

# PROSTHETIC GRAFT INFECTION IN FEMOROPOPLITEAL BYPASS

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## Abstract

**Introduction:** Peripheral artery disease, a manifestation of systemic atherosclerosis, often necessitates surgical revascularization in advanced stages, with femoropopliteal bypass serving as a primary intervention to restore adequate lower limb perfusion. When autologous vein grafts are not available, prosthetic conduits are commonly used. However, these heterologous materials carry an increased risk of infectious complications, which, although rare, are associated with substantial morbidity and mortality. This study aims to review the current literature on prosthetic graft infections in femoropopliteal bypass surgeries, focusing on epidemiology, risk factors, microbiology, diagnostic methods, treatment strategies, and preventive measures.

**Materials and methods:** A narrative review of the literature was conducted using databases such as PubMed to identify relevant studies on vascular prosthetic infections, particularly in femoropopliteal bypass surgeries.

**Results:** Prosthetic graft infections occur in approximately 2.6% of femoropopliteal bypass surgeries. *Staphylococcus epidermidis* is the most commonly isolated pathogen. Other relevant Gram-positive bacteria include *Staphylococcus aureus*, and Gram-negative bacteria such as *Pseudomonas aeruginosa*. Accurate identification of the etiological agent through microbiological and diagnostic methods is essential for improving clinical outcomes. Early diagnosis is crucial to enable timely and effective treatment, which generally combines antibiotic therapy with surgical intervention, often necessitating graft removal. Furthermore, adopting preventive measures, such as perioperative antibiotic prophylaxis, is fundamental to reducing the incidence of these complications and minimizing the morbidity and mortality associated with prosthetic graft infections.

**Conclusion:** Prosthetic graft infections in femoropopliteal bypass surgeries remain a challenging complication. A multidisciplinary approach encompassing early detection, evidence-based treatment, and targeted prevention strategies is essential to improve outcomes, preserve limb function, and mitigate long-term morbidity.

**Keywords:** vascular graft infection; femoropopliteal bypass; prosthetic vascular graft; peripheral artery disease; postoperative complications.

## INTRODUCTION

Peripheral artery disease (PAD) is a manifestation of atherosclerosis, characterized by the progressive narrowing of peripheral arteries, and is a significant indicator of systemic atherosclerosis<sup>1, 2</sup>. Often asymptomatic, PAD compromises blood circulation, particularly in the lower limbs, and affects more than 230 million people worldwide, with a higher

prevalence among older people<sup>2, 3</sup>. This condition represents a substantial burden on global health systems due to its impact on morbidity, quality of life, and healthcare costs<sup>4, 5</sup>.

The management of PAD includes conservative therapies, pharmacological treatments, and, in severe cases, endovascular interventions or surgical revascularization<sup>1</sup>. In advanced PAD, surgical revascularization can be decisive in restoring blood flow to the lower limbs and prevent severe

complications<sup>6</sup>. The preferred conduit for bypass grafting is an autologous vein, typically the great saphenous vein. When autologous veins are unavailable or unsuitable, prosthetic conduits serve as a valid alternative. Various synthetic graft materials, such as polytetrafluoroethylene (PTFE) and polyethylene terephthalate (Dacron), have been created and employed. The most commonly used prosthetic graft for lower extremity bypass is PTFE, whereas Dacron grafts, typically preferred for aortic replacement, are rarely used in the lower extremities<sup>7</sup>.

Despite technical and material advances, femoropopliteal bypass surgery carries significant morbidity, with up to one-third of patients experiencing postoperative complications<sup>8</sup>. One of the most serious complications is bypass graft infection, which, although uncommon, is associated with high morbidity and, in some cases, death<sup>5, 9</sup>. Such infections are particularly challenging when they involve prosthetic materials, frequently requiring multiple interventions, graft removal, and, in severe cases, limb amputation<sup>10</sup>. These complications substantially affect patients' quality of life and contribute to rising healthcare costs. For instance, in a large teaching hospital in England, surgical site infections (SSIs) in vascular surgeries were associated with a mean additional hospital stay of 9.72 days and an extra cost of £3,776 per patient<sup>11</sup>.

Graft infections are associated with multiple risk factors namely the patient's comorbidities, procedural variables and perioperative complications<sup>12</sup>. Early identification and mitigation of these factors is crucial to reduce infection rates and improve clinical outcomes.

In confronting the complexities of graft infections, among the most daunting challenges vascular surgeons face, it is essential to understand their primary mechanism through which they occur<sup>13</sup>. These infections may stem from direct intraoperative contamination, where pathogens are introduced during surgery, or through hematogenous spread, with bacteria from a distant site reaching the graft via the bloodstream<sup>14</sup>. Once bacteria adhere to the prosthetic surface, biofilm formation ensues, protecting the bacteria from immune defenses and antibiotic treatments, promoting persistence and resistance<sup>15</sup>. Given these severe implications, early diagnosis and appropriate treatment are crucial for improving clinical outcomes.

The femoropopliteal region, commonly affected by PAD in the lower limbs, is the most frequent site for vascular bypass surgeries. Its proximity to the inguinal area, a region with abundant resident flora and a higher likelihood of surgical site contamination, significantly increases the risk of severe infections<sup>16-18</sup>.

This narrative review aims to analyze the current literature on prosthetic infections in femoropopliteal bypass surgery, focusing on epidemiology, risk factors, microbiology and pathogenesis, diagnostic methods, treatment strategies, and preventive measures. Understanding these dynamics is critical, as such complications can lead to serious consequences.

## EPIDEMIOLOGY

Although relatively rare, vascular infections of prosthetic grafts remain a serious complications, with a reported incidence ranging between 1% and 6%<sup>5</sup>. Specifically, studies indicate an average infection rate of 2.6% in femoropopliteal bypass surgeries, with most infections occurring within the first year after surgery and a median time to diagnosis of approximately 100 days<sup>18</sup>.

The high rate of complications, including multiple reintervention surgeries and extended hospital stays, has a substantial impact on both patients' quality of life and healthcare costs<sup>11</sup>. The associated morbidity and mortality are substantial: approximately 26.5% of patients with confirmed graft infections require major amputation, and the associated mortality rate can reach up to 29.4% within one year<sup>10, 18</sup>.

## RISK FACTORS

Vascular graft infections arise from a complex interplay of patient characteristics, procedural factors, and perioperative complications. A thorough assessment of risk factors is essential for the implementation of preventive strategies and improving clinical management.

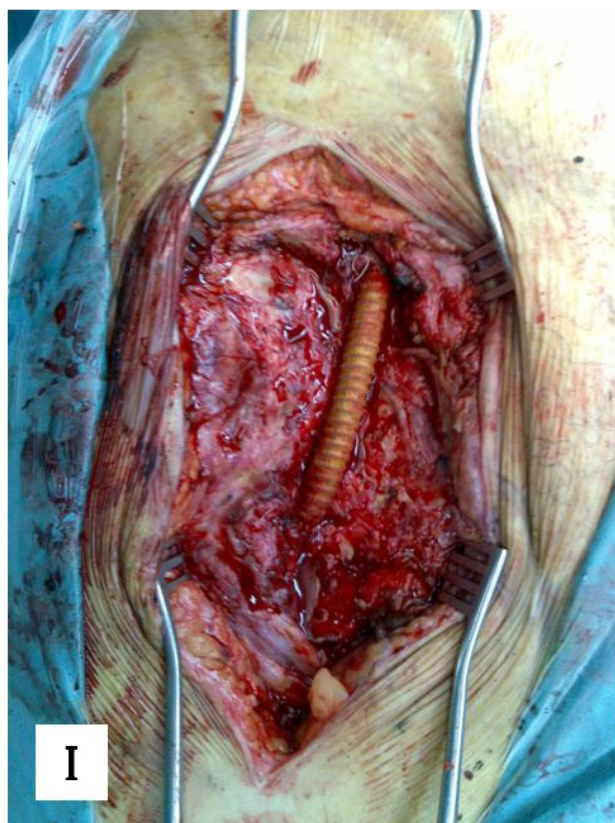
Regarding patient-related factors, conditions such as female sex, obesity (BMI  $\geq 30$  kg/m<sup>2</sup>), ischemic heart disease, diabetes mellitus, and postoperative hyperglycemia are particularly significant<sup>19, 20</sup>. Additionally, nasal colonization by *Staphylococcus aureus*, especially methicillin-resistant strains (MRSA), increases the risk of early infections, while periodontal diseases may predispose patients to late-onset infections<sup>21, 22</sup>.

Among the factors associated with surgical procedures, groin incisions stand out as a significant risk factor for vascular graft infections. This region is rich in microorganisms due to its proximity to the perineum, and the superficial location of grafts further increases the risk for contamination and infection<sup>16-18</sup>. Local complications, such as hematomas and superficial wound infections, are strongly associated with an increased risk of graft infection<sup>18</sup>. Additionally, emergency procedures also elevate the risk of infection, often due to limited patient preparation time and inadequate antimicrobial prophylaxis<sup>23</sup>.

Additional risk factors include early hospital readmissions, particularly unplanned readmissions within 30 days of surgery, and prolonged operative times<sup>14, 18</sup>.

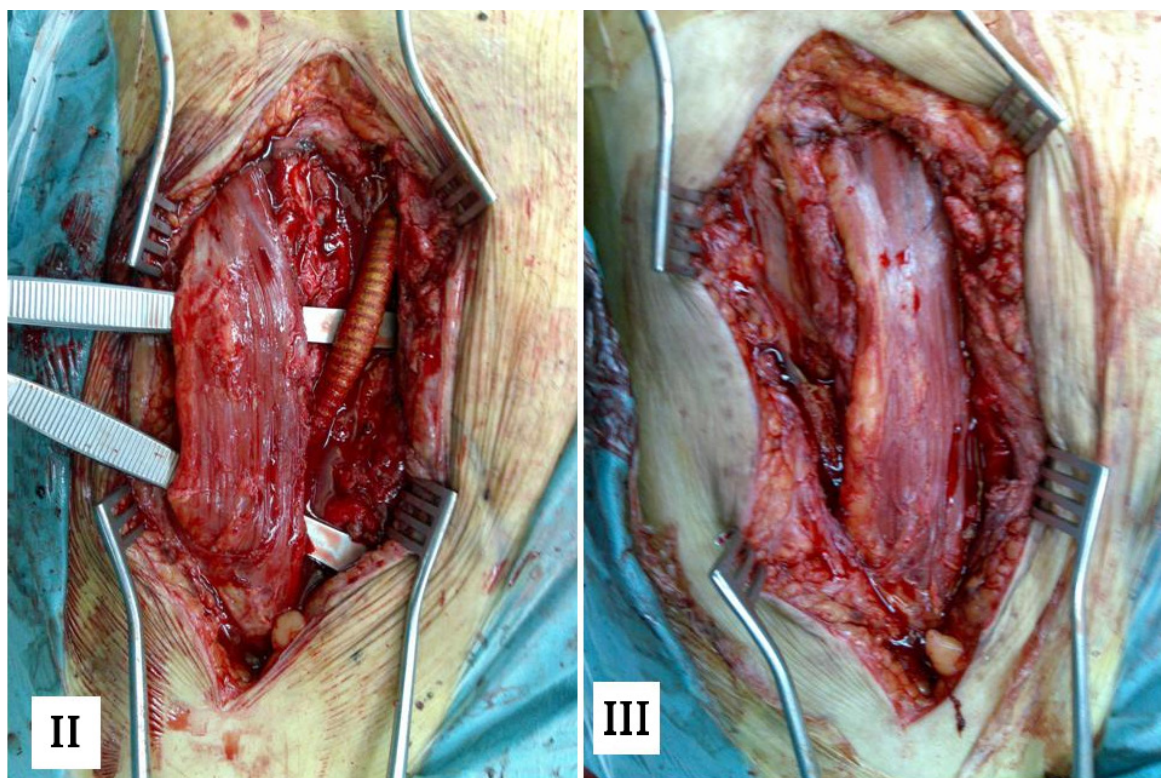
## PATHOGENESIS

The pathogenesis of prosthetic graft infections is not completely established and is considered multifactorial. Multiple factors contribute to infection risk, including graft type, implantation site, prolonged surgical time, the use of antibiotic prophylaxis, the patient's immune and nutritional status, the presence of infections in other anatomical locations,



**Figure 1**

Debridement of the wound and replacement of the infected graft with a silver-bonded synthetic graft. Adapted from Ktenidis K, Giannopoulos A. Current Management of Vascular Infections [Internet]. Vascular Surgery - Principles and Practice. InTech; 2012. Available from: <http://dx.doi.org/10.5772/54027>



**Figure 2**

Preparation of the sartorius muscle (II) followed by coverage of the graft with the muscle flap (III). Adapted from Ktenidis K, Giannopoulos A. Current Management of Vascular Infections [Internet]. Vascular Surgery - Principles and Practice. InTech; 2012. Available from: <http://dx.doi.org/10.5772/54027>

and the virulence of the contaminating organisms<sup>24</sup>. Unlike autologous grafts, synthetic materials lack natural defense mechanisms, making them more susceptible to bacterial adhesion and proliferation. The negative surface charge present in synthetic materials, such as PTFE and Dacron, also favors bacterial colonization<sup>5</sup>.

Graft infections generally occur by one of two mechanisms: direct contamination during surgery, which typically occur earlier; or bacteremia non related to the surgery and microorganism adhesion to the graft, which usually occurs later<sup>23</sup>. Consequently, these infections can also be classified by timing, in early onset (occurring within the first 4 months post-surgery) and late onset (4 months after surgery)<sup>25</sup>.

Most infections occur within the first two months after surgery<sup>12</sup>, typically during the early postoperative period and are mostly caused by direct contamination of the prosthetic material during surgery. In contrast, late onset infections, which are much less common, are primarily associated with bacteremia and bacterial adhesion to the graft originating from other anatomical sites of infection<sup>10, 12, 14, 26</sup>.

A central mechanism in these infections is the formation of biofilms, particularly on prosthetic surfaces. Biofilm development proceeds through three phases: attachment, maturation, and detachment. In the attachment phase, surface proteins facilitate the adhesion of microorganisms to host matrix proteins like fibrinogen and fibronectin. During maturation, intercellular aggregation occurs, mediated by polysaccharide intercellular adhesin leads to a structured biofilm. Finally, in the detachment phase, individual cells or clusters of cells separate from the biofilm, allowing the infection to spread<sup>27</sup>. The biofilm, therefore, consists of a polymeric matrix that encapsulates the microorganisms, offering a favorable environment for proliferation.

Biofilms protect bacteria in two main ways: first, they prevent antibiotics from penetrating the matrix and reaching the bacteria, reducing the efficacy of various classes of medications<sup>27, 28</sup>; additionally, they act as a barrier against the immune system, preventing immune cells from reaching and eliminating the bacteria. Therefore, biofilms play a significant role in treatment failure, promoting persistence and recurrence of infection by shielding microorganisms from both the host's immune defenses and pharmacological therapy<sup>14</sup>.

## MICROBIOLOGY

Vascular prosthesis infections involve a broad spectrum of microorganisms, predominantly bacteria. In most cases (over 75%), microorganisms can be isolated<sup>25</sup>. Gram-positive bacteria are the most common pathogens, with coagulase-negative staphylococci, particularly *Staphylococcus epidermidis*, being the most common, followed by *Staphylococcus aureus* (including both methicillin-sensitive and methicillin-resistant strains) and *Enterococcus* spp.; Gram-negative bacteria are also present, with *Pseudomonas aeruginosa* being the most prevalent, and, more rarely, anaerobes<sup>23, 29, 30</sup>.

Early infections (within the first 4 months post-surgery), typically involve highly virulent bacteria, such as *Staphylococcus aureus* and as well as Gram-negative bacteria, including *Pseudomonas aeruginosa* and *Escherichia coli*. In contrast, late infections are often linked to less virulent Gram-positive bacteria, such as *Staphylococcus epidermidis* and other Coagulase-negative Staphylococci.<sup>12, 23</sup>

Coagulase-negative staphylococci spp have been frequently identified as the causative agent of vascular graft infections, being detected in up to 37% of infected grafts especially in cases of late-onset infections<sup>12</sup>. In femoral artery grafts, *S. epidermidis* has emerged as the primary pathogen, with its incidence rising notably over the past decade<sup>31</sup>. Such infections typically manifest later, often months or even years after graft implantation, and progress more insidiously, typically triggering a low-grade inflammatory response. Over time, this can lead to severe complications such as anastomotic aneurysms and fistula formation. *S. epidermidis* has a particular affinity for prosthetic materials and has the capacity to form biofilms on biomaterial surfaces, creating a mucinoid extracellular matrix that ensures persistence and complicates treatment<sup>32</sup>. Although *S. epidermidis* lacks the well-defined virulence factors found in *S. aureus*, its structural characteristics are crucial for adhesion and persistence on foreign materials, making it one of the most challenging pathogens to eradicate in prosthetic vascular infections<sup>23</sup>.

In contrast, *Staphylococcus aureus* is a highly virulent pathogen, particularly in early infections, due to its potent virulence factors. Its pathogenicity involves biofilm formation, production of coagulase, alpha-toxin, and multiple adhesion proteins. *S. aureus* can form fibrin clots that shield its bacterial cells from the host's immune defences<sup>12</sup>. Alpha-toxin further destabilizes host cell membranes by forming pores, leading to cell lysis and promoting the spread of infection<sup>33</sup>. Moreover, *S. aureus* also expresses several cell wall-anchored proteins (CWAs), such as fibronectin-binding proteins, clumping factors, and collagen-binding proteins. These CWAs are crucial for tissue adhesion and invasion, essential for infection establishment and persistence. They also promote immune evasion by impairing opsonization and hindering phagocytosis<sup>34, 35</sup>.

Gram-negative bacteria, such as *Pseudomonas aeruginosa*, *Escherichia coli*, and *Klebsiella pneumoniae*, also play a significant role in vascular graft infections, particularly in polymicrobial and early onset infections<sup>10, 36</sup>. These bacteria are often associated with severe clinical manifestations, such as haemorrhage and tissue necrosis, due to the production of proteolytic enzymes that degrade extracellular matrix components and weaken anastomosis. Additionally, their high antimicrobial resistance further complicate treatment and frequently result in poor clinical outcomes.

## DIAGNOSIS

Early diagnosis of infections in prosthetic grafts for femoropopliteal bypass is challenging but essential to reduce severe complications and enable more effective therapeutic interventions. Achieving an accurate diagnosis requires

a multidisciplinary approach involving detailed medical history, thorough physical examination, laboratory tests, and imaging methods<sup>37, 38</sup>.

### MEDICAL HISTORY AND PHYSICAL EXAMINATION

Patient evaluation should start with a thorough review of the patient's medical history, aiming to recognize symptoms and risk factors. It is equally essential to evaluate signs of infection, specifically inflammation in the perigraft area, which may present as pain, erythema, edema, and purulent drainage<sup>39</sup>. In addition to local signs and symptoms, systemic indicators such as fever and chills may be present. In severe cases, sepsis may occur, or there may also be anastomotic rupture with hemorrhage, potentially leading to hypovolemic shock<sup>37</sup>.

### LABORATORY TESTS

Inflammatory markers such as leukocytosis, C-reactive protein (CRP), and erythrocyte sedimentation rate are frequently elevated in cases of graft infection, although they have limited specificity<sup>38</sup>. Persistently elevated CRP in the postoperative period suggest the need to investigate potential infectious complications, such as perigraft infection, or secondary infection sites<sup>30</sup>. Identifying the causative microorganism and its antibiotic susceptibility is an essential condition for targeted antibiotic treatment; therefore, before starting antimicrobial therapy, it is essential to perform blood cultures. Ideally, prosthetic graft material should be removed, and sent to the microbiology laboratory. Whenever possible, microbiological cultures from perigraft samples should be obtained, however this is not always possible as they would compromise the bypass integrity, hence the importance of blood cultures<sup>30, 38</sup>. Molecular biology techniques, such as polymerase chain reaction (PCR), are advantageous and complementary to classical microbiology techniques, as they allow for a fast and precise identification of microorganisms, particularly useful in detecting slow-growing or difficult-to-culture organisms. They are, however limited to the primers used and the sample provided<sup>39-41</sup>. Additionally, 16S ribosomal RNA PCR has a promising role for the future, as it has already been shown to have a high sensitivity in diagnosis of prosthetic joint infections when used in conjunction with clinical data and microbiological results<sup>42</sup>.

### IMAGING STUDIES

Confirming prosthetic graft infection often relies on imaging methods, including ultrasonography, contrast-enhanced computed tomography (CT), and positron emission tomography (PET) with fluorodeoxyglucose (FDG)<sup>25</sup>.

Doppler ultrasonography is generally used in the initial evaluation to visualize blood flow and identify possible fluid collections around the graft, though the presence of air introduced during surgery may interfere with the accuracy of

ultrasound imaging in assessing graft patency and detecting signs of infection in a very early postoperative phase<sup>30, 39</sup>.

Contrast-enhanced CT is considered the first-choice imaging modality and the standard imaging technique for detecting prosthetic graft infections, suggested by signs such as perigraft fluid or gas collections, increased perigraft fat density, and pseudoaneurysm formation<sup>10, 37, 43</sup>.

FDG PET-CT is an imaging modality in which radionuclides are used to detect increased glucose consumption, and therefore is much more sensitive than conventional imaging techniques. However, it should be reserved for cases with strong clinical suspicion and inconclusive previous imaging. It is especially valuable in subclinical or late-onset infections, though early postoperative inflammation can limit specificity<sup>25, 39, 44-46</sup>.

### IMPORTANCE OF A MULTIDISCIPLINARY TEAM

The relevance of a multidisciplinary team cannot be overstated, as collaboration across specialties facilitates an integrated approach, enabling more accurate interpretation of clinical and diagnostic findings and promoting more precise and evidence-based decision-making<sup>47</sup>. Centralizing the diagnosis and treatment of infections, as demonstrated in orthopedic care, further enhances the consistency and efficacy of interventions, streamlining protocols and leveraging specialized expertise<sup>48</sup>.

### TREATMENT

Vascular graft infections are serious, life-threatening complications that require prompt and effective treatment to control infection. The main goals are to fully eradicate the infection, ensure long-term graft patency, and preserve limb function while minimizing morbidity and mortality.

Treatment often involves removing the infected vascular graft and its replacement, along with antimicrobial therapy to control the infection. Effective infection management requires a multifaceted approach, which may involve conservative management, surgical reconstruction, and antimicrobial therapy, tailored to each patient's unique clinical presentation.

### CONSERVATIVE TREATMENT

The decision not to remove the infected vascular graft is rarely advisable due to high mortality rates and risks of persistent infection, anastomotic disruption, and bleeding<sup>49</sup>. However, in patients where surgery is not possible, conservative strategies may be considered.

One option is negative pressure wound therapy (NPWT), especially when suspicion of localized graft infection, typically in the groin. NPWT can promote healing and tissue regeneration following debridement, although careful pressure regulation is necessary to prevent bleeding, and limited certainty regarding the complete elimination of the

infection remains<sup>50-52</sup>. Another strategy involves combining NPWT with irrigation, which is commonly used in the groin area after wound debridement, aiming to reduce bacterial colonization and improve healing<sup>25, 53</sup>.

## SURGICAL TREATMENT

Surgical treatment often involves removing the infected graft, followed by in situ or extra-anatomic reconstructions. The timing of the surgical intervention(s) is crucial, as prompt action is often critical. In cases of bleeding anastomoses or abscesses, surgery should be performed as soon as possible. Any infected graft material must be removed during the same procedure, and if limb ischemia is not imminent, revascularization can be delayed until wound healing occurs<sup>25</sup>. Studies have shown that patients undergoing surgical removal of infected grafts achieve significantly longer infection-free survival compared to those who do not undergo the procedure, emphasizing the importance of surgical decision-making in the treatment of vascular graft infections<sup>54, 55</sup>.

In situ reconstructions generally consider the severity of limb ischemia and the choice of graft material. For patients whose initial surgical indication was claudication, immediate revascularization may be unnecessary; however, in cases of chronic limb-threatening ischemia or significant progression of arterial disease, immediate redo bypass after graft removal is essential to avoid major amputation. Regarding graft material choice, when feasible, the great saphenous vein or femoral vein is preferred due to lower re-infection rates<sup>31, 56</sup>. This option has increasingly been accepted over extra-anatomical bypasses<sup>30, 57</sup>; however, when not possible, there remains ongoing debate about which graft type should be preferred. Prosthetic grafts are readily available and lead to shorter surgical times, although they have higher re-infection rates. Silver-impregnated and rifampicin-soaked grafts are potential alternatives with most of the supporting evidence coming from aortic infection studies and remaining limited (figure 1)<sup>58, 59</sup>. Cryopreserved allografts are an option with lower infection rates, although long-term complications, such as graft degeneration, may occur<sup>60-62</sup>. Finally, xenografts, such as bovine pericardial patches, have been shown to be more resilient to infection than synthetic prostheses<sup>63</sup>.

To optimize graft and limb preservation, muscle flap coverage is recommended to enhance graft and limb preservation. The sartorius muscle flap is commonly used for groin infections (figure 2), while the rectus femoris muscle flap may be preferred for larger defects due to its robust blood supply<sup>64, 65</sup>. The gracilis muscle flap is effective for complex infected wounds<sup>66</sup>, and the rectus abdominis flap provides reliable soft tissue coverage, especially when skin closure of the surgical site is impracticable, although it may cause complications such as donor site hernias<sup>25</sup>. Additionally, antibiotic-loaded beads can be placed adjacent to the infected graft to aid in infection control, providing continuous local release of antibiotics; however, reinfection rates can reach up to 20% for in situ<sup>67, 68</sup>.

Extra-anatomic reconstructions involve re-routing

around the infected areas and are generally preferred in cases with multidrug-resistant organisms. There are several approaches for this procedure such as the obturator bypass and lateral retroversartorius bypass, which are among the most frequently applied techniques. As well as the use of perigeniculate arteries or the lateral approach to crural arteries. Each of these techniques have different and specific indications<sup>25</sup>.

## ANTIMICROBIAL THERAPY

Antimicrobial therapy is recommended for all patients with an infected graft (or endograft)<sup>69, 70</sup>. In patients requiring immediate start of antibiotic treatment (patients who are septic or hemodynamically unstable) empiric antibiotics covering the most common pathogens in accordance with the local antibiotic resistance data should be initiated, following the collection of blood cultures. Empiric antibiotic combinations should provide coverage for both gram-positive and gram-negative bacteria<sup>12</sup>, options often include vancomycin or daptomycin in association with an antipseudomonal beta-lactams, such as piperacillin/tazobactam or meropenem<sup>14, 71</sup>. Patients with prior antibiotic exposure or complex comorbidities may benefit from infectious disease consultation to optimize therapy<sup>25</sup>.

After identifying pathogens and susceptibilities, therapy can be adjusted or de-escalated to target the implicated organisms more precisely. When selecting antimicrobial therapy, it is essential to consider the potential formation of biofilm on the graft material, as penetrating the biofilm and eliminating slow-growing bacteria associated with vascular graft infections are critical factors for treatment effectiveness and are influenced by local patterns of antimicrobial resistance.

The duration of antimicrobial therapy depends on the treatment strategy. If the infected graft can be removed and thorough debridement performed, at least two weeks of IV antibiotics followed by two to four weeks of oral therapy is recommended. In cases where the infected graft is replaced, four to six weeks of treatment is typically advised, with some experts suggesting a total treatment duration of three to six months, or even up to a year. In cases where surgery is contraindicated, suppressive antibiotic therapy or lifelong antimicrobial therapy may be considered<sup>25, 69, 72</sup>.

Many experts currently favour in situ reconstruction using infection-resistant materials, mainly autologous. This approach involves removing infected graft material, thoroughly debriding the arterial area, and administering targeted antimicrobial therapy<sup>70</sup>. This decision should be left to a multidisciplinary team.

## PREVENTION

Preventive measures are essential to minimize the infection risk and associated complications, ultimately protecting patient's health and improving surgical outcomes.

Autologous conduits, like the great saphenous vein,

should be prioritized for superior long-term patency and lower infection rates compared to prosthetic grafts<sup>73, 74</sup>. If prosthetic grafts are necessary, material selection is crucial, though studies show no clear advantage between expanded polytetrafluoroethylene (ePTFE) or polyethylene terephthalate (Dacron)<sup>25</sup>. Studies also indicate that the initial use of silver- or rifampicin-coated grafts does not significantly reduce the risk of infection<sup>75, 76</sup>.

Most vascular grafts are constructed with ePTFE or Dacron, based on their structural stability and microbial colonization resistance. Factors like device's shape, the initial adhesion of plasma proteins, and the healing process can influence infection risk<sup>77</sup>. Tissue-engineered grafts are emerging as a potential solution to address limitations associated with ePTFE grafts, which lack natural endothelialization. Studies suggest that coating ePTFE grafts with an extracellular matrix and CD34 monoclonal antibodies can promote the adhesion of CD34+ endothelial progenitor cells, encouraging endothelial formation on the graft surface<sup>78</sup>. While promising, this approach is still under development and may reduce the thrombogenic and immunogenic risks in the future<sup>79</sup>.

Another option is Collatamp G® (Schering-Plough, Stockholm, Sweden), a collagen implant impregnated with gentamicin sulfate, which has shown effectiveness in reducing SSIs in various procedures, including vascular surgeries. In a study, Collatamp G® reduced the infection rate from 20% (6 out of 30 patients) in the control group to 0% (0 out of 30) in the treated group. These findings suggest potential benefits of Collatamp G® in preventing vascular graft infections, though larger randomized controlled trials are needed to confirm these results<sup>80</sup>.

An important preoperative consideration is the nasal carriage of *Staphylococcus aureus*, a common finding in the general population that can lead to severe postoperative infections. Decolonization of *S. aureus* carriers with mupirocin nasal ointment and chlorhexidine body washes has been shown to reduce SSI, as well as 30-day mortality and re-intervention rates. Screening for *S. aureus* and treating positive patients is a highly effective strategy to minimize *S. aureus*-related SSIs<sup>81</sup>.

While perioperative glucose control in diabetic patients is beneficial for reducing cardiovascular complications, it has not been shown to reduce wound complications, likely due to other diabetes-related factors<sup>31</sup>.

Perioperative and intraoperative measures further reduce infection risks. Preoperative antiseptic showering

offers no additional benefit compared to unmedicated bathing<sup>82</sup>, but maintaining normothermia, preoperative hair removal, and strict adherence to aseptic protocols can reduce SSI rates by up to 51%, making these essential components of infection prevention<sup>83</sup>.

Antimicrobial prophylaxis plays a critical role for reducing the risk of wound and early graft infections in arterial reconstructions. Systemic antibiotics, particularly first- or second-generation cephalosporins, are recommended for their coverage of common SSI pathogens. Ideally, antibiotics should be administered within 30 minutes before the incision, with additional doses during longer procedures as indicated by the antibiotic's half-life, to ensure adequate tissue levels.<sup>82</sup>

Preventing postoperative hematomas is essential, as they can lead to superinfection and graft infection after femoropopliteal bypass<sup>18</sup>. For wound closure, monofilament absorbable sutures are preferred over staples, reducing SSIs in lower extremity revascularization<sup>84</sup>.

Proper postoperative wound care is essential, as nearby wound infections can spread. Maintaining a sterile environment supports healing, with negative pressure wound therapy proving effective in reducing infection risk and supporting tissue regeneration<sup>85</sup>.

## CONCLUSION

Infections of femoropopliteal bypasses with prosthetic grafts represent a significant clinical challenge due to their high morbidity, the potential risk of limb loss, and the complexities involved in their management. Prevention remains the cornerstone, emphasizing meticulous surgical techniques, judicious use of prophylactic antibiotics, and early identification of risk factors. However, once infection is established, successful treatment relies on prompt diagnosis and a multidisciplinary approach that includes appropriate surgical interventions and prolonged, effective antimicrobial therapy.

The studies reviewed highlight the importance of strategies such as removal of the infected graft, vascular reconstructions using autologous materials when feasible, and the utilization of biologic grafts or antibiotic-impregnated prostheses. Despite recent advancements, further research is needed to optimize the management of these infections and mitigate associated complications. Ongoing research and the development of novel technologies and protocols are essential to improve clinical outcomes and the quality of life for affected patients.

## REFERENCES

1. Shamaki GR, Markson F, Soji-Ayoade D, Agwuegbo CC, Bamgbose MO, Tamunoinemi BM. Peripheral Artery Disease: A Comprehensive Updated Review. *Curr Probl Cardiol.* 2022;47(11):101082.
2. Mandaglio-Collados D, Marin F, Rivera-Caravaca JM. Peripheral artery disease: Update on etiology, pathophysiology, diagnosis and treatment. *Med Clin (Barc).* 2023;161(8):344-50.
3. Criqui MH, Matsushita K, Aboyans V, Hess CN, Hicks CW, Kwan TW, et al. Lower Extremity Peripheral Artery Disease: Contemporary Epidemiology, Management Gaps, and Future Directions: A Scientific Statement From the American Heart Association. *Circulation.* 2021;144(9):e171-e91.
4. Verma S, Leiter LA, Mangla KK, Nielsen NF, Hansen Y, Bonaca MP. Epidemiology and Burden of Peripheral Artery Disease in People With Type 2 Diabetes: A Systematic Literature Review. *Diabetes Ther.* 2024;15(9):1893-961.
5. Leroy O, Meybeck A, Sarraz-Bournet B, d'Elia P, Legout L. Vascular graft infections. *Curr Opin Infect Dis.* 2012;25(2):154-8.
6. Halena G, Krievins DK, Scheinert D, Savlovskis J, Szopinski P, Kramer A, et al. Percutaneous Femoropopliteal Bypass: 2-Year Results of the DETOUR System. *J Endovasc Ther.* 2022;29(1):84-95.
7. Ciaramella M, LoGerfo F, Liang P. Lower Extremity Bypass for Occlusive Disease: A Brief History. *Ann Vasc Surg.* 2024;107:17-30.
8. van de Weijer MA, Kruse RR, Schamp K, Zeebregts CJ, Reijnen MM. Morbidity of femoropopliteal bypass surgery. *Semin Vasc Surg.* 2015;28(2):112-21.
9. Madden NJ, Calligaro KD, Dougherty MJ, Zheng H, Troutman DA. Lateral femoral bypass for prosthetic arterial graft infections in the groin. *J Vasc Surg.* 2019;69(4):1129-36.
10. Wilson WR, Bower TC, Creager MA, Amin-Hanjani S, O'Gara PT, Lockhart PB, et al. Vascular Graft Infections, Mycotic Aneurysms, and Endovascular Infections: A Scientific Statement From the American Heart Association. *Circulation.* 2016;134(20):e412-e60.
11. Totty JP, Moss JWE, Barker E, Mealing SJ, Posnett JW, Chetter IC, et al. The impact of surgical site infection on hospitalisation, treatment costs, and health-related quality of life after vascular surgery. *Int Wound J.* 2021;18(3):261-8.
12. Gharamti A, Kanafani ZA. Vascular Graft Infections: An update. *Infect Dis Clin North Am.* 2018;32(4):789-809.
13. Chung J, Clagett GP. Neo-aortoiliac System (NAIS) procedure for the treatment of the infected aortic graft. *Semin Vasc Surg.* 2011;24(4):220-6.
14. Young MH, Upchurch GR, Jr., Malani PN. Vascular graft infections. *Infect Dis Clin North Am.* 2012;26(1):41-56.
15. Frei E, Hodgkiss-Harlow K, Rossi PJ, Edmiston CE, Jr., Bandyk DF. Microbial pathogenesis of bacterial biofilms: a causative factor of vascular surgical site infection. *Vasc Endovascular Surg.* 2011;45(8):688-96.
16. Antonios VS, Noel AA, Steckelberg JM, Wilson WR, Mandrekar JN, Harmsen WS, et al. Prosthetic vascular graft infection: a risk factor analysis using a case-control study. *J Infect.* 2006;53(1):49-55.
17. Engin C, Posacioglu H, Ayik F, Apaydin AZ. Management of vascular infection in the groin. *Tex Heart Inst J.* 2005;32(4):529-34.
18. Kim Y, DeCarlo C, Jessula S, Latz CA, Chou EL, Patel SS, et al. Risk factors and consequences of graft infection after femoropopliteal bypass: A 25-year experience. *J Vasc Surg.* 2022;76(1):248-54.
19. Vriesendorp TM, Morelis QJ, Devries JH, Legemate DA, Hoekstra JB. Early post-operative glucose levels are an independent risk factor for infection after peripheral vascular surgery. A retrospective study. *Eur J Vasc Endovasc Surg.* 2004;28(5):520-5.
20. Groin wound Infection after Vascular Exposure Study G. Groin wound infection after vascular exposure (GIVE) multicentre cohort study. *Int Wound J.* 2021;18(2):164-75.
21. Thomas S, Ghosh J, Porter J, Cockcroft A, Rautemaa-Richardson R. Periodontal disease and late-onset aortic prosthetic vascular graft infection. *Case Rep Vasc Med.* 2015;2015:768935.
22. Bandyk DF. Vascular surgical site infection: risk factors and preventive measures. *Semin Vasc Surg.* 2008;21(3):119-23.
23. Chiesa R, Astore D, Frigerio S, Garriboli L, Piccolo G, Castellano R, et al. Vascular prosthetic graft infection: epidemiology, bacteriology, pathogenesis and treatment. *Acta Chir Belg.* 2002;102(4):238-47.
24. O'Brien T, Collin J. Prosthetic vascular graft infection. *Br J Surg.* 1992;79(12):1262-7.
25. Chakfe N, Diener H, Lejay A, Assadian O, Berard X, Caillon J, et al. Editor's Choice - European Society for Vascular Surgery (ESVS) 2020 Clinical Practice Guidelines on the Management of Vascular Graft and Endograft Infections. *Eur J Vasc Endovasc Surg.* 2020;59(3):339-84.
26. Laohapensang K, Arworn S, Orrapin S, Reanpang T, Orrapin S. Management of the infected aortic endograft. *Semin Vasc Surg.* 2017;30(2-3):91-4.
27. Otto M. Staphylococcal biofilms. *Curr Top Microbiol Immunol.* 2008;322:207-28.
28. Keren I, Kaldalu N, Spoering A, Wang Y, Lewis K. Persister cells and tolerance to antimicrobials. *FEMS Microbiol Lett.* 2004;230(1):13-8.
29. Erb S, Sidler JA, Elzi L, Gurke L, Battegay M, Widmer AF, et al. Surgical and antimicrobial treatment of prosthetic vascular graft infections at different surgical sites: a retrospective study of treatment outcomes. *PLoS One.* 2014;9(11):e112947.
30. Legout L, D'Elia PV, Sarraz-Bournet B, Haulon S, Meybeck A, Senneville E, et al. Diagnosis and management of prosthetic vascular graft infections. *Med Mal Infect.* 2012;42(3):102-9.
31. Siracuse JJ, Nandivada P, Giles KA, Hamdan AD, Wyers MC, Chaikof EL, et al. Prosthetic graft infections involving the

- femoral artery. *J Vasc Surg.* 2013;57(3):700-5.
32. Geary KJ, Tomkiewicz ZM, Harrison HN, Fiore WM, Geary JE, Green RM, et al. Differential effects of a gram-negative and a gram-positive infection on autogenous and prosthetic grafts. *J Vasc Surg.* 1990;11(2):339-45; discussion 46-7.
33. Bhakdi S, Trantum-Jensen J. Alpha-toxin of *Staphylococcus aureus*. *Microbiol Rev.* 1991;55(4):733-51.
34. Foster TJ, Geoghegan JA, Ganesh VK, Hook M. Adhesion, invasion and evasion: the many functions of the surface proteins of *Staphylococcus aureus*. *Nat Rev Microbiol.* 2014;12(1):49-62.
35. Foster TJ, Hook M. Surface protein adhesins of *Staphylococcus aureus*. *Trends Microbiol.* 1998;6(12):484-8.
36. Andercou O, Marian D, Olteanu G, Stancu B, Cucuruz B, Noppeney T. Complex treatment of vascular prostheses infections. *Medicine (Baltimore).* 2018;97(27):e11350.
37. Lyons OT, Baguneid M, Barwick TD, Bell RE, Foster N, Homer-Vanniasinkam S, 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(6):758-63.
38. Legout L, Sarraz-Bournet B, D'Elia PV, Devos P, Pasquet A, Caillaux M, et al. Characteristics and prognosis in patients with prosthetic vascular graft infection: a prospective observational cohort study. *Clin Microbiol Infect.* 2012;18(4):352-8.
39. Wouthuyzen-Bakker M, van Oosten M, Bierman W, Winter R, Glaudemans A, Slart R, et al. Diagnosis and treatment of vascular graft and endograft infections: a structured clinical approach. *Int J Infect Dis.* 2023;126:22-7.
40. Puges M, Pereyre S, Berard X, Accoceberry I, Le Roy C, Stecken L, et al. Comparison of Genus Specific PCR and Culture with or without Sonication for Microbiological Diagnosis of Vascular Graft Infection. *Eur J Vasc Endovasc Surg.* 2018;56(4):562-71.
41. Kokosar Ulcar B, Lakic N, Jeverica S, Pecavar B, Logar M, Cerar TK, et al. Contribution of sonicate-fluid cultures and broad-range PCR to microbiological diagnosis in vascular graft infections. *Infect Dis (Lond).* 2018;50(6):429-35.
42. Zhang Y, Feng S, Chen W, Zhang QC, Shi SF, Chen XY. Advantages of 16S rRNA PCR for the diagnosis of prosthetic joint infection. *Exp Ther Med.* 2020;20(4):3104-13.
43. Orton DF, LeVeen RF, Saigh JA, Culp WC, Fidler JL, Lynch TJ, et al. Aortic prosthetic graft infections: radiologic manifestations and implications for management. *Radiographics.* 2000;20(4):977-93.
44. Keidar Z, Pirmisashvili N, Leiderman M, Nitecki S, Israel O. 18F-FDG uptake in noninfected prosthetic vascular grafts: incidence, patterns, and changes over time. *J Nucl Med.* 2014;55(3):392-5.
45. Saleem BR, Pol RA, Slart RH, Reijnen MM, Zeebregts CJ. 18F-Fluorodeoxyglucose positron emission tomography/CT scanning in diagnosing vascular prosthetic graft infection. *Biomed Res Int.* 2014;2014:471971.
46. Sah BR, Husmann L, Mayer D, Scherrer A, Rancic Z, Puipe G, et al. Diagnostic performance of 18F-FDG-PET/CT in vascular graft infections. *Eur J Vasc Endovasc Surg.* 2015;49(4):455-64.
47. Anagnostopoulos A, Mayer F, Ledergerber B, Bergada-Pijuan J, Husmann L, Mestres CA, et al. Editor's Choice - Validation of the Management of Aortic Graft Infection Collaboration (MAGIC) Criteria for the Diagnosis of Vascular Graft/Endograft Infection: Results from the Prospective Vascular Graft Cohort Study. *Eur J Vasc Endovasc Surg.* 2021;62(2):251-7.
48. Haddad FS. Corrigenda. *Bone Joint J.* 2019;101-B(8):1032.
49. Saleem BR, Meerwaldt R, Tiellu IF, Verhoeven EL, van den Dungen JJ, Zeebregts CJ. Conservative treatment of vascular prosthetic graft infection is associated with high mortality. *Am J Surg.* 2010;200(1):47-52.
50. Verma H, Ktenidis K, George RK, Tripathi R. Vacuum-assisted closure therapy for vascular graft infection (Szilagyi grade III) in the groin-a 10-year multi-center experience. *Int Wound J.* 2015;12(3):317-21.
51. Andersson S, Monsen C, Acosta S. Outcome and Complications Using Negative Pressure Wound Therapy in the Groin for Perivascular Surgical Site Infections after Vascular Surgery. *Ann Vasc Surg.* 2018;48:104-10.
52. Chatterjee A, Macarios D, Griffin L, Kosowski T, Pyfer BJ, Offodile AC, 2nd, et al. Cost-Utility Analysis: Sartorius Flap versus Negative Pressure Therapy for Infected Vascular Groin Graft Management. *Plast Reconstr Surg Glob Open.* 2015;3(11):e566.
53. Thermann F, Wollert U. Continuous irrigation as a therapeutic option for graft infections of the groin. *World J Surg.* 2014;38(10):2589-96.
54. Ali AT, Modrall JG, Hocking J, Valentine RJ, Spencer H, Eidt JF, et al. Long-term results of the treatment of aortic graft infection by in situ replacement with femoral popliteal vein grafts. *J Vasc Surg.* 2009;50(1):30-9.
55. Coste A, Poinot M, Panaget S, Albert B, Kaladji A, Le Bars H, et al. Use of rifampicin and graft removal are associated with better outcomes in prosthetic vascular graft infection. *Infection.* 2021;49(1):127-33.
56. Ehsan O, Gibbons CP. A 10-year experience of using femoro-popliteal vein for re-vascularisation in graft and arterial infections. *Eur J Vasc Endovasc Surg.* 2009;38(2):172-9.
57. Zetrenne E, McIntosh BC, McRae MH, Gusberg R, Evans GR, Narayan D. Prosthetic vascular graft infection: a multi-center review of surgical management. *Yale J Biol Med.* 2007;80(3):113-21.
58. Earnshaw JJ. The current role of rifampicin-impregnated grafts: pragmatism versus science. *Eur J Vasc Endovasc Surg.* 2000;20(5):409-12.
59. Berard X, Stecken L, Pinaquy JB, Cazanave C, Puges M, Pereyre S, et al. Comparison of the Antimicrobial Properties of Silver Impregnated Vascular Grafts with and without Triclosan. *Eur J Vasc Endovasc Surg.* 2016;51(2):285-92.
60. Minga Lowampa E, Holemans C, Stiennon L, Van Damme H, Defraigne JO. Late Fate of Cryopreserved Arterial Allografts. *Eur J Vasc Endovasc Surg.* 2016;52(5):696-702.
61. Lejay A, Delay C, Girsowicz E, Chenesseau B, Bonnin E, Ghariani MZ, et al. Cryopreserved Cadaveric Arterial Allograft

- for Arterial Reconstruction in Patients with Prosthetic Infection. *Eur J Vasc Endovasc Surg.* 2017;54(5):636-44.
62. McCready RA, Bryant MA, Fehrenbacher JW, Beckman DJ, Coffey AC, Corvera JS, et al. Long-term results with cryopreserved arterial allografts (CPAs) in the treatment of graft or primary arterial infections. *J Surg Res.* 2011;168(1):e149-53.
63. McMillan WD, Leville CD, Hile CN. Bovine pericardial patch repair in infected fields. *J Vasc Surg.* 2012;55(6):1712-5.
64. Brewer MB, Ochoa CJ, Woo K, Wartman SM, Nikolian V, Han S, et al. Sartorius Muscle Flaps for Vascular Groin Wound Complications. *Am Surg.* 2015;81(11):1163-9.
65. Fischer JP, Mirzabeigi MN, Sieber BA, Nelson JA, Wu LC, Kovach SJ, et al. Outcome analysis of 244 consecutive flaps for managing complex groin wounds. *J Plast Reconstr Aesthet Surg.* 2013;66(10):1396-404.
66. Ali AT, Rueda M, Desikan S, Moursi MM, An R, Spencer H, et al. Outcomes after retroflexed gracilis muscle flap for vascular infections in the groin. *J Vasc Surg.* 2016;64(2):452-7.
67. Stone PA, Mousa AY, Hass SM, Dearing DD, Campbell JR, 2nd, Parker A, et al. Antibiotic-loaded polymethylmethacrylate beads for the treatment of extracavitary vascular surgical site infections. *J Vasc Surg.* 2012;55(6):1706-11.
68. Poi MJ, Pisimisis G, Barshes NR, Darouiche RO, Lin PH, Kougias P, et al. Evaluating effectiveness of antibiotic polymethylmethacrylate beads in achieving wound sterilization and graft preservation in patients with early and late vascular graft infections. *Surgery.* 2013;153(5):673-82.
69. Darouiche RO. Treatment of infections associated with surgical implants. *N Engl J Med.* 2004;350(14):1422-9.
70. Revest M, Camou F, Senneville E, Caillon J, Laurent F, Calvet B, et al. Medical treatment of prosthetic vascular graft infections: Review of the literature and proposals of a Working Group. *Int J Antimicrob Agents.* 2015;46(3):254-65.
71. Hodgkiss-Harlow KD, Bandyk DF. Antibiotic therapy of aortic graft infection: treatment and prevention recommendations. *Semin Vasc Surg.* 2011;24(4):191-8.
72. Kahlberg A, Melissano G, Mascia D, Loschi D, Grandi A, Chiesa R. How to best treat infectious complications of open and endovascular thoracic aortic repairs. *Semin Vasc Surg.* 2017;30(2-3):95-102.
73. Ambler GK, Twine CP. Graft type for femoro-popliteal bypass surgery. *Cochrane Database Syst Rev.* 2018;2(2):CD001487.
74. Klinkert P, Schepers A, Burger DH, van Bockel JH, Breslau PJ. Vein versus polytetrafluoroethylene in above-knee femoropopliteal bypass grafting: five-year results of a randomized controlled trial. *J Vasc Surg.* 2003;37(1):149-55.
75. Ricco JB, InterGard Silver Study G. InterGard silver bifurcated graft: features and results of a multicenter clinical study. *J Vasc Surg.* 2006;44(2):339-46.
76. Rocha-Neves J, Ferreira A, Sousa J, Pereira-Neves A, Vidoedo J, Alves H, et al. Endovascular Approach Versus Aortobifemoral Bypass Grafting: Outcomes in Extensive Aortoiliac Occlusive Disease. *Vasc Endovascular Surg.* 2020;54(2):102-10.
77. Zdanowski Z, Ribbe E, Schalen C. Influence of some plasma proteins on in vitro bacterial adherence to PTFE and Dacron vascular prostheses. *APMIS.* 1993;101(12):926-32.
78. Chen L, He H, Wang M, Li X, Yin H. Surface Coating of Polytetrafluoroethylene with Extracellular Matrix and Anti-CD34 Antibodies Facilitates Endothelialization and Inhibits Platelet Adhesion Under Shear Stress. *Tissue Eng Regen Med.* 2017;14(4):359-70.
79. Naito Y, Shinoka T, Duncan D, Hibino N, Solomon D, Cleary M, et al. Vascular tissue engineering: towards the next generation vascular grafts. *Adv Drug Deliv Rev.* 2011;63(4-5):312-23.
80. Costa Almeida CE, Reis L, Carvalho L, Costa Almeida CM. Collagen implant with gentamicin sulphate reduces surgical site infection in vascular surgery: a prospective cohort study. *Int J Surg.* 2014;12(10):1100-4.
81. Langenberg JCM, Kluytmans J, Mulder PGH, Romme J, Ho GH, Van Der Laan L. Peri-Operative Nasal Eradication Therapy Prevents Staphylococcus aureus Surgical Site Infections in Aortoiliac Surgery. *Surg Infect (Larchmt).* 2018;19(5):510-5.
82. Stewart AH, Evers PS, Earnshaw JJ. Prevention of infection in peripheral arterial reconstruction: a systematic review and meta-analysis. *J Vasc Surg.* 2007;46(1):148-55.
83. van der Slegt J, van der Laan L, Veen EJ, Hendriks Y, Romme J, Kluytmans J. Implementation of a bundle of care to reduce surgical site infections in patients undergoing vascular surgery. *PLoS One.* 2013;8(8):e71566.
84. Parizh D, Ascher E, Raza Rizvi SA, Hingorani A, Amato M, Johnson E. Quality improvement initiative: Preventative Surgical Site Infection Protocol in Vascular Surgery. *Vascular.* 2018;26(1):47-53.
85. Matatov T, Reddy KN, Doucet LD, Zhao CX, Zhang WW. Experience with a new negative pressure incision management system in prevention of groin wound infection in vascular surgery patients. *J Vasc Surg.* 2013;57(3):791-5.