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Original Article

Characteristics and Surgical Results of Acute Type A Aortic Dissection in Patients Younger Than 50 Years of Age

Kentaro Tamura, MD, PhD, Genta Chikazawa, MD, PhD, Arudo Hiraoka, MD, PhD, Toshinori Totsugawa, MD, PhD, and Hidenori Yoshitaka, MD, PhD

Objectives: The aim of this study is to investigate the characteristics and surgical outcomes of acute type A aortic dissection (AAAD) in patients younger than 50 years of age.
Methods: We retrospectively evaluated 307 patients who consecutively underwent surgical treatment for AAAD in our institute from January 2007 to June 2017. Patients were classified into two groups: the young group with 31 patients aged younger than 50 and the old group with 276 patients aged 50 years or older.
Results: In-hospital mortality was similar in both groups (3.2% vs. 9.4%, p=0.19). Overall survival at 5 years was higher in the young group than that in the old group (97% vs. 71%, p=0.017). No significant differences were observed in freedom from aorta-related death and distal aortic reoperation at 5 years (97% vs. 87%, p=0.26; 86% vs. 92%, p=0.093). The percentage of young patients with postoperative patent false lumen at the descending aorta was significantly higher than that of old patients (76% vs. 30%, p<0.001) in spite of primary entry resection.
Conclusion: Early and mid-term outcomes for AAAD in young patients were satisfactory. However, future follow-up is important because postoperative patent false lumen is at a high rate in young patients in spite of entry resection.

Keywords: aortic dissection

Department of Cardiovascular Surgery, Sakakibara Heart Institute of Okayama, Okayama, Okayama, Japan

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Corresponding author: Kentaro Tamura, MD, PhD. Department of Cardiovascular Surgery, Sakakibara Heart Institute of Okayama, 2-5-1 Nakaicho, Kita-ku, Okayama, Okayama 700-0804, Japan
Tel: +81-86-225-7111, Fax: +81-86-223-5265
E-mail: tamuken0801@yahoo.co.jp

Introduction

Acute type A aortic dissection (AAAD) typically develops in elderly patients, and the reported mean age of patients with AAAD is in the early 70s.[1,2] The number of elderly patients undergoing emergency surgery for AAAD is increasing; therefore, the optimal management of elderly patients is often discussed.[3–6] By contrast, it is relatively rare to have young patients with AAAD. In young patients, AAAD is usually related to connective tissue disorders, such as Marfan syndrome and bicuspid aortic valve. However, there are only few reports on young AAAD patients without connective tissue disorders, and those few are based on age only rather than etiology. The aim of this study is to investigate the characteristics and surgical outcomes of AAAD in patients aged younger than 50.

Methods

Patients and definitions

A total of 307 patients who underwent emergency surgery for AAAD at our institute from January 2007 to June 2017 were retrospectively reviewed. Of those patients, one patient (0.3%) was younger than 30 years old, 11 patients (3.6%) were younger than 40 years old, and 31 patients (10%) were younger than 50 years old. Therefore, we used 50 years old as the cut-off age for comparison between younger and older patients. The patients were classified into two groups: the young group with 31 patients aged younger than 50 years (42±5.6 years) and the old group with 276 patients aged 50 years or older (72±9.6 years). Clinical characteristics and surgical outcomes of both groups were compared and clearly investigated.

Contrast-enhanced computed tomography (CT) and echocardiography were performed on all the patients before emergency surgery. If the contrast medium was found anywhere in the distal aortic lesions, then the false lumen was considered patent. Branch vessel involvement (BVI) was defined as a branch vessel with the involvement of dissection and presence of false lumen or branch vessel originating from the false lumen. BVI was counted at the celiac, mesenteric, bilateral renal, and bilateral iliac arteries for patients with dissection extended to the abdominal aorta. Malperfusion syndromes are defined as symptoms due to disrupted blood flow to peripheral arteries. Shock is defined as systolic blood pressure (SBP)$\leqq$80 mmHg measured while entering the operating room. The definition of tamponade is based on the presence of pericardial effusion with transient or persistent hypotension (SBP $\leqq$80 mmHg) or syncope. DeBakey type I dissection includes dissection of the ascending and descending aorta with entry tear in the descending or abdominal aorta.

After written informed consent was obtained from all patients or their families, the patients received emergency surgery under the diagnosis of AAAD. Approval from the Institutional Review Board was granted for this study and for reporting patient information. The cord number of the Institutional Review Board is B201811-03.

Surgical procedure

Median sternotomy was performed under general anesthesia. Cardiopulmonary bypass (CPB) was established via double direct cannulations of the right axillary and femoral arteries with bicaval drainage, and systemic cooling was initiated. The ascending aorta was clamped after onset of ventricular fibrillation. The proximal stump of the aorta was made during the cooling period. The aorta was transected and trimmed 10 mm distal to the sinotubular junction. The false lumen was closed with BioGlue (CryoLife, Inc., Kennesaw, GA, USA). Two Teflon felt strips (Meadox Medicals Inc., Oakland, NJ, USA) were placed inside and outside of the proximal stump. When the bladder temperature reached 25°C, systemic perfusion was stopped, and the ascending aorta was opened. Selective antegrade cerebral perfusion was established by clamping the brachiocephalic artery and inserting balloon catheters into the left common carotid artery and left subclavian artery. In cases of single arterial perfusion through the unilateral femoral artery, the balloon catheter was also inserted into the brachiocephalic artery. If the entry was located at the distal aortic arch, then the total arch replacement (TAR) was performed with a branched graft, and the intimal tear was covered using the conventional or frozen elephant trunk technique to facilitate thrombosis inside the residual false lumen. When there was an intimal tear in the aortic root, or the aortic root was dilated, the aortic root was replaced.

Follow-up

Patients were followed up at our outpatient clinic or were contacted via telephone or letter. The follow-up rate of survivors was 98% (273/280) and the mean duration of the follow-up was 42±32 months, ranging from 6 to 133 months.

Statistical analysis

Continuous data were presented as a mean±standard deviation and were analyzed using the unpaired t-test or Mann–Whitney U test for independent data, as appropriate. Categorical variables were examined by the χ^2 and Fisher's exact tests. The actual survival rate and freedom from sudden death and reoperation for residual dissecting lesions were calculated by the Kaplan–Meier method. The log-rank test was used for comparison between the two groups. P-values <0.05 were statistically significant. All data were analyzed using the Statistical Analysis System software JMP 11.0 (SAS Institute Inc., Cary, NC, USA).

Results

The clinical characteristics of the patients in the young and old groups are presented in **Table 1**. The mean age of the young group was 42±5.6 years (range, 27–49) and that of the old group was 72±9.6 years (range, 50–91). The male/female ratio was significantly higher in the young group than that in the old group ($p<0.0001$). Body mass index (BMI) was significantly higher in the young group than that in the old group (26±5.0 vs. 23±3.7, $p=0.027$). Patients in the old group were more likely to have diabetes, chronic obstructive pulmonary disease, and a history of smoking than those in the young group. No significant differences on the diagnosis of Marfan syndrome were observed between the two groups, but the young group had a greater percentage of patients with bicuspid aortic valve. No other connective tissue diseases were observed in both groups. The diagnosis of Marfan syndrome was based only on phenotypic and morphologic criteria and not on strict genetic criteria. Preoperative CT showed the rate of patients with dissection extended to the abdominal aorta. The rate of patients with patent false lumen was significantly higher in the young group than in the old group. The number of BVI was also significantly higher in the young group than in the old group. No significant differences in the incidence of malperfusion were found between the two groups, but the percentage of patients with brain malperfusion was significantly lower in the young group than in the old group.

Operative data

Table 2 shows the comparison of operative details between the young and old groups. In the young group, more extensive aortic replacement, including TAR (21/31, 68%) and root reconstruction (7/31, 21%), was required, which led to a long operation time. No significant differences in the locations of primary tear were observed. We achieved entry tear resection in most of the cases, and

Table 1 Patient characteristics

Variables	Young group (n=31)	Old group (n=276)	P-value
Age (years, mean±SD)	42±5.6	72±9.6	< 0.0001
Male, n (%)	25 (81)	118 (43)	< 0.0001
BMI (mean±SD)	26±5.0	23±3.7	0.027
Hypertension, n (%)	21(68)	205 (74)	0.44
Hyperlipidemia, n (%)	9 (29)	70 (25)	0.66
History of smoking, n (%)	17 (59)	87 (32)	0.0051
Diabetes, n (%)	0 (0)	21 (7.6)	0.031
COPD, n (%)	0 (0)	18 (5.5)	0.047
CKD (S-Cre >1.5 mg/dl), n (%)	7 (23)	36 (13)	0.17
Marfan syndrome, n (%)	2 (6.5)	8 (2.8)	0.29
Bicuspid aortic valve, n (%)	3 (10)	2 (0.7)	0.0002
AAE, n (%)	4 (13)	8 (2.9)	0.024
DeBakey type I, n (%)	30 (97)	235 (85)	0.0365
Dissection extended to the abdominal aorta, n (%)	30 (97)	225 (82)	0.012
Patent false lumen, n (%)	29 (94)	203 (74)	0.0057
Preoperative patent false lumen at the Th8 level, n (%)	29 (94)	148 (56)	< 0.0001
Number of BVI, n	3.4±1.3	1.9±1.3	< 0.0001
Malperfusion, n (%)	5 (16)	82 (30)	0.094
Cerebral, n (%)	0 (0)	44 (16)	0.0014
Coronary, n (%)	0 (0)	11 (4.1)	0.12
Mesenteric, n (%)	0 (0)	10 (3.6)	0.14
Renal, n (%)	1 (3.2)	8 (2.9)	0.92
Spinal, n (%)	0 (0)	3 (1.1)	0.42
Limb, n (%)	4 (13)	29 (11)	0.69
Aortic regurgitation (> mild), n (%)	11 (35)	68 (25)	0.21
Tamponade, n (%)	2 (6.5)	58 (21)	0.085
Preoperative CPR, n (%)	0 (0)	6 (2.2)	0.26
Shock (SBP ≦80 mmHg), n (%)	1 (3.2)	24 (8.7)	0.24

SD: standard deviation; BMI: body mass index; COPD: chronic obstructive pulmonary disease; CKD: chronic kidney disease; S-Cre: serum creatinine; AAE: annuloaortic ectasia; BVI: branch vessel involvement; CPR: cardiopulmonary resuscitation; SBP: systolic blood pressure

the groups had no significant differences (95% vs. 96%, p=0.61). We also examined the postoperative status of false lumen at the Th8 level. In the young group, the percentage of patients with postoperative patent false lumen at the descending aorta was significantly higher than that in the old group (76% vs. 30%, p<0.001) in spite of primary entry resection.

Mortality and morbidity

The in-hospital mortality was 3.2% (1 of 31 patients) in the young group. The cause of death was low cardiac output syndrome due to preoperative rupture of the ascending aorta. The in-hospital mortality in the old group was 9.4% (26 of 276 patients). The causes of death were visceral malperfusion (six patients), sepsis (five patients), low cardiac output syndrome (five patients, including three patients with preoperative cardiopulmonary resuscitation), cerebral infarction (four patients), pneumonia (two patients), rupture of residual thoracoabdominal aneurysm (two patients), and cerebral hemorrhage (two patients). No significant difference in in-hospital mortality was found between the groups (p=0.19). Postoperative complications are shown in **Table 3**. The percentage of patients with postoperative stroke was significantly lower in the young group than in the old group (0% vs. 11%, p=0.0094).

The overall survival rate of the young group at 3 and 5 years after surgery was 97% and 97%, respectively. In the old group, the actual survival rate at 3 and 5 years after surgery was 80% and 70%, respectively (**Fig. 1**). There were 35 late deaths in the old group during follow-up and no late death in the young group. The causes of late death were stroke (eight patients), malignant neoplasm (five patients), heart failure (four patients), aortic rupture (four patients), sepsis (three patients), senility (three patients), pneumonia (two patients), renal failure (one patient), and ileus (one patient). Unknown causes of death occurred in three patients.

Table 2 Operative data

Variables	Young group (n=31)	Old group (n=276)	P-value
Operative procedure			
Total arch replacement (TAR), n (%)	21 (68)	121 (44)	0.011
Root reconstruction (RR), n (%)	7 (23)	17 (6.2)	0.0058
TAR+RR, n (%)	3 (9.7)	3 (1.1)	0.012
AVR, n (%)	2 (6.5)	33 (12)	0.33
CABG, n (%)	2 (6.5)	19 (6.9)	0.93
Limb bypass, n (%)	1 (3.2)	5 (1.8)	0.62
Procedure-related data			
OP time, min (mean±SD)	492±104	401±115	< 0.0001
CPB time, min (mean±SD)	272±60	216±64	< 0.0001
SCP time, min (mean±SD)	97±59	67±32	0.024
ACC time, min (mean±SD)	169±43	135±40	0.0002
Minimum bladder temperature, °C (mean±SD)	24±1.6	25±1.7	0.24
Location of the entry, n (%)			
Ascending aorta	17 (55)	169 (61)	0.49
Arch	6 (19)	77 (28)	0.29
Distal arch	6 (19)	18 (6.5)	0.06
Descending or unknown	2 (6.5)	12 (4.3)	0.22
Entry resection, n (%)	29 (95)	264 (96)	0.61
Postoperative patent false lumen at the Th8 level, n (%)	22/29 (76)	77/259 (30)	< 0.001

AVR: aortic valve replacement; CABG: coronary artery bypass grafting; OP: operation; CPB: cardiopulmonary bypass; SCP: selective cerebral perfusion; ACC: aortic cross clamp; SD: standard deviation

Table 3 Postoperative outcomes

Variables	Young group (n=31)	Old group (n=276)	P-value
30-day mortality, n (%)	1 (3.2)	23 (8.3)	0.26
In-hospital mortality, n (%)	1 (3.2)	26 (9.4)	0.19
Postoperative complication, n (%)			
Prolonged ventilation (> 72 h)	4 (13)	69 (25)	0.11
Renal failure	1 (3.2)	15 (5.4)	0.58
Stroke	0 (0)	30 (11)	0.0094
Mesenteric ischemia	1 (3.2)	8 (2.9)	0.92
Re-exploration for bleeding	1 (3.2)	8 (2.9)	0.92
Mediastinitis	1 (3.2)	1 (0.36)	0.15
Spinal ischemia	1 (3.2)	3 (1.1)	0.39

Freedom from aorta-related death in the young group at 3 and 5 years after surgery was 97% and 97%, respectively. In the old group, freedom from aorta-related death at 3 and 5 years after surgery was 91% and 87%, respectively (**Fig. 2**). There were five sudden deaths, including four patients with aortic rupture and one patient from an unknown cause. Freedom from distal aortic reoperation in the young group at 3 and 5 years after surgery was 94% and 92%, respectively. In the old group, freedom from distal aortic reoperation at 3 and 5 years after surgery was both 86% (**Fig. 3**). Reoperations in the young group during follow-up consisted of thoracic endovascular aortic repair (TEVAR) in three patients, replacement of the descending aorta in one patient, and replacement of thoracoabdominal aorta in one patient. In the old group, 15 patients required TEVAR.

Discussion

The focus of the current study is to assess the characteristics and surgical results of AAAD repair in patients aged 50 years and younger. Although the majority of the younger patients required more extensive aortic replacement, excellent outcomes were achieved. No significant differences in freedom from aorta-related death and distal aortic reoperation were observed, in spite of a significantly high percentage of patients in the young group with postoperative patent false lumen at the descending aorta.

The German Registry for Acute Aortic Dissection type A (GERAADA) reported that 7% of patients (160/2,137)

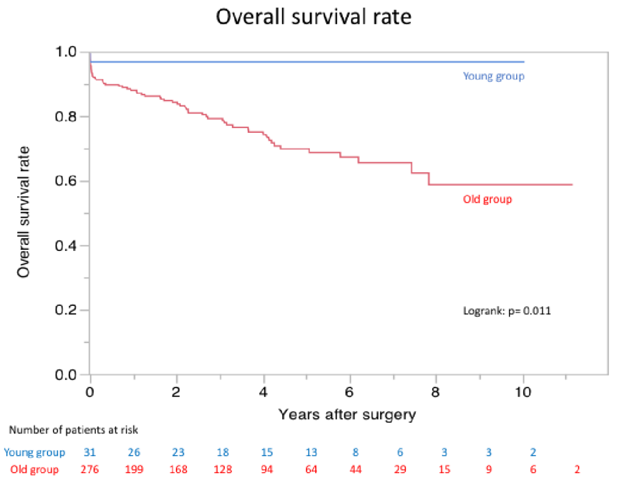

Fig. 1 Kaplan–Meier curves of the overall survival rate in the young and old groups.

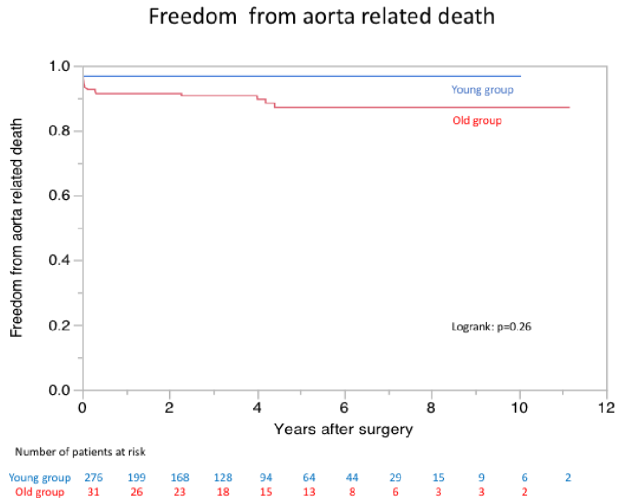

Fig. 2 Kaplan–Meier curves of freedom from aorta-related death in the young and old groups.

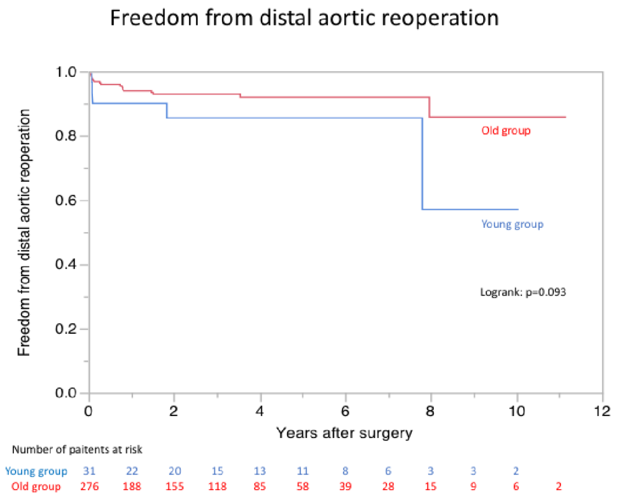

Fig. 3 Kaplan–Meier curves of freedom from distal aortic reoperation.

were younger than 40 years old.[2] In the present study, 3.6% of patients (11/307) were younger than 40 years old and 10% of patients (31/307) were younger than 50 years old. Although we defined our young group as patients younger than 50 years old, no clear universal cut-off age with regard to younger patients with AAAD has been established. Only a few reports have focused on young patients with AAAD. Januzzi et al.[7] used 40 years and Kimura et al.[8] used 45 years as the cut-off age of young patients. The reasons for setting these cut-off ages are not clarified in these papers, but the ratio of Marfan syndrome is one of the deciding factors of the cut-off age. On the other hand, in several reports on aortic aneurysm, 50 years is set as the cut-off age.[9,10] We referred to reports on aortic aneurysm with regard to cut-off age because our aim in this study is to clarify the characteristics and surgical results of young patients with AAAD, regardless of any underlying connective tissue diseases.

In the present study, 81% of the patients in the young group were male. In other studies, the ratio of male to female is similarly high among young patients with AAAD.[1,2,7] Rylski et al. reported that the cut-off age for male ratio dominance was 75 years old; above this age, most patients were female.[2] BMI was significantly higher in the young group. Obesity and the accompanying sleep apnea syndrome (SAS) may be related to the onset of aortic dissection in young patients. The relationship between SAS and aortic dissection has been pointed out in several reports.[11,12] However, we have not tested for SAS in our patients. Such examination will be the subject of the next study.

We considered entry resection as a standard strategy. The rate of entry resection was 95% in the entire cohort. Moreover, when operating on young patients with no serious preoperative complications, TAR was aggressively adopted regardless of the location of the primary entry. We performed TAR in 46% of the entire cohort and 68% in the young group. The rate of TAR was equal or higher than that in previous reports (15%–48%).[1,2,13–16] However, whether extensive aortic replacement should be performed in the emergency setting still remains controversial. Di Eusanio et al. reported that TAR is one of the independent risk factors for in-hospital mortality on the basis of the complete International Registry of Aortic Dissection (IRAD) database (1,995 surgery patients from January 1996 to January 2013).[13] Another report of the IRAD database identified that early and mid-term results between patients who underwent hemiarch replacement and those who underwent extensive TAR had no significant differences in a propensity score-adjusted multivariable analysis (1,241 patients from March 1996 to March 2015).[14] On an analysis of the GERAADA data, Easo et al. reported that the aggressive approach of TAR can be performed in patients with AAAD at an acceptable operative risk compared with the standard treatment with the replacement of the ascending aorta.[15] However, they also reported that a subgroup analysis without a pre-existing neurologic deficit demonstrates a high mortality for patients treated with TAR.

The young group had no cerebral malperfusion and stroke complications. Furukawa et al. reported that partial or complete thrombosis of the supra-aortic branch vessels is an independent risk factor of perioperative cerebral malperfusion.[16] Most patients in the young group had completely patent false lumen. Thus, the incidence of cerebral malperfusion due to thrombosis at the false lumen of the supra-aortic branch vessels is low. In addition, young patients are less likely to have cerebral complications due to arteriosclerosis.

Patients in the young group had more patent false lumen, a wider range of dissection, and more BVI than those in the old group. Residual patent false lumen is reported to be a risk factor for future aortic enlargement and reoperation of the downstream aorta. The rate of residual patent false lumen has been reported to be 43%–80%.[17–20] In the present study, the percentage of patent false lumen at the descending aorta after AAAD repair was 34%. Our overall false lumen thrombus rate was satisfactory. However, the postoperative patency of the false lumen at the descending aorta was significantly higher in the young group than that in the old group in spite of entry resection. The large number of BVI, which is associated with multiple re-entries, is the cause of postoperative patent false lumen in the young patients. Kamman et al. reported that the number of vessels originating from the false lumen is an independent risk factor of false lumen growth in patients with type B aortic dissection.[21] On the other hand, no significant differences in freedom from aorta-related death and freedom from distal aortic reoperation were observed between the groups although the percentage of the patients with postoperative patent false lumen at the descending aorta was significantly higher in the young group. Therefore, our aggressive approach of extended aortic arch replacement at the time of the initial operation is acceptable. Kimura et al. reported that the leading causes of late death of the younger patients after AAAD repair was aortic rupture.[8] In the present study, there was no late death in the young group. Although our results were favorable, future follow-up is necessary to be attentive for the enlargement of the false lumen at the downstream aorta.

This study has several limitations. First, the study population was small and was retrospectively conducted using a single-center cohort. Second, the diagnosis of Marfan syndrome was based only on phenotypic and morphologic criteria and not on strict genetic criteria. Third, the follow-up period is relatively short with a mean follow-up period of 3.6 years (range, 0.5–11 years). Halstead reported that the growth of the distal aorta after type A aortic dissection repair is typically slow and linear. Therefore, with a longer follow-up period, there is a possibility of a significant difference in freedom from the reoperation of the downstream aorta in the young patients, necessitating further study.

Conclusion

In this study, early and mid-term outcomes for AAAD repair in young patients were satisfactory. Compared with the old group, the young group had more extended dissection, more patent false lumen, more multiple re-entries, and more postoperative patent false lumen in spite of entry resection. Although the freedom from aorta-related death and distal aortic reoperation had no significant difference between the two groups, careful follow-up is necessary to examine the enlargement of the false lumen at the downstream aorta.

Disclosure Statement

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Author Contributions

Study conception: KT
Data collection: KT
Analysis: KT
Investigation: KT
Writing: KT
Critical review and revisions: all authors
Final approval of the article: all authors
Accountability for all aspects of the work: all authors

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