

The Roles of Open and Endovascular Repair in Aortic Infection

A review of the approach to treatment for primary and secondary aortic infections.

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Primarily and secondary aortic infections are a major challenge to both the patient and the interventionalist. Endovascular treatment for aortic infections has long been met with skepticism; however, new data indicate that endovascular aneurysm repair (EVAR) can play an important role in treatment, either as a primary and durable solution or as a life-saving bridge in cases in which there is acute bleeding. This article reviews the role of EVAR in primary aortic infection, graft infection with concurrent sepsis, and aortoduodenal fistulas and discusses EVAR as bridge versus a permanent solution.

PRIMARY AORTIC INFECTION

A primary aortic infection resulting in aneurysm formation is also known as a mycotic aortic aneurysm (MAA). The infection starts in the aortic endothelium by blood-borne bacteria. Within days, degradation of the intimal and medial layers may occur, resulting in the development of an aneurysm.^{1,2} MAAs are rare in Western countries, with an estimated incidence of 0.6% to 2% of all aortic aneurysms; however, an incidence rate of up to 13% has been reported in Taiwan.³⁻⁵ MAAs have a tendency to grow rapidly and have a high risk of rupture, and patients often have pain and severe comorbidities such as immunodeficiency and coexisting septic conditions.^{4,6-8} The most frequent pathogens are *Salmonella* sp, *Streptococcus* sp, and *Staphylococcus* sp.^{4,7-9}

There is no consensus on the diagnostic criteria for aneurysms due to infection. Currently, the most used diagnostic workup for MAA is syndromic and based on different combinations of the following criteria: (1) clinical presentation (ie, pain, fever, circulatory and/or septic shock, presence of concomitant infection, and/or immunosuppressive states), (2) laboratory findings (ie, increased inflammatory parameters such as C-reactive protein [CRP], leukocytosis, and/or positive culture), (3) findings on CT or MRI (ie, saccular, eccentric, or multilobular aneurysm with periaortic mass and/or gas, and rapid aortic expansion/rupture), and (4) intraoperative findings.



Figure 1. CTA showing a MAA in the distal descending aorta, before and after thoracic endovascular aortic repair.

	CLINICAL / SURGICAL	RADIOLOGY	LABORATORY
MAJOR CRITERIA	<ul style="list-style-type: none"> • Pus (confirmed by microscopy) around graft or in aneurysm sac at surgery • Open wound with exposed graft or communicating sinus • Fistula development e.g. aorto-enteric or aorto-bronchial • Graft insertion in an infected site e.g. fistula, mycotic aneurysm or infected pseudoaneurysm 	<ul style="list-style-type: none"> • Peri-graft fluid on CT scan \geq 3 months after insertion • Peri-graft gas on CT scan \geq 7 weeks after insertion • Increase in peri-graft gas volume demonstrated on serial imaging 	<ul style="list-style-type: none"> • Organisms recovered from an explanted graft • Organisms recovered from an intra-operative specimen • Organisms recovered from a percutaneous, radiologically-guided aspirate of peri-graft fluid
MINOR CRITERIA	<ul style="list-style-type: none"> • Localized clinical features of AGI e.g. erythema, warmth, swelling, purulent discharge, pain • Fever \geq38°C with AGI as most likely cause 	<ul style="list-style-type: none"> • 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 	<ul style="list-style-type: none"> • Blood culture(s) positive and no apparent source except AGI • Abnormally elevated inflammatory markers with AGI as most likely cause e.g. ESR, CRP, white cell count

Figure 2. MAGIC's proposed definition of suspected and diagnosed AGI. AGI is suspected in a patient with any isolated major criterion or minor criteria from two of the three categories: clinical/surgical, radiologic, or laboratory. AGI is diagnosed in the presence of a single major criterion, plus any other criterion (major or minor) from another category. Note: Where microbiologic investigations identify potential "contaminant" organisms (ie, coagulase-negative staphylococci, propionibacteria, corynebacteria, and 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 sample based on antibiograms or a recognized typing method (ie, pulsed-field electrophoresis). ESR, erythrocyte sedimentation rate; FDG, fluorodeoxyglucose. Reproduced with permission from Lyons OT, Baguneid M, Barwick TD, et al. Diagnosis of aortic graft infection: a case definition by the management of aortic graft infection collaboration (MAGIC). *Eur J Vasc Endovasc Surg.* 2016;52:758–763.

Treatment of MAAs consists of antibiotic therapy combined with surgery, either by open surgical repair (OSR) or EVAR. OSR has been considered the gold standard, despite a lack of evidence supporting its superiority compared with EVAR. OSR includes resection of the aneurysm and the infected tissue, followed by revascularization, either by in situ reconstruction or extra-anatomic bypass, which is partly dependent on localization of the aneurysm. Extra-anatomic bypass might be used in infrarenal MAAs but has been associated with complications such as aortic stump blow-out and graft occlusion. Most modern research describes the use of in situ grafting. There is no evidence comparing graft materials for treating MAAs; however, most data have evaluated synthetic grafts and have demonstrated fairly good results. Use of autograft material, such as femoropopliteal veins as a conduit, also known as neoortoiliac system (NAIS), is appealing because of the supposed superior

resistance to infection; however, it is time consuming and may add to patient morbidity. The use of cryopreserved homografts as a conduit for MAAs has only been reported in a few cases.

EVAR offers a minimally invasive surgical solution in the elderly, comorbid septic patient with an anatomically challenging aneurysm (Figure 1). Concerns about not resecting the infected tissue, including the aneurysm itself, and the risk of recurrent/persistent infection have been expressed, and consequently, treatment with EVAR was initially regarded with skepticism. There is no randomized controlled trial comparing OSR and EVAR for MAA, but the two largest published studies of MAA patients to date demonstrate a clear time trend toward a preferred endovascular approach to treatment rather than OSR,⁴ and today, EVAR is considered an equal if not superior option over OSR for treating MAAs.^{4,7,8}

The largest study on MAAs was a Swedish population-based cohort study consisting of 132 patients with abdominal MAAs. In that cohort, OSR and EVAR were performed in 62 and 70 patients, respectively.⁴ Overall survival was 86%, 79%, 59%, and 39% at 3 months and 1, 5, and 10 years, respectively. Survival was significantly lower for OSR compared with EVAR at 3 months (74.2% vs 95.7%) and at 1 year (72.5% vs 83.9%); data were confirmed by a propensity score-weighted analysis. There was no difference in long-term survival or incidence of infection-related complications or frequency of reoperation between the two groups. A retrospective European multicenter study

including 123 patients treated with EVAR for MAAs in the abdominal and thoracic aorta demonstrated that EVAR was feasible and durable treatment option for most MAA patients. Survival was 91%, 75%, 55%, and 41% after 1 month and 1, 5, and 10 years, respectively.⁷

Among all treated MAAs, 20% develop infection-related complications such as sepsis, graft infections, recurrent MAAs, or aortoenteric fistulas (AEFs), regardless of surgical approach, with most occurring during the first year after surgery.^{4,7,8} Postoperatively, MAA patients treated with EVAR should be followed closely with clinical follow-up that includes laboratory testing and imaging, especially at

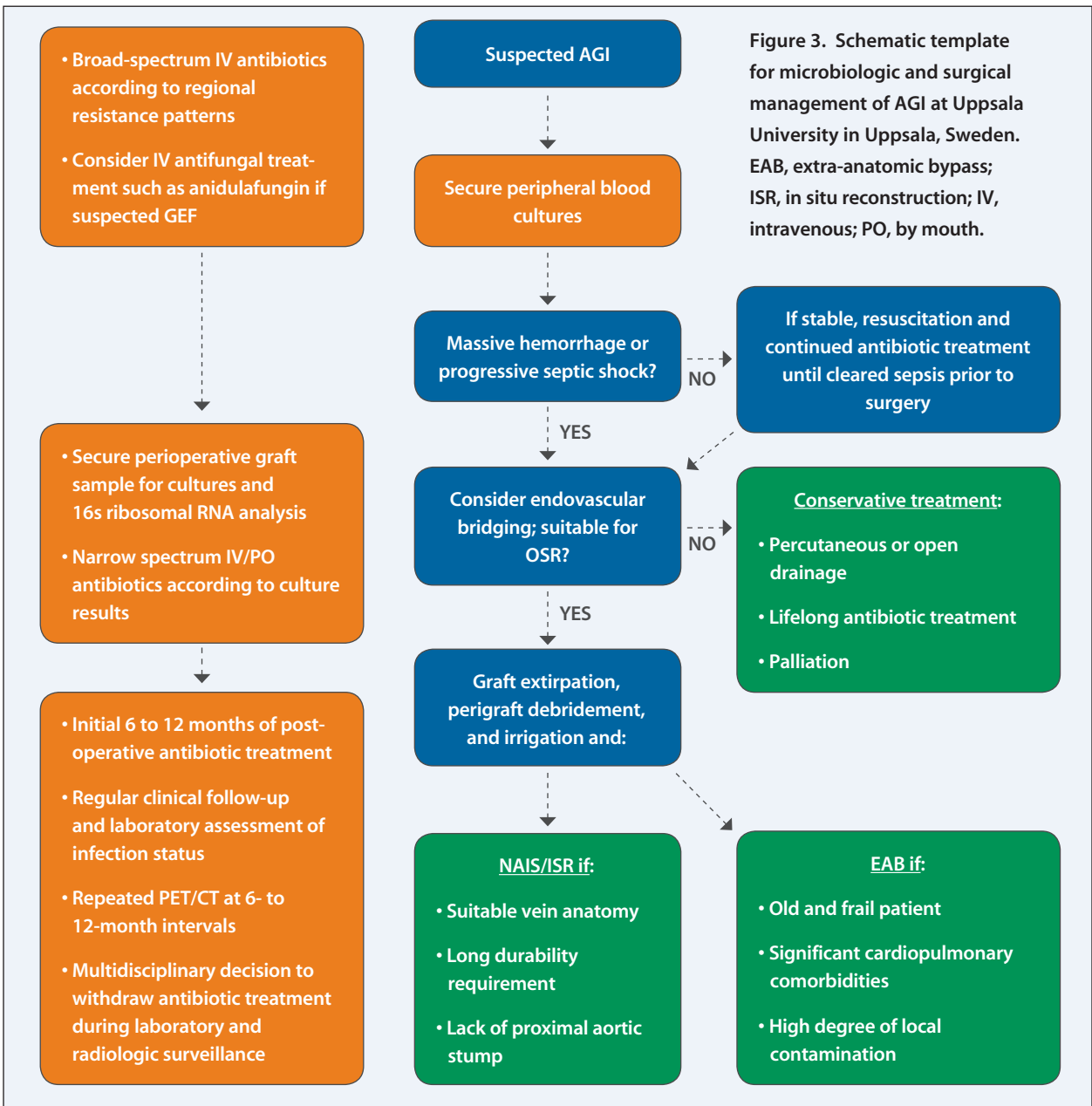


Figure 3. Schematic template for microbiologic and surgical management of AGI at Uppsala University in Uppsala, Sweden. EAB, extra-anatomic bypass; ISR, in situ reconstruction; IV, intravenous; PO, by mouth.

1 year to detect possible development of infection-related complications. As a result, antibiotic treatment should be administered for at least 6 to 12 months postoperatively and possibly lifelong.

SEPTIC PATIENT WITH GRAFT INFECTION

Although aortic graft infections (AGIs) represent a difficult situation for the interventionalist, a patient presenting with concurrent sepsis poses an even greater challenge. By virtue of the Sepsis-3 guidelines, sepsis is currently defined as a life-threatening organ dysfunction caused by a dysregulated host response to infection.¹⁰ Although studies have shown that the addition of sepsis or septic shock among patients undergoing surgery for AGI increases in-hospital mortality, there is a lack of stringent definition and severity grading.^{11,12}

Once presented with a septic patient who has an AGI, one of the major questions is that of early surgical intervention (if suitable) versus surgical delay during antibiotic administration, as well as pulmonary and circulatory resuscitation while waiting for the organ dysfunction to diminish. Ongoing bacteremia during surgery likely increases the risk of recurrent graft infection and concurrent sepsis, which greatly increases the perioperative morbidity and mortality in patients undergoing major surgery.^{13,14} However, in the AGI patient, a lack of early source control may contribute to conservative treatment failure, septic shock, and increased mortality. Due to the lack of randomized studies and the selection bias in retrospective studies where surgical delay was favored in stable patients, no conclusions can be drawn about the optimal strategy. Instead, the absence of current evidence highlights the need for a multidisciplinary approach and decision-making strategy.

Not limited to the septic patient, appropriate culture samples to guide long-term antibiotic treatment is an important factor to reduce the frequency of recurrent AGI and infection-related mortality. The literature supports an estimated positive culture sample in 60% to 80% of patients with AGI.¹⁵ Studies on primary MAAs and AGIs have shown that the infectious etiology at presentation correlates with long-term mortality.^{11,16} As such, culture samples provide risk assessment information and assist in decision-making regarding duration of long-term antibiotic treatment. Because of this and in light of the Management of Aortic Graft Infection Collaboration's (MAGIC) proposed criteria for diagnosis of AGI (Figure 2), we routinely secure blood cultures, perioperative tissue cultures, and explanted graft cultures, as well as 16s ribosomal RNA analysis of graft material.¹⁶ Figure 3 illustrates a suggested schematic template for microbiologic and surgical management of suspected AGI.

In terms of a definitive treatment strategy for AGIs, OSR is the gold standard. This includes complete removal of

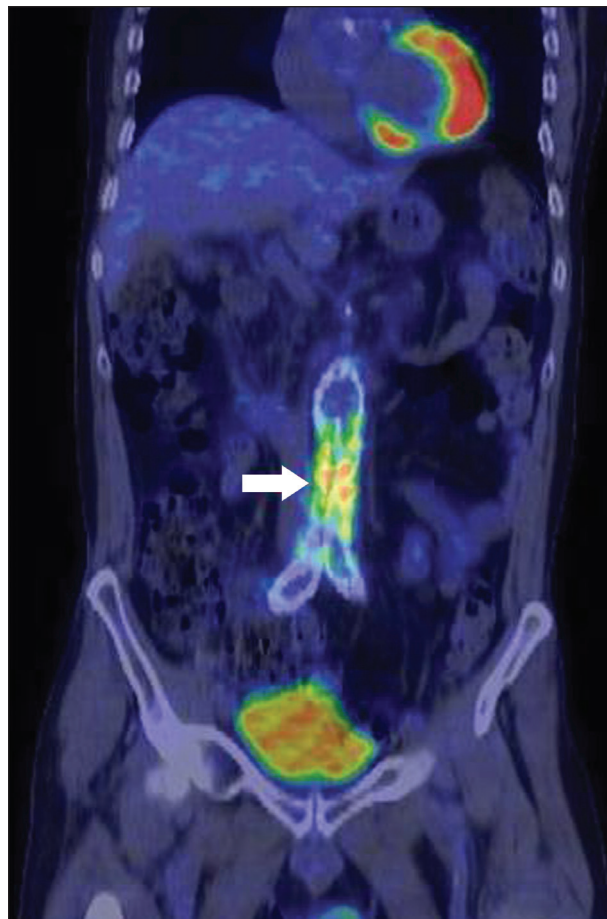


Figure 4. A 74-year-old patient previously treated with EVAR for MAA presented with back pain and intermittent fever at 1-year follow-up, and 18-fluorodeoxyglucose PET/CT showed pathologic F18 tracer uptake (arrow) in the old stent graft.

the infected graft, perigraft tissue debridement combined with in situ reconstruction as previously described, or alternatively, extra-anatomic bypass. Both perigraft debridement and extra-anatomic bypass are feasible options with similar perioperative mortality rates ranging from 10% to 50%, depending on patient selection, presence of rupture/anastomosis dehiscence, AEF, and sepsis.^{11,17,18} It is likely that long-term durability and freedom from new graft infection favor in situ reconstruction, although an extra-anatomic reconstruction is more suitable in the elderly and frailer AGI patient cohorts.¹⁹

Conservative approaches without graft removal are described and might be the only feasible strategy in patients with a high predicted perioperative mortality or complicated suprarenal or thoracic graft anatomy. This often includes percutaneous drainage and irrigation of the infectious cavity or open perigraft debridement, local antibiotic treatment, as well as lifelong antibiotic suppressive strategies.²⁰ Currently,

no studies have compared conservative treatment versus graft removal strategies; however, among conservatively treated patients, poor long-term outcomes and a 1-year mortality of approximately 50% have been reported in small retrospective studies,²¹ indicating that conservative treatment should be regarded as a palliative treatment. Consensus dictates that AEF/graft enteric fistula (GEF), pseudoaneurysm at the site of anastomosis, rupture, and anastomosis dehiscence are contraindications for this approach.

There are no established guidelines on appropriate duration of antibiotic treatment, and retrospective studies comparing strategies have limitations such as residual confounders and competing risks. Furthermore, it is likely that multiple factors such as concurrent AEFs, bacteriology, level of contamination, and surgical technique contribute to recurrent AGI risk and as such should be taken into consideration when determining the duration of antibiotic regimen. At our institution, we adhere to 6 to 12 months of postoperative antibiotic treatment, followed by clinical, laboratory, and radiologic reassessment with positron emission tomography (PET)/CT to determine withdrawal or prolonged treatment (Figure 4).

STABLE PATIENT WITH AN AORTODUODENAL FISTULA

The majority of aortoduodenal fistulas are secondary and occur after previous aortic surgery with fistulation between the aortic graft and the duodenum, typically several years after the primary repair. The prevalence of aortoduodenal fistulas is reported at 0.5% to 1% after previous aortic surgery.²²⁻²⁴ Unfortunately, this complication occurs at equal frequency after both OSR and EVAR.

The classic presentation of aortoduodenal fistulation, with herald bleeding and gastrointestinal bleeding in a patient with previous aortic repair, should initiate investigation to rule out presence of a fistulas. In stable patients with suspicion of an aortoduodenal fistula, workup includes gastroduodenoscopy aiming to visualize the full length of the duodenum (Figure 5), CTA to assess for signs of graft infection and pseudoaneurysm formation, and sometimes functional imaging with PET/CT to verify and evaluate the extent of the graft infection.

If an aortoduodenal fistulation is verified in a stable patient with a previous herald bleed, urgent intervention is required to reduce the risk of a massive and fatal bleeding episode. Mortality for surgical repair of aortoduodenal fistulas is highly independent of surgical strategy used, and the risks with the operation are naturally increased in patients with hemodynamic instability or ongoing sepsis.²⁵ Endovascular stent graft coverage of the fistula is an excellent damage control technique to treat ongoing bleeding or avoid rebleeding as a bridge to open surgery.

As surgery for aortoduodenal fistulas is rare and highly demanding, it is advisable that stable patients are transferred to high-volume centers prior to definitive repair. Final management includes closure of the duodenal fistula, resection of the infected graft material, and reconstitution of blood flow to the lower body either through extra-anatomic or in situ reconstruction. The gold standard surgical technique is to avoid arterial reconstruction in the infected field using extra-anatomic reconstruction with axillobifemoral bypass prior to graft resection and aortic stump closure. However, as this procedure is associated with the risk of aortic stump blowout, NAIS reconstruction in situ using femoral veins is advocated by some and may result in lower risk for late failure, although in situ reconstruction in deeply infected field should still be avoided.

Enteric repair can be performed with duodenorrhaphy with or without omentum interposition and with or without enterostomy or duodenal resection/reconstruction. A literature review that included 331 secondary AEF cases suggested that the use of omentum interposition and in situ vascular reconstruction may be advantageous and that duodenal derivation is preferable to the simple closure of the fistula.²⁶ In a recent pooled analysis that included 823 patients, in-hospital mortality after repair of AEF was 31%.²⁵

EVAR AS A BRIDGE VERSUS A PERMANENT SOLUTION

In patients with a ruptured MAA, EVAR has been suggested as a bridge to radical OSR. However, studies demonstrate that most patients either do too well after EVAR



Figure 5. Exposed stent graft during gastroscopy in a patient with an aortoduodenal fistula. Sörelius K, Sundbom M, Mani K, et al. Hybrid treatment of a post-EVAR aortic fistula. *Vascular*. 2014;22(5):385–389. Copyright © 2014. Reprinted by permission of SAGE Publications, Ltd.

to justify a later major open surgical conversion or are too fragile to undergo OSR.⁷

In case of AGI with bleeding or AEF, endovascular stent graft coverage of the bleeding site or fistula is an excellent technique to treat ongoing bleeding or avoid rebleeding as a bridge to open surgery.²⁷ Stent graft coverage of the fistula can often be achieved through insertion of a commercially available EVAR cuff both in patients with previous OSR and EVAR. As definitive management of graft infections requires extirpation of all foreign material, and also closure of the duodenal fistula in case of AEF, a stent graft cuff without suprarenal fixation may be used to facilitate proximal surgical control above the graft.

Endovascular sealing of AEF provides time to treat shock, local and systemic infection, and comorbidity and creates a better situation to perform radical OSR in the future with a possibly better outcome. However, the rate of reinfection remains high and endovascular sealing of AEF should therefore be used as a short bridge to OSR, except for patients remaining unfit for OSR even after maximal supportive therapy. In those patients, long-term antibiotic treatment and lifelong surveillance are mandatory.²⁷

CONCLUSION

Evidence suggests that EVAR for a primary infected aortic aneurysm is associated with improved short-term outcomes, without compromising long-term results. EVAR can thus be regarded as an acceptable and durable treatment alternative to OSR for MAA. EVAR also has an important role as a life-saving bridge in acute bleeding states associated with AGIs and AEFs, with later OSR, if feasible. ■

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