large cohort is urgently needed. Considering these factors in the preoperative patient evaluation may lead to an improved patient selection and reduce perioperative complication rates. Risk factor analyses have primarily been performed in specific pathologies like acute type A aortic dissection. A more generalized approach is needed to improve patient care in both, elective and emergent thoracic aortic surgery. We aimed to identify independent risk factors associated with new postoperative stroke in a cohort that underwent the whole spectrum of thoracic aortic surgery. Moreover, we compared early and late survival rate between the stroke and no stroke group. We present the following article in accordance with the STROBE reporting checklist (available at https://jtd.amegroups.com/article/view/10.21037/jtd-21-1591/rc).

Methods

Study design, setting and participants

Data from patients undergoing thoracic aortic surgery at the German Aortic Center Hamburg were collected using our dedicated institutional aortic database and evaluated to identify independent risk factors for the occurrence of postoperative stroke. Data acquisition was performed anonymized and retrospectively.

The German Aortic Center Hamburg is a high-volume aortic center in Northern Germany offering the whole spectrum of thoracic aortic procedures. Our registry comprises all patients who were planned to undergo thoracic aortic surgery before starting the procedure, since we included patients based on our digital operating room schedule. Therefore, the rare cases in which the decision to operate on the thoracic aorta was taken intraoperatively

were not included into our database. Besides that, our registry is fully comprehensive. Follow-up data was collected retrospectively from the patient's chart if available. All patients undergoing thoracic aortic surgery from January 2010 to February 2020 were included. All procedure types in thoracic aortic surgery were included, such as root replacement, supracoronary ascending replacement, and hemi- or total arch repair including extension into the proximal descending aorta using the frozen elephant trunk (FET) procedure. These procedures were performed by a total of 25 different cardiac surgeons. This implies all urgency statuses (elective, urgent, emergent, salvage) with or without hypothermic circulatory arrest (HCA) and selective antegrade cerebral perfusion (SACP) as well as concomitant procedures.

As the study was performed anonymized and retrospectively, in accordance with German law, no ethical approval is needed and informed patient consent was waived. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013).

Definitions of variables

Based on the Valve Academic Research Consortium-2 criteria (9), stroke was defined as a new focal or global postoperative neurological deficit (ND) of ischemic or hemorrhagic origin, persisting at least 7 days. ND was diagnosed by clinical signs and symptoms confirmed by a neurologist and brain imaging using computed tomography (CT) or magnetic resonance imaging (MRI). In case the patient already presented with a ND upon admission, the endpoint of postoperative ND was only triggered, if a change in symptoms lead to a higher modified Rankin Scale (mRS) (10) of at least one point difference before and after the procedure. Stroke was further divided into embolic/territorial, hemodynamic, hemorrhagic, and lacunar by brain imaging and as reported by a neurologist or neuroradiologist.

Focal ND was defined as symptoms affecting specific body areas. Global ND was defined as coma or ND affecting the whole brain.

Urgency statuses were defined according to the EuroSCORE II as (11):

- *elective*: *routine admission for operation*;
- *urgent*: *patients not electively admitted for operation but who require surgery on the current admission for medical reasons and cannot be discharged without a definitive procedure*;

- *emergency*: *operation before the beginning of the next working day after decision to operate*;
- *salvage*: *patients requiring cardiopulmonary resuscitation (external cardiac massage) en route to the operating theatre or before induction of anaesthesia. This does not include cardiopulmonary resuscitation after induction of anaesthesia.*

Any atherosclerotic entity was defined as either coronary artery disease in the patient's history and/or extracardiac arteriopathy as defined by the EuroSCORE II. Extracardiac arteriopathy includes claudication, carotid stenosis >50%, amputation for arterial disease or preceding or prospective intervention on the abdominal aorta, carotids or arteries of extremities (11).

Further definitions can be found in Appendix 1.

Study size

Of all 1,392 consecutive patients in the study period, patients with missing data on clinical parameters (n=7) and endocarditis (n=32) were excluded. Furthermore, we excluded patients who died intraoperatively (n=19) since occurrence of intraoperative stroke could not be determined.

Statistical analysis

Categorical variables were reported as frequencies and percentages and compared between study groups (ND *vs.* no ND group) using chi-square test or Fisher's exact test, as appropriate. Continuous variables were expressed as mean ± standard deviation (SD) and compared between groups using the two-sided Student's *t*-test. Continuous variables such as age and surgical times were converted into binary variables using cut-off values between the 70th and 85th percentile of each value based on clinical experience. Temperature was considered as low below the 25th percentile. Potential pre- and intraoperative factors (candidates) identified by significant differences in the univariate analysis were further tested using multivariate logistic regression to explore independent variables associated with postoperative stroke. Variables in the logistic regression model were selected by a stepwise backward elimination process. Adjusted odds ratio (OR), 95% confidence intervals (CIs) and P values were reported.

To identify specific risk factors, risk factor analysis was repeated for the secondary endpoints embolic and hemodynamic stroke. Additionally, we performed subgroup analyses for patients presenting with acute type A dissection (ATAD), presenting with aneurysm, undergoing root surgery and undergoing total arch replacement.

To retrospectively evaluate long-term survival, Kaplan-Meier estimations were calculated. In landmark analyses, patients that died within 30 or 90 days were excluded, respectively. To compare ND and no ND groups, Cox regression analysis was conducted, and adjusted hazard ratio (HR) and P value were reported. Apart from stroke, covariates entered in this model were age, gender, peripheral arterial disease, ejection fraction under 30%, chronic lung disease, renal function, preoperative critical state, ATAD and high extracorporeal circulation (ECC) time, as these factors are known to be associated with increased postoperative mortality after aortic surgery (2,12-14).

Patients with missing data on cannulation technique (n=7) were excluded from our study since they could not be included in the logistic regression analysis.

The level of significance for all analyses was set at alpha =0.05.

Statistical analyses were performed using IBM SPSS version 26.0.0.0 (IBM Corp., Armonk, NY, USA).

Results

Preoperative patients' characteristics

The mean age of all 1,334 analyzed patients was 61.4±14.2 years with 34.9% being female. The mean EuroSCORE II was 8.6±10.1. Genetic aortic syndrome was diagnosed in 123 patients (9.2%). Underlying aortic pathologies mainly were thoracic aortic aneurysms (71.1%, n=948) and aortic syndromes (27.8%, n=371). Of all patients presenting with aortic syndrome, most patients suffered from ATAD (n=240, 18.0% of the total cohort). Further baseline characteristics are depicted in *Table 1*.

Procedural data

Of all aortic procedures, 999 (74.9%) were elective, 47 (3.5%) were urgent, and 286 (21.4%) were emergent or salvage. Aortic root replacement was performed in 451 patients (33.8%). Of these, 221 (16.6% of the total cohort) underwent valve sparing root replacements. Isolated supracoronary ascending replacement without HCA was performed in 82 (6.1%) patients. Hemiarch and total arch replacement using HCA was performed in 419 (31.4%) and 203 patients (15.2%), respectively. Of these, most patients underwent aortic surgery using HCA with SACP for cerebral protection (n=530, 86.0%). The mean HCA,

Table 1 Baseline characteristics

Characteristics	All (n=1,334)	No stroke (n=1,240)	Stroke (n=94)	P value
Age (years), mean ± SD	61.4±14.2	61.0±14.3	67.2±11.5	<0.001
Female gender, n (%)	466 (34.9)	434 (35.0)	32 (34.0)	0.851
Obesity (BMI >35 kg/m²), n (%)	81 (6.1)	79 (6.4)	2 (2.1)	0.097
Arterial hypertension, n (%)	1,040 (78.0)	958 (77.3)	82 (87.2)	0.024
Any atherosclerotic entity, n (%)	493 (37.0)	445 (35.9)	48 (51.1)	0.003
Coronary artery disease	380 (28.5)	341 (27.5)	39 (41.5)	0.004
Extracardiac arteriopathy	184 (13.8)	164 (13.2)	20 (21.3)	0.029
Atrial fibrillation, n (%)	209 (15.7)	192 (15.5)	17 (18.1)	0.504
IDDM, n (%)	31 (2.3)	28 (2.3)	3 (3.2)	0.476
Chronic lung disease, n (%)	134 (10.0)	117 (9.4)	17 (18.1)	0.007
Smoker, n (%)	525 (39.4)	484 (39.0)	41 (43.6)	0.380
Chronic kidney disease, n (%)	256 (19.2)	224 (18.1)	32 (34.0)	<0.001
Previous cardiac surgery, n (%)	136 (10.2)	126 (10.2)	10 (10.6)	0.883
EuroSCORE II, mean ± SD	8.6±10.1	8.1±9.5	15.0±13.9	<0.001
Preoperative stroke, n (%)	114 (8.5)	103 (8.3)	11 (11.7)	0.256
Linked to aortic syndrome	34 (2.5)	33 (2.7)	1 (1.1)	0.508
Not linked to aortic syndrome	80 (6.0)	70 (5.6)	10 (10.6)	0.049
Preoperative critical state, n (%)	134 (10.0)	110 (8.9)	24 (25.5)	<0.001
Preoperative cerebral malperfusion, n (%)	56 (4.2)	44 (3.5)	12 (12.8)	<0.001
Genetic aortic syndrome, n (%)	123 (9.2)	121 (9.8)	2 (2.1)	0.014
Malfunction or infection of TEVAR or aortic graft, n (%)	14 (1.0)	11 (0.9)	3 (3.2)	0.070
Aneurysm, n (%)	948 (71.1)	914 (73.7)	34 (36.2)	<0.001
ATAD, n (%)	240 (18.0)	202 (16.3)	38 (40.4)	<0.001
IMH, n (%)	43 (3.2)	36 (2.9)	7 (7.4)	0.027
PAU, n (%)	13 (1.0)	11 (0.9)	2 (2.1)	0.232
Chronic dissection, n (%)	56 (4.5)	61 (4.6)	5 (5.3)	0.613
Aortic rupture, n (%)	68 (5.1)	56 (4.5)	12 (12.8)	0.002
Maximum thoracic aortic diameter (mm), mean ± SD	5.49±1.18	5.49±1.19	5.45±1.09	0.766
Urgency status, n (%)				
Elective	999 (74.9)	960 (77.4)	39 (41.5)	<0.001
Urgent	47 (3.5)	42 (3.4)	5 (5.3)	0.375
Emergent or salvage	286 (21.4)	236 (19.0)	50 (53.2)	<0.001

SD, standard deviation; BMI, body mass index; IDDM, insulin-dependent diabetes mellitus; TEVAR, thoracic endovascular aortic repair; ATAD, acute type A dissection; IMH, intramural hematoma; PAU, penetrating atherosclerotic ulcer.
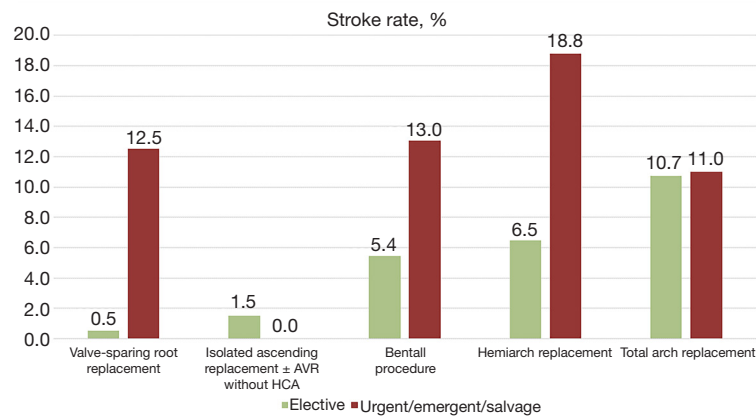
Figure 1 Postoperative stroke rate in different surgical procedures. The postoperative stroke rate differs between specific aortic procedures. While the stroke rate for elective valve-sparing root replacement and ascending replacement with or without concomitant AVR without HCA is as low as 0.5% and 1.5%, respectively, the rate after elective aortic arch surgery is as high as 10.7%. In urgent, elective or emergent procedures, the stroke rate is higher. In isolated ascending replacement, the stroke rate is 0%. AVR, aortic valve replacement; HCA, hypothermic circulatory arrest.

SACP and ECC times were 36.8±25.3 min, 44.1±32.8 min, and 185.9±79.8 min, respectively. The most common site of cannulation was the ascending aorta or aortic arch (n=903, 67.7%), followed by the subclavian (n=211, 15.8%) and the innominate artery (n=182, 13.6%). In only 34 (2.5%) patients, the femoral artery was cannulated for cardiopulmonary bypass.

Stroke rate

In 7.0 % (n=94) of all patients who underwent thoracic aortic surgery, a new permanent postoperative ND was detected. Of all patients, 2.5% suffered transient ND. In 48.9% (n=46) of the permanent strokes, the ND was considered focal. In 51.1% (n=48) it was considered global. In cranial MRI or CT imaging, lesions were observed in the left and right hemisphere in 17 (20.0%) and 19 patients (22.4%), respectively. In 49 patients (57.6%) both hemispheres were involved. In 9 patients, MRI or CT images weren't available for retrospective analysis anymore. Of all patients suffering from postoperative stroke we could evaluate the mRS score of 63 patients at discharge. Of these, 79.4% (n=50) had a score of 3 or higher. The highest stroke rate with 15.8% occurred in patients undergoing surgery for ATAD. In elective procedures the overall stroke rate was 3.9%. *Figure 1* shows postoperative stroke rates for different procedures. Of these, patients who underwent total arch surgery had the highest rate with 10.7%. However, if the total arch was replaced using a simplified FET technique

performed by an experienced aortic surgeon in an elective setting, no stroke was observed. The lowest surgeon-independent stroke rate was found after elective valve-sparing root replacement (0.5%).

Risk factor analysis of the total cohort

Univariate analysis

Table 1 shows baseline characteristics of the analyzed patient cohort. Patients suffering from postoperative ND were significantly older, had a higher EuroSCORE II, and were more likely to have comorbidities such as coronary artery disease, chronic kidney disease, or history of cerebrovascular accident compared to patients without neurological impairment after surgery. Patients with postoperative ND presented with a higher rate of ATAD, preoperative critical state, preoperative cerebral malperfusion, and aortic rupture. Genetic aortic syndromes and elective procedures were less common in the ND group (*Table 1*).

Table 2 shows surgical procedures performed in our cohort. Patients suffering from postoperative stroke more often underwent aortic arch replacement and concomitant coronary artery bypass grafting (CABG). Valve-sparing root replacements and Wheat procedures were less common in the ND group.

Table 3 shows intraoperative data. Here, ECC time was significantly increased in patients showing postoperative neurological impairment. Aortic clamp time, HCA and cerebral perfusion (CP) time did not significantly differ

Table 2 Surgical procedures

Procedures	All (n=1,334)	No stroke (n=1,240)	Stroke (n=94)	P value
Aortic root surgery, n (%)	451 (33.8)	431 (34.8)	20 (21.3)	0.008
Bentall procedure	230 (17.2)	214 (17.3)	16 (17.0)	0.953
Valve-sparing root replacement	221 (16.6)	217 (17.5)	4 (4.3)	0.001
Isolated ascending replacement, n (%)	82 (6.1)	80 (6.5)	2 (2.1)	0.092
Wheat (supracoronary + AVR), n (%)	251 (18.8)	241 (19.4)	10 (10.6)	0.035
Arch procedure, n (%)	622 (46.6)	446 (44.0)	76 (80.9)	<0.001
Hemiarch	419 (31.4)	365 (29.4)	54 (57.4)	<0.001
Total arch	203 (15.2)	181 (14.6)	22 (23.4)	0.022
Conventional	69 (5.2)	61 (4.9)	8 (8.5)	0.143
FET	134 (10.0)	120 (9.7)	14 (14.9)	0.105
Simplified FET technique	70 (5.2)	67 (5.4)	3 (3.2)	0.475
Descending procedure, n (%)	9 (0.7)	8 (0.6)	1 (1.1)	0.483
Concomitant surgery, n (%)				
CABG	193 (14.5)	169 (13.6)	24 (25.5)	0.002
TVR	21 (1.6)	20 (1.6)	1 (1.1)	>0.990
MVR	58 (4.3)	55 (4.4)	3 (3.2)	0.793
VAD implantation	2 (0.1)	2 (0.2)	0 (0.0)	>0.990

AVR, aortic valve replacement; FET, frozen elephant trunk; CABG, coronary artery bypass grafting; TVR, tricuspid valve replacement; MVR, mitral valve repair; VAD, ventricular assist device.

between the groups. The ND group more frequently underwent HCA with SACP and was cooled to lower body temperatures intraoperatively.

Table 4 shows outcome parameters. The overall 30-day mortality was 5.9% (n=79) and was significantly increased in patients with ND compared to patients without ND (34.0% *vs.* 3.8%, P<0.001). Rates of postoperative paraplegia, and reanimation or shock were significantly higher in the ND group. ND patients showed a higher rate of resternotomy.

Multivariate risk factor analysis

The results of the multivariate risk factor analysis are shown in *Table 5*. Advanced age (>70 years; adjusted OR, 1.83; 95% CI, 1.16–2.88; P=0.009), ATAD (adjusted OR, 1.69; 95% CI, 1.00–2.84; P=0.0495), aortic arch surgery (adjusted OR, 3.24; 95% CI, 1.78–5.88; P<0.001), and concomitant CABG (adjusted OR, 2.19; 95% CI, 1.27–3.79; P=0.005) were identified as independent risk factors for postoperative stroke. Of all surgical times, only high ECC time (>230 min) was identified as independent risk factor (adjusted OR, 1.70; 95% CI, 1.04–2.77; P=0.034).

Concomitant CABG

As concomitant CABG was identified as independent risk factor, we further analyzed CABG specific procedural data. Of all patients that underwent concomitant CABG, 99 (55.0%) underwent complete arterial bypass grafting. In 81 patients (45.0%) a central anastomosis to the aorta was performed. Within the group of patients undergoing concomitant CABG, the rate of patients receiving central anastomoses to the aorta was significantly higher in the stroke group (no stroke 41.8% *vs.* stroke 68.2%, P=0.020).

Risk factor analysis of secondary endpoints and subgroups

Further risk factor analyses were performed to identify specific risk factors for the occurrence of embolic or hemodynamic stroke, respectively (Tables S1-S10).

Of all postoperative strokes, 59 (62.8%) were of embolic and 23 (24.5%) of hemodynamic origin. Two strokes were caused by hemorrhage. One stroke was considered lacunar. In nine patients, strokes could not be clearly classified.

Table 3 Intraoperative data

Intraoperative data	All (n=1,334)	No stroke (n=1,240)	Stroke (n=94)	P value
Aortic surgeon (>20 aortic procedures per year), n (%)	771 (57.8)	721 (58.2)	50 (53.2)	0.344
Time of surgery, n (%)				
Weekend surgery	63 (4.7)	52 (4.2)	11 (11.7)	0.003
Night-time surgery	197 (14.8)	165 (13.3)	32 (34.0)	<0.001
ECC time (min), mean ± SD	185.9±79.8	181.6±76.3	242.3±101.5	<0.001
Aortic clamp time (min), mean ± SD	105.3±50.5	104.6±49.6	115.3±61.3	0.108
HCA with SACP, n (%)	530 (39.7)	466 (37.6)	64 (68.1)	<0.001
Unilateral CP, n (%)	53 (4.1)	46 (3.8)	7 (7.8)	0.087
Bilateral CP, n (%)	546 (41.7)	481 (39.5)	65 (72.2)	<0.001
Cerebral hypothermic arrest, n (%)	19 (1.5)	18 (1.5)	1 (1.1)	1.000
CP flow (mL/min), mean ± SD	1,240.8±425.8	1,240.5±435.4	1,242.4±353.7	0.973
CP volume (liter), mean ± SD	58.1±54.5	57.5±53.8	62.9±59.4	0.465
CP temperature (℃), mean ± SD	22.4±4.5	22.5±4.6	21.8±3.2	0.215
Cerebral monitoring, n (%)	576 (49.1)	515 (47.2)	61 (73.5)	<0.001
Circulatory arrest time (min), mean ± SD	36.8±25.3	36.1±24.7	41.6±29.5	0.082
CP time (min), mean ± SD	41.6±31.7	40.9±31.0	46.4±36.1	0.158
Deepest body temperature (℃), mean ± SD	28.7±4.0	28.9±4.0	25.9±3.5	<0.001
Site of arterial cannulation, n (%)				
Ascending aorta or aortic arch	903 (67.7)	857 (69.1)	46 (48.9)	<0.001
Innominate artery	182 (13.6)	169 (13.6)	13 (13.8)	0.956
Subclavian artery	211 (15.8)	181 (14.6)	30 (31.9)	<0.001
Femoral artery	34 (2.5)	29 (2.3)	5 (5.3)	0.085

ECC, extracorporeal circulation; SD, standard deviation; HCA, hypothermic circulatory arrest; SACP, selective antegrade cerebral perfusion; CP, cerebral perfusion.

Risk factor analysis for the occurrence of an embolic stroke identified aortic arch surgery (adjusted OR, 3.95; 95% CI, 2.08–7.51; P<0.001), preoperative cerebral malperfusion (adjusted OR, 2.52; 95% CI, 1.10–5.77; P=0.028), and concomitant CABG (adjusted OR, 2.09; 95% CI, 1.11–3.96; P=0.023) as independent risk factors.

For the occurrence of a hemodynamic stroke, risk factor analysis identified advanced age (adjusted OR, 2.46; 95% CI, 1.02–5.92; P=0.046), any atherosclerotic entity (adjusted OR, 2.66; 95% CI, 1.10–6.42; P=0.030), ATAD (adjusted OR, 3.92; 95% CI, 1.59–9.66; P=0.003) and aortic arch surgery (adjusted OR, 14.26; 95% CI, 1.82–111.74; P=0.011) as independent risk factors.

Further subgroup analyses are shown in Tables S11-S30.

Risk factors identified in the subgroup of patients presenting with aneurysm were any atherosclerotic entity, chronic kidney disease, preoperative critical state. In patients with ATAD no risk factors could be identified. Risk factors in patients undergoing root surgery were advanced age and ATAD. In patients undergoing total arch replacement, concomitant CABG was a risk factor. Furthermore, in this subgroup, the FET procedure using aortic arch zone 2 as landing zone was revealed to be a protective factor against stroke.

Long-term survival

Figure 2 shows the estimated Kaplan-Meier curves of patients with and without postoperative stroke for the

Table 4 Outcome parameters

Parameters	All (n=1,334)	No stroke (n=1,240)	Stroke (n=94)	P value
In-hospital/30-day mortality, n (%)	79 (5.9)	47 (3.8)	32 (34.0)	<0.001
One-year mortality, n (%)	106 (17.8)	65 (12.2)	41 (65.1)	<0.001
Transient ND, n (%)	34 (2.5)	34 (2.7)	–	–
Resternotomy for bleeding or tamponade, n (%)	139 (10.4)	116 (9.4)	23 (24.5)	<0.001
Reanimation or shock, n (%)	77 (5.8)	59 (4.8)	18 (19.1)	<0.001
Paraplegia, n (%)	14 (1.0)	9 (0.7)	5 (5.3)	0.002
Recurrent nerve palsy, n (%)	29 (2.2)	27 (2.2)	2 (2.1)	>0.999
Pneumonia or other respiratory insufficiency, n (%)	174 (13.0)	143 (11.5)	31 (33.0)	<0.001
Sepsis, n (%)	30 (2.2)	18 (1.5)	12 (12.8)	<0.001
New-onset atrial fibrillation, n (%)	265 (19.9)	243 (19.6)	22 (23.4)	0.372
Myocardial infarction, n (%)	10 (0.7)	9 (0.7)	1 (1.1)	0.520

ND, neurological deficit.

overall cohort including early mortality, a 30-day, and a 90-day landmark analysis. Adjusted Cox regression analysis revealed a significantly increased long-term mortality in stroke patients when evaluating the overall cohort (Cox regression: HR, 4.38; 95% CI, 2.99–6.04; P<0.001). The 30-day landmark analysis still showed a decreased survival in stroke patients (Cox regression: HR, 3.52; 95% CI, 1.76–7.04; P<0.001). However, after excluding patients who died within 90 days after surgery, Cox regression did not show a statistically significant difference anymore (P=0.393).

In a non-adjusted analysis, patients with a more severe stroke (global or both hemispheres) had a higher 30-day (8.0% *vs.* 43.5%, P=0.001) and 1-year mortality (31.3% *vs.* 76.6%, P=0.001) than patients with a focal and one-sided stroke.

In patients with postoperative stroke, we evaluated the mRS score before discharge and 1 year after the operation in our aortic outpatient clinic. Unfortunately, mRS score data after 1 year is only available of 16 out of a total of 22 stroke patients surviving the first year after surgery. At discharge, 79.4% (n=50) of stroke patients had a mRS score higher than 3. One year after surgery, this rate decreased to 68.8% (n=11) of patients with a score higher than 3.

Discussion

The rate of postoperative ND after thoracic aortic surgery in our cohort was 7.0%. Adjusted logistic regression analysis revealed preoperative factors, such as advanced age and ATAD, as well as surgical parameters, such as arch replacement, concomitant CABG, and high cardiopulmonary bypass time as independent risk factors for all types of strokes after aortic surgery.

Survival

This study showed an association of a postoperative stroke after thoracic aortic surgery with an impaired early and long-term survival, as demonstrated by Kaplan-Meier curves and Cox regression analyses (*Figure 2*). Stroke was also associated with further complications such as pneumonia and prolonged intensive care unit stay. A landmark analysis after 90 days, however, did not show a significant difference in the survival between the groups. This demonstrates that perioperative strokes have a significant impact on early survival within the first 3 months. However, if the patient survived these first 3 months after surgery, perioperative neurological dysfunction is not significantly associated with impaired mid- and long-term survival. An impaired survival after stroke in patients undergoing aortic surgery has also been shown by other groups. Okada *et al.* reported that patients with stroke after aortic surgery had a significantly higher early mortality than patients without (15). In contrast to the present study, Okada *et al.* observed an impaired late survival after 5 years in the stroke group. Here, Okada *et al.* did not perform a landmark analysis and therefore included early perioperative deaths in their analysis, which may have triggered the impaired overall and long-term survival in the

Table 5 Risk factors for stroke after thoracic aortic surgery

Risk factors	OR	95% CI	P value
Advanced age (>70 years)	1.83	1.16–2.88	0.009
Arterial hypertension	–	–	0.662
Any atherosclerotic entity	–	–	0.397
Chronic kidney disease	–	–	0.061
History of cerebrovascular accident	–	–	0.230
Preoperative cerebral malperfusion	–	–	0.126
Preoperative critical state	–	–	0.101
ATAD	1.69	1.00–2.84	0.0495
Aortic rupture	–	–	0.096
Aortic surgeon	–	–	0.421
Weekend surgery	–	–	0.300
Night-time surgery	–	–	0.200
Valve-sparing root replacement	–	–	0.071
Aortic arch surgery	3.24	1.78–5.88	<0.001
FET	–	–	0.315
Concomitant CABG	2.19	1.27–3.79	0.005
High ECC time (>230 min)	1.70	1.04–2.77	0.034
High aortic clamp time (>155 min)	–	–	0.479
HCA with SACP	–	–	0.843
High circulatory arrest time (>60 min)	–	–	0.752
High CP time (>90 min)	–	–	0.235
Low body temperature (<25 ℃)	–	–	0.286
Site of arterial cannulation			
Ascending aorta or aortic arch	–	–	0.512
Innominate artery	–	–	0.114
Subclavian artery	–	–	0.121
Femoral artery	–	–	0.123

P value of acute type A dissection is reported with 4 decimals to show significance. ATAD, acute type A dissection; FET, frozen elephant trunk; CABG, coronary artery bypass grafting; ECC, extracorporeal circulation; HCA, hypothermic circulatory arrest; SACP, selective antegrade cerebral perfusion; CP, cerebral perfusion; OR, odds ratio; CI, confidence interval.

stroke group. Summarizing, we conclude, that postoperative stroke is indeed relevant for an impaired long-term outcome. The impaired long-term outcome is mainly caused by events within the first 90 days after surgery. We observed a low rate of recovery in the long-term follow-up. We cautiously conclude that only few patients recover from a severe postoperative stroke after aortic surgery if

symptoms remained until hospital discharge.

High-risk patients

The present study showed that especially older patients over 70 years of age and patients presenting with ATAD have a higher stroke risk after thoracic aortic surgery.
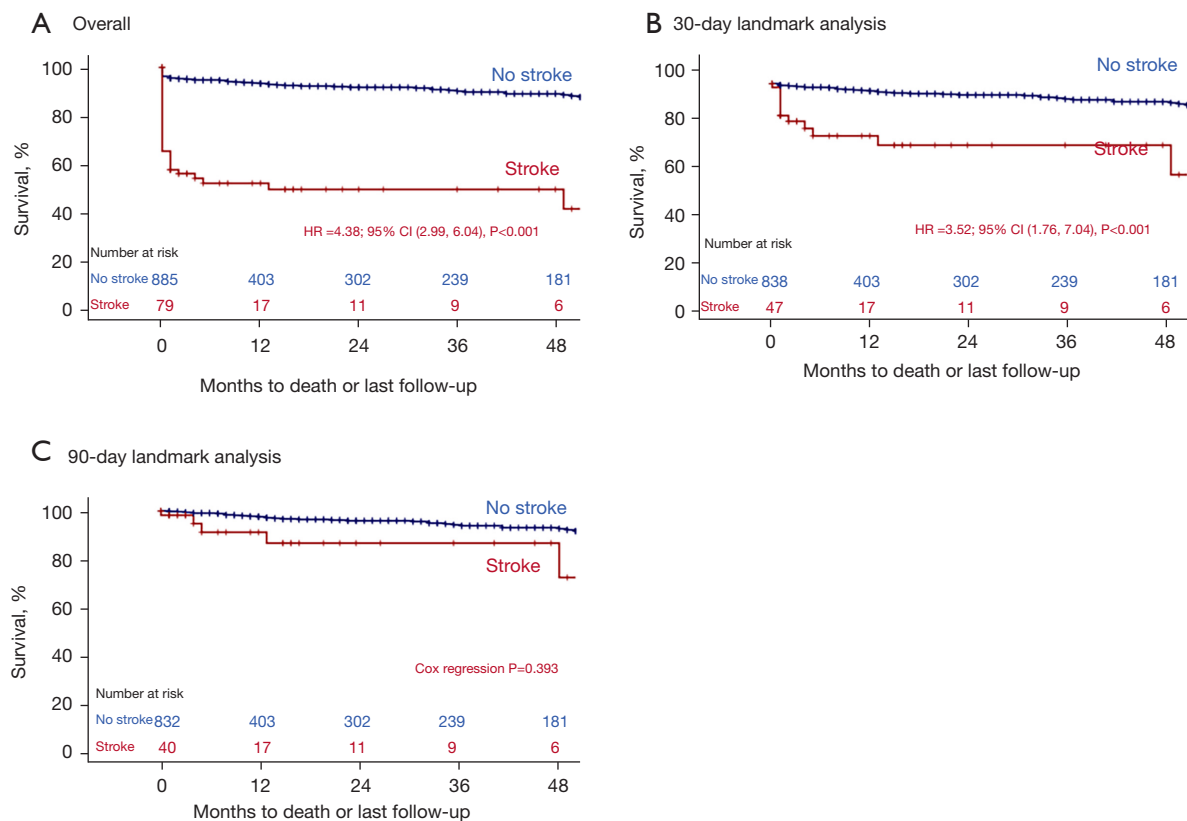
Figure 2 Kaplan-Meier overall, 30-, and 90-day landmark survival analyses. Long-term survival was compared between the stroke and no stroke group using Cox regression analysis adjusting for known risk factors for mortality after aortic surgery (age, gender, peripheral arterial disease, ejection fraction under 30%, chronic lung disease, renal function, preoperative critical state, ATAD, and high ECC time). Survival in stroke patients was significantly lower than in patients without postoperative stroke in the overall cohort (A) and in the 30-day landmark analysis (B). Overall mean survival was 45.8 (95% CI, 32.9–58.7) months in the stroke group *vs.* 107.0 (95% CI, 103.4–110.6) months in the no stroke group. Mean survival in the 30-day landmark analysis was 69.4 (95% CI, 52.6–86.2) months in the stroke and 111.2 (95% CI, 107.7–114.7) months in the no stroke group. Contrary, survival did not show a statistically significant difference between groups in the 90-day landmark Cox regression analysis anymore (C). In the 90-day landmark analysis mean survival was 80.8 (95% CI, 63.4–98.1) months in the stroke and 111.9 (95% CI, 108.5–115.4) months in the no stroke group. HR, hazard ratio; CI, confidence interval; ATAD, acute type A dissection; ECC, extracorporeal circulation.

Prior studies already identified ATAD as independent risk factor for stroke (2,16,17). In the literature, stroke rates after surgery for ATAD are reported from 3.4% to 26.5% (18,19). Accordingly, the subgroup of ATAD patients in our cohort showed a stroke rate of 15.8%. Especially patients with dissection affecting supra-aortic vessels are at high risk since CP might be impaired perioperatively and lead to insufficient oxygen supply to the brain (20,21). Stroke prevention strategies in this patient cohort are of utmost importance. This may include pressure controlled SACP during HCA, near-infrared spectroscopy (NIRS) monitoring to detect early perfusion impairment, or specific

cannulation techniques to improve CP (22,23).

Age is a well-known risk factor for the occurrence of stroke in the general population (24). An analysis of Hagl *et al.* in 2001 already revealed age as a risk factor for stroke in patients undergoing aortic surgery in HCA with or without SACP (7). Analyses using data of the German Registry for Acute Aortic Dissection type A (GERAADA) did not find age to be an independent risk factor for stroke in patients with ATAD (25). In the present study, a more heterogeneous patient group undergoing both elective or emergency surgery for aortic aneurysm or dissection was analyzed. Here, advanced age was identified as independent

risk factor. We conclude that advanced age may especially play a role as stroke risk factor in patients with other pathologies than ATAD undergoing aortic surgery. This cautious assumption needs to be evaluated in further studies.

Arch surgery as a high-risk procedure

The analysis of the overall cohort as well as the subgroup analyses identified aortic arch surgery, including hemi- and total arch replacement, as independent risk factor for strokes of hemodynamic as well as embolic origin. In each risk factor analysis, arch surgery showed the highest OR of all identified independent risk factors. This underlines the importance of neuroprotection and adequate perfusion strategy when performing arch surgery in HCA.

Due to the manipulation of calcified head vessels and the complexity of arch procedures using HCA in combination with CP strategies as well as increased ECC times due to prolonged cooling and rewarming times, aortic arch surgery is well known to impose a relevant stroke risk (26). Therefore, preoperatively, brain-supplying vessels should be evaluated thoroughly using doppler sonography. In patients with history of TIA or stroke and in patients with relevant stenoses or dissections further imaging is necessary. CT angiography with imaging of extra- and intracranial brain-supplying arteries should be performed to evaluate the degree of known stenoses and to rule out an incomplete circle of Willis.

Intraoperatively, neuroprotective measures include monitoring of cerebral oxygen saturation via NIRS, the individual adjustment of the arterial blood pressure as well as an adapted CP flow based on the patient's individual range of cerebral autoregulation and monitored brain oxygen saturation.

It is an ongoing debate which CP strategy provides the best neuroprotection. A current meta-analysis by Hameed *et al.* including 26,968 patients of 68 studies, showed antegrade or retrograde CP each leading to a better neurological outcome than deep HCA alone. Despite the wide consensus about the use of SACP, Hameed and colleagues did not observe a difference in outcome between antegrade and retrograde CP (27). Accordingly, a meta-analysis by Takagi *et al.* comparing antegrade and retrograde CP did not find a difference in postoperative ND either (28).

Nevertheless, especially in procedures with presumed circulatory arrest times beyond 30 to 40 minutes, bilateral CP should be used to reduce stroke risk (29). At our center

and in most European centers, SACP has been used as the preferred method for cerebral protection in the last decade (30). Surgical techniques continuously need to be facilitated and improved to lower the risk of early mortality and perioperative stroke in arch surgery. Accordingly, the simplified FET technique with the distal anastomosis in landing zone 2 and an extra-anatomic bypass to the distal left subclavian artery has been shown to reduce stroke risk as previously reported by our group (31). In addition, the use of endovascular techniques to accelerate the supra-aortic vessel anastomoses and to reduce circulatory arrest times by simplifying the surgical procedure seems to be a valid option (32).

Secondary endpoints

Additional analyses of the present study revealed different risk factors for the secondary endpoints hemodynamic and embolic strokes.

Hemodynamic stroke origin

Advanced age, any atherosclerotic entity, ATAD, and aortic arch surgery were identified as independent risk factors for the occurrence of a hemodynamic stroke. The spectrum of hemodynamic stroke ranges from borderline infarcts due to impaired cerebral microcirculation to massive hypoxic encephalopathy caused by hypoperfusion.

In older patients and patients with atherosclerosis microcirculation in the brain is diminished. In elderly, blood pressure and flow might not be adapted by autoregulation as quickly to changes that occur perioperatively. Already minor decreases in cerebral blood flow or pressure changes may negatively affect oxygen supply. This leads to insufficient oxygen saturation especially in distal brain areas and watershed strokes may occur. In patients with atherosclerosis this effect might be further enhanced due to relevant stenoses of brain-supplying arteries. In cardiac surgery, intraoperative drops in blood pressure were already found to be a risk factor for watershed stroke (33).

Embolic stroke origin

Apart from arch surgery, subgroup analysis identified concomitant CABG and preoperative cerebral malperfusion as independent risk factors for embolic stroke.

The role of atherosclerosis in the occurrence of embolic strokes during aortic surgery appears complex. In our study, CABG was identified as independent risk factor for the development of an embolic stroke. In these patients,

atherosclerosis may not be limited to the coronary arteries but might also affect the aorta as well as the supraaortic and intracranial brain-supplying vessels. Here, especially thrombi formed on ruptured atherosclerotic plaques are a well-known disease mechanism (34). Whether atherosclerotic plaques on their own might be mobilized during aortic surgery and thereby cause embolic strokes is not well investigated so far. Nevertheless, the presence of atherosclerotic plaques in the ascending aorta and the aortic arch is known to be associated with stroke of unknown cause (35).

However, atherosclerosis itself was not found to be an independent risk factor for occurrence of embolic strokes in our analysis. This leads to the assumption, that atherosclerosis during aortic surgery does not mainly increase the stroke risk by causing emboli, but by impairing cerebral microcirculation. In the general population, stroke often is caused by a combination of both atherosclerotic stenotic vessels and embolism of diverse origins (36).

Moreover, preoperative cerebral malperfusion was identified as risk factor for embolic, but not for hemodynamic stroke. Cerebral malperfusion may induce thrombus formation in the false and true lumen preoperatively that not yet cause stroke. Due to hemodynamic changes and/or SACP, these thrombi may be dislocated during surgery resulting in postoperative embolic stroke. However, this field is scarcely investigated, and more studies are needed to further examine underlying mechanisms.

Limitations

The main limitation of our study is its single-center and retrospective nature. Multicenter analyses are needed. Nevertheless, our study included a high number of patients over a significant time period of 10 years. Our cohort is very heterogenic including a broad range of patients presenting with different pathologies and undergoing the whole variety of surgical procedures of the thoracic aorta. However, this could also be seen as a strength as the presented cohort and study results may well represent clinical practice and may substantially improve preoperative risk evaluation of aortic patients. Moreover, our data represent the outcome of a high-volume aortic center. It is not certain if these results apply to lower volume centers as well.

When defining stroke for our analyses, we did not distinguish between different grades of severity and excluded strokes resolving within 7 days. Also, we excluded

patients who died intraoperatively, since it is not possible to evaluate whether these patients suffered from a stroke or not. This might influence our results in either one or the other direction and leading to an over- or underestimation of the stroke risk.

Another limitation regarding the statistical analysis is that ECC time was the only procedural time which correlated with stroke. This might be caused by statistical multicollinearity, as the length of the ECC time correlates with the length of other surgical times (e.g., aortic clamp time or CP time).

Conclusions

Stroke remains a major complication after thoracic aortic surgery. To lower the risk of postoperative ND, attention to pre- and intraoperative factors should be paid. Especially in elderly patients and in patients with ATAD, the least complex surgical technique possible should be used to improve neurological outcome. In these patients, ECC time should be kept short and the indication for arch replacement should only be given cautiously. As concomitant CABG was found to be a risk factor for stroke, percutaneous coronary intervention (PCI) might be a more favorable option in elderly patients who are suffering from coronary artery disease and undergo thoracic aortic surgery. In the case of prior PCI, the risk of bleeding might be increased due to postinterventional dual antiplatelet therapy (DAPT). Therefore, the individual stroke and bleeding risk needs to be evaluated in these patients to decide between concomitant CABG and PCI. Postponing aortic surgery in elective cases with low risk for spontaneous complications (dissection or rupture) until DAPT after PCI may be discontinued might be an option in selected cases. Especially in arch surgery, a particular focus should be placed upon the whole spectrum of neuroprotective measures and simplified surgical techniques.

Acknowledgments

Footnote

Reporting Checklist: The authors have completed the STROBE reporting checklist. Available at https://jtd.

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Data Sharing Statement: Available at https://jtd.amegroups.com/article/view/10.21037/jtd-21-1591/dss

Peer Review File: Available at https://jtd.amegroups.com/article/view/10.21037/jtd-21-1591/prf

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://jtd.amegroups.com/article/view/10.21037/jtd-21-1591/coif). CD is a proctor for Terumo Aortic. The other authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). Data acquisition was performed anonymized and retrospectively. Therefore, in accordance with German law, no ethical approval is needed and informed patient consent was waived (§12 HmbKHG, hospital law of Hamburg, and §15 Medical Association's professional code of conduct).

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Further definitions

History of cerebrovascular accident was defined as any ND any time before surgery. Cerebral malperfusion was assessed through imaging modalities. It was defined as a clear border between the well-perfused and the malperfused part of at least one carotid or vertebral artery characterized by a visually identifiable difference in Hounsfield units/brightness in CT- or MR-angiography.

According to the KDIGO guidelines (1), chronic renal failure was defined by a glomerular filtration rate of less than 60 mL/min that was not due to acute renal failure.

Genetic aortic syndromes included Marfan, Ehlers-Danlos and Loeys-Dietz syndrome, as well as familial thoracic aortic aneurysm and dissection (FTAAD) with positive family history, or pathological mutation in a known causal gene for FTAAD (2,3).

Aortic surgeon was defined as a surgeon who performed more than 20 aortic procedures per year. Surgery was considered to be performed at nighttime when time of skin incision and closure was not within 7 am and 10 pm and as weekend surgery if the date of the procedure was at the weekend or a local public holiday.

mRS

"0—No symptoms at all; 1—No significant disability despite symptoms: able to carry out all usual duties and activities; 2—Slight disability: unable to carry out all previous activities but able to look after own affairs without assistance; 3—Moderate disability: requiring some help, but able to walk without assistance; 4—Moderately severe disability: unable to walk without assistance, and unable to attend to own bodily needs without assistance; 5—Severe disability: bedridden, incontinent, and requiring constant nursing care and attention" (10).

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Table S1 Baseline characteristics including univariate analysis for embolic stroke

Characteristics	All (n=1,334)	No embolic stroke (n=1,275)	Embolic stroke (n=59)	P value
Age (years), mean ± SD	61.4±14.2	61.2±14.3	66.0±11.5	0.011
Female gender, n (%)	466 (34.9)	445 (34.9)	21 (35.6)	0.913
Obesity (BMI >35 kg/m^2), n (%)	81 (6.1)	80 (6.3)	1 (1.7)	0.257
Arterial hypertension, n (%)	1040 (78.0)	986 (77.3)	54 (91.5)	0.010
Any atherosclerotic entity, n (%)	493 (37.0)	466 (36.5)	27 (45.8)	0.152
Coronary artery disease	380 (28.5)	357 (28.0)	23 (39.0)	0.068
Extracardiac arteriopathy	184 (13.8)	172 (13.5)	12 (20.3)	0.136
Atrial fibrillation, n (%)	209 (15.7)	196 (15.4)	13 (22.0)	0.169
IDDM, n (%)	31 (2.3)	28 (2.2)	3 (5.1)	0.154
Chronic lung disease, n (%)	134 (10.0)	124 (9.7)	10 (16.9)	0.071
Smoker, n (%)	525 (39.4)	503 (39.5)	22 (37.3)	0.740
Chronic kidney disease, n (%)	256 (19.2)	237 (18.6)	19 (32.2)	0.009
Previous cardiac surgery, n (%)	136 (10.2)	132 (10.4)	4 (6.8)	0.375
EuroSCORE II, mean ± SD	8.6±10.1	8.3±9.8	14.1±14.1	0.003
Preoperative stroke, n (%)	114 (8.5)	108 (8.5)	6 (10.2)	0.648
Linked to aortic syndrome	34 (2.5)	34 (2.7)	0 (0.0)	0.398
Not linked to aortic syndrome	80 (6.0)	74 (5.8)	6 (10.2)	0.161
Preoperative critical state, n (%)	134 (10.0)	120 (9.4)	14 (23.7)	<0.001
Preoperative cerebral malperfusion, n (%)	56 (4.2)	48 (3.8)	8 (13.6)	0.002
Genetic aortic syndrome, n (%)	123 (9.2)	122 (9.6)	1 (1.7)	0.041
Malfunction or infection of TEVAR or aortic graft, n (%)	14 (1.0)	13 (1.0)	1 (1.7)	0.471
Aneurysm, n (%)	948 (71.1)	922 (72.3)	26 (44.1)	<0.001
ATAD, n (%)	240 (18.0)	220 (17.3)	20 (33.9)	0.001
IMH, n (%)	43 (3.2)	39 (3.1)	4 (6.8)	0.114
PAU, n (%)	13 (1.0)	11 (0.9)	2 (3.4)	0.110
Chronic dissection, n (%)	61 (4.6)	57 (4.5)	4 (6.8)	0.341
Aortic rupture, n (%)	68 (5.1)	60 (4.7)	8 (13.6)	0.008
Maximum thoracic aortic diameter (mm), mean ± SD	5.49±1.18	5.48±1.18	5.68±1.16	0.251
Urgency status, n (%)				
Elective	999 (74.9)	971 (76.2)	28 (47.5)	<0.001
Urgent	47 (3.5)	44 (3.5)	3 (5.1)	0.460
Emergent or salvage	286 (21.4)	258 (20.2)	28 (47.5)	<0.001

SD, standard deviation; BMI, body mass index; IDDM, insulin-dependent diabetes mellitus; TEVAR, thoracic endovascular aortic repair; ATAD, acute type A dissection; IMH, intramural hematoma; PAU, penetrating atherosclerotic ulcer.

Table S2 Surgical procedures including univariate analysis for embolic stroke

Procedures	All (n=1,334)	No embolic stroke (n=1,275)	Embolic stroke (n=59)	P value
Aortic root surgery, n (%)	451 (33.8)	438 (34.4)	13 (22.0)	0.051
Bentall procedure	230 (17.2)	219 (17.2)	11 (18.6)	0.770
Valve-sparing root replacement	221 (16.6)	219 (17.2)	2 (3.4)	0.005
Isolated ascending replacement, n (%)	82 (6.1)	80 (6.3)	2 (2.1)	0.577
Wheat (supracoronary + AVR), n (%)	251 (18.8)	245 (19.2)	6 (10.2)	0.082
Arch procedure, n (%)	622 (46.6)	576 (45.2)	46 (78.0)	<0.001
Hemiarch	419 (31.4)	387 (30.4)	32 (54.2)	<0.001
Total arch	203 (15.2)	189 (14.8)	14 (23.7)	0.063
Conventional	69 (5.2)	63 (4.9)	6 (10.2)	0.120
FET	134 (10.0)	126 (9.9)	8 (13.6)	0.358
Simplified FET technique	70 (5.2)	67 (5.3)	3 (5.1)	1.000
Descending procedure, n (%)	9 (0.7)	8 (0.6)	1 (1.7)	0.335
Concomitant surgery, n (%)				
CABG	193 (14.5)	179 (14.0)	14 (23.7)	0.039
TVR	21 (1.6)	21 (1.6)	0 (0.0)	1.000
MVR	58 (4.3)	55 (4.3)	3 (5.1)	0.740
VAD implantation	2 (0.1)	2 (0.2)	0 (0.0)	1.000

AVR, aortic valve replacement; FET, frozen elephant trunk; CABG, coronary artery bypass grafting; TVR, tricuspid valve replacement; MVR, mitral valve repair; VAD, ventricular assist device.

Table S3 Intraoperative data including univariate analysis for embolic stroke

Intraoperative data	All (n=1,334)	No embolic stroke (n=1,275)	Embolic stroke (n=59)	P value
Aortic surgeon, n (%)	771 (57.8)	739 (58.0)	32 (54.2)	0.571
Time of surgery, n (%)				
Weekend surgery	63 (4.7)	57 (4.5)	6 (10.2)	0.055
Night-time surgery	197 (14.8)	180 (14.1)	17 (28.8)	0.002
ECC time (min), mean ± SD	185.9±79.8	183.6±77.7	233.2±105.8	0.001
Aortic clamp time (min), mean ± SD	105.3±50.5	104.7±49.7	119.1±66.0	0.108
HCA with SACP, n (%)	530 (39.7)	492 (38.6)	38 (64.4)	<0.001
Circulatory arrest time (min), mean ± SD	36.8±25.3	36.3±24.5	42.2±34.5	0.139
CP time (min), mean ± SD	41.6±31.7	41.3±30.8	45.1±42.1	0.559
Deepest body temperature (℃), mean ± SD	28.7±4.0	28.8±4.0	26.3±3.5	<0.001
Site of arterial cannulation, n (%)				
Ascending aorta or aortic arch	903 (67.7)	872 (68.4)	31 (52.5)	0.011
Innominate artery	182 (13.6)	176 (13.8)	6 (10.2)	0.427
Subclavian artery	211 (15.8)	193 (15.1)	18 (30.5)	0.002
Femoral artery	34 (2.5)	30 (2.4)	4 (6.8)	0.059

ECC, extracorporeal circulation; SD, standard deviation; HCA, hypothermic circulatory arrest; SACP, selective antegrade cerebral perfusion; CP, cerebral perfusion.

Table S4 Outcome parameters including univariate analysis for embolic stroke

Parameters	All (n=1,334)	No embolic stroke (n=1,275)	Embolic stroke (n=59)	P value
Overall in-hospital-/30-day mortality, n (%)	79 (5.9)	64 (5.0)	15 (25.4)	<0.001
One-year mortality, n (%)	106 (17.8)	88 (15.7)	18 (51.4)	<0.001
Transient ND, n (%)	34 (2.5)	34 (2.7)	–	–
Resternotomy for bleeding or tamponade, n (%)	139 (10.4)	127 (10.0)	12 (20.3)	0.011
Reanimation or shock, n (%)	77 (5.8)	72 (5.6)	5 (8.5)	0.383
Paraplegia, n (%)	14 (1.0)	13 (1.0)	1 (1.7)	0.471
Recurrent nerve palsy, n (%)	29 (2.2)	28 (2.2)	1 (1.7)	1.000
Pneumonia or other respiratory insufficiency, n (%)	174 (13.0)	155 (12.2)	19 (32.2)	<0.001
Sepsis, n (%)	30 (2.2)	22 (1.7)	8 (13.6)	<0.001
New-onset atrial fibrillation, n (%)	265 (19.9)	251 (19.7)	14 (23.7)	0.447
Myocardial infarction, n (%)	10 (0.7)	9 (0.7)	1 (1.7)	0.365

ND, neurological deficit.

Table S5 Risk factors for embolic stroke after aortic surgery

Risk factors	OR	95% CI	P value
Advanced age (>70 years)	–	–	0.655
Arterial hypertension	–	–	0.123
Any atherosclerotic entity	–	–	0.952
Chronic kidney disease	–	–	0.098
Genetic aortic syndrome	0.20	0.03–1.44	0.109
Preoperative cerebral malperfusion	2.52	1.10–5.77	0.028
Preoperative critical state	–	–	0.294
ATAD	–	–	0.668
Aortic rupture	–	–	0.099
Night-time surgery	–	–	0.761
Valve-sparing root replacement	–	–	0.132
Aortic arch surgery	3.95	2.08–7.51	<0.001
Concomitant CABG	2.09	1.11–3.96	0.023
High ECC time (>230 min)	–	–	0.159
HCA with SACP	–	–	0.973
High circulatory arrest time (>60 min)	–	–	0.627
High CP time (>90 min)	–	–	0.382
Low body temperature (<25 ℃)	–	–	0.677
Site of arterial cannulation			
Ascending aorta or aortic arch	–	–	0.700
Subclavian artery	–	–	0.127
Femoral artery	–	–	0.066

ATAD, acute type A dissection; CABG, coronary artery bypass grafting; ECC, extracorporeal circulation; HCA, hypothermic circulatory arrest; SACP, selective antegrade cerebral perfusion; CP, cerebral perfusion; OR, odds ratio; CI, confidence interval.

Table S6 Baseline characteristics including univariate analysis for hemodynamic stroke

Characteristics	All (n=1,334)	No hemodynamic stroke (n=1,311)	Hemodynamic stroke (n=23)	P value
Age (years), mean ± SD	61.4±14.2	61.3±14.3	70.3±8.2	<0.001
Female gender, n (%)	466 (34.9)	462 (35.2)	4 (17.4)	0.075
Obesity (BMI >35 kg/m²), n (%)	81 (6.1)	80 (6.1)	1 (4.3)	1.000
Arterial hypertension, n (%)	1,040 (78.0)	1,021 (77.9)	19 (82.6)	0.588
Any atherosclerotic entity, n (%)	493 (37.0)	479 (36.5)	14 (60.9)	0.017
Coronary artery disease	380 (28.5)	370 (28.2)	10 (43.5)	0.108
Extracardiac arteriopathy	184 (13.8)	179 (13.7)	5 (21.7)	0.233
Atrial fibrillation, n (%)	209 (15.7)	207 (15.8)	2 (8.7)	0.562
IDDM, n (%)	31 (2.3)	31 (2.4)	0 (0.0)	1.000
Chronic lung disease, n (%)	134 (10.0)	133 (10.1)	1 (4.3)	0.722
Smoker, n (%)	525 (39.4)	513 (39.1)	12 (52.2)	0.204
Chronic kidney disease, n (%)	256 (19.2)	247 (18.8)	9 (39.1)	0.027
Previous cardiac surgery, n (%)	136 (10.2)	131 (10.0)	5 (21.7)	0.076
EuroSCORE II, mean ± SD	8.6±10.1	8.4±9.9	16.0±14.5	0.020
Preoperative stroke, n (%)	114 (8.5)	110 (8.4)	4 (17.4)	0.126
Linked to aortic syndrome	34 (2.5)	33 (2.5)	1 (4.3)	0.451
Not linked to aortic syndrome	80 (6.0)	77 (5.9)	3 (13.0)	0.155
Preoperative critical state, n (%)	134 (10.0)	128 (9.8)	6 (26.1)	0.022
Preoperative cerebral malperfusion, n (%)	56 (4.2)	54 (4.1)	2 (8.7)	0.251
Genetic aortic syndrome, n (%)	123 (9.2)	123 (9.4)	0 (0.0)	0.261
Malfunction or infection of TEVAR or aortic graft, n (%)	14 (1.0)	13 (1.0)	1 (4.3)	0.217
Aneurysm, n (%)	948 (71.1)	944 (72.0)	4 (17.4)	<0.001
ATAD, n (%)	240 (18.0)	227 (17.3)	13 (56.5)	<0.001
IMH, n (%)	43 (3.2)	41 (3.1)	2 (8.7)	0.168
PAU, n (%)	13 (1.0)	13 (1.0)	0 (0.0)	1.000
Chronic dissection, n (%)	61 (4.6)	60 (4.6)	1 (4.3)	1.000
Aortic rupture, n (%)	68 (5.1)	68 (5.2)	0 (0.0)	0.626
Maximum thoracic aortic diameter (mm), mean ± SD	5.49±1.18	5.49±1.19	5.11±0.83	0.185
Urgency status, n (%)				
Elective	999 (74.9)	994 (75.8)	5 (21.7)	<0.001
Urgent	47 (3.5)	46 (3.5)	1 (4.3)	0.565
Emergent or salvage	286 (21.4)	269 (20.5)	17 (73.9)	<0.001

SD, standard deviation; BMI, body mass index; IDDM, insulin-dependent diabetes mellitus; TEVAR, thoracic endovascular aortic repair; ATAD, acute type A dissection; IMH, intramural hematoma; PAU, penetrating atherosclerotic ulcer.

Table S7 Surgical procedures including univariate analysis for hemodynamic stroke

Procedures	All (n=1,334)	No hemodynamic stroke (n=1,311)	Hemodynamic stroke (n=23)	P value
Aortic root surgery, n (%)	451 (33.8)	447 (34.1)	4 (17.4)	0.093
Bentall procedure	230 (17.2)	227 (17.3)	13(13.0)	0.783
Valve-sparing root replacement	221 (16.6)	220 (16.8)	1 (4.3)	0.156
Isolated ascending replacement, n (%)	82 (6.1)	82 (6.3)	0 (0.0)	0.393
Wheat (supracoronary + AVR), n (%)	251 (18.8)	248 (18.9)	3 (13.0)	0.599
Arch procedure, n (%)	622 (46.6)	600 (45.8)	22 (95.7)	<0.001
Hemiarch	419 (31.4)	401 (30.6)	18 (78.3)	<0.001
Total arch	203 (15.2)	199 (15.2)	4 (17.4)	0.769
Conventional	69 (5.2)	69 (5.3)	0 (0.0)	0.628
FET	134 (10.0)	130 (9.9)	4 (17.4)	0.279
Simplified FET technique	70 (5.2)	70 (5.3)	0 (0.0)	0.629
Descending procedure, n (%)	9 (0.7)	9 (0.7)	0 (0.0)	1.000
Concomitant surgery, n (%)				
CABG	193 (14.5)	188 (14.3)	5 (21.7)	0.363
TVR	21 (1.6)	21 (1.6)	0 (0.0)	1.000
MVR	58 (4.3)	58 (4.4)	0 (0.0)	0.621
VAD implantation	2 (0.1)	2 (0.2)	0 (0.0)	1.000

AVR, aortic valve replacement; FET, frozen elephant trunk; CABG, coronary artery bypass grafting; TVR, tricuspid valve replacement; MVR, mitral valve repair; VAD, ventricular assist device.

Table S8 Intraoperative data including univariate analysis for hemodynamic stroke

Intraoperative data	All (n=1,334)	No hemodynamic stroke (n=1,311)	Hemodynamic stroke (n=23)	P value
Aortic surgeon, n (%)	771 (57.8)	760 (58.0)	11 (47.8)	0.329
Time of surgery, n (%)				
Weekend surgery	63 (4.7)	60 (4.6)	3 (13.0)	0.091
Night-time surgery	197 (14.8)	187 (14.3)	10 (43.5)	0.001
ECC time (min), mean ± SD	185.9±79.8	184.8±79.5	246.7±79.0	<0.001
Aortic clamp time (min), mean ± SD	105.3±50.5	105.3±50.6	108.1±50.2	0.800
HCA with SACP, n (%)	530 (39.7)	512 (39.1)	18 (78.3)	<0.001
Circulatory arrest time (min), mean ± SD	36.8±25.3	36.7±25.6	37.0±17.7	0.957
CP time (min), mean ± SD	41.6±31.7	41.6±32.0	41.9±23.0	0.966
Deepest body temperature (℃), mean ± SD	28.7±4.0	28.8±4.0	24.7±1.6	<0.001
Site of arterial cannulation, n (%)				
Ascending aorta or aortic arch	903 (67.7)	894 (68.2)	9 (39.1)	0.003
Innominate artery	182 (13.6)	178 (13.6)	4 (17.4)	0.542
Subclavian artery	211 (15.8)	202 (15.4)	9 (39.1)	0.006
Femoral artery	34 (2.5)	33 (2.5)	1 (4.3)	0.451

ECC, extracorporeal circulation; SD, standard deviation; HCA, hypothermic circulatory arrest; SACP, selective antegrade cerebral perfusion; CP, cerebral perfusion.

Table S9 Outcome parameters including univariate analysis for hemodynamic stroke

Parameters	All (n=1,334)	No hemodynamic stroke (n=1,311)	Hemodynamic stroke (n=23)	P value
Overall in-hospital-/30-day mortality, n (%)	79 (5.9)	70 (5.3)	9 (39.1)	<0.001
One-year mortality, n (%)	106 (17.8)	94 (16.2)	12 (75.0)	<0.001
Transient ND, n (%)	34 (2.5)	34 (2.6)	–	–
Resternotomy for bleeding or tamponade, n (%)	139 (10.4)	132 (10.1)	7 (30.4)	0.007
Reanimation or shock, n (%)	77 (5.8)	71 (5.4)	6 (26.1)	0.001
Paraplegia, n (%)	14 (1.0)	10 (0.8)	4 (17.4)	<0.001
Recurrent nerve palsy, n (%)	29 (2.2)	29 (2.2)	0 (0.0)	1.000
Pneumonia or other respiratory insufficiency, n (%)	174 (13.0)	165 (12.6)	9 (39.1)	0.001
Sepsis, n (%)	30 (2.2)	28 (2.1)	2 (8.7)	0.092
New-onset atrial fibrillation, n (%)	265 (19.9)	260 (19.8)	5 (21.7)	0.793
Myocardial infarction, n (%)	10 (0.7)	10 (0.8)	0 (0.0)	1.000

ND, neurological deficit.

Table S10 Risk factors for hemodynamic stroke after aortic surgery

Risk factors	OR	95% CI	P value
Advanced age (>70 years)	2.46	1.02–5.92	0.046
Any atherosclerotic entity	2.66	1.10–6.42	0.030
Chronic kidney disease	–	–	0.078
Preoperative critical state	–	–	0.877
ATAD	3.92	1.59–9.66	0.003
Night-time surgery	–	–	0.556
Aortic arch surgery	14.26	1.82–111.74	0.011
High ECC time (>230 min)	–	–	0.287
High aortic clamp time (>155 min)	–	–	0.503
HCA with SACP	–	–	0.873
High circulatory arrest time (>60 min)	–	–	0.915
High CP time (>90 min)	–	–	0.998
Low body temperature (<25 ℃)	–	–	0.830
Site of arterial cannulation			
Ascending aorta or aortic arch	–	–	0.629
Subclavian artery	–	–	0.695

ATAD, acute type A dissection; ECC, extracorporeal circulation; HCA, hypothermic circulatory arrest; SACP, selective antegrade cerebral perfusion; CP, cerebral perfusion; OR, odds ratio; CI, confidence interval.

Table S11 Baseline characteristics of patients with ATAD

Characteristics	All (n=240)	No stroke (n=202)	Stroke (n=38)	P value
Age (years), mean ± SD	62.4±13.0	61.5±13.3	66.7±10.3	0.026
Female gender, n (%)	74 (30.8)	63 (31.2)	11 (28.9)	0.784
Obesity (BMI >35 kg/m^2), n (%)	15 (6.3)	14 (6.9)	1 (2.6)	0.477
Arterial hypertension, n (%)	203 (84.6)	170 (84.2)	33 (86.8)	0.674
Any atherosclerotic entity, n (%)	77 (32.1)	63 (31.2)	14 (36.8)	0.493
Coronary artery disease	38 (15.8)	28 (13.9)	10 (26.3)	0.054
Extracardiac arteriopathy	46 (19.2)	39 (19.3)	7 (18.4)	0.899
Atrial fibrillation, n (%)	34 (14.2)	31 (15.3)	3 (7.9)	0.227
IDDM, n (%)	6 (2.5)	4 (2.0)	2 (5.3)	0.242
Chronic lung disease, n (%)	16 (6.7)	14 (6.9)	2 (5.3)	1.000
Smoker, n (%)	96 (40.0)	82 (40.6)	14 (36.8)	0.665
Chronic kidney disease, n (%)	46 (19.2)	39 (19.3)	7 (18.4)	0.899
Previous cardiac surgery, n (%)	17 (7.1)	13 (6.4)	4 (10.5)	0.321
EuroSCORE II, mean ± SD	18.0±14.6	17.7±14.6	19.6±14.8	0.450
Preoperative stroke, n (%)	38 (15.8)	35 (17.3)	3 (7.9)	0.144
Linked to aortic syndrome	25 (10.4)	24 (11.9)	1 (2.6)	0.143
Not linked to aortic syndrome	13 (5.4)	11 (5.4)	2 (5.3)	1.000
Preoperative critical state, n (%)	112 (46.7)	94 (46.5)	18 (47.4)	0.925
Preoperative cerebral malperfusion, n (%)	45 (18.8)	36 (17.8)	9 (23.7)	0.396
Genetic aortic syndrome, n (%)	13 (5.4)	13 (6.4)	0 (0.0)	0.231
Aortic rupture, n (%)	29 (12.1)	26 (12.9)	3 (7.9)	0.587
Maximum thoracic aortic diameter (mm), mean ± SD	5.42±1.24	5.55±1.31	4.90±0.63	0.001

ATAD, acute type A dissection; SD, standard deviation; BMI, body mass index; IDDM, insulin-dependent diabetes mellitus.

Table S12 Surgical procedures of patients with ATAD

Procedures	All (n=240)	No stroke (n=202)	Stroke (n=38)	P value
Aortic root surgery, n (%)	53 (22.1)	45 (22.3)	8 (21.1)	0.867
Bentall procedure	36 (15.0)	31 (15.3)	5 (13.2)	0.729
Valve-sparing root replacement	17 (7.1)	14 (6.9)	3 (7.9)	0.738
Isolated ascending replacement, n (%)	5 (2.1)	5 (2.5)	0 (0.0)	1.000
Wheat (supracoronary + AVR), n (%)	7 (2.9)	6 (3.0)	1 (2.6)	1.000
Arch procedure, n (%)	225 (93.8)	190 (94.1)	35 (92.1)	0.648
Hemiarch	163 (67.9)	136 (67.3)	27 (71.1)	0.652
Total arch	62 (25.8)	54 (26.7)	8 (21.1)	0.463
Conventional	32 (13.3)	29 (14.4)	3 (7.9)	0.282
FET	30 (12.5)	25 (12.4)	5 (13.2)	0.796
Simplified FET technique	8 (3.3)	5 (2.5)	3 (7.9)	0.116
Concomitant surgery, n (%)				
CABG	24 (10.0)	19 (9.4)	5 (13.2)	0.553
TVR	2 (0.8)	2 (1.0)	0 (0.0)	1.000
MVR	2 (0.8)	2 (1.0)	0 (0.0)	1.000
VAD implantation	0 (0.0)	0 (0.0)	0 (0.0)	–

ATAD, acute type A dissection; AVR, aortic valve replacement; FET, frozen elephant trunk; CABG, coronary artery bypass grafting; TVR, tricuspid valve replacement; MVR, mitral valve repair; VAD, ventricular assist device.

Table S13 Intraoperative data of patients with ATAD

Intraoperative data	All (n=240)	No stroke (n=202)	Stroke (n=38)	P value
Aortic surgeon (>20 aortic procedures per year), n (%)	103 (42.9)	85 (42.1)	18 (47.4)	0.546
Time of surgery, n (%)				
Weekend surgery	45 (18.8)	38 (18.8)	7 (18.4)	0.955
Night-time surgery	157 (65.4)	133 (65.8)	24 (63.2)	0.750
ECC time (min), mean ± SD	246.4±84.0	245.6±81.9	251.0±95.9	0.723
Aortic clamp time (min), mean ± SD	120.1±70.6	120.5±70.8	117.8±70.3	0.834
HCA with SACP, n (%)	188 (78.3)	158 (78.2)	30 (78.9)	0.920
Circulatory arrest time (min), mean ± SD	45.6±30.5	46.3±29.5	41.7±35.9	0.432
CP time (min), mean ± SD	48.5±36.3	48.8±35.5	46.5±41.3	0.739
Deepest body temperature (℃), mean ± SD	24.2±2.1	24.2±2.1	24.4±2.3	0.658
Site of arterial cannulation, n (%)				
Ascending aorta or aortic arch	88 (36.7)	75 (37.1)	13 (34.2)	0.732
Innominate artery	38 (15.8)	34 (16.8)	4 (10.5)	0.329
Subclavian artery	104 (43.3)	85 (42.1)	19 (50.0)	0.366
Femoral artery	12 (5.0)	10 (5.0)	2 (5.3)	1.000

ATAD, acute type A dissection; ECC, extracorporeal circulation; SD, standard deviation; HCA, hypothermic circulatory arrest; SACP, selective antegrade cerebral perfusion; CP, cerebral perfusion.

Table S14 Outcome parameters of patients with ATAD

Parameters	All (n=240)	No stroke (n=202)	Stroke (n=38)	P value
In-hospital-/30-day mortality, n (%)	33 (13.8)	17 (8.4)	16 (42.1)	<0.001
One-year mortality, n (%)	36 (27.9)	19 (18.4)	17 (65.4)	<0.001
Transient ND, n (%)	18 (7.5)	18 (8.9)	–	0.085
Resternotomy for bleeding or tamponade, n (%)	43 (17.9)	30 (14.9)	13 (34.2)	0.004
Reanimation or shock, n (%)	23 (9.6)	13 (6.4)	10 (26.3)	0.001
Paraplegia, n (%)	9 (3.8)	6 (3.0)	3 (7.9)	0.156
Recurrent nerve palsy, n (%)	12 (5.0)	12 (5.9)	0 (0.0)	0.222
Pneumonia or other respiratory insufficiency, n (%)	61 (25.4)	49 (24.3)	12 (31.6)	0.342
Sepsis, n (%)	14 (5.8)	8 (4.0)	6 (15.8)	0.012
New-onset atrial fibrillation, n (%)	52 (21.7)	45 (22.3)	7 (18.4)	0.597
Myocardial infarction, n (%)	1 (0.4)	1 (0.5)	0 (0.0)	1.000

ATAD, acute type A dissection; ND, neurological deficit.

Table S15 Risk factors for stroke after thoracic aortic surgery of patients with ATAD

Risk factors	OR	95% CI	P value
Advanced age (>70 years)	–	–	0.137
Preoperative cerebral malperfusion	–	–	0.396
Aortic diameter >5.90 cm	–	–	0.253
Preoperative critical state	–	–	0.925
Aortic arch surgery	–	–	0.648
High circulatory arrest time (>60 min)	–	–	0.195

ATAD, acute type A dissection; OR, odds ratio; CI, confidence interval.

Table S16 Baseline characteristics of patients with aneurysm

Characteristics	All (n=948)	No stroke (n=914)	Stroke (n=34)	P value
Age (years), mean ± SD	61.2±14.5	61.0±14.5	67.1±13.0	0.015
Female gender, n (%)	340 (35.9)	326 (35.7)	14 (41.2)	0.511
Obesity (BMI >35 kg/m^2), n (%)	64 (6.8)	64 (7.0)	0 (0.0)	0.161
Arterial hypertension, n (%)	711 (75.0)	681 (74.5)	30 (88.2)	0.070
Any atherosclerotic entity, n (%)	353 (37.2)	330 (36.1)	23 (67.6)	<0.001
Coronary artery disease	302 (31.9)	281 (30.7)	21 (61.8)	<0.001
Extracardiac arteriopathy	98 (10.3)	90 (9.8)	8 (23.5)	0.018
Atrial fibrillation, n (%)	149 (15.7)	143 (15.6)	6 (17.6)	0.753
IDDM, n (%)	24 (2.5)	23 (2.5)	1 (2.9)	0.588
Chronic lung disease, n (%)	101 (10.7)	89 (9.7)	12 (35.3)	<0.001
Smoker, n (%)	385 (40.6)	366 (40.0)	19 (55.9)	0.065
Chronic kidney disease, n (%)	171 (18.0)	154 (16.8)	17 (50.0)	<0.001
Previous cardiac surgery, n (%)	71 (7.5)	69 (7.5)	2 (5.9)	1.000
EuroSCORE II, mean ± SD	5.8±6.2	5.5±5.5	12.9±15.0	0.008
Preoperative stroke, n (%)	59 (6.2)	56 (6.1)	3 (8.8)	0.464
Linked to aortic syndrome	5 (0.5)	5 (0.5)	0 (0.0)	1.000
Not linked to aortic syndrome	54 (5.7)	51 (5.6)	3 (8.8)	0.436
Preoperative critical state, n (%)	7 (0.7)	4 (0.4)	3 (8.8)	0.001
Preoperative cerebral malperfusion, n (%)	2 (0.2)	2 (0.2)	0 (0.0)	1.000
Genetic aortic syndrome, n (%)	80 (8.4)	79 (8.6)	1 (2.9)	0.352
Aortic rupture, n (%)	13 (1.4)	11 (1.2)	2 (5.9)	0.076
Maximum thoracic aortic diameter (mm), mean ± SD	5.50±1.16	5.49±1.17	5.88±0.95	0.060
Urgency status, n (%)				
Elective	917 (96.7)	889 (97.3)	28 (82.4)	0.001
Urgent	22 (2.3)	19 (2.1)	3 (8.8)	0.041
Emergent or salvage	7 (0.7)	4 (0.4)	3 (8.8)	0.001

SD, standard deviation; BMI, body mass index; IDDM, insulin-dependent diabetes mellitus.

Table S17 Surgical procedures of patients with aneurysm

Procedures	All (n=948)	No stroke (n=914)	Stroke (n=34)	P value
Aortic root surgery, n (%)	368 (38.8)	359 (39.3)	9 26.5)	0.132
Bentall procedure	177 (18.7)	169 (18.5)	8 (23.5)	0.459
Valve-sparing root replacement	191 (20.1)	190 (20.8)	1 (2.9)	0.011
Isolated ascending replacement, n (%)	76 (8.0)	74 (8.1)	2 (5.9)	1.000
Wheat (supracoronary + AVR), n (%)	240 (25.3)	232 (25.4)	8 (23.5)	0.807
Arch procedure, n (%)	266 (28.1)	246 (26.9)	20 (58.8)	<0.001
Hemiarch	196 (20.7)	184 (20.1)	12 (35.3)	0.032
Total arch	70 (7.4)	62 (6.8)	8 (23.5)	0.002
Conventional	18 (1.9)	18 (2.0)	0 (0.0)	1.000
FET	52 (5.5)	44 (4.8)	8 (23.5)	<0.001
Simplified FET technique	29 (3.1)	29 (3.2)	0 (0.0)	0.620
Descending procedure, n (%)	6 (0.6)	5 (0.5)	1 (2.9)	0.197
Concomitant surgery, n (%)				
CABG	154 (16.2)	143 (15.6)	11 (32.4)	0.010
TVR	14 (1.5)	13 (1.4)	1 (2.9)	0.402
MVR	53 (5.6)	51 (5.6)	2 (5.9)	0.715
VAD implantation	2 (0.2)	2 (0.2)	0 (0.0)	1.000

AVR, aortic valve replacement; FET, frozen elephant trunk; CABG, coronary artery bypass grafting; TVR, tricuspid valve replacement; MVR, mitral valve repair; VAD, ventricular assist device.

Table S18 Intraoperative data of patients with aneurysm

Intraoperative data	All (n=948)	No stroke (n=914)	Stroke (n=34)	P value
Aortic surgeon (>20 aortic procedures per year), n (%)	564 (59.5)	545 (59.6)	19 (55.9)	0.662
Time of surgery, n (%)				
Weekend surgery	4 (0.4)	4 (0.4)	0 (0.0)	1.000
Night-time surgery	5 (0.5)	5 (0.5)	0 (0.0)	1.000
ECC time (min), mean ± SD	161.7±65.9	159.2±63.5	210.1±101.4	0.007
Aortic clamp time (min), mean ± SD	101.1±43.4	100.7±43.1	112.6±51.5	0.129
HCA with SACP, n (%)	225 (23.7)	208 (22.8)	17 (50.0)	<0.001
Circulatory arrest time (min), mean ± SD	26.5±16.4	25.4±15.2	38.5±24.1	0.023
CP time (min), mean ± SD	30.3±23.4	28.9±21.6	47.1±35.2	0.034
Deepest body temperature (℃), mean ± SD	30.4±3.3	30.5±3.2	28.1±4.1	0.002
Site of arterial cannulation, n (%)				
Ascending aorta or aortic arch	758 (80.0)	735 (80.4)	23 (67.6)	0.068
Innominate artery	119 (12.6)	114 (12.5)	5 (14.7)	0.605
Subclavian artery	51 (5.4)	47 (5.1)	4 (11.8)	0.104
Femoral artery	13 (1.4)	11 (1.2)	2 (5.9)	0.076

ECC, extracorporeal circulation; SD, standard deviation; HCA, hypothermic circulatory arrest; SACP, selective antegrade cerebral perfusion; CP, cerebral perfusion.

Table S19 Outcome parameters of patients with aneurysm

Parameters	All (n=948)	No stroke (n=914)	Stroke (n=34)	P value
In-hospital-/30-day mortality, n (%)	31 (3.3)	–	–	–
One-year mortality, n (%)	46 (12.0)	33 (9.12)	13 (65.0)	<0.001
Transient ND, n (%)	11 (1.2)	11 (1.2)	–	–
Resternotomy for bleeding or tamponade, n (%)	81 (8.5)	75 (8.2)	6 (17.6)	0.062
Reanimation or shock, n (%)	43 (4.5)	38 (4.2)	5 (14.7)	0.016
Paraplegia, n (%)	3 (0.3)	1 (0.1)	2 (5.9)	0.004
Recurrent nerve palsy, n (%)	4 (0.4)	3 (0.3)	1 (2.9)	0.136
Pneumonia or other respiratory insufficiency, n (%)	81 (8.5)	66 (7.2)	15 (44.1)	<0.001
Sepsis, n (%)	10 (1.1)	5 (0.5)	5 (14.7)	<0.001
New-onset atrial fibrillation, n (%)	187 (19.7)	182 (19.9)	5 (14.7)	0.454
Myocardial infarction, n (%)	8 (0.8)	7 (0.8)	1 (2.9)	0.254

ND, neurological deficit.

Table S20 Risk factors for stroke after thoracic aortic surgery of patients with aneurysm

Risk factors	OR	95% CI	P value
Advanced age (>70 years)	–	–	0.056
Any atherosclerotic entity	2.62	1.22–5.61	0.014
Chronic kidney disease	4.13	2.00–8.54	<0.001
Preoperative critical state	15.97	3.01–84.85	0.001
Total arch replacement	–	–	0.090
High circulatory arrest time (>60 min)	–	–	0.297

OR, odds ratio; CI, confidence interval.

Table S21 Baseline characteristics of patients undergoing root surgery

Characteristics	All (n=451)	No stroke (n=431)	Stroke (n=20)	P value
Age (years), mean ± SD	54.9±15.5	54.6±15.5	61.6±14.0	0.048
Female gender, n (%)	114 (25.3)	110 (25.5)	4 (20.0)	0.579
Obesity (BMI >35 kg/m²), n (%)	31 (6.9)	31 (7.2)	0 (0.0)	0.384
Arterial hypertension, n (%)	304 (67.4)	286 (66.4)	18 (90.0)	0.027
Any atherosclerotic entity, n (%)	122 (27.1)	112 (26.0)	10 (50.0)	0.018
Coronary artery disease	100 (22.2)	93 (21.6)	7 (35.0)	0.171
Extracardiac arteriopathy	38 (8.4)	32 (7.4)	6 (30.0)	0.004
Atrial fibrillation, n (%)	58 (12.9)	54 (12.5)	4 (20.0)	0.308
IDDM, n (%)	9 (2.0)	9 (2.1)	0 (0.0)	1.000
Chronic lung disease, n (%)	38 (8.4)	34 (7.9)	4 (20.0)	0.078
Smoker, n (%)	178 (39.5)	169 (39.2)	9 (45.0)	0.605
Chronic kidney disease, n (%)	61 (13.5)	55 (12.8)	6 (30.0)	0.040
Previous cardiac surgery, n (%)	48 (10.6)	45 (10.4)	3 (15.0)	0.460
EuroSCORE II, mean ± SD	7.9±9.3	7.5±9.1	15.4±11.8	0.008
Preoperative stroke, n (%)	23 (5.1)	21 (4.9)	2 (10.0)	0.271
Linked to aortic syndrome	4 (0.9)	4 (0.9)	0 (0.0)	1.000
Not linked to aortic syndrome	19 (4.2)	17 (3.9)	2 (10.0)	0.204
Preoperative critical state, n (%)	33 (7.3)	28 (6.5)	5 (25.0)	0.011
Preoperative cerebral malperfusion, n (%)	10 (2.2)	8 (1.9)	2 (10.0)	0.068
Genetic aortic syndrome, n (%)	88 (19.5)	87 (20.2)	1 (5.0)	0.145
Malfunction or infection of TEVAR or aortic graft, n (%)	4 (0.9)	4 (0.9)	0 (0.0)	1.000
Aneurysm, n (%)	368 (81.6)	359 (83.3)	9 (45.0)	<0.001
ATAD, n (%)	53 (11.8)	45 (10.4)	8 (40.0)	0.001
IMH, n (%)	5 (1.1)	4 (0.9)	1 (5.0)	0.204
PAU, n (%)	2 (0.4)	2 (0.5)	0 (0.0)	1.000
Chronic dissection, n (%)	13 (2.9)	12 (2.8)	1 (5.0)	0.450
Aortic rupture, n (%)	12 (2.7)	11 (2.6)	1 (5.0)	0.424
Maximum thoracic aortic diameter (mm), mean ± SD	5.58±1.52	5.59±1.54	5.47±1.04	0.740
Urgency status, n (%)				
Elective	381 (84.5)	370 (85.8)	11 (55.0)	0.001
Urgent	9 (2.0)	9 (2.1)	0 (0.0)	1.000
Emergent or salvage	61 (13.5)	52 (12.1)	9 (45.0)	<0.001

SD, standard deviation; BMI, body mass index; IDDM, insulin-dependent diabetes mellitus; TEVAR, thoracic endovascular aortic repair; ATAD, acute type A dissection; IMH, intramural hematoma; PAU, penetrating atherosclerotic ulcer.

Table S22 Surgical procedures of patients undergoing root surgery

Procedures	All (n=451)	No stroke (n=431)	Stroke (n=20)	P value
Bentall procedure, n (%)	230 (51.0)	214 (49.7)	16 (80.0)	0.008
Valve-sparing root replacement, n (%)	221 (49.0)	217 (50.3)	4 (20.0)	0.008
Arch procedure, n (%)	145 (32.2)	132 (30.6)	13 (65.0)	0.001
Hemiarch	100 (22.2)	94 (21.8)	6 (30.0)	0.410
Total arch	45 (10.0)	38 (8.8)	7 (35.0)	0.002
Conventional	13 (2.9)	13 (3.0)	0 (0.0)	1.000
FET	32 (7.1)	25 (5.8)	7 (35.0)	<0.001
Simplified FET technique	14 (3.1)	12 (2.8)	2 (10.0)	0.124
Concomitant surgery, n (%)				
CABG	61 (13.5)	53 (12.3)	8 (40.0)	0.002
TVR	6 (1.3)	6 (1.4)	0 (0.0)	1.000
MVR	20 (4.4)	20 (4.6)	0 (0.0)	1.000
VAD implantation	2 (0.4)	2 (0.5)	0 (0.0)	1.000

FET, frozen elephant trunk; CABG, coronary artery bypass grafting; TVR, tricuspid valve replacement; MVR, mitral valve repair; VAD, ventricular assist device.

Table S23 Intraoperative data of patients undergoing root surgery

Intraoperative data	All (n=451)	No stroke (n=431)	Stroke (n=20)	P value
Aortic surgeon (>20 aortic procedures per year), n (%)	301 (66.7)	289 (67.1)	12 (60.0)	0.513
Time of surgery, n (%)				
Weekend surgery	14 (3.1)	13 (3.0)	1 (5.0)	0.475
Night-time surgery	51 (11.3)	41 (9.5)	10 (50.0)	<0.001
ECC time (min), mean ± SD	219.0±77.7	214.5±70.8	318.5±138.7	0.004
Aortic clamp time (min), mean ± SD	142.0±49.4	140.4±47.5	178.0±71.8	0.036
HCA with SACP, n (%)	124 (27.5)	113 (26.2)	11 (55.0)	0.005
Circulatory arrest time (min), mean ± SD	35.2±31.3	33.2±27.8	52.1±51.5	0.181
CP time (min), mean ± SD	39.8±35.3	36.6±30.2	70.7±60.2	0.065
Deepest body temperature (℃), mean ± SD	29.5±3.4	29.7±3.3	26.5±4.1	<0.001
Site of arterial cannulation, n (%)				
Ascending aorta or aortic arch	346 (76.7)	336 (78.0)	10 (50.0)	0.011
Innominate artery	55 (12.2)	52 (12.1)	3 (15.0)	0.723
Subclavian artery	39 (8.6)	32 (7.4)	7 (35.0)	0.001
Femoral artery	4 (0.9)	4 (0.9)	0 (0.0)	1.000

ECC, extracorporeal circulation; SD, standard deviation; HCA, hypothermic circulatory arrest; SACP, selective antegrade cerebral perfusion; CP, cerebral perfusion.

Table S24 Outcome parameters of patients undergoing root surgery

Parameters	All (n=451)	No stroke (n=431)	Stroke (n=20)	P value
In-hospital-/30-day mortality, n (%)	17 (3.8)	12 (2.8)	5 (25.0)	<0.001
One-year mortality, n (%)	25 (10.6)	15 (6.8)	10 (66.7)	<0.001
Transient ND, n (%)	10 (2.2)	10 (2.3)	–	–
Resternotomy for bleeding or tamponade, n (%)	52 (11.5)	42 (9.7)	10 (50.0)	<0.001
Reanimation or shock, n (%)	28 (6.2)	24 (5.6)	4 (20.0)	0.029
Paraplegia, n (%)	2 (0.4)	1 (0.2)	1 (5.0)	0.087
Recurrent nerve palsy, n (%)	6 (1.3)	6 (1.4)	0 (0.0)	1.000
Pneumonia or other respiratory insufficiency, n (%)	51 (11.3)	43 (10.0)	8 (40.0)	0.001
Sepsis, n (%)	8 (1.8)	6 (1.4)	2 (10.0)	0.045
New-onset atrial fibrillation, n (%)	79 (17.5)	76 (17.6)	3 (15.0)	1.000
Myocardial infarction, n (%)	6 (1.3)	5 (1.2)	1 (5.0)	0.239

ND, neurological deficit.

Table S25 Risk factors for stroke after thoracic aortic surgery of patients undergoing root surgery

Risk factors	OR	95% CI	P value
Advanced age (>70 years)	3.23	1.23–8.48	0.017
Preoperative critical state	–	–	0.668
ATAD	6.58	2.48–17.46	<0.001
Total arch replacement	–	–	0.042

ATAD, acute type A dissection; OR, odds ratio; CI, confidence interval.

Table S26 Baseline characteristics of patients undergoing total arch replacement

Characteristics	All (n=203)	No stroke (n=181)	Stroke (n=22)	P value
Age (years), mean ± SD	62.1±14.2	61.9±14.0	64.5±15.7	0.408
Female gender, n (%)	86 (42.4)	77 (42.5)	9 (40.9)	0.884
Obesity (BMI >35 kg/m²), n (%)	7 (3.4)	7 (3.9)	0 (0.0)	1.000
Arterial hypertension, n (%)	179 (88.2)	159 (87.8)	20 (90.9)	1.000
Any atherosclerotic entity, n (%)	102 (50.2)	88 (48.6)	14 (63.6)	0.183
Coronary artery disease	59 (29.1)	49 (27.1)	10 (45.5)	0.073
Extracardiac arteriopathy	67 (33.0)	58 (32.0)	9 (40.9)	0.404
Atrial fibrillation, n (%)	24 (11.8)	21 (11.6)	3 (13.6)	0.730
IDDM, n (%)	7 (3.4)	6 (3.3)	1 (4.5)	0.558
Chronic lung disease, n (%)	33 (16.3)	28 (15.5)	5 (22.7)	0.367
Smoker, n (%)	71 (35.0)	62 (34.3)	9 (40.9)	0.537
Chronic kidney disease, n (%)	85 (41.9)	75 (41.4)	10 (45.5)	0.718
Previous cardiac surgery, n (%)	44 (21.7)	38 (21.0)	6 (27.3)	0.583
EuroSCORE II, mean ± SD	14.9±14.6	14.7±14.8	17.5±13.4	0.390
Preoperative stroke, n (%)	23 (11.3)	22 (12.1)	1 (4.5)	0.478
Linked to aortic syndrome	7 (3.4)	7 (3.9)	0 (0.0)	1.000
Not linked to aortic syndrome	16 (7.9)	15 (8.3)	1 (4.5)	1.000
Preoperative critical state, n (%)	44 (21.7)	40 (22.1)	4 (18.2)	0.790
Preoperative cerebral malperfusion, n (%)	19 (9.4)	14 (7.7)	5 (22.7)	0.039
Genetic aortic syndrome, n (%)	35 (17.2)	33 (18.2)	2 (9.1)	0.380
Malfunction or infection of TEVAR or aortic graft, n (%)	4 (2.0)	2 (1.1)	2 (9.1)	0.059
Aneurysm, n (%)	70 (34.5)	62 (34.3)	8 (36.4)	0.844
ATAD, n (%)	62 (30.5)	54 (29.8)	8 (36.4)	0.530
IMH, n (%)	8 (3.9)	8 (4.4)	0 (0.0)	0.603
PAU, n (%)	8 (3.9)	7 (3.9)	1 (4.5)	1.000
Chronic dissection, n (%)	45 (22.2)	42 (23.2)	3 (13.6)	0.419
Aortic rupture, n (%)	21 (10.3)	16 (8.8)	5 (22.7)	0.059
Maximum thoracic aortic diameter (mm), mean ± SD	5.80±1.38	5.83±1.41	5.59±1.18	0.469
Urgency status, n (%)				
Elective	121 (59.6)	108 (59.7)	13 (59.1)	0.958
Urgent	18 (8.9)	16 (8.8)	2 (9.1)	1.000
Emergent or salvage	64 (31.5)	57 (31.5)	7 (31.8)	0.975

SD, standard deviation; BMI, body mass index; IDDM, insulin-dependent diabetes mellitus; TEVAR, thoracic endovascular aortic repair; ATAD, acute type A dissection; IMH, intramural hematoma; PAU, penetrating atherosclerotic ulcer.

Table S27 Surgical procedures of patients undergoing total arch replacement

Procedures	All (n=203)	No stroke (n=181)	Stroke (n=22)	P value
Aortic root surgery, n (%)	45 (22.2)	38 (21.0)	7 (31.8)	0.278
Bentall procedure	27 (13.3)	22 (12.2)	5 (22.7)	0.183
Valve-sparing root replacement	18 (8.9)	16 (8.8)	2 (9.1)	1.000
Wheat (supracoronary + AVR), n (%)	11 (5.4)	10 (5.5)	1 (4.5)	1.000
Conventional, n (%)	69 (34.0)	61 (33.7)	8 (36.4)	0.803
FET, n (%)	134 (66.0)	120 (66.3)	14 (63.6)	0.803
Simplified FET technique	70 (34.5)	67 (37.0)	3 (13.6)	0.029
Concomitant surgery, n (%)				
CABG	20 (9.9)	13 (7.2)	7 (31.8)	0.002
TVR	4 (2.0)	4 (2.2)	0 (0.0)	1.000
MVR	3 (1.5)	2 (1.1)	1 (4.5)	0.292

AVR, aortic valve replacement; FET, frozen elephant trunk; CABG, coronary artery bypass grafting; TVR, tricuspid valve replacement; MVR, mitral valve repair.

Table S28 Intraoperative data of patients undergoing total arch replacement

Intraoperative data	All (n=203)	No stroke (n=181)	Stroke (n=22)	P value
Aortic surgeon (>20 aortic procedures per year), n (%)	159 (78.3)	140 (77.3)	19 (86.4)	0.421
Time of surgery, n (%)				
Weekend surgery	13 (6.4)	11 (6.1)	2 (9.1)	0.637
Night-time surgery	46 (22.7)	39 (21.5)	7 (31.8)	0.286
ECC time (min), mean ± SD	263.8±78.5	256.1±71.8	327.1±102.5	0.004
Aortic clamp time (min), mean ± SD	130.5±54.7	126.7±50.3	161.1±77.1	0.053
HCA with SACP, n (%)	195 (96.1)	174 (96.1)	21 (95.5)	1.000
Circulatory arrest time (min), mean ± SD	55.8±27.7	54.4±26.2	68.4±36.7	0.028
CP time (min), mean ± SD	74.0±32.5	72.3±31.7	88.0±36.7	0.031
Deepest body temperature (℃), mean ± SD	24.2±1.9	24.2±1.9	23.7±1.6	0.215
Site of arterial cannulation, n (%)				
Ascending aorta or aortic arch	75 (36.9)	66 (36.5)	9 (40.9)	0.683
Innominate artery	42 (20.7)	36 (19.9)	6 (27.3)	0.411
Subclavian artery	83 (40.9)	76 (42.0)	7 (31.8)	0.360
Femoral artery	4 (2.0)	4 (2.2)	0 (0.0)	1.000

ECC, extracorporeal circulation; SD, standard deviation; HCA, hypothermic circulatory arrest; SACP, selective antegrade cerebral perfusion; CP, cerebral perfusion.

Table S29 Outcome parameters of patients undergoing total arch replacement

Parameters	All (n=203)	No stroke (n=181)	Stroke (n=22)	P value
In-hospital-/30-day mortality, n (%)	26 (12.8)	14 (7.7)	12 (54.5)	<0.001
One-year mortality, n (%)	34 (28.8)	20 (20.2)	14 (73.7)	<0.001
Transient ND, n (%)	14 (6.9)	14 (7.7)	–	–
Resternotomy for bleeding or tamponade, n (%)	26 (12.8)	19 (10.5)	7 (31.8)	0.011
Reanimation or shock, n (%)	18 (8.9)	13 (7.2)	5 (22.7)	0.031
Paraplegia, n (%)	7 (3.4)	6 (3.3)	1 (4.5)	0.558
Recurrent nerve palsy, n (%)	24 (11.8)	23 (12.7)	1 (4.5)	0.482
Pneumonia or other respiratory insufficiency, n (%)	50 (24.6)	44 (24.3)	6 (27.3)	0.761
Sepsis, n (%)	11 (5.4)	7 (3.9)	4 (18.2)	0.021
New-onset atrial fibrillation, n (%)	21 (10.3)	18 (9.9)	3 (13.6)	0.708
Myocardial infarction, n (%)	1 (0.5)	1 (0.6)	0 (0.0)	1.000

ND, neurological deficit.

Table S30 Risk factors for stroke after total aortic arch replacement

Risk factors	OR	95% CI	P value
Preoperative cerebral malperfusion	–	–	0.105
Simplified FET	0.28	0.08–1.02	0.053
Concomitant CABG	5.73	1.94–16.9	0.002
High circulatory arrest time (>60 min)	–	–	0.709

FET, frozen elephant trunk; CABG, coronary artery bypass grafting; OR, odds ratio; CI, confidence interval.