Infra-Inguinal Synthetic Graft Infection: A Clinical and Microbiological Outcome.

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ABSTRACT

Background: Synthetic graft infection is a major complication after infra-inguinal bypass. We investigated the records for patients who had lower extremity prosthetic graft infection in our vascular surgery unit over a 5 year period, with a potential effort to identify potential risk factors related.

Methods: The medical records of patients with vascular graft infections over a five-year period from January 2014 to March 2019 were retrospectively reviewed. All patients with a graft infection involving the femoral artery were included. Patient demographics including comorbidities, indications for intervention, location of bypass, date of graft insertion, date of graft related infection, type of prosthetic material, and bacteriology and the treatment and outcome were collected.

Result: 468 prosthetic graft bypass procedures were performed in 412 patients. Out of these 352 (75%) were males. Infectious complications of the prosthetic graft (PG) were found in 28/468 grafts (6%) .The mean age±SD of the patients was 62±19 years. The number of infected grafts in female patients was 16 (57%). The median follow up duration was 18 months .We found that graft preservation yielded good outcome in selected patients, 7 (25%) PGI were successfully salvaged using a conservative approach . There were 468 patients enrolled in this study; 440 patients were controls and 28 patients had PGI. Bivariate analysis of categorical variables identified that the presence of diabetes mellitus (P value=0.01), end-stage-renal disease (ESRD)(P value= 0.01), female gender (P value =0.004) and major or minor tissue loss (P value =0.01) are risk factors for PGI. Considering continuous variables, high white blood cells (WBCs) was more frequently associated with PGI with a statistically significant P value .The use of an omniflow biosynthetic graft resulted in an 80% (8 of 10 patients) success rate of limb salvage in our patients. There was no late reinfection during the follow-up period. The replaced grafts were successful in 88% of cases. Staphylococcus aureus was the most common isolated bacteria present in 32% of cultures, followed by Coliforms/gram-negative organisms 25%. The amputation rate was 7% and the mortality among the PGI group during the study period was in 3 patients (11%).

Conclusion: That graft preservation yielded good outcome in selected patients, and the biosynthetic prosthesis appears to be a promising alternative in the absence of an appropriate autologous conduit. There were statistically differences in female, diabetes ,elevated WBC, End-stage renal disease and tissue loss in both groups.

Key words: graft infection, infrainguinal bypass, prosthetic graft complications

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Introduction

The reported incidence of infection involving vascular prosthesis varies and is influenced by the implant site, indication for the intervention, underlying disease, and host defense mechanisms.

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Infections involving a vascular prosthesis are associated with a high mortality rate and a significant amputation rate that can be as high as 70% (range 1–70%) (1, 2).

Graft infections are reported with less frequency compared to wound infections. Infection is more likely to involve prosthetic grafts implanted during emergency procedure and when the prosthesis is placed in a subcutaneous tunnel (1).Prosthetic graft infections(PGI) can be classified according to time of appearance after implantation, early (<4 months) or late (>4 months), or the relationship to postoperative wound infection. Vascular infections are divided into 3 groups according to Szilagyi classification, depending on the extent of the inflammation whether being superficial, deep and mixed types (3).
The goals of managing vascular graft infections involve initial and long-term eradication of the local and systemic septic process and maintenance of normal arterial perfusion to the involved end-organ and limb tissue. Staphylococci (Staphylococcus aureus and coagulase negative staphylococci) account for more than 75% of vascular graft-related infections. In fact, S. aureus is the most prevalent pathogen. Gram-negative bacteria such as Pseudomonas, E. coli, Klebsiella, Enterobacter, and Proteus species are particularly virulent (4).
The goal of this study was to investigate the outcomes associated with lower extremity prosthetic graft infections and to identify potential risk factors as group sub-analysis.

Table (I) Patient demographics and analysis of risk factor

Characteristic *prosthetic graft bypass*	*Number of patients with* *(n= 440)*	*Number of patients PGI %* *(n=28)*	*P value*
Male	*322(73%)*	*12(43%)*	*0.06*
Female	*118(27%)*	*16(57%)*	*0.004*
Heart Failure	*45(10%)*	*2(7%)*	*0.06*
Coronary Disease	*111(25%)*	*8(29%)*	*0.82*
Anaemia	*98(22%)*	*4(14%)*	*0.066*
COPD	*59(13%)*	*4(14%)*	*0.9*
DM	*277(63%)*	*15(54%)*	*0.01*
HTN	*118(27%)*	*8(29%)*	*0.17*
Tissue loss	*24(5%)*	*7(25%)*	*0.04*
End-stage-renal disease	*23(5%)*	*6(21%)*	*0.001*
High white blood cells	*22(5%)*	*8(29%)*	*0.03*

Materials and methods

The medical records for patients with vascular graft infections in the department of Vascular Surgery/Royal Medical Services over a five-year period from January 2014 to March 2019 were retrospectively reviewed. 28 graft infections were identified in 468 patients. All patients with graft infection involving the femoral artery were included. Patients with grafts involving the aorta were excluded owing to lack of sufficient follow up period . The patient demographics including comorbidities, indications for intervention, location of bypass, date of graft insertion, date of graft related infection, type of prosthetic material, and bacteriology and the treatment and outcome were recorder (Table I).

The prosthetic grafts were made of polytetrafluoroethylene (PTFE) material in 81% of cases and Dacron (polyethylene terephthalate) material in the remaining cases. The previous operations performed in patients with prosthetic graft bypasses were ilio-femoral bypass in 11% (n=52), femoro-popliteal + femoro-distal(composite) bypass 61% (n=286), femoro-femoral bypass in 13% (n= 63) and in 67 cases (14%) axillo-bifemoral or axillo- femoral bypass

We used longitudinal or transverse incision in the groin depending on the surgeon's preference, which were closed utilizing two layers of running absorbable suture material followed by skin closure with non-absorbable sutures. Our protocol includes the administration of an antibiotic at 30 minutes before skin incision, usually with cefazolin, which is then repeated every 8hours for a period of 24 to 48hours, postoperatively. Our regimen has evolved over time during this study period and we have switched from cefazolin to vancomycin as per hospital policy protocols. These protocols are being monitored and modulated accordingly by the infection control committees at the Royal Medical services. During the study period, we switched to chlorhexidine gluconate as our standard preparation solution followed by treatment with povidone-iodine intraoperatively with cleaning of the groin with povidone-iodine 12 hours preoperatively. We switched to electrical clips instead of razors and started using an antimicrobial incise drape.

PGI was identified by clinical, ultrasound, and microbiological findings. Clinical presentation was categorized as a draining sinus tract, exposed graft, purulent drainage, erythema, cellulitis, pain overlying the graft, and hemorrhage. Our treatment plans are preservation of the graft if the infection is superficial and debridement, excision without revascularization, in situ with vein, in situ with omniflow (LeMaitre) biosynthetic graft (integrated biosynthetic composite of polyester mesh and ovine connective tissue components), extra-anatomical

reconstruction. All the patients received empirical treatment to protect against gram-negative and positive microorganisms, prior administration of antibiotics, swabbing of open wounds or exposed grafts or aspiration with a needle. Gram stains and wound cultures were routinely sent for microbiology analysis.

Identification of bacteria and determination of sensitivity to antibiotics

The bacterial strains were isolated from clinical materials (pus, tissue biopsy, blood, part of the graft) and identified with a VITEK2 ID/AST Testing System (BioMerieux, UA). The majority of bacterial sensitivity testing was investigated using VITEK2 and some were modified or confirmed by manual susceptibility testing using Etest and Disc diffusion methods based on the clinical and laboratory standard institute guidelines(CLSI)

Statistical analysis

Patients' characteristics were summarized using descriptive statistics analysis. Results of continuous variables were given as mean ± standard deviation and categorical variables were presented as counts and percentages. Continuous variables were compared by the use of the Student's t test. Categorical variables were compared by the use of the chi-square test or Fisher's exact test when the chi-square test was not appropriate. Differences between groups were considered to be significant for variables yielding a p-value of <0.05. The statistical analyses of the data were performed using SPSS v.19 for windows statistical software (Chicago, IL, USA).

Results

During the time period covered by the study, 468 prosthetic graft bypasses were performed in 412 patients. 352(75%) patients were male. Infectious complications of the prosthetic graft (PG) were found in 28/468 grafts (6%).The mean age±SD of the patients was 62±19years. The number of infected grafts in female patients was 16(57%). The median follow up duration was 18 months .The median time before the detection of a graft infection was 21 days. The time interval from the initial intervention to the diagnosis of the infection ranged from 11 days to 5 months. There is no documentation to report the exact operating time.

The diagnosis of PGI was established by clinical examination, laboratory tests (C-reactive protein, high white blood cells), microbiologic profile, ultrasonography, computed tomography, and a PET scan for certain patients.

The indications for primary revascularization were limb threatening ischemia(n=12) and claudication (n=8). Emergency revascularization procedures (n= 8)were performed for acute

ischemia. The localization of the infection was in the inguinal area in 13 cases, whereas in 15 cases it was at different areas of the grafts.

All patients were treated with wide spectrum antibiotics. 2(7%) patients had superficial wound infections as cellulites that did not invade the deep tissue, which was treated conservatively with antibiotics. 26 PGI patients had an infection involving the deep tissue reaching the grafts;2(7%) patients were claudicant and did not undergo vascular reconstruction treated by removal of grafts.7(25%)PGI patients were treated by saphenous vein bypass and graft explantation, 7(25%) PGI patients (all grafts were patent, had a single gram-positive organisms not associated with systemic sepsis, involving a short length of the graft)were treated conservatively by debridement of tissue, sartorius flap, and vacuum–assisted closure(VAC).10(36%) patients were treated by omniflow bypass owing to the lack of veins. All patients underwent debridement of the infected tissue and passive wound irrigation. In 2 PGI patients, the replaced bypass was an omniflow graft (ilio-fem and fem-pop bypass

had persistence of infection in the groin area and were treated by wide debridement of tissue necrosis and the inflamed surrounding tissue, a sartorius flap and VAC was placed.Unfortunately,they bled owing to infection at the anastomotic site after 21 and 23 days. Therefore, we decided to remove the bypass and they ended up with major amputation. One patient underwent hip disarticulation and the second patient underwent above knee amputation(AKA) owing to poor perfusion of the limb and infection. The amputation rate was 7% among patients with PGI. The replaced grafts were successful in 88% of cases. All preserved grafts were successfully salvaged. The mortality among the PGI group during the study period was 3(11%), the cause of death was septicemia in two patients and myocardial infarction in the third one.

There were 468 patients enrolled in this study; 440 patients were controls and 28 patients had PGI. Bivariate analysis of categorical variables identified that the presence of diabetes mellitus (P value=0.01), end-stage-renal disease (ESRD)(P value=0.01),female gender (P value =0.004) and major or minor tissue loss (P value =0.01) are risk factors for PGI. Considering continuous variables, high white blood cells (WBCs) was more frequently associated with PGI with a statistically significant P value (Table I).

The microorganisms causing the infection were identified based on the microbiological examination. Bacterial culture was available for 96% of the patients. Suture lines were involved in 86% of the time, body of the graft in 22% of the cases. Staphylococcus aureus was the most common isolated bacteria present in 32% of cultures, followed by Coliforms/gram-negative organisms 25%. MRSA (methicillin-resistant S. aureus) was cultured in 7% of the graft infections (Table II). In 14% of the cases, a polymicrobial infection was present. All the patients were treated empirically with antibiotics effective against Staphylococcus and gram-negative microbes, such as flucloxacillin, clindamycin, vancomycin, cephalosporin, then they

were treated according to the sensitivity result. The antibiotic treatment usually extended for more than 6 weeks.

Table II: Microorganisms identified in prosthetic graft infections of patients in this study.

Bacterial species	Number(%)
Staphylococcus aureus	9(32%)
Coliforms/gram-negative organisms * And Pseudomonas spp	7(25%)
S. epidermidis	2(7%)
No growth	4(14%)
MRSA	2(7%)
Mixed growth	4(14%)

DISCUSSION

The clinical manifestations of prosthetic vascular infection vary depending on the anatomic location and the virulence of the pathogen (3).Our graft infection rate of 6% was similar to previously published rates ranging from 0.2% to 6% at a mean follow-up of 18 months(1,2).The presence of an active infection at the time of the operation is predictive of PGI, most likely owing to contamination during the procedure or the perioperative period. In this study, 25% of cases that had lower limb ulcers or toes gangrene were associated with PGI(P=0.04). Siracuse et al(5)., in their retrospective study about PGIs involving the femoral artery, concluded that female gender, diabetes, and active infection at the time of bypass are associated with a higher risk for graft infection, which is identical to our findings

The association of female gender with PGI could be owing to a higher fat distribution in the lower extremities or incontinence causing wound contamination(5,6,7).We found diabetes to be predictive of graft infection, which is not surprising because it is also associated with surgical site infections not only in the lower extremities but also in other surgical procedures(8).Diabetic patients with critical ischemia are more likely to present with tissue loss and infection (9).

Another factor that plays a role in PGI is patients with ESRD. Numerous studies have demonstrated that chronic inflammation may contribute to the morbidity and mortality among dialysis patients(3,10). Moreover, deterioration of renal function in uremia increases the risk of infection and various abnormalities of the immune system.25% of our patients with ESRD had a graft infection. Individuals with ESRD are at high risk of foot ulceration and major lower extremity amputation (11). The basic diagnosis of PGI depends on the clinical picture, imaging and elevated WBCs. Our results showed that the WBC levels were more elevated in patients with PGI and that it is predictive of graft infection. These results were in accordance with other studies [2,3,12].

The goals of managing vascular graft infections are initial and long-term eradication of the local and systemic septic process and maintenance of normal arterial perfusion to the involved limb tissue.
Our management of these graft infections has changed over time. Previously we removed all PGI whatever the site or kind of bacteria. We advocate patient-specific treatment algorithm. The selection criteria for specific treatment modalities are primarily based on the clinical findings, extent of graft involvement, and microbiology. Basic principles involved in the management of PGI include total graft excision and extra-anatomic bypass or in situ replacement, as well as occasional conservative treatment with antibiotics coverage, debridement, sartorius or gracilis muscle flaps with and without VAC devices (13,14). Nowadays, the graft preservation technique is our preferred approach in selected patients. We found that graft preservation yielded good outcome,7 (25%) PGI were successfully salvaged using a conservative approach. Current recommendations for conservative treatment of PGI are limited to a specific group(3);Patent grafts with single gram-positive organisms other than with polymicrobial organisms not associated with systemic sepsis, involving a shorter length not involving the anastomosis can be considered for preservation. The exception is invasive infections caused by pseudomonas species,MRSA or other potentially virulent gram-negative bacteria(4).

Various replacement vascular materials (in situ or extra-anatomic) are available such as antibiotic or silver-coated vascular prostheses, autologous or heterologous venous or arterial grafts and biosynthetic vascular prosthesis(15).The greater saphenous vein remains the conduit of choice for vascular procedures. However, autologous vein grafts are not feasible in a significant number of patients.The use of a biosynthetic vascular graft (Omniflow®II) might be a viable alternative.They have excellent re-infection resistance. Limb salvage, morbidity, and the mortality rate are similar to those obtained with autologous vein grafts in infected fields(16,17,18).The use of an omniflow graft resulted in an 80% (8 of 10 patients) success rate of limb salvage in our patients. There was no late reinfection during the follow-up period.The biosynthetic prosthesis appears to be a promising alternativein the absence of an appropriate autologous conduit.

The most common bacteria cultured from infected grafts include *Staphylococcus aureus,*
epidermidis, and gram-negative enteric organisms and MRSA(3,19). Our result indicated the presence of a variety of microorganisms; the most predominant was *Staphylococcus aureus*(32%),but other microorganisms such as gram-negative organisms and *Pseudomonas spp* were prevalent. Empirical antimicrobial treatment for PGI should cover all susceptible organism with broad-spectrum antibiotics. The incidence of MRSA has significantly increased and it has become an important pathogen in PGI,contributing to 33% of infections in patients undergoing vascular surgery (20). Our results shows that MRSA was present in only 7% of PGIs. The current literature suggests that MRSA-infected graft preservation should only be

attempted with minor graft involvement(21).In our cases, we explanted all the grafts with MRSA infection because of the fear of morbidity and mortality.

As reported by Revest et al. (22),analysis of the treatment duration from different studies is difficult to interpret because of the non-comparative nature of these studies, which do not include standardized durations. The duration of antibiotic therapy are variable, ranging from 2 weeks after surgery to 6 months. Our protocol consists of 6 weeks parenteral antibiotic treatment followed by at least 6 weeks of oral antibiotics; we did not observe a relapse of infection during the study period.

Our study has a number of limitations. It is a single center retrospective review, which makes it vulnerable to collection bias and to potential inaccuracy in data collection, it was performed in a short period of time and there was small to a modest sample size and events. Furthermore, we excluded PGI involving the aorta owing to the loss of some patients to follow up. The choice of conduit depended on the surgeon's preference, which could cause selection bias. Despite these limitations, in our study we identified the most important clinical events, highlighted the importance of early detection of PGIshow our treatment outcome and potential risk factors.

Conclusions

PGI is a frequent complication associated with significant mortality and morbidity.To date, there is no consensusor randomized control trial about the best management algorithm of PGI. That graft preservation yielded good outcome in selected patients, and the biosynthetic prosthesis appears to be a promising alternative in the absence of an appropriate autologous conduit. There were statistically differences in female, diabetes , elevated WBC, End-stage renal disease and tissue loss from both groups

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