Opinion: Aortic Graft Infection—Any Guidelines or Just Surgeon's Experience Lines!

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Aggressive strategies for thoracic aortic graft infection, including resection of all infected tissues, in situ replacement with a rifampicin-bonded graft, and omental flap installation, resulted in improved survival.

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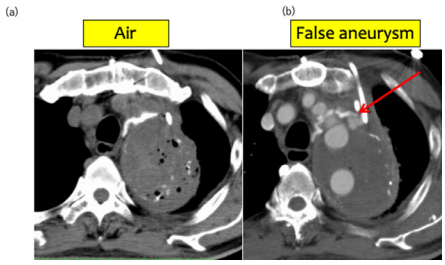

(a) CT scan image of TGI, where many air bubbles exist around the elephant trunk after total arch replacement. (b) False aneurysm formation between the anastomosis between the arch graft and the elephant trunk.

Central Message

Aggressive strategy for thoracic aortic graft infection, including resection of all infected tissues, in situ replacement with a rifampicin-bonded graft and omental flap installation, resulted in improved survival.

INTRODUCTION

Although the infection involving aortic graft prostheses is infrequent, it is a devastating complication of reconstructive aortic graft surgery and is associated with high mortality. Fortunately, thoracic aortic graft infection (TGI) is reported less frequently than the graft infection in the groin or the abdomen. Underlying comorbidities, such as diabetes mellitus, the elderly, or immune compromise, increase the risk of infection and infection-related complications. Clinical experiences for treating the TGI were so sparse, and no comparative studies with a large number of patients have been achieved. There have been few guidelines where the treatment strategies for the TGI were described. We describe our approach for the TAGI based on our experiences.

INCIDENCE OF TGI

The incidence of TGI has been reported as 1–5% after open surgery for the thoracic aorta graft replacement and 0.5–5% after thoracic endovascular insertion (TEVAR), which was less than those of the aortic graft infection in the abdomen or graft infection at the groin.[1–5]

PATIENTS

From November 1999 to July 2017, 105 patients with aorta-related infection underwent surgical intervention at the Department of Cardiovascular Surgery, Kobe University Hospital. These patients consisted of 3.5% of all surgical procedures for the thoracic surgery in the same periods. Patients who had postoperative deep sternal infections immediately after surgery were excluded. Fifty-nine had native aorta infection, and 46 had aortic graft infection. The clinical data and outcome of 31 patients who had the TGI were analyzed. The patients' age was 69.9 ± 12.4 years. The locations of the TGI were aortic root to arch in 7 patients (23%), descending aorta in 22 (71%), and thoracoabdominal aorta in 2 (2.3%). There were aortobronchial fistula in 3 patients and aortoesophageal fistula in 10. Fifteen patients (48%) had comorbidities, and the most common comorbidity was diabetes (10 patients), followed by malignancy (3 patients) and collagen disease (2 patients).

MICROBIOLOGY

The microbiological cause of TGI has changed over the years. Gram-positive cocci, such as *Staphylococcus aureus* or Streptococci accounts for more than half of the TGI. Among *S aureus* infections, methicillin-resistant *S aureus* (MRSA) infections are increasing in frequency. Among the gram-negative infections, *Pseudomonas aeruginosa* is now the most common cause. Recently, thoracic aortic surgery has been performed on elderly patients with multiple underlying comorbidities, and the increased frequency of emergency procedures has contributed to the changing spectrum of infection, which includes multidrug-resistant strains.[1]

DIAGNOSIS OF THE TGI

A diagnosis of TGI was made by the patient's clinical course, blood examination, computed tomography (CT) aortic

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imaging, positive results from blood cultures, and the histopathologic examination of the intraoperative specimens.[6] Thirteen patients (42%) had a body temperature higher than 38°C. The preoperative C-reactive protein level, white blood cell count, and hemoglobin level were 10.0 ± 9.2 mg/dL, 10,043 ± 4985/μL, and 9.3 ± 2.0 g/dL, respectively. Our experience disclosed that only 39% (38/105) of patients with aorta-related infections had positive blood cultures.

Typically, the aortic CT images showed bizarre shapes, air, enhancement with low-density areas, and thickened aneurysmal walls but this finding is not always present in the TGI cases (Fig. 1). Moreover, the CT test is not capable of determining the extent of the graft resection when multiple prosthetic grafts were implanted, or extended replacement of aorta was performed. Intraoperative identification of pus around a graft or fistulae formation is the definitive diagnostic criteria of the TGI.

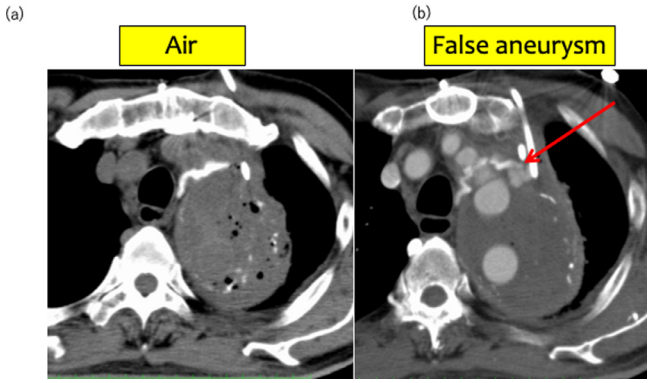


Figure 1. (a) CT scan image of TGI, where many air bubbles exist around the elephant trunk after total arch replacement. (b) False aneurysm formation between the anastomosis between the arch graft and the elephant trunk.

Recently, FGP-PET/CT has been used in the diagnosis of infectious disease. The standardized uptake value (SUV) is commonly applied as a relative measure of 18F-FDG uptakes, in which areas of maximal focal 18F-FDG uptakes are visually detected, and the SUVmax in each area is measured (Fig. 2a). Tokuda et al reported that FDG-PET/CT was useful to promptly and precisely confirm the presence of graft infection. They stated that SUVmax greater than 8.0 around a graft suggested the presence of graft infections.[7] Sah et al noted that the SUVmax cut off the value of ≥3.8 to differentiate between infected and noninfected grafts.[8] Our study done in nondiabetic patients demonstrated that the SUVmax cut-off value was 6.02 for discriminating the infection (Fig. 3b, sensitivity 100%, specificity 74.1%).[9] However, SUV is affected by factors such as physique, blood glucose level, renal function, and the uptake duration between the injection and scan. Moreover, not only infection but also various types of inflammation can cause high uptake because FDG-PET/CT is based on the uptake of radioactive-labeled glucose in metabolically active cells. Keidar et al reported that 18F-FDG uptakes were found in 92% of noninfected vascular prostheses because of foreign body response.[10] Our results showed no difference of the SUVmax value between the infected aorta and noninfected ones (Figs. 3a and 4).

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 (2017)[11] and the "Vascular Graft Infections, Mycotic Aneurysms, and Endovascular Infections: A Scientific Statement from the American Heart Association (2016)."[1] In 1 patient who had the infected Crawford extension II thoracoabdominal graft was treated with the continuous irrigation of the perigraft space for 2 months.

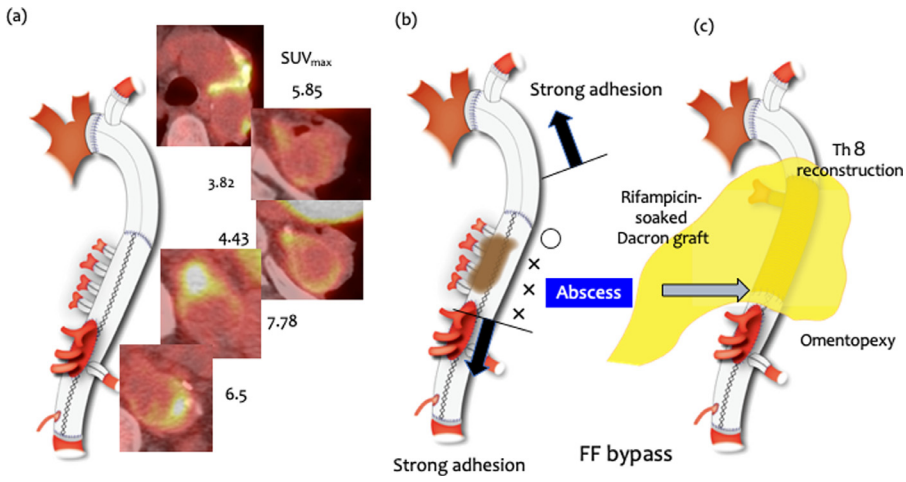


Figure 2. The illustrations of TGI after thoracoabdominal aorta replacement. (a) The images of the FDG-PET and each SUVmax values were shown. (b) There was abscess formation around the lower descending aortic portion and the other portions of the graft strongly adhered to the surrounding tissues. (c) The descending aortic portion of the graft was replaced by a new graft and reconstruction of the Th 9 segmental artery was reconstructed. A pedicle of the omentum wrapped the graft.

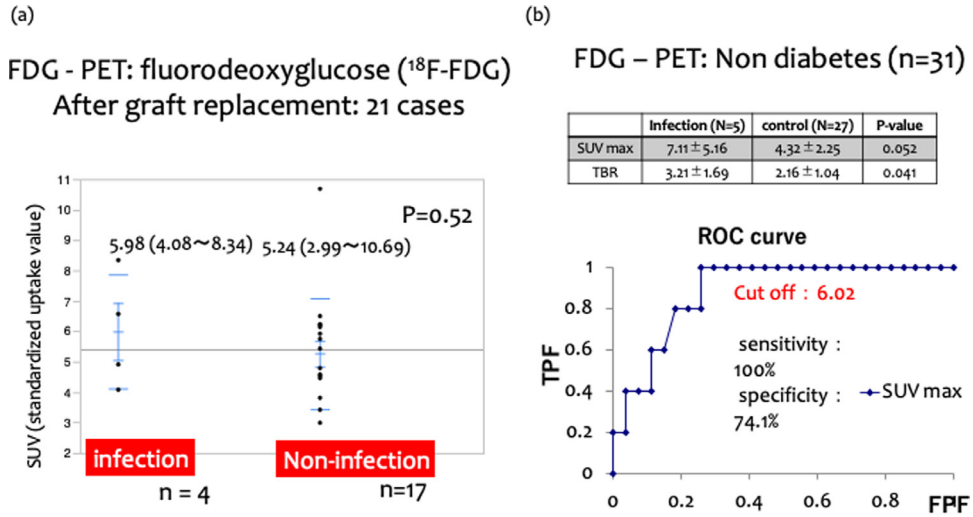


Figure 3. (a) Comparison of the SUVmax of FDG-PET between the patients with aortic infection and noninfection. (b) The ROC curve of the SUVmax values of the FDG-PET in nondiabetic patients with aortic infection. The cut-off value is 6.02. The sensitivity or specificity was 100% and 74%, respectively.

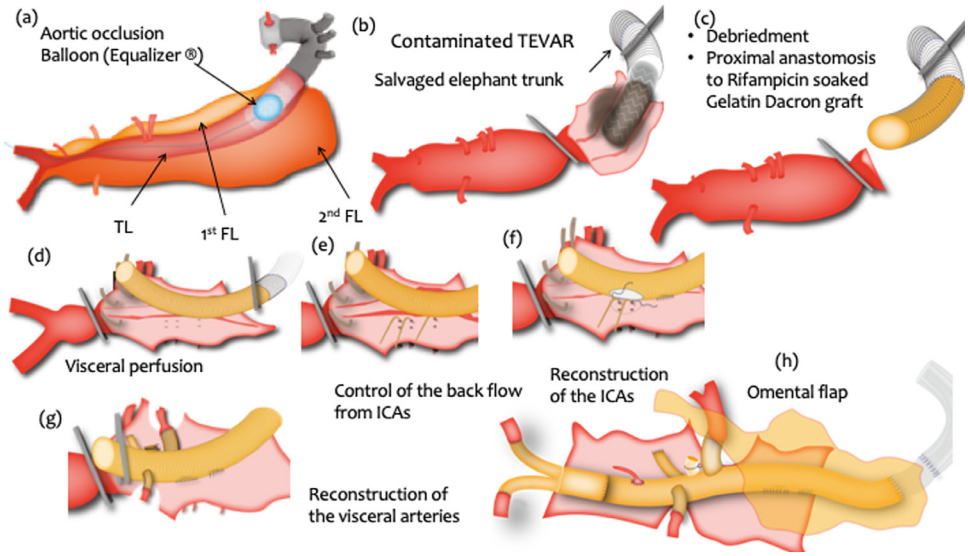


Figure 4. The illustrations of TGI after total arch replacement with the elephant trunk and additional TEVAR (video case). (a) After starting the partial cardiopulmonary bypass from the femoral artery and vein, the aortic occlusion balloon was inflated inside the elephant trunk. (b) The descending aorta was open after aortic clamping. The infected TEVARs and the elephant trunk were resected. Extensive debridement of the infected tissue was achieved, and copious irrigation was made using the Toluidine blue solution. (c) A new Dacron graft soaked with Rifampicin was anastomosed to the previous healthy graft. (d) The thoracoabdominal portion was opened, and the visceral perfusion was initiated using balloon tipped cannulae. (e) The back flow from the segmental arteries was controlled by several balloon catheters. (f) The lower segmental arteries were reattached to the graft. (g) The buttons of each visceral artery were anastomosed to the aortic graft using small branches. (h) The pedicle of the omentum was introduced to the left chest and wrap the new graft.

SURGICAL TREATMENT

Surgical treatment is very challenging and involves major interventions in patients who are often critically ill. It is essential to decide the timing of operation depending on the condition of the patient with TGI. However, we are cautious about the timing of operation not to miss an opportunity.

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 aorta ruptured, the contaminated site was localized, and the patient was an immunocompromised host (such as those with advanced cancer) or as a bridge to open surgical repair. 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 hemodynamic instability. A review reported by Kan et al

identified 22 reports, 48 cases of endovascular repair of mycotic thoracic and abdominal aortic aneurysms, and they concluded that a definite surgical treatment should be considered when fever persisted after endovascular repair.[12] Using the meta-analysis of endograft infection, Moulakakis et al reported that a trend of a better outcome with endograft explantation compared with endograft preservation and that the mortality rate of surgical conversion was much higher in the presence of a fistula.[2] Similarly, Li et al analyzed clinical data of 402 patients and concluded that surgical treatment is a better option compared with conservative management in selected patients with aortic endograft infection. The outcome was worse in patients with infected TEVAR and aortoesophageal fistula.[13] Our experiences showed that the infected TEVAR should be resected as much as possible.[6] Coselli et al reported their experiences of open aortic surgery after TEVAR and showed that patients with infected TEVAR had a worse outcome.[14]

Historically, extra-anatomical bypass in combination with debridement of infected tissues and excision of the infected aorta with oversewing of the noninfected aortic stump was considered to be a standard treatment. However, the patency rates of long axillobifemoral bypass grafts are not optimal, and fatal aortic stump bleeding has been reported.[15] In our experiences, most of the patients who underwent extra-anatomical bypass were in poor preoperative conditions and had a worse outcome.

The 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 (Fig. 2).[6,14] Complete resection of the foreign graft was possible in 14 patients (45%). Resection of the infected graft and salvaging the noninfected graft was done in 17 patients (55%). In situ graft replacement was performed in 26 patients (84%), extra-anatomical bypass in 2 (6.5%), and endovascular repair in 3 (9.7%). Three patients (in situ graft replacement, $n = 2$; extra-anatomical bypass, $n = 1$) had endovascular repair as a bridge alternative to open surgery. The omental flap was simultaneously installed in 18 (58%) patients, and when an omental flap was not available, a pedicled muscle flap was used in 3 (9.6%) later.

As for the graft material, some studies have shown excellent results for in situ aortic reconstruction using allografts.[16] However, cryopreserved allografts may not be available in emergencies, and also the limitation of the caliber and the length may exclude the usage of the allograft for the TGI. The use of antibiotics-soaked graft has been controversial. The rifampicin was effective against for *Staphylococcus epidermidis*, whereas no efficacy was recognized against either MRSA or *Escherichia coli*. As the other options for graft, the good results of autologous superficial femoral vein and bovine pericardial conduit were reported.[17]

RESULTS

Hospital mortality was 23% (7/31). Causes of death were persistent sepsis in 2 patients, multiple organ failure in 2, surgical bleeding in 1, cerebral bleeding in 1, and rupture of the aortic stump in 1. Hospital mortality was 19% (5/26) in patients with in situ graft replacement, 33% (1/3) in patients with endovascular repair, and 100% (1/1) in patients with extra-anatomical bypass. Follow-up was completed in 97% of patients, and the mean follow-up period was 24.2 ± 27.1 months. Late deaths occurred in 4 patients, and 2 patients died due to aortic infection. Causes of late death were hemoptysis or hematemesis in 2 cases (6.5 and 74.5 months after surgery), multiple organ failure in 1 (4.7 months after surgery) and malignancy in 1. Overall, 5-year survival was 69.6 ± 11.2% and freedom from infection-related death at 5 years for patients was 75.8 ± 8.0%.

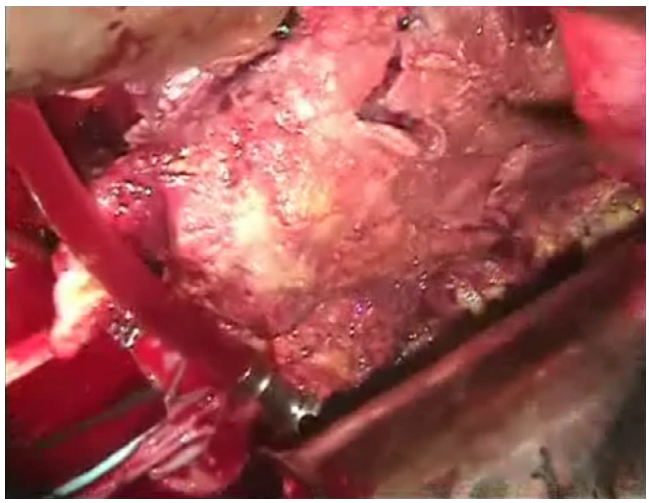
Our experiences of treatment for the esophageal fistula secondary to the TGI showed that hospital mortality was noted in 2/10 patients (20%) and late death occurred in 3 patients due to pneumonia, cerebral bleeding, and persistent infection.[18] A multidisciplinary approach is essential for successful treatment. Multicenter studies done in both Europe[19] and Japan[20] demonstrated that preservation of the esophageal was a major risk factor for the worse outcome. Survival in patients with esophageal fistula has been improved by complete resection of all infected tissues (including the aneurysmal wall), simultaneous esophagectomy, in situ reconstructions of the aorta using a rifampicin-soaked gelatin-impregnated Dacron graft, and installing an omental flap.

CONCLUSIONS

Aortic graft-related infections are associated with high mortality and morbidity. However, aggressive surgical strategy, such as 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.

SUPPLEMENTARY MATERIAL

The following is the supplementary data to this article:



Video 1. Preoperative CT scans showed post-total arch replacement with elephant trunk insertion and additional endografts insertion. The proximal descending aorta was dilated to 100 mm in diameter with staining the adventitia with the contrast, and the false lumen was filled with huge amounts of thrombi. The distal descending aorta showed a 4-channel dissection. The visceral arteries were branched from the true lumen. The dissection terminated at the bifurcation of the left common iliac artery.

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