Characteristics of Abdominal Aortic Aneurysm in Japanese Patients Aged 50 Years or Younger

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Objective: We investigated the characteristics and surgical outcomes of abdominal aortic aneurysm (AAA), which typically occurs in elderly persons, in Japanese patients aged 50 years or younger.

Materials and Methods: Clinical records of 999 patients who underwent open or endovascular repair for AAA at our hospital between 2007 and 2015 were reviewed to identify the clinical characteristics and surgical outcomes of young patients with AAA. The cohort included 14 patients aged 50 years or younger (mean, 40.4 years; young group) and 985 patients aged older than 50 years (mean, 72.8 years; old group).

Results: Marfan syndrome, prior aortic dissection, and a history of aortic surgery were more prevalent in the young group, and 50% of the patients in the young group had dissecting aneurysms. All patients in the young group underwent open repair. Overall in-hospital mortality rates were 7.1% (1/14) and 1.9% (19/985) in the young and old groups, respectively (P=0.67). Seven-year survival and aortic event-free survival rates in the young group were 82.5%±11.5%, and 71.2±14.5%, respectively.

Conclusion: AAA in patients aged 50 years or younger tended to be associated with Marfan syndrome, a history of aortic surgery, and prior aortic dissection. Early outcomes of AAA among young patients are acceptable, but close postoperative monitoring is important.

Keywords: abdominal aortic aneurysm, young age, aortic dissection

Introduction

Abdominal aortic aneurysm (AAA) typically develops in elderly persons on a background of arteriosclerosis. According to a recent nationwide database study conducted in the USA, which included 166,443 subjects, the average age of patients who underwent elective surgical intervention for AAA between 2007 and 2011 was 73.0 years.1 In step with an aging global population, the number of elderly patients requiring elective or urgent surgery for AAA is expected to increase.2 Many studies reported the characteristics of AAA as well as treatment outcomes in elderly patients.2-4 Findings of these studies assisted physicians in choosing the optimal management strategy on a case-by-case basis, which include endovascular or open repair and continuous clinical monitoring. In contrast, there are a limited number of studies characterizing AAA in people aged 50 years or younger, as AAA is not common in this age group.5,6 Ruptured AAA remains one of the most serious cardiovascular emergencies, with vast economic and social impact especially when it occurs in young people. Thus, in this retrospective study conducted in Japan, we investigated the characteristics of AAA and outcomes of surgical interventions for AAA in patients aged 50 years or younger and compared with those in patients aged 51 years or older.

Materials and Methods

Between January 2007 and May 2015, 999 patients (852 males, 147 females; mean age, 72.4±8.5 years) underwent open (n=796) or endovascular aortic repair (n=203) for AAA at Saitama Medical Center at Jichi Medical University in Saitama, Japan. Age distribution of the entire cohort is shown in Fig. 1. In this cohort of 999 patients, 14 (1.4%; 14/999) were 50 years or younger who were followed up for a mean of 3.7 years (range, 0.1–7.0 years; follow-up rate, 100%).

The clinical records of 14 patients in the young group as well as the remaining 985 patients (the old group) were reviewed to collect information on the following clinical
variables: age, sex, risk factors, comorbidities, history of aortic disease, family history of aortic disease, smoking status, computed tomography (CT) findings of AAA, type of surgery performed, and immediate postoperative clinical outcomes including in-hospital death. Late outcomes (survival or death, aortic events, i.e., re-intervention for a graft-related event, intervention involving another aortic area, death due to aortic rupture, or sudden death) were investigated in the young group. The ethics committee of Saitama Medical Center at Jichi Medical University approved the study (approval ID, S16-086), and the need for individual informed consent was waived.

Data were presented as means ± standard deviation or numbers with percentages. Between-group differences in clinical variables were analyzed by $\chi^2$ or Fisher’s exact test or by unpaired Student’s t test or Mann–Whitney U test, as appropriate. Calculations for 7-year actuarial survival and 7-year aortic event-free survival rates in the young group were conducted using the Kaplan–Meier method. All analyses were performed with IBM SPSS Statistics version 23.0 for Windows (IBM, Armonk, NY, USA). For all analyses, $P$ values < 0.05 were considered as statistically significant.

**Results**

Clinical characteristics of patients in the young group are detailed in Table 1. Mean age of the young group was 44.0 ± 4.7 years (range, 35–50), and male/female ratio was 11:3. The following AAA-associated risk factors

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**Table 1** Clinical characteristics of all patients aged 50 years and younger (young group) who were diagnosed with abdominal aortic aneurysm

| Patient | Age (years)/ sex | MFS | Comorbidity | FH | Current smoking | Etiology | Aneurysm site | Maximum size | Aneurysm rupture | Surgery | Immediate outcome |
|---------|------------------|-----|-------------|----|-----------------|----------|--------------|--------------|-----------------|---------|------------------|
| 1       | 35/M yes         | none no yes no | dissection | abdominal | 75 mm yes | aortic repair | survival |
| 2       | 40/M yes         | HT no yes | dissection | abdominal | 50 mm no | aortic repair | survival |
| 3       | 40/M no          | HT, DM no yes | dissection | abdominal | 48 mm no | aortic repair | survival |
| 4       | 40/F yes         | HT, IHD yes yes | no dissection | abdominal | 49 mm no | aortic repair | survival |
| 5       | 40/F no          | HT, DM, no yes | no dissection | iliac | 22 mm yes | aortic repair | death |
| 6       | 41/M no          | none no yes | dissection | iliac | 22 mm yes | aortic repair | survival |
| 7       | 44/M no          | HT, DM, DL no no | dissection | abdominal | 46 mm no | aortic repair | survival |
| 8       | 45/M no          | HT, Behçet’s disease no yes | no dissection | abdominal | 100 mm yes | patch plasty | survival |
| 9       | 47/M no          | HT, DM, DL, IHD no yes | no dissection | abdominal | 75 mm yes | aortic repair | survival |
| 10      | 48/M no          | none no yes | no dissection | iliac | 25 mm no | aortic repair | survival |
| 11      | 48/M no          | HT, DL no yes | no dissection | abdominal | 54 mm no | aortic repair | survival |
| 12      | 48/M no          | HT, DM, DL no yes | dissection | abdominal | 48 mm no | aortic repair | survival |
| 13      | 50/F no          | HT, DL no no | dissection | abdominal | 50 mm no | aortic repair | survival |
| 14      | 50/M no          | HT, DM no yes | no dissection | abdominal | 42 mm no | aortic repair | survival |

M: male; F: female; MFS: Marfan syndrome; FH: family history; HT: hypertension; DM: diabetes mellitus; DL: dyslipidemia; IHD: ischemic heart disease
were present in the young group: current smoking (n = 10, 71%), hypertension (n = 10, 71%), dyslipidemia (n = 5, 36%), and family history of aortic disease (n = 3, 21%). Comorbidities included Marfan syndrome (n = 3, 21%), diabetes (n = 5, 36%), ischemic heart disease (n = 2, 14%), and Behçet’s disease (n = 1, 7%).

Seven (50%) patients in the young group had dissecting AAAs; five of these patients (patients 2, 3, 7, 12, and 13) underwent elective aortic repair. The remaining two patients (patients 1 and 6) underwent urgent aortic repair for ruptured AAAs. The causes in the remaining seven patients in the young group with non-dissecting AAAs were atherosclerosis (n = 3, 21%), inflammation (n = 1, 7%), infection (n = 1, 7%), Marfan syndrome (n = 1, 7%), and vascular-type Behçet’s disease (n = 1, 7%). Aneurysms in the young group included juxtarenal abdominal aorta (n = 2, 14%), non-juxtarenal abdominal aorta (n = 10, 71%), and iliac artery (n = 2, 14%). Urgent surgery due to the rupture of AAA was required in four patients in the young group (29%), whereas elective surgery was performed in the remaining ten patients with non-ruptured AAAs.

Table 2 shows the comparison of clinical characteristics between the young and old patient groups. Patients in the young group were more likely to have Marfan syndrome and to have a history of aortic dissection and/or aortic surgery. Mean preoperative platelet count and estimated glomerular filtration rate were lower in the young group than in the old group. Patients in the young group were more likely than those in the old group to have AAA diagnosis by CT. Median aortic diameter did not differ between the two groups.

All patients in the young group underwent open aortic repair that was achieved by replacement with a vascular prosthesis (n = 13) or patch repair (n = 1). The only patient in this cohort who underwent patch repair (patient 8) was

| Table 2 | Clinical characteristics of the young and old groups with aortic abdominal aneurysms |
|---------|-----------------------------------------------|
| Young group | Old group | P value |
| Age ≤50 years (n = 14) | Age >50 years (n = 985) |
| Age (years) | 44±4.6 | 72.8±7.8 | <0.01 |
| Sex, male | 11 (79%) | 841 (85%) | 0.73 |
| Marfan syndrome | 3 (21%) | 3 (0.3%) | <0.01 |
| History of smoking | 10 (71%) | 722 (73%) | 1.0 |
| Hypertension | 10 (71%) | 788 (80%) | 0.64 |
| Dyslipidemia | 5 (36%) | 401 (41%) | 0.71 |
| Diabetes mellitus | 5 (36%) | 167 (17%) | 0.14 |
| COPD or asthma | 0 (0%) | 101 (10%) | 0.41 |
| Hemodialysis | 0 (0%) | 16 (2%) | 1.0 |
| Ischemic heart disease | 2 (14%) | 362 (37%) | 0.083 |
| History of cerebrovascular disease | 0 (0%) | 126 (13%) | 0.15 |
| Prior aortic dissection | 5 (36%) | 44 (4%) | <0.01 |
| History of aortic surgery | 4 (29%) | 48 (5%) | <0.01 |
| LVEF (%)† | 66.3±4.3 | 62.7±10.1 | 0.28 |

| Laboratory findings |
|---------------------|
| Hematocrit (%) | 39.9±6.1 | 37.7±10.6 | 0.43 |
| Platelet (×10³/µL) | 20.6±8.3 | 26.2±8.3 | 0.025 |
| eGFR (mL/min/1.73 m²) | 60.9±29.7 | 77.4±25.8 | 0.039 |
| Albumin (g/mL) | 3.8±0.8 | 3.8±0.9 | 0.97 |

| CT findings |
|-------------|
| AAA | 12 (86%) | 948 (96%) | 0.98 |
| IIA | 2 (14%) | 142 (14%) | 0.25 |
| Solitary CIA and/or IIA | 2 (14%) | 37 (4%) | 0.19 |
| Dissecting aneurysm | 7 (50%) | 50 (5%) | <0.01 |
| Aortic diameter (mm), median (IQR)†† | 50.0 (48.0–69.8) | 51.0 (45.0–60.0) | 0.41 |
| Urgent surgery | 4 (28%) | 116 (12%) | 0.13 |
| Elective surgery | 10 (71%) | 869 (88%) | 0.13 |

Numbers with percentages or means±standard deviation are shown unless otherwise indicated. † Measured only in patients who underwent elective surgery. †† Measured only in patients with abdominal aortic aneurysm. COPD: chronic obstructive pulmonary disease; LVEF: left ventricular ejection fraction; eGFR: estimated glomerular filtration rate; CT: computed tomography; AAA: abdominal aortic aneurysm; IIA: internal iliac aneurysm; CIA: common iliac aneurysm; IQR: interquartile range
a 45-year-old male with Behçet’s disease. Aneurysm grew rapidly from 3 cm to 10 cm within three months in this patient, and conventional aortic repair could not be performed due to the presence of severe adhesions between the aneurysmal wall and surrounding tissues. Therefore, patch repair was performed with a Dacron prosthesis that covered the ruptured area.

The in-hospital mortality rate in the young patient group was 7.1% (1/14). The only patient with AAA in the young group who died at the hospital (patient 6) was a 41-year-old male with a limited dissecting aneurysmal enlargement of the right iliac artery; the patient suffered cardiopulmonary arrest preoperatively due to aneurysmal rupture. As shown in Table 3, the in-hospital mortality rate following open aortic repair did not differ significantly between the two groups.

Three of the young patients suffered an aortic event during the follow-up period. Patient 8 (45-year-old male with Behçet’s disease) had a pseudo-aneurysm at the site of patch repair and underwent successful endovascular aneurysm repair with a Powerlink stent graft (Endologix, Irvine, CA, USA) eight months after the initial surgery. Patient 2 (40-year-old male with Marfan syndrome) underwent thoracoabdominal aorta replacement 17 months after the initial repair, and the second repair was successful. Patient 3 (40-year-old male without Marfan syndrome) had a history of aortic dissection and died from the rupture of a thoracoabdominal aneurysm 39 months after the initial surgery. There were no other late mortalities in the young group. Among young patients with AAA, 7-year overall and 7-year aortic event-free survival rates were 82.5% ± 11.5% and 71.2% ± 14.5%, respectively (Fig. 2).

### Discussion

Most studies including young patients with AAA define 65 or 75 years as the age cutoff criterion. A large-scale population-based study showed that the prevalence of AAA, defined as an abdominal aortic diameter ≥ 3 cm determined by ultrasonography, was 0.05% among a total of 333,369 quadragenarians.7) Studies investigating truly young (aged 50 year or less) patients with AAA are limited, even in Western countries, due to the small number of AAA patients aged 50 years or younger.5,6) To the best of our knowledge, this is the first study investigating the characteristics of young patients with AAA in an Asian population to determine treatment outcomes. In two studies conducted in the USA, patients aged 50 years or younger were shown to be more likely than those older than 50 years to show symptoms associated with AAA.5,6) Twenty-nine percent (4/14) of the patients in the young group in the present study underwent urgent aortic

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**Table 3** In-hospital mortality rates of patients with abdominal aortic aneurysms

| Variables          | Young group | Old group | P value |
|--------------------|-------------|-----------|---------|
|                    | Age≤50 years | Age>50 years |         |
| Overall            | 7.1% (1/14)  | 1.9% (19/985) | 0.67    |
| Open repair†       | n=14        | n=782     |         |
| Urgent surgery     | 25.0% (1/4)  | 12.7% (14/110) | 0.73    |
| Elective surgery   | 0% (0/10)   | 0.6% (4/672)  | 1.0     |
| Endovascular repair†† | n=0       | n=203     |         |
| Urgent surgery     | NA          | 0% (0/6) | NA      |
| Elective surgery   | NA          | 0.5% (1/197) | NA      |

† 14 patients in the young group and 782 patients in the old group underwent open repair. †† 0 patients in the young group and 203 patients in the old group underwent endovascular repair. NA: not applicable

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**Fig. 2** Kaplan–Meier curves for actuarial survival (A) and aortic event-free survival (B) among patients 50 years or younger who underwent surgery for abdominal aortic aneurysm.
The prevalence of symptomatic AAA among the young group in the current study was 12% (116/985; Table 2). This difference in the prevalence of symptomatic AAA between the young and old groups was not significant, although the prevalence of symptomatic AAA among young patients was fairly high.

Environmental factors are known to play a role in the development of AAA. Smoking is the strongest risk factor for AAA. Indeed, 71% of young AAA patients in the current study were smokers. Furthermore, high prevalence rates of lifestyle-related disorders including hypertension, diabetes, and dyslipidemia were observed among the young patients. These findings suggest that atherosclerosis promoted by environmental factors was responsible for the development of AAA in young patients with no genetic risk factors.

Genetic factors are known to play a role in the development of AAA. Sakalihasan et al. reported that 10% of AAA cases were familial, with a prevalence of 13% among family members and a staggering 25% among brothers. Twenty-one percent of the patients in the young group in the present study had a first-degree relative with aortic disease. Thus, the development of AAA in young patients in the current study might indicate a strong genetic component. Akai et al. recently reported that the growth rate of small AAAs in patients with a positive family history of AAA was twice that of AAAs in patients without a family history (4.2 mm/year vs. 2.0 mm/year, \( P < 0.009 \)). Therefore, comprehensive follow-up is recommended for young AAA patients and their family members including those with normal-diameter aortas.

Marfan syndrome is an autosomal dominant disorder that affects connective tissue in a wide range of organs including musculoskeletal, ocular, and cardiovascular systems. Common cardiovascular manifestations of Marfan syndrome include ascending aorta (aortic root) dilation, aortic dissection, and mitral regurgitation. In the current study, three patients in the young group had Marfan syndrome, including two with dissecting AAA and one with non-dissecting AAA. Non-dissecting AAA in patients with Marfan syndrome is relatively rare. Takayama et al. recently reported treatment outcomes in six patients with true AAAs. Of these, two patients presented with rupture, one died during surgery, and two died during the follow-up period either from sudden death or aortic dissection. The three patients with Marfan syndrome in the current study had previously undergone aortic surgery (aortic root replacement, \( n = 2 \); descending aorta replacement, \( n = 1 \)), and one of the patients (patient 2) required additional thoracoabdominal replacement 1.5 years after the surgery for AAA. These findings altogether emphasize the importance of careful follow-up in patients with Marfan syndrome.

Behçet’s disease is a multi-system autoimmune disorder that tends to occur in young adults. The peak age of disease onset ranges between 20 and 50 years of age. Behçet’s disease can affect blood vessels of any size. A large-scale study conducted in China recently reported that the incidence of vascular involvement in Behçet’s disease was 12.8% (102/796). Venous involvement was shown to be more common than arterial involvement (9.0% [72/796] vs. 7.0% [56/792]), which most often implies the involvement of the aorta, arteries of the lower extremities, pulmonary artery, coronary artery, and/or subclavian artery. Arterial involvement is an indication for surgical intervention. Postoperative anastomotic pseudo-aneurysm is a life-threatening complication associated with Behçet’s disease. Hosaka et al. reported an incidence of pseudo-aneurysm of 10.2% (5 of 49 anastomoses) among ten patients with Behçet’s disease who underwent surgical treatment for arterial aneurysm. In the current study, one of the patients with Behçet’s disease required additional endovascular repair for a pseudo-aneurysm nine months after the patch repair of AAA. Endovascular repair should be considered as an effective treatment option for AAA in patients with Behçet’s disease, although its indication should be considered carefully on a case-by-case basis.

Conclusion

In this retrospective study conducted in Japan, AAA in people aged 50 years or younger was relatively rare, with an incidence rate of 1.4% (14/999). AAA in young patients was likely to be associated with Marfan syndrome, a history of aortic dissection, and prior aortic surgery. In addition, AAA in young patients tended to be symptomatic. Furthermore, early outcomes among young patients with AAA were generally acceptable, although some patients required additional surgical intervention during the follow-up period. Overall, these findings emphasize the critical importance of close postoperative clinical monitoring of young patients with AAA.

Disclosure Statement

The authors have no conflicts of interest to disclose.

Author Contributions

Study conception: NK
Data collection: MN
Analysis: MN
Investigation: MN, NK
Writing: MN, NK
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Critical review and revision: all authors
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Accountability for all aspects of the work: all authors

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