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Original Article

Effect of orthoptic cardiac surgery on the outcome and prognosis of recurrent aortic dissection surgery

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Abstract: Objective: To explore the effect of orthoptic cardiac surgery on the outcome and prognosis of recurring aortic dissection surgery. Methods: A retrospective study was conducted among 196 patients admitted to our hospital who had a history of orthoptic cardiac surgery and recurring aortic dissection surgery. In this study, we investigated the survival status of the patients and grouped them as the death group containing 40 cases and the survival group containing 156 cases. We compared their general information, test parameters, the preoperative and postoperative parameters of the two groups of patients and analyzed the relevant factors affecting the patients who underwent recurrent aortic dissection surgery after orthoptic cardiac surgery using one-way analysis of variance and multivariate logistic regression. Results: Among the 196 patients, 40 died within 60 days of the perioperative period with a total mortality rate of 20.41% and a median survival time of 19.000 days (95% CI: 14.048-23.952). The body mass index, D-dimer (D-D2), ascending aorta diameter, ratio of moderate to severe pericardial effusion, aortic regurgitation, operation time, extracorporeal circulation time, aortic block time, postoperative ICU stay time, postoperative brain injury, postoperative low cardiac output, postoperative hypoxia, postoperative liver function abnormality, postoperative septic shock and postoperative blood purification were significantly higher in the death group than in the survival group (all $P<0.05$). After multivariate regression analysis, it was found that body mass index, postoperative brain injury, postoperative low cardiac output, postoperative hypoxia, and postoperative blood purification are independent risk factors for poor prognosis of patients undergoing recurrent aortic dissection surgery after orthoptic cardiac surgery ($P<0.05$). Conclusion: The increased postoperative mortality rate in those who underwent recurrent aortic dissection surgery after orthoptic cardiac surgery may be related to body mass index, postoperative brain injury, low cardiac output postoperatively, postoperative hypoxia, and postoperative blood purification.

Keywords: Orthoptic cardiac surgery, aortic dissection, prognosis, influencing factors

Introduction

Orthoptic cardiac surgery is an open heart surgical procedure performed to restore cardiac structure and function, which requires achieving extracorporeal circulation support [1-3]. It is currently used for various types of heart valve diseases, aortic dissection, coronary artery bypasses, atrial fibrillation and other diseases [4, 5]. However, it has been found that inflammation and oxidative stress often occur after orthoptic cardiac surgery, leading to an increased incidence of myocardial injury and lung injury [6, 7]. Aortic dissection (AD) is a major vascular disease treatment with a high mortality rate. Previous studies have revealed that AD in China is as prevalent as 2.8/100,000 which is lower than the global estimate of 2.9-3.5/100,000 [8]. However, it is believed that the statistical number in China is lower than the actual number of patients with AD, which is related to the omission of information from deceased patients [9]. The majority of patients with AD in China are young adults [10]. The pathogenesis of AD is mainly the formation of a false cavity within the middle layer of the aorta or between the adventitia [11]. Surgery is the best way to treat AD, reduce the mortality rate and save lives [12]. Although great progress has been made in the surgical treatment of AD, the postoperative mortality rate is still high, with foreign countries reporting a postoperative mortality rate of 14-44%, and China's postoperative mortality rate being slightly lower than that of other countries by 4.8-16.6% [13, 14]. Currently, there are several studies on the postoperative mortality rate and factors affecting the prognosis of patients who have undergone previous orthoptic cardiac surgery and surgery for AD. Based on the inclusion of patients with a previous history of orthoptic cardiac surgery for recurrent AD surgery, this study was intended to explore the perioperative mortality and the influencing factors, which may provide a theoretical basis for disease prevention and treatment of such patients in the clinic.

Materials and methods

General information

In this study, we selected 196 patients who had a history of orthoptic cardiac surgery and recurrent AD surgery and who were treated by our hospital from January 2009 to December 2018 for a retrospective study. They were aged 30-70 years old, with an average age of 53.2±10.9 years old. This study was approved by the Ethics Committee of our hospital, and all the participants signed an informed consent.

Inclusion and exclusion criteria

Patients were aged 18 years or above, all included patients met the diagnostic criteria of AD and underwent median thoracotomy due to AD [15]. They had complete clinical data and a history of orthoptic cardiac surgery. Their course of disease was less than 14 days.

Patients who were excluded: patients with missing or incomplete clinical data; patients who were treated in the emergency department only, not admitted to hospital or died before the hospital for any cause; patients with iatrogenic aortic dissection which meant that AD occurred in the course of PCI, or catheterization surgery and so on; patients who were lost to follow-up after surgery.

Methods

In this study, we collected general and relevant information, including the onset season, age, gender, body mass index, length of hospital stay, type of aortic dissection, time from previous orthoptic cardiac surgery to the onset of AD, and complications such as chronic obstructive pulmonary (COPD), hypertension, chronic renal failure, diabetes, heart failure, cerebrovascular disease, coronary artery disease, Marfan syndrome and so on.

The patients included in this study gave 5 mL of venous blood which was analyzed using an enzyme-linked immunosorbent assay and a fully automated immunoassay analyzer (Germany, Siemens) to determine D-dimer (D-D2), white blood cells (WBC), platelet count and neutrophil percentage. A cardiac ultrasound was performed upon admission using a cardiac colorimeter (Philips), which measured the ascending aortic diameter, left ventricular ejection fraction (LVEF), aortic valve regurgitation, ratio of moderate to severe pericardial effusion, and moderate to severe aortic insufficiency.

Intraoperative and postoperative relevant data included operation time, extracorporeal circulation time, aortic block time, low flow time, minimum nasal temperature, red blood cell infusion, plasma, secondary thoracotomy to stop bleeding, postoperative ICU stay time, postoperative brain injury, postoperative atrial fibrillation, postoperative pleural effusion, postoperative low cardiac output, postoperative hypoxia, postoperative liver function abnormalities, postoperative septic shock, postoperative blood purification, and postoperative mechanical ventilation time. The diagnostic indicators of the above complications were determined by the *Chinese Expert Consensus on the Diagnosis and Treatment of Aortic Dissection* [16]. According to the outcome of death or survival within 60 days after the operation, the patients were divided into (40 cases) the death group and (156 cases) the survival group [13].

Outcome measures

(1) We investigated the postoperative survival of patients. (2) We compared general information, test parameters, relevant preoperative and intraoperative parameters, and postoperative conditions between the two groups of patients. (3) We used univariate analysis of variance and multivariate logistic regression to analyze the relevant factors that affected the recurrent AD surgery after orthoptic cardiac surgery.

Statistical analysis

In this study, SPSS 17.0 was used to analyze the data. Measurement data conforming to a normal distribution and continuous variables were represented by mean ± standard devia-

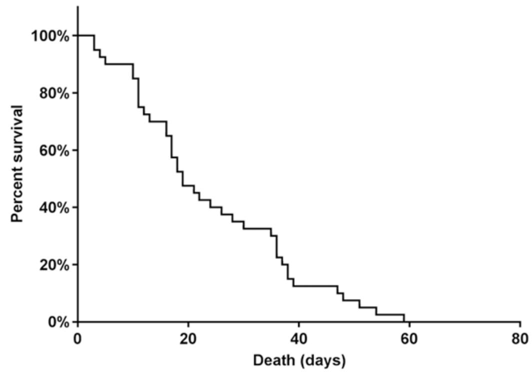

Figure 1. Survival curve of the 40 dead patients.

tion ($\overline{x}$ ± sd), data with a non-normal distribution was represented by M (P25, P75). Independent sample t-test was used for variables conforming to a normal distribution and homogeneity. The independent sample t-test was used for comparison between groups, while the paired sample t-test was used for comparison within groups. Multigroup comparisons were performed by one-way analysis of variance combined with post-hoc Bonferroni test. Rank sum test was used for non-normal distribution and homogeneity of variance, represented by Z. The count data was subject to Pearson's chi-square test and expressed as chi-square. Logistic regression analysis was used to analyze the risk factors influencing the prognosis of patients undergoing recurrent AD surgery after orthoptic cardiac surgery. For variables with differences in univariate analysis, the stepwise forward (Ward) method was used for variable screening. The inclusion level was 0.05 and the exclusion level was 0.1. The risk of death was expressed by the adjusted odds ratio (OR value), and the difference was statistically significant when $P<0.05$.

Results

Survival of 196 patients

Among the 196 patients, 40 died within 60 days of the perioperative period. The overall mortality rate was 20.41%, and the median survival time of the dead patients was 19.0 days (95% CI: 14.048-23.952), as shown in **Figure 1**.

Comparison of general information of the two groups of patients

The body mass index in the death group was significantly higher than that of the survival group ($P<0.001$), and there was no difference in other indexes ($P>0.05$), as shown in **Table 1**.

Comparison of pre-hospital detection indicators between the two groups

D-dimer, ascending aorta diameter, ratio of moderate to severe pericardial effusion, and aortic valve regurgitation rates in the death group at admission were higher than those in the survival group ($P<0.05$). There was no statistical difference in other indicators between the two groups ($P>0.05$), as shown in **Table 2**.

Comparison of intraoperative and postoperative related indexes between the two groups of patients

Operation time, extracorporeal circulation time, aortic block time, postoperative ICU stay time, postoperative brain injury, postoperative low cardiac output, postoperative hypoxia, postoperative liver function abnormalities, postoperative septic shock and postoperative blood purification were higher than those in the survival group ($P<0.001$). There was no statistical difference in other indicators between the two groups ($P>0.05$), as shown in **Table 3**.

Multivariate logistic regression analysis of the prognosis of patients undergoing recurrent aortic dissection surgery after orthoptic cardiac surgery

We took the mean of the included samples as the cut-off point of the included indicators. Multivariate regression analysis found that body mass index, postoperative brain injury, postoperative low cardiac output, postoperative hypoxia, and postoperative blood purification were independent risk factors for the prognosis of patients undergoing recurrent AD surgery after orthoptic cardiac surgery ($P<0.05$), as shown in **Tables 4**, **5**.

Discussion

AD is a dangerous disease with a high mortality rate. Some studies have revealed that the mortality rate increases by 1% for each additional hour within 48 hours after the onset of AD, and the mortality rate can reach 50% and 75% in patients who do not undergo surgery within 2 days and 2 weeks, respectively [17]. The refinement of surgical methods has led to a significant decrease in mortality after the onset of AD, but some studies have revealed that post-

Table 1. Comparison of general information of the two groups of patients ($\bar{x}$ ± sd, n, %)

Items	Survival group (n = 156)	Death group (n = 40)	χ^2/t	P
Age (years)	52.9±9.7	53.8±11.6	0.502	0.616
Gender (Male/Female)	111/45	29/11	0.028	0.886
Body mass index (kg/m²)	23.45±2.42	25.26±2.64	4.412	<0.001
Types of AD			2.201	0.138
Type A	135	38		
Type B	21	2		
Length of hospital stay (d)	24.99±2.95	24.15±2.37	1.667	0.097
Time from previous orthoptic cardiac surgery to the onset of AD (years)	4.6±1.3	4.9±1.6	1.243	0.217
Types of diseases treated by orthoptic cardiac surgery in the past			4.703	0.195
Aortic valve disease	46	12		
Aortic dissection	5	4		
Coronary artery bypass	35	11		
Mitral valve and other diseases	70	13		
Complications				
Hypertension	130	32	0.247	0.619
Type 2 diabetes	5	2	0.298	0.585
Chronic obstructive pulmonary	12	3	0.002	0.967
Chronic renal failure	18	8	1.981	0.159
Cerebrovascular disease	10	3	0.061	0.805
Coronary artery disease	12	4	1.018	0.313
Marfan syndrome	6	2	0.108	0.742

Table 2. Comparison of pre-hospital detection indicators between the two groups ($\bar{x}$ ± sd, n, %)

Items	Survival group (n = 156)	Death group (n = 40)	χ^2/t	P
D-D2 (mg/L)	5.02±3.12	6.22±3.87	2.129	0.035
WBC (×10⁹/L)	10.56±5.32	11.46±4.89	0.970	0.333
Platelets count (×10⁹/L)	149.65±20.56	155.35±30.26	0.125	0.262
Neutrophil percentage (%)	80.69±16.58	82.62±11.67	0.693	0.489
LVEF (%)	62.14±7.26	61.54±8.24	0.453	0.651
Ascending aortic diameter (mm)	36.29±8.24	43.27±13.37	4.417	<0.001
Moderate to severe pericardial effusion (cases)	16 (10.26)	10 (25.00)	6.015	0.014
Aortic regurgitation (cases)	19 (12.18)	12 (30.00)	7.593	0.006
Moderate to severe aortic insufficiency (cases)	20 (12.82)	6 (15.00)	0.131	0.717

Note: D-D2: D-dimer; WBC: White blood cells; LVEF: Left ventricular ejection fraction.

operative death in the hospital can reach 22-31%. With the development of technology, postoperative death in hospitals has decreased to 18-22% compared to before [18]. Previous studies have shown that the in hospital mortality rate of AD patients after thoracotomy can reach 32%, and high mortality rates after AD remains an important challenge [19]. The present study demonstrated that mortality in the hospital after recurrent AD surgery in patients with previous orthoptic cardiac surgery can reach 20.41%, and this mortality rate is consistent with previous reports of postoperative mortality after AD.

The study of influencing factors for mortality in the hospital among patients undergoing recurrent AD surgery after orthoptic cardiac surgery has important implications for the management of high-risk patients. Through univariate and multivariate analysis, we found that body mass index, postoperative brain injury, postop-

Table 3. Comparison of intraoperative and postoperative related indexes between the two groups of patients ($\overline{x}$ ± sd, n, %)

Items	Survival group (n = 156)	Death group (n = 40)	χ^2/t	P
Operation time (min)	453.67±111.29	583.65±152.71	6.073	<0.001
Extracorporeal circulation time (min)	172.69±38.74	283.24±139.47	8.267	<0.001
Aortic block time (min)	111.68±28.47	134.25±54.63	3.605	<0.001
Low flow time (min)	24.64±10.21	21.89±12.12	1.461	0.148
Minimum nasal temperature (°C)	25.43±3.54	25.36±2.72	0.116	0.907
Intraoperative fluid infusion (mL)	1615.36±643.85	1689.46±753.25	0.627	0.532
Red blood cell infusion (u)	17.32±5.31	19.45±11.32	1.730	0.185
Plasma (Ml)	893.41±534.74	1025.32±796.35	1.248	0.214
Secondary thoracotomy to stop bleeding (cases)	14 (8.97)	7 (17.50)	2.419	0.120
Postoperative ICU stay time (d)	5.38±7.21	12.67±9.36	5.348	<0.001
Postoperative brain injury (cases)	2 (1.28)	9 (22.50)	27.057	<0.001
Postoperative atrial fibrillation (cases)	25 (16.02)	10 (25.00)	1.748	0.186
Postoperative pleural effusion (cases)	30 (19.23)	9 (22.50)	0.213	0.644
Postoperative low cardiac output (cases)	18 (11.54)	23 (57.50)	40.655	<0.001
Postoperative hypoxia (cases)	50 (32.05)	29 (72.50)	21.649	<0.001
Postoperative liver function abnormalities (cases)	10 (6.41)	17 (42.50)	30.579	<0.001
Postoperative septic shock (cases)	16 (10.26)	13 (32.50)	12.459	<0.001
Postoperative blood purification (cases)	18 (11.54)	19 (47.50)	26.886	<0.001
Postoperative mechanical ventilation time (d)	6.38±5.23	7.35±6.54	0.992	0.323

Table 4. Assignment table of independent variables influencing the prognosis of patients undergoing recurrent aortic dissection surgery after orthoptic cardiac surgery

Factors	Independent variable	Assignment
Body mass index (kg/m^2)	X1	≥25 = 1, <25 = 0
D-D2 (mg/L)	X2	≥0.55 = 1, <0.55 = 0
Ascending aorta diameter (mm)	X3	≥35 = 1, < = 0
Moderate to severe pericardial effusion	X4	Yes = 1, no = 0
Aortic regurgitation	X5	Yes = 1, no = 0
Operation time (min)	X6	≥500 = 1, <500 = 0
Extracorporeal circulation time (min)	X7	≥222 = 1, <222 = 0
Aortic block time (min)	X8	≥122 = 1, <122 = 0
Postoperative ICU stay time (d)	X9	≥8 = 1, <8 = 0
Postoperative brain injury	X10	Yes = 1, no = 0
Postoperative low cardiac output	X11	Yes = 1, no = 0
Postoperative hypoxia	X12	Yes = 1, no = 0
Postoperative liver function abnormality	X13	Yes = 1, no = 0
Postoperative septic shock	X14	Yes = 1, no = 0
Postoperative blood purification	X15	Yes = 1, no = 0

Note: D-D2: D-dimer.

erative low cardiac output, postoperative hypoxia, and postoperative blood purification were independent risk factors for poor prognosis in those who underwent recurrent AD surgery after orthoptic cardiac surgery. Previous studies have shown a significant increase in the proportion of the overweight population in China in recent years, which is a main contributor for the increased incidence of chronic metabolic diseases (hypertension, diabetes mellitus, cerebrovascular diseases, etc.). At the same time, it has been found that overweight patients with AD had a higher mortality rate than those with normal weight, so being overweight was taken into account as a risk factor for postoperative death after AD [17]. Postoperative neurological complications have been shown to be a contributing factor to the increased postoperative mortality rate in AD patients [20]. In 2017, an

Table 5. Multivariate logistic regression analysis of prognosis of patients undergoing recurrent aortic dissection surgery after orthoptic cardiac surgery

Factor	β	SE	Wald value	OR value (95% CI)	P
Body mass index	2.023	0.849	7.965	7.521 (0.379-10.268)	0.006
Postoperative brain injury	1.941	0.702	7.832	7.102 (1.726-27.369)	0.004
Postoperative low cardiac output	1.016	0.279	3.123	3.792 (1.742-7.693)	0.002
Postoperative hypoxia	2.312	0.789	4.265	10.254 (2.247-22.214)	0.035
Postoperative blood purification	1.436	0.708	4.156	4.236 (1.057-16.879)	0.043

expert consensus demonstrated that the occurrence of cerebrovascular diseases before and after surgery is a vital factor in increasing the postoperative mortality of AD patients. Further studies have also pointed out that patients who had cerebrovascular disease before surgery were more likely to have brain injury after surgery. The postoperative mortality rate can be as high as 20% in those who have complications of cerebrovascular disease in the perioperative period [16]. Postoperative cerebral injury was associated with prolonged surgery leading to coagulation disorders and intraoperative thrombosis. Another study also revealed that postoperative neurological injury was a risk factor for postoperative death in hospitalization [21]. Postoperative hypoxia was a consequence of postoperative pulmonary ventilation and exchange impairment due to intraoperative lung injury, and an investigation of 130 patients with AD found an incidence up to 50% of postoperative hypoxia [22]. Another study illustrated that the use of early assisted ventilation in postoperative AD patients can effectively reduce the occurrence of hypoxemia and improve patient outcomes [23]. The incidence of lung injury was increased in patients who had undergone previous orthoptic cardiac surgery, which can aggravate the lung injury, and was thus further exacerbated by recurrent AD surgery [24]. Postoperative low cardiac output was a common and severe complication after AD surgery and often required extracorporeal membrane oxygenation (ECMO) support. One study demonstrated that 65% of postoperative AD deaths were associated with postoperative low cardiac output using ECMO [16]. Since previous orthoptic cardiac surgery can contribute to myocardial damage, secondary myocardial damage after recurrent operations led to an increased incidence of low cardiac output complications [25]. Previous studies have revealed that AD promoted renal injury after surgery. The mechanism was mainly due to postoperative inflammation and oxidative stress leading to renal ischemia reperfusion, resulting in renal injury. After renal injury, toxins in the body cannot be eliminated normally, leading to the development of toxins and water and sodium retention, which further affected the function of other organs and increased the postoperative mortality rate [26]. Another study illustrated that the incidence of postoperative acute kidney injury in patients with AD could be as high as 54%, and 11% of these patients required long-term blood purification therapy. Postoperative mortality was positively correlated with the degree of acute kidney injury [27].

The present study was a single-center retrospective study with a small sample size, and the sample size can be further increased for a multicenter prospective study. Additionally, the follow-up time could be further increased to observe the long-term prognosis of those who underwent recurrent AD surgery after orthoptic cardiac surgery.

In summary, increased postoperative mortality in those who underwent recurrent AD surgery after orthoptic cardiac surgery may be related to body mass index, postoperative brain injury, postoperative low cardiac output, postoperative hypoxia, and postoperative blood purification.

Disclosure of conflict of interest

None.

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