

CLINICAL MANAGEMENT

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- 17 clinical data are identical with the clinical data of Russu2009 -

VASCULAR GRAFT INFECTIONS MANAGEMENT

Support paper for several PhD theses

Russu2009 (NOT mentioned)

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INTRODUCTION

Despite antibiotic prophylaxis and the development of more refined surgical techniques, microbial infection of the vascular prostheses are well known, not rare and redutable coplications.

The literature-reported incidence may vary between 0,2 and 5% and it is influenced by: the site of the implant, the underlying disease and the host defense mechanism.

Infection affects especially prosthetic grafts which are implanted during emergency procedures (for example emergency surgery for the ruptured abdominal aortic aneurysm) and prostheses anastomosed to the femoral artery or placed into an subcutaneous tunnel (for example the axillofemoral or axillobifemoral grafts).

Vascular graft infections are classified by their appearance time (early infections-which appear earlier than 4 months after graft implantation; late infections-which appear after 4 months), their relationship to the postoperative wound and the extent of graft involvement.

Szilagy's classification [2] is referring to the grades of postoperative's wound infection. So we have three grades,as follows:

- grade I: cellulitis involving wound;
- grade II: infection involving subcutaneous tissue;
- grade III: infection involving the vascular prosthesis.

An early infection correlates with a Szilagy grade III wound infection. These infections are caused by virulent hospital-acquired bacteria and present with sepsis signs like: fever, leukocytosis, bacteremia and easy-noticeable signs of an infected wound (inflamated tissues around it, pus emerging from it).

Late infections are a result of graft colonization by "low-virulence" organisms such as: Staphylococcus epidermidis or Candida spp. They are characterized by the fact that they are indolent and have no signs of sepsis and cultures of the perigraft tissues are not growing any germs.

IV.1. Pathogenesis of graft infection

The initiating event is the bacterial adherence to the biomaterial surfaces, followed by colonization and development of a bacterial biofilm that resist host defenses and antibiotic penetration.

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Introduction: Despite routine antibiotic prophylaxis and refinements in implantation technique, microbial infection of the vascular prosthesis can occur. Infection involving a vascular graft is difficult to eradicate. If not recognized or treated promptly, implant failure will occur by producing sepsis, hemorrhage or thrombosis. Management involves graft excision alone, graft preservation within the implant wound, in-situ graft replacement, or graft excision in conjunction with extra-anatomic bypass grafting.

Material and method: We retrospectively analysed the operative registers of our clinic as well as the regular archives, from 2000 until 2008, searching for reported graft infections which needed excisions and extraanatomical bypasses or for conservative therapy. There were 50 patients in this interval admitted and treated in Surgical Clinic No.1, out of a total of 950 vascular interventions. 10 of them were early graft infections (< 4 months), 40 were late ones (> 4 months).

Using Szilagy's classification, 10 were grade I, 17 were grade II and 23 grade III. We followed antibiotic prophylaxis protocols in all of the cases, prior to first vascular intervention. Staphylococcus aureus was the most prevalent pathogen (95%) found affecting our grafts.

Results: We performed 20 graft excisions for infrainguinal graft infections, with the removal of the entire graft, radical debridement of infected perigraft tissues, closure of the arteriotomies with monofilament suture and the administration of systemic and topical antibiotics. We attempted graft preservation in 3 cases of infrainguinal prosthetic bypass graft infection (with serial surgical wound debridement, coupled with antibiotic therapy, early muscle flap coverage and repeated wound cultures to identify any development of bacterial resistance or change in the microbial flora). We used the staged approach in 20 cases, beginning with drainage of the perigraft abscess, followed in 2 or 3 days by graft excision and autogenous vein grafting. We performed none in-situ replacements with Rifampin-bonded prosthesis, partly because they were not available until a few years. For the patients with infection localized to only a portion of an aortofemoral graft, we preferred, for the decreased morbidity, the excision of the infected portion of the graft (partial graft excision) and after solving the inguinal infection, a staged extra-anatomical bypass- in cases. As for the gold standard regarding the aortic graft- total graft excision and ex-situ bypass, we only performed 3 of them. 3 patients died and 2 required major amputation.

Conclusions: Dissatisfaction with the morbidity and the mortality of treating vascular graft infections, regardless of location, by total graft excision and remote bypass has been the impulse for the expanded application of lately performed in-situ bypasses or even for the prophylactic use of antibiotic-bonded grafts, in carefully selected cases.

Keywords: vascular graft, algorithm of evaluation, therapeutic solutions

The presence of a foreign body potentiates the infectivity of bacteria. Elek [1] and Cone demonstrated in 1957 that a single-braided silk suture significantly reduced the inoculum of staphylococci required to produce a local infection. The risk of foreign body infection can be predicted by the formula:

Risk of biomaterial infection = (Dose of bacterial contamination × virulence) / Host resistance

Bacterial adherence to polyester grafts is 10 to 100 times greater than to PTFE grafts. Gram-positive bacteria produce an extracellular glycoocalix made out of mucine which makes them much more adherent than, for example, Gram-negative ones.

Etiologic factors involved in graft colonization: perioperative contamination; bacteremia seeding of the biomaterial; mechanical erosion into bowel or genitourinary tract or through skin.

The risk factors for graft infection are:

1. Bacterial contamination of the graft (Faulty sterile technique; Prolonged preoperative stay; Emergency surgery; Extended operative time; Reoperative vascular procedure; Simultaneous gastrointestinal procedure; Remote infection; Postoperative superficial wound infection/skin necrosis/seroma/lymphocele).

2. Altered host defenses

Local factors (Biomaterial foreign body reaction: Bacterial slime producing a protective biofilm).

Systemic factors (Malnutrition; Leukopenia/ lympho-proliferative disorders; Malignancy; Corticosteroid administration; Chemotherapy; Diabetes mellitus; Chronic renal failure; Autoimmune disease).

IV.2 Prevention

Vascular infections can be minimized if some simple principles are applied:

- avoid a prolonged preoperative stay to minimize the development of skin flora resistant to commonly used antibiotics;
- have patients shower or scrub with an antibacterial soap the night before the operation;
- control the remote infections before an elective operation;
- remove operative site hair immediately before surgery using scissors rather than razors, to minimize skin trauma;
- protect vascular grafts from contact with contaminating sources, especially the exposed adjacent skin, using iodine-impregnated plastic drapes or antibiotic-soaked towels;
- avoid simultaneous gastrointestinal procedures during grafting;
- use prophylactic antibiotics whenever a graft or stent is implanted;
- longer duration of perioperative antibiotics (>48 hours) may be considered whenever patients present more than two risk factors for wound infection, including extremes of age, malnutrition, chronic illnesses such as diabetes, remote infections or prior irradiation of the surgical site.

Antibiotic prophylaxis protocols for vascular procedures are as follows:

- Cefazolin 1-2 g IV slowly prior to induction of anesthesia and repeated (1-2g) each 8 hours for 24-48 hours, or cefuroxime 1.5 g IV and each 12 hours for a total of 6 g; a single dose of cefazolin 1 g IV is recommended prior to endovascular stent implantation;
- When MRSA (methicillin-resistant Staphylococcus aureus) is cultured from body surfaces or is a known important pathogen in hospitalized patients, add vancomycin 1 g IV infused over 1 hour;
- If the patient has a cephalosporin allergy, give aztreonam 1g IV each 8 hours for 24 hours;
- If the patient has a vancomycin allergy, give clindamycin 900 mg IV over 20-30 minutes followed by 450-900 mg IV each 8 hours for 24 hours.

In some vascular centers, prophylactic antibiotics are continued for 3 to 5 days in patients being at high risk for infection from bacteremia, prolonged preoperative hospitalization or high institutional wound infection rates (>10%).

IV.3 Bacteriology

S. aureus is the most prevalent pathogen, one fourth of prosthetic infections being caused by it.

Lately, prosthetic infections caused by *S. Epidermidis* or Gram-negative bacteria have emerged.

This change in the microbiology of graft infections is the result of reporting both early and late infections and of surgeons becoming more aware of the false-negative microbiological results taken from many late infections, owed to the low bacteria numbers present within the graft surface biofilm.

Graft infections associated with negative culture results are caused by *S. epidermidis* or other coagulase-negative staphylococci, or by *Candida* species.

Infections due to Gram-negative bacteria as *E. coli*, *Pseudomonas*, *Klebsiella*, *Enterobacter* and *Proteus* spp are very virulent.

The incidence of anastomotic dehiscence and artery rupture is high and is due to the ability of these organisms to produce destructive endotoxins.

Fungal infections are very rare and most of the patients having them are immunosuppressed or have an established fungal infection elsewhere.

MRSA is responsible for one fourth of early graft infections, nowadays. This recent increase in MRSA graft infections may justify the use of specific antibiotic prophylaxis for all vascular implant procedures.

Infection diagnosis is reached upon clinical examination, microbiology findings and intraoperative aspects.

IV.4 Diagnosis

Clinical evaluation includes: patient history, physical examination and vascular imaging (arteriography, ultrasonography, contrast-enhanced CT, endoscopy).

IV.5 Therapy

Surgical therapy is mandatory, antibiotic therapy alone not being enough.

General principles of the overall management strategies:

Determining the extent of graft infection; ± removing the graft; Debridement of the arterial wall and perigraft tissues; Draining and antibiotic therapy.

The therapeutic options are: Graft excision without revascularization; Graft preservation; Excision + EAB [6]; Excision + in-situ replacement [8].

Calligaro and colleagues recommended specific criteria for selective graft preservation:

- patent graft that is not constructed of polyester (Dacron);
- anastomoses are intact and not involved in the infection;
- patient has no clinical signs of sepsis.

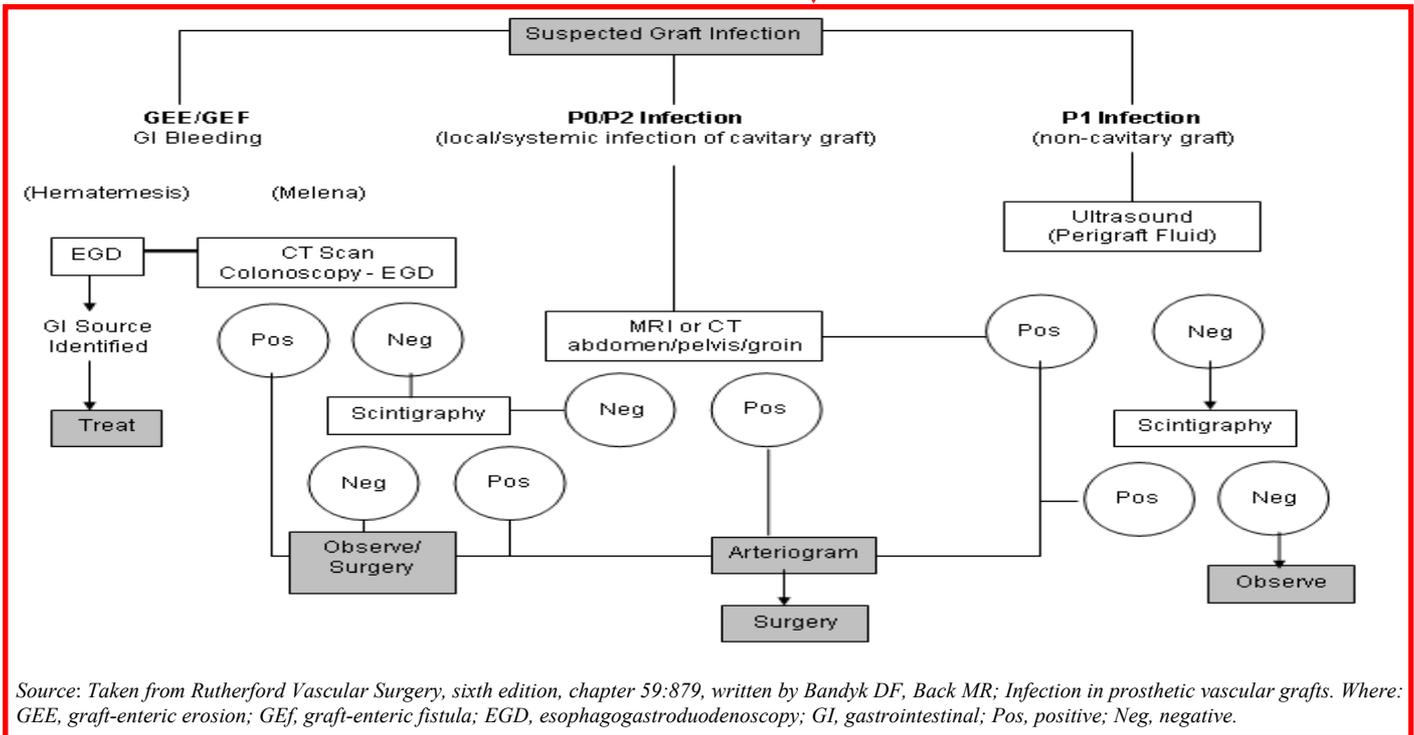
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coincident Figure with Table I from Russu2009

Algorithm for evaluation of a suspected prosthetic graft infection [3]



Treatment selection criteria for graft infection patients, considering their symptoms and the microbiological findings:

Treatment options	Clinical presentation	microbiology
Graft preservation [9]	Early infection and no sepsis	All except Pseudomonas
Excision alone	Graft thrombosis and adequate collaterals	Positive cultures
In-situ replacement - autogenous vein - allograft - Rifampin-bonded graft	- invasive garft infections without sepsis or GEE/GEF - invasive graft infections without sepsis and no suitable autogenous conduit - localized biofilm graft infections	- positive cultures - positive cultures - S. epidermidis
Excision and ex-situ bypass - simultaneous - staged [10] ⁰	- unstable patient with GEE/GEF - stable patient with aortic infection ± GEE/GEF	- no exclusion criteria - no exclusion criteria

Maneuvers associated to **graft preservation:**

- repeated and aggressive wound debridement in the operating room;
- daily wound dressing change at each 8 hours using dilute povidone-iodine solution (1ml of 1% povidone solution in 1 l saline solution);
- if wound is closed between serial wound debridement , antibiotic (vancomycin, tobramycin) – impregnated methylmethacrylate beds are implanted in the subcutaneous tissue;
- administration of culture-specific antibiotics;
- rotational muscle coverage [4] of the exposed prosthetic graft segment.

Referring to revascularisation, several RCTs demonstrated a decrease of morbidity and mortality for Staged treatment vs. Traditional graft excision associated to extra-anatomical procedures.

If a monophasic Doppler arterial signal is present at the ankle after graft excision or if arterial systolic pressure is greater than 40 mm Hg at the ankle or forearm, delayed reconstruction is an option because sufficient collaterals are present to maintain limb viability.

In the presence of critical limb ischemia signs, revascularisation shouldn't be delayed.

18 In- situ replacemnts using revolutionary matherials is probably the future in this field.



Selection criteria for in-situ reconstruction candidates:

- *Clinical criteria* (presentation months or years after graft implantation; no systemic signs of infection: afebrile, normal white blood cells count, sterile blood culture).
- *Anatomic* (inflammation of tissue adjacent to prosthetic graft; perigraft cavity with absence of graft incorporation; weakening of graft-artery anastomosis(pseudoaneurysm);
- *Microbiologic* (perigraft fluid Gram stain: white blood cells, no bacteria; perigraft fluid culture: no growth; graft biofilm culture: coagulase- negative staphylococci(S. Epidermidis).

Treatment components for these patients are:

- preoperative and perioperative administration of vancomycin- beginning 3 days prior to replacement;
- wide debridement of inflamed perigraft tissue;
- excision of anastomotic sites;
- cleansing/debridement of tissues and retained graft segment with wound irrigation system;
- replace with rifampin-soaked (60 mg/ml) polyester gelatin or collagen-impregnated polyester vascular prosthesis;
- muscle flap coverage of replacement graft segment in groin, if feasible;
- prolonged (6-week) parenteral administration of culture-specific antibiotics.

Prophylactic use of antibiotic impregnated grafts in patients at high infection risk does bring benefits.

big difference betw this value and the one from Russu2009

In order to summarize our center's experience, we analysed retrospectively the operative registries, from 2000 until 2008. 50 cases of graft infections were reported, out of a total of 950 vascular procedures.

Using Szilagyi's classification, 10 case were grade I infections, 17 were grade II and 23 grade III infections. 10 cases were early infections and 40 were late infections (>4-months after surgery).

We were not able to determine the impact of all risk factors, but the more common were, by far, Diabetes Mellitus (25%) and reoperative procedures(72%).

The most frequently infecting pathogen was S. aureus (growing out of cultures taken from the postoperative wound), but in the last year (2008) there was a significantly increase in the number of patients infected with S. epidermidis and Gram-negatives.

We reached the diagnosis after clinical evaluation, microbiology findings and sometimes after operative exploration.

Clinical evaluation was done as follows: patient history, physical examination, vascular imaging.

After reaching diagnosis and having taken material from the wounds, management was done using the principles exposed previously, using additional risk scoring systems for deciding which stable patients were at high risk for in-situ replacements.

We performed 20 graft excisions for infrainguinal infections with:

- removal of the whole graft;
- radical debridement of perigraft tissues;
- closing of the arteriotomies;
- antibiotic administration.

We tried to preserve the grafts in 5 cases of infrainguinal infections [5], using serial debridement in association with antibiotherapy and muscle flap coverage. Serial approach was used in 20 cases presenting perigraft collections, beginning with the drainage and followed after 2 or 3 days by graft excision and autogenous graft implantation.

We were unable to perform in-situ replacement using Rifampicin-impregnated prostheses, since we had none available.

In patients presenting with well-localised infections affecting only the end of an aorto-femoral graft, we preferred to perform excision of the terminal portion of the graft and, after healing of the tissues surrounding it, extra-anatomical revascularization [7].

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