Impact of High Tibial Osteotomy on Cartilage Regeneration (biology) of The Knee: A Systematic Review

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Background

• Most studies focus on restoration of alignment and clinical outcomes
• Few have studied on **impact of cartilage regeneration**
Aim

- Review current literature available regarding HTO and impact on cartilage regeneration at follow-up
- No systematic review conducted to date on this topic to the authors’ best knowledge
Results


Articles Overview

• Impact of pre-operative cartilage status on clinical outcome of HTO
  (1 article: Niemeyer et al.)

• Impact of HTO on cartilage regeneration with arthroscopic and histologic findings
  (2 articles: Koshino et al., Wakabayashi et al.)

• Impact of HTO and post-operative limb alignment on cartilage regeneration
  (1 article: Jung et al.)

• Impact of HTO and combination strategies on cartilage regeneration
  (3 articles: Jung et al., Matsunaga et al., Saw et al.)
Open-Wedge Osteotomy Using an Internal Plate Fixator in Patients With Medial-Compartment Gonarthritis and Varus Malalignment: 3-Year Results With Regard to Preoperative Arthroscopic and Radiographic Findings

Philipp Niemeyer, M.D., Hagen Schmal, M.D., Oliver Hauschild, M.D., Johanna von Heyden, M.D., Norbert P. Södkamp, M.D., Ph.D., Wolfgang Kustler, M.D.

Department of Orthopedic Surgery and Traumatology, Freiburg University Hospital, Freiburg, Germany
Study Design

- 69 patients with a minimum follow-up of 36 months
- IKDC and Lysholm scores.
- **Arthroscopic** findings before HTO were correlated with clinical outcome.
- Defects were localized and graded according to the International Cartilage Research Society (ICRS).
Table 1. Distribution of Cartilage Damage of Different Compartments of Knee Joint

<table>
<thead>
<tr>
<th></th>
<th>No. of Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>ICRS Grade 0</td>
</tr>
<tr>
<td>Medial compartment</td>
<td>0</td>
</tr>
<tr>
<td>Lateral compartment</td>
<td>39</td>
</tr>
<tr>
<td>Anterior compartment</td>
<td>13</td>
</tr>
</tbody>
</table>

NOTE. Patients with full-thickness defects of the lateral compartment were excluded from the study.
FIGURE 4. Effect of severity of cartilage defects of the different knee compartments on IKDC score before surgery and at 6, 12, 24, and 36 months’ follow-up. Within the inclusion criteria of this study, partial-thickness defects of the lateral compartment and all grades of asymptomatic cartilage defects of the anterior compartment were tolerated. Within these inclusion criteria, no influence of severity of cartilage damage could be found. Furthermore, the improvement of function after HTO and the clinical outcome also did not depend on the severity of cartilage damage of the medial compartment.
Discussion

• Regardless of preop stage of cartilage
• HTO was not the only modality.
• Additional surgical procedures were performed in 55 of 69 patients:
  – 31 cases of microfracturing
  – 13 cases of autologous chondrocyte implantation
• No direct cartilage evaluation post-HTO
Regeneration of degenerated articular cartilage after high tibial valgus osteotomy for medial compartmental osteoarthritis of the knee

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Department of Orthopaedic Surgery, Yokohama City University, School of Medicine, 3-9 Fukuura, Kanazawa-ku, Yokohama 236-0004, Japan
Study Design

• Lateral closing wedge HTO (Koshino plate)
• 140 knees with medial compartmental OA in 115 patients
• Intra-articular assessment of cartilage twice:
  – At HTO
  – Second look at removal of implants at 2 years
Fig. 1. Medial compartmental osteoarthritis of left knee of 67-year-old man. (a) Anteroposterior radiograph taken in standing, showing narrowing of medial joint space and osteosclerosis. Standing femorotibial angle is 185° (5° of anatomical varus angulation). High tibial osteotomy was performed with removal of a 15° laterally-based wedge. The proximal and the distal fragments were fixed with a Koshino blade plate. (b) Anteroposterior radiograph taken standing 20 months after initial high tibial osteotomy. The medial joint space is a little widened and standing femorotibial angle is 166° (14° of anatomical valgus angulation). (c) Articular surface of medial femoral condyle at the time of high tibial osteotomy, showing a large ulcerative lesion in the weight-bearing portion with eburnation of subchondral bone (Grade 4-C). (d) Articular surface of medial femoral condyle at removal of blade plate 20 months after the initial high tibial osteotomy, showing almost complete coverage by white regenerated cartilage over the previous ulcerative lesion (Stage C).
Fig. 1 (Continued).

Fig. 1. Medial compartmental osteoarthritis of left knee of 67-year-old man. (a) Anteroposterior radiograph taken in standing, showing narrowing of medial joint space and osteosclerosis. Standing femorotibial angle is 185° (5° of anatomical varus angulation). High tibial osteotomy was performed with removal of a 15° laterally-based wedge. The proximal and the distal fragments were fixed with a Koshino blade plate. (b) Anteroposterior radiograph taken standing 20 months after initial high tibial osteotomy. The medial joint space is a little widened and standing femorotibial angle is 166° (14° of anatomical valgus angulation). (c) Articular surface of medial femoral condyle at the time of high tibial osteotomy, showing a large ulcerative lesion in the weight-bearing portion with eburnation of subchondral bone (Grade 4-C). (d) Articular surface of medial femoral condyle at removal of blade plate 20 months after the initial high tibial osteotomy, showing almost complete coverage by white regenerated cartilage over the previous ulcerative lesion (Stage C).
Grading System Used

- Grade 0: normal
- Grade 1: yellowish discoloration
- Grade 2: unevenness and softening
- Grade 3: fasciculation and attrition
- Grade 4-a: partly to subchondral bone
- Grade 4-b: ulceration with subchondral bone exposure
- Grade 4-c: eburnation of subchondral bone
- Grade 5-a: worn-off defect of the tibial plateau with depth less than 5 mm
- Grade 5-b: worn-off defect with depth more than 5 mm

In 47 knees out of 146, covered by a white cartilage layer (Stage C: mature regeneration).

In majority of patients (86 knees), partially by a pink and yellowish fibrous layer or white fibrocartilaginous tissue (Stage B).

Few patients (13 knees) have no regeneration or repair or cartilage at follow-up.
Fig. 4. Photomicrographs of histopathological sections of regenerated cartilage. (a) Superficial layer of regenerated cartilage, with round or spindle-shaped cells (arrows) scattered in extracellular matrix showing mild safranin-O staining. The area is composed of fibrocartilage (×400). (b) Middle to deep layer of regenerated cartilage, with hyaline cartilage and clusters of round cells accompanying matrix with strong safranin-O staining (×400). (c) Type I collagen immunostaining. Extracellular matrix in the superficial layer of repaired cartilage shows staining for type I collagen (×200). (d) Type II collagen immunostaining. Round hyaline cartilage cells in the middle and deep layers of repaired cartilage are positive for type II collagen (×200).
Table 2
Limb alignment after high tibial osteotomy

<table>
<thead>
<tr>
<th>Regeneration</th>
<th>Anatomical valgus angulation</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>≥5</td>
</tr>
<tr>
<td>Stage A and B</td>
<td>86</td>
</tr>
<tr>
<td>(Immature\textsuperscript{a})</td>
<td></td>
</tr>
<tr>
<td>Stage C</td>
<td>46</td>
</tr>
<tr>
<td>(Mature\textsuperscript{b})</td>
<td></td>
</tr>
<tr>
<td></td>
<td>132</td>
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<td></td>
<td></td>
</tr>
</tbody>
</table>

Regeneration was more mature in knees with greater valgus angulation after osteotomy.

\textsuperscript{a} Immature indicates the same as in Table 1.

\textsuperscript{b} Mature indicates the same as in Table 1.
Discussion

- HTO regenerate even in the severely degenerated knee.
- Cartilage regeneration is not limited to fibrocartilage.
- Greater correction of varus deformity appears to increase potential for cartilage regeneration.
Second-Look Arthroscopic Assessment of Cartilage Regeneration After Medial Opening-Wedge High Tibial Osteotomy

Woon-Hwa Jung, M.D., Ryohei Takeuchi, M.D., Chung-Woo Chun, M.D., Jung-Su Lee, M.D., Jae-Hun Ha, P.A., Ji-Hyae Kim, P.A., Jae-Heon Jeong, M.D.
Fig 2. Images from a 58-year-old woman show varus limb alignment before (A) medial opening-wedge HTO, (B) valgus limb alignment after medial opening-wedge HTO, and (C) well-maintained valgus limb alignment at hardware removal. (D) The articular surface shows eburnation of the articular surfaces before osteotomy. (E) The articular surface shows even coverage with fibrocartilage at 24 months postoperatively. The Knee Society knee score significantly improved from 65 points preoperatively to 95 points at the time of second-look arthroscopy. The preoperative mechanical tibiofemoral angle was $-5.4^\circ$. The postoperative mechanical tibiofemoral angle was $1.9^\circ$ at 24 months after osteotomy.
Study Design

- **Medial opening wedge HTO, no adjuncts**
- 159 knees divided into 3 groups based on post-operative limb alignment (mechanical TFA):
  - Group A: $\leq 0$ deg
  - Group B: $> 0$ deg, $< 6$ deg (ideal correction group)
  - Group C: $\geq 6$ deg
Degenerative cartilage was partially regenerated in almost all cases and fully regenerated in only some cases.

Postoperative limb alignment influenced the clinical outcome and regeneration of the cartilage.

### Table 3. Medial Femoral Condyle Articular Cartilage Regeneration Grade According to Postoperative Limb Alignment

<table>
<thead>
<tr>
<th>Group</th>
<th>Immature</th>
<th>Mature (Grade)</th>
<th>Grade 1</th>
<th>Grade 2 (Grade)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group A</td>
<td>15</td>
<td>1 (6%)</td>
<td>4</td>
<td>12 (75%)</td>
</tr>
<tr>
<td>Group B</td>
<td>129</td>
<td>4 (3%)</td>
<td>7</td>
<td>126 (95%)</td>
</tr>
<tr>
<td>Group C</td>
<td>9</td>
<td>1 (10%)</td>
<td>1</td>
<td>9 (90%)</td>
</tr>
</tbody>
</table>

NOTE. $P = .462$ for statistical analysis between immature and mature regeneration. $P = .018$ for statistical analysis between grade 1 and grade 2 regeneration.
Discussion

• Mechanical improvement positive influence on cartilage regeneration.

• Mature cartilage in knees in patients with more than 5 degree of anatomic valgus angulation after osteotomy compared with less

• Limitation: short-term follow-up
Comparison of Results of Medial Opening-Wedge High Tibial Osteotomy With and Without Subchondral Drilling

Woon-Hwa Jung, M.D., Ryohei Takeuchi, M.D., Chung-Woo Chun, M.D., Jung-Su Lee, M.D., Jae-Heon Jeong, M.D.

DOI: http://dx.doi.org/10.1016/j.arthro.2014.11.035 | CrossMark
Study Design

• Group I: HTO + subchondral drilling (30 knees)
• Group II: HTO only (31 knees)
• Arthroscopic assessment at time of HTO and follow-up.
• Group 1: Grade II formation of fibrocartilage in 100% of patients (30 of 30) with immature appearance in 90% of patients (27 of 30) and maturation in 10% (3 of 30) in Group 1.
• Group 2: Grade II formation of fibrocartilage in 94% of patients (29 of 31), immature appearance in 90% (28 of 31) and maturation in 3% (1 of 31).
• Only two knees (7%) showed no formation of fibrocartilage (grade I) in this study.
High Tibial Osteotomy in Combination With Chondrogenesis After Stem Cell Therapy: A Histologic Report of 8 Cases

Khay-Yong Saw, M.Ch.Orth., F.R.C.S.(Edin), Adam Anz, M.D., Caroline Siew-Yoke Jee, Ph.D. (Lond), Reza Ching-Soong Ng, M.D., Norhafizah Mohtarrudin, M.B.B.S., M.Path., Kunaseegaran Ragavanaidu, M.B.B.S., M.Path.
Study Design

• Aim: histological evaluation of quality of articular cartilage regeneration after:
  – arthroscopic subchondral drilling
  – + post-operative intra-articular injections of autologous peripheral blood stem cells (PBSCs) and hyaluronic acid
  – + medial open-wedge HTO.

• All 8 patients have ICRS grade 4 OA

• Hypothesis: combining HTO with the developed cartilage repair technique would regenerate repair cartilage that closely resembled the normal articular cartilage
<table>
<thead>
<tr>
<th>Image Location</th>
<th>Intra-operative</th>
<th>2 years</th>
<th>H&amp;E</th>
<th>Tissue morphology</th>
<th>Safranin-O</th>
<th>Collagen I</th>
<th>Collagen II</th>
</tr>
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<tbody>
<tr>
<td>MFC</td>
<td><img src="image1" alt="Image" /></td>
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<td><img src="image6" alt="Image" /></td>
<td><img src="image7" alt="Image" /></td>
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<tr>
<td>MTP</td>
<td><img src="image8" alt="Image" /></td>
<td><img src="image9" alt="Image" /></td>
<td><img src="image10" alt="Image" /></td>
<td><img src="image11" alt="Image" /></td>
<td><img src="image12" alt="Image" /></td>
<td><img src="image13" alt="Image" /></td>
<td><img src="image14" alt="Image" /></td>
</tr>
</tbody>
</table>

Fig 7. Findings of second-look arthroscopy and histologic assessment of medial femoral condyle (MFC) and medial tibial plateau (MTP) at 2 years in a 49-year-old male patient (same patient shown in Figs 4 and 6).
Discussion

- Small sample size (8 patients)
- Short follow-up
- Grade 4 bone-on-bone lesions are treatable arthroscopically while regenerating repair cartilage approaching normal articular cartilage histologically.
Injectable Cultured Bone Marrow–Derived Mesenchymal Stem Cells in Varus Knees With Cartilage Defects Undergoing High Tibial Osteotomy: A Prospective, Randomized Controlled Clinical Trial With 2 Years’ Follow-up

Keng Lin Wong, M.R.C.S.(Edin), Kevin Boon Leng Lee, F.R.C.S.(Edin, Orth), Bee Choo Tai, Ph.D.(Stats), Ping Law, Ph.D., Eng Hin Lee, M.D., and James H. P. Hui, F.R.C.S.(Edin), F.A.M.S.(Sing), M.D.
High Tibial Osteotomy
N = 56 patients randomized

HTO + HA+ MSC : 28 patients
Cell recipient group

1) Arthroscopy
2) Microfracture
3) HTO
4) BM Harvesting

3 week MSC culture

3rd week post op: HA +MSC
4th week post op: HA
5th week post op: HA

HTO + HA: 28 patients
Control Group

1) Arthroscopy
2) Microfracture
3) HTO

3rd week post op: HA
4th week post op: HA
5th week post op: HA

Follow for 2 years with scoring systems and MRI 1 year post op
Surgical Procedure and BM Harvest

- **Surgical Procedure:**
- Done under General Anaesthesia (GA)
- Tourniquet control

- **1) Arthroscopy:**
  - ICRS classification
  - Lesion size measured using standardized tool

- **2) Microfracture:**
  - Microfracture technique as described by Steadman et al\(^\text{9}\)

- **3) Medial opening wedge HTO:**
  - Fixed with long fixed angle locking plate

TFA = 12 deg

TFA = 13 deg
TFA = 0 deg
(corrected 12 deg)
TFA = 15 deg

TFA = 20 deg
Left Knee Post-HTO
TFA = 1.5 deg
(corrected 13.5 deg)

TFA = 6 deg
(corrected 14 deg)
Learning points

• HTO good for cartilage
• Regardless of stage
• Hyaline?
• Overcorrection?
• Adjunct procedures?
• Long term results?
Thank You
Background
ARTHRROSCOPY
The Journal of Arthroscopic and Related Surgery