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Clinical Benefits of Cartilage Repair in High Tibial Osteotomy Can Only Be Expected in Patients with Successfully Regenerated Cartilage

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Background: The clinical benefits of combining cartilage procedures with high tibial osteotomy (HTO) remain undetermined. This study aimed to evaluate the additional clinical benefits by comparing a combined procedure group with an isolated HTO group, with stratification based on the success of cartilage regeneration.

Methods: Patients who underwent medial open-wedge HTO from 2010 to 2022 with a minimum 2-year follow-up were retrospectively reviewed. Patients were divided into 2 groups: HTO + combined cartilage procedures (C group) and isolated HTO (I group). C group was further divided into 2 subgroups based on the medial femoral condyle (MFC) cartilage status assessed on second-look arthroscopy: well-regenerated cartilage (C1 group) and poorly regenerated cartilage (C2 group). Propensity score-matched I groups were formed for each C1 and C2 group (C1-matched and C2-matched group I), based on baseline factors affecting clinical outcomes. Comparative analysis was performed for each matched pair based on patient-reported outcomes (PROs).

Results: A total of 313 patients were retrospectively reviewed in this study, with 199 patients included in the analysis: 83 patients in the C group (49 in the C1 group and 34 in the C2 group) and 116 patients in the I group. Baseline characteristics showed no significant difference between the matched groups after propensity score matching. The mean follow-up period for all groups was approximately 3 years with no significant differences. The C1 group showed significantly better PROs and improved PROs at the final follow-up compared to the C1-matched I group (visual analog scale score, $p < 0.001$; Lysholm, $p = 0.004$; Knee injury and Osteoarthritis Outcome Score subscales, $p \leq 0.018$). However, the C2 group did not show any differences in PROs compared to the C2-matched I group at the final follow-up.

Conclusions: Only patients with well-regenerated cartilage after combined cartilage repair procedures showed additional clinical outcome improvements with HTO. When considering combined cartilage repair procedures with HTO, selecting appropriate candidates for achieving successful cartilage regeneration is necessary to yield additional clinical benefits.

Keywords: *Osteoarthritis, Articular cartilage, Cartilage injuries, Osteotomy, Cartilage sugery*

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High tibial osteotomy (HTO) is an effective treatment for young, active patients with medial compartment osteoarthritis and varus deformity, demonstrating good-to-excellent clinical outcomes from the short to long term.[1,2] The long-term survival rate after HTO ranges approximately 64%–97.6% at 10 years and 44%–90.4% at 15 years, indicating a significant potential for future conversion to total knee arthroplasty given the young age of the patient cohort.[1,2] Accordingly, to improve the surgical outcomes, various studies on influencing factors, precise bone correction, and optimal target alignment for each patient are underway.[3-7]

Additionally, efforts are being made to improve long-term survival and clinical outcomes after HTO in a slightly different way, which is to implement additional cartilage procedures on the medial femoral condyle (MFC) in combination with HTO.[8-10] However, evidence for the clinical benefits of these combined procedures remains insufficient. A recent systematic review of studies comparing HTO with combined cartilage repair versus isolated HTO concluded that the heterogeneity of studies makes it difficult to ascertain the additional clinical benefits of combined cartilage procedures.[11] Nevertheless, studies analyzing outcomes differently reported that patients with successful cartilage regeneration after HTO had significantly higher long survival[12] and better intermediate-term clinical outcomes.[13,14]

A considerable portion of patients undergoing HTO exhibits diffuse cartilage defects and impaired meniscal function, leading to a high probability of failure even after cartilage repair.[15] The lack of clear clinical benefit in combined cartilage procedures compared to isolated HTO in previous studies may be attributed to the high proportion of patients failing to achieve sufficient cartilage regeneration. If clinical benefits are demonstrated in only patients with well-regenerated cartilage, it can be interpreted that selective combined cartilage procedures could be advantageous for appropriately indicated patients.

Therefore, this study aimed to determine the additional clinical benefits of combined cartilage procedures by comparing them with isolated HTO, with stratification based on the success of cartilage repair. Given that patients with successful cartilage regeneration may inherently have superior underlying factors, we planned to create matched groups for comparison. Our hypothesis was that combined cartilage repair procedures would provide additional clinical benefits in patients with successful cartilage regeneration.

METHODS

This study was reviewed and approved by Gangnam Severance Institutional Review Board (IRB No. 3-2024-0183). Due to the retrospective nature of the study and the minimal risk involved, patient consent was waived by the IRB.

Patients

This retrospective study reviewed patients who underwent medial open-wedge HTO (MOWHTO) for medial compartment osteoarthritis between September 2010 and April 2022, with a minimum follow-up of 2 years. Exclusion criteria included (1) no follow-up patient-reported outcomes (PROs) evaluation at the final follow-up, (2) no second-look arthroscopy performed, (3) previous knee ligament surgery or injury, (4) surgical history in the involved limb, (5) complications after MOWHTO (e.g. nerve injury, nonunion after hinge fracture), (6) severe involved limb pain due to other pathology (e.g. lumbar radiculopathy).

Indications for MOWHTO were as follows: (1) relatively young (< 65 years) and active patients with medial knee pain refractory to conservative treatment for at least 3 months, (2) medial compartment osteoarthritis with varus deformity (mechanical tibiofemoral angle > 5°), and (3) a relatively good range of motion (arc of motion > 100° and flexion contracture < 15°) without joint instability. Combined cartilage repair procedures included microfracture, microdrilling, and allogeneic umbilical cord blood-derived mesenchymal stem cell-hyaluronic acid composite implantation (UCB-MSC-HA, Cartistem; MEDIPOST

Co. Ltd.). These procedures were considered for patients with near full-thickness MFC cartilage defects classified as International Cartilage Repair Society (ICRS) grade ≥ 3b. Since the clinical benefits and appropriate indications for combining cartilage procedures with MOWHTO have not been fully established, these procedures were not actively recommended. Instead, decisions were primarily based on patient preference following a comprehensive explanation of the procedure. The type of cartilage procedure was also determined by the patient after the senior surgeon (SHK) thoroughly explained the procedure details and associated costs. It was fully communicated that the primary contributor to symptom improvement would be MOWHTO, while the cartilage procedure might assist in cartilage defect filling but lacks well-established clinical benefits.[16] For patients with extensive defects, potential for poor outcomes was explained, and cartilage repair was performed only if the patient desired it and it was deemed feasible during arthroscopy.

Patients were categorized into 2 groups: those who underwent concomitant cartilage repair procedures (C group) and those who underwent isolated HTO (I group). Group C was further divided into 2 subgroups based on the MFC cartilage status assessed by ICRS Cartilage Repair Assessment (CRA) grades on second-look arthroscopy: good cartilage regeneration (ICRS grade 1–2, C1 group) and poor cartilage regeneration (ICRS grade 3–4, C2 group).[17,18] Propensity score-matched I groups were created for each C1 group and C2 group (C1-matched and C2-matched I groups). Demographic, radiographic, and arthroscopic baseline characteristics were assessed. Baseline factors affecting outcomes after HTO, including age, sex, body mass index, Kellgren-Lawrence (K-L) grade, MFC cartilage defect size, and pre- and postoperative alignment, were used in propensity score matching.

Surgical Procedures and Rehabilitation

All surgical procedures, including biplanar MOWHTO and combined cartilage repair, were performed by a single senior orthopedic surgeon (SHK). For cartilage repair, arthroscopic procedures (microfracture or microdrilling) were conducted prior to the HTO, while mini-open arthrotomy (UCB-MSC implantation) was performed after HTO. The HTO procedures were consistent between the groups in terms of bone correction and fixation methods, adhering to previously described methods.[6] The target for valgus realignment was the Fujisawa point (weight-bearing line [WBL] ratio, 62.5%). Two guidance pins for transverse osteotomy were inserted from the medial tibial cortex, approximately 35–40 mm below the medial joint line, extending to the fibular tip to ensure the osteotomy was within the safe zone as described in the literature.[19] For the biplanar osteotomy, proximal tibial tubercle osteotomy was performed at an angle of about 110° to transverse osteotomy.[5] After achieving the planned correction angle, the osteotomy site was rigidly fixed using a locking plate (Tomofix locking plate; DePuy Synthes) and screws.

The combined cartilage procedures in this patient cohort included microfracture with an arthroscopic awl, microdrilling with a small-diameter drill, and implantation of an allogeneic UCB-MSCs-HA composite (Car-

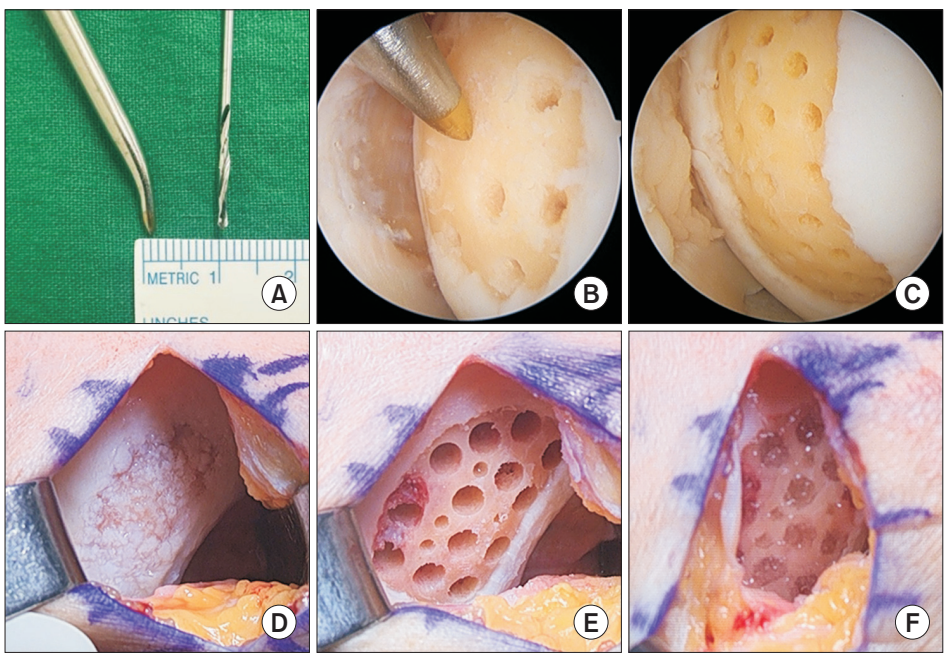

Fig. 1. Combined cartilage repair procedures. (A) Arthroscopic microfracture awl and 1.5-mm diameter drill bit used for the microdrilling procedure. (B) Arthroscopic microfracture on the medial femoral condyle (MFC) cartilage defect. (C) Arthroscopic microdrilling on the MFC cartilage defect. (D, E) Umbilical cord blood-derived mesenchymal stem cell-hyaluronic acid composite (UCB-MSC-HA) implantation procedures. (D) Baseline MFC cartilage defect. (E) Multiple drill holes were made after cartilage defect preparation. (F) UCB-MSC-HA implantation.

tistem; MEDIPOST Co. Ltd.) (Fig. 1). Cartilage defect preparation followed the same principles for all 3 procedures. Cartilage margins were trimmed using a gouge to create vertical healthy edges, and the underlying calcified layer was meticulously removed.[20] For microfracture, subchondral perforations were made using an arthroscopic awl (Arthrex) with a width of 2–3 mm and a depth of 5–8 mm. For microdrilling, subchondral perforations were created using a 1.5 mm-diameter drill bit (ECT Internal Fracture Fixation Drill Bits, Zimmer Biomet) to achieve smaller diameter and deeper perforations (13–15 mm in depth).[20] A guide (B-IP-1512; Bioretec Ltd.) was used to control the microdrilling procedure and prevent drill bit breakage. In the marrow stimulation technique, numerous closely spaced (2–3-mm intervals) perforations were made to maximize the quantity of bone marrow cells derived from the perforations. For UCB-MSC-HA composite implantation, a mini-open arthrotomy was performed. After the defect preparation, multiple drill holes of 2 different sizes (4 mm × 7 mm and 2 mm × 7 mm [diameter × depth]) were made in the subchondral bone. The prepared UCB-MSC-HA composite was subsequently implanted into the holes and then covered prepared defect. Information about the UCB-MSC-HA product and preparation process are provided in Supplementary Material 1.

Rehabilitation protocols varied slightly depending on the performance of combined cartilage repair. Patients who underwent isolated HTO were instructed to begin crutch-assisted ambulation with partial weight-bearing after surgery. Passive range of motion exercises started 2 days postoperatively with a hinged knee brace starting at 60°, increasing by 30° every 2 weeks. After 6 weeks, patients discontinued the use of crutches and the knee brace. For those with combined cartilage repair, weight-bearing was initially more restricted. Passive range of motion exercise was emphasized using a continuous passive motion machine to promote early cartilage healing.[21] Weight-bearing was restricted for 4 weeks with crutches, followed by partial weight-bearing for an additional 6 weeks.

Radiographic and Arthroscopic Assessment

Preoperative K-L grade was assessed using standing anteroposterior (AP) and Rosenberg view knee radiographs, with the worse radiograph among the 2 being used for grading. Preoperative and postoperative mechanical alignment was evaluated using the WBL ratio measurement on standing whole lower extremity radiographs taken preoperatively and at 1 year postoperatively.

Arthroscopic assessments were performed at baseline (before HTO during the primary surgery) and at second-look arthroscopy during plate removal approximately 1 year after surgery. Baseline arthroscopic evaluation included the size of the MFC cartilage defect. The medial meniscus status was assessed secondarily based on the combined meniscus procedure (none, partial meniscectomy, or subtotal meniscectomy). In the combined cartilage repair group (C group), repaired MFC cartilage was evaluated using the ICRS CRA grading system: grade 1 (normal), grade 2 (near normal), grade 3 (abnormal), and grade 4 (severely abnormal) (Fig. 2).[17] In the isolated HTO group (I group), cartilage procedures were not performed; therefore, evaluation methods such as the original ICRS grading system or Koshino stage[22] would typically be more appropriate for assessing cartilage status. However, to facilitate a relative comparison with the C group, the cartilage status in the I group was assessed using the categories and criteria of the ICRS CRA system.

Clinical Outcome Assessment

Clinical outcomes were assessed using several PROs: pain

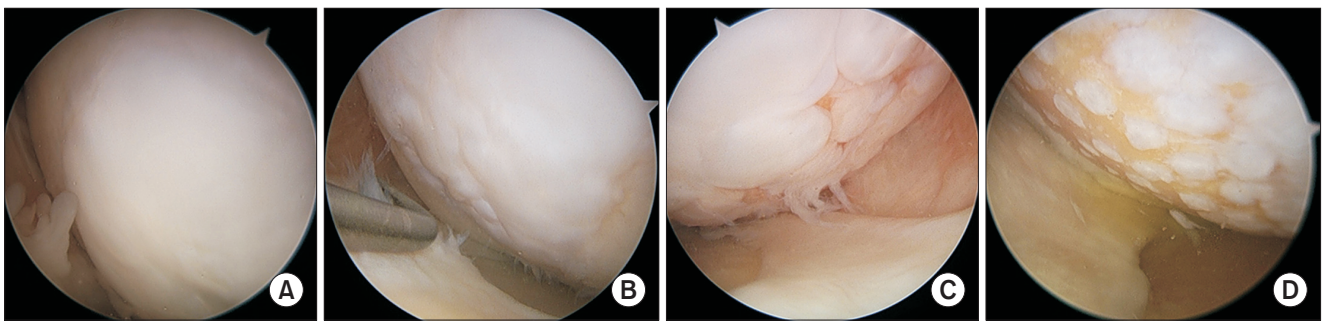

Fig. 2. Assessment of the repaired medial femoral condyle cartilage using International Cartilage Repair Society Cartilage Repair Assessment (ICRS CRA). Second-look arthroscopic images of patients who underwent umbilical cord blood-derived mesenchymal stem cell-hyaluronic acid composite implantation (A-C) and of a patient who underwent arthroscopic microdrilling (D). These images were classified according to the ICRS CRA grading system as follows: grade 1 (A), grade 2 (B), grade 3 (C), and grade 4 (D).

visual analog scale (VAS), Lysholm knee score, and Knee injury and Osteoarthritis Outcome Score (KOOS). Each PRO was evaluated preoperatively and at the final follow-up (minimum 2 years). The minimal clinically important differences (MCIDs) for each PRO were based on previous related studies: VAS, 27;[23] Lysholm score, 10.1;[23] KOOS pain, 15.4; KOOS symptoms, 15.1; KOOS activities of daily living, 17; KOOS sports/recreation, 11.2; and KOOS quality of life, 16.5.[24] The MCID achievement rate for each PRO was evaluated.

Statistical Methods

All statistical analyses were performed using IBM SPSS version 26.0 (IBM Corp.), with statistical significance set at $p < 0.05$. Continuous variables were presented as mean ± standard deviation, and categorical variables as number (percentage) unless otherwise indicated. The primary purpose of this study was to compare the PROs between the combined cartilage repair procedure group (C group) and the isolate HTO group (I group) based on the cartilage regeneration status of patients in C group (C1 and C2 groups). Since numerous factors affect the clinical outcome after MOWHTO, matching baseline factors was necessary to determine the superiority between the groups. The C1, C2, and I groups showed differences in baseline characteristics, which was related to the baseline severity of the osteoarthritis. Propensity score-matched I groups were formed for each C1 group and C2 group (C1-matched and C2-matched I groups). The unbalanced baseline factors (age, sex, body mass index, preoperative K-L grades, MFC cartilage defect size, and preoperative and postoperative 1-year WBL ratio) between the groups were utilized as matching factors for propensity score matching. Using the greedy matching algorithm, 1:1 propensity score matching was applied to maximize the number of patients in C group and minimize differences between the groups. Standardized mean difference (SMD) was used to evaluate the quality of matching. Comparisons between each matched pair group were performed using an independent *t*-test or Mann-Whitney *U*-test, depending on the normality test results (Shapiro-Wilk test). Categorical variables from the 2 groups were compared using chi-square tests. Logistic regression analysis was performed to identify the factors affecting the success or failure of the cartilage regeneration. To select factors for inclusion in the logistic regression analysis, demographic factors (age, sex, and body mass index) and arthritis- and surgery-related factors (MFC defect size, K-L grade, meniscal procedure, and postoperative WBL ratio) were initially screened using the Spearman correlation test to identify variables significantly associated with successful cartilage regeneration. Factors that showed significant correlations were subsequently included in the logistic regression analysis. Receiver operating characteristic curve analysis was utilized to determine

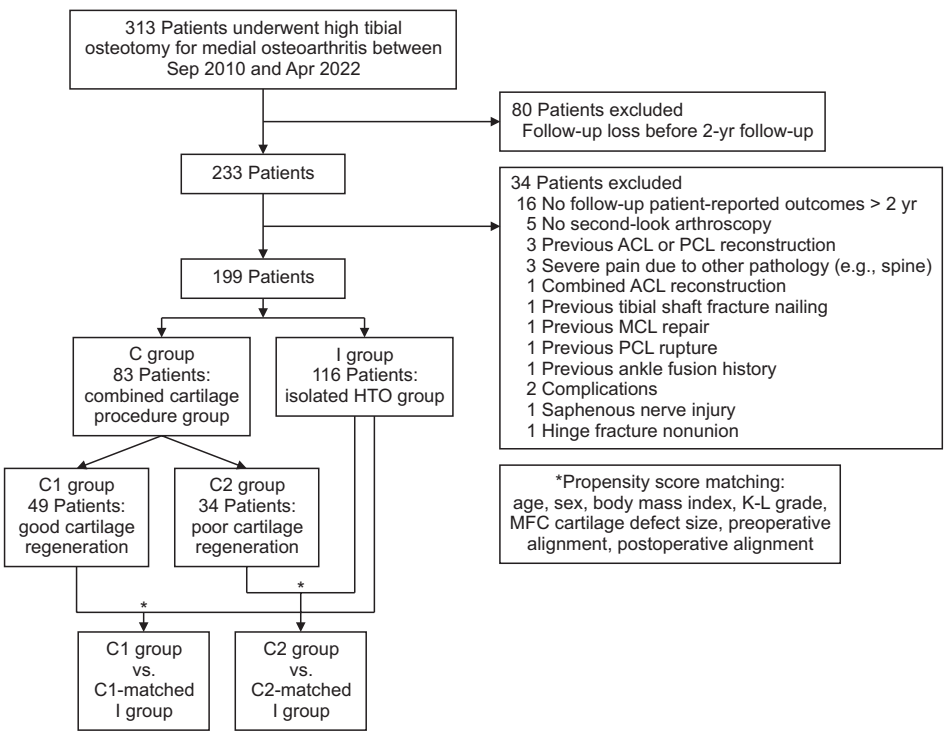

Fig. 3. Patient flow diagram. The C1 group is the group of patients with good cartilage regeneration, assessed as International Cartilage Repair Association Cartilage Repair Assessment (ICRS CRA) grade I–II. The C2 group is the group of patients with poor cartilage regeneration, assess as ICRS CRA grade III–IV. C1-matched group I and C2-matched group I were formed by the 1:1 propensity matching using the factors indicated by the asterisk (*) in the flow diagram. ACL: anterior cruciate ligament, PCL: posterior cruciate ligament, MCL: medial collateral ligament, HTO: high tibial osteotomy, K-L: Kellgren-Lawrence, MFC: medial femoral condyle.

the cutoff value for a significant factor in predicting the failure of cartilage regeneration.

RESULTS

A total of 313 patients were retrospectively reviewed in this study, with 199 patients included in the analysis: 83 patients in the C group (49 in the C1 group and 34 in the C2 group) and 116 patients in the I group (Fig. 3). Demographic, radiographic, and arthroscopic baseline characteristics of the patients are presented in Table 1. Baseline characteristics did not differ significantly between the C and I groups, except for a high proportion of patients with K-L grade IV osteoarthritis in the I group (25.9% vs. 15.7%).

In the comparison between the C1 and C2 groups, the MFC defect size was significantly larger in the C2 group than in the C1 group (7.0 ± 2.5 cm^2 vs. 5.7 ± 2.6 cm^2, p = 0.027). The proportion of K-L grade IV osteoarthritis was also higher in the C2 group compared to the C1 group (23.1% vs. 10.2%). Logistic regression analysis identified MFC defect size as the only significant factor associated with successful cartilage repair (p = 0.031; odds ratio, 0.822; 95% CI, 0.688–0.982). The cutoff value of the defect

Table 1. Baseline Characteristics of the Patients

Variable	C group (n = 83)	I group (n = 116)	*p*-value (C vs. I)	C1 group (n = 49)	C2 group (n = 34)	*p*-value (C1 vs. C2)
Age (yr)	57.8 ± 5.9	56.2 ± 6.1	0.074	57.5 ± 5.7	58.2 ± 6.1	0.552
Sex			0.893			0.920
Male	20 (24.1)	27 (23.3)		12 (24.5)	8 (23.5)	
Female	63 (75.9)	89 (76.7)		37 (75.5)	26 (76.5)	
Body mass index (kg/m^2)	26.2 ± 2.9	26.9 ± 3.7	0.198	26.0 ± 2.5	26.5 ± 3.4	0.464
K-L grade			0.109			0.265
Grade I	1 (1.2)	0	-	1 (2.0)	0	-
Grade II	20 (24.1)	17 (14.7)	0.091	14 (28.6)	6 (17.7)	0.252
Grade III	49 (59.0)	69 (59.5)	0.950	29 (59.2)	20 (58.8)	0.974
Grade IV	13 (15.7)	30 (25.9)	0.085	5 (10.2)	8 (23.5)	0.100
MFC defect size (cm^2)	6.2 ± 2.6	6.7 ± 2.6	0.244	5.7 ± 2.6	7.0 ± 2.5	0.027*
Preoperative WBL ratio	18.0 ± 11.4	16.3 ± 13.0	0.327	17.4 ± 11.1	19.0 ± 11.9	0.531
Postoperative WBL ratio	67.6 ± 9.7	68.2 ± 10.4	0.657	68.8 ± 9.0	65.8 ± 10.6	0.182
Meniscus procedure			0.132			0.277
None	23 (27.7)	38 (32.8)		13 (26.5)	10 (29.4)	
Partial meniscectomy	18 (21.7)	32 (27.6)		14 (28.6)	4 (11.8)	
Subtotal meniscectomy	34 (41.0)	43 (37.1)		17 (34.7)	17 (50.0)	
Root repair	8 (9.6)	3 (2.6)		5 (10.2)	3 (8.8)	
Cartilage procedure			-			0.075
Microfracture	23 (27.7)	-		12 (24.5)	11 (32.4)	
Microdrilling	35 (42.1)	-		17 (34.7)	18 (52.9)	
UCB-MSC implantation	25 (30.1)	-		20 (40.8)	5 (14.7)	

Values are presented as mean ± standard deviation or number (%).
K-L: Kellgren-Lawrence, MFC: medial femoral condyle, WBL: weight-bearing line, UCB-MSC: umbilical cord blood-derived mesenchymal stem cell.
*Statistical significance, $p < 0.05$.

size to predict cartilage repair failure was 5.7 cm^2 (area under curve, 0.647; 95% CI, 0.526–0.768; $p = 0.023$) (Fig. 4).

Comparisons of the baseline characteristics of the C1 and C2 groups with the I group before and after propensity score matching are presented in Table 2. The C1 and I groups showed significant differences in baseline characteristics before matching, but these were considered balanced after matching based on the SMD. The C2 group exhibited baseline characteristics similar to those of the I group, with no significant mean differences. After matching, the SMD indicated reduced differences between the groups. Upon evaluating the second-look cartilage status of the I group, only a small proportion of patients (10.3%) demonstrated relatively good cartilage status, classified as ICRS CRA grade 2, while the majority of patients were categorized as ICRS CRA grades 3–4. Detailed information regarding the cartilage status of patients in each group is presented in Table 2.

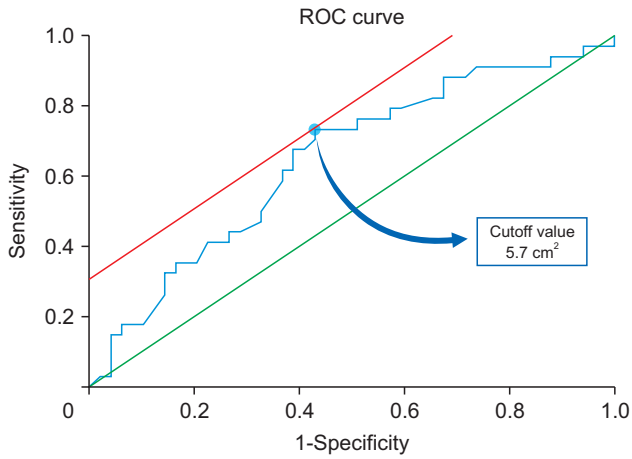

Fig. 4. Receiver operating characteristics (ROC) curve analysis to determine the cutoff value for cartilage defect size in predicting the failure of cartilage regeneration combined with high tibial osteotomy. The analysis identified a cutoff value of 5.7 cm^2, with area under curve of 0.647 (95% CI, 0.526–0.768).

Clinical Outcome

Preoperative, improved, and final PROs and the MCID achievement rate for each PRO were compared between 3 pairs of groups: (1) C group vs. I group, (2) C1 group vs. C1-matched I group, (3) C2 group vs C2-matched I group. The mean final follow-up periods for each group were approximately 3 years and did not differ significantly.

The C group showed significantly better pre- and postoperative outcomes in several PROs compared to I

Table 2. Baseline Characteristics of I Group vs. C1 and C2 Groups (before and after Propensity Score Matching)

Variable	Before matching				After matching			
	I group	C1/C2 Group	*p*-value	SMD	Matched I group	C1/C2 Group	*p*-value	SMD
I group vs. C1 group	I group (n = 116)	C1 group (n = 49)			Matched I group (n = 49)	C1 group (n = 49)		
Age (yr)	56.2 ± 6.1	57.5 ± 5.7	0.230	–0.208*	57.2 ± 4.9	57.4 ± 5.7	0.835	–0.042
Sex			0.867	–0.029			0.460	–0.183
Male	27 (23.3)	12 (24.5)			9 (18.4)	12 (24.5)		
Female	89 (76.7)	37 (75.5)			40 (81.6)	37 (75.5)		
BMI (kg/m^2)	26.9 ± 3.7	26.0 ± 2.5	0.110	0.253*	26.0 ± 3.4	26.0 ± 2.5	0.929	–0.018
MFC defect size (cm^2)	6.7 ± 2.6	5.7 ± 2.6	0.031*	0.372*	5.7 ± 2.5	5.7 ± 2.6	0.985	0.004
K-L grade			0.019*				0.767	
I	0	1 (2.0)		0.204*	0	1 (2.0)		0.204*
II	17 (14.7)	14 (28.6)		0.343*	15 (30.6)	14 (28.6)		–0.045
III	69 (59.5)	29 (59.2)		–0.006	28 (57.1)	29 (59.2)		0.041
IV	30 (25.9)	5 (10.2)		–0.416*	6 (12.2)	5 (10.2)		–0.065
Preoperative WBL ratio	16.3 ± 13.0	17.4 ± 11.1	0.609	–0.090	16.8 ± 13.1	17.3 ± 11.1	0.809	–0.049
Postoperative WBL ratio	68.2 ± 10.4	68.8 ± 9.0	0.749	–0.056	67.8 ± 10.4	68.8 ± 9.0	0.621	–0.100

Table 2. Continued

Variable	Before matching				After matching			
	I group	C1/C2 Group	*p*-value	SMD	Matched I group	C1/C2 Group	*p*-value	SMD
Meniscus procedure			0.202				0.572	
None	38 (32.8)	13 (26.5)			17 (34.7)	13 (26.5)		
Partial meniscectomy	32 (27.6)	14 (28.6)			12 (24.5)	14 (28.6)		
Subtotal meniscectomy	43 (37.1)	17 (34.7)			18 (36.7)	17 (34.7)		
Root repair	3 (2.6)	5 (10.2)			2 (4.1)	5 (10.2)		
Second-look MFC cartilage status, ICRS CRA grade			< 0.001				< 0.001	
Grade 1	0	9 (18.4)			0	9 (18.4)		
Grade 2	12 (10.3)	40 (81.6)			8 (16.3)	40 (81.6)		
Grade 3	40 (34.5)	0			17 (34.7)	0		
Grade 4	64 (55.2)	0			24 (49.0)	0		
I group vs. C2 group	I group (n = 116)	C2 group (n = 34)			Matched I group (n = 34)	C2 group (n = 34)		
Age (yr)	56.2 ± 6.1	58.2 ± 6.1	0.092	–0.329*	58.2 ± 4.7	58.2 ± 6.1	0.965	–0.010
Sex			0.975	–0.006			1.000	0.000
Male	27 (23.3)	8 (23.5)			8 (23.5)	8 (23.5)		
Female	89 (76.7)	26 (76.5)			26 (76.5)	26 (76.5)		
BMI (kg/m^2)	26.9 ± 3.7	26.5 ± 3.4	0.648	0.091	26.4 ± 4.0	26.5 ± 3.4	0.905	–0.029
MFC defect size	6.7 ± 2.6	7.0 ± 2.5	0.526	–0.125	7.2 ± 2.1	7.0 ± 2.5	0.682	0.100
K-L grade			0.899				0.713	
I	0	0			0	0		
II	17 (14.7)	6 (17.7)		0.081	4 (11.8)	6 (17.7)		0.166
III	69 (59.5)	20 (58.8)		–0.013	23 (67.7)	20 (58.9)		–0.183
IV	30 (25.9)	8 (23.5)		–0.054	7 (20.6)	8 (23.5)		0.071
Preoperative WBL ratio	16.3 ± 13.0	19.0 ± 11.9	0.282	–0.216*	18.3 ± 14.5	19.0 ± 11.9	0.836	–0.050
Postoperative WBL ratio	68.2 ± 10.4	65.8 ± 10.6	0.261	0.226*	66.6 ± 10.2	65.8 ± 10.6	0.781	0.067
Meniscus procedure			0.090				0.161	
None	38 (32.8)	10 (29.4)			8 (23.5)	10 (29.4)		
Partial meniscectomy	32 (27.6)	4 (11.8)			9 (26.5)	4 (11.8)		
Subtotal meniscectomy	43 (37.1)	17 (50.0)			17 (50.0)	17 (50.0)		
Root repair	3 (2.6)	3 (8.8)			0	3 (8.8)		
Second-look MFC cartilage status, ICRS CRA grade			0.027				0.117	
Grade 1	0	0			0	0		
Grade 2	12 (10.3)	0			2 (5.9)	0		

Table 2. Continued

Variable	Before matching				After matching			
	I group	C1/C2 Group	*p*-value	SMD	Matched I group	C1/C2 Group	*p*-value	SMD
Grade 3	40 (34.5)	19 (55.9)			12 (35.3)	19 (55.9)		
Grade 4	64 (55.2)	15 (44.1)			20 (58.8)	15 (44.1)		

Values are presented as mean ± standard deviation or number (%).
SMD: standardized mean difference, BMI: body mass index, MFC: medial femoral condyle, K-L: Kellgren-Lawrence, WBL: weight-bearing line, ICRS CRA: International Cartilage Repair Society Cartilage Repair assessment.
*Statistical significance < 0.05 for *p*-value and > 0.2 for SMD.

Table 3. Preoperative, Improved, and Final PROs (Total I Group Vs. Total C Group)

Variable	Preoperative PRO			Improved PRO			PRO at final follow-up		
	C group (n = 83)	I group (n = 116)	*p*-value	C group (n = 83)	I group (n = 116)	*p*-value	C group (n = 83)	I group (n = 116)	*p*-value
VAS	54.4 ± 24.4	58.5 ± 23.6	0.232	32.6 ± 31.8	31.1 ± 29.3	0.731	21.8 ± 20.7	27.4 ± 24.0	0.085
Lysholm	46.7 ± 18.6	40.8 ± 17.9	0.025*	25.5 ± 21.1	24.0 ± 20.8	0.630	73.1 ± 17.4	64.8 ± 21.1	0.004*
KOOS pain	49.6 ± 19.4	46.8 ± 17.5	0.289	26.6 ± 24.4	23.7 ± 20.3	0.360	76.2 ± 16.8	70.5 ± 16.9	< 0.001*
KOOS symptoms	50.8 ± 19.4	46.0 ± 19.1	0.084	24.4 ± 21.1	20.8 ± 22.9	0.839	72.2 ± 15.1	66.7 ± 17.8	0.024*
KOOS ADL	57.4 ± 19.2	51.8 ± 19.4	0.046*	24.4 ± 21.1	23.0 ± 19.0	0.610	81.8 ± 12.8	74.8 ± 15.5	0.001*
KOOS sports/ recreation	23.3 ± 20.6	22.0 ± 20.8	0.665	25.7 ± 32.2	15.8 ± 29.0	0.024*	49.0 ± 26.3	37.8 ± 26.2	0.003*
KOOS QOL	29.8 ± 16.1	26.3 ± 13.8	0.102	21.6 ± 23.5	22.4 ± 20.2	0.796	51.5 ± 20.4	48.8 ± 20.8	0.363

Values are presented as mean ± standard deviation. The mean follow-up periods were 37.0 months for C group and 36.5 months for I group ($p = 0.776$).
PRO: patient-reported outcome, VAS: visual analog scale, KOOS: Knee injury and Osteoarthritis Outcome Score, ADL: activities of daily living, QOL: quality of life.
*Statistical significance, $p < 0.05$.

group (Table 3). The improvement in KOOS sports/recreation was significantly greater in C group than in I group among the improved PROs. However, there were no differences in MCID achievement rates for each PRO between the groups (Fig. 5). In the comparative analysis between the C1 group and the C1-matched I group, the C1 group showed significantly better improved and final postoperative PROs. Even after matching for baseline factors, the C1 group showed better preoperative PROs in 2 measures (Lysholm and KOOS activities of daily living [ADL]). The MCID achievement rates for VAS and KOOS sports/recreation were higher in the C1 group than in the C1-matched I group (VAS, $p = 0.042$; KOOS sports/recreation, $p = 0.040$). The C2 group showed no significant differences in all PROs compared to the C2-matched I group, including MCID achievement rates (Table 4, Fig. 6).

DISCUSSION

The principal finding of this study is that when combined cartilage repair was performed with HTO, the group with well-regenerated cartilage (C1 group) showed superior clinical outcomes compared to the isolated HTO group with matched baseline factors (C1-matched I group). Conversely, the group with poorly regenerated cartilage (C2 group) did not show superior outcomes compared to the matched isolated HTO group (C2-matched I group). These results suggest that the additional clinical benefits of performing cartilage repair procedures with HTO are limited to patients with well-regenerated cartilage.

Currently, there is insufficient evidence to determine whether an additional cartilage repair procedure during HTO provides clinical benefits compared to isolated HTO.[8,11,25] Despite advancements in various cartilage

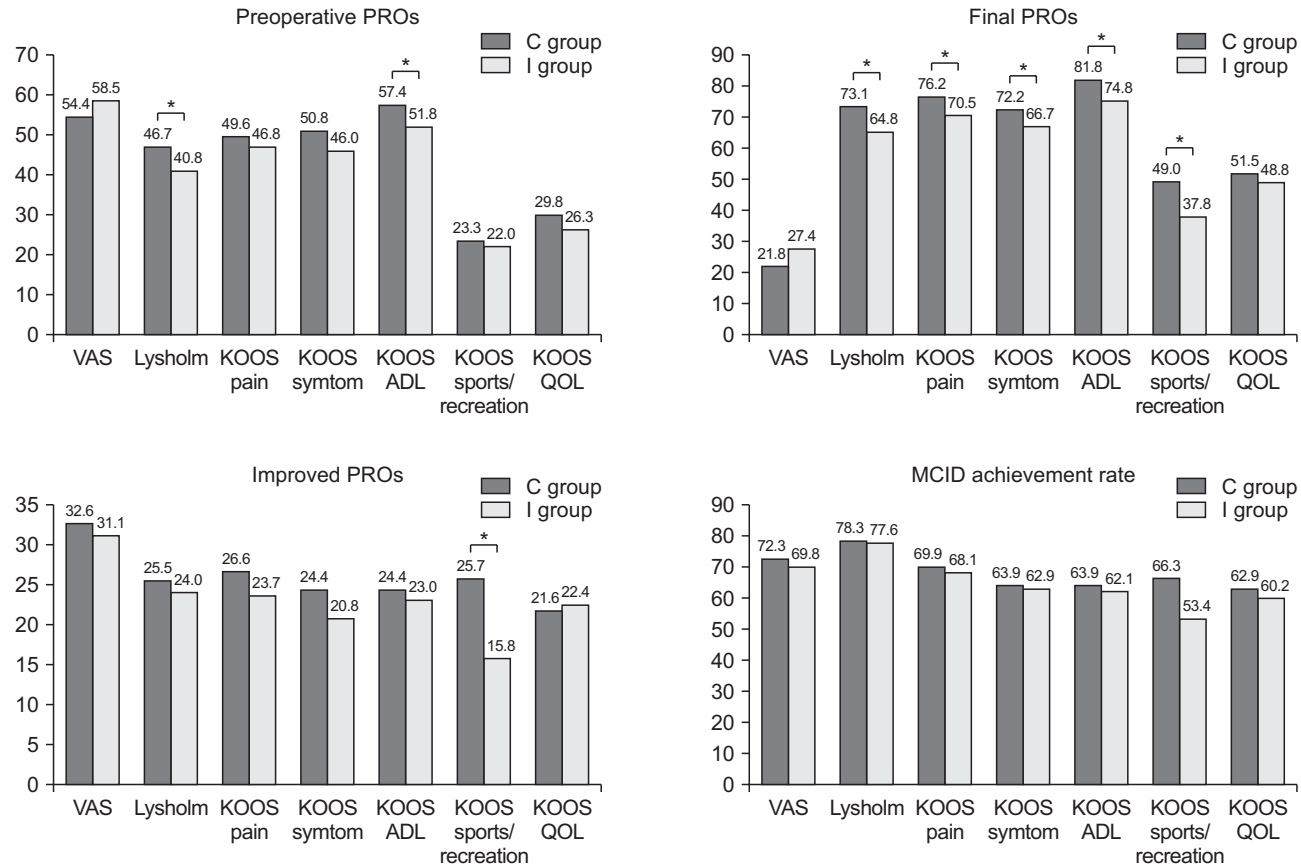

Fig. 5. Comparison of patient-reported outcomes (PROs) and minimal clinically important difference (MCID) achievement rate between the C group and I group. C group showed significantly higher PROs in several preoperative, improved, and final postoperative PROs. The MCID achievement rate did not differ significantly between the groups. VAS: visual analog scale, KOOS: Knee injury and Osteoarthritis Outcome Score, ADL: activities of daily living, QOL: quality of life. *$p < 0.05$.

repair techniques, few studies have directly compared patients undergoing isolated HTO with those undergoing combined cartilage procedures. Ferruzzi et al.[25] compared patients who underwent isolated HTO with those who received HTO combined with autologous chondrocyte implantation (ACI) or microfracture. They reported no significant difference in clinical outcomes between the isolated HTO and combined ACI groups in 11-year follow-up results, while the microfracture group exhibited inferior results. Lee et al.[16] reported better cartilage regeneration on magnetic resonance imaging with combined microfracture but no clinical benefit at 2 years. Similarly, Jung et al.[8] found no clinical benefit with combined microdrilling. In contrast, Bode et al.[26] reported a higher 10-year survival rate for combined ACI compared to HTO alone (94.3% vs. 84.4%). However, a closer review of baseline characteristics in the combined ACI group, as presented in their study, revealed that these patients had less varus deformity and a lower joint line convergence angle than the isolated HTO group, with a mean age of 39.4 years. This makes it difficult to classify them as typical osteoarthritis patients. Overall, previous studies have not demonstrated a clear clinical benefit when comparing the combined cartilage procedure with HTO to the isolated HTO group. Additionally, a recent systematic review highlighted the challenge of drawing conclusions due to substantial heterogeneity among the studies.[11]

When comparing outcomes between the 2 groups of patients who underwent HTO by dividing them based on a specific factor, it is necessary to consider the baseline factors related to arthritis. This is because outcomes after HTO are significantly influenced by baseline factors and the severity of osteoarthritis.[12,27,28] As demonstrated in the comparison between the combined ACI group and the isolated HTO group in above-mentioned study,[26] if 1 group has a more severe initial arthritis condition, no definitive conclusion can be drawn from the comparison. In this study, to determine whether there were clinical

Table 4. Preoperative, Improved, and Final PROs (C1 Group vs. C1-Matched I Group/C2 Group vs. C2-Matched I Group)

Variable	Preoperative PRO			Improved PRO			PRO at final follow-up		
	C1/C2 group	C1/C2-matched I group	*p*-value	C1/C2 group	C1/C2-matched I group	*p*-value	C1/C2 group	C1/C2-matched I group	*p*-value
C1 vs. C1-matched I group	C1 group	C1-matched I group		C1 group	C1-matched I group		C1 group	C1-matched I group	
VAS	52.2 ± 24.3	57.8 ± 23.7	0.248	37.9 ± 24.4	26.4 ± 34.7	0.060	14.3 ± 13.5	31.5 ± 26.7	< 0.001*
Lysholm	51.0 ± 18.5	40.5 ± 18.1	0.005*	25.0 ± 22.2	23.4 ± 20.7	0.707	76.1 ± 17.6	63.9 ± 23.0	0.004*
KOOS pain	51.7 ± 16.3	49.9 ± 15.5	0.575	26.8 ± 20.6	19.4 ± 21.1	0.083	78.5 ± 16.6	69.4 ± 17.8	0.010*
KOOS symptom	53.5 ± 18.5	48.3 ± 18.2	0.160	21.2 ± 19.5	18.4 ± 23.6	0.511	74.8 ± 13.5	66.6 ± 19.4	0.018*
KOOS ADL	59.7 ± 17.4	52.2 ± 19.7	0.048*	24.7 ± 18.1	20.4 ± 19.6	0.266	84.4 ± 11.3	72.6 ± 17.4	< 0.001*
KOOS sports/recreation	21.3 ± 18.9	23.4 ± 21.5	0.618	30.7 ± 27.5	15.5 ± 25.4	0.005*	52.0 ± 23.3	38.8 ± 26.5	0.010*
KOOS QOL	30.6 ± 15.7	27.4 ± 12.8	0.280	22.3 ± 23.8	20.5 ± 19.9	0.674	52.9 ± 19.9	47.9 ± 20.9	0.227
C2 vs. C2-matched I group	C2 group	C2-matched I group		C2 group	C2-matched I group		C2 group	C2-matched I group	
VAS	57.5 ± 24.7	61.0 ± 25.5	0.571	24.9 ± 39.2	30.0 ± 29.0	0.550	32.6 ± 24.3	31.0 ± 23.3	0.788
Lysholm	40.5 ± 17.1	42.1 ± 16.4	0.707	26.1 ± 19.8	18.2 ± 18.8	0.096	68.6 ± 16.4	60.2 ± 20.4	0.068
KOOS pain	46.4 ± 23.0	44.7 ± 14.7	0.721	26.4 ± 29.4	23.1 ± 18.3	0.580	72.8 ± 16.6	67.8 ± 16.1	0.214
KOOS symptom	46.8 ± 20.2	46.5 ± 16.3	0.939	21.7 ± 24.1	17.2 ± 19.5	0.397	68.5 ± 16.7	63.7 ± 17.9	0.249
KOOS ADL	54.0 ± 21.3	51.7 ± 19.6	0.653	24.1 ± 25.0	20.8 ± 18.0	0.534	78.1 ± 14.0	72.5 ± 16.2	0.135
KOOS sports/recreation	26.1 ± 22.9	22.4 ± 20.9	0.486	18.5 ± 37.1	13.6 ± 28.3	0.547	44.6 ± 29.8	36.0 ± 28.4	0.229
KOOS QOL	28.8 ± 16.8	28.3 ± 14.9	0.894	20.6 ± 23.2	22.7 ± 21.8	0.705	49.4 ± 21.2	51.0 ± 21.4	0.763

Values are presented as mean ± standard deviation. The final mean follow-up periods were 34.7 months for C1 group and 38.3 months for C1-matched I group ($p = 0.124$). The final mean follow-up periods were 36.0 ± 10.2 months for C2-matched I group and 40.3 ± 11.1 months for C2 group ($p = 0.073$).
PRO: patient-reported outcomes, VAS: visual analog scale, KOOS: Knee injury and Osteoarthritis Outcome Score, ADL: activities of daily living, QOL: quality of life.
*Statistical significance, $p < 0.05$.

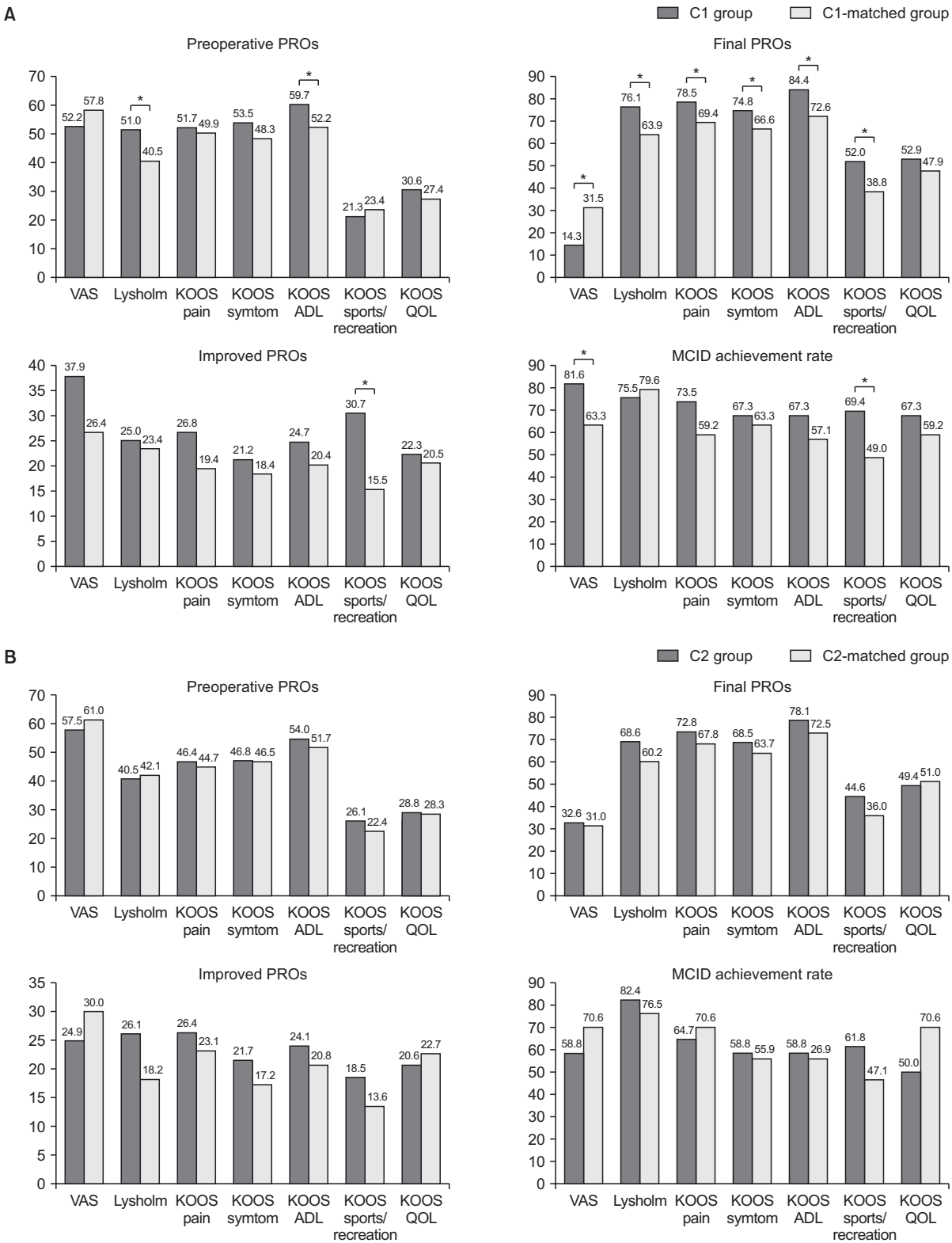

Fig. 6. Comparison of patient-reported outcomes (PROs) and minimal clinically important difference (MCID) achievement rate between the C1 group versus C1-matched I group (A) and C2 group versus C2-matched I group (B). C1 group showed significantly higher PROs in preoperative, improved, and final postoperative PROs compared to C1-matched I group, including MCID achievement rates (A). However, C2 group showed no significant differences in all measures compared to the C2-matched I group. VAS: visual analog scale, KOOS: Knee injury and Osteoarthritis Outcome Score, ADL: activities of daily living, QOL: quality of life. *$p < 0.05$.

benefits of the combined cartilage procedure compared to the isolated HTO group according to the status of cartilage regeneration, matched isolated HTO groups (matched I groups) were formed where baseline factors were matched for each group. Although strict matching was not performed to minimize the loss of study group patients and to include many factors for matching, acceptable matching was confirmed with SMDs. The authors believe that the results obtained are sufficient to draw conclusions.

There are studies that compared clinical outcomes after HTO between groups with good cartilage status and poor cartilage status.[13,14] In these studies, the good cartilage group showed better clinical outcomes in midterm follow-up compared to the poor cartilage status group. The differences between these previous studies and our study can be described in 3 points: First, previous studies included both patients who underwent combined microfracture and isolated HTO, dividing them into good or poor cartilage status groups. In contrast, our study only divided patients who underwent combined cartilage procedures into good or poor cartilage status groups, sparing the isolated HTO group as a control. Second, while previous studies directly compared the good versus poor cartilage status groups, our study compared each of these groups with the isolated HTO group. Third, previous studies did not match baseline factors before comparison, increasing the possibility of confounding factors. In our study, baseline factors were matched, minimizing the potential for confounding. Therefore, our study is considered to have a unique design that has not been previously conducted.

This study's principal finding suggests that the additional clinical benefits of performing cartilage repair procedures with HTO are limited to patients with well-regenerated cartilage. If patients are selected based on appropriate indications likely to result in favorable cartilage regeneration, the proportion of patients with well-regenerated cartilage could increase, potentially leading to superior outcomes when comparing the entire combined cartilage procedure group to the isolated HTO group. When comparing our entire patient group, the C group and the I group, there can be 2 reasons why the C group demonstrated superior clinical outcomes compared to the I group. First, although not statistically significant, the severity of osteoarthritis tended to be more severe in the I group. Second, the proportion of patients with favorable cartilage regeneration was larger in the C group (C1 group, 49 / 83).

The prognostic factors for cartilage regeneration following cartilage procedures combined with HTO in patients with osteoarthritis have not been extensively studied. Patients with osteoarthritis often exhibit diffuse cartilage lesions rather than focal defects, coupled with meniscal functional loss, creating a less favorable environment for cartilage regenerative procedures.[15,29] Jung et al.[15] suggested that significant prognostic factors for cartilage regeneration in osteoarthritis patient include cartilage defect size, meniscal insufficiency, and postoperative alignment. Tsushima et al.[14] identified the WBL ratio as a significant factor affecting MFC cartilage improvement after HTO. Cartilage defect size has been frequently mentioned in several studies as a significant factor affecting cartilage regeneration outcomes.[30] This study also demonstrated that the cartilage defect size was significantly smaller in the well-regenerated cartilage group (C1 group) compared to the C2 group. Additional logistic regression analysis identified cartilage defect size as the only significant factor in this study. Although not statistically significant, the C1 group had a lower proportion of K-L grade IV patients than the C2 and I groups. The K-L grade is the most widely used evaluation system, incorporating joint space and osteophytes[31] and can comprehensively indicate the severity of osteoarthritis, including meniscal loss or the depth and extent of cartilage defects. K-L grade is considered an important factor in selecting good candidate for combined cartilage procedure with HTO.[27,28]

Considering the results of this study and the current literature comprehensively, it is recommended to select appropriate candidates for the combined cartilage procedure with HTO to obtain additional benefits. Candidates likely to succeed in cartilage regeneration should be prioritized. When selecting appropriate candidates, the size of the cartilage defect size should be considered, and it would be advisable to exclude patients with K-L grade IV osteoarthritis. Additionally, based on previous studies, achieving a certain degree of valgus alignment, rather than near neutral alignment, during HTO would be necessary for favorable cartilage regeneration.

This study is not without limitations. First, being a retrospective study, it is susceptible to selection bias. Additionally, patients who underwent cartilage repair were not blinded to their cartilage repair outcomes. Patients in group C1 or C2, where cartilage repair was deemed successful or unsuccessful, were likely informed of their results approximately 1 year postoperatively. This may have influenced their subjective PROs at subsequent follow-ups. Second, the study used 1 : 1 propensity score matching to create matched groups for each comparison. The propensity score matching process also carries risk of selection bias in selecting patients for the matched groups. Third, some preoperative PROs in the C1-matched I group showed significant differences compared to those in the C1 group.

Although matching was performed based on baseline factors and statistical balance was confirmed, the possibility of unidentifiable baseline factors contributing to these differences cannot be ruled out. Additionally, since multiple factors influence the outcomes of MOWHTO, there is a possibility that unrecognized confounding factors may have affected the observed differences between the matched groups in this study. Meniscus function would be one of these influential factors. In our study, meniscus status was indirectly assessed based on the type of procedures performed on the meniscus, which may not have fully reflected its functional integrity. Fourth, because we analyzed patients who underwent HTO over an extended period, there may be heterogeneity in the detailed procedures of HTO performed during that time, and the surgeon's technical proficiency may have changed over time. However, the main HTO procedure (bony correction, target point, fixation method, etc.) remained consistent, and we do not believe the surgeon's skill level has changed enough to affect the outcome within this study period. Lastly, 3 different cartilage procedures were performed, introducing potential heterogeneity. However, the purpose of this study was to determine whether there was a difference between the group with well-regenerated cartilage and the group with poorly regenerated cartilage compared to the isolated HTO group, regardless of the specific procedure used.

Only patients with well-regenerated cartilage after concomitant cartilage repair procedures showed additional clinical outcome improvements with HTO. When considering combined cartilage repair procedures with HTO, selecting appropriate candidates for achieving successful cartilage regeneration is necessary to yield additional clinical benefits.

CONFLICT OF INTEREST

No potential conflict of interest relevant to this article was reported.

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SUPPLEMENTARY MATERIAL

Supplementary material is available in the electronic version of this paper at the CiOS website, www.ecios.org.

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