

Combined Cartilage Procedures After High Tibial Osteotomy: Cartilage Status, Early Functional Recovery, and Short-term Clinical Outcomes

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Background: The clinical benefit of performing cartilage procedures concurrently with high tibial osteotomy (HTO) remains uncertain. While these procedures aim to enhance cartilage regeneration, concerns persist regarding increased early postoperative pain and delayed functional recovery.

Purpose: To evaluate whether adding cartilage procedures increases pain or delays functional improvement during early recovery after HTO.

Study Design: Cohort study; Level of evidence, 3.

Methods: Patients who underwent HTO between March 2015 and December 2022 were included if patient-reported outcomes (PROs) were available at 6, 12, and 24 months postoperatively. Patients were categorized into 3 groups: isolated HTO (group I), HTO with microdrilling (group M), and HTO with umbilical cord blood-derived mesenchymal stem cell implantation (group C). PROs were retrospectively reviewed. Factors such as osteoarthritis severity, cartilage defect size, kissing lesions, and postoperative alignment were analyzed. For patients with 1-year postoperative magnetic resonance imaging (MRI) studies, subchondral edema severity and depth were assessed. Postoperative cartilage status was evaluated using second-look arthroscopy.

Results: Among 234 knees, 93 were included: 38 in group I, 32 in group M, and 23 in group C. Baseline characteristics were comparable, although group M had smaller medial femoral condyle cartilage defects (group I: $6.5 \pm 2.6 \text{ cm}^2$ vs group M: $4.4 \pm 2.4 \text{ cm}^2$ vs group C: $7.4 \pm 2.1 \text{ cm}^2$; $P < .001$). At 6 months, group C demonstrated significantly less improvement in Lysholm (5.3 ± 20.1 vs 20.8 ± 21.5 ; $P = .018$) and International Knee Documentation Committee Function (0.0 ± 2.7 vs 2.3 ± 3.3 ; $P = .014$) scores compared with group I. Minimal clinically important difference achievement rates at 6 months were lower in groups M and C than in group I (Lysholm score: $P = .041$; Knee injury and Osteoarthritis Outcome Score Activities of Daily Living: $P = .020$). These differences were no longer significant at 12 and 24 months. No baseline factor correlated significantly with PROs. MRI showed that subchondral edema correlated with greater pain and poorer function ($r = 0.250\text{--}0.380$; $P < .05$). Although second-look arthroscopy indicated improved cartilage status in the cartilage procedure groups, these findings did not correlate with PROs.

Conclusion: Combined cartilage procedures involving subchondral drilling after HTO are associated with increased early postoperative pain and delayed functional recovery during the first 6 months. Although second-look arthroscopy demonstrated improved cartilage status in the cartilage procedure groups, clinical outcomes at 12 and 24 months were comparable to those observed after isolated HTO.

Keywords: knee osteoarthritis; high tibial osteotomy; articular cartilage; cartilage repair; cartilage regeneration

arthroplasty.^{26,34} Because many of these patients have concomitant cartilage defects, there has been growing interest in performing cartilage repair procedures concurrently with HTO.^{3,6} Techniques such as marrow stimulation or the implantation of mesenchymal stem cells (MSCs) have been proposed to enhance cartilage regeneration and improve outcomes.^{6,14}

The clinical benefits of these procedures remain unclear, primarily due to the high heterogeneity among existing studies and the limited number of high-quality investigations available.^{3,6} Several studies have reported that the addition of cartilage procedures resulted in improved cartilage defect filling; however, short-term follow-up has not demonstrated significant differences in patient-reported outcomes (PROs) when these procedures are combined with HTO.^{15,21,22} This uncertainty persists even in the short-term period of up to 2 years. HTO is typically performed in younger, more active patients with higher functional demand who are often part of the working population.⁸ Therefore, facilitating rapid recovery to enable early return to work and daily function is an important consideration. Cartilage repair procedures involving subchondral drilling inherently introduce additional iatrogenic injury and may therefore increase postoperative pain. Subchondral drilling induces bleeding and marrow stimulation, leading to hematoma formation and subsequent biological remodeling of the osteochondral unit.¹⁹ These processes may provoke local inflammatory responses and joint effusion, potentially contributing to increased early postoperative pain and delayed functional recovery.²⁰ These concerns may be further exacerbated in some procedures in which large-diameter subchondral drilling is performed. In the absence of clearly demonstrated long-term clinical benefits,³ if these procedures are found to increase early postoperative pain and delay recovery, their addition should be reconsidered with caution. However, the current literature lacks analysis on early postoperative PROs within 2 years (6 months and 12 months) related to these procedures.

This study aimed to evaluate whether combined cartilage procedures performed during HTO are associated with increased pain or delayed functional improvement in the early postoperative period. Additionally, we assessed postoperative magnetic resonance imaging (MRI) findings to explore correlations with functional outcomes. We hypothesized that the additionally performed cartilage procedures would induce increased postoperative pain and delay functional recovery during the early period after HTO.

METHODS

Study Design and Patient Selection

This study was reviewed and approved by our institutional review board (IRB No. 4-2025-0729). Given the retrospective design and minimal risk to patients, the requirement for informed consent was waived by the IRB. This retrospective study included patients who underwent medial opening-wedge HTO (MOWHTO) for medial compartment osteoarthritis between March 2015 and December 2022 at a single institution by a single surgeon (S.H.K.). Exclusion criteria were (1) unavailability of PROs at 6, 12, and 24 months postoperatively; (2) contralateral HTO or other knee surgeries within 2 years; (3) Kellgren-Lawrence (KL) grade 4 osteoarthritis; (4) patients who underwent conventional microfracture on the medial femoral condyle (MFC) during surgery; and (5) patients who developed postoperative infections or experienced traumatic events or complications that could significantly affect subjective outcomes. The indications for HTO included (1) patients <65 years of age who were physically active and had persistent medial knee pain unresponsive to nonoperative therapy for a minimum of 3 months, (2) presence of medial compartment osteoarthritis accompanied by varus alignment (defined as a mechanical tibiofemoral angle >5°), and (3) adequate range of motion >100° and flexion contracture <15°, with no evidence of joint instability. Cartilage repair procedures were generally considered when the cartilage defect was a near-full-thickness defect classified as International Cartilage Regeneration & Joint Preservation Society (ICRS) grade ≥3B. Cartilage repair performed concurrently with HTO in this study consisted of arthroscopic microdrilling and allogenic umbilical cord blood-derived MSC (UCB-MSC; Cartistem, MEDIPOST Co, Ltd) implantation. During the early phase of the study period, cartilage procedures were not considered except for focal defects. From 2018 onward, cartilage procedures were more actively considered to improve clinical outcomes. The type of cartilage procedure was determined based on the patient's informed choice after a thorough explanation of the procedure, its advantages and disadvantages, and associated costs. Patients were also informed that the long-term clinical benefits of cartilage procedures have not been clearly established. In cases in which patients declined the procedure due to additional costs or uncertain outcomes, cartilage procedures were not performed. Moreover, in patients with diffuse, extensive cartilage defects, a simple

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Ethical approval for this study was obtained from the Severance Institutional Review Board (IRB No. 4-2025-0729).

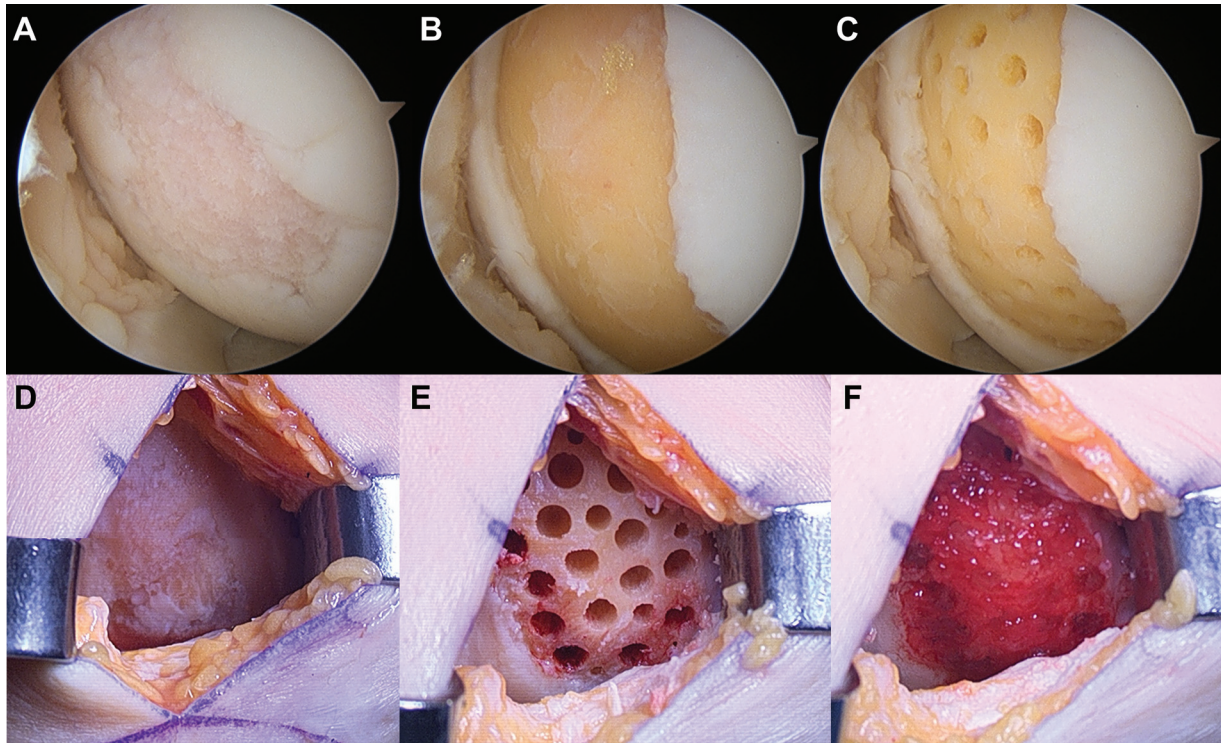


Figure 1. (A-C) Arthroscopic microdrilling procedures. (A) The cartilage defect status of the medial femoral condyle (MFC) was evaluated through the anterolateral portal before microdrilling. (B) Cartilage defect preparation was performed by creating a vertical wall at the margin of the cartilage defect and debriding the defect bed. (C) Arthroscopic microdrilling was performed using a 1.5-mm drill bit, with perforations spaced 2 to 3 mm apart. (D-F) Umbilical cord blood-mesenchymal stem cell (UCB-MSC) implantation. (D) A mini-open arthrotomy was performed to expose the MFC for UCB-MSC implantation, allowing direct visualization of the cartilage defect. (E) After cartilage defect preparation, drilling was performed on the subchondral bone. (F) The UCB-MSCs mixed with hyaluronic acid gel were implanted into the prepared defect area.

marrow stimulation procedure was not considered, as its efficacy was expected to be limited in such cases. The final included patients were categorized into 3 groups: isolated HTO (group I), HTO with microdrilling (group M), and HTO with UCB-MSC implantation (group C).

Surgical Procedures

All surgeries, including MOWHTO and any accompanying cartilage restoration procedures, were performed by a single experienced orthopaedic surgeon (S.H.K.). The MOWHTO technique, including osteotomy, bony correction, and fixation, followed standardized procedures described in previous literature.¹³ The target for valgus correction was the Fujisawa point, corresponding to a weightbearing line (WBL) ratio of 62.5%.⁵ Regarding the management of the superficial medial collateral ligament (sMCL), the transection technique was predominantly used in most cases, in which the sMCL was transected at the level of the osteotomy. In a minority of cases, the release technique was applied, where the sMCL was reflected from its distal attachment with the underlying periosteum using a periosteal elevator without

transection.¹⁰ For the transverse osteotomy, 2 guide pins were inserted from the medial tibial cortex toward the fibular tip, starting approximately 40 mm below the medial joint line and targeting the safe zone within the proximal tibiofibular joint.²³ The biplanar osteotomy included an additional cut at the proximal tibial tubercle, angled at approximately 110° to the transverse osteotomy.¹² After completing the osteotomy, the opening was performed using an adjustable spreader based on the preoperatively planned correction angle. Once the desired alignment was achieved, the osteotomy site was stabilized using a locking plate system (Tomofix; DePuy Synthes). In cases involving combined cartilage repair, arthroscopic microdrilling was conducted before the osteotomy, while UCB-MSC implantation via mini-open arthrotomy was performed after the osteotomy.

The cartilage repair methods used in this study included arthroscopic microdrilling (with a small-diameter drill) and implantation of UCB-MSCs (Figure 1). Cartilage defects were prepared using a uniform technique: vertical edges were created by trimming the margins with a gouge, and the calcified cartilage layer was carefully removed. For microdrilling, a 1.5 mm-diameter drill bit (Zimmer Biomet) was used to create 13 to 15 mm-deep perforations

spaced 2 to 3 mm apart, guided by a device (B-IP-1512; Bioretec Ltd) to ensure precision and avoid communication between holes (Figure 1, A-C). In cases undergoing UCB-MSC implantation, a mini-open arthrotomy was performed. Through this window, the cartilage defect was prepared, followed by subchondral bone drilling. To align with the original technique introduced during its development,²⁸ relatively large-diameter drill holes were created. Drillings with a 4-mm diameter and 7-mm depth were performed, with additional 2 mm-diameter drillings intermittently placed in the remaining spaces. The UCB-MSCs mixed with hyaluronic acid were then implanted to fill those drill holes and to cover the entire defect area (Figure 1, D-F). Further product details and preparation procedures are provided in Appendix Material 1.

Postoperative rehabilitation protocols differed depending on whether cartilage repair was performed. Patients treated with HTO alone began partial weightbearing ambulation with crutches shortly after surgery. Passive range of motion exercises started on postoperative day 2 using a hinged knee brace initially set to 60° of flexion, with the flexion range increased by 30° every 2 weeks. Both the crutches and brace were discontinued by 6 weeks. For patients who underwent combined cartilage procedures, weightbearing was more restricted. These patients used crutches for a total of 10 weeks: nonweightbearing to toe-touch weightbearing during the first 4 weeks, followed by partial weightbearing for the next 6 weeks. Passive range of motion was gradually increased following the same protocol used for patients who underwent HTO alone, and a hinged knee brace was applied in all cases. Continuous passive motion devices were used early to promote cartilage healing for first 4 weeks.³⁰

Assessment of Baseline Status

Patient data, including age, sex, affected side, and body mass index, were collected. Preoperative radiographs were reviewed to determine the KL grade on anteroposterior knee radiographs and the WBL ratio on whole lower extremity radiographs.³⁹ During initial arthroscopy, the size of the cartilage defect on the MFC was measured after defect preparation, and the presence of kissing lesions was assessed. A kissing lesion was defined as near-full-thickness cartilage defects (ICRS grade ≥ 3 B) on both the femoral and tibial articular surfaces. Postoperative alignment was evaluated using whole lower extremity radiographs obtained 1 year after surgery, considering that early postoperative stiffness may gradually resolve over time. On these radiographs, the postoperative WBL ratio and joint line obliquity (JLO) were measured.¹³

Outcome Measures

The following prospectively collected PROs were retrospectively reviewed: pain visual analog scale (VAS) score (0-100 scale), Lysholm knee score,¹ International Knee Documentation Committee (IKDC) subjective score,⁹ and Knee Injury and Osteoarthritis Outcome Score (KOOS).² PROs

were obtained at baseline (preoperatively) and at 6, 12, and 24 months postoperatively. The degree of improvement from baseline at each follow-up point was calculated. Additionally, the achievement rates of minimal clinically important differences (MCIDs) were determined and compared between groups. Because no established MCID values exist for patients undergoing cartilage procedures combined with HTO, cohort-specific MCIDs were calculated using the distribution-based method, defined as one-half of the standard deviation of the change in scores.^{25,29} The baseline data used for MCID calculations are presented in Appendix Table 1. The resulting MCID values were as follows: 13.4 for VAS score, 10.8 for Lysholm knee score, 9.3 for IKDC score, 10.9 for KOOS Pain, 10.0 for KOOS Symptoms, 10.3 for KOOS Activities of Daily Living (ADL), 12.9 for KOOS Sports, and 10.5 for KOOS Quality of Life (QOL).

Postoperative MRI evaluation at approximately 1 year was performed in patients who consented to evaluation of overall knee joint condition and cartilage regeneration. The cartilage repair tissue in patients who underwent cartilage procedures was evaluated using the MOCART (magnetic resonance observation of cartilage repair tissue) 2.0 scoring system.³² The MOCART 2.0 scoring system, primarily designed to evaluate cartilage repair tissue, is not suitable for chondral lesions in patients who did not undergo cartilage procedures. Therefore, in the MRI analysis of all groups, including the isolated HTO group (group I), only the “subchondral change” subscore was used to assess the extent of subchondral edema, which may be influenced by subchondral drilling during cartilage procedures. Patients were categorized into 2 groups based on this subscore: no or mild edema (subscores 15-20) and severe edema (subscores 0-10) (Figure 2A). Additionally, the depth of subchondral edema was measured on the sagittal MRI slice showing the greatest edema. A best-fit circle was drawn over the femoral condyle, and the depth was measured from the articular surface toward the center of the circle at the point of maximal edema (Figure 2B). The analysis of subchondral edema was conducted using MRI views that included the SEMAC (slice encoding for metal artifact correction) sequence, a technique designed to reduce metal artifacts.

At approximately 1 year postoperatively, plate removal was performed. For patients who consented to second-look arthroscopy during the plate removal, cartilage status was assessed arthroscopically using the ICRS Cartilage Repair Assessment (CRA) form.³⁶

Statistical Analysis

All statistical analyses were performed using SPSS Version 26.0 (IBM), with statistical significance set at a *P* value $< .05$. Continuous variables are presented as mean $\pm$ standard deviation, and categorical variables as number (percentage) unless otherwise indicated. Comparisons of continuous variables among the 3 groups were performed using either analysis of variance or the Kruskal-Wallis test, depending on whether the assumption of normality was satisfied (Shapiro-Wilk test). For categorical

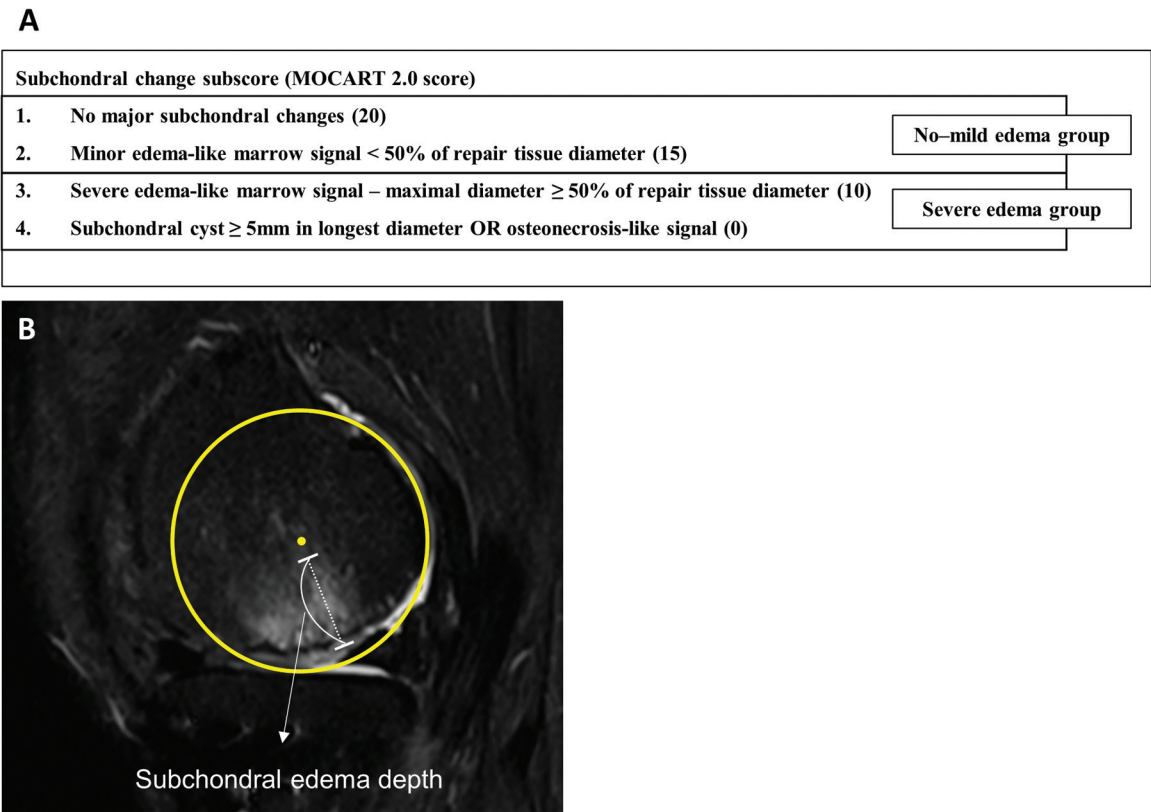


Figure 2. (A) Schematic illustration of the evaluation criteria for the subchondral change subscore in the MOCART (magnetic resonance observation of cartilage repair tissue) 2.0 scoring system, along with the method used in this study to classify patients into the no to mild edema group and the severe edema group. (B) On the sagittal SEMAC (slice encoding for metal artifact correction) magnetic resonance imaging sequence, the slice showing the maximal depth of subchondral edema was selected. A best-fitting circle was drawn on the medial femoral condyle, and the depth of the edema was measured from the subchondral plate toward the center of the circle at the point of maximal edema.

variables, the chi-square test or Fisher exact test was used, as appropriate. Post hoc analysis was performed with Bonferroni correction. Correlations between various factors and PROs were assessed using Spearman correlation coefficients. To determine the statistical power of the significant findings, power analysis was performed using G*Power Version 3.1 (Heinrich Heine University Düsseldorf, Düsseldorf, Germany). For MRI evaluations of the subchondral edema subscore and depth, intra- and interobserver reliability were assessed using the intraclass correlation coefficient (ICC). Two evaluators (S.H.J. and B.H.J.) independently measured each parameter twice, with a minimum interval of 3 weeks between measurements.

RESULTS

Baseline Characteristics

A total of 93 knees (93 patients) were included: 38 in group I, 32 in group M, and 23 in group C (Figure 3).

No significant differences were observed in age, sex, body mass index, KL grade, or pre- and postoperative mechanical alignment among the 3 groups (all $P > .05$) (Table 1). However, group M had a significantly smaller MFC cartilage defect size than groups I and C ($4.4 \pm 2.4 \text{ cm}^2$ vs $6.5 \pm 2.6 \text{ cm}^2$ and $7.4 \pm 2.1 \text{ cm}^2$, respectively; $P < .001$).

Patient-Reported Outcomes

At 6 months postoperatively, group C showed significantly smaller improvements in Lysholm (5.3 ± 20.1 vs 20.8 ± 21.5 , $P = .018$) and IKDC Function (0.0 ± 2.7 vs 2.3 ± 3.3 ; $P = .014$) scores compared with group I. While other PROs also trended lower in group C, the differences were not statistically significant. By 12 and 24 months, improvements in PROs were comparable across all groups, with no significant intergroup differences (Figure 4). The MCID achievement rates for each PRO are presented in Table 2. Among the 3 groups, a statistically significant difference in MCID achievement rates was observed only at 6 months

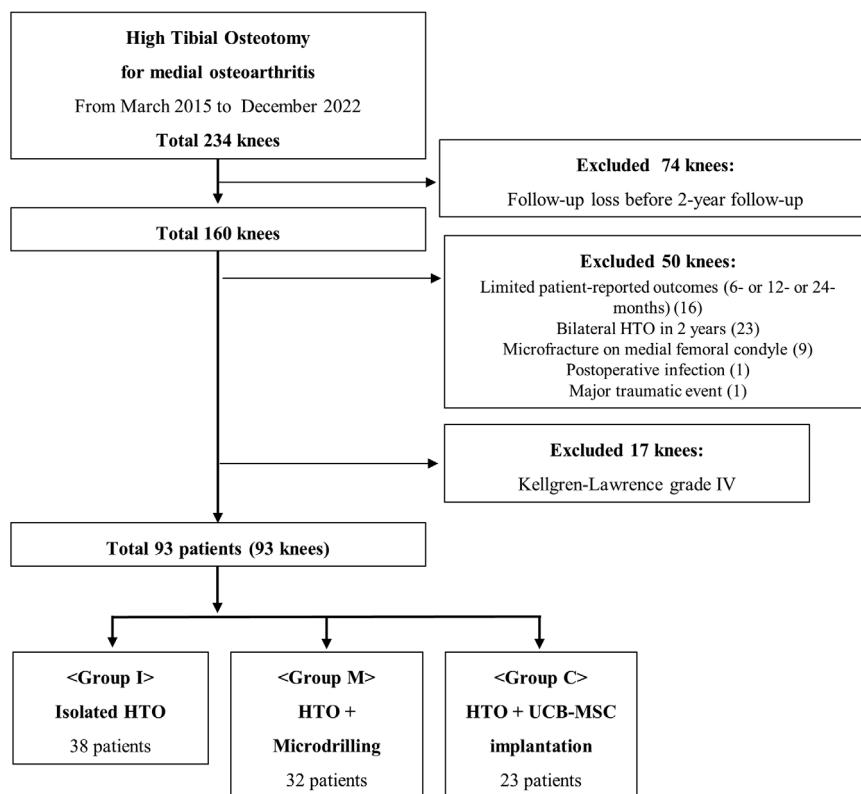


Figure 3. Patient flow diagram. HTO, high tibial osteotomy; UCB-MSC, umbilical cord blood-derived mesenchymal stem cell.

TABLE 1
Patient Characteristics and Baseline Status^a

	Group I (n = 38)	Group M (n = 32)	Group C (n = 23)	P Value
Age, y	58.0 ± 4.7	58.0 ± 7.7	58.1 ± 6.2	.996
Sex, male/female	10/28	7/25	5/18	.882
Affected side, right/left	16/22	16/16	12/11	.696
Body mass index	26.9 ± 4.2	26.8 ± 2.8	26.1 ± 2.8	.645
MFC cartilage defect size, cm ²	6.5 ± 2.6	4.4 ± 2.4	7.4 ± 2.1	<.001 ^b
Kissing lesions, yes/no	14/24	16/16	6/17	.190
Preoperative KL grade, 0/1/2/3/4	0/7/31/0	0/10/22/0	0/5/18/0	.439
Preoperative WBL ratio, %	19.7 ± 11.7	18.5 ± 11.5	19.2 ± 11.0	.904
Postoperative WBL ratio, %	68.0 ± 8.0	67.1 ± 9.2	68.1 ± 9.4	.626
Postoperative JLO, deg	3.6 ± 2.6	3.0 ± 2.3	2.5 ± 2.5	.253

^aData are presented as number or mean ± SD. Group I, isolated HTO; Group M, HTO with microdrilling; Group C, HTO with UCB-MSC implantation. JLO, joint line obliquity; KL, Kellgren-Lawrence; MFC, medial femoral condyle; WBL, weightbearing line.

^bThis significant difference was attributable to group M showing significantly lower values compared with both groups I and C (vs group M, $P = .002$; vs group C, $P < .001$).

for the Lysholm and KOOS ADL scores. For the other outcomes, no significant differences were found. Overall, the groups that underwent additional cartilage procedures showed a trend toward lower MCID achievement rates at 6 months; however, by 12 and 24 months, their MCID

achievement rates became comparable to those of the isolated HTO group (Figure 5). The statistically significant results in the comparison of improved PROs and MCID achievement rates demonstrated statistical power ranging from 0.85 to 0.99.

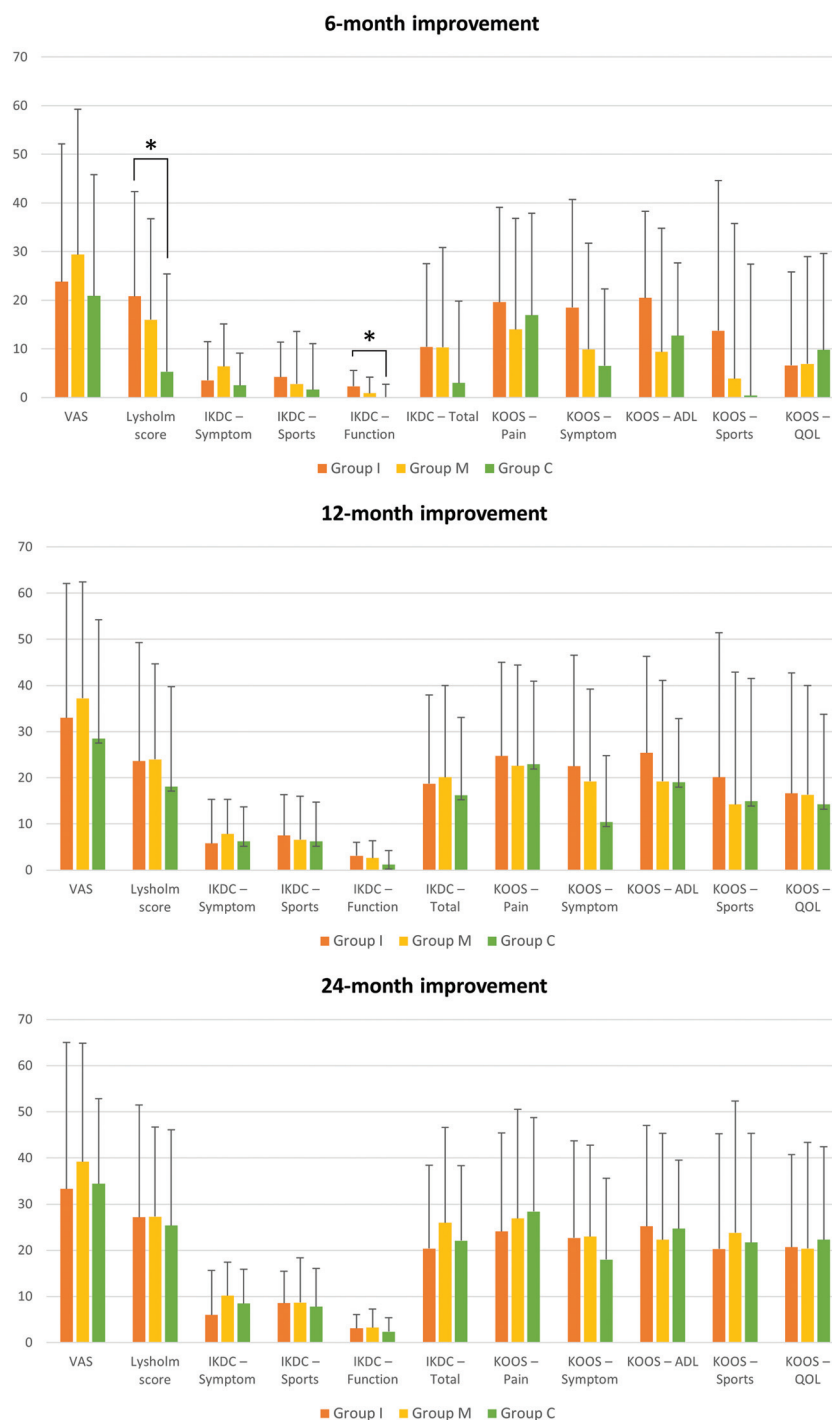


Figure 4. Graphs illustrating the improvement in patient-reported outcomes at 6, 12, and 24 months postoperatively compared with baseline. At 6 months, there were statistically significant differences among the groups in both the Lysholm knee score and the IKDC Function score. Specifically, group C demonstrated significantly less improvement compared with group I. However, at 12 and 24 months, no significant differences were observed among the groups, and the magnitude of the differences tended to diminish over time. *Statistically significant. Group I, isolated HTO; Group M, HTO with microdrilling; Group C, HTO with UCB-MSC implantation. ADL, Activities of Daily Living; IKDC, International Knee Documentation Committee; KOOS, Knee injury and Osteoarthritis Outcome Score; QOL, Quality of Life; VAS, visual analog scale.

TABLE 2
MCID Achievement Rates and Between-Group Comparisons at 6-, 12-, and 24-Month Follow-ups^a

	Group I (n = 38)	Group M (n = 32)	Group C (n = 23)	P Value
VAS score				
6 mo	65.8 (25)	71.9 (23)	73.9 (17)	.763
12 mo	73.7 (28)	84.4 (27)	69.6 (16)	.391
24 mo	78.9 (30)	84.4 (27)	91.3 (21)	.443
Lysholm score				
6 mo	63.2 (24)	56.3 (18)	30.4 (7)	.041
12 mo	71.1 (27)	68.8 (22)	65.2 (15)	.893
24 mo	76.3 (29)	84.4 (27)	73.9 (17)	.457
IKDC total score				
6 mo	50.0 (19)	46.9 (15)	26.1 (6)	.162
12 mo	63.2 (24)	75.0 (24)	65.2 (15)	.548
24 mo	76.3 (29)	84.4 (27)	73.9 (17)	.592
KOOS Subscale				
Pain				
6 mo	68.4 (26)	46.9 (15)	52.2 (12)	.167
12 mo	71.1 (27)	71.9 (23)	78.3 (18)	.812
24 mo	71.1 (27)	78.1 (25)	87.0 (20)	.352
Symptoms				
6 mo	60.5 (23)	50.0 (16)	43.5 (10)	.404
12 mo	68.4 (26)	65.6 (21)	43.5 (10)	.101
24 mo	71.1 (27)	71.9 (23)	65.2 (15)	.851
ADL				
6 mo	73.7 (28)	40.6 (13)	56.5 (13)	.020
12 mo	78.9 (30)	68.8 (22)	73.9 (17)	.624
24 mo	76.3 (29)	68.8 (22)	82.6 (19)	.492
Sports				
6 mo	47.4 (18)	34.4 (11)	34.8 (8)	.462
12 mo	63.2 (24)	43.8 (14)	60.9 (14)	.228
24 mo	68.4 (26)	71.9 (23)	69.6 (16)	.951
QOL				
6 mo	44.7 (17)	40.6 (13)	52.2 (12)	.696
12 mo	57.9 (22)	56.3 (18)	47.8 (11)	.731
24 mo	78.9 (30)	59.4 (19)	69.6 (16)	.206

^aData are presented as percentage (n). Boldface type indicates statistical significance. Group I, isolated HTO; Group M, HTO with microdrilling; Group C, HTO with UCB-MSC implantation. ADL, Activities of Daily Living; IKDC, International Knee Documentation Committee; KOOS, Knee injury and Osteoarthritis Outcome Score; MCID, minimal clinically important difference; QOL, Quality of Life; VAS, visual analog scale.

MRI Findings and PROs

A total of 62 patients (66.7%) who provided consent underwent follow-up MRI evaluation approximately 1 year postoperatively (group I: 12 patients; group M: 31 patients; group C: 19 patients). The total MOCART score was 53.4 ± 17.3 in group M and 50.3 ± 11.2 in group C, with no significant difference between the 2 groups. The subchondral change subscore was significantly lower in groups M and C compared with group I (group I: 16.3 ± 3.8 ; group M: 11.9 ± 4.6 ; group C, 12.4 ± 3.1 ; group I vs group M, $P = .008$; group I vs group C, $P = .034$). A weak but statistically significant correlation was observed between the subchondral change subscore and several PROs at 6 months and 2 years postoperatively (Table 3). The measured subchondral edema depth showed no statistical difference between the groups (group I: 6.7 mm; group M: 12.6 ± 7.9 mm; group C, 12.0 ± 7.0 mm; $P = .067$). The subchondral edema depth

was found to be associated with VAS score, Lysholm score, KOOS Pain, KOOS Symptoms, and KOOS ADL at 6 months postoperatively. At 12 months postoperatively, it remained associated with VAS scores, and at 24 months, it was significantly associated with VAS score, IKDC Symptoms score, IKDC Sports score, IKDC total score, and KOOS Pain (Table 3). The ICC values for the measurement of subchondral edema subscore and depth were 0.942 and 0.961, respectively, for intraobserver reliability, and 0.954 and 0.985, respectively, for interobserver reliability.

Patients with severe edema demonstrated higher VAS score and lower KOOS Pain and KOOS ADL at 6 months compared with those with no or mild edema ($P = .004$, $P = .027$, and $P = .043$, respectively). Additionally, at 2 years postoperatively, patients with severe subchondral edema showed significantly higher pain VAS scores, indicating more persistent pain, than those with no or mild subchondral edema ($P = .010$).

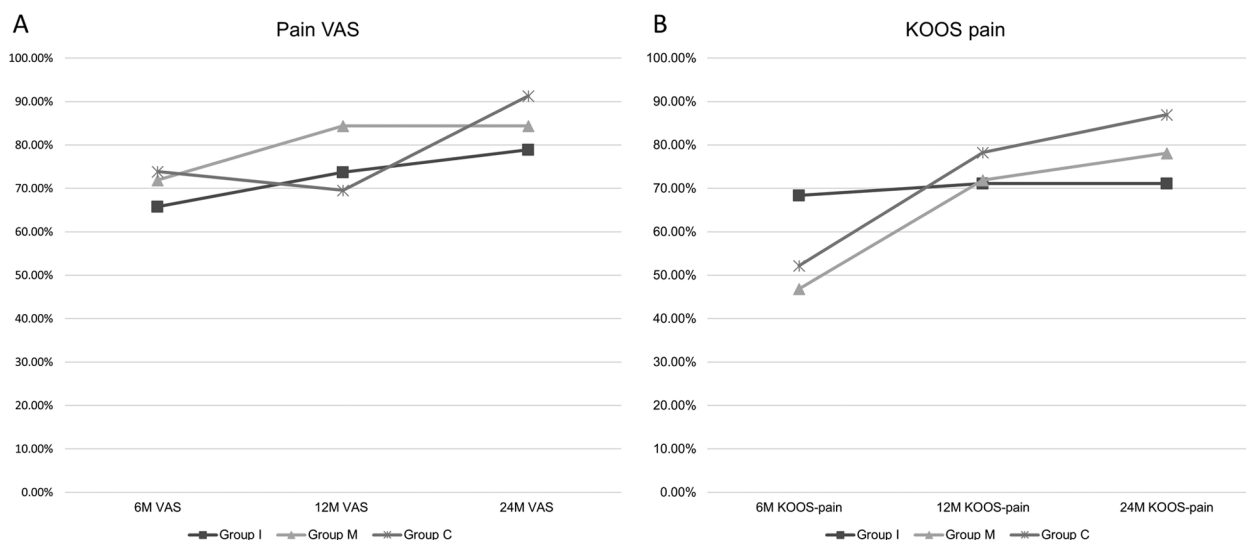


Figure 5. Graphs displaying the serial minimal clinically important difference (MCID) achievement rates for the (A) visual analog scale (VAS) pain score and (B) Knee injury and Osteoarthritis Outcome Score (KOOS) Pain across the 3 groups. Although no statistically significant differences were observed, group I demonstrated a relatively consistent MCID achievement rate over time. In contrast, groups M and C, which underwent additional cartilage repair procedures, exhibited a trend of initially lower rates that increased over time. Group I, isolated HTO; Group M, HTO with microdrilling; Group C, HTO with UCB-MSC implantation.

Second-Look Arthroscopic Cartilage Status and PROs

Cartilage status evaluated through second-look arthroscopy performed approximately 1 year postoperatively using the ICRS CRA grading system showed a statistically significant difference among the groups (Table 4). However, the ICRS grade did not demonstrate a statistically significant correlation with any PROs at any time point.

DISCUSSION

The principal findings of this study are as follows. First, combining cartilage procedures involving subchondral drilling, such as microdrilling or UCB-MSC implantation, with HTO was associated with delayed functional recovery at 6 months postoperatively compared with isolated HTO, as evidenced by less improvement in some PROs and lower MCID achievement rates. However, by 12 to 24 months, these differences were no longer statistically significant. Notably, these comparable clinical outcomes persisted despite the fact that the combined procedure groups demonstrated arthroscopically superior cartilage regeneration compared with the isolated HTO group. Second, the extent and depth of subchondral edema on the MFC observed on MRI at approximately 1 year postoperatively showed a significant correlation with patients' subjective pain and functional outcomes during the short-term postoperative period.

Although cartilage procedures combined with HTO may enhance cartilage defect filling, their additional clinical benefit—especially regarding PROs—remains unclear.^{4,15,21}

Validating these potential benefits requires well-designed direct comparative studies between isolated HTO and HTO with cartilage procedures, but such studies are limited and often heterogeneous.³ Given that the clinical benefits of these combined procedures remain unproven or insufficiently established, their use should be carefully considered. These procedures may impose considerable financial burdens on patients, and their potential adverse effects must also be weighed. HTO is typically performed in younger, more active patients who are often engaged in socioeconomic activities.⁸ Therefore, facilitating rapid recovery to enable early return to work and daily function is an important consideration. However, most comparative studies between isolated HTO and HTO with cartilage procedures have focused on clinical outcomes beyond 2 years postoperatively.^{7,15,16,21} As a result, data regarding early postoperative pain and functional recovery within 2 years are currently very limited. Among the few available studies, Ferruzzi et al⁴ compared isolated HTO with HTO combined with autologous chondrocyte implantation (ACI) or microfracture. However, early clinical outcomes within 2 years were presented only as trend graphs, without detailed numeric values or statistical comparisons. According to the trends shown in those graphs, the group that underwent cartilage repair procedures tended to report lower PROs compared with the isolated HTO group—similar to the findings observed in the present study.

In this study, at the 6-month follow-up, certain PROs and MCID achievement rates were significantly lower in the groups that underwent additional cartilage procedures than in the isolated HTO group. The reason for this difference remains unclear; however, several contributing

TABLE 3
Correlation Test Results Between PROs
and Subchondral Edema Subscores/Subchondral
Edema Depth at 6, 12, and 24 Months
Postoperatively in All Included Patients^a

	6 Mo	12 Mo	24 Mo
PROs and subchondral edema subscore			
VAS score	-0.339	-0.134	-0.362
Lysholm score	0.187	0.074	0.150
IKDC score			
Symptoms	0.144	0.148	0.238
Sports	0.001	0.052	0.272
Function	0.057	-0.012	0.051
Total	-0.013	0.088	0.250
KOOS subscale			
Pain	0.333	0.047	0.259
Symptom	0.221	0.034	0.045
ADL	0.264	0.107	0.265
Sports	0.022	0.001	0.116
QOL	-0.014	-0.113	0.085
Improved PROs and subchondral edema subscore			
VAS score	0.005	-0.190	0.019
Lysholm score	0.101	-0.061	-0.003
IKDC score			
Symptoms	0.042	0.032	0.085
Sports	-0.022	-0.066	0.131
Function	0.142	0.097	0.108
Total	-0.054	0.005	0.132
KOOS subscale			
Pain	0.255	-0.002	0.156
Symptom	0.079	-0.075	0.003
ADL	0.198	0.064	0.151
Sports	0.187	0.036	0.230
QOL	-0.028	-0.127	0.059
PROs and subchondral edema depth			
VAS	0.332	0.260	0.380
Lysholm score	-0.301	-0.191	-0.187
IKDC score			
Symptoms	-0.245	-0.246	-0.270
Sports	0.017	-0.062	-0.282
Function	-0.120	-0.070	-0.136
Total	-0.055	-0.143	-0.280
KOOS subscale			
Pain	-0.348	-0.223	-0.295
Symptom	-0.270	-0.198	-0.138
ADL	-0.314	-0.224	-0.247
Sports	.076	-0.013	-0.096
QOL	-0.019	.037	-0.080

^aSpearman correlation coefficients (*r*) were calculated following normality testing. Boldface type indicates statistical significance. ADL, Activities of Daily Living; IKDC, International Knee Documentation Committee; KOOS, Knee injury and Osteoarthritis Outcome Score; PRO, patient-reported outcome; QOL, Quality of Life; VAS, visual analog scale.

factors can be inferred. These include subchondral bone drilling, additional exposure for cartilage repairs (such as arthrotomy or arthroscopic debridement), and more restrictive postoperative protocols, including prolonged weightbearing restrictions, all of which may delay

TABLE 4
Cartilage Status During the Second-Look
Arthroscopy Assessed Using ICRS CRA^a

ICRS CRA Grade	Group I	Group M	Group C	P Value ^b
1	0	7 (21.9)	3 (13.0)	<.001
2	4 (11.4)	11 (34.4)	14 (60.9)	
3	10 (28.6)	7 (21.9)	5 (21.7)	
4	21 (60.0)	7 (21.9)	1 (4.3)	

^aData are presented as n (%). CRA, Cartilage Repair Assessment; ICRS, International Cartilage Regeneration & Joint Preservation Society.

^bP values were calculated using the chi-square test.

functional recovery.³¹ To more specifically investigate the factors related to subchondral bone, this study focused on subchondral edema on MRI, demonstrating that both the severity and depth of edema were significantly associated with early pain and certain PROs during the early postoperative period. The relationship between subchondral edema and clinical outcomes has not yet been clearly established. While some studies have suggested that preoperative subchondral edema may be associated with early clinical outcomes,²⁴ others have reported no such correlation.¹⁷ Likewise, the clinical significance of postoperative subchondral changes or edema remains unclear, with several reports indicating minimal or no effect on outcomes.^{18,40} Koenig et al¹⁸ reported that postoperative bone marrow edema did not affect clinical outcomes after matrix-induced ACI or microfracture in a 5-year follow-up. Similarly, Zak et al⁴⁰ found that although subchondral changes frequently appeared on long-term follow-up MRI scans after ACI, they did not influence clinical outcomes. However, in our study involving cartilage procedures that included subchondral drilling, the degree of subchondral edema observed on follow-up MRI performed approximately 1 year after surgery was associated with early postoperative pain and clinical outcomes assessed between 6 months and 24 months, although the strength of this association was relatively weak.

In this study, when cartilage procedures were performed in conjunction with HTO, arthroscopic evaluation demonstrated markedly superior cartilage status compared with isolated HTO. However, this improved cartilage status did not translate into better PROs in the short term. Nevertheless, the significance of improved cartilage status after HTO should be considered from a broader perspective. Although it remains unclear whether combining cartilage repair with HTO improves clinical outcomes,³ several studies have reported that better postoperative cartilage status is linked to superior mid- to long-term outcomes and increased long-term survival.^{33,35,37} Yang et al³⁷ assessed cartilage status approximately 20 months postoperatively using second-look arthroscopy in patients who underwent HTO. Patients were classified into groups with good or poor cartilage status and followed for

a mean of 5.2 to 5.4 years, with the better cartilage group showing significantly superior PROs. Similarly, Tsushima et al³⁵ found that patients with postoperative improvement in cartilage status demonstrated significantly better mid-term outcomes at 5 years. Schuster et al³³ reported higher 10-year survival rates in patients achieving complete defect filling compared with those with incomplete filling. These findings highlight that postoperative cartilage status can have an effect on mid- to long-term outcomes and survival after HTO.^{33,35,37} Therefore, if cartilage procedures can reliably achieve successful cartilage regeneration, favorable mid- to long-term outcomes may be expected. However, successful cartilage regeneration is not guaranteed, especially in patients with osteoarthritis undergoing HTO.^{14,15,21,38} For instance, in the study by Jung et al,¹⁵ subchondral drilling combined with HTO resulted in even cartilage coverage with maturation in only 3 of 30 patients (10%) on second-look arthroscopy, while 56.7% showed partial and immature regeneration, and the remainder showed minimal or no regeneration. Even in studies that attempted more advanced procedures such as UCB-MSC^{14,38} or bone marrow aspirate concentration implantation,³⁸ favorable cartilage restoration (ICRS CRA grades 1 and 2) was achieved in 64% to 67% of cases.^{14,38} Taken together, these findings indicate that a subset of patients fail to achieve favorable cartilage restoration, potentially leading to limited long-term benefit despite additional cost, particularly in cases involving MSC treatment, while also experiencing increased early postoperative pain and delayed recovery, as shown in our results. Therefore, careful patient selection may be critical when considering combined cartilage repair procedures with HTO, ideally focusing on individuals most likely to achieve successful cartilage regeneration.¹¹

Limitations

This study has several limitations. First, it was conducted retrospectively, which inherently introduces the potential for selection bias. A considerable number of patients were excluded from the analysis, which may also contribute to selection bias. Second, the study focused exclusively on patients who underwent cartilage procedures that were most frequently performed by us—microdrilling and implantation of UCB-MSCs. The findings of our study may not be generalizable to all types of cartilage restoration procedures. Third, baseline cartilage defect size differed significantly among groups, primarily because group M (microdrilling) had smaller defects. As microdrilling is less applicable to diffuse cartilage lesions, smaller defects were expected in this group. Given that the isolated HTO group exhibited greater early improvements in pain and functional scores despite larger defects, cartilage defect size is unlikely to have biased the study's conclusions. Fourth, the rehabilitation protocols differed between the isolated HTO and combined cartilage procedure groups. However, because immediate weightbearing, as in isolated HTO, is not feasible after cartilage procedures, the more restricted rehabilitation should be regarded as an

inherent component of the cartilage procedures itself. Lastly, the surgical procedures were not performed contemporaneously. Given the retrospective nature of the study, certain procedures may have been more commonly performed during specific time periods. Nonetheless, all surgeries were performed by a single experienced surgeon, and we believe there were no meaningful differences in surgical proficiency over the study period.

CONCLUSION

Combined cartilage procedures involving subchondral drilling after HTO are associated with increased early postoperative pain and delayed functional recovery during the first 6 months. Although second-look arthroscopy demonstrated improved cartilage status in the cartilage procedure groups, clinical outcomes at 12 and 24 months were comparable to those observed after isolated HTO.

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APPENDIX

Appendix material 1

Preparation of UCB-MSCs

For UCB-MSCs, Cartistem® (MEDIPOST Co. Ltd., Seongnam-si, Gyeonggi-do, South Korea), an off-the-shelf cartilage regeneration product. UCB-MSCs were produced at the cell manufacturing facility in full compliance with the Good Manufacturing Practice requirements of the Ministry of Food and Drug Safety, as well as donor screening, cell isolation and expansion, and quality control measures. This product was approved for cartilage regeneration by the Korea Food and Drug Administration in January 2012 and consists of 1.5mL hUCB-MSCs (7.5×10^6 cells/vial) and 4% hyaluronic acid hydrogel. Safety was assessed by a previous clinical trial by Park et al. and no serious adverse events were reported. The therapeutic dose was determined by preoperative measurement of the cartilage defect size on magnetic resonance imaging: $500 \mu\text{L}/\text{cm}^2$ was recommended according to the manufacturer's instructions. During preparation, 1.5 mL of cells was drawn into a syringe and gently dropped into the freeze-

dried HA hydrogel. After incubating at room temperature for 30 minutes, the mixture was transferred to a syringe for implantation.

APPENDIX TABLE 1

The mean and standard deviation of the patient-reported outcomes for the entire patient cohort, and the minimal clinically important difference (MCID) derived based on these values

	All patients	MCID
VAS	35.6±26.8	13.4
Lysholm score	26.8±21.6	10.8
IKDC – Total	22.8±18.5	9.3
KOOS – Pain	26.2±21.7	10.9
KOOS – Symptom	20.9±19.9	10.0
KOOS – ADL	24.1±20.6	10.3
KOOS – Sports	21.8±25.7	12.9
KOOS – QOL	21.0±20.9	10.5

VAS, visual analog scale; IKDC, International Knee Documentation Committee; KOOS, Knee injury and Osteoarthritis Outcome Score; ADL, activity of daily living; QOL, quality of life.