The Pathogenesis of Vascular Graft Infection

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Introduction

Vascular graft infection is a rare, but serious, complication of vascular surgery. It is a problem of prosthetic grafts, although less commonly it may affect autologous vein grafts. The long delay between the time of surgery and the presentation of the infection makes it difficult to estimate the true incidence of vascular graft infection. The current incidence of vascular graft infection is estimated at 1–6% for all operations.

The infection of aortic grafts is associated with considerable morbidity and mortality. The associated mortality ranges from 33 to 58%. In contrast, infrainguinal graft infection carries a lower mortality rate, ~22%, yet the consequences are devastating. Vascular graft infection may result in the loss of organ function, amputation, and death. In some studies the amputation rate following infrainguinal graft infection is as high as 79%.

Infection of the native vessels results in weakening of the vessel wall and disruption of the anastomosis. The inflammatory process results in the precipitation of aneurysmal dilatation, haemorrhage and fistula formation. Death may occur due to overwhelming sepsis or haemorrhage.

Microbiology

Bacterial infection accounts for the majority of vascular graft infection. Less frequently fungi\(^{2,6}\) (Candida albicans, aspergillus), mycoplasma\(^{7}\) and mycobacterium\(^{8}\) have also been identified. In recent years, there has been a gradual change in infection pattern. In earlier studies, Staphylococcus aureus accounted for 50% of all vascular graft infections.\(^{2,3,9}\) More recently this incidence has diminished and Staphylococcus epidermidis now accounts for 60% of all graft infections.

Vascular graft infection may be divided into early and late infections.\(^{10-12}\) Most vascular graft infections occur in the early postoperative period (<4 months). During this period, the most commonly identified pathogens include coagulase-positive S. aureus and Gram-negative bacteria, Escherichia coli, Proteus and Pseudomonas aeruginosa. In the late postoperative phase (>4 months), the most commonly identified is coagulase negative S. epidermidis, and less commonly fungal infections.

The response of the host to the infective organism is influenced by the virulence of the organism. Early infections tend to present with septicemia, wound infection, anastomotic bleeding, leukocytosis or the development of a mass at the site of implantation. Late infections are typically more difficult to diagnose. In these cases the clinical signs may vary, but are typically absent; a leukocytosis is frequently absent, but the erythrocyte sedimentation rate may be raised. As the infection progresses, local signs develop, including tenderness and erythema of the skin overlaying the graft, a perigraft mass, or a discharging sinus.\(^{13}\)

The virulence of S. aureus is associated with the production of enzymes which cause haemolysis and cell necrosis. In particular, S. aureus produces coagulase and a wide variety of toxic proteolytic enzymes. This virulent Gram-positive cocci produces an extracellular glyocalyx (mucin) which promotes its adherence to the prosthetic graft. This “mucin” protects the organism against antibiotics and phagocytosis. In contrast, S. epidermidis is a normal skin commensal, is a coagulase-negative organism, is less virulent and has minimal capacity for invasion. This pathogen has a predilection for prosthetic materials, and in general requires the presence of a foreign body for contained growth.\(^{14,15}\)

Like S. aureus, it is capable of producing a mucin which binds itself to the prosthetic material and has
a protective action by reducing the penetration of antibiotics and inhibiting the action of antibodies and phagocytes. The organism induces a low grade inflammatory response which over a prolonged time course may result in anastomotic aneurysmal and fistulae formation. Characteristically, *S. epidermidis* graft infections present late. In previous studies the mean time of presentation after surgery was 41 months.

Gram-negative pathogens may also be highly virulent. Aggressive tissue invasion is particularly characteristic of *Pseudomonas* graft infections. Like *S. aureus*, *Pseudomonas* produces proteolytic enzymes (proteases) which breakdown elastin, collagen and fibrin leading to tissue necrosis. Typically these infections present acutely, with delayed haemorrhage following breakdown of the anastomosis.

**Identification of the Infective Organism**

The causative organisms of vascular graft infection may be difficult to identify. Standard clinical practices for organism isolation, such as swab cultures, are frequently unreliable, and despite the presence of infection, negative culture results are obtained. Aspiration of the perigraft fluid yields leukocytes, but frequently no organisms.

The micro-organisms become entrapped in an organised biofilm surrounding the infected graft. The surface biofilm is a complex structure and is composed of coalescing colonies of bacteria and a fibrous polysaccharide matrix (glycocalyx/slime). The sampling error of routine culture methods can be reduced if the bacterial laden biofilm is disrupted. This may be achieved either physically or by sonification of the graft, using high frequency, low energy sound waves. The optimal method for identification of the infective organism is to culture segments of the graft and disrupted membrane in tryptic soy broth.

An improvement in culture techniques may explain the recent change in the pattern of vascular graft infection.

**Source of Infection**

Contamination of the graft with bacteria may occur either during surgery, at the time of implantation, or in the postoperative period. Most commonly contamination of the graft occurs at the time of surgery. In these cases the most frequent source of infection is from endogenous pathogens from the patient’s skin. The organisms most frequently identified correspond with the abundant skin commensals, notably *staphylococci*. Contamination of the graft is most likely following direct contact between the graft and the patient’s skin or after excessive handling of the graft.

Other potential sources of graft contamination at the time of surgery include inadequate graft sterilisation and a breakdown in surgical technique. Airborne particles may be an important source of micro-organisms which contaminate the sterile field. In orthopaedic theatres, stringent measures are taken to ensure ultraclean air circulation. The high flow rate laminar ventilation system was first introduced by Charnley in an attempt to reduce prosthesis infection in joint replacement surgery. Limited benefit has been shown in reducing the incidence of infection following hip replacement surgery; however, this practice is not undertaken in vascular surgery.

Haematogenous and lymphatic spread of infection has been implicated in the pathogenesis of graft infection, particularly in association with lower limb infection, skin ulceration, cellulitis and gangrene. The division of lymphatic channels during groin dissections may result in the spread of infection; however, this remains unproven.

Bacteria have been identified in the thrombus within the aneurysm sac and in the arterial wall. These are a further potential source of vascular graft infection; however, their significance is unclear.

**Risk Factors for Graft Infection**

Clearly patients who are at greatest risk of graft infection include those who are aged with debilitating disease, diabetic, uraemic, jaundiced, obese, taking steroids or are immunocompromised.

The risk of prosthetic vascular graft infection is closely linked with the development of superficial and wound infections. Consequently, the factors which might precipitate a wound infection, including lymphocele, seroma and haematoma formation, are all associated with a higher rate of graft infection. The groin in particular poses a problem, as the area tends to be relatively dirty. Its close proximity to the perineum and the redundant folds of skin considerably increase the colonisation of the area with skin pathogens, and as a result increase the risk of wound and graft infection. The presence of a groin haematoma following preoperative femoral arteriography may contribute to the risk of vascular graft infection, and a benefit may be observed from increasing the interval between intervention in the groin and surgery. Direct extension of
infection locally results in an increased risk of vascular graft infection in association with wound complications.

The incidence of graft infection increases with emergency surgery, performed for ruptured abdominal aortic aneurysm and for acutely ischaemic limb. In addition early reoperation, wound and graft exploration has also been shown to significantly increase graft infection rates and should be avoided whenever possible. Particular care is required in these cases.

A significant factor determining the risk of graft infection is the choice of conduit. Vascular graft infection is predominantly limited to prosthetic grafts. It appears that saphenous vein has an inherent resistance to graft infection, whereas prosthetic grafts act as any foreign body and harbour organisms within the interstices of the grafts. The initiating event in prosthetic graft infection is bacterial adherence. The physical property of the graft material which influences the risk of prosthetic graft infection is the relative bacterial adherence of the graft. The bacterial adherence of Dacron is 10 to 100 times greater than polytetrafluoroethylene (PTFE) and varies with bacterial species; however, to date clinical trials have failed to demonstrate any difference in infection rates between Dacron and PTFE.

Patients with lower limb infection, cellulitis, gangrene or infected leg ulcers, are at increased risk. Controversy remains as to whether the spread of infection is haematogenous or via the lymphatic channels. In experiments performed in animals, organisms injected into the hind limb of dogs have been cultured in the ipsilateral groin wounds. Whenever possible, in these cases of increased risk, the use of vein as the bypass conduit is preferred.

Prevention of Infection

The methods available to prevent vascular graft infection may be considered to be preoperative, perioperative and postoperative.

There is now considerable evidence that the use of prophylactic antibiotics reduces the incidence of vascular graft infection, and their use perioperatively is now considered to be mandatory. There are, however, no strict guidelines concerning the choice of antibiotic or the duration of treatment. The choice of antibiotic will be determined by the sensitivities of the organisms most frequently encountered. In general, a broad spectrum of antibiotic cover is required and should cover Gram-positive organisms, particularly *S. aureus* and *S. epidermidis*, and Gram-negative organisms. Adequate cover is not achieved using single agents. A combination of antibiotics is usually advocated, including third generation cephalosporins or amoxycillin and clavulanic acid (Augmentin). These have particular activity against *S. epidermidis* and Gram-negative organisms. Fluloxacinill may be used in combination for its increased activity against staphylococci. When the resistance of organisms to antibiotics is suspected, for example after prolonged hospital admission or in cases of reoperation, then the combination of vancomycin and gentamicin may be used. In the U.K., the commonest form of antibiotic prophylaxis used in vascular surgery is a systemic, broad spectrum cephalosporin. The third generation cephalosporin has significant Gram-negative and positive activity. Specific cover against anaerobes using metronidazole is occasionally added.

Antibiotic prophylaxis should certainly commence prior to surgery. It is our practice to give the first dose prior to surgery, on induction of anaesthesia, and to give antibiotic prophylaxis for three doses postoperatively. Several studies have now shown that three doses of antibiotic over 24 h is adequate and a significant benefit from prolonged courses of antibiotic has not been demonstrated. In addition, the prolonged administration of antibiotics may be associated with the proliferation of resistant organisms. More recently, the use of ciprofloxacin administered orally has been favourably compared to a three-dose regimen of systemic cefuroxime.

The influence of antibiotic impregnated and gelatin sealed grafts on the prevention of vascular graft infection is currently being assessed. Much of the work has been performed in animals, but early results from clinical studies are now available. Powell et al. were the first to describe the technique using a collagen-rifampicin release system. Rifampicin is a semi-synthetic derivative of rifamycin B, and is the most effective antibiotic against both coagulase positive and negative staphylococci, and highly effective against Gram-negative micro-organisms.

Preparation of the skin prior to surgery may reduce skin contamination, and hence the risk of graft infection. Preoperative cleaning with antiseptic solutions, povidone iodine or chlorhexidine prior to surgery is recommended; however, there is no evidence to suggest that either solution is superior. Two studies have been performed examining the benefit of preoperative bathing in antiseptic solutions and the results are conflicting. The instillation of antiseptic solutions into the wound prior to closure is an accepted practice, although there is little evidence to demonstrate any benefit.

Hair may be removed from the operative field either
by shaving or by using depilatory creams. If shaving is performed then this should be done as close to the time of surgery as possible. Sterile plastic adhesive drapes are used extensively; however, this practice has not been shown to reduce the incidence of wound infection, even when the incision crosses the groin.22

Clearly the most important consideration in reducing the incidence of wound infection and consequently the risk of vascular graft infection is meticulous surgical technique. Careful tissue handling with minimal dissection of the lymphatic channels and haemostasis can prevent both haematoma and seroma formation. Preoperative marking of the long saphenous vein reduces the incidence of skin flap necrosis caused by undercutting the skin edge in search of the vein.22 Surgical technique is considerably more effective in preventing haematoma formation than suction drainage. The routine vacuum drainage of groin wounds does not appear to prevent either lymphocele or wound infection.23 A careful layered closure of the groin wound is advised.

Conclusion

Vascular graft infection is the most feared complication of vascular surgeons and is associated with considerable morbidity and mortality. Improving our understanding of the pathogenesis of vascular graft infection may lead to developments in technique, resulting in both the prevention and treatment of graft infection and a reduction in its overall incidence. The role of prophylactic antibiotics in reducing the risk of graft infection has already been proven, and for patients at particular risk of vascular graft infection the role of antibiotic impregnated grafts is being investigated.

It is currently our practice to use sparingly chlorhexidine liberally applied directly to prosthetic grafts prior to wound closure, and dry povidone iodine spray to the subcutaneous layers prior to closure of the skin. There is, of course, no substitute for good surgical technique in minimising the incidence of complications.

References


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