Does Change in Femorotibial Cartilage Thickness Differ Between Acutely Anterior-Cruciate Ligament Injured Knees Treated with and without Reconstructive Surgery

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Disclosures

- Wolfgang Wirth: Freelancer for Chondrometrics GmbH, Ainring, Germany; Share-holder of Chondrometrics GmbH, Ainring, Germany; Received consulting fees from Merck Serono S.A.
- Martin Hudelmaier: Part-time employment with Chondrometrics GmbH
- Felix Eckstein: CEO and share-holder of Chondrometrics GmbH, Ainring, Germany; Received consulting fees from Merck Serono S.A., Novartis, Abbvie, and Sanofi Aventis
- Stefan Lohmander & Richard Frobell: No disclosures
Anterior cruciate ligament (ACL) tears

- Common injury in young adults (soccer, skiing)

- ACL injuries associated with elevated risk of developing knee OA
  - Molecular & cellular changes
  - Chronic alterations in joint biomechanics

- Model for early OA
  - Post-traumatic OA
  - Defined baseline
  - Healthy knees
  - Monitor disease onset
  - Identify biomarkers
The KANON trial

- Comparison of surgical vs. non-surgical treatment in young, active adults with rotational trauma to previously uninjured knee

- Randomization to either:
  - early ACL reconstruction and structured rehabilitation or
  - structured rehabilitation with optional delayed ACL reconstruction

- **Primary objective:** Patient reported outcomes (Knee injury and Osteoarthritis Outcome Score, KOOS)

- No significant differences in patient reported outcomes after 2 (Frobell et al. N Engl. J. Med. 2010) and 5 years (Frobell et al. BMJ 2013).
Objectives

- Does the surgical reconstruction of an acute ACL tear influence the change in femorotibial cartilage thickness over the first five years after the injury?
KANON Baseline Characteristics

- **N=121** young, active adults:
  - 62 randomized to early ACL reconstruction surgery (3 lost to follow-up)
  - 59 randomized to structured rehabilitation only with optional delayed ACL reconstruction surgery

<table>
<thead>
<tr>
<th></th>
<th>Early ACR reconstruction</th>
<th>Delayed ACL reconstruction</th>
<th>Structured rehabilitation only</th>
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</thead>
<tbody>
<tr>
<td><strong>N</strong></td>
<td>59</td>
<td>30</td>
<td>29</td>
</tr>
<tr>
<td><strong>Age</strong></td>
<td>26.6±5.1 y</td>
<td>25.2±4.5 y</td>
<td>26.4±4.9</td>
</tr>
<tr>
<td><strong>Female sex</strong></td>
<td>12 (20%)</td>
<td>11 (37%)</td>
<td>9 (31%)</td>
</tr>
<tr>
<td><strong>BMI</strong></td>
<td>24.5±3.2 kg/m²</td>
<td>23.3±2.0 kg/m²</td>
<td>24.3±3.1 kg/m²</td>
</tr>
</tbody>
</table>
MRI

- Sagittal FLASH (1.5T, 0.29mm in-plane, 1.5mm slice spacing)
- Image acquisition at visits:
  - Recruitment (BL = baseline, n=117)
  - Year 2 (Y2) follow-up (n=112)
  - Year 5 (Y5) follow-up (n=112)
Quantitative cartilage analysis

- Manual segmentation of cartilages:
  - Medial and lateral tibia (MT/LT)
  - Central 75% of the medial and lateral femoral condyle (cMF/cLF)

- Computation of cartilage thickness in cartilage plates and subregions

  \[ FTJ = MFTC + LFTC \]
Ordered values of subregional changes

- Sorting of changes observed in the 16 subregions within each knee in ascending order (Buck et al. Arthritis Rheum. 2009)

Subject #1

- OV 2 ← ccMF

Subject #2

- OV 16 ← ccLF
- OV 16 ← aMT
- OV 2 ← aLT

- OV 1 ← cLT
- OV 1 ← eMT

- Quantitative analysis of ordered values 1-16 (OV 1 – OV 16)
Statistical analysis

- **Primary outcome**: Change in entire femorotibial joint (FTJ)
- **Secondary outcomes**:
  - Ordered value 1 (OV 1)
  - Ordered value 16 (OV 16)
  - Medial femorotibial compartment (MFTC)
  - Lateral femorotibial compartment (LFTC)
- **Observation periods**:
  - Baseline → Year 5 (BL→Y5)
  - Baseline → Year 2 (BL→Y2)
  - Year 2 → Year 5 (Y2→Y5)
- **As-treated analysis**:
  - Early ACL reconstruction
  - Delayed ACLR
  - Rehabilitation only (no ACL reconstruction)
- **T-test** (crude analysis)
- **Analysis of covariance** (analysis with adjustment for age, sex & BMI)
Entire femorotibial joint (FTJ)

- Increase in cartilage thickness observed over the entire 5 years
- No significant differences between treatment groups (crude/adjusted $p \geq 0.38 / p \geq 0.39$)

Mean change $\pm$ 95% confidence intervals

- BL→Y5: (n=59/27/26)
- BL→Y2: (n=58/27/27)
- Y2→Y5: (n=58/25/24)
Medial femorotibial compartment (MFTC)

- FTJ increase driven by increase in MFTC
- No significant differences between treatment groups (crude/adjusted p≥0.19 / p ≥ 0.20)

Mean change ± 95% confidence intervals

- BL→Y5: (n=59/27/26)
- BL→Y2: (n=58/27/27)
- Y2→Y5: (n=58/25/24)
Lateral femorotibial compartment (LFTC)

- Small magnitude of change
- No significant differences between treatment groups (crude/adjusted p≥0.41 / p ≥ 0.42)

Mean change ± 95% confidence intervals

- Early ACLR
- Delayed ACLR
- Rehab Only

BL→Y5 (n=59/27/26)
BL→Y2 (n=58/27/27)
Y2→Y5 (n=58/25/24)
Ordered value 1

- OV 1 ↓ for early ACLR than rehabilitation only (BL→Y5: crude/adjusted p=0.04/0.03; BL→Y2: crude/adjusted p=0.007/0.005)
- OV 1 ↓ for delayed ACLR than rehabilitation only (BL→Y2: p=0.04/0.04)
Ordered value 16

- OV 16 ↑ for early ACLR than rehab only (BL→Y5: crude/adjusted p=0.02/0.01, BL→Y2: crude/adjusted p=0.06/0.08)
- OV 16 tended to be greater for delayed ACLR than rehabilitation only (BL→Y5: crude/adjusted p=0.07/0.08)

Mean change ± 95% confidence intervals

<table>
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<tr>
<th></th>
<th>Early ACLR</th>
<th>Delayed ACLR</th>
<th>Rehab Only</th>
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<tbody>
<tr>
<td>BL→Y5 (n=59/27/26)</td>
<td>300±100</td>
<td>250±100</td>
<td>200±100</td>
</tr>
<tr>
<td>BL→Y2 (n=58/27/27)</td>
<td>250±100</td>
<td>200±100</td>
<td>150±100</td>
</tr>
<tr>
<td>Y2→Y5 (n=58/25/24)</td>
<td>200±100</td>
<td>150±100</td>
<td>100±100</td>
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</table>
Conclusions

- No significant differences observed for primary outcome (FTJ) between treatment groups
- No significant differences observed for MFTC / LFTC
- Greater magnitude of subregional cartilage thickness changes (both decrease and increase) after ACL reconstruction surgery
- Surgical ACL reconstruction may induce greater magnitudes of subregional cartilage thickness changes
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