Diagnosis and treatment of prosthetic aortic graft infections: confusion and inconsistency in the absence of evidence or consensus

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Prosthetic aortic graft infections represent a major diagnostic and therapeutic challenge. Although a combination of clinical assessment, imaging and microbiological investigations is usually helpful, there are no agreed criteria to confirm a diagnosis. Potential pathogens isolated from superficial specimens may be misleading but influence the choice of antimicrobial agents. Removal of the infected material is strongly recommended. However, this is not always possible in the very debilitated or clinically unstable patient. The choice of which antimicrobial agents to administer as empirical or definitive therapy and the duration of treatment are unclear. A multi-disciplinary group is required to offer guidance, based on what evidence there is, and to provide expert consensus (as is the case for infective endocarditis) to optimize the management of these difficult infections.

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Prosthetic aortic grafts are used to treat abdominal aortic aneurysm and occlusive vascular disease. Graft insertion is complicated by infection in 0.5–2% of cases1 and is associated with considerable morbidity and mortality. Staphylococcus species are the most commonly implicated causative organisms,2 with Staphylococcus aureus more likely in early infection and coagulase-negative staphylococci such as Staphylococcus epidermidis more likely in late infections.3,4 Gram-negative bacilli and Enterococcus species are regularly recovered from cultures as are anaerobes and fungi,5 but these often represent colonization when isolated from superficial wound swabs. In addition, a sizable minority (14%) of infections are polymicrobial.6 However, many suspected aortic graft infections are treated without knowing the identity or antimicrobial susceptibilities of the causative organism, because suitable specimens were not obtained or because antibiotic treatment was instituted before the collection of appropriate samples for culture.

The diagnosis of aortic graft infection is usually made on the basis of clinical findings, supported by radiological and microbiological investigations. Clinical manifestations of aortic graft infection may vary according to the length of time that has elapsed since the procedure. In early-onset infections (usually defined as those occurring within 4 months of surgery) the patient may be systemically toxic with fever and leucocytosis. Bloodstream infection (BSI), wound infection, abdominal discomfort and graft dysfunction from recent thrombosis or anastomotic bleeding may also occur. The presentation of late-onset infections (those occurring more than 4 months after surgery) tends to be more subtle with non-specific signs and symptoms. Fever is usually absent. These patients are more likely to present with signs of complications of aortic graft infection, such as false aneurysm, gastrointestinal bleeding resulting from erosion of the graft into the gastrointestinal tract, hydronephrosis or osteomyelitis.3

CT is the imaging modality of choice but, in suspected early infection, it may be difficult to distinguish changes due to the surgery itself from changes secondary to infection. CT also permits the aspiration of infected fluid for culture to confirm the diagnosis and to guide treatment. The role of MRI has yet to be clarified but unlike CT, it can distinguish haematoma from peri-graft fluid and inflammatory changes.3,7,8 Other investigations include technetium-99m-hexametazime-labelled leucocyte scanning, which has a sensitivity of up to 100%.9 and sinography, which can determine whether a draining sinus extends to the graft, which is diagnostic of graft infection.

Desirable specimens for culture include explanted graft tissue and material aspirated from peri-graft collection. Organisms isolated from overlying wounds or sinuses may represent colonizing flora, e.g. methicillin-resistant S. aureus (MRSA), but may be interpreted as causative leading to prolonged treatment with a glycopeptide antibiotic or linezolid. Blood cultures are often negative, particularly in late-onset infection. Various techniques such as broth culture and sonication of the graft may be used to enhance the recovery of biofilm-forming organisms10 from graft or infected material, and, in the future, molecular methods such as PCR may contribute significantly. Greater efforts to confirm a

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microbiological diagnosis of aortic graft infection should be made by the use of less invasive sampling procedures such as CT-guided aspiration of fluid collections and in postponing antibiotic treatment in the non-critically ill patient until after cultures are collected and processed. Finally, assays to detect serum antibodies against staphylococcal slime polysaccharide antigens have been developed with initial reports of high sensitivity and specificity, but this remains to be confirmed.11

The routine approach to the diagnosis of aortic graft infection is often somewhat ad hoc and varies from centre to centre. A more systematic approach to the investigation of suspected infections would facilitate earlier and more accurate diagnosis, thus permitting prompt treatment. In the absence of evidence from well-constructed trials on diagnosis, a provisional set of diagnostic criteria, such as the Duke criteria used for the diagnosis of infective endocarditis, could be formulated, and then these could be tested in prospective trials.3

The gold standard for treatment of an infected prosthetic aortic graft remains explantation of the graft and reperfusion of the area by placement of a new graft through an extra-anatomic uninfected route.12 This approach may be complicated by aortic stump blow-out or graft failure; the incidence of these unfavourable outcomes has declined with refinements in surgical technique and of the graft material used in the extra-anatomic bypass. In a series of 60 patients with infra-renal aortic infection who were conventionally managed (50 of whom had graft infection), 5 year survival rates were 47% and 5 year primary bypass graft patency was 73%. Moreover, although extra-anatomical grafting has theoretically less risk of infection than in situ replacement, because of the distance from the infected area, secondary infection was reported in 10% of patients.13 In many cases, the procedure may not be anatomically feasible or the patient may not be surgically fit. Alternative techniques have been reported including retroperitoneal in-line bypass14 and in situ revascularization. These procedures can avoid some of the problems associated with total graft excision and extra-anatomic bypass, such as lengthy procedure, aortic stump blow-out and lower flow rates. In situ revascularization may be carried out using normal graft,15 silver-coated polyester graft, rifampicin-impregnated grafts, allografts or autogenous vein. Revascularization with silver-coated grafts may be a suitable option for patients with persistent infection with organisms of low virulence.16 A series of 11 patients who had in situ revascularization with rifampicin-bonded prostheses showed no evidence of recurrent infection in the seven surviving patients.17 Cryopreserved allografts have been proposed as an alternative for in situ revascularization because of theoretically reduced re-infection rates—however, preliminary data from the United States Cryopreserved Aortic Allograft Registry fail to justify the preferential use of this method over the gold standard.18 Autogenous reconstruction with femoral vein grafts may reduce the risk of recurrent infection, but problems have been encountered with graft blood flow due to the smaller lumen of the vein conduit.19 Complete or partial graft preservation is an option in those high-risk patients in whom conventional management is precluded because of severe co-morbid illness or a hostile abdomen.20 Some authors advocate the use of local antibiotics by instillation or irrigation.20,21 However, much of this work is in the form of case studies or uncontrolled trials. Surgical management ultimately varies, depending on surgical preference, and the requirements of the individual patient.

Antimicrobial therapy is a vital adjunct to surgical management, and, in some cases, it may be the only option if the patient is not fit for further operative intervention. There have been few if any well-designed trials to study antimicrobial therapy in the treatment of prosthetic aortic graft infection. Most studies are carried out by surgeons, and, as such, antibiotic treatment is mentioned as an adjunct to surgical therapy. Details on the specifics of antimicrobial therapy are usually absent. There is no evidence on which to decide the optimal duration of antibiotic therapy. This may vary from 11 days to more than a year, although a minimum of 6 weeks intravenous therapy followed by up to 6 months of oral therapy is commonly recommended.19 A small number of cases in which operative treatment was deemed unsuitable have reported success from long-term suppressive treatment, including in some cases life-long antibiotics.22,24

Where positive culture results are available, antibiotic treatment should be guided by the results of antibiotic susceptibility. However, there is no consensus on which classes of agents are preferred or what might be appropriate for initial empirical treatment. The British Society for Antimicrobial Chemotherapy (BSAC) Steering Group on the treatment of hospital infections25 has recommended treatment with cefuroxime and metronidazole, with or without amoxicillin, as suitable empirical therapy for early-onset prosthetic vascular graft infections. Ciprofloxacin and clindamycin should be considered as alternative agents in penicillin-allergic patients. However, as S. aureus is the organism most likely to be isolated in early infection, and as methicillin resistance is increasingly common, empirical treatment of early-onset infection should perhaps include a glycopeptide where MRSA is prevalent.26 With regard to late-onset infections, the guidelines recommend that antibiotic treatment be deferred until the infective aetiology has been confirmed, except in the very ill patient. However, more specific and evidence-based recommendations are required for empirical therapy in this group of patients and in those in whom no pathogen is ever identified, as well as for pathogen-specific therapy and prophylaxis. Furthermore, these recommendations need to include the criteria for diagnosis, to clearly indicate when antibiotics should be commenced, as well as offering advice on the total duration of therapy, including if and when life-long suppressive treatment is indicated. A detailed treatment algorithm for the management of prosthetic joint infections, along with specific antimicrobial recommendations and a proposed infection score to assist in diagnosis has been devised and would be a useful template.27

There are many unresolved questions concerning the optimal choice of antibiotic therapy for patients with aortic graft infections that need to be addressed. Do the BSAC recommendations for prosthetic vascular graft infections directly apply to aortic graft infections? Because tissue or pus may not be accessible for laboratory processing unlike with many other vascular infections, and because aortic rupture may be fatal, is a different approach to empirical therapy warranted? Should a glycopeptide be routinely used to empirically cover MRSA and methicillin-resistant coagulase-negative staphylococci? A retrospective review of the impact of MRSA in a vascular unit found that ~50% of vascular patients known to be colonized with MRSA developed clinical infection due to MRSA, and that the proportion of wound and graft infections caused by MRSA had increased from 4% to 63% over the 6 year study period.28 Is the choice and duration of antibiotic therapy influenced by whether or not partial graft excision can be carried out, or when any form of surgical intervention is not possible? What is the appropriate duration of therapy for these differing categories of patients? There are a small number of cases reported in the
literature, in which long-term suppressive antibiotic treatment was successfully used when surgery was not possible or complete, but such therapy puts the patient at risk of adverse drug reactions and the acquisition of resistant organisms. Successful antibiotic treatment with implant retention has been described in the setting of other prosthetic infections, including cochlear implants, spinal instrumentation and prosthetic joints. However, only in the last group has a randomized controlled trial confirmed the efficacy of this approach; in the other groups, as in prosthetic aortic graft infection, details of this conservative approach come from case reports and series only. What is appropriate for the patient in whom aortic graft infection is suspected, but not confirmed, but who cannot tolerate surgery to remove the infected graft and to obtain appropriate specimens? Infection of aortic endografts has been reported and as their use becomes more widespread, consideration should also be given to the optimal management of this infection.

In many clinical scenarios, including those outlined above, there are no easy answers and decisions must be made following the input of all clinicians involved, i.e. vascular surgeon, microbiologist/infectious disease physician, interventional radiologist and others, taking due cognisance of the individual patient’s condition and state. However, as there is an incomplete evidence base, due in part to the considerable difficulty that would be involved in successfully recruiting sufficient numbers for each of the diverse patient groups to a randomized controlled trial, there is need for a multi-disciplinary group to provide expert consensus on this issue. The BSAC has set up a working group to research this difficult topic and their conclusions are awaited. Such guidelines on diagnosis and management, including antibiotic therapy, could subsequently be audited to assess their effectiveness in clinical practice.

Transparency declarations

None to declare.

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