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ORIGINAL ARTICLE

Vascular Graft Infections: a Decade's Clinical Experience in Indian Population

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Abstract

Vascular graft infection with its morbidity and mortality has tormented the world of vascular reconstruction overlong. India despite carrying a sizable burden of patients requiring vascular reconstruction has minimal research on the subject. We attempted to chronicle clinical profiles, symptom variability, risk factors, prophylactic measures, and various therapeutic options extended to patients with vascular graft infection, in this medical record-based case series analysis, of a decade (years 2010–2020), of patients presenting with vascular graft infections. Statistical comparison was done with chi-square and Fisher's exact probability test. A total of 70 patients presented with vascular graft infection, 92.9% men and 7.1% women (mean age of 58 SD 11.8 years). Diabetes and coronary artery disease were the commonest comorbid conditions (24.7% each). The most common site of infection was the groin, and femoropopliteal bypass graft was the most infected segment (48.5%). The average time interval from index surgery to presentation with infection was 308 days. Early graft infection was seen in 60% patients, with extra-cavitary graft infections manifesting earlier than others. Local symptoms with discharging sinuses and cellulitis were common clinical presentations. *Staphylococcus aureus* was the commonest organism isolated (31.4%). A total of 58.5% patients underwent graft explantation and 40% were managed conservatively. Incidence of infection in patients who underwent immediate post-operative re-intervention was statistically significant when compared with Bunt's classification (P value < 0.05). The distribution of incidence of post-operative infection differed significantly across various sites and the type of graft material used (P value < 0.05). Prosthetic vascular grafts provide unparalleled benefit to a patient in maintenance of life and limb. Our Indian experience of a decade when summed up reflects that extra-cavitary graft infections express early and anatomical predisposition of the groin makes femoropopliteal segment the worst affected in VGI. Remote infections and re-interventions are hidden caveats of VGI. Apt to say that "Aegrescit medendo"—"the cure is worse than the disease"—holds good for vascular graft infections.

Keywords Peripheral arterial disease · Vascular graft infection · Prosthetic vascular grafts

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Introduction

Vascular graft infection (VGI) is an extremely vexatious condition that leads to a significant morbidity in patients undergoing vascular reconstruction. The morbidity associated with the condition is often more debilitating than the natural history of the primal vascular indication, making management of VGI a colossal task [1, 2].

The journey of prosthetic grafts has come a long way from the time Debakey together with Prof Thomas Edman developed a knitting machine to make seamless polyester (Dacron), way back in 1954 [3]. Despite the refinements in operative techniques, graft handling, and peri-operative sterilization techniques, VGI continues to haunt the surgical fraternity with an incidence of 0.2–6% [1, 4–8].

The study was formulated with the aim to chronicle clinical profiles, symptom variability, risk factors, prophylactic measures, and various therapeutic options extended to the patients of VGI, in the last decade at our center.

Methods

A patient medical record-based case series analysis was carried out, including all the patients who presented with VGI following a vascular reconstruction over a 10-year period, from the year 2010 to 2020. This included all patients with VGI operated for revascularization surgery at this center and also the ones received from other centers. Evaluation of the degree of infection was done by segregating the cohort using relationship to post-operative wound infection (Samson's classification) and the extent of graft involvement using Bunt classification (modified) [9, 10].

Infection was diagnosed by clinical evaluation, biochemical investigations supported with sonological examination, nuclear imaging (18F-fluorodeoxyglucose positron emission tomography–computed tomography (PET-CT)), and computed tomography angiography (CTA). Samples from the infected sites were obtained either indirectly (blood culture, culture from superficial wound/draining sinus) or directly (intra-operative tissue/graft biopsy and/or portion of infected explanted graft).

Statistical Data Analysis

The data on categorical variables is shown as *n* (% of patients), and the data on continuous variables is presented as mean and standard deviation (SD) or average. The inter-group statistical comparison of the distribution of categorical variables was tested using chi-square test or Fisher's exact probability test for 2 × 2 contingency table.

All the hypotheses were formulated using two-tailed alternatives against each null hypothesis (hypothesis of no difference) [11–13]. Statistical significance was defined as *P* value less than 0.05. The entire data was statistically analyzed using Statistical Package for Social Sciences (SPSS version 22.0, IBM Corporation, USA) for MS Windows.

Results

In our case series analysis spreading over a decade, a total of 70 cases were found to have VGI. The cohort comprised 65 (92.9%) men and 5 (7.1%) women. The mean age was 58 SD 11.8 years (age range 24–90 years). As the study population also incorporated patients received with established VGI from other institutes, reporting of a true incidence for this cohort was difficult.

Out of this cohort, 68.5% (*n* = 48) were smokers, while reformed smokers and non-smokers comprised 20% (*n* = 14) and 11.4% (*n* = 8), respectively. Coronary artery disease and diabetes mellitus II were identified as the commonest comorbidities with an incidence of 24.2% (*n* = 17) each, closely followed by hypertension in 22.8% (*n* = 16) patients. Immunocompromised conditions in the patients comprised chronic kidney disease (CKD), hepatitis C virus infection, and pulmonary tuberculosis in 5.7%, 4.2%, and 2.8% patients, respectively, either as a stand-alone disease or in conjugation with other comorbidities. The cohort had 30% patients (*n* = 21) with no comorbidities.

The biomaterial of the grafts used for revascularization in the infected cases were ePTFE in 81.4% (*n* = 57), Dacron in 15.7% (*n* = 11), and reversed saphenous vein bypass graft (RSVG) in 2.8% (*n* = 2) patients. Majority of infected vascular reconstructions were femoropopliteal bypasses, i.e., 48.5% (*n* = 34), including two RSVG. Patients with infected aortofemoral bypasses comprised 14.3% (*n* = 10) and those with infected iliofemoral bypasses comprised 15.7% (*n* = 11) of the cohort. Complex revascularization procedures like aortofemoral bypasses complimented with a distal femoropopliteal bypass were found infected in 7.1% (*n* = 5). Patients of CKD undergoing arteriovenous graft (AV) for hemodialysis access comprised 5.7% (*n* = 4). Carotid endarterectomy with prosthetic patch repair and carotid-subclavian bypass graft infection was seen in one patient, each. Groin was the most infected anatomical site (62.8% patients) (Table 1). A total of 20 patients (28.5%) had extremity ischemic ulcers pre-operatively and 50% (*n* = 10) of them required graft explantation.

The average time interval from last reconstructive vascular surgery to the patient reporting with graft infection was 308

Table 1 Incidence of vascular graft infection: (a) segment and (b) anatomical sites

(a) VGI as per the vascular segment involved	*n* (%)
Femoropopliteal bypasses	34 (48.5)
Aortofemoral bypass grafts	10 (14.3)
Iliofemoral bypass	11 (15.7)
Arteriovenous grafts	4 (5.7)
Axillofemoral bypasses	3 (4.2)
Aortofemoral with femoropopliteal grafts	5 (7.1)
Carotid endarterectomy with patch repair	1 (1.4)
Carotid-subclavian bypass	1 (1.4)
Femorofemoral bypass	1 (1.4)
(b) VGI as per the anatomical sites	*n* (%)
Groin	44 (62.8)
Thigh	20 (28.5)
Arm	4(5.7)
Neck	2 (2.8)

days, onset of infection varying between 2 and 1863 days. There were 15.7% (n = 11) patients who had a previous ipsilateral vascular reconstructive surgery.

On classifying the clinical presentation with respect to extent of wound infection (Samson classification), we found discharging groin sinuses and wound erythema with cellulitis as the commonest clinical presentations, with an incidence of 35.7% (n = 25) and 31.4% (n = 22), respectively. The extent of graft involvement (Bunt classification) revealed 61.4% (n = 43) of the grafts involved were non-cavitary (Table 2). Mass at the operated site, depicting a pseudoaneurysm, was observed in 10% (n = 7). One of the patients presented with a herald bleed. Other clinical presentations comprised a non-healing ulcer at the operated scar and wound hematoma. Doppler imaging (n = 21), CTA (n = 19), and PET-CT (n = 51) were the diagnostic modalities employed, PET-CT being the commonest with a standardized uptake value (SUVmax > 10) in the perigraft area, with linear and diffuse uptake and projection of the vessel as the most common findings (Fig. 1).

Microbiological evaluation revealed positive cultures for gram-positive bacteria. *Staphylococcus aureus* was the most prevalent organism, in 31.4% (n = 22), followed by *Pseudomonas* in 7.2% (n = 5) patients. The genetically distinct and feared strain of *Staphylococcus aureus*, methicillin-resistant *Staphylococcus aureus* (MRSA), was found in 5.7% (n = 4) patients. The infected RSVG bypasses grew gram-negative rod-shaped bacteria, *Klebsiella*. A total of 52.8% (n = 37) patients had no growth in their culture specimens. As an institutional protocol, all patients on diagnosis of VGI, irrespective of the bacterial ecology, were treated with broad-spectrum parenteral antibiotic agents, i.e., piperacillin/tazobactum 4.5 g IV q8 and vancomycin 1 g IV q 12 for gram-positive and gram-negative coverage, respectively. Pseudomonal infections were managed with third-generation cephalosporins, carbapenems, and levofloxacin. A combination of piperacillin/tazobactam and ticarcillin/clavulanic acid was used in some patients as it has shown an edge over cephalosporins in covering obligate anaerobes [14].

The patients who underwent some form of re-intervention in the immediate post-operative period (n = 22) usually presented with a VGI within an average of 9 months, mostly with a discharging groin sinus. Graft explantation was carried out for 17 such patients, and intraoperatively in all such patients, graft disincorporation was found. Extra-cavitary graft infection manifested early, whereas cavitary infections were seen later with a reported mean time of 34 months. Early graft infection (< 4 months) was observed in 60% (n = 42) patients, and amongst this subset, 57% patients (n = 24) underwent graft explantation, and 42.8% (n = 18) patients were managed conservatively [8].

The incidence of VGI differed significantly across various anatomical sites and the type of graft used (P value 0.011). Similarly, the distribution of incidence of immediate post-op complications differed significantly across the extent of graft involvement (Bunt's classification) in the study group (P value < 0.05) (Tables 3 and 4).

A total of 58.5% (n = 41) patients underwent graft explantation (Table 2). Conservative management comprising culture-based antibiotics, incision and drainage, and supportive wound care was offered to 40% (n = 28) patients. Graft repositioning was done in one patient. A total of 12.8% (n = 9) patients underwent amputation of the affected limb, including two patients who presented with class III acute limb ischemia and were offered upfront amputation of the affected extremity. The only mortality of the cohort was in a patient of disseminated tuberculosis who died because of complications of his comorbidity.

Table 2 Incidence of wound and vascular graft infection as per (a) Samson's and (b) modified Bunt's classification

(a) Samson's classification (extent of wound infection)	n (%)	Graft explantation (%)
Group 1: no deeper than the dermis	24 (34.2)	9 (37.5)
Group 2: subcutaneous tissue, no direct contact with the graft	29 (41.4)	18 (62)
Group 3: body of the graft but not anastomosis	8 (11.4)	5 (62.5)
Group 4: exposed anastomosis, no bleeding, no bacteremia	1 (1.4)	1 (100)
Group 5: anastomosis involved, bleeding, bacteremia	8 (11.4)	8 (100)
(b) Bunt's classification (extent of graft involvement)		
Peripheral graft infection		
P0: infection of the cavitary graft	12 (17.1)	6 (50)
P1: infection of a non-cavitary graft	43 (61.4)	23 (32.8)
P2: infection of the extra-cavitary part of a graft whose origin is cavitary	14 (20)	12 (85.7)
P3: infection of prosthetic patch angioplasty	1 (1.4)	0
Graft-enteric erosion	0	0
Graft-enteric fistula	0	0
Aortic stump sepsis after excision of infected graft	0	0

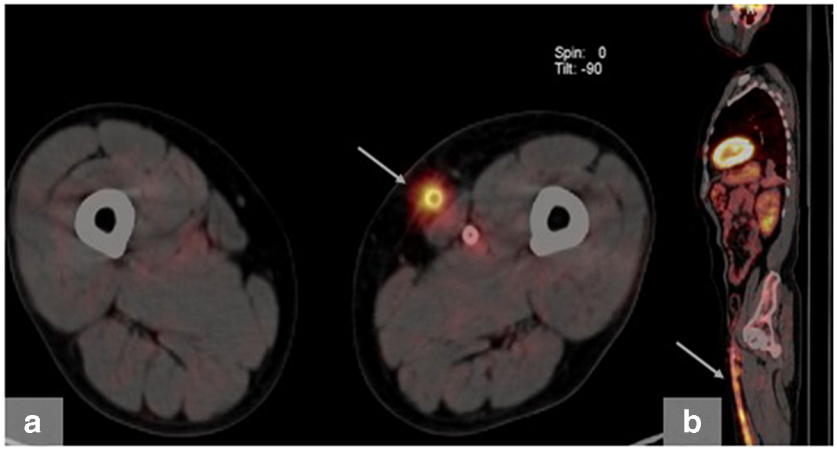

Fig. 1 18F-FDG PET-CT showing FDG avid uptake in the perigraft region of a left femoropopliteal graft suggestive of a graft infection: **a** axial plane and **b** sagittal plane (highlighted with the arrow)

Intraoperatively, vancomycin incorporated in calcium sulfate biodegradable beads was implanted into the hematoma cavity in four patients as part of a wound sterilization algorithm for treatment of extra-cavitary graft infection (Fig. 2). Flap coverage for the post-debridement exposed prosthetic graft (example: Sartorius muscle flap in the groin and omental patch cover in aortic grafts) was offered to 26% (n = 18), under culture-based antibiotic shield, and vein patch closure was done for the residual patent arteries. Infected aortofemoral bypass grafts with pseudoaneurysm, but no systemic signs of infection and adequate graft incorporation, underwent in situ prosthetic replacement of the infected graft limb.

Patients who had *Staphylococcus aureus* graft infection, including MRSA, presented early and 76% (n = 16) had to undergo prosthesis explantation. Patients who underwent conservative management were given 2 weeks of intravenous culture-based antibiotics followed by 4 weeks of oral regimen. Those who underwent graft explantation, with or without rescue extra-anatomical bypasses, were given an antimicrobial cover for 6 weeks.

Extremity amputation as a measure of limb and life-saving surgery was offered to 12.8% (n = 7) patients in the form of trans-femoral, trans-tibial amputation, and hip disarticulation in five, two, and two patients, respectively. These patients had presented within an average time period of 7 months from the date of last surgery, had a discharging sinus over the operated scar, and were elderly with a mean age of 60 years. However, no statistical correlation with remote infection was found.

Discussion

The presence of foreign body has been long known to increase bacterial infectivity in surgical fields [8]. Surgery itself by virtue of being a soft tissue trauma temporarily potentiates the bacterial inoculum, and a subcritical concentration of cocci can express enhanced infectivity [14]. This makes vascular surgery clientele, often with their underlying comorbidities an inherently high-risk group, where even a smaller infective microbial presence can proliferate on the inert surfaces of the graft materials. Szilagyi, in the year 1972, had forecasted that infection in a synthetic graft is such a disastrous complication that it would provoke the growth of a rather massive literature [15].

The observed gender composition of the study had a predilection for men, similar to those cited in the world literature [6]. Active smokers in this Indian cohort comprised mostly

Table 3 Distribution of incidence of VGI across various anatomical sites and graft material used

Anatomical site	Site-specific graft infection (%)	Graft material			Graft explantation			
		Dacron, *n* (%)	ePTFE, *n* (%)	RSVG, *n* (%)	Site-specific graft explantation, *n* (%)	Dacron	ePTFE	RSVG
Groin	44 (62.8)	6 (13.6)	38 (86.3)	0	27 (61.3)	4 (14.8)	23 (85.1)	0
Thigh	20 (28.5)	2 (10)	16 (80)	2 (10)	12 (60)	0	12 (100)	0
Arm	4 (5.7)	3 (75)	1 (25)	0	2 (50)	1 (50)	1 (50)	0
Neck	2 (2.8)	0	2(100)	0	0	0	0	0
P value		0.011*				0.105^{NS}		

P value by chi-square test (Fisher's exact probability test for 2 × 2 table). *P* value < 0.05 is considered to be statistically significant. **P* value < 0.05, *NS* statistically non-significant

Table 4 Distribution of incidence of VGI across extent of graft involvement (Bunt classification)

Extent of graft involvement	P0	6 (50)	6 (50)	0.026*
	P1	28 (65.1)	15(34.9)	
	P2	3 (21.4)	11 (78.6)	
	P3	0 (0)	1 (100)	

P value by chi-square test (Fisher's exact probability test for 2 × 2 table). *P* value < 0.05 is considered to be statistically significant. **P* value < 0.05, *ns* statistically non-significant

men, with an incidence higher than reported in most studies [16]. This incidence reflects the societies smoking pattern.

Majority of the clientele presenting for prosthetic vascular reconstruction had underlying comorbidities that predisposed them to graft infections. We noticed diabetes as an influential risk factor, with 61% of diabetics requiring graft explantation and presenting with a graft infection within an average of 9 months from the index surgery. Taking into consideration the low-risk threshold of Indians for diabetes, the authors hypothesize that the added burden of microangiopathy and leucocyte dysfunction in the Indian population can be ascribed as the culprit for the observed higher rates of morbidity [17, 18].

In our analyzed results, the foremost symptoms of graft infection were local, potentiating the dictum of regular inspection of the operated site and maintaining its sterility [1]. The most common anatomical site of VGI in our study was the groin which is the preferred approach in most patients with critical limb-threatening ischemia (CLTI) and carries an inherent risk of contamination due to its anatomical disposition (Table 1). This idea was accentuated on co-relating groin VGI with PET-CT where we observed that the infection did not show any extension beyond the level of the prosthetic limb shaft or to the proximal anastomotic site. On extrapolating, the spectrum of graft infections, standardized by Bunt in the year 1988, we found that a majority of our patients had infections in the extra-cavitary prosthetic grafts (Bunt classification: P1), mostly early graft infections, a finding less scrutinized in world literature [8, 10].

The clinical relevance of early and late graft infections has often been debated [1]. Our perusal of the time interval between the surgical intervention and presentation with graft infection revealed a wide range. It is noteworthy that the patients who required surgical re-intervention in the immediate post-operative period had an early onset of infection. In our study, 50% of cases presenting with early graft infection were successfully managed conservatively. The authors feel that this may be attributable to the limited extent of graft involvement, with most cases in Samson groups 1 and 2 (Table 2). This finding affords proof that not all infected grafts require explantation and the act to salvage a functional patent graft is justified to prevent complex revascularization surgery. Graft salvage however was most rewarding when managing portion of a thrombosed infected graft where the femoral artery was used as an inflow vessel, as any surgical adventure would have compromised collateral limb perfusion.

Microbiological spectrum of our cohort revealed a noteworthy share of negative bacteriological cultures. Inflow of patients from other institutes for management of VGI after being under antibiotic coverage seems like a plausible explanation. In consilience with the world literature, *Staphylococcus aureus* was the most prevalent organism [1, 8]. When co-relating outcomes with organisms involved, we found that despite being present in a small subset, MRSA's existence in grafts required graft explantation and one such affected extremity had to be amputated. The infected RSVG bypass is attributed to *Klebsiella*, considering its high virulence and tendency to destroy the vessel wall [19, 20].

Some of the findings of the present study suggest possibilities of a remote infection causing bacteremia, subsequently leading to graft infection, and the authors feel they deserve consideration. Such patients presented within 3 months of index vascular reconstruction surgery and 50% underwent graft explantation. Patients of CKD who presented with requirement of a prosthetic arteriovenous access usually had a hemodialysis access catheter in situ. If we put the theory of remote infection to test in these patients, all patients of CKD who developed VGI had a history of hemodialysis catheter in

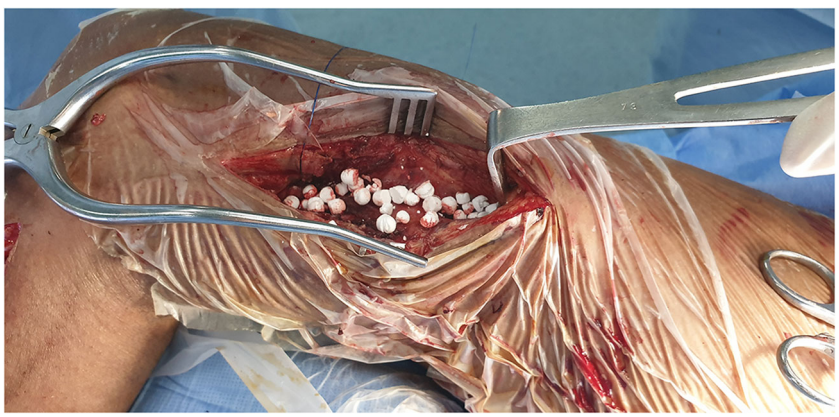

Fig 2 Vancomycin-incorporated beads implanted in the graft bed after graft explantation (highlighted with the arrow)

situ at the time of reconstructive vascular surgery. Patients who presented after a relatively pristine follow-up were attributed to hematogenous seeding of the graft following dental procedures or bacteremia. These findings potentiate the world opinion on this matter [1, 21].

Majority of the cohort with infected grafts in our study had undergone re-intervention in the post-operative period. The authors would like to postulate that circumstances of infection rather than the infective inoculum dose dictates the outcome.

Our institutional sterilization algorithm mandated staged debridement and antibiotic-loaded beads for graft bed sterilization [8, 22]. Vancomycin was our drug of choice for antibiotic-loaded beads (Fig. 2). Immediate sartorius muscle flap coverage was used as a part of in situ replacement or graft preservation in cases of graft exposure and repair. The indication for this type of usage is firm. Though not associated with complete elimination of re-infection risk, the use of the sartorius flap technique has shown promising results in complex groin wound restoration [23, 24].

Apart from the finding of VGI differing significantly across the anatomical site and type of graft material used, one of the most encouraging yields of this study was the statistically significant distribution of immediate post-operative complications across ascending grades of Bunt's classification communicating the fact that immediate post-operative complications are a direct function of increased chances of VGI.

Conclusion

Prosthetic vascular grafts provide unparalleled benefit to a patient in the maintenance of life and limb. Our Indian experience of a decade when summed up reflects that extra-cavitary graft infections express early and anatomical predisposition of groin makes femoropopliteal segment the worst affected in VGI. Remote infections and re-interventions are hidden caveats of VGI. Apt to say that "Aegrescit medendo"—"the cure is worse than the disease"—holds good for VGI.

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(f) Supervision: Vikram Patra and Rishi Dhillan

Compliance with ethical standards

Conflict of Interest The authors declare that they have no conflict of interest.

Consent to Publish Informed consent was obtained from all individual participants included in the study. The authors affirm that the participant provided informed consent for the publication of images in Figs. 1 and 2.

Ethical Approval Ethical approval was waived by the local ethics committee in view of the retrospective nature of the study and all the procedures being performed were part of the routine care.

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