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Surgical treatment of graft infection combined with aortoesophageal fistula after TEVAR: a retrospective single-center, single-arm study

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Abstract

Objective Aortoesophageal fistula (AEF) secondary to thoracic aortic endovascular repair (TEVAR) is rare and fatal. The author reports the treatment methods and outcomes of 10 patients with a TEVAR graft infection and an aortoesophageal fistula.

Method A retrospective analysis was conducted on the clinical data of 10 patients who developed a secondary AEF and a graft infection after TEVAR from March 2018 to March 2024.

Result The perioperative mortality rate was 70%. Two patients had TEVAR only and all died of bleeding and infection. Eight patients underwent open surgery, five died within 30 days, four of them died due to massive bleeding, the one patient died of a serious infection after surgery. Three patients recovered well and were discharged. One patient died of severe pneumonia 3 months after discharge, and two patients survived for 6 years and 3 months, respectively.

Conclusion Extra-anatomical bypass reconstruction is feasible for treating graft infection combined with aortoesophageal fistula after TEVAR but related to bad outcomes in most of the patients. It is reserved for highly select patients and is performed at centers with experience with this procedure.

Keywords Aortoesophageal fistula, Transplants, Infection, Thoracic aortic endovascular repair surgery

Introduction

An endograft infection after thoracic endovascular aortic repair (TEVAR) is a dramatic event and associated with a high mortality rate that exceeds 70% [1]. Endograft infection combined with aortoesophageal fistula (AEF) is more rare and portends significantly worse prognosis [2, 3]. As a minimally invasive treatment method for patients with thoracic aortic aneurysm and dissection, TEVAR has been widely used in clinical practice in recent years due to its advantages of minimal trauma and fast recovery, it seems that there has been an increased number of secondary AEF cases after TEVAR [4]. The presence of AEF lead to potential of acute exsanguination, anemia and constant septic that put the patient in a poor condition [5, 6]. Nowadays, the "gold standard" of treatment for endograft infections remains total endograft explantation with arterial reconstruction, resection of infected tissues, extensive debridement, and repair of the fistula [1, 7]. However, the poor condition of patients and great trauma of surgery associated result in a high risk of

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operative complications or death [8]. Due to the rarity of this disease, there are currently no large-scale multicenter studies reporting the efficacy of various treatment strategies for secondary AEF, and the optimal treatment strategy remains unknown. The aim of this study is to report our experiences and discusses our surgical strategy for AEF.

Materials and methods

This was a retrospective analysis of the clinical data of patients who developed a graft infection and an aortoesophageal fistula after undergoing TEVAR at Beijing Friendship Hospital, Capital Medical University, from March 2018 to March 2024. The study protocol was approved by the Ethics Committee of the Beijing Friendship Hospital, and the study was conducted in accordance with the Declaration of Helsinki. Written informed consent was obtained from all study participants. The inclusion criteria were the development of both a graft infection and an aortoesophageal fistula after TEVAR, and the diagnosis was based on contrast-enhanced CT, endoscopy, and PET-CT (Fig. 1A and B). The exclusion criteria were AEF secondary to esophageal tumors or esophageal surgery. This study involved 10 consecutive patients who met the inclusion criteria, and no patients were excluded. Afterward, their medical records were reviewed. On contrast-enhanced CT, air surrounding the prosthesis was considered as the leading radiographic

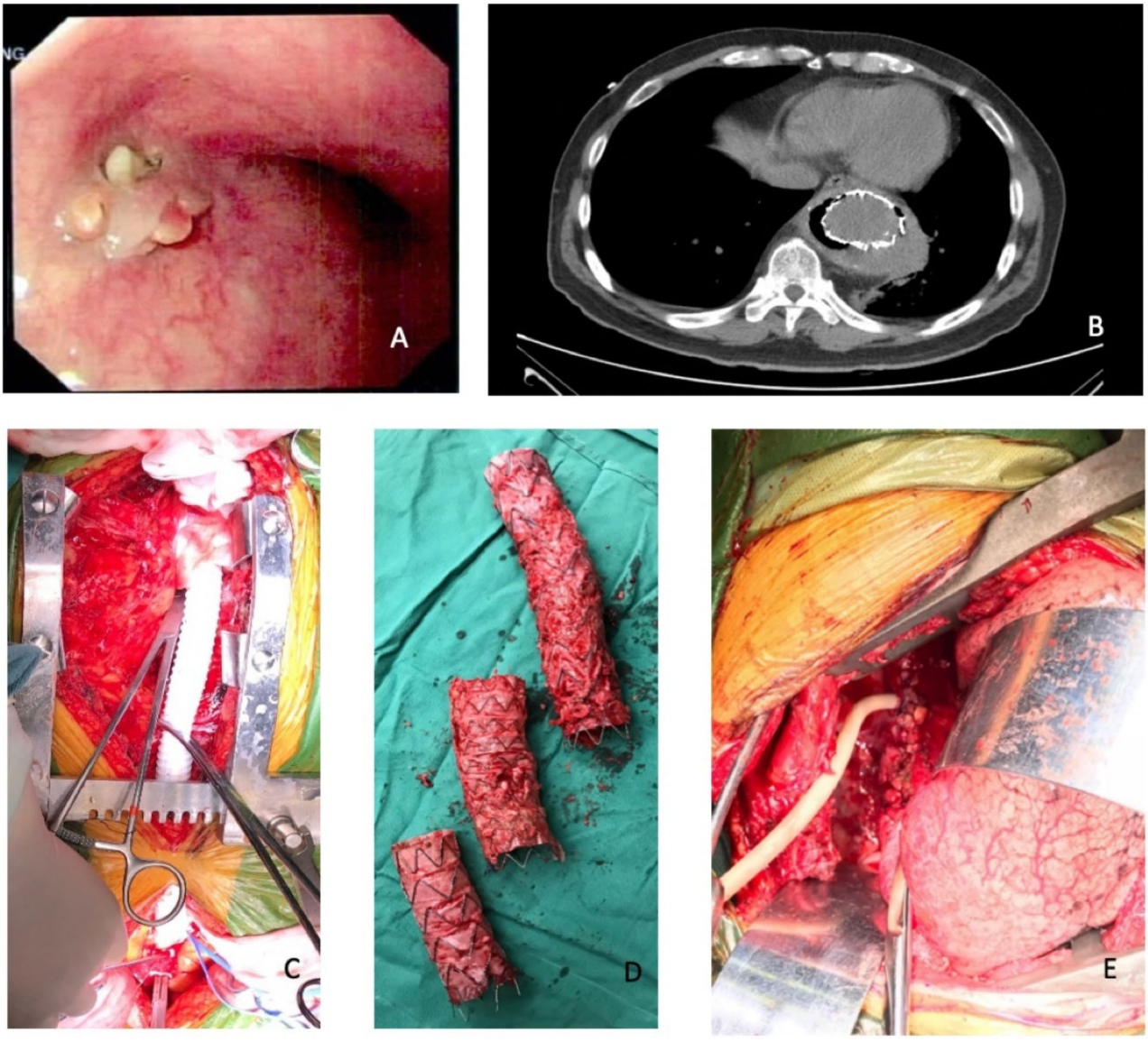

Fig. 1 Preoperative examinations and intraoperative pictures **A**: Endoscopic view showing exposure of the stent and infection lesion; **B**: The enhanced CT scan demonstrating air surrounding the prosthesis and esophagus; **C**: Extra-anatomical bypass from ascending aorta to abdominal aorta; **D**: The removed infected stent-graft; **E**: Drainage of the oesophageal fistula

sign. The diagnosis was confirmed by endoscopy in the half of patients with simple mucosal fistula or indentation. The PET-CT showed an abnormal increase in metabolism around the thoracic aorta and prosthesis.

Therapeutic methods

Parenteral nutrition support and antibiotics were provided after admission. Due to the patient's graft infection and esophageal fistula, the surgical plan including external artificial graft bypass surgery from ascending aorta to abdominal aorta without nonextracorporeal circulation, and resection of infected tissues and graft, extensive debridement. Patients with hemodynamic instability underwent emergency TEVAR, and open surgery was performed after the patient's general condition improved.

Surgical method

Stepwise surgery was performed without extracorporeal circulation under general anesthesia. Step 1: A midline incision was made in the chest to expose the proximal end of the ascending aorta, and a midline incision was made in the abdomen to expose the abdominal aorta. After whole-body heparinization (1 mg/kg), the ascending aorta and abdominal aortic sidewalls were clamped with sidewall forceps, and 16 mm x 35 cm polyester artificial blood vessels were used (BARD, Germany). The proximal graft was anastomosed with the ascending aorta, and the distal graft was anastomosed with the abdominal aorta (Fig. 1C). Then, the thoracic aorta distal to the left subclavian artery was ligation. Step 2: In the right lying position, the fourth intercostal incision on the left anterior lateral side of the chest was made, the 5th, 6th, and 7th ribs were cut, purulent secretions around the aorta and endograft were removed, and if necessary, some lung tissue was removed. After blocking the distal ends of the thoracic aorta, the aorta was incised, the stent graft was removed, and the proximal and distal stumps of the thoracic aorta were closed with Prolene (2−0) (Fig. 1D). Step 3: The adhesions between the esophagus and thoracic aorta were separated, a "mushroom head" drainage tube was placed near the esophageal fistula, and a drainage tube was placed at the site of the mediastinal infection (Fig. 1E).

After admission, empirical antibiotics were administered until discharge. All patients had parenteral intravenous nutrition or enteral nutrition though jejunal nutrition tubes for one months at least one month untill the fistula was healed (confirmed with endoscopy). Antiinfection treatment was adjusted according to the bacteriological examination and treatment progress. After discharge, oral antibiotics were continued for 12 weeks.

Follow-up and outcomes

Patients had contrast-enhanced CT and endoscopy before discharge. They were followed up through telephone calls and outpatient clinic visits after then. The perioperative and late mortality rates, causes of death, major adverse aortic events, and freedom from infection-related death were evaluated.

Results

All the patients were male, with an average age of 57.8 years (36–77 years). All 10 patients underwent TEVAR before, the AEF occurred with an average interval of 5.6 years (3 months to 11 years) after the previous TEVAR. All patients denied a history of esophageal tumors or esophageal surgery. Pathogenic bacteria were detected in three patients (30%), *Enterococcus faecalis* and *Pseudomonas aeruginosa* were detected in one patient, *Pseudomonas aeruginosa* was detected in one patient, and Klebsiella pneumonia was detected in one patient. All 10 patients showed air surrounding the prosthesis on contrast-enhanced CT. Five patients (50%) underwent digestive endoscopy to further confirm the diagnosis, and all located 30–35 cm away from the incisors, the diameter of fistula were between 0.4 and 1.5 cm. Two patients underwent PET-CT, which revealed an abnormal increase in metabolism around the thoracic aorta and prosthesis, suggesting the possibility of infection.

In terms of outcomes, four patients admitted to the hospital in critical condition with unstable hemodynamics. TEVAR was performed in emergency. Two of them died of septic shock and re-bleeding before open surgery. The rest of eight patients underwent open surgery. Unfortunately, five patients (62.5%) died in 30-days after the surgery, four of them died due to massive bleeding, the last patient died of a serious infection after surgery. Only three patients recovered well and were discharged from the hospital. One of them died of severe pneumonia 3 months later, and 2 patients survived for 6 years and 3 months respectively till now. Overall, the perioperative mortality rate was 70%, seven patients were freedom from infection-related death. Table 1 summarizes the characteristics, surgical strategies, and outcomes of these patients.

Discussion

Graft infection combined with AEF is an extremely serious complication after TEVAR, with the main symptoms being hematemesis, fever, or shock (sepsis or hemorrhagic). Delaying treatment can have serious consequences. Secondary AEF after TEVAR is rare, with an incidence rate of 1.5–5% [5, 9–11]. Although the incidence rate is very low, once it occurs, most cases are fatal. At present, there is no consensus on which surgical method is the best treatment. In previous studies,

Table 1 Study population, surgical strategies, and outcomes

Number	Age	Sex	Primary aortic disease	Interval between TEVAR and AEF (years)	symptom	Surgical method	30 days postoperative results	Follow up time (months)
1	48	male	thoracic aortic dissection	0.58	Fever, chest and back pain	Open surgery	survival	3(survival)
2	61	male	Thoracic aortic aneurysm, thoracic aortic dissection	11	Fever, cough, hematemesis	Open surgery	survival	72(survival)
3	50	male	thoracic aortic dissection	9	Fever, chills, chest and back pain	Open surgery	death	——
4	50	male	Aortic ulcer with intramural hematoma	5	Fever, hematemesis, and black stools	Open surgery	death	——
5	49	male	thoracic aortic dissection	7	Fever, hematemesis	TEVAR, Open surgery	death	——
6	36	male	Thoracic aortic aneurysm	11	Fever and black stools	TEVAR	death	——
7	67	male	Aortic intramural hematoma with multiple penetrating ulcers	0.25	Fever, chest pain, hematemesis	TEVAR	death	——
8	75	male	thoracic aortic dissection	4	Fever and abdominal pain	Open surgery	death	——
9	77	male	Thoracic aortic aneurysm	5	Fever and hematemesis	TEVAR, Open surgery	survival	3(death)
10	65	male	thoracic aortic dissection	3	Fever and hematemesis	Open surgery	death	——

TEVAR: Thoracic aortic endovascular repair

graft-enteric fistulas like AEF were contraindications to conservative treatment alone [12]. On the one hand, timely surgical intervention after patients are diagnosed with AEF is crucial for survival, on the other hand, surgical management also carries a high risk of morbidity and mortality up to 64% in previous studies [13].

In previous studies, surgical treatment can be roughly divided into several categories [14–17]: TEVAR, esophageal stenting, esophagostomy or esophageal exclusion, and endograft explantation with arterial reconstruction. The trauma of TEVAR is relatively minor, and bridging TEVAR to the open surgery is a useful adjunct in patients with AEF with hemorrhagic shock [4]. However, although TEVAR has a predominant role in controlling hemorrhage in emergency, infectious lesions and esophageal repair remains [18]. Antoniou et al.'s systematic review included 18 infection related aorto-enteric fistula patients treated with TEVAR alone, showed that 13 patients (72.22%) developed persistent or recurrent sepsis during the follow-up period [19]. The presence of AEF serves as a nidus for continuing bacterial growth and persistent infection. In this study, four patients underwent TEVAR in emergency due to their critical condition and unstable hemodynamics. They were scheduled to underwent open surgery, but two of them died of septic shock and re-bleeding before open surgery. This also proves that TEVAR alone cannot achieve a good prognosis for patients with AEF combined with graft infection. The author believes that it can be used as a bridging treatment, attempting to control bleeding quickly with a minimally trauma and creating opportunities for further open surgery. Some scholars have also attempted to temporarily stop bleeding and reduce the overflow of esophageal contents through esophageal stents to promote esophageal healing and prevent bleeding, but the risk of persistent infection may be high in situations where contamination from the esophageal lesion is ongoing [20]. This disadvantage resulted in a worse prognosis of esophageal stent therapy compared to esophagectomy [21].

Published reports suggest that the combination of graft explantation with arterial reconstruction, resection of infected tissues, extensive debridement, and esophagectomy resulted in the most favorable prognosis of all therapies [4, 21]. There are two methods to rebuild the blood supply of thoracic aorta after endograft explantation: extra-anatomical bypass and in situ repair [7]. The extra-anatomical repair was designed to avoid insertion of new aortic prosthesis in the infected mediastinal tissue. However, the bleeding complications lead by residual aortic stumps were terrible. On the other hand, cryopreserved aortic homograft or rifampicin-bonded Dacron graft accompanied with omental flap provides a better chance to perform in situ aortic repair [22]. Yamazato et al. studied 18 patients who had AEF secondary to aortic lesions [4]. The aortic infection–related death rate in patients had extra-anatomical bypass was 66.7%, which was much higher compared to patients had in situ reconstruction (15.4%). Another review included 41 patients with thoracic endograft infection had endograft explantation, most patients (85.4%) underwent an in situ reconstruction with either a silver-coated graft or a cryopreserved allograft and the mortality rate was 42.8% (15 of 35 succumbed), whereas in patients with extra-anatomic bypass, it was 66.7% (4 of 6 patients died) [1]. Unfortunately, rifampicin-bonded Dacron graft or

cryopreserved allograft were not obtainable in our center, we can only use ordinary graft to achieve the reconstruction, and extra-anatomical bypass was the only choice. Finally, the mortality was 62.5%, and 50% of patients succumbed because of the major bleeding after surgery. Our frustrated result also confirms the advantage of in situ reconstruction in perioperative mortality rate. Otherwise, all endografts in our study were located at zone 3 or 4. Because the proximal thoracic aorta is hard to be clamped if the landing zone is proximal to left subclavian artery or even left common carotid artery. This also limits the application of this surgery strategy in these patients, especially when fenestrated or chimney techniques are applied.

The presence of fistula significantly increased the mortality rate, and esophagectomy is considered mandatory in most studies [1, 22]. The esophagectomy can help control the infection especially in patients had in situ repair. In this study, we didn't perform esophagectomy for two reasons. First, all patients had extra-anatomical bypass, no grafts were left near the fistula. Second, to reduce surgical time and trauma, as the extra-anatomical bypass take more time compare to in situ reconstruction. After removing the infected graft, relieving the local esophageal compression caused by the stent and infected mediastinal tissue, and fully draining of infected area, the AEF of all three surviving patients were healed. These results indicate that, in patients had extra-anatomical bypass reconstruction, preserving the esophagus is feasible based on thorough debridement, drainage, and decompression.

Moreover, previous studies showed that wrapping implanted artificial aortic grafts with omental flaps could prevent or reduce the occurrence of subsequent infection [23]. Unfortunately, we didn't use omental flap because we performed an extraanatomical graft bypass to avoid graft infection, but the infection of AEF area and subsequent re-bleeding of proximal stumps of the thoracic aorta still occurs. Using omental flap in the surrounding area of AEF in the future may be helpful to improve this poor outcome.

Among these 10 patients, 3 had positive blood culture results. Throughout the treatment process, our team provided broad-spectrum anti-infection treatment and recommended extending the course of anti-infection treatment. Canaud et al. [24] noted that in more than 40% of AEF patients after TEVAR, bacteriological tests were positive, and there was a strong negative correlation between prolonged antibiotic treatment and mortality.

Finally, these patients usually have a poor nutritional status, accompanied by symptoms such as infection and bleeding, which increases the difficulty of nursing care. Postoperative respiratory management for patients should be strengthened, coughing and expectoration should be guided. Patients should be provided with sufficient nutritional support and receive a combination of enteral nutrition and parenteral nutrition. For enteral nutrition, the principle of gradual progression from less to more should be followed, and placing jejunal nutrition tubes can reduce the likelihood of aspiration and gastroesophageal reflux. Patients should receive psychological support, encouraged to engage in good communication, and encouraged to actively seek treatment, which promotes patient recovery.

This study has the following limitations. First, due to the rarity of postoperative graft infection combined with AEF in TEVAR patients, the number of patients included in this study was small, this disadvantage inherently limits the generalizability of the findings. Second, this study is inherently subject to selection bias, as the patients with complex endograft landing zone were not considered for open surgery in our center, the results of this study do not reflect the general characteristics of patients, and the surgical plan should be adjusted according to the situation of different patients.

Conclusion

In summary, the treatment of AEF secondary to TEVAR with concurrent infection is highly challenging and has a high mortality rate. Extra-anatomical bypass reconstruction combined with removal of the infection graft and esophageal fistula open drainage surgery is feasible for treating graft infection combined with AEF after TEVAR but related to bad outcomes. The bleeding complications lead by residual aortic stumps were frequent and fatal. It is reserved for highly select patients and is performed at centers with experience with this procedure.

Author contributions

SJ was involved in protocol/project development, data collection and management, data analysis and manuscript writing. GW and XQ were involved in project development and data analysis. WL was involved in project development, manuscript review and editing. All authors have read and approved the manuscript.

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Data availability

No datasets were generated or analysed during the current study.

Declarations

Ethical approval

The studies involving human participants were reviewed and approved by the Institutional Ethical Review Board of Beijing Friendship Hospital. The patients/participants provided their written informed consent to participate in this study.

Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Competing interests
The authors declare no competing interests.

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