Approach to Prosthetic Vascular Graft Infections and Alternative Treatments: Review of the Literature with Two Cases

Prosthetic Vascular Graft Infections; Partial Resection; VAC

ABSTRACT The aim of this study is to discuss the prosthetic vascular graft (PVG) approach, which has been still widely used in peripheral arterial and aortic surgery, and the infections develop in the early or late postoperative periods. The classical way of treatment is considered as resection of the infected graft, wide debridement of necrotic tissues, obtaining bacterial cultures, revascularization with a different approach, and administration of suitable antibiotics. However, treatment strategy cannot be always applied due to several reasons related to the patient and/or the disease. As an alternative, prosthetic vascular graft infection (PVGI) can be done either with partial graft resection or with negative pressure wound therapy (the vacuum assisted wound closure) together with irrigation with antimicrobial solutions and without any resection. We reviewed the literature with two cases of our center. In PVGI, there are some treatment options other than resection and revascularization. PVGI has significantly high mortality and morbidity rates. More studies are needed to solve those problems, and make a consensus on diagnosis and treatment for vascular and cardiovascular surgeons.

Key Words: Prosthetic vascular graft infections; partial resection; VAC

ÖZET Bu derlemedeki amacımız günümüzde hala yaygın olarak periferik arter ve aort cerrahisinde kullanılan prostatik vasküler greftlerin (PVG) postoperatif erken veya geç dönemde gelişen enfeksiyonlarını yaklaşımı tartışmaktır. Klasik olarak, tedavide enfekte greftin çıkarılması, geniş debidman yapılması, kültür alınması ve sonrasında farklı bir yoldan revaskülarize edilmesi ile uygun antibiyoterapi düşünülmektedir. Fakat bu tedavi hassasiyet ve/veya hastalığı bağlı sebeplerden dolayı her zaman uygulanamamaktadır. Prostistik vasküler greft enfeksiyonların (PVGE) tedavisinde alternatif olarak parsiyel greft resezisyonu ile veya hiç resezisyon yapmadan antimikrobiyal sivıların irrigasyonuyla beraber negatif basınçlı yara tedavi sistemleri (vakum yardımıyla yara kapatması) kullanılabılır. İki olgu eşliğinde literatür bilgilerini gözden geçirdik. PVGE’lere de resezisyon ve revaskülarizasyondan başka tedavi seçenekleri de vardır. PVGE mortalite ve morbiditesi yüksek bir sorundur. Bu problemlerin çözümü için vasküler ve kardiyovasküler cerrahlar olarak daha fazla çalışma yapamaz ve teşhis ve tedavi için konsensus oluşturamaz gerekmektedir.

Anahtar Kelimeler: Prostistik vasküler greft enfeksiyonları; parsiyel resezisyon; VAC

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Surgery and interventions related to peripheral arterial disease (PAD) are used more frequently due to increasing world population and aging population, particularly in the developed countries. At the same time, increase in smoking habit, and increasing rates of diabetes and hypertension result in advanced atherosclerosis in the population. Prosthetic...
vascular grafts (PVG) are still the essential surgical materials although numerous alternative methods are present in treatment of PADs. PVGs are unquestionably beneficial for saving the life of the patient, and to maintain viability of the extremity. PVGs have increasingly been used in both aortic and lower extremity in parallel to the increase in the number of patients.\(^1\) PVGIs are not commonly seen; however, they are still a significant cause of mortality and morbidity. Annual treatment cost of PVGIs has been calculated as 640 million dollars in USA.\(^2\) Today, surgeons are more experienced about such problems, but virulent bacteria resistant to antimicrobial agents remain as the main problem.\(^3\) The incidence of PVGI varies between 1 and 6%.\(^4,5\) Depending on the location of the graft, prevalences of infrainguinal, aortofemoral and aortic area infections are 2-5%, 1-2%, and 1%, respectively.\(^1\) The mortality rates of intra-abdominal aortic graft infections and amputation rates in lower extremity prosthetic grafts have been reported up to 75% and 70%, respectively.\(^6\) The main reasons for infection are bacterial colonization of the wound and the prosthetic material, and direct contamination from the skin and/or bowel during surgery. There is still no exact consensus regarding the best treatment option and the diagnostic criteria of PVGIs.\(^7\)

**CASE 1**

A 55-year-old male patient was referred with complaints of fever, warmth in the inguinal region, swelling, and poor general status after aorto-bifemoral bypass surgery performed due to peripheral arterial disease. On laboratory examinations, hemoglobin was 12 g/dL, white blood cell count was 17,100/mm\(^3\), platelet count was 223,000/mm\(^3\), C-reactive protein was 22.56 mg/dL (0-0.5). Peripheral blood smear revealed polymorphonuclear leukocytes (PMNL) as 83% and lymphocytes as 17%. Arterial blood gas and biochemistry, and urinalysis were normal. Empiric teicoplanin and meropenem treatment were started. Circulatory system was examined using computerized tomographic angiography. On scintigraphic examination, an appearance was observed conforming an infection, only in the left side of the graft. Under general anesthesia, an incision was made starting from the left groin, and extending to the retroperitoneal area. Left leg of the synthetic graft was cut immediately after the bifurcation. Femoral artery anastomosis was resected. Infected and necrotic tissues were debrided. *E. coli* was cultured from the pus sample obtained. Teicoplanin was discontinued, and meropenem was continued to be administered. The wound was left open for one week, and it was irrigated twice a day by dissolving 20 ml of a surgical hand disinfection solution (including Povidone iodine 7.5%, ISOSOL scrub 1000 ml) in 500 ml physiological saline, and then the wound was debrided. Vacuum assisted wound closure (VAC) system was applied to the open wound for four weeks. The sponge was changed every three days, and it was made smaller. After the culture yielded a negative result, the wound was primarily closed. No revascularization was planned due to the sufficient circulation of the left leg, and improvement of the symptoms. No infection findings were observed in the follow-up period more than two years (Figures 1, 2).

**CASE 2**

A 61-year-old male patient was referred to our hospital with the diagnosis of sepsis. His history revealed an aorto-bifemoral bypass three years ago, and he underwent femoropopliteal bypass surgery one year ago upon development of ischemia in his left foot. His femoropopliteal PVG was infected, and the foot was necrotized due to thrombosis of the graft. A left below-knee amputation had been performed in another medical center. The laboratory examinations of the patient with a wound discharge in the groin was as follows: hemoglobin was 9.2 g/dL, white blood cell count was 25420 / mm\(^3\), platelet count was 379,000 / mm\(^3\), C-reactive protein was 23.16 mg/dL (0-0.5), albumin was 2.49 g/dL, and sodium was 119 mmol/L. Peripheral blood smear showed 85% PMNLs, and 15% lymphocytes. Arterial blood gas values were normal. Empirical teicoplanin and meropenem was started. The patient was undertaken to surgery when his clinical
status became stable, a left retroperitoneal incision was performed under general anesthesia, and left leg of the synthetic graft was transected and removed. The wound that was left open, and irrigated twice a day for two weeks by using a surgical hand disinfection solution (Povidone iodine 7.5%, ISOSOL scrub 1000 ml), prepared by dissolving 20 ml of it in 500 ml physiological saline. Then, VAC system was applied. The sponge was changed every three days for five weeks, it was made smaller, and the wound site was closed. *Acinetobacter baumanii* was cultured from the pus obtained from the wound. The patient’s clinical picture and laboratory values improved, and he did not have any circulation problems. He was discharged with full recovery at the end of a 60-day treatment. He did not have any problems on his monthly examinations performed for six months (Figures 3, 4).

**DISCUSSION**

Predefining the risk factors in PVGI provides significant advantages for determining high-risk patients, and taking protective measures in treatment. Primarily, patient-related risk factors include old age, male gender, a high body mass index, heart failure, immune system deficiency, diabetes, renal failure, and chronic obstructive pulmonary disease. The main risk factor for development of PVGI is groin incisions. High load of microbial flora and dense lymphatics in the inguinal region are rational causes. Additionally, incision from the angiography intervention site, overmanipulation of tissues and damage to the lymphatics, redo surgeries, and intestinal injuries...
during surgery constitute other surgical risk factors.\textsuperscript{7,5,10}

Wound-site infection is an independent risk factor. It has been considered that direct dissemination of the wound site makes the graft infected.\textsuperscript{11} In the early postoperative period, it is difficult to distinguish whether PVGI and wound site infection involve PVG or not. Air and fluid accumulation around the graft may be a radiological evidence.\textsuperscript{12} Aspiration of this fluid is not preferred, because the graft may get infected during this procedure. Radiologically, presence of air and fluid accumulation around the graft for 8 weeks or other supportive clinical, surgical, and microbial findings are suggestive of diagnosis of PVGI. Every wound site infection may not cause PVGI, also PVGI does not progress with the wound site infection in early postoperative period.\textsuperscript{1} Bleeding at the wound site or a pseudoaneurysm caused by the hematoma or seroma increases the risk of wound site infection, and thus PVGI.\textsuperscript{7}

Emergency cases such as ruptured or dissecting abdominal aortic aneurisms may particularly be risk factors. The skin ulcers in the lower extremity at the time of surgery, and infection in the circulatory system constitute other risk factors for development of PVGI.\textsuperscript{1,7} However, relatively small number of these cases may not show a statistically increased risk.\textsuperscript{1} Prolonged lower extremity surgery and length of hospital stay are other risk factors.\textsuperscript{10}

Thomas et al. presented four cases, and determined that 3 PVGs and one endovascular graft were infected from the oral flora in the late postoperative period. In this study, it was also found that the infected tissue was debrided, and the tissues removed were sent for microbiological analysis. On 16s rDNA real-time PCR study, mixed bacteria indicated possible oral flora.\textsuperscript{13} Therefore, it is recommended for the patients, who will undergo a complex aortic surgery, to have a dental examination before surgery, and to receive the necessary treatment.
When the polyester and polytetrafluoroethylene (PTFE) grafts were compared in terms of the incidence of infection; it was thought that polyester grafts were more resistant to eradication of infection.10

Since numerous PVGIs arise from the wound-site infection in the groin, it is required to avoid prolonged hospital stay before surgery, and to shave the incision site. Gastrointestinal system interventions should also be avoided during surgery, and nasal carriage of *S. aureus* should be treated. A number of studies pointed out the starting antibiotic prophylaxis, normothermia, blood glucose control, and eradication of nasal *S. aureus* were important.14

PVGIs usually develop due to the wound site infection that occur as a result of contamination from skin flora during surgical procedure. Hematologic dissemination may occur during urological, dental, and endoscopic procedures. Another type of infection dissemination occurs by the bacterial colonization of the atherosclerotic plaque and thrombus within the aneurysm sac that is covering the graft or from the tissue covering its surface.15 Soft tissue edema or disruption in the skin integrity may also pose a risk.16 The biofilm developed by the microorganisms around PVG both provides bacterial colonization and keeps away these microorganisms from effect of the immune system.7 In fact, any microorganism may cause an infection at the wound site. However, gram-positive bacteria, especially *S. aureus*, is responsible for these infections in up to 75% of cases.17 In the study conducted by Hodgkiss–Harlow et al., it was observed that the rates of methicillin-resistant *S. aureus* (MRSA) increased four times in prosthetic arterial graft infections that have been treated by the vascular surgery group from 1990s to 2000s. In 12% of the patients to whom inguinal incision was applied, wound site infection developed, and gram-positive bacteria were determined at the rate of 75%. In one fourth of the wound site infections, MRSA was determined, and vancomycin resistance was observed in two-thirds of them.17 In another study conducted by Texas Galveston University vascular surgery group in 2005, it was reported that the rate of wound site infections after lower extremity bypass surgery was 11%, *S. aureus* was cultured in 64%, and half of them were methicillin resistant.18 Thus, *S. aureus* should be absolutely considered in the wound site infections developing in the patients to whom PVG is used, including the non-healing amputations. Suitable antibiotic prophylaxis should be administered to the patients who have more than one risk, for nasal colonization and before surgery.18

PVGIs occurring in the first three postoperative months are called as early infections. They usually present with acute fever, bacteremia, painful erythema, swelling, fever, local bleeding, ulcer formation, graft occlusion or mycotic pseudoaneurysm-related pulsatile mass in the groin.7

PVGIs seen after three months are called as late infections. They usually present with less significant symptoms such as back pain, fistula development, graft occlusion, formation of an asymptomatic pseudoaneurysm, and separation in the relationship of the graft with the surrounding tissue. Blood cultures are usually negative. Systemic symptoms are not encountered particularly in diabetic patients. It is hard to differentiate inflammation on the soft tissue covering the graft from PVGI.7 There are two classifications of PVGIs, suggested by Szilagyi and Samson.19,20 In Szilagyi classification; in group 1, infection involves only the dermis. In group 2, it extends into the subcutaneous tissue, but does not invade the arterial implant. In the last group, it involves the arterial implant. In Samson classification; in group 1, infection is limited in the dermis. In group 2, it extends into the subcutaneous tissue, but does not invade the arterial implant. In the last group, it involves the arterial implant. In group 4, infection surrounds an exposed anastomosis, but bacteremia or anastomotic bleeding does not occur. In the last group, it involves a graft-to-artery anastomosis, and is associated with septicemia and/or bleeding at the time of presentation.19,20

Infection may arise from gram-positive or gram negative bacteria or a mixed flora, thus wide-spectrum antibiotics should be administered. The patient should be hospitalized, and drainage cultures should be obtained. The late infections are usually formed by low-virulence bacteria like *S.*
As a result of the development of a biofilm layer by the bacteria, a superinfection may develop due to more virulent bacteria such as methicillin-sensitive or resistant *S. aureus*. In this case, a fistula develops between the graft and the skin. In aortic graft infections, positive culture of gram-negative bacteria implicates possible graft-related enteric erosion.\(^7\)

While assessing whether graft is infected or not, generally ultrasound, contrasted computed tomographic angiography (CTA), 18F-fluorodeoxyglucose positron-emission tomography (FDG-PET), and fusion PET/computed tomography are used as the imaging methods. Although ultrasound is a rapid method for determining fluid accumulation and inflammation around the graft, computed tomography (CT) is mostly preferred for diagnostic purposes. Fluid and gas accumulation around the graft, assessment of the soft tissue, and aneurysm development and maintenance are recognized by CTA.\(^21\)

CTA sensitivity in advanced PVGs is about 100%.\(^22\) False negativity ratio is high in slowly progressive PVGs.\(^23\) Specificity and positive predictive value of FDG-PET is 95% in the determination of graft infections.\(^24\) Combination of FDG-PET and CTA at the same session exactly determines the location of FDG involvement.\(^7\)

As a glucose analogue, 18F-fluoro-2-deoxy-D-glucose (18F-FDG) is taken up by the viable cells using the membrane glucose transport protein, and then phosphorylated by hexokinase. During metabolic inflammation; granulocytes, especially neutrophils and monocytes use glucose as the energy source. Thus, 18F-FDG accumulation in inflammatory cells provides the imaging of infection and inflammation.\(^25\)

Samples received from deep side or surface of the infected wound may simply show the colonized flora. It is possible to determine the most reliable bacteria with samples obtained as a result of surgical removal of infected graft and its surrounding infected tissue. The samples taken for 16S rRNA polymerase chain reaction or bacterial culture are used in the diagnosis of PVG.\(^7\)

The decision whether or not graft replacement is necessary at the time of surgery is based on the onset of the symptoms, prevalence of the graft involvement, and its microbiology. It is quite important to determine whether whole aortic graft or only its one segment is infected. In fact, it is recommended to remove the infected graft together with aggressive debridement and administration of antibiotics at the same session, and to revascularize with a new graft by passing it through the non-infected site.\(^7\) If there is a prevalent, virulent infection in the samples obtained during surgical exploration, in-situ restructuring should be planned with an autogenous vein. Preoperative implantation of antibiotic-impregnated beads makes contribution to the sterilization of the graft bed. In the presence of an aortic graft infected with graft-enteric fistula, the graft is surgically excised and extra anatomical bypass such as axillofemoral bypass should be planned.\(^7\) However, extra-anatomic bypass is not preferred since it takes a long time, and low patency and high amputation rates.\(^7\)

If the infection keeps only the leg of aortofemoral graft, the retroperitoneal oblique incision is extended from the groin to the lower abdomen. If the infection progresses or an abscess is formed, multi-stage surgery is recommended. At the beginning, the abscess around the graft is drained, necrotic tissue is debrided, and the cavity is irrigated with a suitable antimicrobial solution. This solution provides a surgical site cleaning. Additionally, antibiotic-impregnated beads can be placed in the spaces around the graft. After those two procedures, the surgical wound is closed. Culture results are obtained, the wound is reopened after 3-5 days, and the leg of the aorta-femoral graft is evaluated in terms of infection. A clamp is placed and the non-infected proximal segment of the graft is transected, then it is separated from the femoral anastomosis, and the graft bed is irrigated with an antibacterial solution. Based on the early culture results, a deep femoral vein or rifampicin-impregnated PTFE graft is implanted.\(^17\) Besides, cryopreserved homografts, fresh arterial allografts, autologous veins and silver-ion or antibiotic-related grafts can be used with or without a muscle flap.\(^26,27\)
Another frequently preferred treatment method is to cover the wound with a muscle flap. Sartorius or rectus femoris muscles can be used for this flap. All the wounds are opened, drained, and debrided. Necrotic tissues are removed with a series of surgical interventions. While sartorius muscle is sufficient for the small ones, rectus femoris muscle can be used alone or together with the skin for wider wounds. Debridement and muscle flap are effective treatment methods for early and localized graft infections.28

Wide spectrum, bactericidal and parenteral antibiotics should be started as soon as possible if an aortic graft infection is suspected. There is no consensus regarding the class of antibiotics to be used for the empirical treatment of PVGIs. The most common-to-rare responsible bacteria are staphylococci (S. aureus, S. epidermidis), E. coli, klebsiella, pseudomonas group and Candida albicans. MRSA is responsible for half of the early aorto-femoral graft infections, and a quarter of the late ones. Thus, first or second generation cephalosporins should be chosen as parenteral antibiotic covering S. aureus and S. epidermis and MRSA. Daptomisin is preferred owing to its rapid onset of action in gram positive infections, dose-dependent bactericidal effect, covering MRSA, and penetration to the bacteria films. Vancomycin and linezolid may be used in treatment of MRSA infections; however, they are show their effect slowly since they cannot penetrate bacteria films, and are bacteriostatic. For a gram negative effect; fluoroquinolones or aminoglycosides are preferred in case of penicillin hypersensitivity.16 Although empirical antifungal treatment is not recommended, rifampicin should be included in the empirical antibacterial treatment in order to penetrate the biofilm layer. Antimicrobial spectrum should be narrowed after culturing the microorganism and performing antibiotic sensitivity tests. Oral antibiotic treatment is not recommended, but quinolones, trimethoprim-sulfamethoxazole, tetracyclines and rifampicin are may be administered if needed, owing to their high oral bioavailability. Recently, many resistant bacteria are being isolated from PVGIs.18,27

Antimicrobial treatment period is not unclear. For superficial infections, one-week oral antibiotherapy is sufficient. The infections including subcutaneous tissues should be treated for a longer time. Treatment periods of Szilagyi grade 3 and Samson grade 3-5 PVGIs are not clear, and they vary in relation with the prevalence of infection, as well as location and the material of the graft (synthetic, biological or vein). They should be treated as done in prosthetic valve endocarditis. Following surgical debridement and the removal of the infected graft, intravenous antibiotics should be administered for 4-6 weeks. Calligaro et al. and Legout et al. recommended oral antibiotics for 6-12 months after a 6-week i.v. antibiotic treatment.14,29

VAC offers a new option for the treatment of infected vascular wounds. Contrary to popular belief, surgical debridement is not sufficient for the infected vascular wound treatment, and it can be used as a bridge for surgical closure or as the primary wound treatment modality. VAC system is primarily developed for chronic ulcers and treatment of pressure wounds, and it is a relatively new non-invasive treatment option enabling formation of granulation tissue. At the beginning, it was used for treatment of osteomyelitis, and then it was originally adapted in 1984 by Durandy et al. for treatment of mediastinal infections.30,31 In some recent studies, it was reported that VAC systems were used with minute irrigation, without replacement of PVGIs. Those non-invasive systems remove the microorganisms and inflammatory mediators with continuous vacuum effect, and provide formation of granulation on the tissues.32

In a study conducted by Berger et al. in 2012, VAC application was investigated after surgical debridement in 17 Szilagyi grade 3 inguinal infections of 15 patients with PVGs. Treatment consisted of continuous application of a double-layer sponge system made up of of polyvinyl alcohol and polyurethane at a pressure of 50 mmHg, and the success rate was reported as 84%. Complementary antibiotics were administered to all patients. Primary endpoint of treatment was determined as complete wound closure. The mean application pe-
riod of the VAC system was 43 (14-76) days, and wound closure was completed in 51 (5-69) days. Eleven of these patients had VAC treatment in the hospital for a mean period of 21 (5-61) days, and then completed their treatment at home in a mean period of 22 (5-69) days. In this respect, VAC treatment has a reduced the hospital expenses.33

In our two cases who had aorto-bifemoral bypass with a synthetic graft, left legs of the grafts were infected. Therefore, the incision in the groin was extended as a retroperitoneal oblique incision at surgery, and the left legs of the infected grafts were removed. Irrigation and debridement were done at first in both patients, and then VAC treatment with irrigation was administered. The remaining part of the graft was recovered.

CONCLUSION
PVGIs are rarely seen but their mortality, morbidity, and treatment costs are high. When the condition of the patient and the disease is evaluated, a wide surgical approach may not always be possible. In such cases, alternative treatment options such as a VAC system present a good option. However, the ideal treatment method, the type of antibiotics, and duration of administration remain to be determined. We, as the surgeons, need to share our experience and knowledge, and should achieve an agreement on this subject.

Conflict of Interest
Authors declared no conflict of interest or financial support.

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