Nuclear medicine and Prosthetic Joint Infections

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Orthopedic prostheses: world market 1996

- Prosthetic joint infections:
  - Uncommon complication (1 to 2%... 8% elderly)!!!!!!!

<table>
<thead>
<tr>
<th>Joint</th>
<th>Number</th>
</tr>
</thead>
<tbody>
<tr>
<td>Shoulder</td>
<td>24,000</td>
</tr>
<tr>
<td>Elbow</td>
<td>3,500</td>
</tr>
<tr>
<td>Hand/finger</td>
<td>2,000/500,000</td>
</tr>
<tr>
<td>Hip</td>
<td>730,000</td>
</tr>
<tr>
<td>Knee</td>
<td>410,000</td>
</tr>
<tr>
<td>Ankle</td>
<td>3,000</td>
</tr>
<tr>
<td>Toe</td>
<td>30,000</td>
</tr>
</tbody>
</table>
Overview

- Prosthetic joint infections:
  - Pathogenesis and microbiology
  - Risk factors
  - Clinical presentation
  - Diagnostic studies
  - Treatment (ABs and Surgery) and prevention
  - Conclusions

Pathogenesis

- Host defense
  - Glycoprotein layer
- Development of biofilm
  - Adherence of bacteria
  - Inhibition of antibiotics and leukocytes
- Contiguous spread (2/3)
  - Direct contamination
  - Trauma
- Hematogenous dissemination (1/3)
Microbiology

- Most common organisms:
  - Staphylococcus aureus (33%)
  - E. coli and Pseudomonas species (38% total)
  - Staphylococcus epidermidis (12%)
  - Enterococcus species (10%)

Microbiology

- Early Infections (<1 year postoperatively)
  - S. epidermidis
  - S. aureus
  - Streptococcus species
  - Gram negative bacilli (E. coli and Pseudomonas)
Microbiology

- Late Infection (>1 year postoperatively)
  - S. epidermidis
  - S. aureus
  - Gram-negative bacilli

Overview

- **Prosthetic joint infections:**
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Risk Factors

Host Factors:
- Advanced age
- Diabetes mellitus
- Malignancy
- Rheumatoid arthritis
- Sickle Cell
- Prior joint replacement

Intraoperative Factors:
- Oversized components
- Wound hematoma
- Conflicting skin incisions
Risk Factors

- Postoperative Factors:
  - Hematogenous dissemination
  - Skin ulceration

Overview

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Clinical Presentation

- Painful joint with swelling (90%)
- Warmth
- Erythema
- Fever
- Drainage
- Hypotension
- Sepsis

Overview

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Diagnosis

- **Gold Standard**: Joint aspiration or intraoperative specimen...
  - Aerobic and anaerobic cultures
  - Fungal and mycobacterium cultures

Diagnosis

- Laboratory Testing:
  - Elevated WBC
  - Elevated ESR (1/2 of all patients)
  - Elevated C-reactive protein
Diagnosis

- Imaging Studies:
  - X-rays
  - Bone scan (immediate, 15 min, 4 hr)
  - WBC scan
  - Colloid scan
  - FDG PET
Hip: Cemented versus cementless

- **Cemented prostheses** (PMMA): spreads forces over large surface
  - < 1 yr:
    - bone scan pattern variable
  - > 1 yr:
    - 80-90% of asymptomatic pts turn normal
    - ± 10-20%: ↑ uptake at the tip and gr trochanter
- **Cementless prostheses:***
  - More distal stress transfer
  - maybe abnormal > 2 years after surgery
  - > 3 yrs:
    - Simultaneous ↑ uptake at tip and lesser trochanter
    - Diffuse periprosthetic uptake
    - Increased bloodpool

Knee prostheses: bone scan

- Uncemented: Value of bone scanning?
  - Bone scan: moderate to high tibial uptake may persist for a long time (blood pool mild +)
  - High negative predictive value
- Asymp uncemented > 2yrs: baseline scan very useful
Nuclear medicine in the infected joint prosthesis

- **Bone scan**: broad screening for complication

  \(\Delta\Delta\) **septic** versus **aseptic** loosening **not possible** even with bloodflow

- **Increasing specificity for infection**
  - **BONE + Gallium-67**: accuracy 70-80%
    - Lacks specificity (<70%) \(\Leftrightarrow\) incidence of infection
  - **Labeled leukocytes** (In-111; Tc-99m HMPAO)?

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**Diagnosis**

- **Imaging Studies**:
  - X-rays
  - Bone scan (immediate, 15 min, 4 hr)
  - **WBC scan**
  - Colloid scan
  - FDG PET
Mechanisms of aseptic loosening in (un)cemented prostheses

- no polymorphonuclears!
- ΔΔ infectious loosening

HIP: Bone/leukocyte imaging

- Interpretation in combination with bone scan improves accuracy (Palestro et al, 1997);
  - « higher congruent uptake »
  - « incongruency »

- Wukich et al, 1987;
  - Johnson et al, 1988 (THP):
    - sensitivity ↓ (100%=>70%-88%),
    - specificity ↑ (35-50%=>80-95%)
Bone/leukocyte imaging

**Bone/leukocyte scan: why not so accurate?**

* Slow uptake process … low grade infections (lymphocytes, monocytes)
  importance of late (24 hr) imaging (sensitivity!)

* Distribution of bone marrow post surgery highly variable

« ectopic hematopoietic marrow »

**Importance of late imaging**

BONE  WBC 4 hr  WBC 24 hr
Diagnosis

- Imaging Studies:
  - X-rays
  - Bone scan (immediate, 15 min, 4 hr)
  - WBC scan
  - Colloid scan
  - FDG PET

Central skeleton
Leucocyte/marrow scan

- Congruent: no infection
- Discongruent: infection

Accuracy ranging from 89% to 98%

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Diagnosis

- Imaging Studies:
  - X-rays
  - Bone scan (immediate, 15 min, 4 hr)
  - WBC scan
  - Colloid scan
  - FDG PET
FDG PET(-CT) IMAGING IN INFECTED PROSTHESIS

Why need for other techniques?:
- Separating, labeling and re-injection of patient’s white blood cells
- Complex, time consuming
- Delayed imaging after 24 h

Use of 18F-FDG-PET in the diagnosis of endoprosthetic loosening of knee and hip implants
- N= 32, 74 components (44 knee, 30 hip endoprosthetic components)
- All underwent revision surgery at a later stage
- Endoprosthetic component was considered septic if the microbiological smear grew cultures

- Interpretation criteria according to other authors
  - Hip: unspecific: head and neck uptake, end of femoral stem
    pathologic: acetabular, bone-prosthesis interface of the stem
  - Knee:
    - unspecific: proximal prosthesis-bone interface, medial or lateral prosthesis-bone interface of tibial plateau
    - pathologic: distal prosthesis-bone interface of femoral shield, prosthesis-bone interface of stem of tibial prosthesis

Mayer-Wagner et al, Arch Orthop Trauma Surg, november 2009
FDG PET(-CT) IMAGING IN INFECTED PROSTHESIS

- Use of 18F-FDG-PET in the diagnosis of endoprosthetic loosening of knee and hip implants

**Table: Sensitivity, Specificity, Positive Predictive Value, Negative Predictive Value**

<table>
<thead>
<tr>
<th>PET in loosening</th>
<th>Sensi</th>
<th>Speci</th>
<th>PPV</th>
<th>NPV</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hip aseptic</td>
<td>80%</td>
<td>87%</td>
<td>86%</td>
<td>81%</td>
</tr>
<tr>
<td>Hip septic</td>
<td>75%</td>
<td>71%</td>
<td>75%</td>
<td>71%</td>
</tr>
<tr>
<td>Knee aseptic</td>
<td>56%</td>
<td>82%</td>
<td>64%</td>
<td>77%</td>
</tr>
<tr>
<td>Knee septic</td>
<td>14%</td>
<td>89%</td>
<td>50%</td>
<td>57%</td>
</tr>
</tbody>
</table>

Mayer-Wagner et al, Arch Orthop Trauma Surg, November 2009

FDG PET(-CT) IMAGING IN INFECTED KNEE AND HIP PROSTHESSES

FDG PET(-CT) IMAGING IN INFECTED PROSTHESIS

<table>
<thead>
<tr>
<th>Accuracy</th>
<th>HIP</th>
<th>KNEE</th>
</tr>
</thead>
<tbody>
<tr>
<td>BONE scintigraphy</td>
<td>80%</td>
<td>81%</td>
</tr>
<tr>
<td>WBC</td>
<td>91%</td>
<td>84%</td>
</tr>
<tr>
<td>FDG-PET</td>
<td>89%</td>
<td>83%</td>
</tr>
</tbody>
</table>

- Results of SUV values to discern septic from aseptic loosening are discouraging
- Use of CT in combination with FDG-PET in metallic implants?
- Advantages of PET: 1 injection, diagnosis within 4 hours, no blood manipulation, slightly lower accuracy than WBC, SENSITIVITY NOT INFLUENCED BY ANTIBIOTICS

Reinartz, Q J Nucl Med Mol Imaging 2009; 53:41-50 FDG-PET in patients with painful hip and knee arthroplasty: technical breakthrough or just more of the same

FDG-PET for diagnosing prosthetic joint infection: systematic review and meta-analysis

Table 3  Patient characteristics of included studies

<table>
<thead>
<tr>
<th>Study and year</th>
<th>Country</th>
<th>No. of patients</th>
<th>Mean age in years (range)</th>
<th>Sex (M:F)</th>
<th>No. of protheses</th>
<th>Age of protheses</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chrysikos et al. [12], 2008</td>
<td>USA</td>
<td>113</td>
<td>59 (31-87)</td>
<td>54:59</td>
<td>127 (H)</td>
<td>12, 18, and 24 months</td>
</tr>
<tr>
<td>Garcia-Barrachina et al. [13], 2007</td>
<td>Spain</td>
<td>24</td>
<td>68 (37-81)</td>
<td>12:12</td>
<td>24 (H)</td>
<td>6 months</td>
</tr>
<tr>
<td>Pill et al. [15], 2006</td>
<td>USA</td>
<td>89</td>
<td>NR (29-85)</td>
<td>NR</td>
<td>92 (H)</td>
<td>NR</td>
</tr>
<tr>
<td>Delenk et al. [17], 2006</td>
<td>Germany</td>
<td>27</td>
<td>NR (45-82)</td>
<td>NR</td>
<td>36 (H+K)</td>
<td>0.8-19.4 years (n=27); NR (n=9)</td>
</tr>
<tr>
<td>Reinartz et al. [19], 2005</td>
<td>Germany</td>
<td>63</td>
<td>68 (43-88)</td>
<td>32:31</td>
<td>92 (H)</td>
<td>1-31 years</td>
</tr>
<tr>
<td>Stumpe et al. [20], 2004</td>
<td>Switzerland</td>
<td>35</td>
<td>69 (46-89)</td>
<td>23:12</td>
<td>35 (H)</td>
<td>12-260 months</td>
</tr>
<tr>
<td>Chucko et al. [23], 2003</td>
<td>USA</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>53 (H+36)</td>
<td>NR</td>
</tr>
<tr>
<td>Vanquickenborne et al. [24], 2003</td>
<td>Belgium</td>
<td>17</td>
<td>NR (42-77)</td>
<td>8:9</td>
<td>17 (H)</td>
<td>2-163 months</td>
</tr>
<tr>
<td>Manthey et al. [27], 2002</td>
<td>Germany</td>
<td>23</td>
<td>70 (55-83)</td>
<td>9:14</td>
<td>14 (H=14K)</td>
<td>NR</td>
</tr>
<tr>
<td>Van Acke et al. [28], 2000</td>
<td>Belgium</td>
<td>21</td>
<td>66 (33-78)</td>
<td>8:13</td>
<td>21 (H)</td>
<td>7 months-9 years</td>
</tr>
<tr>
<td>Zhuang et al. [30], 2001</td>
<td>USA</td>
<td>62</td>
<td>NR (27-84)</td>
<td>NR</td>
<td>36 (H)+36 (K)</td>
<td>3 months-8 years</td>
</tr>
</tbody>
</table>

H hip prosthesis, K knee prosthesis, NR not reported

Kwee et al, EJNMI 2008;35:2122-2132
FDG-PET for diagnosing prosthetic joint infection: systematic review and metaanalysis

Kwee et al, EJNMI 2008;35:2122-2132

FDG-uptake patterns and clinical correlates in (hip) arthroplasty

by Mumme

by Reinartz
FDG PET VS BONE SCINTIGRAPH PATTERN I

FDG PET VS BONE SCINTIGRAPH PATTERN II
FDG PET VS BONE SCINTIGRAPH PATTERN V

FDG PET(-CT) IMAGING IN INFECTED PROSTHESIS

- No final conclusion in literature to diagnose septic from aseptic loosening in THR
- Pooled average sensitivity 84%, pooled specificity 84%
- Lower specificity than bone scintigraphy combined with leukocyte scintigraphy
- More accurate in hip than knee prostheses
- Difficult to differentiate between metal-wear induced chronic inflammatory and infectious processes seen around prostheses
- FDG uptake patterns need to be defined
FDG PET for prosthetic infections

false positive result: aseptic loosening of left total knee prosthesis on FDG PET (surgically proven); normal prosthesis at right side

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### Treatment

- I&D with systemic antibiotics (prosthetic salvage)
- Systemic antibiotics with removal of hardware and reimplantation
  - Immediate replacement (84% cure rate)
  - Delayed replacement (90%)
- Antibiotics plus permanent removal of hardware
- Joint arthrodesis after removal of components
- Amputation
- Antibiotic therapy

### Prevention

- Preoperative
  - Host factor optimization
  - Surgical antibiotic prophylaxis
- Perioperative
  - Wound hemostasis
  - Decreased operative time
  - Proper prosthetic size
  - Incision placement
- Postoperative
  - Wound care
  - Prevention of bacteremia
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Conclusions

Nuclear Medicine strategy dependent on clinical question:

Question: COMPLICATION?
- 3F bone scan reasonable strategy

Question: INFECTION?
- Leukocyte scan (24 hrs!)
  - if any periprosthetic uptake proceed with
- Marrow scan (sulfur colloid)