Chapter 9

Infected Aortic Aneurysms

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Additional information is available at the end of the chapter

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Abstract

Infected aortic aneurysms are surgical urgencies, requiring prompt management to avoid the development of catastrophic complications. Although traditional open surgery composed of radical debridement and aortic reconstruction remains the gold-standard, many favorable results of the endovascular repair strategy have been reported. In this chapter, the etiology, bacteriology, clinical manifestation, and diagnostic criteria of infected aortic aneurysms will be discussed in detail at first, followed by a comprehensive review of both traditional open surgery and endovascular repair, based on current evidences and the authors' institutional experience. Along with long-term oral antibiotic suppression and aggressive adjunctive procedures, endovascular repair for uncomplicated infected aortic aneurysms could be a definite treatment alternative to traditional open surgery in the endovascular era.

Keywords: infected aortic aneurysm, mycotic aortic aneurysm, antibiotic, aortic reconstruction, graft, endovascular aortic repair (EVAR), thoracic endovascular aortic repair (TEVAR)

1. Introduction

An infected aneurysm, commonly known as "mycotic aneurysm", is an abnormal dilatation of the artery associated with an infectious process [1–5]. In 1885, Sir William Osler first used the term "mycotic aneurysm" to describe multiple bead-like aneurysms of the aortic arch, resulting from suppuration in vessel wall in one patient with infective endocarditis-related aortic valve vegetations [1]. Currently, mycotic aneurysm is widely accepted as synonymous with infected aneurysm, describing all kinds of infected aneurysms with different etiologies, but not only those caused by septic emboli from a cardiac origin [6]. Moreover, the majority of infected (mycotic) aneurysms is caused by bacteria, but not fungus [4]. In this chapter, we will discuss in detail and review the current literatures about infected aneurysm, and we will present the authors'

institutional experience of infected aneurysms involving the aorta. Here, the term "infected aortic aneurysm" instead of "mycotic aortic aneurysm" is used to prevent any misunderstanding.

Infected aortic aneurysms are generally surgical urgencies and comprise about 0.7–2.6% of all cases of aortic aneurysms [7–12]. The therapeutic considerations for infected aortic aneurysms include perioperative medical management (i.e., preoperative and postoperative antibiotic selection and course), timing and type of surgical procedures (traditional excision, debridement, and reconstruction versus endovascular technique), and the necessity of adjunctive procedures [7–15]. Complications occasionally occur at the initial presentation, including massive exsanguination due to free rupture and the development of aneurysm-related fistulations. Emergency operation is indispensable to salvage patients presenting with ruptured infected aortic aneurysms. Since the infectious process is usually not suppressed sufficiently even with proper antibiotic treatment course at the time of operation in these patients, the risk of postoperative persistent or even outbreak of infection is high [16–18]. Furthermore, the management of infected aortic aneurysms with aerodigestive communications is much more complex and remains inconclusive according to current evidence [18–23]. Thus, we will focus on uncomplicated infected aortic aneurysm in this chapter and propose strategies in managing this rare but severe disease in the endovascular era.

2. Etiology

Vascular infections with infected aneurysm formation generally have four types of etiologies according to Wilson's classification [4, 6]: (1) aneurysm formation after microbial arteritis due to bacteremia or local infection invasion, (2) posttraumatic infected pseudoaneurysms, which were usually related to drug abuse in the past and with increased incidence with the use of endovascular procedures [24] (3) infection of preexisting aneurysms, and (4) infected (mycotic) aneurysm resulting from infective endocarditis-related septic emboli (as described by Sir Osler) [1]. The intima of the arterial structure is normally resistant to infection; however, the presence of injury or pathological change makes it vulnerable to microorganisms, especially *Staphylococcus* and *Salmonella* species [25, 26]. Untreated local infection or arteritis that is not suppressed by host immunity in the early stage could progress to abscess formation, vascular perforation, and pseudoaneurysm formation. Furthermore, since the aorta is the most common site of atherosclerosis and aneurysm formation, infected aortic aneurysms usually result from bacteremic seeding to the diseased intima [6]. Rarely, infected aortic aneurysms secondary to an infectious process of adjacent structures, such as intraabdominal infection, empyema, mediastinitis, and vertebral osteomyelitis, have also been reported in Refs. [27–30].

Infected aortic aneurysms are also often developed in patients with various degrees of immunosuppressed status, such as in diabetes mellitus, liver cirrhosis, end-stage renal disease, alcoholism, chronic glucocorticoid therapy, chemotherapy, posttransplantation immunosuppression, human immunodeficiency virus infection, and malignancy [10, 31–34]. These patients frequently present with atypical clinical features that make the diagnosis difficult and uncommonly delayed [10]. In our institutional experience, more than 70% of the operated patients with infected aortic aneurysm had impaired immunity due to the aforementioned conditions at the time of operation.

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3. Bacteriology

Overall, blood cultures were positive in more than half of patients with an infected aortic aneurysm, and intraoperative cultures could provide an even higher positive rate [5, 6, 35]. The causative microbiology of infected aortic aneurysms has changed after the advent of the antibiotic era and has a significant geographical difference. Before the popularized use of antibiotics, nonhemolytic *Streptococcus* species have once been the most common infectious organisms; subsequently, they account for less than 10% of infection cases after the advent of the antibiotic era [5, 36]. Currently, in Western countries, *Staphylococcus* species are generally the most common pathogens, accounting for 28–71% of cases based on published literatures [13, 37, 38]. It is also noteworthy that methicillin-resistant *Staphylococcus aureus* (MRSA) prevalence is continuously rising, and some reports indicated MRSA as the most dominant pathogen [39, 40]. Vancomycin-intermediate *Staphylococcus aureus* (VISA) has also been associated with infected aneurysms [41]. Gram-negative bacterium–related infected aortic aneurysms are less prevalent in Western countries than in East Asia, where *Salmonella* species are the most frequent Gram-negative bacteria causing aortic infections [11, 13, 38]. A diseased aorta, such as that with significant atherosclerotic change or preexisting aneurysm, is more vulnerable to *Salmonella* species [11]. In the literatures from Taiwan and in our institutional experience, *Salmonella* species account for 50–83% of cases of infected aortic aneurysms [11, 12, 14, 15].

Furthermore, the bacteriological spectrum may also be broader than that expected [37]. A recent report on endovascular treatment of infected aortic aneurysms from a European multicenter study revealed that 62% of the cases had a positive blood culture in which 20% was *Staphylococcus* species, 12% *Salmonella* species, and 11% *Streptococcus* species; approximately 19% were caused by other microorganisms [42]. A less common organism should always be considered in patients with infected aortic aneurysms, especially those in an immunosuppressed state [43]. Several Gram-negative bacterium–related infected aortic aneurysms have been described, including *Pseudomonas*, *Klebsiella*, *Escherichia coli*, *Campylobacter*, *Yersinia*, *Brucella*, *Haemophilus influenzae*, *Coxiella burnetii*, *Acinetobacter*, *Burkholderia pseudomallei*, *Campylobacter*, *Enterobacter cloacae,* and *Bacteroides fragilis* [44–55]. A Gram-negative bacterium–related infection is usually associated with more aneurysm rupture and mortalities. Moreover, infected aortic aneurysms due to various fungal infections have also been reported, such as *Candida*, *Cryptococcus*, and *Aspergillus* [56–58]. *Mycobacterium* species could also result in infected aortic aneurysms [59, 60], while *Bacillus* Calmette-Guérin–related abdominal aorta infection has also been reported in Ref. [61].

4. Clinical manifestation and diagnostic criteria

Unlike superficial infected aneurysms, which normally presents with painful, pulsatile masses along with local or systemic infection features, the clinical manifestation of infected aortic aneurysms is often obscure. Patients with an infected thoracic aortic aneurysm may have deep and vague chest or upper back pain, while those with infected abdominal aortic aneurysm may have abdominal or lower back pain. Oftentimes, patients with infected aortic aneurysms may only present with fever of unknown origin, and a diagnosis is made typically

only after the aneurysms rupture or other complications develop. The structures adjacent to the infected aorta could be affected by direct bacterial invasion or a mass effect, resulting in gastrointestinal bleeding, dysphagia, hoarseness, hemoptysis, or the development of empyema, arteriovenous fistula, osteomyelitis, or psoas abscess [10, 62, 63].

The diagnosis of an infected aortic aneurysm is made by imaging studies and evidence of infection. Computed tomography (CT) angiography, which has been the diagnostic modality employed, could timely and clearly provide information on the size and location of the aneurysm as well as the anatomic relationship and possible involvement of the surrounding structures. The typical CT image suggestive of the presence of infectious process in the aorta shows irregular aortic wall, periaortic fat stranding, and presence of periaortic soft tissue mass, and fluid or air accumulation [64–66]. The aneurysm is usually saccular or multilobulated [65, 66]. Active extravasation of intravascular contrast medium is seen in ruptured aneurysm. A retropleural or retroperitoneal hematoma formation adjacent to the aneurysm can be observed if the aneurysm has a contained rupture. If contrast medium exposure is contraindicated, magnetic resonance angiography is the alternative choice of imaging study. As previously mentioned, it is not uncommon that no microorganism is identified in the blood sample from patients with infected aortic aneurysms; thus, a negative blood culture could not exclude the presence of infected aortic aneurysms.

Moreover, an infected aortic aneurysm should be distinguished from an inflammatory aortic aneurysm, although not always easy especially considering that both have the following clinical symptoms: chest, abdominal, or back pain and low-grade fever. The presence of positive serial antinuclear antibody (ANA) and elevated IgG4 in patients with aortitis or aortic aneurysm could imply an underlying autoimmune disease [67, 68]. A "mantle sign" on CT imaging is suspicious of an inflammatory aortic aneurysm, which displays a thickened wall of the aortic aneurysm with periaortic inflammation and fibrosis [67].

5. Management

Infected aneurysms are clinically serious, and those involving the aorta could result in more significant morbidity and mortality despite prompt surgical interventions. With the high percentage of disease evolution to aneurysm rupture, antibiotic treatment alone results in extremely poor prognoses and should be only reserved for those with very high surgical risk and significant medical comorbidities [69]. Aggressive debridement with aortic reconstruction remains the gold-standard operative procedure; however, a complicated postoperative course generally could be anticipated [7]. Furthermore, for infected aneurysms affecting the thoracic aorta and aortic arch, the surgical procedure typically employs extracorporeal circulation, cardiopulmonary bypass, and even a period of deep hypothermic circulatory arrest (DHCA), further increasing the operative risks. The feasibility of endovascular aortic repair (EVAR) for infected aortic aneurysms has been investigated in numerous studies, which in turn provided encouraging short-term results [18, 42, 70–74]. However, the long-term survival and late-onset complications, especially recurrent or persistent infections, are of greater concerns [74].

5.1. Antibiotic therapy

If an infected aortic aneurysm is suspected clinically, systemic broad-spectrum antibiotics should be initiated immediately before definite pathogen identification [69, 75]. Because of the high prevalence of *Salmonella* species infection in our country, we prefer administering ceftriaxone in every case of an infected aortic aneurysm if there is no contraindication [12, 69, 71]. Once the culture and susceptibility results are available, antibiotics should be tailored accordingly. The minimum inhibitory concentration (MIC) of every susceptible antibiotic should be assessed and specialist consultation for infectious diseases should be liberal.

The optimal duration of antibiotic therapy both before and after surgical repair of an infected aortic aneurysm remains inconclusive. Generally, 4–8 weeks of systemic antibiotic course is accepted as the minimum treatment duration for infected aortic aneurysms [75]. The treatment effectiveness should be assessed, and the therapeutic course should be based on subsequent blood culture, serial examination of the inflammatory markers, and persistent evaluation of the clinical progress. Patients infected with highly drug-resistant organisms usually require a longer antibiotic therapy duration [76]. Furthermore, since the infected aorta is generally either reconstructed by prosthetic graft implantation or repaired with endovascular prosthesis deployment, suppressive oral antibiotics for a prolonged period following completed parenteral antibiotic therapy is often warranted [18, 69, 77]. Further details of the antibiotic therapy will be discussed in Sections 7.2 and 7.5.

5.2. Traditional open repair

Open surgical repair for an infected aortic aneurysm is composed of excision of the diseased aorta, debridement of the surrounding infected tissue, and immediate, and usually in situ, reconstruction of the aortic continuity. This operation technique for infected aortic aneurysms is generally consistent with that for noninfected aortic aneurysms. Patient positioning and surgical exposure depend on the anatomical and pathological conditions of the aneurysm, and the adjunctive monitoring or protective measures should be prudently executed based on the consensus between the surgeon and anesthesiologist. The operative considerations for infected aortic aneurysms with different anatomical locations are discussed below, and some representative completed reconstructions are illustrated in **Figure 1**.

5.2.1. Infected ascending aortic and aortic arch aneurysms

To replace an infected aneurysm of the ascending aorta and aortic arch, cardiopulmonary bypass is absolutely required, and an interval of DHCA is often necessary. Electroencephalographic monitoring or continuous recording of cerebral oxygen saturation is advisable. Intraoperative transesophageal echocardiography (TEE) is performed to assess cardiac function [78]. A full median sternotomy is the standard approach, and an extension to the neck or even a "trapdoor" incision is sometimes needed for better exposure of the distal arch and its branches. If aortic valve replacement is necessary for infective endocarditis or a concomitant pathology of the aortic valve, a composite graft replacement, or a separated replacement of the valve and aorta, is performed. Coronary arteries are reimplanted to the prosthetic graft with buttons of the aorta tissue (Button-Bentall procedure) if the aortic root is replaced [79, 80]. Occasionally,

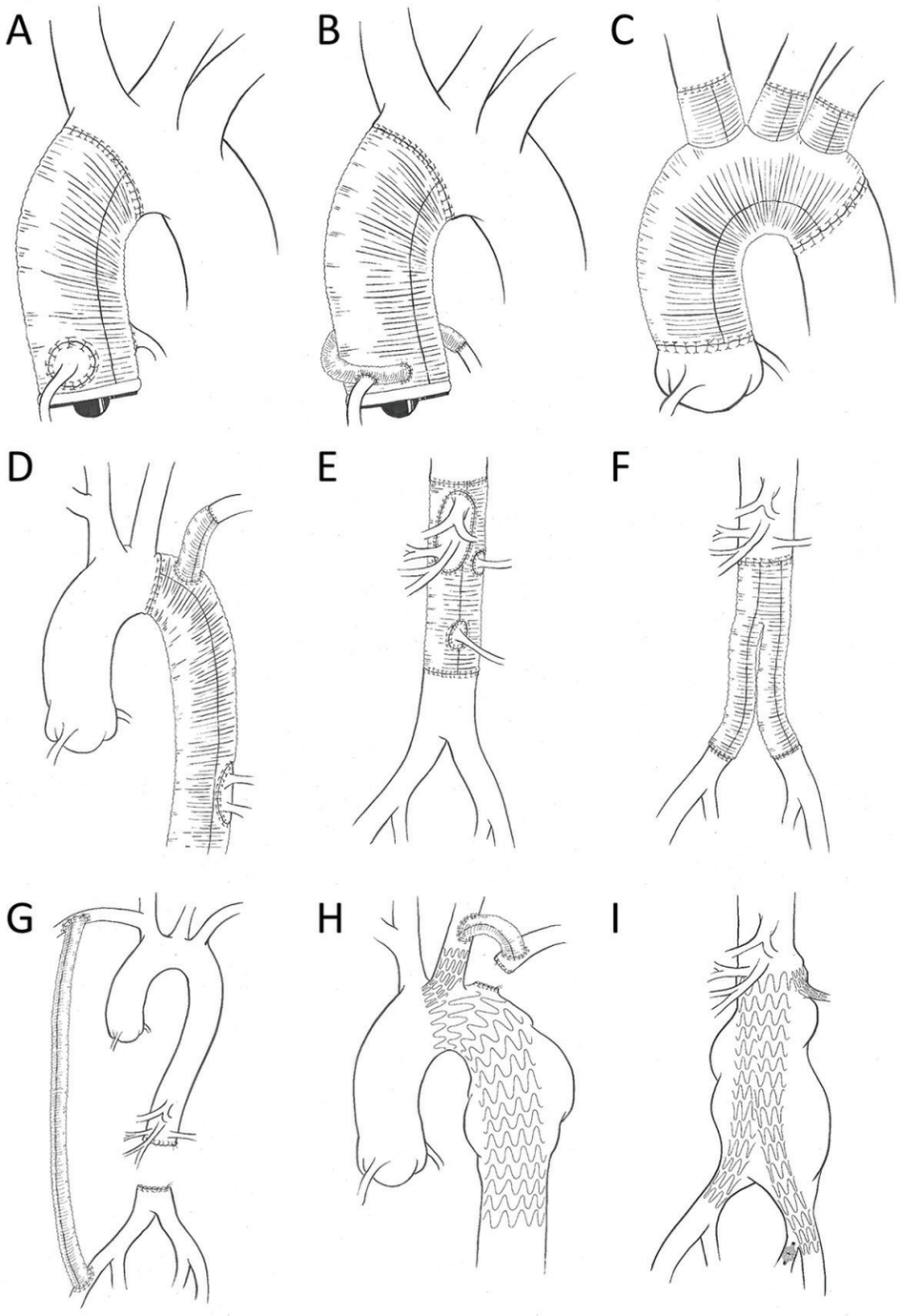

Figure 1. Illustrations of different aortic reconstructions. (A) Ascending aorta and aortic root replacement, with a composite graft with a mechanical valve and reimplantation of the coronary arteries with buttons of the aorta tissue (Button-Bentall procedure). (B) Ascending aorta and aortic root replacement, with a composite graft with Cabrol modification. (C) Total arch replacement. (D) Descending thoracic aorta and proximal left subclavian artery replacement (semi-arch replacement), with reimplantation of the important spinal arteries (e.g., Adamkiewicz artery). (E) Juxta-renal abdominal aorta replacement, with reimplantation of all visceral arteries. (F) Infra-renal abdominal aorta and iliac arteries replacement, with a bifurcated graft. Note the inferior mesenteric artery is not reimplanted. (G) Axillo-femoral bypass (extra-anatomical reconstruction), with aortic stumps closure. (H) Thoracic endovascular aortic repair (TEVAR), with chimney technique for left carotid artery debranching and a carotid-subclavian bypass for proximal sealing zone at zone I. (I) Endovascular aortic repair (EVAR), with chimney technique for left renal artery debranching and plug embolization for left internal iliac artery.

no adequate healthy tissue for coronary artery reimplantation is found; a Cabrol technique or coronary artery bypass graft (CABG) can be used to reestablish the coronary flow [81, 82].

5.2.2. Infected thoracic and thoracoabdominal aortic aneurysms

Similar to noninfected thoracic and thoracoabdominal aortic aneurysms, an infected thoracic aortic aneurysm is repaired through a left thoracotomy with suitable intercostal spaces or a more extended thoracoabdominal incision [11, 77]. A simple clamp-and-sew technique, partial cardiopulmonary bypass, or left heart bypass can be chosen according to the characteristics of the aneurysm and the preference of the surgical team. If there is no space for proximal clamping, proximal anastomosis under a period of DHCA is necessary, and the use of intraoperative cerebral monitoring is also advisable. Cerebrospinal fluid (CSF) drainage should be routinely performed in all suitable patients, and evoked potential measurement should be considered [83, 84]. If the operation is performed with simple aortic clamping, some adjunctive protective measures in addition to CSF drainage could be done, such as hypothermia (cool the patient to 34°C or slightly lower with low operation room temperature or cold intravenous fluid) and cold renal perfusion with crystalloid or blood [77, 83–85]. Of note, the adoption of clamp-and-sew technique during an infected thoracic aortic aneurysm repair should be carefully evaluated because excising the infected aorta and performing debridement often takes a considerably more time, which increases the distal ischemic time despite the utilization of various protective strategies.

5.2.3. Infected abdominal (juxta-renal, supra-renal, and infra-renal) aortic aneurysms

Infected abdominal aortic aneurysms are generally repaired using a simple clamp-and-sew method through a median laparotomy, without extracorporeal circulatory support [9, 86]. Renal protective measures as previously described should be considered for those with a juxta-renal or supra-renal location. The involved visceral arteries are reimplanted to the graft [87]. Historically, aortic reconstruction with an autologous femoropopliteal venous graft has been advocated [88]. The time consumed and the morbidities caused by femoropopliteal vein harvest, along with the lack of availability of cryopreserved allografts, have urged more surgeons to prefer using prosthetic grafts, usually a Dacron graft, as alternatives [12, 14, 89–91]. An omental flap with preserved vascular supply is usually transposed to cover the graft and the anastomosis sites. Omental flaps separate the prosthesis from the surrounding contaminated structures and fill a dead space. The highly vascularized flap could also facilitate the systemic antibiotic delivery to the infected area [14].

5.2.4. Extra-anatomical reconstruction

To avoid prosthetic graft placement in the contaminated field and to restore the aortic flow with a remote route, extra-anatomical reconstruction is an attractive alternative to in situ reconstruction [9, 87, 92, 93]. Extra-anatomical reconstruction also includes excision of the infected aorta and debridement of the surrounding contaminated tissue, with aortic stump closure and aortic revascularization through a noninfected pathway. A unilateral or bilateral axillo-femoral bypass after an infra-renal abdominal aorta excision is the most common procedure. Extra-anatomical reconstruction has also been used for the repair of infected aneurysm of the aortic arch [94]. Because of the residual aortic tissue fragility, a sustained risk

of aortic stump disruption exists [87, 95]. A two-layer closure is generally recommended, with coverage of a vascularized omental flap.

5.3. Endovascular technique

Since the first report by Semba et al. [96], an increasing number of investigations on endovascular technique utilization in infected aortic aneurysm management, including one European multicenter study published in 2014 [15, 18, 42, 70–74, 97, 98], was noted. The general principle and considerations of endovascular treatment for infected aortic aneurysms are identical to those for noninfected aortic aneurysms, including consideration of the characteristics of each device, arterial access route assessment (usually the iliac and femoral artery), anatomical characteristics of the aneurysm, and proximal and distal sealing zones.

A high-resolution multi-slice CT angiography providing essential information and a well-reconstructed three-dimensional image is usually necessary for surgical planning. The endovascular procedure is performed in a hybrid operating room equipped with a fluoroscopic unit, where prompt conversion to traditional open surgery is possible. Depending on the patient's situation, the procedure could be performed under general anesthesia, spinal anesthesia, or even local anesthesia. For patients with long-segment descending thoracic aorta coverage by the stent graft or, ideally for all patients undergoing thoracic endovascular aortic repair (TEVAR), CSF drainage should be performed for neuroprotection [99, 100]. Although controversial, the artery of Adamkiewicz, normally located between T8 and L2, should be preserved if possible [100]. If essential branches of the aorta are to be covered by stent grafts, revascularization by either a bypass surgery, open debranching, or endovascular debranching with a chimney technique or a fenestrated stent graft is necessary [101–105]. Adjunctive procedures, such as open debridement and percutaneous drainage, could be performed, based on the clinical judgment [74].

Although endovascular treatment for ascending aortic pathologies, including those with an infectious process, has been sporadically investigated [106–109], its use remains "off-label" for current commercially available aortic stent grafts. Further advances in the design of the devices and well-constructed studies are both necessary. Consequently, endovascular management for infected ascending aortic aneurysms is not discussed herein.

6. Outcomes

6.1. Antibiotic therapy alone

It was believed that patients with infected aortic aneurysms treated medically without undergoing aortic resection surviving to hospital discharge is almost impossible [38, 69]. In 2009, Hsu and colleagues from Taiwan reported the institutional experience of medical treatment of infected aortic aneurysms in high-risk patients, which revealed that the prognosis was not uniformly fatal [69]. The treatment strategy is composed of 6–8 weeks parenteral antibiotic administration during hospitalization, followed by lifelong oral antibiotics. Of the 22 patients (8 thoracic and 14 abdominal aortic aneurysms), the overall in-hospital mortality rate was 50% and the 1-year event-free survival rate was 32%. Ruptured aneurysm was the major cause of death, accounting for 40.9% (9/22) of patients treated medically. Of note, two in-hospital deaths due to massive gastrointestinal tract bleeding, whose etiology was not mentioned,

were reported; aortoesophageal or aortoenteric fistulations could be the possible causes. The most common causative agent was the *Salmonella* species, which is responsible for 50% (11/22) of the cases, and the authors found that the prognosis of medically treated *Salmonella*-infected aneurysms was better than that of non-*Salmonella* infected cases. However, the prognosis of medically treated *Salmonella*-infected aortic aneurysm remains a subject of debate as most of the early reports from Western countries showed an extremely dismal result [38, 110, 111] (see more details in Section 7.1). The authors concluded that although the results of antibiotic treatment alone in patients with infected aortic aneurysm remained poor, it could still be an alternative treatment, especially in *Salmonella*-infected patients with very high surgical risks.

6.2. Traditional open repair

Due to the rarity of the disease, most reports regarding the surgical outcome of infected aortic aneurysms after traditional open repair have very heterogeneous case characteristics, with various aortic segments involved and different methods for aortic reconstruction [9–14, 16, 17, 77, 112–118]. Although admirable surgical outcomes have been reported, with both early and late mortalities as low as 5%, an early mortality rate of 5–40% and an at least 30% late mortality rate after open surgical repair of infected aortic aneurysms were demonstrated in most literatures [9–14, 16, 17, 77, 112–118]. Generally, the surgical outcomes for infected aneurysms with an infrarenal location were better than those involving the aortic arch and descending thoracic, thoracoabdominal, supra-renal, and juxta-renal aorta [11, 13, 16, 116]. An infected aneurysm of the ascending aorta is rare, and a successful surgical treatment has been reported in Refs. [119–123].

More than 50% of the patients undergoing open surgical repair of infected aortic aneurysms had early major complications, such as acute kidney injury, respiratory failure, and spinal ischemia. Late vascular complications, mostly a prosthetic graft infection, developed in up to 30% of the survivors [9–14, 16, 17, 77, 112–118]. Although the late outcomes are similar between in situ and extra-anatomical reconstruction, the latter is related to higher vascular complications, including aortic stump disruption (8–19%) and limb amputation (17–27%) [91–95]. Re-infection of the prosthetic graft is also possible in patients undergoing extra-anatomical reconstruction [93, 95]. Nevertheless, extra-anatomical reconstruction is still a reasonable option for patients who are unsuitable for in situ reconstruction.

6.3. Endovascular technique

The short-term advantage of endovascular infected aortic aneurysm repair has been gradually clarified, although most reports comprise small case numbers and limited follow-ups [15, 70–74, 97, 98]. In 2007, Kan and colleagues reviewed English literatures investigating the efficiency of EVAR for infected aortic aneurysms [18]. The estimated overall 30-day survival rate was 89.6%, and the 2-year survival rate was 82.2% for the extracted 48 cases. Ruptured aneurysm, including those complicated with aortic fistulations, and fever at the time of EVAR procedure were found to be the significant predictors of persistent infection. Several studies continuously demonstrated that EVAR is a possible alternative procedure for infected aortic aneurysm patients with high surgical risks, with an early mortality rate less than 20%, which is comparable to that of traditional open repair. A poorer outcome was still evident in patients with aneurysm-related fistulation complication [71, 72, 124–127]. Persistent infection greatly contributed to both early and late mortalities; thus, adjunctive procedures to eliminate contamination and prolonged

antibiotic therapy duration after EVAR were usually advocated in the literatures [18, 72, 74] (see more details in Sections 7.4 and 7.5).

In 2014, Sörelius and colleagues conducted a European multicenter study, the largest retrospective study, to investigate the durability of EVAR for infected aortic aneurysms [42]. The 30-day, 1-year, 5-year, and 10-year survival rate of the 123 patients identified was 91, 75, 55, and 41%, respectively. Of note, infected aortic aneurysms caused by non-*Salmonella* microorganisms were identified to have a worse long-term prognosis. Location of the aneurysm, presence of shock, or ruptured aneurysm at the time of operation showed no effects on the late outcome. Aneurysm-related infection complications developed in 33 patients (26.83%) postoperatively, 23 of whom had an either early or late lethal outcome. The authors concluded that EVAR could be a feasible and durable choice for most patients with infected aortic aneurysms. Persistent or recurrent infection remained a great concern, necessitating a long-term antibiotic therapy and regular follow-up.

6.3.1. The institutional experience of endovascular management for uncomplicated infected aortic aneurysms from National Cheng Kung University Hospital, Tainan, Taiwan

National Cheng Kung University Hospital is a tertiary medical center in southern Taiwan and serves as a first-line hospital in Tainan City with an urban population of 1.8 million and also as a referral center for the whole southern Taiwan. As of the writing of this manuscript, a total of 338 EVAR procedures (including TEVAR and hybrid procedures) for various purposes have been performed.

Since the first case of infected thoracic aortic aneurysm treated by TEVAR in March 2009, 25 patients have undergone endovascular management for infected aortic aneurysms in our hospital. Six complicated cases were excluded from this study: two presented with aneurysm-free rupture and hemorrhagic shock and received emergency EVAR and four were associated with aortoesophageal or aortobronchial fistulas. Finally, 19 cases, with a mean age of 68.68 years (range: 43.94–83.65 years) and a mean follow-up of 20.54 months (range: 0.59–85.13 months), were included. Several valuable preoperative and postoperative images from selected patients are shown in (**Figures 2–5**). There was one in-hospital mortality that had persistent periaortic graft infection despite continuous parenteral antibiotic treatment.

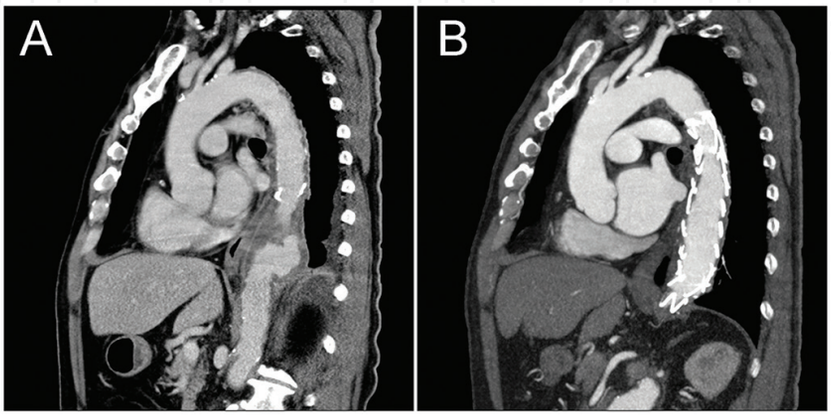

Figure 2. (A) Infected descending thoracic aortic aneurysm in a 70-year-old male patient (B) Oral antibiotic treatment continued for 1 year after TEVAR and CT angiography 2 years after TEVAR showed no residual aneurysm or periaortic infection. No adjunctive procedure was ever done for this patient.

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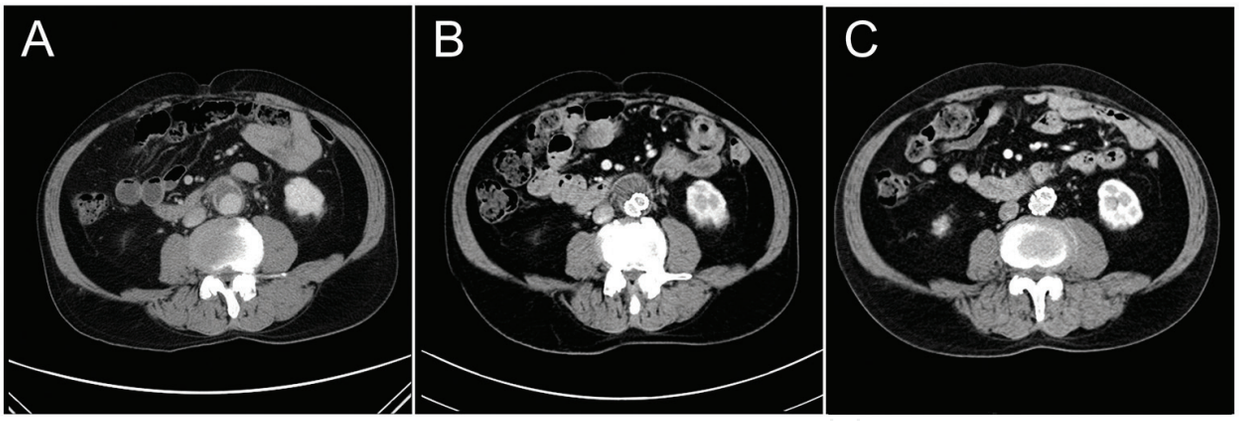

Figure 3. (A) Infected infra-renal abdominal aortic aneurysm in a 68-year-old diabetic male patient (B) CT angiography 2 weeks after EVAR showed residual aneurysm but resolved periaortic inflammation. Percutaneous drainage of the aneurysm was done. (C) With long-term oral antibiotic suppression, the aneurysm disappeared completely on CT angiography 2 years later.

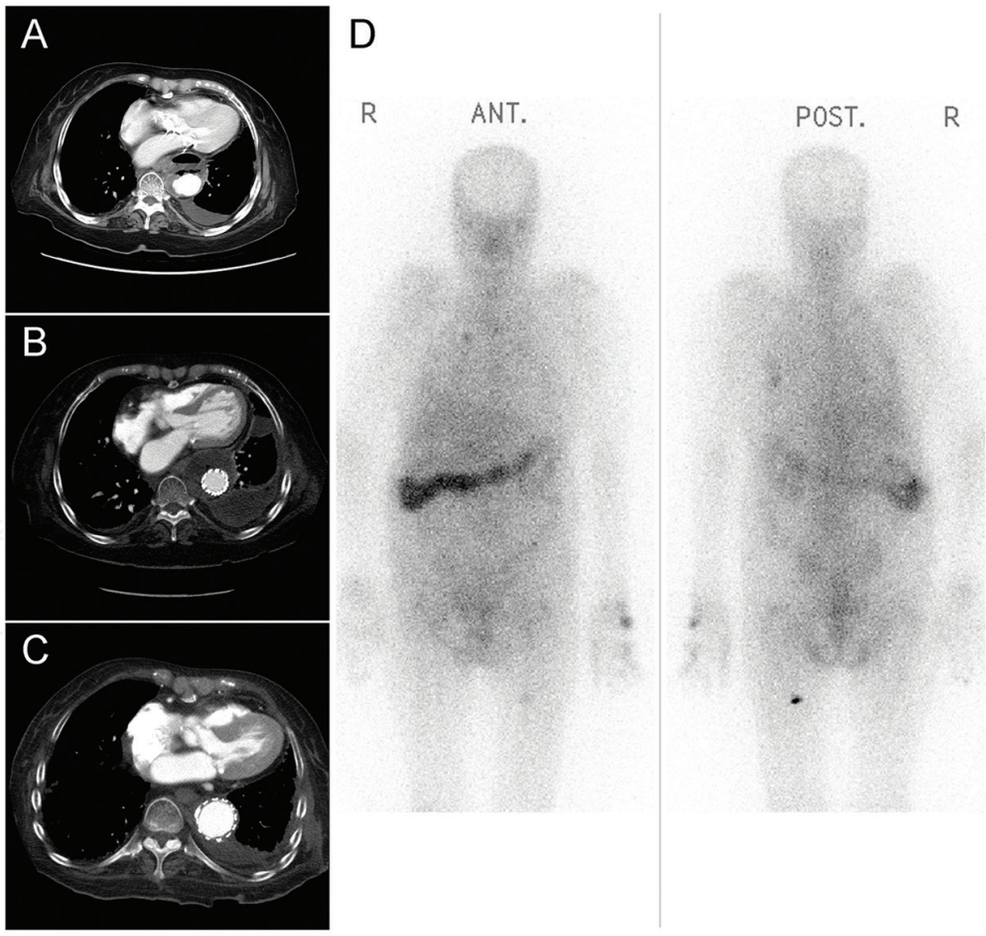

Figure 4. (A) Infected descending thoracic aortic aneurysm with periaortic foamy air collection (emphysematous aortitis) in an 83-year-old diabetic female patient. (B) Two weeks after TEVAR, there was still fluid accumulation around the stent graft and also abundant pleural effusion. Debridement through left mini-thoracotomy was done. (C) With long-term oral antibiotic suppression, the periaortic inflammation resolved 6 months later, despite this there was still some pleural effusion. (D) Gallium inflammation scan confirmed that there was no residual infection process.

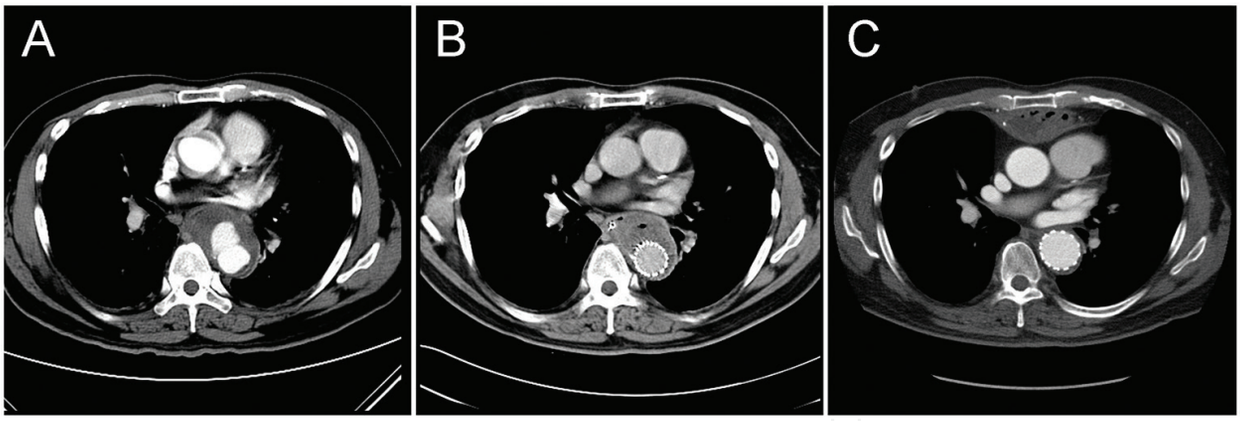

Figure 5. (A) Infected descending thoracic aortic aneurysm caused by *Salmonella enteritidis* in a 60-year-old male patient. (B) The patient was complicated with persistent local infection and esophageal perforation 1 week after TEVAR. Debridement and esophagectomy by a video-assisted thoracic surgery (VATS) was done. (C) Oral antibiotics were kept for 1 year after hospital discharge and CT angiography 3 years after TEVAR showed completely resolved periaortic infection. Note the retrosternal gastric tube for esophagus reconstruction.

The patient refused open debridement and died 2 months after the EVAR procedure. Major postoperative early complications developed in nine patients (47.37%), including respiratory failure requiring tracheostomy in four, acute kidney injury in three, esophageal perforation in two, spinal cord ischemia in one, lower extremity ischemia in one, and hypoxic encephalopathy in one. The two cases developing esophageal perforation had no hematemesis at initial presentation and their preoperative CT angiographies did not reveal any feature of aortoesophageal fistula. Persistent local infection or ischemic esophageal necrosis after TEVAR should be the cause resulting in esophageal perforation. Both these patients underwent subsequent radical debridement and esophagectomy and were alive during the last follow-up.

Three late mortalities occurred, of which one was aneurysm-related mortality. The patient developed recurrent periaortic infection and subsequent aortoenteric fistula 2 years after the operation and died because of massive exsanguination. The estimated 30-day, 1-year, and 5-year aneurysm-related survival rate was 100, 94.1, and 78.4%, respectively. No endoleak was detected by CT angiography beyond 30 days postoperatively. All patients with a follow-up duration more than 6 months had disappearance of aneurysms along with complete resolution of periaortic inflammation.

Long-term antibiotics were prescribed in nine patients (47.37%) in the study population. Adjunctive procedures to eliminate the infectious environment were performed in seven patients (36.84%), including open debridement in four (two patients also underwent concomitant esophagectomy for postoperative esophageal perforation as previously mentioned) and percutaneous drainage in three patients. Due to the rarity of both early and late mortalities, the evaluation of the benefit of long antibiotic therapy duration and adjunctive procedures is challenging. For the same reason, analysis of other predictors of inferior early and late outcomes was not performed.

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7. Controversies

7.1. *Salmonella*-related versus non-*Salmonella*-related infected aortic aneurysm

Infected aortic aneurysms caused by *Salmonella* species were thought to be more virulent and tend to have a worse outcome, in view of the higher risk of early aneurysm rupture and prosthetic graft infection [110, 111, 128–132]. In 2010, Kan and colleagues compared the surgical outcomes of 41 cases of infected aortic aneurysms identified from relevant literature reports and institute cases from 1990 to 2008 and found that *Salmonella* infection was a risk factor of postoperative aneurysm-related morbidity and mortality [71]; however, the type of procedures (i.e., traditional open repair versus EVAR) was not.

With the advent of effective modern antibiotics, improved outcomes of *Salmonella*-related infected aortic aneurysms were reported in most of the recent literatures [12, 15, 118]. *Salmonella* infection prevalence in our institution is high; thus, we routinely prescribe ceftriaxone as one of the empiric antibiotic agents (usually, vancomycin or oxacillin is added for a better coverage of Gram-positive microorganisms), provided that no contraindications are noted, once a diagnosis of an infected aortic aneurysm was made even before the availability of definite culture result. We also found a favorable outcome in patients with infected aortic aneurysms caused by *Salmonella* species in our institution. On the other hand, some studies identified a positive culture of non-*Salmonella* species as a predictor of a poorer outcome after both open surgery and endovascular procedures [17, 42, 77]. Thus, although still inconclusive, *Salmonella* infection should at least not be considered as a predictor of a worse outcome for infected aortic aneurysm.

7.2. Preoperative antibiotic course

Infected aortic aneurysms are surgical urgencies, and our mentors used to inculcate in us the cliché "avoid undue delay of operation." Nevertheless, implanting a vascular prosthesis into a contaminated field in a patient with an active systemic infection might result in a catastrophic graft infection. Thus, the usual practice is to perform the operation after a period of parenteral antibiotic treatment if the patient's condition permits [17, 18, 77, 116].

Hsu and colleagues retrospectively analyzed the clinical outcome of infected aortic aneurysms in National Taiwan University Hospital, Taipei, Taiwan, from 1995 to 2011 [118]. Of the 109 patients identified, 85 underwent surgical intervention, including open repair in 77 and endovascular repair in eight. The median preoperative antibiotic treatment duration was 8 days (interquartile range: 2–21 days). Ten deaths (early or late) directly related to persistent/recurrent periaortic infection or prosthesis infection were reported. The authors found that shorter preoperative antibiotic treatment duration was associated with more aneurysm-related moralities: a median preoperative antibiotic duration of 3 days (interquartile range: 0–7 days) in the deceased and 16 days (interquartile range: 3–26 days) in the survivors. In the systemic review of infected aortic aneurysms treated with EVAR by Kan et al. [18], 22 of the 48 patients received preoperative antibiotics for more than 1 week, and two patients had a postoperative persistent infection. In the univariate analysis, preoperative antibiotic treatment more than 1 week had a

protective effect against persistent infection; however, its benefit was not significant in the multivariate analysis. In fact, the decision on the preoperative antibiotic course is highly determined by other clinical conditions, which in turn could be confounding factors for worse prognosis. For example, the presence of aneurysm-related complications or profound sepsis would urge the surgeon to perform operation earlier, and both situations could affect the surgical outcome.

No study investigating the optimal surgical timing for infected aortic aneurysms after initial antibiotic treatment has so far been conducted; thus, the ideal preoperative antibiotic treatment duration remains controversial. If the clinical condition permits, we favor performing operation (either open or endovascular repair) at least when fever subsides after adequate systemic parenteral antibiotic treatment or, more desirably, after a 7-day antibiotic course or confirmation of a negative culture result.

7.3. Choice of graft materials for in situ reconstruction

Numerous graft materials to reestablish the aortic continuity in situ are available, such as a prosthetic graft, an autologous venous graft, a cryopreserved allograft, and even an autologous or xenologous pericardial patch [91, 117, 133, 134]. An autologous venous graft or an allograft was considered to be more resistant to microorganisms than a prosthetic graft and thus used to be the preferred material for infected aorta reconstruction [88]. Despite the low reinfection rate and good durability of the autologous femoropopliteal venous grafts, considerable major morbidities are associated with femoropopliteal vein harvest, including compartment syndrome requiring fasciotomy in 12% and chronic venous insufficiency in 15% of the patients [89]. The availability of cryopreserved allografts in Taiwan and most countries in East Asia is limited [14, 117].

The reinfection rate after in situ reconstruction with prosthetic grafts for infected aortic aneurysms, which was as high as 20% in early reports [135], has decreased significantly recently. Several studies in Taiwan, including our institutional experience, have demonstrated a graft infection rate of 8.0–10.4% after in situ prosthetic graft replacement for infected aortic aneurysms [11, 12, 113–116, 118]. In a more recent study investigating the outcomes of open repair of infected descending thoracic and thoracoabdominal aortic aneurysms by Lau et al., no postoperative graft infection occurred in 14 patients who had in situ prosthetic graft reconstruction [77].

In 2011, Bisdas et al. analyzed the prognosis of cryopreserved allografts and silver-coated Dacron grafts for abdominal aortic infections with positive intraoperative culture and found comparable short-term and mid-term survival rates [91]. None of the 22 patients in the cryopreserved allograft group developed graft infection, while two of the 11 patients in the silver-coated Dacron graft group had an ongoing or recurrent infection. Of interest, the costs of therapy were significantly higher for cryopreserved allografts. Moreover, other studies have revealed favorable results of in situ antibiotic-bonded prosthetic graft replacement for infected aortic aneurysms [117, 136]; nevertheless, its effectiveness still requires further investigations.

7.4. Adjunctive procedures after the initial EVAR

The major concern of endovascular treatment for infected aortic aneurysms is the residual infectious environment surrounding the deployed device. Additional surgical procedures,

such as debridement of the infected tissue and drainage of the abscess, could aid in eradicating the infection and thus improve the outcome [18, 74, 137]. Furthermore, additional culture information could be obtained through the specimen derived from these procedures.

In our systemic review, performing adjunctive procedures after EVAR serves as a protective factor against persistent infection in the univariate analysis; however, the benefit was insignificant in the multivariate analysis [18]. In 2011, Kritpracha and colleagues published their institutional experience of endovascular therapy for infected aortic aneurysms and showed an impressive mid-term outcome for those without an aortic fistulation [72]. They routinely prescribed lifelong antibiotics to the patients, and no adjunctive procedure was conducted. During a mean follow-up of 22 months, no late mortality or aneurysm-related complication in the 15 patients surviving to hospital discharge was reported. Complete resolution of periaortic inflammation and shrinkage of the aneurysms were observed in most of the patients starting at the 6-month follow-up. The authors thus suggested that aggressive debridement of the infected tissue may not be necessary for those with uncomplicated infected aortic aneurysms.

Determining the effectiveness of each adjunctive procedure is also difficult, and the selection should be individualized. We prefer performing CT-guided drainage if the patient remains febrile or unsterilized blood sample persists after EVAR provided that the periaortic abscess has been adequately liquefied. Irrigation of the abscess cavity with antibiotics or disinfectants could also be performed [74]. A more extensive open debridement is generally reserved for those with an unsatisfactory response to the aforementioned less-invasive measures.

7.5. Postoperative antibiotic course

No consensus on the optimal postoperative antibiotic treatment duration is available. For other cardiovascular infections, at least 4–8 weeks of parenteral antibiotic therapy after surgical intervention is generally accepted, and the course should be carefully tailored according to the clinical and laboratory parameters [75]. Several authors have advocated long-term oral antibiotic suppression after hospital discharge for all operated patients, especially those who underwent endovascular repair [9, 10, 15, 42, 77]. However, drug adherence is typically less than ideal, mainly because of the development of antibiotic-related adverse reactions or patient noncompliance.

In the early institutional experience of in situ prosthetic graft replacement for infected abdominal aortic aneurysms published in 2003, Luo and colleagues found that oral antibiotic suppression, prolonged or not, was not related to the development of late graft infection [12]. Thereafter, we did not routinely prescribe oral antibiotics to patients who had received open repair at hospital discharge. Following our strategy of both pre- and postoperative antibiotic treatment, as previously mentioned, only two patients have developed late graft infections after in situ prosthetic graft replacement for infected abdominal aortic aneurysms [14].

Moreover, in our practice, long-term oral antibiotic suppression is generally planned at hospital discharge for those who had endovascular repair for infected aortic aneurysms [15]. The

surgeon's decision on antibiotic treatment termination, provided that no residual infection based on clinical, imaging, and laboratory evidence is noted, is individualized. Of 18 hospital survivors with uncomplicated infected aortic aneurysms treated with EVAR, along with long-term oral antibiotic suppression and aggressive adjunctive procedures, only one patient (5.6%) developed a late aneurysm-related complication (i.e., recurrent periaortic infection complicated with aortoenteric fistula).

8. Epilogue

Based on current evidence and our institutional experience, we have introduced and adopted the following therapeutic strategy for infected aortic aneurysms in the endovascular era:

1. Open repair through the excision of the infected aorta and radical debridement of the surrounding contaminated structure with immediate aortic reconstruction remains the gold standard. Although a higher reinfection rate is theoretically possible, in situ reconstruction with a prosthetic graft, along with adequate perioperative antibiotic course, is a safe and durable choice and could be applied in most patients. Long-term oral antibiotic suppression is not necessary provided that no evidence of ongoing infection after completion of parenteral antibiotic therapy is found.
2. For uncomplicated infected aortic aneurysms, endovascular treatment can be a reasonable alternative, especially for patients with significant comorbidities. If clinically feasible, an EVAR procedure can be performed after controlling overt infection, usually at least 3–7 days after parenteral broad-spectrum antibiotic treatment. The postoperative parenteral antibiotic treatment duration is at least 4–8 weeks. Long-term or even lifelong oral antibiotic suppression is recommended, and adjunctive procedures to eliminate the infectious environment are also considered. With the adoption of the abovementioned therapeutic strategies, the role of EVAR for uncomplicated infected aortic aneurysms has evolved from a temporary palliation to a reliable definite therapy.

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