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Effects of unloader bracing on clinical outcomes and articular cartilage regeneration following microfracture of isolated chondral defects: a randomized trial

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Abstract

Purpose To determine whether the use of an unloading brace can increase the thickness of cartilage regenerate after microfracture surgery.

Methods This is a randomized (1:1) controlled clinical trial. Twenty-four patients who underwent microfracture between 2012 and 2015 were identified and were randomly assigned to an unloading brace group or a no-brace group. All patients were kept non-weight bearing for the first eight weeks after surgery and then patients in the intervention group began using an unloading brace for an average of 63.9 (SD = 41.6) days to protect clot stability by exerting a varus or valgus force on the knee to decrease the force on the knee's lateral or medial compartment, respectively. Quality of the cartilage repair was assessed with knee magnetic resonance imaging to determine repair tissue thickness (primary outcome), repair tissue volume, and T2 relaxation times at 12 and 24 months after surgery. Clinical outcomes were evaluated with KOOS, Tegner, SF12, and Lysholm questionnaires at six, 12 and 24 months after surgery.

Results Three patients were lost to follow-up, resulting in 21 patients ultimately analyzed. The unloading brace repair tissue was greater than the no-brace group in volume (26.8 ± 23.7 mm^3 vs -8.4 ± 22.7 mm^3, $p = 0.005$) and thickness (0.2 ± 0.2 mm versus -0.4 ± 0.3 mm, $p = 0.001$) at 12 months and in cartilage thickness in the unloading brace group at 24 months (0.4 ± 0.4 mm versus -0.1 ± 0.3 mm, $p = 0.029$). There was a positive correlation between wearing the brace longer and improved 6-month KOOS symptom scores ($r = 0.82$, $p = 0.013$), 6-month KOOS QOL scores ($r = 0.80$, $p = 0.017$), 6-month Tegner scores ($r = 0.94$, $p = 0.002$), and Tegner score changes from baseline to 6 months ($r = 0.80$, $p = 0.032$).

Conclusion This study found a significant mid-term increase in cartilage repair tissue thickness following unloading bracing in patients recovering from microfracture for isolated chondral defects.

Level of evidence II.

Introduction

The optimal treatment of isolated chondral defects has historically been challenging as damaged articular cartilage possesses limited spontaneous healing or regenerative capacity [8, 15]. Current treatment options include conservative measures with mild symptoms or debridement, microfracture, osteochondral grafting, autologous chondrocyte implantation (ACI), and matrix-assisted ACI (MACI) for more severe cases [4, 8].

Microfracture surgery is one of the most cost-effective and common methods for treating isolated chondral defects [8, 9]. During microfracture surgery, the calcified cartilage layer is removed and small holes are then made into the subchondral bone [17]. Bone marrow that contains mesenchymal progenitor cells can then travel through these holes, forming a clot at the site of the defect [18]. The stability of this blood clot is thought to be particularly important for the successful formation of fibrocartilaginous repair tissue.

Following microfracture surgery, patients are typically made non-weight bearing for at least 6–8 weeks to protect the blood clot and to allow for subsequent fibrocartilaginous

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repair tissue formation [20]. Decreased force at the site of microfracture after this 6–8-week non-weight-bearing period could possibly allow for additional repair tissue generation and more successful clinical outcomes.

Unloading braces exert a varus or valgus force on the knee and, as a result, can decrease the force on the knee's lateral or medial compartment, respectively [5]. The longer-term use of an unloading brace could, thus, enhance clot stability by protecting it from disruptive shear forces during active movement. To our knowledge, no study to date has examined the use of an unloading brace after microfracture surgery.

The aim of this study is to analyze the MRI and clinical outcomes following microfracture of isolated chondral defects with or without wearing an unloading brace during their post-operative rehabilitation. The hypothesis is that late weight-bearing bracing will increase repair tissue thickness, volume, and T2 signaling, as well as decrease post-operative symptoms.

Materials and methods

This is a single-site, parallel-group randomized (1:1), superiority trial conducted in the United States (Trial Registration: NCT02016300). The trial was approved by the Stanford University Institutional Review Board (ID number: 17985). Patients undergoing microfracture surgery by a single board-certified orthopaedic surgeon (JD) from 2012 to 2015 were evaluated for study eligibility and recruited. No changes were made to the methods from the start of the study.

Inclusion criteria included a discrete, contained chondral defect less than 2.5 cm by 2.5 cm in size located on the medial or lateral femoral condyle, age between 18 and 50 years, and overall neutral lower limb mechanical alignment (< 5 degrees varus or valgus). Exclusion criteria included previous chondral regenerative or debridement procedures, current use of NSAIDs or platelet modifying medications, moderate to severe osteoarthritis (Kellgren–Lawrence Grade > 3), morbid obesity (Body Mass Index > 40), known or suspected pregnancy, and any risk factors for magnetic resonance imaging (MRI) such as the presence of metallic internal devices, pacemakers, aneurysm clips, or intra-uterine devices. Of note, concomitant knee pathology, such as meniscal injuries, and patients with a history of knee surgery were not excluded. If patients had more than one chondral defect, they were excluded. Data were collected at clinic visits.

Fifty individuals were assessed for eligibility and 26 did not meet inclusion criteria. There were no eligible participants who declined to participate in the study. The surgeon principle investigator for this study enrolled patients. In total, there were 24 eligible patients with isolated chondral defects who were consented for study inclusion following microfracture surgery and were randomized (1:1) using a non-blocked, computer-generated randomization sequence by a research coordinator into two groups: the unloading brace group versus the no-brace group. Three participants were withdrawn from the study due to their inability to follow-up [10]. Those three patients had originally been allocated to the no-brace group. All individuals in the brace group received the intervention. Twenty-one patients were analyzed in the final data analyses: 12 in the unloading brace group and 9 in the no-brace group. Zero participants were excluded from the analysis. Researchers assessing MRI outcomes were blinded to the groups by removing identifying information on the MRI. All scans were sent to a neutral site (Chondrometrics, Germany) for evaluation. The test–retest error (reliability) of local cartilage thickness and volume measurements has been reported previously, and was shown to range from 19 µm (1.5%) to 84 µm (4.7%) [23]. The reliability and reproducibility of T2 measurements has been evaluated in relation to other quantitative parameters of articular cartilage [11], and recently in comparison to cartilage T2 using a qDESS and an MESE MRI sequence; [3] however, previous studies have not specifically analyzed the local measurements performed in the current study. Researchers assessing clinical outcomes were blinded to the groups by not allowing patients to wear unloading braces into the clinic. It was not possible to blind the participants, as it was not feasible to create a similar intervention to the brace group; therefore, participants in each group knew whether they were in the experimental or control groups.

Surgical technique

Standard knee arthroscopy was performed to identify the cartilage defect. A curette was used to stabilize the cartilage walls of the lesion and to remove the calcified cartilage at the base. An awl was then used to perform the microfracture technique. Bleeding from each microfracture site was confirmed arthroscopically. Meniscal tears were also treated during the same procedure and then sutures were placed to close the incisions. All surgeries were performed as outpatient procedures, and patients were seen in the clinic the next day.

During their first eight weeks following microfracture surgery, all patients were kept non-weight bearing and participated in physical therapy two times per week using a continuous passive motion device for 4 h per day with no range of motion restrictions and a standardized physical therapy protocol. At 8 weeks, baseline clinical and radiographic outcomes were recorded and patients in the unloading brace group were fitted by a licensed orthotist for an unloading brace (Össur Unloader One Brace, Össur Inc). Clinical outcomes were additionally obtained at clinic visits at six, 12

and 24 months following surgery; while, MRI outcomes were also obtained at 12 and 24 months following surgery. Patient follow-up and the trial ended in January 2018.

Brace characteristics

Patients in the unloading brace group were asked to wear their braces until their six-month post-operative visit. Each unloading brace was equipped with an iButton temperature sensor (iButtonLink, LLC) that acquired temperature readings every 20 min to objectively document brace compliance, which participants were not aware of. The temperature threshold to determine brace wear was set at 25 °C. The iButton captures and stores these measurements for 1 month after which it must be downloaded; all participants, therefore, underwent up to five iButton downloads. These visits were managed by the orthotist who performed the initial brace fitting. Four of the 12 patients in the unloading brace group were not included in final iButton brace use analyses for the following reasons: one patient developed a pressure urticaria (not secondary to the brace) and had to stop wearing their brace prematurely, one wore the brace over their pants, and two were non-compliant. However, these patients were included in the final analyses.

MRI outcomes

The primary outcome with respect to the efficacy of the brace was a significant increase in repair tissue thickness from baseline 8 weeks to 24 months. Quality of the cartilage repair was assessed with knee MRI scans using a 3.0-T clinical scanner (GE Medical Systems—Discovery MR 750). Cartilage T2 relaxation times, volume, and thickness were analyzed from manual segmentations performed by a radiologist with expertise in cartilage segmentation analysis blinded to the experimental groups and acquisition date using CubeQuant T2 MRIs. The segmentations comprised 2–3 slices covering the repair tissue region of interest, and one anterior and one posterior reference in the same condyle as well as three additional corresponding comparisons in the non-affected condyle that reflected similar locations for the repair tissue region, anterior reference, and posterior reference. As a result, three regions were analyzed on each condyle for a total of six regions analyzed. For each of the six regions, cartilage T2 times were computed from the CubeQuant MRIs using a non-linear method fitting mono-exponential decay curves to the measured signal intensities for each voxel, similar to that used in a previous study [23]. Cartilage volume of the six regions was calculated by multiplying the number of segmented voxels with the respective resolution of the MRIs. The mean cartilage thickness of the six regions was approximated for each region by dividing the volume by the size of the subchondral bone area of the respective region, similar to that used in a previous study [22]. To address any biases introduced by inconsistent image acquisition conditions, the comparisons were not performed by directly comparing the repair tissue region between knees treated with and without unloading braces. Instead, the comparison was performed by (a) calculating the difference between the repair tissue region and both the anterior and the posterior reference regions, (b) calculating the difference between the corresponding regions in the non-affected condyle, and (c) calculating the difference of (a) and (b) between the condyles. In other words, an example calculation for (c) is the following: (anterior reference of the affected condyle − repair region of the affected condyle) − (anterior reference of the unaffected condyle − repair region of the unaffected condyle). The final difference calculated in (c) was the variable that was then compared between the unloading brace and no-brace groups (Fig. 1). Due to similar results from the anterior reference and posterior reference regions, all the MRI-reported values were subtracted from references in the opposite condyle using the anterior reference region. As a result, some T2 relaxation times, volume, and thickness may be reported as negative.

Clinical outcomes

Differences in clinical outcomes were assessed with the Knee Injury and Osteoarthritis Outcome Score (KOOS) sub-scores [14], Tegner activity level scale [19], VR-12 quality of life questionnaire [21], and Lysholm score [19]. KOOS sub-scores included symptoms, pain, function in daily living (ADL), function in sport and recreation, and quality of life (QOL). Clinical outcomes were recorded at clinic visits at two, six, 12 and 24 months following surgery.

Statistical analyses

The primary endpoints were change in three MRI outcomes at 24 months: T2 relaxation times, repair region volume, and repair region thickness. Secondary endpoints included the KOOS sub-scores, the VR-12 score, the Lysholm score, and the Tegner score. All data were reported as the mean "*M*" and standard deviation "SD". For the primary and secondary endpoints, differences in the groups for T2 relaxation time, repair region volume, and repair region thickness and clinical outcomes were examined using t-tests (reported in the tables). No correction was made for multiple comparisons because the analyses were considered exploratory. A significant p value of 0.05 was used. We aimed to assess whether the data provided evidence of superiority of the unloading brace in recovery after microfracture surgery. Also, the normality of the residuals of each multilevel linear regression was assessed using q–q plots. All residuals were normally distributed.

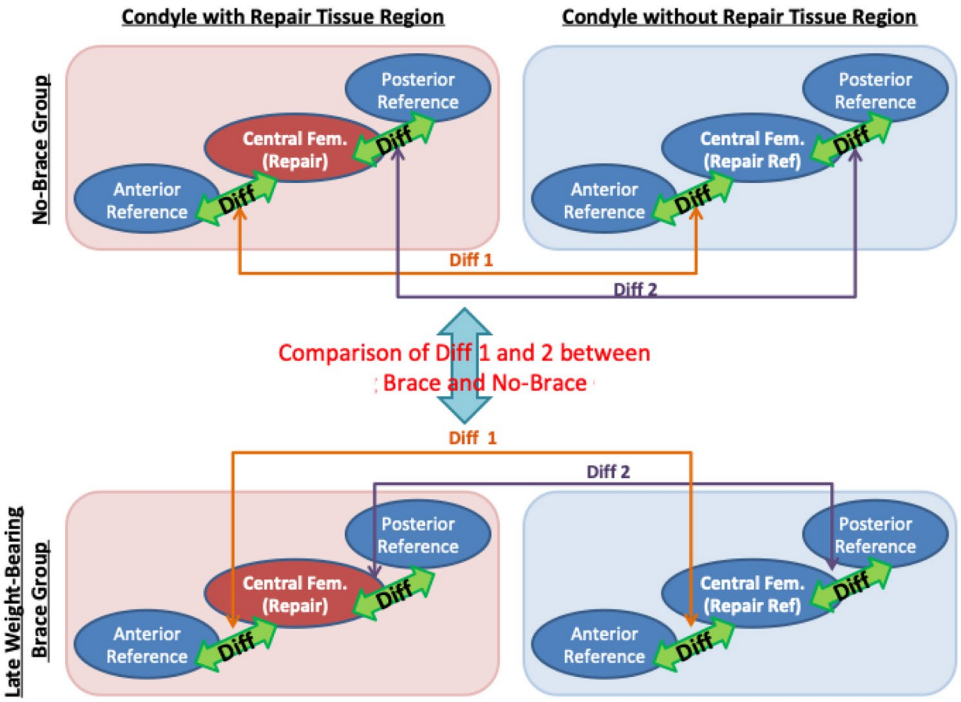

Fig. 1 Schematic of the MRI analysis. *Diff* Difference, *Ref* Reference

Subgroup analyses examining correlations between questionnaire items and brace data were conducted with analyses limited to patients in the unloading brace group. The number of days the brace was worn, the average number of minutes per day that the brace was worn, and the total number of minutes the brace was worn were calculated for patients in the unloading brace group. Correlations were also examined between either the questionnaire items at each time point or the change from baseline to each time point in relationship to the total number of days the brace was worn or the total number of minutes the brace was worn over all days. Similarly, correlations were assessed between the MRI data at each time point and the change from baseline to each time point and the total amount of time the brace was worn. Data were analyzed using R and Rstudio (R Core Team, 2018; Rstudio Team, 2016). No interim analyses were performed. An a priori power analysis was conducted to test the difference between the unloading brace and no-brace groups using an estimated effect size of 1.11 and alpha of 0.05. Results indicated that 14 participants per group were needed to detect 80% power.

Results

Final analysis included 12 patients in the unloading brace group and nine patients in the no-brace group. There was only one provider (XX) in each group and only one center was used (X). The trial stopped after all patients had attended their two-year follow-up visit. There was no delay between randomization and the initiation of the intervention.

Demographics (age, sex, body mass index (BMI), smoking history, and ethnicity) and surgical details (history of knee surgery, alignment, Kellgren–Lawrence (KL) grade, inciting event, American Society of Anesthesiologists (ASA) class, side of surgery, concomitant surgical procedures, articular cartilage lesion size, and articular cartilage lesion location) are listed in Table 1. The average age was 40.0 ± 9.0 years, and the average BMI was 25.4 ± 3.8. Patients in the unloading brace group had a lower BMI ($M = 23.7$, SD = 2.1) compared to patients in the no-brace group ($M = 27.6$, SD = 4.5) ($p = 0.04$). There were no perioperative complications.

MRI outcomes

Unloading brace and no-brace groups exhibited no baseline differences at 2 months post operatively for T2 relaxation times, regenerate cartilage volume, or regenerate cartilage thickness (Table 2). At 12 months following microfracture surgery, the unloading brace regenerate cartilage was larger in volume ($M = 26.8$ mm^3, SD = 23.7 mm^3, $p = 0.005$) and thickness ($M = 0.2$ mm, SD = 0.2 mm, $p = 0.001$) compared to the no-brace group ($M = -8.4$ mm^3, SD = 22.7 mm^3) ($M = -0.4$ mm, SD = 0.3 mm) (Table 2, Fig. 2). The negative values are a result of the reading being less than the reference zone as depicted in Fig. 1. '*M*' represents the mean and 'SD' the standard deviation.

Table 1 Demographics and surgical characteristics in the unloading brace group versus the no-brace group

	Percent or mean (SD)		*p* value
	Brace ($n=12$)	No brace ($n=9$)	
Left side	25.0	55.6	n.s
Female sex	50.0	33.3	n.s
Age	40.3 (8.5)	39.6 (10.2)	n.s
BMI	23.7 (2.1)	27.6 (4.5)	**0.036**
Smoking			
None	100.0	77.8	n.s
Marijuana	0.0	11.1	
Yes	0.0	11.1	
Inciting event			
Insidious	66.7	22.2	n.s
Trauma	16.7	44.4	
Twisting	16.7	33.3	
History of knee surgery	50.0	66.7	n.s
Alignment			
Anatomic valgus	0.0	33.3	n.s
Anatomic varus	33.3	22.2	
Neutral	66.7	44.4	
KL grade			
1	0.0	33.3	n.s
2	75.0	55.6	
3	25.0	11.1	
ASA class			
1	41.7	44.4	n.s
2	58.3	55.6	
Intra-operative additional procedures			n.s
Menisectomy	33.3	55.5	
Meniscal repair	8.3	33.3	
ACL reconstruction	8.3	0	
Other	33.3	0	
None	16.6	11.1	
Lesion size	238.3 (159.1)	206.2 (107.4)	n.s
Lesion location			
Lateral femoral condyle	75.0	44.4	n.s
Medial femoral condyle	25.0	55.6	

n.s. not significant

Bold value indicates $p < 0.05$

Clinical outcomes

The KOOS ADL, SF12, Lysholm, and Tegner scores at each time point are displayed in Table 3. The median Tegner score and range from minimum to maximum for the brace group were 2 (1–5), 4 (2–6), 5 (2–7), and 4 (2–8), and for the no-brace group were 2 (0–6), 3 (0–5), 4 (2–5), 3.5 (0–4) at 2, 6, 12, and 24 months, respectively. There were no differences between the unloading brace group and the no-brace group at each time point for any of these measures or for the other KOOS sub-scores (pain, QOL, symptoms, and function in sport and recreation), except that the brace group had a higher Tegner score at 24 months ($M=4.5$, SD = 1.6) compared to the no-brace group ($M=2.9$, SD = 1.6, $p=0.039$). There was no difference in the groups in the change between baseline and each of the follow-up time points (6 months, 12 months, and 24 months) except that the brace group had a higher KOOS ADL change from baseline to 24 months ($M=17.8$, SD = 16.7) compared to the no-brace group ($M=4.6$, SD = 10.3, $p=0.043$).

Table 2 Microfracture cartilage regenerate T2 relaxation time (ms), volume (mm^3), and thickness (mm)

Time point	MRI parameter	Mean (SD)		*T* value	*p* value	95% confidence interval
		Brace	No brace			
2 mo	T2	31.4 (38.1)	42.8 (96.8)	0.31	n.s	−71.08, 93.89
	Volume	−6.5 (36.3)	−6.3 (46.3)	0.01	n.s	−42.91, 43.37
	Thickness	−0.1 (0.3)	−0.2 (0.4)	−0.60	n.s	−0.46, 0.26
12 mo	T2	8.6 (25.0)	10.2 (23.5)	0.15	n.s	−22.12, 25.40
	Volume	26.8 (23.7)	−8.4 (22.7)	−3.27	**0.005**	−57.92, -12.29
	Thickness	0.2 (0.2)	−0.4 (0.3)	−4.64	**0.001**	−0.89, -0.32
24 mo	T2	2.8 (22.9)	−6.1 (4.4)	−1.19	n.s	−25.54, 7.76
	Volume	48.7 (38.3)	12.0 (28.8)	−2.08	n.s	−75.83, 2.41
	Thickness	0.4 (0.4)	−0.1 (0.3)	−2.53	**0.029**	−0.91, -0.06
Change 2 mo.–12 mo:	T2	−24.5 (25.3)	−32.6 (73.8)	−0.29	n.s	−70.61, 54.43
	Volume	31.4 (31.8)	−2.1 (37.5)	−2.01	n.s	−69.16, 2.28
	Thickness	0.3 (0.3)	−0.2 (0.4)	−2.67	**0.020**	−0.91, -0.10
Change 2 mo.– 24 mo:	T2	−25.1 (25.1)	−17.6 (5.6)	0.86	n.s	−12.19, 27.14
	Volume	49.2 (35.8)	17.8 (52.3)	−1.20	n.s	−95.28, 32.49
	Thickness	0.3 (0.3)	0.1 (0.2)	−1.84	–	–

Negative values indicate that the reading was less than the reference zone as depicted in Fig. 1. Patients began wearing their braces at the 2-month post-operative follow-up visit; therefore, the 2-month time point is the baseline value

mo. month, *n.s.* not significant

Bold value indicates $p < 0.05$

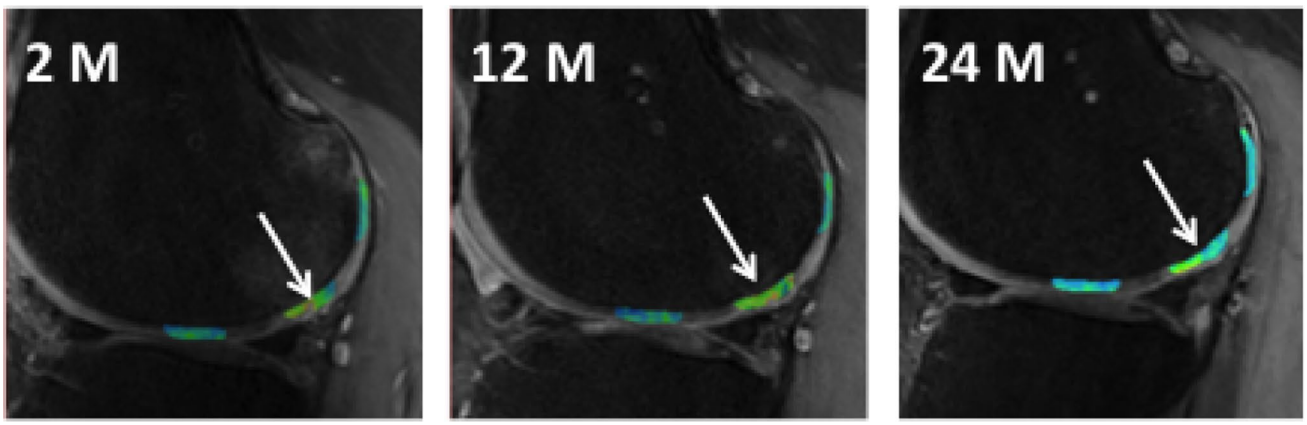

Fig. 2 Example unloading brace T2 relaxation times at 2 months (2 M), 12 months (12 M), and 24 months (24 M). White arrow indicates site of microfracture; region to the right of the arrow is the posterior reference point; region to the left of the arrow is the anterior reference point

Correlations with time wearing brace

There were eight patients who wore braces with sensors during the course of the study for an average of 63.9 (SD = 41.6, median = 43.5, IQR = 67) days, with the total number of days patients wore braces ranging from 28 to 126 days. On average, patients wore their brace 8.0 (SD = 3.5) hours per day with a range of 2.3 to 12.5 h per day on average (median = 9.2 h, IQR: 4.4 h). The average total number of hours patients wore their braces was 557.9 (SD = 473.5), ranging from 97.3 to 1214.3 total hours (median = 379.3 h, IQR: 816.9 h).

More days wearing the brace was positively correlated with a higher 6-month KOOS symptom score ($r = 0.82$, $p = 0.013$), 6-month KOOS QOL score ($r = 0.80$, $p = 0.017$), 6-month Tegner score ($r = 0.94$, $p = 0.002$), and Tegner score change from baseline to 6 months ($r = 0.80$, $p = 0.032$) (Fig. 3). A higher total number of minutes wearing the brace was positively correlated with a 6-month KOOS symptom score ($r = 0.76$, $p = 0.028$), 6-month KOOS QOL score ($r = 0.76$, $p = 0.030$), 6-month

Table 3 Unloading brace and no-brace clinical outcome measures

	Mean (SD)		*T* value	*p* value	95% confidence interval
	Brace ($n=12$)	No Brace ($n=9$)			
KOOS ADL					
2 months	76.8 (18.9)	79.6 (16.1)	0.36	n.s	−13.32, 18.79
6 months	88.8 (12.1)	83.7 (19.4)	−0.70	n.s	−21.03, 10.79
12 months	95.9 (4.7)	87.7 (12.6)	−1.86	n.s	−18.14, 1.66
24 months	94.6 (4.7)	83.4 (20.3)	−1.53	n.s	−28.21, 5.85
Change—baseline to:					
6 months	12.0 (12.2)	4.1 (12.2)	−1.46	n.s	−19.19, 3.48
12 months	19.1 (16.9)	8.1 (11.5)	−1.77	n.s	−23.99, 2.04
24 months	17.8 (16.7)	4.6 (10.3)	−2.18	**0.043**	−25.91, −0.50
SF12					
2 months	28.8 (2.9)	28.9 (2.4)	0.12	n.s	−2.28, 2.56
6 months	30.9 (2.1)	31.8 (4.3)	0.56	n.s	−2.54, 4.26
12 months	31.2 (2.9)	31.2 (3.6)	0.04	n.s	−3.08, 3.19
24 months	29.5 (3.2)	31.0 (5.4)	0.71	n.s	−3.21, 6.21
Change—baseline to:					
6 months	2.2 (3.0)	2.9 (5.5)	0.36	n.s	−3.73, 5.17
12 months	2.4 (4.1)	2.3 (3.0)	−0.05	n.s	−3.32, 3.15
24 months	0.8 (5.1)	2.1 (6.8)	0.49	n.s	−4.76, 7.51
Lysholm					
2 months	63.6 (24.7)	51.3 (24.7)	−1.12	n.s	−35.22, 10.72
6 months	77.8 (13.6)	62.4 (21.1)	−1.91	n.s	−32.78, 2.00
12 months	89.3 (22.7)	71.7 (29.1)	−1.50	n.s	−42.54, 7.37
24 months	83.9 (11.3)	69.0 (26.8)	−1.49	n.s	−37.69, 7.85
Change—baseline to:					
6 months	14.3 (16.2)	11.1 (23.1)	−0.35	n.s	−22.51, 16.23
12 months	25.7 (33.9)	20.3 (21.7)	−0.44	n.s	−30.80, 20.13
24 months	20.3 (20.5)	18.8 (17.1)	−0.19	n.s	−19.43, 16.26
Tegner					
2 months	2.2 (1.3)	2.0 (1.9)	−0.22	n.s	−1.79, 1.45
6 months	3.9 (1.4)	2.9 (1.6)	−1.50	n.s	−2.46, 0.42
12 months	4.8 (1.3)	3.9 (1.1)	−1.81	n.s	−2.04, 0.15
24 months	4.5 (1.6)	2.9 (1.6)	−2.25	**0.039**	−3.16, −0.09
Change—baseline to:					
6 months	1.7 (1.2)	0.9 (2.6)	−0.90	n.s	−2.89, 1.21
12 months	2.7 (1.1)	1.9 (2.2)	−1.00	n.s	−2.49, 0.94
24 months	2.3 (1.9)	1.4 (1.2)	−1.40	n.s	−2.40, 0.48

mo. month, *n.s.* not significant

Bold value indicates $p<0.05$

Tegner score ($r=0.85$, $p=0.016$), change from baseline to 6 months for Tegner score ($r=0.88$, $p=0.010$), and change from baseline to 6 months for KOOS function in sports and recreation ($r=0.76$, $p=0.029$). There were no other significant correlations between clinical outcome scores and total time wearing the brace; there were also no significant correlations between MRI outcomes and total time wearing the brace.

Discussion

Conclusions from the present study include: (1) unloading bracing results in increased cartilage repair tissue thickness at longer-term follow-up (1 year and 2 year), and (2) unloading bracing results in short-term decreased symptoms (6 months). This randomized trial examined

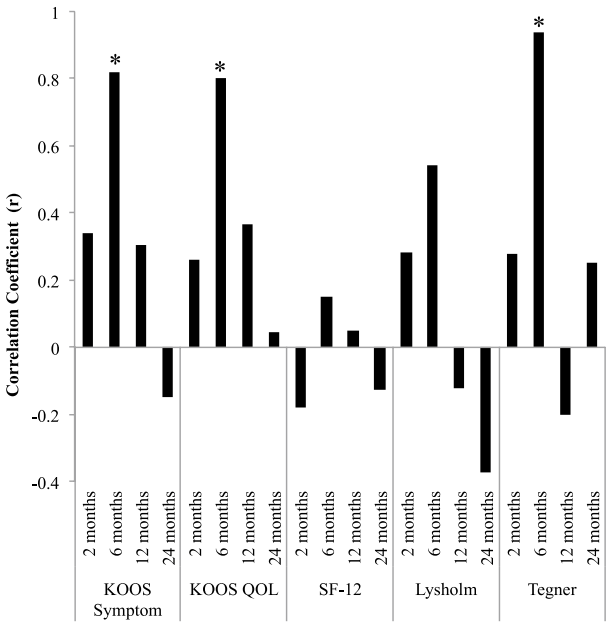

Fig. 3 Correlation between clinical outcomes scores (KOOS Symptom, KOOS QOL, SF12, Lysholm, and Tegner) and total number of days the brace was worn (*$p < 0.05$)

the influence of an unloading brace worn after an eight-week non-weight-bearing period to determine if additional unloading of the cartilage regenerate would further improve MRI and clinical outcomes following microfracture surgery for isolated chondral defects. These results can be best generalized to patients who are not morbidly obese and who present with a discrete, contained chondral defect less than 2.5 cm by 2.5 cm in size located on the medial or lateral femoral condyle, age between 18 and 50 years, and overall neutral lower limb mechanical alignment (< 5° varus or valgus).

The present study also provides evidence that unloading bracing delivers lasting effects on the cartilage regenerate. Even though patients stopped wearing their braces by their 6-month post-operative visit, the unloading brace regenerate cartilage volume was larger at 12 months ($p = 0.005$) and larger in thickness ($p = 0.001$) than in the no-brace group. The significant difference in thickness between the unloading and no-brace groups lasted through their 24-month follow-up MRI ($p = 0.029$). MRI analysis exhibited a sustained long-term increase in repair tissue thickness.

No changes in T2 relaxation times were detected between groups at any time points. Correlations have been found between T2 values and cartilage hydration and collagen fiber orientation, suggesting some degree of specificity for cartilage arrangement [2, 12]. Therefore, wearing an unloading brace after microfracture surgery is unlikely to change repair tissue arrangement given the similar T2 relaxation times, but more likely results in a greater amount of fibrocartilaginous repair tissue at the site of microfracture since increased regenerate volume and thickness were observed.

In theory, increased lesion volume and thickness should provide additional support and as a result, increased function and decreased pain. Other studies have in fact shown cartilage volume to directly correlate with a patient's knee pain [1, 7]. Thicker fibrocartilaginous repair tissue is of particular importance given that unlike normal articular cartilage, which is composed of chondrocytes and a dense extracellular matrix of water, collagen, and proteoglycans [16], fibrocartilaginous repair tissue contains more of a mixture of fibrous tissue and cartilage. This difference in composition is partly why fibrocartilaginous repair tissue is thought to be not as robust as articular cartilage. Patients in the current study had increased repair tissue thickness but limited differences in symptoms at two years, but it is possible that after additional years of mechanical stress at the knee joint, patients with thinner fibrocartilaginous repair tissue, a weaker tissue by nature, may be more susceptible to further cartilage degradation. Differences in symptoms may take many years to arise.

Patients in the bracing group were asked to start wearing their braces at their 2-month post-operative visit until their 6-month visit, and though there were no differences when directly comparing clinical outcomes between groups, a statistically significant positive correlation was found between the total number of days the brace was worn and the 6-month KOOS symptom score ($p = 0.013$), KOOS QOL score ($p = 0.017$), and Tegner score ($p = 0.002$). No differences were seen in SF12 and Lysholm scores or at 12- or 24-month follow-up visits. Overall, individuals who wore their unloading brace longer had decreased symptoms, improved quality of life, and improved activity levels as reported by their questionnaire responses compared to those who wore their brace less. Though no other studies have examined the use of unloading braces for isolated chondral defects before or after microfracture, those that have looked at the use of unloading braces in the management of unilateral osteoarthritis have found sustained and increased KOOS scores after wearing the brace for up to 1 year [6, 13].

Even though this was a randomized trial, this study was limited by a small sample size, significant differences in BMI between groups, and an inability to blind participants to the experimental group. As patients in the brace group had a lower BMI compared to patients in the no-brace group, it is possible that this influenced this study's outcomes and a sedentary versus active lifestyle may have also influenced results as Tegner scores were noted to be higher for those in the brace group compared to the non-brace group. Also, even though researchers assessing clinical outcomes were blinded to the groups by not allowing patients to wear the unloader braces into the clinic, it is possible that the providers were not truly blinded. Furthermore, patients in

the unloading brace group wore their braces irregularly as detected by the iButton temperature sensor. Additional research would benefit not only from braces being worn for a more uniform length of time, but also from examining clinical outcomes greater than 2 years out from microfracture as well as the effects of longer-term use of the brace since the present study did not find lasting improvements in symptoms. Some patient also underwent concomitant meniscectomy or meniscal repairs, and though there were no significant differences between groups in the number of participants who underwent additional procedures, this may have influenced baseline symptoms and patient functional recovery both in the short term and long term. It would also be interesting if future studies were to analyze the influence of lesion size on clinical and radiologic results. However, through this research, surgeons may find it useful to use unloader bracing as a part of their post-operative protocol to improve patient outcomes following microfracture surgery for isolated chondral defects. This study suggests that the following post-op treatment protocol may be useful in the recovery of patients following microfracture surgery for isolated chondral defects: (1) non-weight bearing for eight weeks while participating in a standardized physical therapy program two times per week and (2) after eight post-operative weeks, an unloading brace may be worn for 1–3 months.

Conclusion

Overall, this study provides evidence that the unloading brace helps to address short-term symptoms for people recovering after microfracture surgery for isolated chondral defects. Wearing the brace for a longer period of time was positively correlated with increased 6-month KOOS scores. Patients who wore the brace also had a larger repair tissue volume and thickness at 12 months, and larger thickness at 24 months. Unloading bracing after microfracture could potentially be a useful intervention in future rehabilitation protocols.

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Compliance with ethical standards

Conflict of interest Author J.D. is a consultant for Ossur, Authors J.K. and A.F. report no conflicts of interest.

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