Management of endovascular graft infections

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Agenda

- Introduction
- Cases
- Vasgra Cohort
- Diagnosis
- Treatment: Surgical treatment approach, Antimicrobial therapy
- PET/CT for treatment response
Background

Vascular graft infections are associated with a significant mortality and morbidity.

Femoropopliteal grafts: 4%

Aortic grafts: 0.5-2%

Hasse et al. Swiss Medical Weekly 2013
Aortic aneurysm: open surgery vs endovascular treatment
Aortic endograft are often used in patients who are unfit for open procedures.

Infection rate < 1%
### Economic consequences

<table>
<thead>
<tr>
<th>Implant</th>
<th>Implants Inserted in the U.S. Annually</th>
<th>Projected Infections of Implants Annually</th>
<th>Average Rate of Infection (†)</th>
<th>Preferred Practice of Surgical Replacement</th>
<th>Estimated Average Cost of Combined Medical and Surgical Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cardiovascular</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mechanical heart valve</td>
<td>85,000</td>
<td>3,400</td>
<td>4</td>
<td>1</td>
<td>50,000</td>
</tr>
<tr>
<td>Vascular graft ‡</td>
<td>450,000</td>
<td>16,000</td>
<td>4</td>
<td>1 or 2</td>
<td>40,000</td>
</tr>
<tr>
<td>Pacemaker-defibrillator</td>
<td>300,000</td>
<td>12,000</td>
<td>4</td>
<td>2</td>
<td>35,000§</td>
</tr>
<tr>
<td>Ventricular assist device</td>
<td>700</td>
<td>280</td>
<td>40</td>
<td>1</td>
<td>50,000</td>
</tr>
<tr>
<td>Orthopedic</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Joint prosthesis</td>
<td>600,000</td>
<td>12,000</td>
<td>2</td>
<td>2</td>
<td>30,000</td>
</tr>
<tr>
<td>Fracture-fixation device ‡</td>
<td>2,000,000</td>
<td>100,000</td>
<td>5</td>
<td>1 or 2</td>
<td>15,000</td>
</tr>
<tr>
<td>Neurosurgical — ventricular shunt</td>
<td>40,000</td>
<td>2,400</td>
<td>6</td>
<td>2</td>
<td>50,000</td>
</tr>
<tr>
<td>Plastic — mammary implant (pair)</td>
<td>130,000</td>
<td>2,600</td>
<td>2</td>
<td>2</td>
<td>20,000</td>
</tr>
<tr>
<td>Urologic — inflatable penile implant</td>
<td>15,000</td>
<td>450</td>
<td>3</td>
<td>2</td>
<td>35,000</td>
</tr>
</tbody>
</table>

Switzerland: 9 /100’000 persons hospitalized with vascular graft infection

Hospitalization costs 72’350 sFr (DRG)

Source: Swiss federal office of Statistics, 2013

Vascular graft infection: interaction microorganisms, host and prosthetic factors

Polyethylenterephthalate (Dacron®)
coated with gelatin or collagen
– Woven
– Knitted

Polytetrafluoroethylen (Gore-Tex®)
Blood-tight, smooth surface, prevents blood clots
Foreign bodys are devoid of microcirculation

### Synthetic material
- PET Polyethylenterephthalate (Dacron)
- PTFE Polytetrafluoroethylen (Gore-Tex)

### Biological material
- Animal Heterologous (Xenografts)
- Cryopreserved Homologous (Homograft)
- Cadaveric arteries
- Produced naturally Autologous (Autograft) in the body

Susceptibility to infection

University Hospital Zurich
Role of the biofilm

http://www2.binghamton.edu/biology/faculty/davies/research.htm
Typical organisms

*Staphylococcus aureus* 20-50%
*Coagulase negative Staphylococci* 15%
*Enterobacteriaceae* 14-41%
Anaerobes 5%
Fungi 1-2%

Polymicrobial infections 20%

Endograft infection

**Case #1 | 61-year-old male**

*2010 EVAR*

*06/2012 Fever, night sweats, belt-shaped abdominal pain; CRP 89 mg/L*

*07/2012 Dx of aortic endograft infection*

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CoNS, *S. agalactiae*
Criteria for vascular graft infections

- Positive bacterial culture of intraoperative specimens or blood samples
- Clinical signs of infection
- Biological signs of infection or other radiological signs of infection (perigraft air or fluid persisting for more than 8 weeks postoperatively, abscess)

FitzGerald et al; Journal of Antimicrobial Chemotherapy (2005) 56, 996–999
No treatment guidelines

Surgical treatment

Antimicrobial therapy
- Empirical therapy?
- Use of the same treatment approach for
  - Endovascular/ open surgery
  - Abdominal/ thoracic or peripheral vascular surgery
Duration unclear – how long is long enough?
Vascular graft cohort Study (VASGRA)

Prospective, observational cohort study, single centre, May 2013
Infectious Diseases specialists, microbiology, vascular surgery, radiology
Methodology

Prospective n=72
Systematic microbiological/histopathological work up
Use of PET/CT scan at diagnosis/ during follow-up

Microbiology
- Deep tissue cultures
- Broad range PCR
- Blood cultures
- Cultures of negative pressure wound therapy foams

Histopathology

PET/CT
- At diagnosis, during FUP, 3 month after stop of antimicrobial therapy
Risk factors
Postoperative wound complications are the most important risk factors for abdominal vascular graft infection

365 patients with 599 vascular grafts; 46 Prosthetic vascular graft infections Incidence 6 (95% 4-10) per 100 PYFUP

<table>
<thead>
<tr>
<th>Variable</th>
<th>Hazard Ratio</th>
<th>95% Confidence interval</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Endovascular operation</td>
<td>0.32</td>
<td>0.13-0.76</td>
<td>0.010</td>
</tr>
<tr>
<td>Postoperative wound infection</td>
<td>4.8</td>
<td>1.7-14</td>
<td>0.004</td>
</tr>
<tr>
<td>Other wound complications</td>
<td>1.8</td>
<td>0.71-4.8</td>
<td>0.209</td>
</tr>
<tr>
<td>Duration of operation in hours</td>
<td>1.2</td>
<td>1.0-1.3</td>
<td>0.012</td>
</tr>
</tbody>
</table>

Cox regression, MV Model

ESCMID eLibrary by author
Diagnosis
Diagnostic work-up: Broad range PCR adds to the diagnostic accuracy

<table>
<thead>
<tr>
<th></th>
<th>Culture negative</th>
<th>Culture positive</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>PCR negative</td>
<td>103</td>
<td>43</td>
<td>146</td>
</tr>
<tr>
<td>PCR positive</td>
<td>22</td>
<td>29</td>
<td>57</td>
</tr>
<tr>
<td>Total</td>
<td>125</td>
<td>72</td>
<td>197</td>
</tr>
</tbody>
</table>

Review of discordant samples:
PCR positive samples added to clinical diagnosis
Culture positive/PCR negative samples among isolates with low bacterial load/contaminants

Bloemberg G et al. unpublished
Bacterial cultures from NPWT foams do not improve diagnostics

Scherrer AU et al. submitted
FDG uptake in non-infected graft as a confounder for PET/CT scan

Diffuse FDG-uptake
No focal uptake
Intensity not changing over time
SUV 1.9 (0.4-6.3)

PET/CT scan is very accurate for vascular graft infections

Accuracy: 94%
No antibiotics: 100%

Treatment
Surgical treatment: Removal of the infected endograft

More proximal aortic cross-clamping than index surgery
Associated with high risk of operative complications or death, or both.

In-line reconstruction

Extraanatomic reconstruction

Surgical treatment and outcomes of aortic endograft infections

206 Endograft infections (180 EVAR; 26 TEVAR)
Surgical management: 96% patients after mean 153 days.
- 90% In situ replacement (cryopreserved allograft, neoaortoiliac system, abx-soaked prosthesis)
- 6% Axillary-bifemoral bypass
Outcome (mean FUP 21 month):
- 11% 30 day mortality, 30 % 1-year mortality, 35% 2-year mortality
- 15% Reinfections
New challenge for medical therapy
Endograft infection

More proximal aortic cross-clamping than index surgery
Associated with high risk of operative complications or death, or both.

Other surgical technique?
Graft preservation, debridement, negative pressure wound therapy (NPWT)

44 patients 30-d-Mortality 0%, 1-y-Mortality 16%

Endograft infection is a challenge for medical therapy

- No blood flow
- No vasa vasorum
- Antibiotics do not reach the thrombus/site of infection
- Biofilm acts as barrier against antibiotic penetration
Abdominal aortic graft infection - empirical therapy

- Coverage of Gram positive, Gram negative and Anaerobes
- Coverage of Methicillin resistant Staphylococci
- Bactericidal against bacteria in stationary growth phase
- Good tissue- and biofilm-penetration and safety profile

<table>
<thead>
<tr>
<th>Clinical situation</th>
<th>First line</th>
<th>Second line Allergy to penicillin</th>
</tr>
</thead>
<tbody>
<tr>
<td>PVGI without sepsis</td>
<td>Piperacillin/tazobactam + Vancomycin or Daptomycin + Gentamicin</td>
<td>Cefepime + Metronidazol + Vancomycin or Daptomycin + Gentamicin</td>
</tr>
<tr>
<td>PVGI with sepsis</td>
<td>Ceftazidim + Metronidazol + Vancomycin or Daptomycin + Gentamicin</td>
<td>Meropenem or imipenem + Vancomycin or Daptomycin + Gentamicin</td>
</tr>
</tbody>
</table>
Do we always need antibiotics in endograft infection?

VAC VeraFlo TM
Instillation of antiseptics
Do we always need antibiotics in endograft infection?
Type of microorganism influences surgical treatment and vice versa

Endovascular graft infections with barely no blood flow, withhold antibiotics in case of instillation
If graft retention/ NPWT therapy prolongation of therapy needed

Surgical excision of infected material and extraanatomic reconstruction recommended:
- *Pseudomonas aeruginosa*, MRSA, Rifampicin-resistant Staphylococci
- Fungi
- *Mycobacterium chimaera*
Case #2 | 61-year-old male

2014 EVAR (PTFE)

04/2015 Fever, night sweats, belt-shaped abdominal pain; CRP 65 mg/L

05/2015 Dx of aortic endograft infection

*Mycobacterium chimaera*  
*CoNS*
Healthcare-associated prosthetic heart valve, aortic vascular graft, and disseminated *Mycobacterium chimaera* infections subsequent to open heart surgery

Philipp Kohler¹, Stefan P. Kuster¹, Guido Bloemberg², Bettina Schulthess², Michelle Frank³, Felix C. Tanner⁴, Matthias Rössle⁵, Christian Böni⁶, Volkmar Falk⁷, Markus J. Wilhelm⁴, Rami Sommerstein¹, Yvonne Achermann⁴, Jaap ten Oever⁹, Sylvia B. Debast⁸, Maurice J.H.M. Wolfhagen⁸, George J. Brandon Bravo Bruinsma¹¹, Margreet C. Vos¹², Ad Bogers¹³, Annerose Serr¹⁴, Friedhelm Beyersdorf¹⁵, Hugo Sax¹, Erik C. Böttger², Rainer Weber¹, Jakko van Ingen¹⁶, Dirk Wagner¹⁷, and Barbara Hasse¹⁸

Extraanatomic reconstruction: axillobifemoral bypass
Treatment duration
Endograft infection

Case #3 | 70-year-old male
Belt-shaped pain in abdomen without fever
EVAR six weeks before…

Stationary aortic aneurysm (5.5 cm)
Focal FDG-uptake on graft, SUVmax12.4

Dx: Aortic graft infection

Coagulase neg Staphylococci
Monitoring of cancer therapy

Adeno-CA: cT1 pN3 cM0
05/2012

Cisplatin and Alimta
07/2012

Recurrence
11/2012
Vascular graft infection: Response of therapy with PET/CT is feasible

10/2012  11/2012  03/2013

06/2013  12/2013  03/2014

Stop antimicrobial therapy
Conclusions

Suggestions for treatment algorithms
Vascular graft infections qualifying for implant preservation

Vascular graft infection

Implant, anastomosis and soft tissue intact
- Preserve graft

Negative pressure wound therapy
- Flap ±

Implant, anastomosis not intact
- Remove parts risk

Prerequisites
- Condition of implant, anastomosis and soft tissue good
- Perioperative culture positive
- Susceptibility to antimicrobial agents with activity against surface-adhering microorganisms
Vascular graft infections not qualifying for implant preservation

Vascular graft infection

- High risk for surgery
  - Comorbidities
- Difficult-to-treat organisms
- Aortoenteric fistula
  - Tissue defect

Suppressive therapy

Extraanatomic reconstruction

In-situ reconstruction

Recommended
- Difficult to treat microorganisms
- Severely compromised tissue
- Comorbidities, Drug abuse (?)
Strategy antimicrobial therapy

Vascular graft infection

- SIRS
  - Delayed surgery
    - Start empirical therapy immediately
  - No SIRS
    - Immediate surgery
      - Await microbiology culture results
- Adapt antimicrobial therapy in accordance with deep tissue and blood culture
Length of antimicrobial therapy depends on surgical strategy

<table>
<thead>
<tr>
<th>Situation</th>
<th>iv</th>
<th>oral</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prosthetic material left in place Debridement, NPWT</td>
<td>6 weeks</td>
<td>6-12 month</td>
</tr>
<tr>
<td>Excision of infection site, extra-anatomic bypass</td>
<td>6 weeks</td>
<td>6 weeks</td>
</tr>
<tr>
<td>Excision of infection site, replacement by cryopreserved homograft</td>
<td>6 weeks</td>
<td>6 weeks</td>
</tr>
<tr>
<td>Infected autogenous vein grafts</td>
<td>2 weeks</td>
<td>4 weeks</td>
</tr>
<tr>
<td>No operation, conservative management</td>
<td>6 weeks</td>
<td>Suppressive therapy</td>
</tr>
</tbody>
</table>

171 patients (FUP 3.4), Healed 75%, Death due to PVGI 9.6 %
Dieter Mayer  
Vascular surgery

Annelies Zinkernagel  
Translational Research

Guido Bloemberg, Microbiologist  
Alexandra Scherrer, Statistics  
Zoran Rancic, Vascular surgery  
Mario Lachat, Vascular surgery

Lars Husmann  
Nuclear medicine

Simone Bürgin, Study nurse  
Marisa Kälín & Ulrich Matt, Infectious Diseases Service  
Rainer Weber, Infectious Disease Service  
Irene Burger & Bert-Ram Sah, Nuclear medicine

Caroline Müller  
Study nurse

Vontobel Foundation  
Rozalia Stiftung