Surgical strategy for aorta-related infection†

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Abstract

OBJECTIVES: This report describes our experience with surgical management of aorta-related infections.

METHODS: From November 1999 to April 2013, 70 patients underwent surgical management for aorta-related infection, including aorto-bronchial fistula in 12 patients, aorto-oesophageal fistula in 14 and aortoduodenal fistula in 4. The location of infection was aortic root to arch in 22 patients, descending aorta in 29, thoraco-abdominal aorta in 12 and abdominal aorta in 7. Forty-seven patients had infections of the native aorta and 23 had postoperative graft infections.

In situ replacement [bridge thoracic endovascular aortic repair (TEVAR); n = 1] was performed in 45 patients, endovascular aortic repair in 18 and extra-anatomical bypass (bridge TEVAR; n = 2) in 7. Omental flap was installed in 29 patients and a pedicled latissimus dorsi muscle flap was used in 3. Since 2008, we have been trying to resect not only the infected tissues, but also the surrounding aneurysmal wall as well.

RESULTS: Hospital mortality was 17.1% (12/70). Late death occurred in 15 patients. Overall survival at 3 years was 60.1 ± 6.7%. Freedom from infection-related death of patients who had in situ graft replacement, endovascular repair or extra-anatomical bypass at 3 years was 88.5 ± 4.9, 75.2 ± 10.9 or 14.3 ± 13.2%, respectively (P < 0.01). In situ graft replacement provided a better freedom from aortic event (recurrent infection and reintervention) at 3 years compared with endovascular repair (85.6 ± 5.5 vs 61.8 ± 12.5%, P = 0.029). Freedom from infection-related death at 3 years improved significantly from 61.1 ± 9.7 (before 2008) to 84.7 ± 5.8% (since 2008) (P = 0.044).

CONCLUSIONS: Surgical treatment for aorta-related infection is still associated with high mortality and morbidity. However, our current strategy, which is aggressive surgical management, including resection of infected tissues, extensive debridement, in situ graft replacement of the aorta and omental or muscle installation provided a better patient survival.

Keywords: Aortic infection • In situ graft replacement • Extra-anatomical bypass • Endovascular repair • Omental flap • Muscle flap

INTRODUCTION

Although aorta-related infection is rare, it is still a challenging problem that is associated with a high mortality. The standard treatment for aorta-related infections consists of open surgical repair with resection of infected aortic segment, debridement of surrounding tissue and in situ graft replacement or extra-anatomical bypass. Recently, some reports have described the usefulness of endovascular repair to treat aorta-related infections. The purpose of this study was to describe our experience with surgical management of aorta-related infections.

MATERIALS AND METHODS

This study was approved by the Institutional Review Board (IRB) of the Kobe University School of Medicine (IRB number: #1490). Individual consent was waived.

Patient profiles

Seventy-one (3.3%) patients had aorta-related infections (Table 1). One who underwent only medical therapy was excluded. Patients' age was 69.9 ± 12.4 years. Seventy patients (50 males and 20 females) who underwent open surgical repair with resection of infected tissue or who underwent endovascular repair were retrospectively investigated. There were aortobronchial fistula (ABF) in 12 (17%) patients, aorto-oesophageal fistula (AEF) in 14 (20%) and

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Twenty-four (34%) patients had comorbidities. Twenty-six (38%) patients were febrile, and blood cultures were positive in 24 (32%) patients. The most common pathogenetic MRSA: methicillin-resistant Staphylococcus aureus; MSSA: methicillin-sensitive Staphylococcus aureus; MRSE: methicillin-resistant Staphylococcus epidermidis.

Table 1: Patient profiles 1

<table>
<thead>
<tr>
<th>Variables</th>
<th>N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of patients</td>
<td>70 (32)</td>
</tr>
<tr>
<td>Postoperative graft infection</td>
<td>23 (68)</td>
</tr>
<tr>
<td>Infection of native aorta</td>
<td>47 (19)</td>
</tr>
<tr>
<td>Aorto-oesophageal fistula</td>
<td>14 (17)</td>
</tr>
<tr>
<td>Aortobronchial fistula</td>
<td>12 (6)</td>
</tr>
<tr>
<td>Aortoduodenal fistula</td>
<td>4 (58)</td>
</tr>
<tr>
<td>No fistula</td>
<td>40 (32)</td>
</tr>
<tr>
<td>Aortic root to arch infection</td>
<td>22 (41)</td>
</tr>
<tr>
<td>Descending aortic infection</td>
<td>29 (17)</td>
</tr>
<tr>
<td>Thoraco-abdominal aortic infection</td>
<td>12 (10)</td>
</tr>
<tr>
<td>Abdominal aortic infection</td>
<td>7 (34)</td>
</tr>
<tr>
<td>Blood culture positive</td>
<td>24</td>
</tr>
<tr>
<td>MRSA</td>
<td>5</td>
</tr>
<tr>
<td>MSSA</td>
<td>3</td>
</tr>
<tr>
<td>Candida albicans</td>
<td>3</td>
</tr>
<tr>
<td>Enterococcus faecalis</td>
<td>3</td>
</tr>
<tr>
<td>Pseudomonas aeruginosa</td>
<td>2</td>
</tr>
<tr>
<td>Salmonella spp</td>
<td>2</td>
</tr>
<tr>
<td>MRSE</td>
<td>1</td>
</tr>
<tr>
<td>Clostridium septicum</td>
<td>1</td>
</tr>
<tr>
<td>Streptococcus dysgalactiae</td>
<td>1</td>
</tr>
<tr>
<td>Bacteroides</td>
<td>1</td>
</tr>
<tr>
<td>Listeria</td>
<td>1</td>
</tr>
<tr>
<td>Enterobacter</td>
<td>1</td>
</tr>
</tbody>
</table>

Surgical treatment

Surgical management consisted of debridement of the infected tissues, copious saline irrigation and in situ graft replacement or extra-anatomical bypass or endovascular repair. Endovascular repair was performed when the infected site was localized, the patient was an immunocompromised host (such as those with advanced cancer) or as a bridge to open surgical repair. Current standard surgical strategy included complete resection of infected tissues and in situ graft replacement of the aorta using a rifampicin-soaked gelatin-impregnated Dacron graft followed by omentopexy. In situ graft replacement was performed in 45 (64%) patients, extra-anatomical bypass in 7 (10%) and endovascular repair in 18 (26%). Three patients (in situ graft replacement, n = 2; extra-anatomical bypass, n = 1) had endovascular repair as a bridge alternative to open surgical repair. Before 2008, we resected the infected tissues and abscess. However, since 2008, we have tried to resect not only the infected tissues and abscess, but also the surrounding aneurysmal wall. When a diagnosis of aorta-related infections was not confirmed preoperatively, Gram’s stain of intraoperative specimen was performed. Complete resection and omentopexy were done if bacteria were detected on Gram’s stain. When an omental flap was not available, a pedicled muscle flap was used. Omental flap installation was performed in 29 (41%) patients, and a pedicled latissimus dorsi muscle flap was used in 3 (4%). Omental flap was installed simultaneously with aortic reconstruction. Two patients had concurrent latisimus dorsi muscle flap installation and 1 had separate surgery.

Medical treatment

We applied pre- and postoperative antibiotic therapy based on the culture results and drug-sensitivity tests according to the Guidelines for the Prevention and Treatment of Infective Endocarditis of the Japanese Circulation Society (2003–) and the Sanford Guide to Antimicrobial Therapy (1999–).
Statistical analysis

The data were processed using the Stat View J-5.0 software (SAS Institute, Inc., Cary, NC, USA). Continuous values are expressed as the mean ± standard deviation. Freedom from infection-related death and from aortic event were assessed using the Kaplan-Meier method. Differences were considered statistically significant when $P < 0.05$.

RESULTS

Hospital mortality was 17.1% (12/70). Causes of death (Table 2) were sepsis in 4 patients, bleeding in 2, multiple organ failure in 1, rupture of aortic stump in 1, pneumonia in 1, perforation of colon in 1, rupture of a residual aneurysm and fever in 1, low output syndrome in 1. Hospital mortality was 13% (6/45) in patients with in situ graft replacement, 11% (2/18) in patients with endovascular repair and 57% (4/7) in patients with extra-anatomical bypass. Hospital mortality was 15% (7/47) for patients with infections of the native aorta and 22% (5/23) for patients with postoperative graft infections.

Follow-up was completed in 98.6% of patients, and the mean follow-up period was 26.7 ± 26.0 months. Late deaths occurred in 15 patients and 6 patients died due to aortic infection. Causes of late death (Table 2) were haemoptysis in 4 cases (1.1, 6.5, 24.8 and 74.5 months after surgery), multiple organ failure in 1 (4.7 months after surgery) and rupture of aortic stump in 1 (3.3 months after surgery). Overall 3-year survival was 60.1 ± 6.7% (Fig. 1A) and freedom from infection-related death at 3 years was 75.8 ± 5.6% (Fig. 1B).

Freedom from infection-related death at 3 years for patients with graft infections was 76.1 ± 9.4% compared with 75.8 ± 6.9% in patients with infections of the native aorta ($P = 0.92$) (Fig. 2A). No significant differences were observed in freedom from infection-related death at 3 years regarding the location of infection (abdominal aorta 71.4 ± 17.1% versus thoraco-abdominal aorta 55.6 ± 15.2% versus descending aorta 79.7 ± 8.2% versus root to arch 76.4 ± 9.3%) (Fig. 2B). Freedom from infection-related death in patients with AEF, ADF, ABF and others at 3 years was 55.6 ± 15.2% versus descending aorta 79.7 ± 8.2% versus root to arch 76.4 ± 9.3% versus thoraco-abdominal aorta 71.4 ± 17.1% (Fig. 2C). Freedom from infection-related death at 3 years in patients with extra-anatomical bypass (14.3 ± 13.2%) was significantly worse than that in patients with in situ graft replacement (88.5 ± 4.9%) and endovascular repair (75.2 ± 10.9%) ($P < 0.001$ and 0.001, respectively) (Fig. 3A).

DISCUSSION

Aorta-related infections are life-threatening and relatively rare conditions. Early diagnosis and the use of a combination of surgical intervention and appropriate antibiotic therapy are essential for patient survival. A variety of surgical techniques have been reported, but standard guidelines regarding operative procedures have not been established. Conventional open surgical treatment consists of debridement of the infected tissues and arterial reconstruction with in situ graft replacement or extra-anatomical bypass. The hospital mortality after conventional open surgical treatment is high, ranging from 12 to 36% [1, 2], and related to the need for emergency intervention in patients who often have multiple pre-existing comorbidities. In this setting, some reports have described the successful use of endovascular repair as an alternative strategy [3].

Endovascular repair for patients with aortic infection has the advantages of being minimally invasive, providing prompt aneurysm exclusion and immediate control of bleeding in the case of haemodynamic instability. However, placement of stent-grafts in an infected environment remains a major concern, and the long-term outcomes of patients who undergo endovascular repair for aortic infections are unknown. In the present study, patients who underwent endovascular repair had more aorta-related events than those who underwent in situ graft replacement. A review reported by Kan et al. [4] identified 22 reports of endovascular repair of mycotic thoracic and abdominal aortic aneurysms, which included a total of 48 cases. The 12-month actuarial survival rate of the persistently infected group was significantly worse than that of the healed group (39.0 ± 17.0 vs 94.0 ± 4.0%, $P < 0.05$). Rupture of the aortic aneurysm and fever were the only significant independent predictors of failure identified by multivariate logistic regression analysis. They emphasized the role of endovascular repair as a feasible alternative treatment for infected aneurysm when the active infection was well controlled without fever. However, they concluded that a definite surgical treatment should be considered when fever persisted after endovascular repair. Kakkos et al. compared outcomes after endovascular repair with those after surgical
Figure 2: (A) Freedom from infection-related death in patients with postoperative graft infection versus infection of the native aorta. (B) Freedom from infection-related death in patients with abdominal aortic infection versus thoraco-abdominal aortic infection versus descending aortic infection versus root to aortic arch infection. (C) Freedom from infection-related death in patients with AEF versus ABF versus ADF versus others. AEF: aorto-oesophageal fistula; ABF: aortobronchial fistula; ADF: aortoduodenal fistula; TAAA: thoraco-abdominal aorta.
open repair of aortoenteric fistulas. Eight patients were managed with endovascular repair and 17 with open repair. The overall long-term survival rates of the two groups were similar. However, endovascular repair had worse recurrence-free rates at 2 years (endovascular 51 vs open 78%), sepsis-free rates at 2 years (28 vs 70%), reoperation-free rates at 2 years (30 vs 64%) and aortoenteric fistula-related death-free rates at 2 years (17 vs 38%) comparing with open repair. They concluded that endovascular repair should preferentially serve only as a bridge to surgical open repair. In contrast to endovascular repair, conventional open surgical treatment allowed surgical cleaning with aggressive debridement of infected tissues. We would perform aggressive resection of all infected tissues, including the removal of endovascular stent-grafts, as soon as the patients’ condition was stabilized.

Our data showed that overall survival at 3 years was 60.1 ± 6.7% and hospital mortality rate was 17.1%, in spite of patients with severe infections, such as thoraco-abdominal aortic infections (12/70, 17%), postoperative graft infections (22/70, 31%) and fistulae complications (29/70, 41%). Also, we have improved freedom from infection-related death significantly since 2008. The reason for better outcome is to resect not only the infected tissues and abscess, but also the surrounding aneurysmal wall. Hsu and Lin [1] stated that one of the possible ways to prevent the recurrence of infection was aggressive surgical debridement. Yamashiro et al. [6] described that the infected aneurysm should be completely resected and maximally debrided along with surrounding tissue to prevent prosthetic graft infection.

There is no consensus regarding the reconstruction method of the aorta in the presence of infections. Historically, extra-anatomical bypass in combination with debridement of infected tissues and excision of the infected aorta with oversewing of the non-infected aortic stump was considered to be a standard treatment. However, despite the administration of lifelong anticoagulation therapy, the patency rates of long axillofemoral bypass grafts are not optimal, and fatal aortic stump bleeding has been reported [7]. Moreover, extra-anatomical bypass is contraindicated if the infection involves a critical anatomic area, such as the aortic arch or visceral arteries. In the present study, most of the patients who underwent extra-anatomical bypass were in complicated and poor conditions.

Recently, some studies [1, 2, 8] have shown that in situ graft replacement in combination with extensive debridement of all infected tissues and antibiotic treatment is a better strategy. Excellent results have been reported for in situ replacement using allografts. Knosalla et al. reported 8 cases who underwent operative repair of mycotic aneurysms using cryopreserved allograft material. Six (75%) patients were treated successfully. They described the efficacy of cryopreserved allograft material for mycotic aneurysms of the thoracic aorta [9]. Saito et al. also reported the efficacy of cryopreserved aortic allografts. Eleven patients received in situ cryopreserved aortic allograft replacement for the treatment of AEF. Hospital mortality was 27% (3/11) and there were no infection-related late deaths [10]. However, cryopreserved allografts may not be available in emergency situations because of the limited availability of allografts in Japan.

The use of antibiotic-bonded grafts (i.e. rifampicin-soaked gelatin-sealed Dacron graft) has been reported to be effective [8]. Lachapelle et al. conducted an experimental study of rifampicin-soaked gelatin-sealed Dacron graft and reported that it was superior to intravenous rifampicin in preventing graft infection. Rifampicin has antimicrobial effects against gram-positive staphylococci, but its effect against gram-negative bacilli is controversial. However, a high local concentration of rifampicin from the graft is thought to protect the prosthetic graft from gram-negative bacilli [11]. Further, Koshiko et al. [12] reported that rifampicin-gelatin grafts were clearly effective against for Staphylococcus epidemidis, whereas no efficacy was recognized against either MRSA or Escherichia coli. As other options for graft, the good results of autologous superficial femoral vein [13] and bovine pericardial conduit [14] were reported.
On the other hand, implanted prosthetic grafts should be covered with omental flap to prevent complications caused by residual infection. The omentum has a rich blood circulation and abundant lymphoid tissues with a high absorptive capacity, and this provides the clearance of bacteria [15]. A pedicled muscle flap can be used when an omental flap is not available, as is the case with the patient who has undergone laparotomy or gastrectomy [16]. Muscle flap installation is also a valid therapeutic option in the management of intrathoracic infection with cavity formation. It not only obliterates the cavity but also delivers a high concentration of oxygen, antibiotics and immune components to the infected area [17].

In western countries, the most common organisms responsible for aortic infection are *S. aureus* and *Streptococcus* species. On the other hand, in Asia, *Salmonella* seems to be the most common responsible organism causing aortic infection. In out cohort, 24 (34%) patients were blood culture-positive preoperatively, and the most common responsible micro-organism was MRSA in 5 patients. Of 24 patients, 5 patients died because of aorta-related infections (MRSA, *n* = 2; MRSE, *n* = 1; *Pseudomonas aeruginosa*, *n* = 1; *Enterococcus faecalis*, *n* = 1). Many Gram-negative bacteria such as *Salmonella*, *Pseudomonas* and *E. coli* species are easy to invade adjacent aortic tissue and eventually lead to anastomotic disruption [18]. It is very important to decide the timing of operation depending on the condition of the patient with Gram-negative bacteria. However, we are very careful about timing of operation not to miss an opportunity. Patient outcomes with MRSA and fungal infection are less favorable with an increase in both mortality and morbidity [19, 20]. Not only our aggressive surgical strategy but also lifelong antibiotics are mandatory to such a patient.

ADF, ABF and aorto-oesophageal fistula are rare but highly fatal conditions that cause massive gastrointestinal and respiratory tract bleeding. These conditions occur most frequently secondary to thoracic trauma, aortic aneurysms, ruptured penetrating aortic ulcers, oesophageal or bronchogenic malignancies, endovascular aortic repair and thoracic or abdominal surgery. A multidisciplinary approach is essential for successful treatment. Contrary to our expectations, freedom from infection-related death of patients with ABF was better in this study, because the lower airways, especially the peripheral bronchi, are aseptic, unlike the oesophagus [21]. Bailey et al. [22] also reported excellent results in patients with ABF. Eleven patients received thoracic endovascular aortic repair as definitive management of ABF. No intraoperative or 30-day deaths occurred. In all 11 patients, no additional haemoptysis or recurrence of infection was noted postoperatively. In the present study, freedom from infection-related death is low in patients with AEF like other reports. However, survival in patients with AEF has been improved by complete resection of all infected tissues (including the aneurysmal wall), simultaneous oesophagectomy, in situ reconstruction of the aorta using a rifampicin-soaked gelatin-impregnated Dacron graft and installing an omental flap. Four patients have been managed by this strategy since 2008. Hospital mortality was 25% (1/4) and the cause of death was pneumonia, but not related to aortic infection. However, hospital mortality was 67% (2/3) before 2008, and causes of death were bleeding from the aorta and sepsis.

Postoperative graft infection, particularly thoracic aortic graft infection, is associated with very high morbidity and mortality. Surgical treatment is very challenging and involves major interventions in patients who are often critically ill. Coselli et al. [23] reported 19 patients with thoracic aortic graft infections (ascending to aortic arch, *n* = 15; descending aorta, *n* = 2; thoraco-abdominal aorta, *n* = 2), and 30-day postoperative survival of 89% and in-hospital mortality of 42%. Although prompt and precise diagnosis of graft infection is essential, the clinical presentation of prosthetic vascular infection is often non-specific and misleading. Positron emission tomography (PET) and leucocyte scanning are useful to diagnose graft infection. Tokuda et al. [24] reported that 18F-fluorodeoxyglucose PET was useful to promptly and precisely confirm the presence of graft infection. They stated that the maximal standardized uptake value greater than 8 around a graft suggested the presence of graft infections (sensitivity: 1.0 and specificity: 0.8). And if multiple prosthetic grafts were implanted, we could not resect all prosthetic grafts. PET-CT is very effective in determining the resection area. And transoesophageal echocardiography is also useful. When vegetation is attached to the graft, graft replacement must be performed. Traditional treatment for this condition is aortic reconstruction with removal of infected prosthetic graft. Some authors reported that removal was not necessary [25]. But the number of reports is limited. Our strategy for patients with postoperative graft infections is resection of all infected tissues (including the infected prosthetic graft), in situ reconstruction and omentopexy, as well as infections of the native aorta.

**STUDY LIMITATIONS**

This is a retrospective non-randomized study conducted in a small number of patients, and all operations were performed at a single institute. Statistical significance was determined regarding the long-term results between surgical options (Fig. 3A and B) and long-term results before 2008 and since 2008 (Fig. 4). However, because the number of patients in each group is small, especially the number of patients with extra-anatomical bypass, the reliability of *P*-values in these analyses may be low. Histopathological examinations were not performed for patients who only underwent endovascular repair.

**CONCLUSIONS**

Aorta-related infections are associated with high mortality and morbidity. However, aggressive surgical strategy (i.e. radical resection of all infected tissues, abscess, aneurysmal wall; in situ replacement with a rifampicin-bonded gelatin-impregnated Dacron graft and omental or pedicled muscle flap installation) resulted in improved survival. When the patients have communications between the aorta and oesophagus, bronchus or intestine, simultaneous resection of the aorta and the affected adjacent organs is essential. Moreover, in haemodynamically unstable patients, endovascular stent-grafts are effective as a bridge alternative.

**Conflict of interest:** none declared.

**REFERENCES**


APPENDIX. CONFERENCE DISCUSSION

Dr T. Sioris (Tampere, Finland): Your results are very impressive, especially related to the patients who have fistulae. When you presented your results before and after you had changed to a very radical debridement, I think your grafts nicely showed the importance of a radical cleaning out of all the infected tissue. Some of the numbers in your statistical comparisons, such as the seven patients who had extra-anatomical bypass, are a little small perhaps for strong P-values, but the grafts clearly indicate the results in spite of this.

Now, when the case is obvious and the patient has a fever and you have CT findings such as you showed, with contrast enhancement of the cavity and fluid accumulation, perhaps even gas, blood culture positivity, then the decision is straightforward. You go in, and, as we all know, you find the prosthesis floating in pus and it comes out just by looking at it, if I may say so. But then you have another problem. Sometimes you have the patient who has the on and off type of fever and the on and off CRP. As you showed, not all are blood culture positive, only a third, only a third had fever, and then you have a graft in the patient, and you have to make a decision, what do I do with the patient who has a graft and maybe has a graft infection? So my first question is, what diagnostic findings do you require before you decide to take the risk of almost 20% mortality for operation and you go in and change the graft, because it is a big undertaking? This is my first question, the diagnostic criteria for graft infection in your decision to go for operation.

Dr Yamanaka: It is very difficult to diagnose graft infection. A diagnosis of graft infection is determined by the patient’s clinical course, blood cultures, blood examination and CT. CT is performed several times, and when the gas appears and when the low density area around the graft has a tendency to enlarge, we diagnose graft infection. In some cases, graft infection in the early postoperative phase is cured by only irrigation. But usually we think graft replacement should be performed. And transoesophageal echocardiography is also useful. When vegetation is attached to the graft, graft replacement must be performed. And we perform a PET scan when we cannot diagnose graft infection.

Dr Sioris: That would have been my next question, what do you think a PET scan or a leukocyte scan will add into your formula for making decisions?

Dr Yamanaka: As I said, PET scan is performed when we cannot diagnose graft infection. In addition, we often perform PET scan to determine the resection area. If multiple prosthetic grafts were implanted, we could not resect all the prosthetic grafts. So we perform PET to determine the resection area. Regarding leukocyte map, we never have performed it.

Dr Sioris: Then there are two kind of microbes which I am particularly worried about which are not very common. One is Pseudomonas and, as we all know, it’s a collagen-eating bacteria which can cause nasty surprises. The second bug is Candida, or actually any fungal infection, Candida being the most common, for being so really, really difficult to eradicate from any tissue. If you have a finding of Pseudomonas or Candida, let’s say, in the blood culture or some other means, how does this affect your timing of surgery, especially if you find Pseudomonas, how fast do you feel the need to go in, and what about if you have a slow but difficult bug like Candida?

Dr Yamanaka: We don’t change the treatment decision and the timing of surgery depending on the bacteria or fungus, but we have the impression that MRSA, Pseudomonas and Candida are very bad. So we must be very careful of your management of the infected patients who had extra-anatomical bypass, are a little small perhaps for strong patients who had a slow but difficult infection. We use the rifampin graft only because xenografts are hard to come by these days, but would you still use the use of xenograft material, such as bovine pericardium or a tissue scaffold like, let’s say, CorMatrix or such xenograft materials, better than prosthetics, or perhaps the use of deep femoral vein grafts from one or both legs instead of using synthetic material?

Dr Yamanaka: We always use the rifampin graft only because xenografts are not available in Japan, and there is a deviation of diameter between the aorta and the deep femoral vein.