Bacterial adherence in infected arthroplasties: material differences

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Increasing importance of implant-related infection

- Increasing numbers of TJR
- Increasing numbers of infected

TJR (TKR: 1.5-3%; THR: 1-2%)

Table 1: Clinical and Economic Consequences of Infections-Associated with Surgical Implants

<table>
<thead>
<tr>
<th>Infections</th>
<th>Implants Removed (n)</th>
<th>Infections (n)</th>
<th>Average Age (y)</th>
<th>Estimated Average Cost (Surgical, Hospital and Implant)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infections Associated</td>
<td>403,000</td>
<td>15,000</td>
<td>63</td>
<td>10,000,000</td>
</tr>
<tr>
<td>Bacteremia</td>
<td>403,000</td>
<td>15,000</td>
<td>63</td>
<td>10,000,000</td>
</tr>
<tr>
<td>Staphylococcus aureus</td>
<td>403,000</td>
<td>15,000</td>
<td>63</td>
<td>10,000,000</td>
</tr>
<tr>
<td>Staphylococcus epidermidis</td>
<td>403,000</td>
<td>15,000</td>
<td>63</td>
<td>10,000,000</td>
</tr>
<tr>
<td>Total</td>
<td>606,000</td>
<td>31,000</td>
<td>63</td>
<td>30,000,000</td>
</tr>
</tbody>
</table>

Kurtz et al., 2008

Dariouche et al., 2004
Implant-related infection

Mechanism of implant-related infection:
- Biomaterials may decrease the immune system efficacy
- Implant surface bacterial adherence:
  - Early reversible inespecific adherence
  - Late irreversible adherence:
    - Class II: inespecific bonds
    - Class III: adhesin-receptor bonds
    
    Gristina et al., OCNA 1991; Garvin et al., JBJS 1995
  - Implant colonization leads to infection (“race for the surface”): adherence followed by biofilm formation.

Orthopaedic biomaterials and implants may facilitate or impede infection.

Biomaterial infection in Orthopaedics

- Limited information available about susceptibility to infection in orthopaedic biomaterials.
  - PMMA: more infection than PE, SS, CrCo. (Petty et al., JBJS-A- 1985)
  - PMMA: more infection than CrCo and Ti. (Cordero et al., JOR 1996)
  - Metals: porous coating increases surface and infection (more than polished, more in CrCo than Ti). (Cordero et al., JBJS-Br- 1994)
  - More cytotoxicity (Co, Ni), more infection.
  - More biocompatibility (Ti, Cr, Mo), less infection.
  - Hydrophobicity increases bacterial adherence (Donlan et al., Clin Inf Dis 2001)
- Yet clinical decisions (i.e. PE exchange) are based on pretended differential infectibility.
Aims of the study

- To isolate the adherent microorganisms in retrieved implants from patients with infected joint replacements.
- To quantify those obtained from each component of infected total hip and knee prosthesis after selective sonication of the parts.
- To analyze the differential bacterial adherence to the each of the retrieved parts in each infected joint.

Material

- 87 total joint components (51 hip and 36 knee components)
- From 32 patients (20 hip and 12 knee arthroplasties)
- With clinical diagnosis of implant-related infection

- Components under study included:
  - 6 femoral heads
  - 14 femoral stems
  - 14 metal cup shells
  - 13 acetabular liners
  - 9 femoral knee components
  - 4 patellas
  - 11 tibial trays
  - 12 tibial polyethylene

- Predominant material in the component surface was CrCo in 33, UHMWPE in 27, HA in 17 (5 fully coated), Ti alloys in 10.
Methods

● Retrieval study protocol:
  • Sonication of separated components after surgical retrieval (previously published protocol, Esteban et al., JCM 2008).

● Microbiological study and quantification:
  • Culture was positive in 75 of the 87 components (all of them from infected joints), and 12 showed more than one microorganism.
  • A ratio of UFC per mm² of the implant surface was obtained to compare components.
Methods

- Implant measurement and categorization:
  - 6 retrieved joint implants (total 24 components) scanned using a Picza 3D Laser Scanner LPX-60 (Roland DG Corporation, Japan).
  - 3D point cloud data converted into polygon meshes using Dr. PICZA3 software for further file conversion and analysis.
  - Measurements (in mm²) obtained with PixformTM Pro software.

Statistical analysis

- Considering the event of bacterial adherence an independent effect, descriptive and comparative (Kruskal-Wallis, Mann-Whitney, Chi square tests) statistics were used (CFU/mm² variables did not follow a normal distribution in the Kolmogorov-Smirnov test).

- Mixed linear models with random effects:
  - The patient is considered the random effect.
  - For both TKA and THA components and for each of them, the models are adjusted for the number of CFU/mm²
  - Fixed effects being the component and the material
**RESULTS**

- Microbiological descriptive analysis on microorganisms:

<table>
<thead>
<tr>
<th>Microorganism</th>
<th>Mean ±SD CFU/mm²</th>
<th># components /patients</th>
<th>Polimicrobial cultures</th>
<th>Hips/Knees</th>
<th>Most freq inf</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>S. epidermidis</strong></td>
<td>2.67±3.73</td>
<td>23/9</td>
<td>7/23</td>
<td>21Hips/2Knees</td>
<td>HA(9)</td>
</tr>
<tr>
<td><strong>S. aureus</strong></td>
<td>5.04±5.43</td>
<td>10/4</td>
<td>2/10</td>
<td>6/4</td>
<td>PE(4)</td>
</tr>
<tr>
<td>P. aeruginosa</td>
<td>0.21±0.21</td>
<td>5/2</td>
<td>1/5</td>
<td>1/4</td>
<td>CrCo(3)</td>
</tr>
<tr>
<td>R. picketti</td>
<td>3.06±4.83</td>
<td>4/3</td>
<td>0/4</td>
<td>0/4</td>
<td>CrCo(3)</td>
</tr>
<tr>
<td>K. pneumoniae</td>
<td>1.55±1.47</td>
<td>4/1</td>
<td>0/4</td>
<td>0/4</td>
<td>PE(2)</td>
</tr>
<tr>
<td>S. lugdunensis</td>
<td>4.51±5.33</td>
<td>4/1</td>
<td>2/4</td>
<td>4/0</td>
<td>CrCo(2)</td>
</tr>
<tr>
<td>E. aerogenes</td>
<td>2.97±5.7</td>
<td>4/1</td>
<td>0/4</td>
<td>4/0</td>
<td>All</td>
</tr>
<tr>
<td>H. kunzi</td>
<td>7.67±6.76</td>
<td>3/1</td>
<td>0/3</td>
<td>0/3</td>
<td>CrCo(2)</td>
</tr>
<tr>
<td>Burkholderia sp.</td>
<td>1.21±1.55</td>
<td>2/2</td>
<td>0/2</td>
<td>2/0</td>
<td>Ti(2)</td>
</tr>
<tr>
<td>E. coli</td>
<td>0.06±0.05</td>
<td>2/1</td>
<td>0/2</td>
<td>2/0</td>
<td>Ti + PE</td>
</tr>
<tr>
<td>Pasteurella sp.</td>
<td>5.09</td>
<td>1/1</td>
<td>0/1</td>
<td>0/1</td>
<td>CrCo(1)</td>
</tr>
<tr>
<td>P. acnes</td>
<td>0.05</td>
<td>1/1</td>
<td>0/1</td>
<td>1/0</td>
<td>PE(1)</td>
</tr>
<tr>
<td>M. abscessus</td>
<td>0.01</td>
<td>1/1</td>
<td>0/1</td>
<td>1/0</td>
<td>CrCo(1)</td>
</tr>
<tr>
<td>G- Anaerobic Bacillus</td>
<td>11.54</td>
<td>1/1</td>
<td>0/1</td>
<td>1/0</td>
<td>CrCo(1)</td>
</tr>
</tbody>
</table>

**RESULTS**

- Microbiological descriptive analysis on infections with one component without adherent microorganisms:

<table>
<thead>
<tr>
<th>Patient #</th>
<th>Hip / Knee</th>
<th>Part/material with negative culture</th>
<th>Microorg. other parts, same Px</th>
<th>CFUs/mm² other parts, same Px</th>
<th>Major adherence part / material in same Px</th>
</tr>
</thead>
<tbody>
<tr>
<td>12</td>
<td>Hip</td>
<td>Shell/HA</td>
<td>S. epidermidis</td>
<td>0.01</td>
<td>Stem/HA</td>
</tr>
<tr>
<td>18</td>
<td>Hip</td>
<td>Stem/HA</td>
<td>S. epidermidis</td>
<td>0.14</td>
<td>Shell/HA</td>
</tr>
<tr>
<td>29</td>
<td>Hip</td>
<td>Liner/UHMWPE</td>
<td>Burkholderia sp.</td>
<td>2.30</td>
<td>Shell/Ti</td>
</tr>
<tr>
<td>83</td>
<td>Knee</td>
<td>Tib surf/UHMWPE, fem comp /CrCo</td>
<td>S. epidermidis</td>
<td>0.16</td>
<td>Tibial tray/CrCo</td>
</tr>
<tr>
<td>100</td>
<td>Hip</td>
<td>Stem/CrCo</td>
<td>M. abscessus</td>
<td>0.01</td>
<td>Shell/CrCo</td>
</tr>
<tr>
<td>109</td>
<td>Hip</td>
<td>Fem head/CrCo, liner/UHMWPE</td>
<td>G- anaerobic bacillus</td>
<td>11.54</td>
<td>Stem/CrCo</td>
</tr>
<tr>
<td>113</td>
<td>Knee</td>
<td>Tib surf/UHMWPE</td>
<td>Pasteurella sp.</td>
<td>5.09</td>
<td>Tibial tray/CrCo</td>
</tr>
<tr>
<td>124</td>
<td>Knee</td>
<td>Tibial tray/CrCo, tib surf/UHMWPE</td>
<td>S. epidermidis</td>
<td>0.05</td>
<td>Fem comp/CrCo</td>
</tr>
<tr>
<td>135</td>
<td>Knee</td>
<td>Tib surf/UHMWPE</td>
<td>R. picketti</td>
<td>10.17</td>
<td>Tibial tray/CrCo</td>
</tr>
<tr>
<td>137</td>
<td>Knee</td>
<td>Fem comp/CrCo, patella/UHMWPE</td>
<td>E. coli</td>
<td>0.1</td>
<td>Tibial tray/CrCo</td>
</tr>
<tr>
<td>140</td>
<td>Knee</td>
<td>Fem comp/CrCo, tib surf/UHMWPE</td>
<td>R. picketti</td>
<td>2.03</td>
<td>Tibial tray/CrCo</td>
</tr>
<tr>
<td>141</td>
<td>Knee</td>
<td>Fem comp/CrCo, tib surf/UHMWPE</td>
<td>R. picketti</td>
<td>0.03</td>
<td>Tibial tray/CrCo</td>
</tr>
</tbody>
</table>
RESULTS

- NOT INFECTED COMPONENTS IN INFECTED JOINTS:
  - CrCo: 7 (at risk: 33)
  - UHMWPE: 9 (at risk: 27)
  - HA coated: 2 (at risk: 17)
  - Ti: 0 (at risk: 10)

- When studying independently the adherence of microorganisms to infected joint prosthetic components:
  - The presence of positive culture was different among materials (p=0.025, Chi square).
  - Significant differences were found in the adhered CFU/mm² among components (p=0.018) and materials (p=0.005).
  - Lower adherence to UHMWPE than to Ti (p=0.001), but not to CrCo or HA.
  - Lower adherence to CrCo than to Ti (p=0.008).
RESULTS

- When studied mixed linear models with random effects:
  - the patient with his/her infection as a random effect
  - Either the adherence to a biomaterial as a fixed effect (in both the hip and the knee, or in the hip, or in the knee)
  - Or the adherence to a component as a fixed effect (in both the hip and the knee, or in the hip, or in the knee)

All 6 models completed the convergence criteria (p=0.000)

None of them reached significance in the association of a fixed effect (material or component) to the random effect (each infection in a particular patient with a particular microorganism).

Discussion and conclusions

- Similar risk of adherence to different biomaterials in an infected joint.
- The main determinant of the microorganism adherence is the particular infection in a particular patient. Patient and microorganism are the leading factors of infection, and differences among biomaterials are secondary factors.
- No clinical confirmation that polymer infection is higher than metal, as classically studied in animal experiments.
- No rationale of exchanging one particular component alone if a joint is infected (i.e. polyethylene selective exchange).
- Complex models, where the infection of a particular patient by a particular microorganism is the independent variable, with large number of infected joints are required to clarify the relative and moderate role of a particular biomaterial.
Nothing to disclose.

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