Long-Term Outcomes of Surgical Treatment for Acute Type-A Aortic Dissection with Coronary Artery Involvement

Shuyang Lu,^{1,*} MD, Yun Zhao,^{2,*} MD, Kai Song,^{1,*} MD, Wangchao Yao,¹ MD, Le Kang,¹ MD, Jun Li,¹ MD, Yongxin Sun,¹ MD, Hao Lai,¹ MD and Chunsheng Wang,¹ MD

Summary

The surgical strategies for acute type-A aortic dissection (aTAAD) with coronary artery involvement have been controversial, and its prognosis remains unclear. Thus, in this study, we aim to determine the characteristics, surgical strategies, and prognosis of patients with coronary artery involvement due to aTAAD.

Retrospective analysis of 65 consecutive aTAAD patients with coronary artery involvement between September 2005 and January 2012 was performed. The patients were divided into two groups: those treated with aTAAD repair and coronary ostia reimplantation (Neri type-A, group A, $n = 37$) and those with aTAAD repair and coronary artery bypass grafting (Neri type B and C, group B, $n = 28$).

Overall in-hospital mortality was determined to be 8.1% for group A and 21.4% for group B ($P = 0.124$). No significant difference was determined between groups A and B in cardiopulmonary bypass time, cross-clamp time, cerebral perfusion time, and hospitalization time. Intensive care unit (ICU) stay was 5.8 ± 7.4 days for group A, whereas it was 12.4 ± 10.6 days for group B ($P = 0.009$). The morbidity of postoperative temporary and permanent neurological dysfunction was similar between the two groups, while renal and respiratory dysfunction were 8.1% versus 25.0% and 16.2% versus 39.3%, respectively ($P = 0.062$, $P = 0.036$). Average follow-up time was 112.0 ± 44.8 months, and survival curves have not shown statistical significance between two groups ($P = 0.386$).

Coronary artery dissection with Neri type B and C in acute TAAD has been associated with higher early death, but comparable long-term survival after discharge. However, combined immediate coronary artery bypass grafting and aortic repair remains a safe, effective, and acceptable approach to these challenging group of patients.

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Key words: Neri type, Coronary malperfusion, Coronary artery bypass grafting

Acute type-A aortic dissection (aTAAD) has been identified to be a catastrophic medical emergency for patients with a high mortality rate if surgery is not performed. According to the International Registry of Acute Aortic Dissection (IRAD), the in-hospital mortality rate for aTAAD patients receiving surgery is as high as 26.6% versus 55.9% for those treated with medical therapy alone (overall 32.5%).¹⁾ However, even when aTAAD is identified early and surgery is timely, operative mortality remains high. Early reports of perioperative mortalities after repair of type-A aortic dissection were 30% to 60%; however, contemporary results have improved because of advances in surgical techniques and improvement of perioperative management, with most recent reports demon-

strating a perioperative mortality of 3.09% to 30%.¹⁻⁵⁾

Predictors of aTAAD mortality can vary between studies; nonetheless, preoperative status has been demonstrated to be the most important predictor of perioperative hospital mortality. Acute myocardial ischemia or/and infarction due to retrograde dissection of the aortic root reaching the coronary artery ostia is believed to be a potentially fatal condition with poor prognosis. Prompt and optimal interventions to re-establish an adequate coronary blood flow and rescue jeopardized myocardium are recommended for patients with aTAAD with coronary artery involvement.⁶⁾ For peripheral malperfusion, some investigators recommend a strategy of initial percutaneous intervention to restore end-organ perfusion and delayed opera-

From the ¹Department of Cardiovascular Surgery, Zhongshan Hospital, Fudan University, The Shanghai Institute of Cardiovascular Diseases, Shanghai, China and ²Department of Cardiovascular Surgery, Shanghai Geriatrics Center, Shanghai, China.

*These authors contributed equally to this work.

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Address for correspondence: Chunsheng Wang, MD, Hao Lai, MD or Yongxin Sun, MD, Department of Cardiovascular Surgery, Zhongshan Hospital, Fudan University, The Shanghai Institute of Cardiovascular Diseases, No. 1609 Xieta Road, Xuhui District, Shanghai 200032, China. E-mail: wang_cs@126.com or lai.hao@zs-hospital.sh.cn or sun.yongxin@zs-hospital.sh.cn

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Table I. Patient Demographics and Characteristics

Characteristic	Group A	Group B	P-value
Number of patients	37	28	
Age (years)	45.4 ± 9.6	55.1 ± 10.0	0.000
Gender			
Male	29 (78.4%)	18 (64.3%)	0.209
Female	8 (21.6%)	10 (35.7%)	0.209
Hypertension	26 (70.3%)	22 (78.6%)	0.451
DM	7 (18.9%)	8 (28.6%)	0.360
Previous CVA	2 (5.4%)	3 (10.7%)	0.426
PVD	0	1 (3.6%)	0.247
Renal dysfunction	3 (8.1%)	6 (21.4%)	0.124
COPD	0	0	
Previous cardiac surgery	2 (5.4%)	1 (3.6%)	0.727
Previous EVR	0	1 (3.6%)	0.247
AR	11 (29.7%)	7 (25.0%)	0.673
Marfan syndrome	1 (2.7%)	0	0.381
BAV	2 (5.4%)	2 (7.1%)	0.773
Acute myocardial infarction	0	2 (7.1%)	0.099

AR indicates aortic regurgitation; BAV, bicuspid aortic valve; DM, diabetes mellitus; COPD, chronic obstructive pulmonary disease; CVA, cerebrovascular accident; EVR, endovascular repair; and PVD, peripheral vascular disease.

tive repair after resolution of malperfusion syndrome.^{7,8)} Girardi, *et al.* suggest that patients with malperfusion in the setting of aTAAD should undergo immediate aortic reconstruction as the primary means of re-establishing end-organ perfusion.⁹⁾

As in the treatment of peripheral malperfusion, surgical strategies for aTAAD patients with coronary artery involvement remain controversial, and its prognosis remains unclear. In this present study, we review our experience with aortic dissection involving the coronary arteries and elucidate the characteristics, surgical strategies, and prognosis of this special patient cohort.

Methods

The protocol of this study was approved by the Committee for the Protection of Human Subjects at Zhongshan Hospital Fudan University (Shanghai, China). Informed consent was obtained from each patient involved in this study. The study design was retrospective and observational.

Patient demographics and characteristics: Between September 2005 and January 2012, we recruited 65 patients with coronary artery involvement out of the 267 patients who had undergone surgical repair of aTAAD. The mean age was 49.6 ± 10.8 years; age range was 26-70 years old, and 47 were male. The acute phase of aortic dissection was defined as being within 2 weeks from symptom onset to the institution of therapy. Preoperative diagnoses of TAAD were based on the computed tomography angiography and echocardiography results. Types of coronary ostial lesions were described by Neri, *et al.*, and they are as follows: type A, ostial dissection defined as a disruption of the inner layer limited to the area of the coronary ostium; type B, dissection with a coronary false channel; and type C, circumferential detachment with an inner cylinder intussusception.⁶⁾ In addition to the three patients who had preoperative electrocar-

diographic signs of myocardial ischemia, all aTAAD patients with coronary artery involvement were testified by the results of the surgical exploration. Among them, 37 patients with mild coronary artery involvement (Neri type-A) were treated with aTAAD repair and coronary ostia reimplantation (group A), whereas 28 patients with moderate to severe coronary artery involvement (Neri type B and C) were treated with aTAAD repair along with coronary artery bypass grafting (group B).

Although the differences were not statistically significant, preoperative hypertension, diabetes mellitus (DM), and renal dysfunction were more common in the patients of group B (78.6% versus 70.3%, $P = 0.451$, 28.6% versus 18.9%, $P = 0.360$, and 21.4% versus 8.1%, $P = 0.124$, respectively). No significant differences were noted in other preoperative medical disorders between the two groups. Further demographic and preoperative data are summarized in Table I.

Operative technique: Our approach for open aortic arch reconstruction has been described previously in detail.^{10,11)} All patients were carried out by a median sternotomy and total cardiopulmonary bypass (CPB) with selective antegrade cerebral perfusion (ACP). The left radial artery and dorsal artery of foot were cannulated for continuous blood pressure monitoring. Temperature probes were placed for esophagopharyngeal and bladder temperature monitoring. Right axillary artery and right femoral artery were routinely used for arterial perfusion cannulation. Circulatory arrest was initiated when the nasopharyngeal temperature reached 17°C to 22°C and bladder temperature reached 26°C to 28°C. Pharmacological agents (thiamylal sodium, phenytoin, and mannitol) were then administered for brain protection in addition to ice packs placed around the head. The right axillary artery was used for selective ACP during arch reconstruction. The flow rate was maintained at 8 mL/kg/minute to 10 mL/kg/minute and the perfusion pressure at 40 mmHg to 50 mmHg.

Open aortic arch reconstruction techniques for this

Table II. Surgical Strategy

Variables	Group A	Group B	<i>P</i> -value
Extent of aortic procedure			
AAR+HAR	9 (24.3%)	5 (17.9%)	0.530
AAR+TAR (4-branch prosthetic graft)	14 (37.8%)	7 (25.0%)	0.273
AAR+TAR (island anastomosis)	13 (35.1%)	15 (53.6%)	0.137
AAR+Triple-branched stent graft implantation	1 (2.7%)	1 (3.6%)	0.841
Elephant trunk technique	21 (56.8%)	20 (71.4%)	0.225
Concomitant procedures			
Ascending aorta replacement	37 (100%)	28 (100%)	
Bentall operation (mechanical valve)	30 (81.1%)	8 (28.6%)	0.000
David operation	5 (13.5%)	4 (14.3%)	0.929
Cabrol operation	2 (5.4%)	0	0.211
Wheat operation	0	3 (10.7%)	0.041
Aortic root reinforcement	0	13 (46.4%)	0.000
CABG (SVG)			
RCA	0	23 (82.1%)	0.000
LAD	0	5 (17.9%)	0.007

AAR indicates ascending aorta replacement; CABG, coronary artery bypass grafting; HAR, hemi-arch replacement; RCA, right coronary artery; SVG, saphenous vein graft; and TAR, total arch replacement.

cohort of patients included total arch replacement (TAR) with four-branch, one-branch, or straight prosthetic graft for island anastomosis, along with a stent graft (MicroPort Medical Co Ltd., Shanghai, China); triple-branched stent graft implantation technique (Yuhengjia Sci Tech Corp Ltd., Beijing, China) for TAR; and hemiarch replacement (HAR). The arch reconstruction strategy was mainly based on intraoperative inspection, including location of the primary tear, extent of the tear, vascular-wall texture, and situation of the supra-arch vessels.

The proximal aortic root procedures were performed during cooling and the systematic rewarming duration and based on the surgical inspection of the involvement of the aortic root, including the aortic valve leaflets as well as the coronary ostia. For the patients of group A, coronary artery ostia involvement was deemed not serious, and coronary artery reimplantation was performed to avoid coronary artery bypass grafting. Specific techniques for aortic root reconstruction of the present group included Bentall, David, and Cabrol surgery. For the patients of group B, the severity of coronary ostia involvement reached Neri type B and C, and intima was fragile and detached with adventitia. All patients of this group underwent coronary artery bypass grafting. Specific aortic root techniques of this group included Bentall, David, Wheat, and aortic root reinforcement surgery.¹¹⁾

Statistical analysis and follow-up: Data were collected from chart review and were entered into a dedicated Microsoft Excel table. Categorical variables are represented as frequency distributions and single percentages. Values of continuous variables are expressed as mean $\pm$ standard deviation. Survived patients were followed yearly in our outpatient department or by phone calls to evaluate their clinical status. Normally distributed continuous variables were compared using Student *t*-test, non-normally distributed continuous variables using Mann-Whitney *U* test, and categorical variables using χ^2 and Fisher's exact test, where appropriate. Long-term survival analysis was conducted using Kaplan-Meier method with log-rank test for

group comparisons. All statistical tests were two-sided. Results were considered statistically significant at a level of *P* less than 0.05. All analyses were performed with the IBM SPSS statistical package version 26.0 (IBM Corp. Armonk, NY, USA).

Results

Perioperative data: Table II shows the extent of aortic repair and concomitant procedures in both groups. The ascending aorta was replaced in all patients. Most patients of both group A and B underwent TAR. However, more island anastomosis operations were performed in group B (35.1% versus 53.6%, *P* = 0.137), while more four-branch prosthetic grafts were used in group A (37.8% versus 25.0%, *P* = 0.273). Composite graft replacement of the aortic root (Bentall procedures) had been extensively applied in group A as compared to group B (81.1% versus 28.6%, *P* < 0.001), while 46.4% of patients of group B underwent aortic root reinforcement operations and avoided Bentall or David operations. In group B, all patients underwent coronary artery bypass grafting (CABG) for Neri type B and C lesions. There were 23 patients (82.1%) who needed right coronary artery bypass, while only 5 patients (17.9%) needed left coronary artery bypass. Other procedures of the David operation, hemiarch replacement, triple-branched stent graft implantation, and elephant trunk technique showed no significant difference between the two groups.

As shown in Table III, there were no significant differences in terms of CPB time (*P* = 0.990), cross-clamp time (*P* = 0.882), cerebral perfusion time (*P* = 0.325), overall in-hospital stay (*P* = 0.179), packed red blood cell transfusions (*P* = 0.118), serum transfusions (*P* = 0.627), and volume of drainage during the first postoperative day (*P* = 0.216). Patients in group B had significantly longer ICU stay (*P* = 0.009) and ventilation time (*P* = 0.025).

In-hospital mortality and morbidity: As shown in Table IV, overall in-hospital mortality and 30-day operative mor-

Table III. Perioperative Data

	Group A		Group B		<i>P</i> -value
	Mean $\pm$ SD	Range percentage	Mean $\pm$ SD	Range percentage	
CPB time (minutes)	177.7 $\pm$ 58.4	94–307	177.5 $\pm$ 44.5	115–303	0.990
Cross-clamp time (minutes)	103.9 $\pm$ 33.4	60–184	102.5 $\pm$ 40.7	34–178	0.882
Cerebral perfusion time (minutes)	34.5 $\pm$ 15.5	10–73	31.0 $\pm$ 11.1	18–55	0.325
Nasopharyngeal temperature ($^{\circ}$ C)	17.8 $\pm$ 2.7	11.9–23.3	18.2 $\pm$ 1.7	14.6–20.8	0.525
Rectal temperature ($^{\circ}$ C)	21.1 $\pm$ 2.5	17.0–25.3	22.7 $\pm$ 2.4	17.7–28.0	0.013
In-hospital stay (days)	19.6 $\pm$ 13.3	1–59	23.7 $\pm$ 10.0	2–41	0.179
ICU stay (days)	5.8 $\pm$ 7.4	1–40	12.4 $\pm$ 10.6	1–39	0.009
Ventilation time (hours)	75.3 $\pm$ 168.0	8–960	193.6 $\pm$ 214.4	11–936	0.025
Transfused RBC (mL)	1439.7 $\pm$ 1351.5	400–7500	1948.1 $\pm$ 1047.8	200–5000	0.118
Transfused serum (mL)	1452.9 $\pm$ 1500.1	400–9000	1607.7 $\pm$ 672.9	400–3000	0.627
Platelet (patients, %)	13	35.10%	11	39.30%	0.731
Platelet (pack)	0.5 $\pm$ 0.8	0–4	0.5 $\pm$ 0.7	0–2	0.832
Drainage of first day (mL)	563.0 $\pm$ 402.9	210–1600	438.5 $\pm$ 252.2	115–1170	0.216

CPB indicates cardiopulmonary bypass; ICU, intensive care unit; and RBC, red blood cell.

Table IV. In-Hospital Mortality and Morbidity

	Group A	Group B	<i>P</i> -value
In-hospital mortality	3 (8.1%)	6 (21.4%)	0.124
Operative mortality within 30 days	2 (5.4%)	3 (10.7%)	0.426
Acute renal dysfunction	3 (8.1%)	7 (25.0%)	0.062
Respiratory dysfunction	6 (16.2%)	11 (39.3%)	0.036
Redo for bleeding	2 (5.4%)	1 (3.6%)	0.727
Mediastinum infection	1 (2.7%)	1 (3.6%)	0.841
TND	2 (5.4%)	1 (3.6%)	0.727
PND	3 (8.1%)	2 (7.1%)	0.885

PND indicates permanent neurological dysfunction; TND, temporary neurological dysfunction.

tality were 8.1%, 5.4% for group A and 21.4%, 10.7% for group B, respectively ($P = 0.124$, 0.426). In group A, causes of in-hospital death were as follows: multiple organ failure with permanent neurological dysfunction, respiratory dysfunction, renal dysfunction, and massive gastrointestinal bleeding in one patient, permanent neurological dysfunction, and respiratory dysfunction in two. In group B, causes of in-hospital death were as follows: multiple organ failure in one patient, low cardiac output syndrome in two, and sepsis in one.

The morbidities of postoperative acute renal dysfunction and respiratory dysfunction were observed to be more common in group B, although there was no statistical difference for renal dysfunction. Acute renal dysfunction was observed in 7 of 28 patients in group B and in 3 of 37 patients in group A ($P = 0.062$). Respiratory dysfunction was observed in 11 of 28 patients in group B and in 6 of 37 patients in group A ($P = 0.036$). The morbidities of temporary neurological dysfunction, permanent neurological dysfunction, redo sternotomy for bleeding, and mediastinal infection were similar in the two groups ($P = 0.727$, $P = 0.885$, $P = 0.727$, $P = 0.841$, respectively).

Follow-up and long-term outcomes: Average follow-up time was 112.7 ± 53.6 months for group A and 111.1 ± 31.2 months for group B ($P = 0.898$). Survival curves (excluding in-hospital deaths) of both surgical techniques showed no statistically significant difference between

group A and group B (log-rank P -value = 0.386 , Figure). Median survival time was 131.8 ± 11.9 months (95% CI, 108.4 – 155.3) for group A and 144.2 ± 8.8 months (95% CI, 126.9 – 161.5) for group B.

As shown in Table V, overall mortality was 20.6% for group A and 13.6% for group B during the follow-up ($P = 0.507$). In group A, early causes of death were cerebral hemorrhage due to warfarin overdose in three patients and infection with secondary descending aortic dissection rupture in one patient, while late causes of death were secondary abdominal aortic dissection rupture in one patient and carcinoma of respiratory and digestive system in two patients. In group B, there were one early death due to warfarin overdose and two late deaths due to rectal cancer and secondary rupture of abdominal aortic dissection. There were no significant differences in complications of cerebral hemorrhage, secondary descending aortic dissection rupture, and cancer, respectively.

Discussion

Acute TAAD has been identified as a life-threatening disease due to its high mortality and morbidity. Once diagnosed, emergent or urgent surgical intervention is required. If aTAAD is concomitant with acute coronary artery malperfusion or myocardial infarction, the condition is more complicated, and the mortality rate is higher. In

Figure. The survivor functions (excluding in-hospital deaths) were not significantly different between group A and group B (Log-rank P -value = 0.386).

Table V. Follow-Up and Long-Term Outcomes

	Group A	Group B	P -value
Overall mortality	7 (20.6%)	3 (13.6%)	0.507
Early death (within 24 months)	4 (11.8%)	1 (4.5%)	0.355
Late death	3 (8.8%)	2 (9.1%)	0.973
Cerebral hemorrhage	3 (8.8%)	1 (4.5%)	0.544
Descending aortic dissection rupture	2 (5.9%)	1 (4.5%)	0.828
Cancer	2 (5.9%)	1 (4.5%)	0.828

this study, we systematically summarized the characteristics, surgical strategies, and prognosis of patients with acute TAAD with coronary artery involvement.

For characteristics of aTAAD patients with coronary involvement, Chen, *et al.* found that patients with acute coronary involvement because of TAAD are much younger (51.8 ± 11.8 years), have a lower incidence of a history of hypertension, and have a higher aortic regurgitation rate.¹²⁾ In our study, patients of group B were much older (55.1 ± 10.0 years) with a high rate of hypertension (78.6%); on the contrary, patients of group A were much younger (45.4 ± 9.6 years) with a relative low rate of hypertension (70.3%). Note that hypertension is the most common risk factor for aTAAD. We have also found that incidence of preoperative renal dysfunction of group B was much higher than group A (21.4% versus 8.1%). It might correlate with the severity of coronary artery involvement and advanced age, which indicate poor prognosis.⁵⁾

The overall rate of aTAAD with coronary artery involvement is not low, and the proportion of cases in this group is as high as 24.3% (65/267). In most cases, although the coronary ostia are involved, there is no myocardial ischemia, so it is difficult to make a definite diag-

nosis before operation. Unless the patient has abnormal changes in the electrocardiogram, or the degree of coronary artery involvement is serious, cardiac echocardiography can catch sight of coronary involvement. In group A, the coronary artery ostia of all patients were slightly involved, and there were no myocardial ischemia manifestations before surgery. All of the diagnoses were confirmed during surgery. Only three patients in group B had myocardial ischemia before operation. Two of them belonged to Neri C type with coronary artery intimal rupture. On the whole, preoperative electrocardiogram (ECG) showed that only 4.6% of all cases were diagnosed with coronary artery involvement (3/65). In literatures, the incidence of acute myocardial ischemia due to type-A aortic dissection has been reported at 5.7% to 11.3%, which is higher than our incidence.^{6,13)} Therefore, although aTAAD involves a high proportion of coronary artery ostia affected, the cases of serious myocardial ischemia are not high. However, its true clinical significance is that it makes aortic root reconstruction become more complex.

The surgical outcomes of TAAD have been dramatically improved in recent years. Sun, *et al.* reported the treatment of 291 patients with TAAD with total aortic arch replacement with stented elephant trunk implantation,

with in-hospital mortality only at 3.09%.³⁾ However, myocardial damage caused by coronary dissection is one of the leading predictors of hospital death. Coronary ischemia and the need for concomitant CABG have been reported to be the independent risk factors for mortality.^{5,13)} On the one hand, insufficient coronary perfusion may increase the difficulty of CPB weaning and prolong the CPB time, exacerbating complement-mediated inflammatory response. Additionally, myocardial ischemia triggers inflammatory “waterfall” responses, thus increasing the incidence of acute respiratory distress syndrome, myocardial stunning, and so on, leading to an increase in mortality.^{14,15)} Eren, *et al.* reported there were three (21.4%) early postoperative deaths for aTAAD patients with coronary involvement in their study, and this mortality rate was significantly worse than that in patients without coronary involvement over the same period of study, having only mortality rate of 13.4% (17/122).¹³⁾ In our study, there were three patients with preoperative electrocardiogram indicating myocardial ischemia, and two of these patients died of multiple organ failure after active treatment. These results are enough to demonstrate the perioperative risk of myocardial ischemia/infarction for aTAAD.

Neri, *et al.* reported that they preferred regional repair of torn coronary arteries to CABG out of technical and hemodynamic considerations.⁶⁾ They thought of the following advantages: (1) reconstruction of the coronary ostia was anatomic, and it avoided extensive revascularization on vessels whose diameter, importance, and status were often undetermined; (2) it avoided ligation of the coronary ostium and the consequent complete graft-dependent perfusion of large territories of the myocardium; and (3) it provided antegrade flow in the coronary tree, thus avoiding the risk of competitive flows and of coronary re-dissection. However, repairing the coronary artery is usually cumbersome and time-consuming since the tissues are dissected and very fragile. We instead prefer grafting the distal coronary due to the simplicity of the procedure, which would also facilitate prompt cardioplegia delivery to protect the affected myocardium via the bypass graft.^{16,17)} For the patients of group A with Neri type-A lesion, we agreed with Neri, *et al.* and performed anatomic reconstruction of coronary ostia. Composite graft replacement of the aortic root for reimplantation of the restored coronary orifices (Bentall procedures) has been extensively applied in this series mostly because of the following reasons: patients are much younger and high incidence of commissural detachment. For the patients of group B with Neri type B and C lesions, we prefer to perform CABG with aortic valve-sparing techniques or aortic root reinforcement techniques when possible. The patients in this series are much older, and preoperative status is complex. The goal of the operation should be to solve the patient's main problems with the simplest and most effective methods.

The follow-up results show that although the in-hospital mortality of the patients in the group A was lower than that in the group B, there were no significant differences in terms of the early and late mortalities. There was also no significant difference between the two groups as regards the causes of the patients' follow-up

death. However, patients of group A developed more cerebral hemorrhage due to warfarin overdose, which was closely related to the higher proportion of mechanical valve use in previous surgery.

Limitations: This present study has some inevitable limitations. First, this is a retrospective observational study, and the nonrandomized design may have affected the results, through unrecognized confounding factors and bias. Second, this study represents only a single-center experience, and not a multi-center one. There surely are some disparities among different centers and surgeons. Finally, with the advances in surgical techniques, anesthesia, cerebral protection, and perioperative care, they surely affect the surgical results of different periods.

Conclusions

Coronary artery dissection with Neri type B and C in acute TAAD has been found to be associated with higher early death, but comparable long-term survival after discharge. However, there are several factors that can affect the outcome, such as advanced age, more renal dysfunction, and worse preoperative conditions. Immediate CABG and aortic repair remains to be a safe, effective, and acceptable approach to these challenging group of patients.

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Disclosure

Conflicts of interest: None.

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