Vascular Graft Infections (VGI): How to isolate the causative microorganisms, a proposal for a diagnostic work-up in aortic and peripheral vascular grafts

Prof. Pierre Tattevin, Infectious Diseases & ICU, Pontchaillou Univ. Hosp., Rennes, France
Disclosure of speaker’s interests

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<tr>
<th>(Potential) conflict of interest</th>
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<td>Potentially relevant company relationships in connection with event</td>
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<td>- Sponsorship or research funding</td>
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Epidemiology of vascular graft infections (VGI)

Microbiology
1. Samples (blood, surgical samples, serology)
2. Techniques (standard, 16S rRNA PCR, FISH)

Guidelines

Conclusions

Courtesy: Prof. Matthieu Revest, Rennes, France
PET (polyethylene terephthalate, Dacron®)

PTFE (polytetrafluoroethylene, Teflon® or Goretex®)

Chafké et al. Ann Chir 2004
Vascular graft infections (VGI): incidence

- Overall, 1.5%
  Litterature review, 2015: 1,914 / 126,649 vascular grafts (98 papers)
- Intra-cavitary VGI = 1%, aortic (abdomen 70%, thoracic 30%)
- Extra-cavitary VGI = 5%, groin 80%, or lower limb 20%

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Mechanisms of VGI

• Two main pathways
  - From contiguous focus of infection/colonization
    • Early, post-operative (within 2 months) = extra-cavitary
    • Late, from digestive tract (fistula) = cavitary
  - Hematogenous: rare
    • Vascular grafts quite resistant to pathogens adhesion (endothelialization)
    • The exception: Intrathoracic VGI involving the aortic root ↔ Endocarditis
**Diagnosis of VGI**

**Clinical**

- **Cavitary**
  - Fever, 75 %
  - Abdominal pain, 25 %

- **Extra-cavitary**
  - Fever, 50%
  - Local signs (pain, erythema, wound drainage, sinus tract), 75%

- **Both**: sudden onset of bleeding, or thrombosis, or emboli

**Median time from vascular graft to infection:**

- Extra-cavitary: **12 months** (1-27)
- Intra-cavitary: **51 months** (4.4-97)
Basic lab abnormalities in VGI

✓ Standard lab

Leucocytosis (25% of cases)
Elevated CRP (95-100%), but not specific (a tool to monitor treatment efficacy)

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Early PVGI (n = 49)</th>
<th>Late PVGI (n = 36)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>White blood count (/mm³)</td>
<td>13 030 ± 6711</td>
<td>9780 ± 3140</td>
<td>0.14</td>
</tr>
<tr>
<td>C-reactive protein (mg/L)</td>
<td>136 ± 79</td>
<td>94 ± 80</td>
<td>0.05</td>
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Microbiology of VGI

- **Blood cultures**
  - At least one positive: 25-40%
  - Largest prospective study: 34%

- **Organisms**:
  - *S. aureus*: 20-50%
  - Coag neg staph: 10-20%
  - Streptococci, enterococci: 15%
  - GNR (*P. aeruginosa* = 10%, *Enterobacteriaceae* 15%)
  - Polymicrobial: 20-30%

In patients with aortic graft, polymicrobial enteric bacteremia highly suggestive of enteric fistula (duodenum)
Blood cultures for diagnosis of VGI

• 25-40% positive (only) in large series of VGI

• **Blood cultures in 2019** (automated blood culture systems)
  – Two main determinants of BC yield
    • Adequate volume of blood (8-10 mL/bottle)
    • No previous antibiotic
  – Prolonged incubation, specific BC bottles => of limited interest

⇒ 6 bottles, 8-10 mL/bottle, before any antibiotic prescription
   + 2 bottles during or just after surgery
An extensive blood culture protocol, including prolonged incubation of cultures, for 215 patients believed to have had endocarditis yielded only 3 clinically relevant results. Twenty-four Haemophilus, Actinobacillus, Cardiobacterium, Eikenella, and Kingella (i.e., HACEK) organisms were recovered from standard 5-day blood cultures during the same time
Surgical samples (1)

- One paradigm: Surgery required for treatment of VGI!

- Basic principles of surgical sampling for VGI
  - Whenever possible, no anti bioprophylaxis
  - No swab (sub-optimal for anaerobic bacteria)
  - Collection / Pus => tube
  - Tissue (peri-prosthetic)
    - 3 distinct samples
  - Material (vascular graft)
    - n=3: Proximal anastomosis / distal anastomosis / intermediate
  - Transport: room temperature (20-25°C), < 2 h before processing

http://www.infectiologie.com/fr/actualites/infections-de-prothese-vasculaire_-n.html
Surgical samples (2)

• #1 = Standard microbiology
  – For solid samples (tissue / material)
    • Grind with water compatible with molecular biology
    • Sonication ?
  – Direct examination after Gram staining
  – Routine cultures, max 14 days, 35-37 °C

• Others
  – Histology of no interest (peri-prosthetic tissues / prosthesis)
  – 16S rRNA PCR, if standard cultures negative
    (NB. no interest if polymicrobial VGI)
  – multiplex PCR / FISH => research ongoing

http://www.infectiologie.com/fr/actualites/infections-de-prothese-vasculaire_-n.html
Other samples

- No sampling of superficial wounds, fistula, etc.
- No sampling from drainage collection recipient
- Q fever serology if risk factors
  - Local epidemiology
  - Contact with cattles / sheeps
Treatment and Prophylactic Strategy for *Coxiella burnetii* Infection of Aneurysms and Vascular Grafts

*A Retrospective Cohort Study*

**TABLE 1. Characteristics of Patients Diagnosed With C. burnetii Vascular Infections**

<table>
<thead>
<tr>
<th></th>
<th>Vascular Graft</th>
<th>No Vascular Graft</th>
<th>Total</th>
<th>P</th>
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<tbody>
<tr>
<td>Mean age</td>
<td>64.7</td>
<td>65.8</td>
<td>65.09</td>
<td>0.6</td>
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<tr>
<td>Male sex</td>
<td>53 (91.4%)</td>
<td>26 (92.9%)</td>
<td>79 (91.9%)</td>
<td>1</td>
</tr>
<tr>
<td>Type of graft</td>
<td></td>
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<tr>
<td>Aortic</td>
<td>51 (87.9%)</td>
<td>/</td>
<td>/</td>
<td></td>
</tr>
<tr>
<td>Nonaortic</td>
<td>7 (12.1%)</td>
<td>/</td>
<td>/</td>
<td></td>
</tr>
<tr>
<td>Surgery</td>
<td>20 (34.5%)</td>
<td>20 (71.4%)</td>
<td>40 (46.5%)</td>
<td>0.002</td>
</tr>
<tr>
<td>Total</td>
<td>58 (67.5%)</td>
<td>28 (32.5%)</td>
<td>86</td>
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Microbiological diagnosis of device-related biofilm infections

Fluorescence *in situ* Hybridization (FISH)

Fig. 4. FISH of a heart valve prosthesis from a patient with *Staphylococcus epidermidis* endocarditis. (A) Overview shows biofilms within the prosthesis material with the bacterial FISH probe EUB338 (95) (orange) and the nucleic acid stain DAPI (blue). Prosthesis material and tissue background appear in green. (B) Insert at higher magnification shows single FISH-positive cocci within the biofilm. Note the discriminative fluorescence intensity in orange indicating differential ribosomal content of the bacteria.

*Xu et al. APMIS 2017*
Medical treatment of prosthetic vascular graft infections: Review of the literature and proposals of a Working Group

M. Revest a,b, F. Camou c, E. Senneville d, J. Caillon e, F. Laurent f, B. Calvet g, P. Feugier h, M. Batt i, C. Chidiac j,*, Groupe de Réflexion sur les Infections de Prothèses vasculaires (GRIP) 1

• Multidisciplinary panel
  – ID physicians
  – Microbiologists (J. Caillon, F. Laurent)
  – Vascular surgeons

• Systematic literature review
Basic principles of antibiotics for VGI

- **Empirical treatment may be beneficial** (grade C, multidisciplinary decision)

- **Bactericidal** (preferably on biofilm ?)

- Active on staphylococci (including meticillin-resistant), and Gram negative (including *P. aeruginosa*)

- Good diffusion

- **Tolerability**
  - Comorbidities
  - High doses

Few days of ATB before surgery have a limited impact on microbiology documentation

Prospective monocentric standardized study
- 38/43 patients with positive per-operative samples if ATB initiated before surgery
- vs. 40/42 if no ATB (*P* = 0.4)

Legout et al. Clin Microbiol Infect 2011
Vascular Graft Infections, Mycotic Aneurysms, and Endovascular Infections
A Scientific Statement From the American Heart Association

Microbiology of PPM/ICD Infections (n=189)

- Culture negative: 7%
- Fungal: 2%
- Polymicrobial: 7%
- Gram negative bacilli: 9%
- Other Gram positive cocci: 4%
- Methicillin-resistant S. aureus: 4%
- Methicillin-sensitive S. aureus: 25%
- Coagulase-negative staphylococci: 42%

Figure 1. Microbiology of prosthetic vascular graft infections.
ICD indicates implantable cardioverter-defibrillator; and PPM, permanent pacemaker. Reprinted from Sohail et al15 with permission from the American College of Cardiology Foundation. Copyright © 2007, the American College of Cardiology Foundation.
Microbiological diagnosis of VGI: Conclusions

- **Complex**, and the **mistakes cost a lot**!  
  \[\Rightarrow\] requires **multidisciplinary team**, to be optimal from the start  
  (as much as complex bone & joint infections, or endocarditis)

- Blood cultures => documentation for one third of cases

- Superficial samples to be avoided

- **Surgical samples = the best tools**
  - Even in patients with previous ATB
  - Tissue (n=3), and material (n=3), if available
  - First = standard microbiology
  - 16S rRNA if standard microbiology negative

- **Q fever serology** if risk factors