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How To Diagnose and Manage Infected Endografts after Endovascular Aneurysm Repair

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Abstract

The prevalence of endograft infections (EI) after endovascular abdominal aortic aneurysm repair is below 1%. With the growing number of patients with aortic endografts and the aging population, the number of patients with EI might also increase. The diagnosis is based on an association of clinical symptoms, imaging, and microbial cultures. Angio-computed tomography is currently the gold-standard technique for diagnosis. Low-grade infection sometimes requires nuclear medicine imaging to make a correct diagnosis. There is no good evidence to guide management so far. In the case of active gastrointestinal bleeding, pseudoaneurysm, or extensive perigraft purulence involving adjacent organs, an invasive treatment should always be attempted. In the other cases (the majority), when there is not an immediate danger to the patient's life, a conservative management is started with a proper antimicrobial therapy. Any infectious cavity can be percutaneously drained. Management depends on the patient's condition and a tailored approach should always be offered. In the case of a patient who is young, has a good life expectancy, or in whom there is absence of significant comorbidities, a surgical attempt can be proposed. Surgical techniques favor, in terms of mortality, patency, and reinfection rate, the in situ reconstruction. Choice of technique relies on the center and the operator's experience. Long-term antibiotic therapy is always required in all cases, with close monitoring of the C-reactive protein.

Key Words

Computed tomography scan · Aortic aneurysm · Epidemiology · Stent graft · Endovascular

Introduction

The incidence of infected endografts (IEs) following endovascular abdominal aortic aneurysm repair (EVAR) is below 1% [1–113]. Most of our knowledge on diagnosis and management of IE is translated from the experience of graft infection following open repair [8–11].

As a complication, IE is one of the most challenging and threatening in vascular surgery and may lead to graft/arterial interface disruption, hemorrhage, or sepsis, and is associated with significant morbidity and mortality [12]. IEs have been shown to present roughly one-third as chronic sepsis, one-third as severe acute sepsis, and one-third as aorto-enteric fistula (AEF) [6,7,11]. IEs can be summed up as low- and high-grade infections [10].

Low-grade infection, caused by low-virulent bacteria, occurs generally late after the original graft im-

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plantation. Usually, these patients have been suffering from nonspecific symptoms and signs, thus potentially delaying diagnosis. Nonspecific symptoms include weakness, weight loss, and malaise. Low-grade infection occurs in one third of total patients (chronic sepsis).

High-grade infection is caused by more aggressive bacteria. Symptoms appear acutely, such as sepsis, fever, abdominal pain, lumbar pain, graft thrombosis, septic embolism, hematemesis, rectal blood loss, and hemorrhagic shock (in the case of aorto-enteric fistula) [10,11,14,15,101].

Etiologies

Experimental data [16–18] showed that stent grafts present lower bacterial resistance and greater bacterial adherence. Bacterial adherence depends on the length of stent graft in contact with the arterial wall and on the extent of endothelialization of the stent graft surface by mature collagen tissue.

Moreover, it has been speculated that an intact aneurysm wall in a patient with a stent graft prevents any bacterial egress and thus produces a more aggressive "closed space" infection. The presence of unevacuated thrombus around the graft could be a nidus for bacterial growth and, in case of endoleak, for septic embolism. Possible etiologies for IEs are perioperative contamination, hematogenous seeding, and mechanical erosion [11].

Secondary procedures with multiple catheter manipulations inside a stent graft have been found responsible for infection as well [10,11,14].

The procedural environment is critical. It is thought that interventional radiology suites offer a lower level of sterility and require significant changes in both equipment [19] and work habits [20] to achieve outcomes similar to those in conventional operating rooms. However, it should be said that no correlation between procedures performed in the angiosuite versus the operating room has been confirmed by published studies [11,21].

Another risk factor associated with IEs is immunodeficiency (primary or secondary), especially that due to corticosteroid therapy or chemotherapy in neoplastic patients [22].

Urgent/emergency procedures are associated with a significantly higher percentage of IEs [14].

Antibiotic prophylaxis in vascular surgery has been proven beneficial to reduce surgical site infections after reconstruction of the aorta, procedures on the leg that involve a groin incision, any procedure that implants a vascular prosthesis, or endoluminal graft [10,11,14,23,24]. Therefore, prophylaxis with a cephalosporin or penicillin is mandatory.

The most frequent causative organism for IE is Staphylococcus [9,11]. *Staphylococcus aureus* has been reported to be the most frequently isolated microorganism in IE [7]. Many of these infections result from perioperative contamination, 50% manifesting after the second year of follow-up. Development of stent graft infection in the presence of other infections has been reported. Bacteria are typically of skin flora or gastroenteric tract origin (including *Staphylococcus aureus*, *Staphylococcus epidermidis*, *Escherichia coli*, Enterococci, and Streptococci). Fungal infections are very rare [10,11,94].

Diagnosis

IE diagnosis [2,6,10,11,14,25–40,55,73,76] is based on an association of clinical symptoms, imaging findings, and microbial cultures. Cultures of blood or even samples collected from the infected field can sometimes be negative (up to 33% of cases) [10,11,14].

Each patient should be investigated for leukocytosis and C-reactive protein values. C-reactive protein has been indicated as a value to be monitored in follow-up in order to grade infection (progression, resolution) and to decide when antibiotic therapy can be discontinued [25].

Angio-computed tomography (CT) scans should be performed in each patient, even in case of hemorrhagic shock. This scan has a high specificity and high sensitivity; it is performed quickly and is available in most centers. For all these reasons the angio-CT scan is considered the gold standard for IE. If an angio-CT scan is not conclusive for the diagnosis of a suspected IE, and the patient's clinical condition is fit to await surgical treatment, MRI and positron emission tomography (PET) combined with CT should be considered [10,11,26,27]. Duplex ultrasound is rarely useful since it has low sensitivity and specificity in detecting IE.

High-grade infections are well diagnosed by angio-CT scan. Peculiar features are perigraft air, tissue infiltration, intrasac collections, fluid accumulation and soft-tissue attenuation, ectopic gas, pseudoaneurysm, or discontinuity of the aneurysmal wall, as well as focal bowel thickening, and direct contrast enhancement in the bowel in the arterial phase (communication between aortic wall and bowel tract) [27]. In case of aorto-enteric fistula, a CT scan confirms diagnosis in only 33-80% of cases. Also, endoscopy, rarely performed in the absence of gastrointestinal bleeding, does not exclude diagnosis if no fistula is seen. The diagnosis of aorto-enteric fistula is most often made on surgical exploration. Some problems arise when a low-grade infection without pathognomonic signs and symptoms is present. MRI has a higher sensitivity in the differentiation of small perigraft fluid collections [28].

Leukocyte scan or scintigraphy is most useful in low-grade infection, and in association with CT scan confirms the diagnosis of infection. Indium-111- and technetium-99-radiolabeled leukocytes have been employed to mark hot spots in suspected graft infection. Sensitivity and specificity range from 50 to 100% [29,30]. Fluorodeoxyglucose (FDG)-PET has been successfully used to detect suspected focal infection when other techniques are negative. To increase both sensitivity and specificity of this technique, the combination of FDG-PET and CT scan is used. Information gained by the exact localization of the site of infection provided by CT scan, combined with metabolic data obtained by FDG-PET, may enhance accurate localization and then treat the infectious process. When a focal intense FDG uptake plus a suspected lesion on CT imaging are present, the predicted prosthetic graft infection probability is around 97% [31–39].

Isolation of the causative bacteria or fungus from either blood- or perigraft-drained fluid material is confirmative of the diagnosis of IE.

Management

The low incidence of this complication has not allowed establishment of a consensus in its management. IE management requires a case-by-case evaluation [1–113].

Patients undergoing EVAR are usually frail patients who are deemed unfit for open surgery due to anatomic or clinical features. The crucial point when there is an infected graft is to decide if the graft has to be removed or not. This decision has to take into account the patient's comorbidities, abdomen hostility (previous abdominal intervention, abdominal radiotherapy, colostomy, nephrostomy, etc), and symptoms and signs (including hemodynamic stability or instability).

Surgery is essential when there is active bleeding or threatening septic shock. Offering a therapeutic strategy should balance the operative risk and patient's life expectancy. On the other hand, the procedure likely to achieve better results in terms of mortality, morbidity and anatomic durability should be offered to the patient.

Conservative Treatment

In selected high-risk patients with multiple comorbidities with or without a hostile abdomen, conservative treatment is likely the only acceptable solution [10,11,14,25,26,40–43,64-69,85-87,90,92]. Sometimes, it is better to cope with suboptimal therapy, as in conservative treatments, and allow the patient some more life years than to be extremely radical [87]. In Italy, the mean life expectancy of a healthy man is a little bit more than 82 years, therefore, in the case of an 80-year-old man with an infected abdominal aortic aneurysm endograft, hypertension, cardiomyopathy, and even renal insufficiency, it is unlikely to give more years to live than Nature has given to that patient (*primum non nˇoc*[macr]*ere*).

Conservative treatment consists of antimicrobial therapy, which should not be empirical but based on the antibiogram and percutaneous drainage (CT guided). For somewhat more aggressive therapy, drainage may be followed by irrigation and extraction of infectious material from the cavity. In selected cases, simple resection of the aneurysm sac has been described, leaving the stent graft behind [42]. Mortality in these frail patients has been up to 40% [43].

Although the consensus is that, in suitable patients, the infected graft material should always be removed, some authors [14] showed no significant difference in mortality between the conservatively and surgically managed groups (possibly related to the small sample size analyzed) [43]. Cernohorsky et al. [14] concluded their study by saying that there may be a role for conservative treatment in selected cases of patients with stent-graft infection, possibly those patients with minor, low-grade infections.

On the contrary, Lyons et al. [4] recently reported that in their large series all patients (abdominal and thoracic) who did not have their endografts explanted died of aortic disease progression, contrasted with a mortality rate of only about 30% when the graft was explanted.

Surgical Treatment

When an infected graft is generating a clinical scenario that is not manageable by a conservative approach, surgical treatment should be considered [2–16,26,40–113]. Young patients with a good life expectancy (these are a minority) should be considered for surgical treatment as the first option.

Surgical treatment consists of two different phases: the stent-graft removal and revascularization. Stent graft removal is a prerequisite for complete healing and cure of the infectious process in a patient with a vascular graft implant [2–16,26,40–113]. The technical aspects of device explantation will vary with the type of graft deployed and the vascular anatomy. Endografts with suprarenal barb fixation require supraceliac control for explantation, whereas endografts with an infrarenal fixation may be managed with a lower clamp placement. In case of endograft with suprarenal barb fixation, supraceliac clamping is required and the bare suprarenal struts of the device may be cut and left in situ [11,102]. In order to facilitate graft removal, a suggested procedure is to routinely dislodge the proximal portion of the stent graft, squeezing the upper stent and gently pushing the stent hooks or barbs in a proximal direction [11]. Dissection of the pararenal aorta and iliac arteries is often described as very difficult, because of the inflammation surrounding the arteries near the graft attachment sites, with a reactive process similar to that encountered with an inflammatory aneurysm.

After excision of the infected graft and debridement of devitalized tissue, in situ or by extra-anatomical routes, reconstruction can be accomplished supported by pre-, intra-, and postoperative broad-spectrum or culture-specific antibiotic therapy [10,89].

The specific revascularization technique currently is based on the experience of the operators and center.

Extra-anatomic bypass (EAB) originating from the axillary artery has been performed widely. The most common reconstruction employed is the axillo-femoro-femoral bypass performed in the same or a later staged procedure. Several authors [7–11,70–75] have reported substantially lower mortality rates with staged EAB and graft removal. Dacron or polytetrafluoroethylene grafts, as well as autologous vein or cryopreserved allograft, can be used.

Concerns about long-term graft patency and reinfection (up to 27%) remain, as well as the risk of aortic stump blow-out during follow-up (up to 25%), in particular in cases of persistent retroperitoneal sepsis [10,11]. Specific follow-up protocols should be applied in order to detect early signs of this fatal complication. Risk of renal complications (renal artery occlusion) has also been described in cases of aortic stump closure. The risk of amputation is reported as high as 29% [92]. In a single center experience, reported mortality for EAB was around 16% while in situ reconstruction mortality was nearly 6%. This may have been due to the preference for performing EAB in high-grade infection [7].

In situ reconstruction avoids aortic stump oversewing, and presents other advantages as well. It avoids the risk of stump blow-out and renal vessel occlusion, avoids prolonged operative time and consequent ischemia, reduces limb loss, and finally avoids long-term anticoagulation associated with EAB.

A recent review reported that in situ reconstructions have surpassed EAB in almost every aspect (mortality, amputation rate, patency) [93]. After having held the position of gold standard for years, EAB is now part of a wide array of treatment options with limited indications [93].

In case of in situ reconstruction, cadaveric homograft tissue has been used in some centers [95,96]. This technique has a lower rate of reinfection (<10%), perianastomotic hemorrhage (<10%), thrombosis (<10%) and recurrent aneurysm formation (2%) compared to EAB.

The well known major drawback of cryopreserved human tissue is the risk of degeneration of the allograft, leading to complications such as calcification, dilatation, or even rupture of the allograft [97]. Dilation has been reported in up to 17% of cases and late occlusion rates in up to 32% [98]. Immunological reactions seem to be partly responsible for degenerative changes occurring in the allograft wall [99]. Moreover, we cannot generalize that in situ allograft replacement is safe for all types of infection. Indeed caution should be used when planning in situ allograft replacement in patients with extensive infection and gross purulence or highly virulent Gram-negative organisms. In these cases, some authors have preferred complete graft removal, extensive debridement, and EAB [97]. EAB continues to be recommended when there is a severe, widespread purulent abdominal infection.

In the largest study of cryopreserved aorto-iliac arterial allografts (220 patients), [14] the authors concluded that this treatment allows for in-line aortic reconstruction in the presence of infection, with lower patient morbidity (24%) and mortality (9%) than other published treatment options. In the long term, use of cryopreserved grafts is associated with low rates of aneurysm formation (3%), allograft rupture (6%), recurrent infection (4%), and early limb loss (0%). Freedom from graft-related complications, graft explant, and limb loss was 80%, 88%, and 97%, respectively, at five years. The use of a fresh allograft has been discontinued in most institutions due to concerns regarding the graft's propensity to dilate over the long term [100].

At present, reconstruction with cryopreserved arterial allografts can be regarded as a safe temporizing maneuver to help eradicate infection and permit subsequent reconstruction with prosthetic material when necessary (bridge solutions) [97,101]. Superficial femoral-popliteal veins in a nonreversed configuration have been used as material for aorto-iliac reconstruction in case of infected stent graft explantation [7]. Some authors called this technique of revascularization a neoartoiliac system procedure. Advantages include avoiding the risk of aortic stump blow-out and the potential patency and reinfection issues of EAB. Thirty-day operative mortality is $<$10%, with 5-year mortality rates of 30-50%. Thirty-day major amputation rates range from 2% to 9%, with 5-year limb-salvage rates ranging between 89% and 96%. Recurrent infection is very rare, occurring in $<$2% of patients [103]. Venous morbidity is similarly low, with fasciotomy rates of 12%, and only 15% of patients experiencing chronic venous insufficiency at five years. Incidence of postoperative deep vein thrombosis is up to 22% for the donor limb [26]. Aneurysmal degeneration is also exceptionally rare. Use of autologous vein grafts for in situ reconstruction of infected grafts represents the standard of care in the treatment of aortic graft infections according to a recent review from Chung and Clagett [103]. In the literature, autogenous veins remain the most effective method to avoid any reinfection. Important factors limiting their applicability are extended surgical trauma (risk of wound infection) and longer operation time [8,103,104].

Some researchers have used antibiotic-impregnated grafts and Dacron silver grafts in order to decrease the risk of infection recurrence (combined with adequate antimicrobial therapy) [105,106]. The reported reinfection rate ranges from 4 to 22% [6,106–109]. Thirty-day mortality ranges from 7 to 21% and morbidity from 2 to 60%. The 5-year survival is near 50%. Amputations are rarely seen in these cases (they are more common following EAB). In a recent paper, [98] cryopreserved arterial homografts were compared to silver-coated grafts, showing no statistical differences between the two groups in terms of early mortality and midterm survival. It was found that homografts are nearly three times more expensive than silver grafts. These authors [98] reported homograft as the preferred implantation in patients without an acute life-threatening status (i.e., gastrointestinal bleeding, free aneurysm rupture, cardiogenic shock) even if more expensive and despite no statistical differences being found in the results.

In a meta-analysis, [6] rifampicin-bonded grafts are associated with fewer amputations, conduit failures, and early mortality than other treatment modalities for aortic graft infection. On the contrary, reinfection was worst for rifampicin-bonded grafts (closely followed by cryopreserved allografts), and lowest for autogenous veins. This systematic review and meta-analysis remarked that in situ replacement may be appropriate in properly selected patients for infected vascular grafts and raised the question whether EAB should remain the gold standard as it was in the past.

Additional strategies during surgery for infected aortic grafts and endografts are used to prevent reinfection: use of viable flaps to obliterate dead space, or of omentum tacked to the aortic stump to reduce risk of blow-out, as well as placement of perigraft catheters for postoperative antibiotic irrigation. Fatima et al. [92] reported Rifampin-soaked polyester grafts wrapped 360° in autogenous tissue (preferably omentum) [4,19,110].

Some authors indicate the need for lifelong appropriate parenteral antibiotic prophylaxis in all patients with prosthetic aortic grafts who are undergoing a late procedure that can cause bacteremia [25].

The duration of antimicrobial treatment in patients after removal of an infected aortic endograft is controversial. No current guidelines exist on this issue and some authors suggest prolonging antibiotic administration until the C-reactive protein level has returned to baseline [25].

The most-preferred antibiotic agents are daptomycin for Gram-positive coverage and piperacillin-tazobactam, cefepime, or levofloxacin for Gram-negative coverage. Vancomycin or linezolid is an alternative for staphylococcal and MRSA (methicillin-resistant Staphylococcus aureus) coverage [111,112].

Aorto-enteric Fistula

Aorto-enteric fistulas (AEFs) are rare, lethal causes of massive gastrointestinal tract bleeding [10,11] and among the most challenging diagnostic and therapeutic problems encountered by vascular surgeons. The morbidity and mortality remain alarmingly high.

The treatment aim is to promptly stop bleeding. The fastest way may be via a further endovascular exclusion by placement of a new endograft to cover the hole in the gastrointestinal tract [89]. This procedure should be considered as "bridge solution" to a more definitive one. Relining should be considered if anatomic criteria are respected inside the AEF. As we know, the source of infection and so the fistulous communication cannot be removed in this way and the infection cannot be solved even with aggressive antibiotic therapy. In the literature, anecdotal attempts to achieve definitive solutions in this way have failed in the long-term and new surgery has been required [12,101].

If the endovascular solution is not possible, open surgery is required (details of surgical techniques are given in the Surgical Treatment section). When the bleeding has been stopped, conventional treatment of an AEF is based on debridement, repair of the enteric fistula, and removal of the inciting factor. In the literature, anatomic bypass (antibiotic-impregnated or silver-coated prosthesis, homograft or allograft), and extra-anatomic bypass (axillo-bifemoral bypass) are all described [4,7,8,10,11,113].

Summary

The prevalence of endograft infections after endovascular abdominal aortic aneurysm repair is below 1%. With the growing number of patients with aortic endografts and the aging population, the number of patients with endograft infections can be expected to increase. The diagnosis is based on an association of clinical symptoms, imaging findings, and microbial cultures. Angio-CT is currently the gold-standard technique for diagnosis. Low-grade infection sometimes requires nuclear medicine imaging to make a correct diagnosis. There is no good evidence to guide management so far. In case of active gastrointestinal bleeding, pseudoaneurysm, or extensive perigraft purulence involving adjacent organs, an invasive treatment should always be attempted. In the other cases (the majority), when there is no immediate danger to the patient's life, a conservative management can be started with appropriate antimicrobial therapy. In case of an infectious cavity, this could be percutaneously drained. Specific management depends on the patient's condition and a tailored approach should always be offered. In case of a young age and good life expectancy without significant comorbidities, a surgical attempt should be proposed. Surgical techniques favor (in terms of mortality, patency and reinfection rate) an in situ reconstruction. Currently, the choice of technique used relies on center and operator experience. Long-term antibiotic therapy is always required in all cases, with close monitoring of the C-reactive protein.

Conflict of Interest

The authors have no conflict of interest relevant to this publication.

Comment on this Article or Ask a Question

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