

# Managing Infected Thoracic Endografts

A review of presentation and diagnosis, medical and surgical management and explantation, and outcomes after explantation.

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First reported in 1993, aortic endograft infection occurs in 1% to 4% of cases, and it remains unclear whether this incidence is rising.<sup>1-4</sup> Thoracic endograft infection (TEI) is associated with a mortality risk of up to 70% and should be treated by multidisciplinary teams in centers with experience in managing this complex problem to optimize outcomes.<sup>2,3,5-7</sup>

## PRESENTATION AND DIAGNOSIS

The clinical presentation of TEI can initially be very nonspecific and can sometimes occur years after

implantation; thus, a high index of suspicion is required for diagnosis.<sup>8</sup> Furthermore, because of the morbidity associated with definitive treatment, a reliable diagnosis of TEI is essential. Presenting features suggestive of TEI vary widely and include life-threatening hemorrhage secondary to fistulas connecting with, for example, the esophagus and the bronchial tree; back pain; and sepsis. Patients may complain of localized pain, anorexia, weight loss, fevers, night sweats, and features of septic emboli.<sup>9</sup> It is important to seek a history of infection at distant sites (eg, cholecystitis, urinary tract infection, animal bites), which may have resulted in inoculation of the endograft by bacteremia.<sup>10</sup> A detailed history and examination are essential not only for diagnosis of TEI but also in determining its etiology and associated features, such as spinal osteomyelitis or fistulas, which must be managed concomitantly.

Figure 1 outlines recently published consensus criteria for establishing a diagnosis of endograft infection.<sup>9</sup> CTA is the most commonly performed first-line imaging investigation and is supplemented by 18F-fluorodeoxyglucose (FDG) positron emission tomography (PET)/CT or single-photon emission CT. Multiple peripheral blood cultures should be obtained concomitantly. Samples for tissue culture and for analysis by 16S-polymerase chain reaction (16S-PCR) for bacterial ribosomal DNA can be obtained by CT-guided biopsy.<sup>10</sup> The advantages of 16S-PCR are its speed, util-

	CLINICAL / SURGICAL	RADIOLOGY	LABORATORY
MAJOR CRITERIA	<ul style="list-style-type: none"> <li>• Pus (confirmed by microscopy) around graft or in aneurysm sac at surgery</li> <li>• Open wound with exposed graft or communicating sinus</li> <li>• Fistula development e.g. aorto-enteric or aorto-bronchial</li> <li>• Graft insertion in an infected site e.g. fistula, mycotic aneurysm or infected pseudoaneurysm</li> </ul>	<ul style="list-style-type: none"> <li>• Peri-graft fluid on CT scan <math>\geq 3</math> months after insertion</li> <li>• Peri-graft gas on CT scan <math>\geq 7</math> weeks after insertion</li> <li>• Increase in peri-graft gas volume demonstrated on serial imaging</li> </ul>	<ul style="list-style-type: none"> <li>• Organisms recovered from an explanted graft</li> <li>• Organisms recovered from an intra-operative specimen</li> <li>• Organisms recovered from a percutaneous, radiologically-guided aspirate of peri-graft fluid</li> </ul>
MINOR CRITERIA	<ul style="list-style-type: none"> <li>• Localized clinical features of AGI e.g. erythema, warmth, swelling, purulent discharge, pain</li> <li>• Fever <math>\geq 38^{\circ}\text{C}</math> with AGI as most likely cause</li> </ul>	<ul style="list-style-type: none"> <li>• Other e.g. suspicious peri-graft gas/fluid/soft tissue inflammation; aneurysm expansion; pseudoaneurysm formation; focal bowel wall thickening; discitis/osteomyelitis; suspicious metabolic activity on FDG PET/CT; radiolabelled leukocyte uptake</li> </ul>	<ul style="list-style-type: none"> <li>• Blood culture(s) positive and no apparent source except AGI</li> <li>• Abnormally elevated inflammatory markers with AGI as most likely cause e.g. ESR, CRP, white cell count</li> </ul>

**Figure 1. Criteria for establishing a diagnosis of endograft infection.** Aortic graft infection (AGI) is suspected in a patient with any isolated major criterion, or minor criteria from two of the three categories: clinical/surgical, radiological, or laboratory. AGI is diagnosed in the presence of a single major criterion, plus any other criterion (major or minor) from another category. CRP, C-reactive protein; ESR, erythrocyte sedimentation rate. Reproduced with permission from Lyons et al, *Eur J Vasc Endovasc Surg* (2016) 52, 758–763.

ity despite prior antibiotic administration, and ability to detect fastidious organisms.

Endograft infection is suspected in a patient with any isolated major criterion, or minor criteria from two of three categories: clinical/surgical, radiologic, or laboratory. Infection is diagnosed in the presence of a single major criterion, plus any other criterion (major or minor) from another category. In the event that microbiologic investigations identify potential “contaminant” organisms (eg, coagulase-negative staphylococci, propionibacteria, corynebacteria, other skin commensals) a minimum of (1) two intraoperative specimens, (2) two blood cultures, or (3) one intraoperative specimen plus one blood culture must be positive with an indistinguishable organism in each of the samples based on antibiograms or a recognized typing method (eg, pulsed-field electrophoresis).<sup>9</sup> Low-virulence organisms (which may produce a biofilm) and oral flora are culprit organisms that require a high degree of suspicion.<sup>11,12</sup>

## MANAGEMENT

Data informing management of TEI are in part extrapolated from the infrarenal aorta where large multicenter retrospective analyses have been performed using the Swedish Vascular Registry, as well as data from France and the United States.<sup>4,13,14</sup> In 2016, the American Heart Association published guidelines on the management of vascular graft infections and mycotic aneurysms.<sup>15</sup> In general, these recommendations were based on a low level of evidence and are not specific to the thoracic aorta. The evidence base used to guide management decisions based on microbial growth and for the duration of antimicrobial therapy is particularly lacking. Multicenter prospective data collection is necessary to begin to address this problem and is underway by the Management of Aortic Graft Infection Collaboration ([www.gsttbr.com/MAGIC](http://www.gsttbr.com/MAGIC)), which welcomes new collaborating centers.<sup>9</sup>

### Medical Management

It is essential that TEI is managed by a multidisciplinary team that includes a physician with expertise in microbiology/infectious diseases. The microbial epidemiology of endograft infection is poorly defined, and there is little correlation between microbiologic data and the site of vascular infection. Attempts at culprit microbial identification are often uninformative due to the difficulties of sample collection, presence of a low density of organisms in a stationary growth mode (ie, within biofilm), failure to sonicate samples, prior initiation of antimicrobials, and use of culture techniques alone without additional molecular methods of identification such as 16S-PCR.

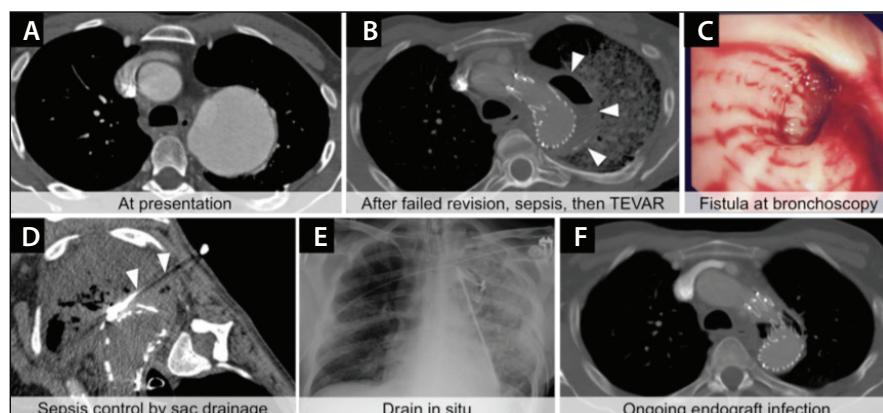
Antibiotic choice is guided by local resistance patterns and is initially a broad-spectrum therapy, with subsequent deescalation and use of agents tailored to specific organisms. Antifungals are an important requirement, in addition to antibiotics, when a visceral fistula is suspected. After endograft explantation, we typically administer intravenous antibiotics for 6 weeks, followed by oral antibiotics for an additional 6 weeks. The agent is initially broad spectrum and later guided by intra-operative samples. We perform 18F-FDG PET/CT after stopping antimicrobials to exclude recurrence of metabolically active infection.

When infected prosthetic material cannot be removed, antimicrobial therapy is usually lifelong, but long-term therapy is also not without risk of major morbidity and mortality. Chronic nausea, hepatotoxicity, bone marrow suppression, adrenal failure, and infective diarrhea (eg, *Clostridium difficile*) are just some of the complications of prolonged therapy.<sup>6,16,17</sup> This is frequently poorly reported in retrospective surgical case series. Antimicrobial resistance is a worsening and global problem. The complications of antimicrobial agents can limit the choice of available drugs and prohibit continuation of suppressive therapy. Chronic sepsis typically causes anorexia and weight loss, and nutritional support should be considered, particularly if endograft explantation is planned. Sepsis-induced cardiomyopathy may further limit quality of life and fitness for future surgical intervention.<sup>18</sup>

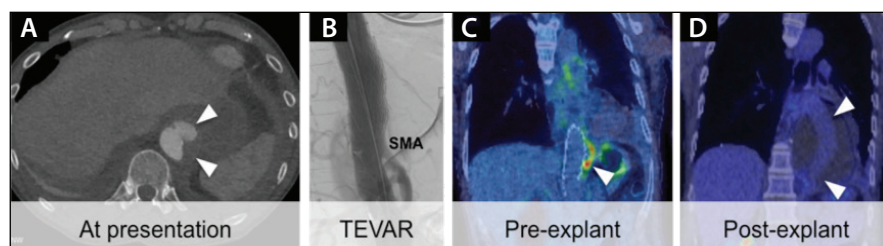
### Surgical Management and Endograft Explantation

Without endograft explantation, in-hospital mortality related to TEI is 42% and increases to 82% after a follow-up period of 9 months.<sup>6</sup> The aortic endoprostheses currently in use are not designed to be removed and the use of barbs and hooks for proximal fixation renders explantation more difficult. Explantation of thoracic grafts that have branches or fenestrations further increases the complexity and may be prohibitively dangerous. When explantation is not possible and provided there is no leakage of blood outside the endograft and aorta, surgical debridement of tissues in the chest and drain placement may allow for control of sepsis when used in conjunction with antimicrobial irrigation (Figure 2).

Endograft explantation necessitates extensive open surgery; however, the risks associated with explantation may be prohibitive in patients who were considered unfit for major open intervention at the time of their index procedure.<sup>19</sup> Where possible, explantation should be electively performed in a stable, optimized patient. Those who present with hemorrhage due to aortoenteric,



**Figure 2.** Sac drainage for sepsis control. This 43-year-old man presented with a large pseudoaneurysm at the site of a childhood coarctation repair (A, B). He had also received talc pleurodesis for recurrent pneumothoraces. Attempted revision surgery was abandoned, and an ascending-to-common carotid bypass was placed. He developed chest sepsis and was later treated with a TX2 thoracic endograft (Cook Medical). An abscess developed within the aneurysm sac (arrowheads) with signs of systemic sepsis and bronchial fistulation (B, C). CT-guided transpleural pigtail drainage of the sac was performed (D, E). Local control of sepsis was achieved with drainage and antibiotics (F). He survived 2.5 years with chronic low-grade sepsis before death from exsanguination.



**Figure 3.** Explantation. A patient with a history of open abdominal aortic aneurysm repair presented with back pain a few weeks after an episode of cholecystitis. CTA demonstrated a large mycotic aneurysm arising above the celiac artery (A). The aneurysm was treated emergently with a thoracic endograft covering the celiac artery (B). Despite antimicrobial therapy, PET/CT demonstrated active aortic graft infection indicating a need for definitive surgery (C). The endograft was explanted via a thoracotomy using left heart bypass and in-line reconstruction with a bovine pericardial tube was carried out (D). Follow-up PET/CT demonstrated absence of active infection and a curative procedure.

aortobronchial, or aortocutaneous fistulas are best managed by a bridging endovascular repair (if this is technically an option), followed by interval graft removal.<sup>20</sup> In any case, the mortality rate of surgical conversion is significantly higher in the presence of fistulas, but the use of endovascular bridging techniques makes exposure and control more predictable and allows preparation of the surgical field with less blood loss and without immediate aortic cross-clamping, thereby shortening the ischemia time.<sup>6</sup> Percutaneous drainage of an infected pseudoaneurysm or collection has been used to

control sepsis, either in addition to palliative antimicrobials or to control sepsis prior to definitive surgery.<sup>6,21-23</sup>

Perioperative mortality from explantation of infected thoracic endografts approaches 40%.<sup>6</sup> Failure to perform adequate debridement of all infected tissues may render the entire operation ineffective. Explantation is usually performed via a thoracotomy and usually with left heart bypass (eg, via the left inferior pulmonary vein), but deep hypothermic circulatory arrest may be required for more proximal endografts. Involvement of the visceral segment similarly increases the complexity of the repair. Expertise is required to manage blood flow rates to the upper and lower body, as well as selective visceral perfusion using appropriate cannulae.

The aims of explantation include excision of all infected native and synthetic material, debridement of infected/necrotic tissue and drainage of fluid collections, arterial (and other tissue) biopsy for microbial culture and/or 16S-PCR, control and repair of fistulas, and arterial reconstruction (ideally in the anatomic position and using a biological conduit), without

compromising visceral perfusion (Figure 3).

The area of infected and friable aorta may extend further than what is evident on the preoperative CT scan, necessitating more extensive exposure. Preoperative PET/CT may help to identify the extent of infected artery. Muscle flaps have been used to obliterate dead space and provide a vascularized coverage of the graft.<sup>24,25</sup> Contiguous spinal column infection can usually be managed with a prolonged course of antimicrobials but may require surgical stabilization. In the case of vertebral osteomyelitis with severe anterior column destruction,



the use of titanium cages in combination with posterior instrumentation may be required.<sup>26</sup> An aortobronchial fistula may require repair or lobectomy with a bovine pericardial patch used as an adjunct.<sup>20</sup> Involvement of the esophagus may require total esophagectomy if repair or control is not feasible by placing drains.

### Choice of Conduit for Reconstruction

Once the aortic stent graft and any other infected prosthetic material have been removed, the arterial circulation must be reconstructed, ideally without placing new prosthetic material in the infected field. Options for reconstruction with a biological conduit include bovine pericardial tube, deep femoral vein, and allograft (or a composite).<sup>6,24,27</sup> If use of a prosthetic graft is essential, grafts soaked in antibiotic and silver-impregnated material are options.<sup>4,6</sup> An alternative option for reconstruction with a prosthetic graft is to use an extra-anatomic approach from the ascending aorta, passing retrohepatic to either the supraceliac or infrarenal aorta.<sup>28</sup> The retrosternal route has also been utilized.<sup>29</sup> Axillofemoral bypass is also possible but may lead to hypertension or mesenteric angina. The mortality associated with extra-anatomic reconstruction is higher than with in situ reconstruction.<sup>6</sup>

### OUTCOMES AFTER EXPLANTATION

There are no large series describing thoracic endograft explantation, and the majority of the available data describe relatively small numbers of patients or report outcomes associated with medical management alone.<sup>4,19,20,24,27,30</sup> A recent systematic review and a meta-analysis suggest a mortality rate of > 80% when the infected thoracic endograft is not explanted and approximately 50% with explantation.<sup>6,31</sup> Endograft preservation in the presence of established TEI should not be considered a definitive or durable solution, particularly in the presence of a fistula, and explantation should be considered the standard of care.

There is no consensus regarding the optimal follow-up of patients after graft explantation. We use clinical, radiologic, and biochemical markers in follow-up. We suggest performing 18F-FDG PET/CT and laboratory tests (particularly C-reactive protein level) to confirm absence of infection after cessation of antimicrobial therapy before considering the patient “cured” of infection. CTA is used to exclude collections and confirm the structural integrity of the repair. Patients who are not candidates for endograft explantation and remain on lifelong suppressive therapy should not be discharged from follow-up. We typically follow these patients with serial 18F-FDG PET/CT scans at 6- to

12-month intervals to monitor the metabolic activity around the endograft and use this as an indicator of response to medical therapy in conjunction with the C-reactive protein measurements.

### CONCLUSION

Without explantation, an infected thoracic endograft is fatal in over half of patients in the midterm, but in the thoracic segment, graft removal in itself carries substantial morbidity and mortality. Many patients will be unfit for surgical repair, and suppression of infection with antimicrobials and nutritional support remain the mainstay of treatment.<sup>16,30</sup> Multidisciplinary management of these cases is essential, with detailed preoperative planning. Attention must be focused toward reducing the incidence of aortic graft infection when possible.<sup>8</sup> The development of diagnostic criteria for aortic graft infection provides a consistent diagnostic standard, which is essential for future clinical trial design and meaningful comparison between diagnostic and therapeutic strategies. Compulsory surveillance of endograft infection within national registries would improve the epidemiologic data available to develop management guidelines. ■

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