Risk factors for cerebral complications after type A aortic dissection surgery: single center's experience

Yunxing Xue[1,2,3#], Chang Liu[2,3,4#], Lin Mi[2,3], Yang Chen[2,3], Dongjin Wang[1,2,3,4]

[1]Nanjing Drum Tower Hospital Clinical College of Nanjing Medical University, Nanjing, China; [2]Department of Cardiothoracic Surgery, Nanjing Drum Tower Hospital, The Affiliated Hospital of Nanjing University Medical School, Nanjing, China; [3]Institute of Cardiothoracic Vascular Disease, Nanjing University, Nanjing, China; [4]Clinical College of Traditional Chinese and Western Medicine, Nanjing University of Chinese Medicine, Nanjing, China

Contributions: (I) Conception and design: Y Xue; (II) Administrative support: Y Chen, D Wang; (III) Provision of study materials or patients: C Liu, L Mi; (IV) Collection and assembly of data: C Liu, L Mi; (V) Data analysis and interpretation: Y Xue; (VI) Manuscript writing: All authors; (VII) Final approval of manuscript: All authors.

[#]These authors contributed equally to this work.

Correspondence to: Dongjin Wang, MD, PhD. 321 Zhongshan Road, Nanjing 210000, China. Email: dongjinwang_gl@163.com.

Background: The objective of this study was to retrospectively review the rate and risk factors of cerebral complications (CC) after type A aortic dissection (TAAD) surgery.

Methods: A total of 746 TAAD patients who underwent hypothermic circulatory arrest (HCA) surgery were enrolled. Postoperative CC were defined as intracranial hemorrhage or ischemic infarct stroke as confirmed by cranial CT scan. Multivariable logistic regression analysis was used to investigate the risk factors for CC and mortality. To identify the risk role of arch repair methods and flow rate in antegrade cerebral perfusion (ACP), propensity-score matching studies were performed (conservative vs. total arch replacement, n=135; low vs. normal flow rate, n=148).

Results: Thirty-five patients developed CC (6 with intracranial hemorrhage and 29 with ischemic stroke). Thirty-day mortality (34.3%) among patients with CC was significantly higher than that among patients without CC (12.2%). Multivariable logistic regression analysis identified preoperative cerebral ischemia, limb ischemia, end-stage renal disease, and salvage surgery as risk factors for postoperative CC. CAR (P=0.044; odds ratio, 4.587; 95% CI: 1.045–20.130) and low flow rate ACP (P=0.046; odds ratio, 2.139; 95% CI: 1.014–4.515) had protective roles. In the propensity-score matching studies, the CAR group (0.7% and 9.6%, P=0.005 and 0.175, respectively) and the low flow rate ACP group had lower rates of mortality (8.8% and 5.4%, P=0.067 and 0.012, respectively) and CC.

Conclusions: CC are common and lethal after TAAD surgery. Low-flow ACP could be a safer and suitable antegrade perfusion method for cerebral protection.

Keywords: Aortic dissection; cerebral complication; cerebral perfusion

Introduction

Cerebral complications (CC) are severe postoperative complications of type A aortic dissection (TAAD) surgery. The rate of CC has been reported be as high as 10–30% and will increase the rate of mortality 2- to 3-fold (1,2).

Previous retrospective studies found that the methods of aortic arch surgery, arterial cannulation, hypothermic strategy and cerebral perfusion were risk factors of CC (3). As results from different studies were controversial, there are no standards of cerebral protection during TAAD surgery. And no prospective randomized trial is available

for TAAD surgery, thus we retrospective reviewed the data from our center with a large cohort to analyze the risk factors for CC after TAAD surgical repair.

We present the following article in accordance with the STROBE reporting checklist (available at https://dx.doi.org/10.21037/apm-20-2365).

Methods

Patients

From January 2010 to December 2017, 746 patients diagnosed with Stanford TAAD underwent surgery in our center. Among them, 711 patients had not developed CC (non-CC group), and 35 patients were diagnosed with CC (CC group) after surgery. Six patients had intra cranial hemorrhage, and 29 patients had ischemic infarct stroke. All patients in the CC group received head CT scans, and positive intracranial lesions were identified. CC referred to those of a focal (stroke) or global (parkinsonism, coma, gait disturbance) nature that persisted at discharge from the hospital (4).

The clinical preoperative, operative, and postoperative characteristics were collected through the electronic charts of all patients. We retrieved the data retrospectively by a review of hospital records, and individual consent for this retrospective analysis was waived. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by the Institutional Review Board of Nanjing Drum Tower Hospital (No. 2020-185-01).

Surgical approach

The surgical approaches were reported in our previous articles on TAAD. We chose different methods for aortic arch repair according to the patients' anatomic indications (5-7). Partial aortic arch replacement was defined as conservative arch repair (CAR), and total arch replacement and arch stent procedures were defined as total arch repair (TAR). In a subsequent propensity-score matching analysis, the TAR group was divided into two subgroups: the Total-arch group and the Arch-stent group. Root repair was performed with the reinforcement reconstruction method as previously reported (8,9). The Bentall procedure was performed as described in the literature.

Cannulation and cerebral perfusion method

The right axillary artery and femoral artery were the first

choices for arterial cannulation. Based on the expected duration of the circulatory arrest and the intended surgical procedure, we decided to use antegrade cerebral perfusion (ACP), retrograde cerebral perfusion (RCP) or no cerebral perfusion. Intraoperative cerebral oxygen testing was used to assess the effectiveness of intraoperative cerebral perfusion. When the value was below 20% of the baseline, we considered the cerebral perfusion to have had an effect and obtained additional measurements. For an expected arrest time of more than 30 minutes, the target value of cerebral temperature (Nasopharyngeal temperature) was 18–20 ℃. For an arrest time of less than 30 minutes, the target value was 20–22 ℃. Only a very small number of patients were assigned a cerebral temperature of 25 ℃. In the ACP subgroup, before December 2015, we used an ACP perfusion rate of 6–10 mL/kg/min. After January 2016, we have further reduced the flow rate to 3–5 mL/kg/min.

Statistical analysis

Continuous variables are presented as the mean ± standard deviation (after verifying the normality of the distribution of the data). Categorical variables are presented as absolute numbers and proportions. Data analysis was performed using SPSS 23 Statistics software (IBM, Herrenberg, Germany). Differences in categorical variables were analyzed using the χ^2 test. Differences in continuous variables were tested using the t-test, or the Mann-Whitney U test, respectively. Multivariable analysis was performed using a binary logistic regression model to discriminate independent risk factors for 30-day mortality and CC. Kaplan-Meier survival analysis was used to compare the long-term follow-up survival rate between the non-CC and CC groups in terms of the odds ratio (OR) and the 95% confidence interval (CI). A value of P<0.05 was considered statistically significant. In the propensity-score matching step, sex, age, and other preoperative characteristics were entered into a logistic regression model to estimate the propensity score. The best balance was reflected by a standardized difference below 10%.

Results

Comparable analysis between the non-CC and CC group

The average age was 52.1±13.0 years, and 75.9% of the patients were male. The mean body mass index (BMI) was 25.6±3.9 (kg/m^2). A total of 575 patients (77.1%) had

7460

Xue et al. Cerebral complication after TAAD surgery

hypertension. Cerebral malperfusion was more common in the CC group (non-CC vs. CC, 9.6 vs. 40.0%, P=0.000). The ratio of permanent preoperative cerebral ischemic events was significantly higher in the CC group (P=0.001). According to the preoperative critical status, more patients in the CC group received emergent or salvage operations, although the difference with the non-CC group was not significant (P=0.060). The total average of operation time was 8.4±2.0 hours, with cardiopulmonary bypass (CPB) and aortic clamp times of 247.3±83.6 and 169.4±64.5 minutes, respectively. The average time of hypothermic cerebral arrest (HCA) was different between the two groups (non-CC vs. CC, 29.3±12.0 vs. 31.1±8.7 minutes, P=0.036). CAR induced significantly lower rates of CC. Access through the axillary artery had the lowest rate of CC. A total of 3.4% of patients with a low flow rate and 7.0% with a normal flow rate experienced CC (P=0.035). The 30-day mortality was 13.3% (99/746); patients in the CC group had significantly higher mortality than those in the non-CC group (non-CC vs. CC, 12.2% vs. 34.3%, P=0.001). The proportion of patients with prolonged mechanical ventilation was higher in the CC group (non-CC vs. CC, 18.3% vs. 37.1%, P=0.006). A total of 1.5% patients of all patients developed paraplegia, which was more common in the CC group (non-CC vs. CC, 1.0% vs. 11.4%, P=0.001). Other morbidities of common complications were nearly similar (*Table 1*).

In multivariable analysis, risk factors for mortality included age, tamponade, end-stage kidney disease (ESKD), operation time, salvage surgery, CC, extracorporeal membrane oxygenation (ECMO) support, continuous renal replacement therapy (CRRT) and re-intubation (*Figure 1A*). The independent risk factors for CC were preoperative cerebral ischemia, limb ischemia, ESKD, and salvage surgery (*Figure 1B*). Postoperative risk factors were paraplegia and mechanical ventilation. A low flow rate in ACP was a protective factor both for both mortality and CC, and CAR acted as a protective factor for CC. After adjustment, CAR (P=0.044; odds ratio, 4.587; 95% CI: 1.045–20.130) and a low flow rate in ACP (P=0.046; odds ratio, 2.139; 95% CI: 1.014–4.515) remained protective against CC (*Table 2*).

In the Kaplan-Meier survival analysis, we found that there were no differences between the non-CC and CC groups (P=0.68, *Figure 2*).

CAR: propensity-score matching analysis

Three groups with 135 patients in each group were compared. Preoperative risk factors were consistent without differences. The times of CPB, X clamp and HCA were all significantly different. The CPB time was longer in total-arch group (non-arch vs. total-arch vs. arch-stent: 218.5±61.5 vs. 265.3±90.0 vs. 223.7±124.6 minutes, P=0.000); similar observations were made for X clamp and HCA time. The morbidity rate for CC was higher in the Arch-stent group (non-arch vs. total-arch vs. arch-stent, 0.7% vs. 3.0% vs. 8.9%, P=0.000), and the mortality rate was higher in the total-arch group (non-arch vs. total-arch vs. arch-stent, 9.6% vs. 17.0% vs. 11.9%, P=0.175) (*Table 3*).

Low flow rate in ACP: propensity-score matching analysis

Two separate groups of 148 patients each were compared. No differences were found in baseline demographic data, surgical methods, or intraoperative details. However, both the rate of CC and mortality were higher in the normal flow rate group (normal vs. low flow rate in ACP, CC: 10.8% vs. 5.4%, P=0.067; mortality: 19.6% vs. 8.8%, P=0.012) (*Table 4*).

Discussion

Prevalence and risk factors

TAAD is a lethal disease with high mortality and morbidity despite improvements in surgical techniques and organ protection methods. CC are the main complications after surgical repair for aortic dissection. In an STS database review, the operative mortality was 17%, and the incidence of postoperative stroke was 13% (3). The German registry for acute aortic dissection type A reported that the incidence of permanent neurological dysfunction (PND) was 13.4%, the 30-day mortality was 15.9%, and PND patient mortality was 21.5% (2). The Japanese adult cardiovascular surgery database revealed a mortality of 6.1% and a stroke rate of 7.0% among all patients with total arch replacement, but the subgroup of aortic dissection comprised only 22.9% of the total (10). Wang and colleagues investigated the largest group from China, consisting of 1,708 patients with 57.8% of acute aortic dissection, and the overall PND rate was 4.8%, with a mortality of 6.1% (11). Our single-center results were are nearly consistent with these results obtained from a patient database.

Preoperative cerebral ischemia has a strong relationship with postoperative CC and mortality, but the indications for emergent surgery for these patients are not clear. Of the 1,873 patients with type A dissection enrolled in IRAD, 87

Table 1 Characteristics in patient with post operation cerebral complications (CC) and without that (non-CC) in a retrospective analysis

Variable	Total (N=746)	Non-CC (N=711)	CC (N=35)	P value
Preoperative characteristics				
Age (years)	52.1±13.0	52.1±13.0	52.4±10.9	0.877
Gender (male), n (%)	566 (75.9)	538 (75.7)	28 (80.0)	0.362
BMI (kg/m²)	25.6±3.9	25.5±3.9	26.7±4.3	0.648
Dissection type, n (%)				0.430
Acute,	684 (91.7)	651 (91.6)	33 (94.3)	
Chronic	62 (8.3)	60 (8.4)	2 (5.7)	
Hypertension, n (%)	575 (77.1)	523 (73.6)	25 (71.4)	0.456
Medicine control	187 (32.5)	179 (34.2)	8 (32.0)	0.503
Diabetes, n (%)	30 (4.0)	24 (3.4)	4 (1.1)	0.037
Smoking, n (%)	133 (17.8)	113 (15.9)	8 (22.9)	0.192
Alcohol, n (%)	86 (11.5)	73 (10.3)	8 (22.9)	0.028
Marfan's, n (%)	19 (2.5)	19 (2.7)	0 (0.0)	0.397
Previous cardiac surgery, n (%)				
AVR/Bentall	10 (1.3)	10 (1.3)	0 (0.0)	0.617
TEVAR/EVAR	19 (2.5)	19 (2.7)	0 (0.0)	0.397
Previous coronary artery disease history, n (%)	19 (2.5)	19 (2.7)	0 (0.0)	0.397
ESKD, n (%)	12 (1.6)	10 (1.4)	2 (5.7)	0.105
Stroke history, n (%)	13 (1.7)	11 (1.6)	2 (5.7)	0.121
Tamponade, n (%)	118 (15.8)	111 (15.6)	7 (20.0)	0.310
Coronary malperfusion, n (%)	113 (15.1)	108 (15.2)	5 (14.3)	0.558
Limb malperfusion, n (%)	102 (13.7)	94 (13.2)	8 (22.9)	0.091
Mesenteric malperfusion, n (%)	41 (5.5)	39 (5.5)	2 (5.7)	0.586
Cerebral malperfusion, n (%)	82 (11.0)	68 (9.6)	14 (40.0)	0.000
Transient	72	64	8	0.001
Permanent	10	4	6	
Operative characteristics				
Surgical status, n (%)				0.060
Salvage	14 (1.9)	13 (1.8)	1 (2.9)	
Emergent	457 (76.4)	426 (59.9)	31 (88.6)	
Elective	162 (21.7)	159 (22.4)	3 (8.6)	
Operation time (h)	8.4±2.0	8.4±2.0	8.6±2.3	0.471
CPB (min)	247.3±83.6	247.3±84.3	248.0±69.2	0.956
X clamp (min)	169.4±64.5	169.5±64.8	166.9±59.9	0.592
DHCA (min)	29.4±11.8	29.3±12.0	31.1±8.7	0.036

Table 1 (*continued*)

7462

Xue et al. Cerebral complication after TAAD surgery

Table 1 (*continued*)

Variable	Total (N=746)	Non-CC (N=711)	CC (N=35)	P value
Arch surgery, n (%)				0.024
CAR	156 (20.9)	154 (21.7)	2 (5.7)	
TAR	590 (79.1)	557 (78.3)	33 (94.3)	
Cannulation site, n (%)				0.405
Right axillary artery	209 (28.0)	203 (28.6)	6 (17.1)	
Femoral artery	101 (13.5)	97 (13.6)	4 (13.4)	
Right axillary artery + femoral artery	424 (56.8)	400 (56.3)	24 (68.6)	
Others	12 (1.6)	11 (1.5)	1 (2.9)	
Perfusion method, n (%)				0.785
Direct hypothermia without perfusion	65 (8.7)	63 (8.9)	2 (5.7)	
Antegrade perfusion	630 (69.1)	600 (84.4)	30 (85.7)	
Unilateral	617 (67.7)	587 (82.6)	30 (85.7)	
Bilateral	13 (1.4)	13 (1.8)	0 (0.0)	
Retrograde perfusion	51 (6.8)	48 (6.8)	3 (8.6)	
Temperature of hypothermia (nasopharyngeal), ℃	20.7±2.8 (14 to 30)	20.9±2.9	21.0±2.2	0.079
Deep, n (%)	465 (62.3)	447 (62.9)	18 (3.9)	0.119
Moderate, n (%)	281 (37.7)	264 (37.1)	17 (6.1)	
Perfusion flow in antegrade perfusion patients	N=630	N=600	N=30	0.035
Low flow perfusion rate (3–5 mL/kg/min), n (%)	388 (53.8)	375 (52.7)	13 (3.4)	
High flow perfusion rate (5–10 mL/kg/min), n (%)	242 (46.2)	225 (31.6)	17 (7.0)	
Postoperative characteristics				
Mechanical ventilation (hours)	71.4±77.7	71.6±77.5	66.1±84.2	0.468
Prolonged ventilation, n (%)	143 (19.2)	130 (18.3)	13 (37.1)	0.006
Re-intubation, n (%)	37 (5.0)	36 (5.1)	1 (2.9)	0.471
Tracheotomy, n (%)	13 (1.7)	12 (1.6)	1 (5.7)	0.121
Paraplegia, n (%)	11 (1.5)	7 (1.0)	4 (11.4)	0.001
ECMO, n (%)	28 (3.8)	7 (3.8)	1 (2.9)	0.364
IABP, n (%)	6 (0.8)	6 (0.8)	0 (0.0)	0.749
CRRT, n (%)	76 (10.2)	72 (10.1)	4 (11.4)	0.486
Re-exploration, n (%)	50 (6.7)	48 (6.8)	2 (5.7)	0.579
GI bleeding, n (%)	6 (0.8)	6 (0.8)	0 (0.0)	0.749
Bowl Ischemia, n (%)	8 (1.1)	8 (1.1)	0 (0.0)	0.680
Surgical site infection, n (%)	20 (2.7)	18 (2.5)	2 (5.7)	0.240
ICU (day)	9.2±9.6	9.1±9.5	15.2±11.1	0.168
30d-mortality, n (%)	99 (13.3)	87 (12.2)	12 (34.3)	0.001

Dissection type: acute ≤2 weeks, chronic >2 weeks. CC, cerebral complications; CAD, coronary artery disease; ESKD, end stage kidney disease; DHCA, deep hypothermia cardiac arrest; CABG, coronary artery bypass graft; MVR, mitral valve replacement; MVP, mitral valve plasty; TVP, mitral valve plasty; CAR, conservative arch replacement; TAR, total arch replacement; CRRT, continuous renal replacement therapy; GI, gastrointestinal; ICU, intensive care unit.
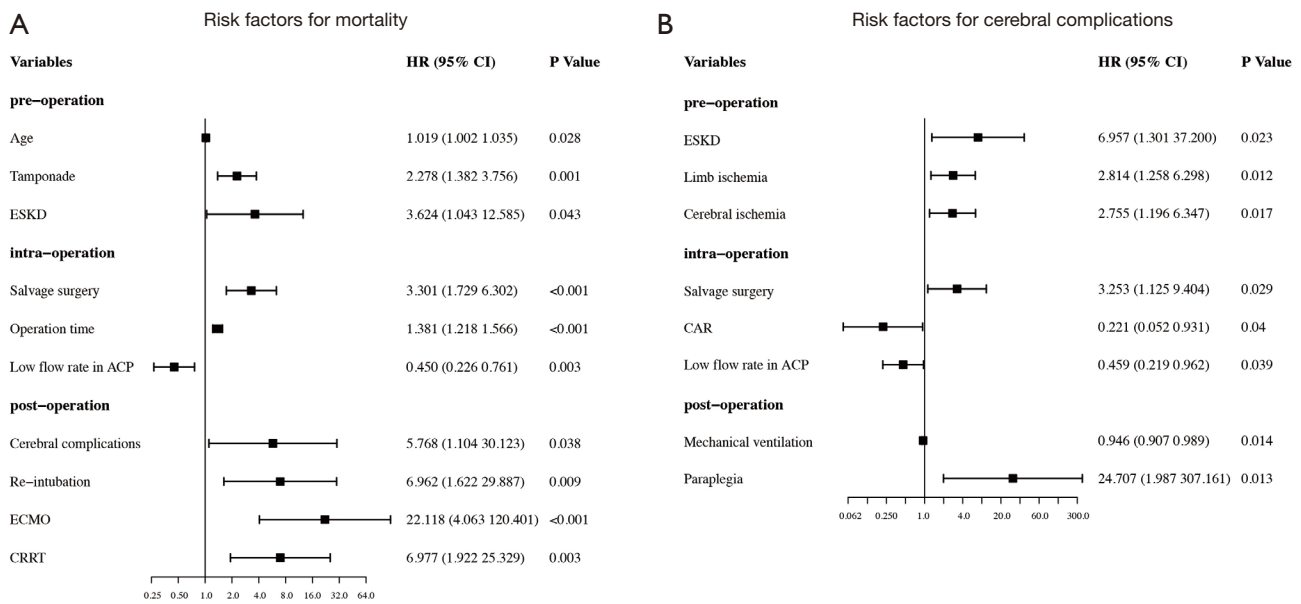
A   Risk factors for mortality

Variables	HR (95% CI)	P Value
pre–operation		
Age	1.019 (1.002 1.035)	0.028
Tamponade	2.278 (1.382 3.756)	0.001
ESKD	3.624 (1.043 12.585)	0.043
intra–operation		
Salvage surgery	3.301 (1.729 6.302)	<0.001
Operation time	1.381 (1.218 1.566)	<0.001
Low flow rate in ACP	0.450 (0.226 0.761)	0.003
post–operation		
Cerebral complications	5.768 (1.104 30.123)	0.038
Re–intubation	6.962 (1.622 29.887)	0.009
ECMO	22.118 (4.063 120.401)	<0.001
CRRT	6.977 (1.922 25.329)	0.003

0.25 0.50 1.0 2.0 4.0 8.0 16.0 32.0 64.0

B   Risk factors for cerebral complications

Variables	HR (95% CI)	P Value
pre–operation		
ESKD	6.957 (1.301 37.200)	0.023
Limb ischemia	2.814 (1.258 6.298)	0.012
Cerebral ischemia	2.755 (1.196 6.347)	0.017
intra–operation		
Salvage surgery	3.253 (1.125 9.404)	0.029
CAR	0.221 (0.052 0.931)	0.04
Low flow rate in ACP	0.459 (0.219 0.962)	0.039
post–operation		
Mechanical ventilation	0.946 (0.907 0.989)	0.014
Paraplegia	24.707 (1.987 307.161)	0.013

0.062 0.250 1.0 4.0 20.0 60.0 300.0

Figure 1 The results of the risk factors for postoperative CC and mortality from multivariate logistic regression analysis. (A) Risk factors for postoperative CC from multivariate logistic regression analysis; (B) risk factors for postoperative mortality from multivariate logistic regression analysis. CC, cerebral complications.

Table 2 Results of multivariable logistic regression of postoperative cerebral complications after adjustment

Variable	OR	95% CI	P value
Age	0.996	0.970–1.023	0.771
Gender (male)	0.783	0.326–1.880	0.584
Cerebral ischemia	0.153	0.071–0.327	0.000
Limb ischemia	0.549	0.240–1.258	0.156
Salvage surgery	0.338	0.149–1.011	0.053
CAR	4.074	1.045–20.130	0.044
Low flow rate	3.981	1.014–4.515	0.046

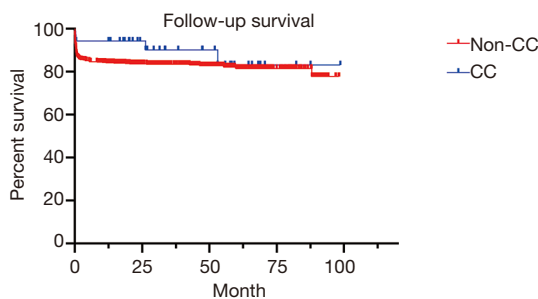CAR, conservative arch replacement.

Figure 2 Follow-up results of comparing CC and non-CC patients. CC, cerebral complications.

(4.6%) presented with cerebrovascular accidents, and 54 (2.9%) presented with coma (12). In our experience, 11.0% (82/746) of patients had preoperative cerebral ischemia, and only 1.3% had preoperative PND. Among them, 14 patients developed CC after surgery, 6 of them with PND before surgery. IRAD found that surgery led to a hospital survival benefit of 49.6% in patients with preoperative neurologic symptoms and 55.6% in those with coma (12). Therefore, we must continue to attempt surgical repair first for these patients with cerebral ischemia.

Brain protections methods: conservative arch repair

In addition to preoperative cerebral ischemia including CC after surgical repair for TAAD, intraoperative brain protection methods are the key factors impacting cerebral outcomes. Ghoreishi listed cannulation strategy, degree of hypothermia, cerebral perfusion method and techniques for arch repair as the main factors that could impact postoperative cerebral complication (3). Among them, hemiarch surgery was shown to play a protective role for the brain. We identified CAR as having a lower rate of CC and mortality than TAR in both the retrospective analysis and propensity-score matching analysis. However, our results are inconsistent with those from retrospective reviews. Rice

Table 3 Among different arch methods group in a perspective study

Variable	CAR (N=135)	TAR, n (%)		P value
		Total-arch (N=135)	Arch-stent (N=135)	
Cerebral complications, n (%)	1 (0.7)	4 (3.0)	11 (8.9)	0.005
Mortality, n (%)	13 (9.6)	23 (17.0)	16 (11.9)	0.175
Age, years	55.7±14.2	49.8±11.8	53.3±13.2	0.429
Cerebral ischemia, n (%)	14 (28.6)	16 (32.7)	19 (38.8)	0.643
Limb ischemia, n (%)	12 (32.4)	13 (35.1)	12 (32.4)	0.971
ESKD, n (%)	2 (1.9)	4 (1.9)	2 (0.9)	0.600
Tamponade, n (%)	29 (26.3)	31 (12.3)	29 (14.4)	0.944
Surgery status (emergency surgery), n (%)	107 (80.1)	96 (76.6)	106 (79.4)	0.220
CPB (min)	218.5±61.5	265.3±89.9	223.7±124.6	0.000
X clamp (min)	153.9±53.0	185.3±62.3	146.0±96.1	0.000
DHCA (min)	28.3±9.7	33.9±9.0	24.9±8.6	0.000
Mechanical ventilation (hours)	41.1±48.1	82.5±92.4	57.3±60.7	0.000
ICU (day)	3.7±4.1	8.0±10.4	4.5±6.1	0.000

Arch stent: including tripled branched arch stent, single branched arch stent and fenestrated arch stent. CAR, conservative arch replacement; TAR, total arch replacement; ESKD, end stage kidney disease; CPB, cardiopulmonary bypass; DHCA, deep hypothermia cardiac arrest; ICU, intensive care unit;

Table 4 Low and high flow rate in ACP in a perspective study

Variable	High flow rate in ACP (6–10 mL/kg/min) (N=148)	Low flow rate in ACP (3–5 mL/kg/min) (N=148)	P value
Cerebral complications, n (%)	16 (10.8)	8 (5.4)	0.067
Mortality, n (%)	29 (19.6)	13 (8.8)	0.012
Age, years	51.1±12.5	51.1±12.7	0.973
Cerebral ischemia, n (%)	20 (13.5)	22 (14.9)	1.000
CPB (min)	252.0±80.0	265.4±108.5	0.307
X clamp (min)	171.9±53.2	176.4±59.1	0.578
DHCA (min)	32.4±8.9	31.0±0.8	0.243

CPB, cardiopulmonary bypass; DHCA, deep hypothermia cardiac arrest; ACP, antegrade cerebral perfusion.

et al. studied 489 patients who underwent TAAD surgery, and the rate of stroke was not significantly different between the total arch group (8.2%) and the hemiarch group (10.5%) (13). Rylski *et al.* also found similar neurological outcomes in a cohort, but TAR was a strong predictor for mortality (14). However, Roselli *et al.* found that the rate of reintervention for patients with hemiarch repair was 38% within 10 years, which suggested more aggressive techniques for arch repair in TAAD (15). In the present study, TAR included arch surgery with arch stents, as described in previous studies (5,6). Arch stents are used to simplify the arch surgery and achieve a reshaping effect with the frozen elephant trunk technique. However, the rate of CC was higher than that of the total arch and CAR groups, while the mortality was lower than that of the total arch group and similar to that of the CAR group. One possible reason for these differences was that the underestimation of the incidence of CC in the case of high

mortality in the total arch group. Another was that arch manipulation could not be avoided during the arch stent procedure. During the HCA period, we had to clamp the innominate artery and left common carotid artery, then insert the arch stent system and release it in anatomical proximity to the proximal artificial vessel. Arterial clamping injury and the potential risk for blood flow from a new stent in the arch position are all possible origins of thrombi and low perfusion, respectively. We considered the possibility of aggressive arch repair to reduce the rate of reintervention, but the method of arch stent repair still has limitations and disadvantages for brain protection based on our results. Investigating the indications and optimizing the surgical manipulations are necessary in future studies.

Brain protection methods: cerebral perfusion and flow rate

In our series, we used different perfusion methods, including direct HCA without perfusion, ACP and RCP, but all had similar rates of CC. HCA is a basic method for aortic arch surgery where body temperature is lowered to preserve organ function and reduce metabolic demand (16). The safety duration of HCA ranges between 25–60 min. The researchers found that an HCA duration longer than 40 minutes will increase the risk of postoperative CC and mortality (17). Despite the safe duration, direct HCA have revealed similar risk for CC. Ghoreishi et al. found that 29% of patients in their cohort had not received an adjunct technique for cerebral perfusion, but it was not found to be a risk factor for postoperative stroke (3). However, in our series, the average time for HCA in the TAR group was longer than 30 minutes, which meant for most patients with HCA, no cerebral perfusion was exposed to damage caused by a prolonged HCA time. This is why adjunct methods are necessary. ACP is widely used and can be physiologically adapted when the duration of ACP is longer (18-21). Keeling et al. retrospectively reviewed 342 patients using moderate hypothermic circulatory arrest and selective ACP. The median circulatory arrest time was 38.9 minutes, the mortality was 11.7%, and the rate of PND was 7.3% (19). In a propensity-score matching analysis consisting of 925 elective aortic arch surgery patients with ACP or HCA alone, the mortality and PND rates were all significantly lower in the ACP group (3.8% and 2.9%, respectively) (21). However, no results on the superiority of ACP in TAAD arch surgery have been confirmed. Angleitner et al.

reported on both unilateral and bilateral ACP for TAAD arch surgery. During the average HCA time of 34 minutes, the rate of PND was 19.0%, and the mortality rate was 14.1% (22). This perplexed us in the early stage after the burden of ischemia resolved with the aid of adjunct ACP. The concepts regarding direct HCA and the clinical findings of facial edema after ACP + HCA surgery inspired us to also consider the burden of luxury-over perfusion from ACP. Autoregulation of cerebral circulation is the key physiological function for maintaining the related normal flow for the brain (23,24). However, cerebral autoregulation can become dysfunctional when the body cools to temperatures lower than 22 ℃. This means that the resistance of cerebral vessels will not increase to adapt to ischemia, and the blood flow of the cerebral circulation will increase, which may be a potential risk factor for increased intracerebral pressures, cerebral edema, and microvascular damage. The weight of normal human adult brain is 1.5% to 3.0% of that of the whole body, and the normal physiological cerebral blood flow is 55 mL/min/100 g of cerebral matter. This means that a blood flow of nearly 8–16 mL/kg/min is necessary at baseline of physiological demand. However, when the temperature decreases, the physiological demand also decrease, reaching is nearly 30% of the baseline at 22 ℃ (25). Therefore, we chose 3–5 mL/kg/min as the perfusion flow rate.

An animal model was used to show that a higher perfusion rate in ACP can not only improve cerebral perfusion to improve metabolism, but also cause intracranial edema (26). No clinical trials can be performed to compare the different flow rates applied for ACP for ethical reasons, but the clinical experiences from our center present new proof of the benefit of a low flow rate for ACP. We used NIRS to detect the cerebral metabolism and adjusted the flow rate based on the baseline value and variated value.

Limitations

This article is a retrospective analysis from a single center. Even with a large cohort of cases, the bias of such a study design cannot be ignored. We attempted to adjust for the preoperative factors in two separated propensity-score matching analyses, but the missing data during this processaffeced the real results. Otherwise, TAAD is primarily emergent or urgent surgery, which we cannot compare factors in an RCT. The data from our single center

7466

Xue et al. Cerebral complication after TAAD surgery

reflect the results from a real-world experience.

Conclusions

In conclusion, our single-center results for TAAD repair, including a mortality of 13.3% and rate of CC of 4.7% were interesting. Preoperative status remained the key factor inducing mortality and adverse cerebral outcomes. Conservative arch repair had lower mortality and morbidity than total arch repair for TAAD, but considering the necessity of TAR, the technique also achieved acceptable results. Low flow rate in ACP may be a safer and potentially better technique for cerebral protection, but it must be compared with traditional methods in the further prospective studies.

Acknowledgments

Footnote

Reporting Checklist: The authors have completed the STROBE reporting checklist. Available at https://dx.doi.org/10.21037/apm-20-2365

Data Sharing Statement: Available at https://dx.doi.org/10.21037/apm-20-2365

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://dx.doi.org/10.21037/apm-20-2365). The 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. We retrieved the data retrospectively by a review of hospital records, and individual consent for this retrospective analysis was waived. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by the Institutional Review Board of Nanjing Drum Tower Hospital (No. 2020-185-01).

Open Access Statement: This is an Open Access article distributed in accordance with the Creative Commons Attribution-NonCommercial-NoDerivs 4.0 International License (CC BY-NC-ND 4.0), which permits the non-commercial replication and distribution of the article with the strict proviso that no changes or edits are made and the original work is properly cited (including links to both the formal publication through the relevant DOI and the license). See: https://creativecommons.org/licenses/by-nc-nd/4.0/.

References

1. Dumfarth J, Kofler M, Stastny L, et al. Stroke after emergent surgery for acute type A aortic dissection: predictors, outcome and neurological recovery. Eur J Cardiothorac Surg 2018;53:1013-20.

2. Kruger T, Weigang E, Hoffmann I, et al. Cerebral protection during surgery for acute aortic dissection type A: results of the German Registry for Acute Aortic Dissection Type A (GERAADA). Circulation 2011;124:434-43.

3. Ghoreishi M, Sundt TM, Cameron DE, et al. Factors associated with acute stroke after type A aortic dissection repair: An analysis of the Society of Thoracic Surgeons National Adult Cardiac Surgery Database. J Thorac Cardiovasc Surg 2020;159:2143-54.e3.

4. Ergin MA, Galla JD, Lansman s L, et al. Hypothermic circulatory arrest in operations on the thoracic aorta. Determinants of operative mortality and neurologic outcome. J Thorac Cardiovasc Surg 1994;107:788-97; discussion 797-9.

5. Pan J, Li QG, Zhou Q, et al. Repair of acute type A aortic dissections using open replacement with triple-branched stent grafts. Ann Thorac Surg 2013;96:559-62.

6. Zhou Q, Xue Y, Cao H, et al. Novel arch fenestrated stent graft for acute Stanford Type A aortic dissection with open antegrade implantation. Interact Cardiovasc Thorac Surg 2018;26:369-75.

7. Xue Y, Pan J, Cao H, et al. Different aortic arch surgery methods for type A aortic dissection: clinical outcomes and follow-up results. Interact Cardiovasc Thorac Surg 2020;31:254-62.

8. Xue Y, Zhou Q, Pan J, et al. Root reconstruction for proximal repair in acute type A aortic dissection. Journal of Thoracic Disease 2019;11:4708-16.

9. Xue Y, Zhou Q, Pan J, et al. "Double Jacket Wrapping" Root Reconstruction for Acute Type A Aortic Dissection. Ann Thorac Surg 2020;110:1060-2.

10. Okita Y, Miyata H, Motomura N, et al. A study of brain

protection during total arch replacement comparing antegrade cerebral perfusion versus hypothermic circulatory arrest, with or without retrograde cerebral perfusion: analysis based on the Japan Adult Cardiovascular Surgery Database. J Thorac Cardiovasc Surg 2015;149:S65-73.

11. Wang X, Yang F, Zhu J, et al. Aortic arch surgery with hypothermic circulatory arrest and unilateral antegrade cerebral perfusion: Perioperative outcomes. J Thorac Cardiovasc Surg 2020;159:374-87.e4.

12. Di Eusanio M, Patel HJ, Nienaber CA, et al. Patients with type A acute aortic dissection presenting with major brain injury: should we operate on them? J Thorac Cardiovasc Surg 2013;145:S213-21.e1.

13. Rice RD, Sandhu HK, Leake SS, et al. Is Total Arch Replacement Associated With Worse Outcomes During Repair of Acute Type A Aortic Dissection? Ann Thorac Surg 2015;100:2159-65; discussion 2165-6.

14. Rylski B, Beyersdorf F, Kari FA, et al. Acute type A aortic dissection extending beyond ascending aorta: Limited or extensive distal repair. J Thorac Cardiovasc Surg 2014;148:949-54; discussion 954.

15. Roselli EE, Loor G, He J, et al. Distal aortic interventions after repair of ascending dissection: the argument for a more aggressive approach. J Thorac Cardiovasc Surg 2015;149:S117-24.e3.

16. Griepp RB, Stinson EB, Hollingsworth JF, et al. Prosthetic replacement of the aortic arch. J Thorac Cardiovasc Surg 1975;70:1051-63.

17. Ganapathi AM, Hanna JM, Schechter MA, et al. Antegrade versus retrograde cerebral perfusion for hemiarch replacement with deep hypothermic circulatory arrest: does it matter? A propensity-matched analysis. J Thorac Cardiovasc Surg 2014;148:2896-902.

18. Comas GM, Leshnower BG, Halkos ME, et al. Acute type a dissection: impact of antegrade cerebral perfusion under moderate hypothermia. Ann Thorac Surg 2013;96:2135-41.

19. Keeling WB, Leshnower BG, Hunting JC, et al. Hypothermia and Selective Antegrade Cerebral Perfusion Is Safe for Arch Repair in Type A Dissection. Ann Thorac Surg 2017;104:767-72.

20. Urbanski PP, Luehr M, Di Bartolomeo R, et al. Multicentre analysis of current strategies and outcomes in open aortic arch surgery: heterogeneity is still an issue. Eur J Cardiothorac Surg 2016;50:249-55.

21. Leontyev S, Davierwala PM, Semenov M, et al. Antegrade selective cerebral perfusion reduced in-hospital mortality and permanent focal neurological deficit in patients with elective aortic arch surgerydagger. Eur J Cardiothorac Surg 2019;56:1001-8.

22. Angleitner P, Stelzmueller ME, Mahr S, et al. Bilateral or unilateral antegrade cerebral perfusion during surgery for acute type A dissection. J Thorac Cardiovasc Surg 2020;159:2159-67.e2.

23. Bachet J. Re: Selective cerebral perfusion using moderate flow in complex cardiac surgery provides sufficient neuroprotection. Are children young adults? Eur J Cardiothorac Surg 2012;42:710-1.

24. Lassen NA. Cerebral blood flow and oxygen consumption in man. Physiol Rev 1959;39:183-238.

25. Ehrlich MP, McCullough JN, Zhang N, et al. Effect of hypothermia on cerebral blood flow and metabolism in the pig. Ann Thorac Surg 2002;73:191-7.

26. Haldenwang PL, Strauch JT, Amann I, et al. Impact of pump flow rate during selective cerebral perfusion on cerebral hemodynamics and metabolism. Ann Thorac Surg 2010;90:1975-84.