Heterotopic Ossification, Is it Clinically Relevant? Clinical Implications and Risk Factors after Cervical Total Disc Replacement at 7-Years

David Cavanaugh, MD; Pierce D. Nunley, MD; Eubulus J. Kerr, III, MD, Andrew Utter, MD, Peter Campbell, MD, Kelly Frank, MS, Marcus B. Stone, PhD

Spine Institute of Louisiana, Shreveport, LA

Disclosure:

D. Cavanaugh: None
Introduction

- Heterotopic ossification (HO) can occur after treatment with cervical disc arthroplasty (CDA).
- HO can limit the motion of the treated segment, with more severe cases resulting in complete ankylosis.
- Risk factors and effects on clinical outcomes associated with HO are not well understood.
- Here we aim to:
  - Assess the prevalence and progression of HO in patients treated with CDA seven years after surgery.
  - Determine if HO is associated with diminished clinical outcomes seven years after surgery.
  - Evaluate potential risk factors associated with HO development.
Methods

- Multi-center, prospective, randomized, concurrently controlled, FDA IDE clinical trial.
  - Investigational treatment: CDA
  - Control: ACDF with anterior plate and allograft bone

- 389 Randomized patients:
  - One-Level: 164 CDA
  - Two-Level: 225 CDA

- CDA patients with data at seven years: 75.7%

HO grades 3 and 4 are classified as clinically relevant (CR) due to restricted ROM.

- Grade 0
- Grade 1
- Grade 2
- Grade 3
- Grade 4

Outcomes

- Preoperative patient characteristics:
  - Age
  - Gender
  - BMI
  - Clinical and radiographic measures

- Radiographic outcomes:
  - HO (McAfee and Mehren Classification)
  - Flexion/extension range of motion (ROM)

- Clinical Outcomes:
  - Neck Disability Index (NDI) score
  - Visual Analog Scale (VAS) for neck pain
  - Short-form 12-item Physical Component Score (SF-12 PCS)
  - Patient Satisfaction
At 7 years, 28.7% of 1-level patients had Grade 3 or 4 HO.

At 7 years, 37.4% of 2-level patients had Grade 3 or 4.
At 7 years, 23.3% of Superior Segments had Grade 3 or 4 HO.

At 7 years, 31.7% of Inferior Segments had Grade 3 or 4 HO.
## Logistic Regression Model

<table>
<thead>
<tr>
<th>Variables</th>
<th>Odds Ratio</th>
<th>95% CI [LB, UB]</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (year)</td>
<td>1.02</td>
<td>[0.95, 1.1]</td>
<td>0.57</td>
</tr>
<tr>
<td>Follow-up Visit (years)</td>
<td>2.59</td>
<td>[2.3, 2.9]</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>Gender (male)</td>
<td>12.66</td>
<td>[3.30, 48.6]</td>
<td>0.0002</td>
</tr>
<tr>
<td>Obese (BMI ≥ 30)</td>
<td>2.68</td>
<td>[0.72, 10.0]</td>
<td>0.14</td>
</tr>
<tr>
<td>Endplate Coverage (%)</td>
<td>0.96</td>
<td>[0.89, 1.04]</td>
<td>0.31</td>
</tr>
<tr>
<td>Levels Treated (two)</td>
<td>0.28</td>
<td>[0.08, 1.03]</td>
<td>0.06</td>
</tr>
<tr>
<td>PreOp ROM (degree)</td>
<td>0.95</td>
<td>[0.85, 1.06]</td>
<td>0.37</td>
</tr>
<tr>
<td>PreOp VAS Neck Pain (score)</td>
<td>1.03</td>
<td>[1.0002, 1.06]</td>
<td>0.048</td>
</tr>
<tr>
<td>PreOp Disc Height (mm)</td>
<td>1.17</td>
<td>[0.61, 2.23]</td>
<td>0.64</td>
</tr>
</tbody>
</table>
## Mixed Effects Cox Proportional Hazards Model

<table>
<thead>
<tr>
<th>Variables</th>
<th>Hazard Ratio</th>
<th>95% CI [LB, UB]</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (year)</td>
<td>1.02</td>
<td>[0.99, 1.05]</td>
<td>0.27</td>
</tr>
<tr>
<td>Gender (male)</td>
<td>2.95</td>
<td>[1.73, 5.06]</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>Obese (BMI ≥ 30)</td>
<td>1.68</td>
<td>[1.004, 2.81]</td>
<td>0.048</td>
</tr>
<tr>
<td>Endplate Coverage (%)</td>
<td>0.95</td>
<td>[0.91, 0.98]</td>
<td>0.004</td>
</tr>
<tr>
<td>Levels Treated (two)</td>
<td>0.51</td>
<td>[0.30, 0.86]</td>
<td>0.012</td>
</tr>
<tr>
<td>PreOp ROM (degree)</td>
<td>0.95</td>
<td>[0.90, 1.01]</td>
<td>0.08</td>
</tr>
<tr>
<td>PreOp VAS Neck Pain (score)</td>
<td>1.02</td>
<td>[1.004, 1.03]</td>
<td>0.008</td>
</tr>
<tr>
<td>PreOp Disc Height (mm)</td>
<td>1.15</td>
<td>[0.86, 1.53]</td>
<td>0.35</td>
</tr>
</tbody>
</table>
Summary & Conclusions

- Results from the largest study to analyze and report HO rates, outcomes, and risk factors.

- Potential risk factors identified here for HO include:
  - Male gender
  - Obesity
  - Endplate coverage
  - Levels treated
  - Pre-op VAS neck pain scores

- Patient outcomes remain unaffected by clinically relevant HO through 7 years.

- Clinically relevant HO should be more accurately described as motion restricting HO.