Increased Risk Of Revision After ACLR With Soft Tissue Allograft Compared To Hamstring Autograft

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ISAKOS
June 6, 2015
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- We have no potential conflicts with this presentation.
- IRB approval was obtained for this investigation.
Background

- Despite years of study, controversy still exists regarding the ideal graft for anterior cruciate ligament reconstruction (ACLR).
- Allograft use is increasingly popular in the US having exceeded 40% in some large hospital and group settings.\(^1,2\)
- Summary studies have reported autografts have better stability and lower revision rates than allografts\(^3-6\) but others report no difference.\(^7-9\)
- Two meta-analyses limited their cohorts to comparing autograft and non-irradiated allograft tissue and reported no differences in outcomes.\(^10,11\)
- One meta-analysis compared hamstring autograft and soft tissue allografts and also found no difference.\(^12\)
- Yet several large cohort studies have reported a 2-4 x higher risk of graft failure when allograft is used.\(^13-16\)
Background

- The lack of clarity regarding graft performance is due to two primary issues:
  - Many studies are underpowered to detect a difference in outcome
  - Allografts are often grouped together despite the different graft types and different processing methods.

Purpose

- (1) To compare the risk of aseptic revision in patients undergoing primary ACLR with soft tissue grafts.
- (2) Specifically to evaluate the risk of revision by tissue type (soft tissue allograft and hamstring autograft) and tissue processing (irradiation, chemical processing, or non-processed)
Methods

- Design: Retrospective cohort study
- Setting: Kaiser Permanente, an Integrated Health Care System covering 9.5 million members in the United States
- Data source: Kaiser Permanente ACLR Registry
  - Prospective data collection
  - Outcomes validated via chart review
- Study sample:
  - Primary single ligament ACLR with BPTB autograft or BPTB allograft
  - 282 surgeons from 43 hospitals
  - 6 regions (Hawaii, Southern California, Northern California, Northwest, Mid-Atlantic, Colorado)
Methods

- **Outcome of interest:** Aseptic revision ACLR
- **Exposures of interest:**
  1. **Graft type:**
     - Hamstring autograft
     - Soft tissue allograft: tibialis anterior or posterior, peroneal tendons, hamstring tendons
  2. **Tissue processing:**
     - Irradiation $< 1.8 \text{ Mrad or } > 1.8 \text{ Mrad}$
     - Chemical processing
       - Allowash (LifeNet Virginia Beach, VA), AlloTrue (AlloSource Centennial, CO)
         - Ultrasonic bath with detergents, antibiotics, alcohol, and peroxide
       - BioCleanse (Regeneration Technologies Inc. Alachua, FLA)
         - Oscillating positive and negative pressure with alcohol and peroxide
     - Sterilely harvested non-processed tissue
- **Analysis:** survival analysis (Kaplan Meier curves and Cox regressions)
## Results

- **Sample Size:** 9458 soft tissue grafts (60.3% Auto, 39.7% Allo)

<table>
<thead>
<tr>
<th></th>
<th>Autograft</th>
<th>Allograft</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Median</td>
<td>24.3</td>
<td>34.6</td>
</tr>
<tr>
<td>IQR</td>
<td>17.7-33.8</td>
<td>24.1-43.2</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>N (%)</th>
<th>N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>2210 (38.7)</td>
<td>1474 (39.3)</td>
</tr>
<tr>
<td>Male</td>
<td>3497 (61.3)</td>
<td>2277 (60.7)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>N (%)</th>
<th>N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Race</td>
<td></td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>2561 (44.9)</td>
<td>2010 (53.6)</td>
</tr>
<tr>
<td>Hispanic</td>
<td>1413 (24.8)</td>
<td>745 (19.9)</td>
</tr>
<tr>
<td>Asian</td>
<td>553 (9.7)</td>
<td>468 (12.5)</td>
</tr>
<tr>
<td>Black</td>
<td>402 (7.0)</td>
<td>214 (5.7)</td>
</tr>
<tr>
<td>Multi/Other</td>
<td>208 (3.6)</td>
<td>105 (2.8)</td>
</tr>
<tr>
<td>Unknown</td>
<td>570 (10.0)</td>
<td>209 (5.6)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Processing Type</th>
<th>N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>All allografts</td>
<td>3751 (100.0)</td>
</tr>
<tr>
<td>No Processing</td>
<td>483 (12.9)</td>
</tr>
<tr>
<td>&lt;1.8Mrad Irradiation</td>
<td>1013 (27.0)</td>
</tr>
<tr>
<td>- w/o Chemical Processing</td>
<td>444 (11.8)</td>
</tr>
<tr>
<td>- with Chemical Processing</td>
<td>258 (6.9)</td>
</tr>
<tr>
<td>≥1.8Mrad Irradiation</td>
<td>1307 (34.8)</td>
</tr>
<tr>
<td>- w/o Chemical Processing</td>
<td>444 (11.8)</td>
</tr>
<tr>
<td>- with Chemical Processing</td>
<td>258 (6.9)</td>
</tr>
<tr>
<td>BioCleanse</td>
<td>246 (6.6)</td>
</tr>
</tbody>
</table>
## Results

<table>
<thead>
<tr>
<th></th>
<th># of Cases</th>
<th># of Revisions</th>
<th>Crude Revision Rate (%)</th>
<th>Cumulative Failure at 3 years with 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Autograft</td>
<td>5707</td>
<td>132</td>
<td>2.3</td>
<td>3.5 (2.9, 4.2)</td>
</tr>
<tr>
<td>Allograft (Total)</td>
<td>3751</td>
<td>83</td>
<td>2.2</td>
<td>3.7 (2.9, 4.7)</td>
</tr>
<tr>
<td>No Processing</td>
<td>483</td>
<td>5</td>
<td>1.0</td>
<td>2.0 (0.8, 5.0)</td>
</tr>
<tr>
<td>&lt;1.8Mrad w/o Chemical Processing</td>
<td>1013</td>
<td>19</td>
<td>1.9</td>
<td>3.0 (1.8, 5.1)</td>
</tr>
<tr>
<td>&lt;1.8Mrad with Chemical Processing</td>
<td>1307</td>
<td>28</td>
<td>2.1</td>
<td>3.2 (2.1, 4.9)</td>
</tr>
<tr>
<td>≥1.8Mrad w/o Chemical Processing</td>
<td>444</td>
<td>15</td>
<td>3.4</td>
<td>4.7 (2.7, 8.0)</td>
</tr>
<tr>
<td>≥1.8Mrad with Chemical Processing</td>
<td>258</td>
<td>9</td>
<td>3.5</td>
<td>6.8 (3.2, 14.2)</td>
</tr>
<tr>
<td>BioCleanse</td>
<td>246</td>
<td>7</td>
<td>2.8</td>
<td>5.3 (2.4, 11.6)</td>
</tr>
</tbody>
</table>

### Total Sample Risk of Revision

<table>
<thead>
<tr>
<th>Risk of Revision</th>
<th>Hazard Ratio (95%CI)</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Allograft within 2.5 years vs. Autograft</td>
<td>1.41 (1.03 - 1.92)</td>
<td>0.031</td>
</tr>
<tr>
<td>Allograft after 2.5 years vs. Autograft</td>
<td>2.94 (1.48 - 5.83)</td>
<td>0.002</td>
</tr>
</tbody>
</table>
Results: Cumulative Revision Probability

< 1.8 Mrad allograft vs autograft

> 1.8 Mrad allograft vs autograft

Log Rank P-Value: 0.363
Results: Revision Risk Factors

Risk Factors vs. Hamstring Autograft (adjusted for age, gender, and race)

- Allograft-No Processing: Hazard Ratio (95%CI) 0.84 (0.34 - 2.05)
- <1.8Mrad Irradiation w/o Chemical Processing: Hazard Ratio (95%CI) 1.50 (0.92 - 2.45)
- <1.8Mrad Irradiation with Chemical Processing: Hazard Ratio (95%CI) 1.44 (0.95 - 2.17)
- ≥1.8Mrad w/o Chemical Processing within 2.5yrs: Hazard Ratio (95%CI) 1.38 (0.72 - 2.64)
- ≥1.8Mrad w/o Chemical Processing after 2.5yrs: Hazard Ratio (95%CI) *3.88 (1.48 - 10.12)
- ≥1.8Mrad with Chemical Processing within 1yr: Hazard Ratio (95%CI) 1.54 (0.37 - 6.32)
- ≥1.8Mrad with Chemical Processing after 1yr: Hazard Ratio (95%CI) *3.43 (1.58 - 7.47)
- BioCleanse: Hazard Ratio (95%CI) *3.02 (1.40 - 6.50)
Discussion

- **Soft tissue allografts** processed with < 1.8 Mrads with and without chemical processing and non processed grafts did not have a significantly different risk of revision compared to hamstring autografts.

- **BioCleanse processed grafts** had a 3.0 X higher risk of revision compared to hamstring autografts.

- **Significant time interactions were noted with the performance of soft tissue allografts compared to hamstring autografts:**
  - Allografts > 1.8 Mrad without chemical processing had a no difference in risk in the first 2.5 years and a 3.9 X higher risk after 2.5 years.
  - Allografts > 1.8 Mrad with chemical processing had a no difference in risk in the first year and a 3.4 X higher risk after one year.
Discussion: Strengths & Limitations

- **Limitations**
  - Surgical technique and rehabilitation were not standardized.
  - Return to sports and activity levels not evaluated.
  - Strength, knee laxity and functional outcomes not available.
  - Loss to f/u : 25.9% (addressed in analysis).

- **Strengths**
  - Large racially diverse sample.
  - Large sample size.
  - Prospective standardized method of data collection and validation.
  - Diverse patient and surgeon sample make the results generalizable to the greater population of ACLR patients and providers/hospitals involved in their care.
Conclusions

- Soft tissue allograft performance is influenced by:
  - Graft processing and time.

- More highly processed tissue leads to a higher risk of revision at earlier time frames.
  - $> 1.8$ Mrads without chemical processing has an increased risk revision after 2.5 years
  - $> 1.8$ Mrads with chemical processing has an increased risk of revision after only one year

- Surgeons and patients need to be aware of the increased risk of revision, and the time interaction, associated with soft tissue allograft usage for ACLR.
References


