Original Article

Low-Intensity Pulsed Ultrasonography Plus Arthroscopic Drilling Does Not Improve Bone Healing More Than Arthroscopic Drilling Alone in Pediatric Patients With Stable Osteochondritis Dissecans of the Knee

Borna Guevel, M.A., M.B., B.Chir., M.R.C.S., M.P.H., Stephen T. Mathew, M.D., Ryan P. Coene, M.S., Kathleen j. Maguire, M.D., Kathryn A. Williams, M.S., Lyle J. Micheli, M.D., and Matthew D. Milewski, M.D.

Purpose: To determine whether adjuvant use of bone stimulation would improve the rate of healing in the operative management of stable osteochondritis dissecans (OCD) of the knee in pediatric patients. **Methods:** This retrospective matched case-control study was performed at a single tertiary care pediatric hospital between January 2015 and September 2018. Patients who underwent antegrade drilling for stable femoral condyle OCD with greater than 2 years' follow-up were included. Preference was for all to receive postoperative bone stimulation; however, some were denied because of insurance coverage. This enabled us to create 2 matched groups of those who received postoperative bone stimulation and those who did not. Patients were matched on skeletal maturity, lesion location, sex, and age at surgery. The primary outcome measure was the rate of healing of the lesions determined by postoperative magnetic resonance imaging measurements at 3 months. **Results:** Fifty-five patients were identified who met the inclusion and exclusion criteria. Twenty patients from the bone stimulator group (BSTIM) were matched to 20 patients from the no bone stimulator group (NBSTIM). Mean age for BSTIM at surgery was 13.2 years ± 2.0 (range, 10.9-16.7) and for NBSTIM at surgery 12.9 years ± 2.0 (range, 9.3-17.3). At 2 years, 36 patients (90%) in both groups went on to clinical healing without further interventions. In BSTIM, there was a mean decrease of 0.9 (±1.8) mm in lesion on coronal width and 12 patients (63%) had overall improved healing; in NBSTIM there was a mean decrease of 0.8 (±3.6) mm in coronal width and 14 patients (78%) had improved healing. No statistical differences in the rate of healing were found between the 2 groups ($P = .706$). **Conclusion:** In antegrade drilling of stable knee OCD lesions in pediatric and adolescent patients, adjuvant bone stimulator use did not appear to improve radiographic or clinical healing. **Level of evidence:** Level III, retrospective case-control study.

Osteochondritis dissecans (OCD) has been defined as a focal idiopathic alteration of subchondral bone with a risk for instability and disruption of adjacent articular cartilage that may result in premature osteoarthritis.[1-3] The condition primarily affects younger patients, with the majority aged 10 to 20 years old, and has an estimated prevalence between 9.5 and 29 per 100,000 population.[4,5] Left untreated, it can lead

From the Boston Children's Hospital, Division of Sports Medicine, Department of Orthopaedic Surgery (B.G., R.P.C., L.J.M., M.D.M.); Boston Children's Hospital, Biostatistics and Research Design Center, ICCTR (K.A.W.); and Harvard Medical School (L.J.M., M.D.M.), Boston, Massachusetts; and the Children's Hospital of Philadelphia (K.M.), Philadelphia, Pennsylvania, U.S.A.; and Baylor Scott & White Health (S.T.M.), Dallas, Texas, U.S.A.

The authors report the following potential conflicts of interest or sources of funding: M.D.M. reports other from Elsevier. The authors report that they have no conflicts of interest in the authorship and publication of this article. Full ICMJE author disclosure forms are available for this article online, as supplementary material.

Presented at Pediatric Research in Sports Medicine Society Meeting (PRISM) in Glendale, AZ, January 23-25, 2020.

Received March 3, 2022; accepted November 9, 2022.

Address correspondence to Matthew Milewski, M.D., Boston Children's Hospital, Division of Sports Medicine, Department of Orthopaedic Surgery, 300 Longwood Avenue, Boston, MA 02115, U.S.A. E-mail: mdmilewski@gmail.com

2666-061X/22251

https://doi.org/10.1016/j.asmr.2022.11.018

to loose body formation, pain, mechanical symptoms and early onset arthritis.[6]

The optimal treatment for OCD is unclear.[7] Both operative and nonoperative methods have been studied. Treatment factors such as skeletal maturity, location of the defect, defect stability, patient symptoms, and surgeon preference may affect treatment decisions.[8] Stable lesions in skeletally immature patients are typically treated with 3 to 6 months of nonoperative treatment, involving activity modification and unloader bracing.[8] Patients with persistent symptoms are then often offered surgery, usually transarticular or retroarticular drilling of the affected lesion to promote revascularization and healing.[9] Although success rates of this approach are high, Heyworth et al.[10] reported a pooled healing rate across 5 studies of 91% at 4.5 months for transarticular drilling, up to 10% of patients still experience a poor outcome.[11]

Bone stimulation has been increasingly used to accelerate bony healing with success seen in fracture care,[12] particularly for delayed/nonunions.[13,14] External bone stimulation can be achieved using a number of modalities, including electric/electromagnetic stimulation, low-intensity pulsed ultrasound (LIPUS), and more recently extracorporeal shock wave therapy (ESWT).[15] With LIPUS in vitro studies highlight a promising mechanism of action in promoting bone healing[16] through inhibition of RANKL-induced osteoclast formation via modulating ERK-c-Fos-NFATcx1 signaling cascades[17] and the upregulation of osteogenic factors increasing osteoblast activity.[18] There is a paucity of literature regarding the use of LIPUS in the treatment of knee OCD but its effect on accelerating OCD healing has been investigated in the capitellum, where LIPUS was found to significantly shorten the repair period.[11]

The purpose of this study was to determine whether adjuvant use of bone stimulation would improve the rate of healing in the operative management of stable osteochondritis dissecans (OCD) of the knee in pediatric patients. Our hypothesis was that LIPUS bone stimulation would decrease time to bone healing.

Methods

This institutional review board-approved retrospective matched case-cohort study was performed at a single tertiary care pediatric hospital, between January 2015 and September 2018 by one senior surgeon (L.J.M.). All patients who had International Cartilage Repair Society stage 1 and stage 2 femoral condyle OCD lesions, had failed a trial of nonoperative management with ongoing pain, and were thus treated with antegrade drilling were identified. The inclusion criteria were patients under 17 years of age with greater than 2 years' follow-up. The exclusion criteria were unstable OCD lesions, traumatic osteochondral fractures, other ligamentous injuries, and patellar or trochlear OCDs.

Electronic medical records were reviewed, and data were collected on demographics, including age at surgery, sex, skeletal maturity (open vs. closed physes) and laterality of OCD (medial femoral condyle [MFC] vs. lateral femoral condyle [LFC]), as well as use of postoperative bone stimulation.

The bone stimulator (Exogen LIPUS device) was used in the transducer parapatellar position, medial for MFC and lateral for LFC, 20 minutes twice a day for 3 months. Preference was for all patients to receive postoperative bone stimulation; however, 20 patients were denied because of insurance coverage. This enabled us to produce 2 matched patient cohorts of those who received postoperative bone stimulation and those who did not. To create the matched patient cohort, patients from the bone simulator patient group (BSTIM) who were similar to the patients with no bone simulator (NBSTIM) were selected based on skeletal maturity, lesion location, sex, and age at surgery. Although an exact 1-1 match was not possible, priority was given to ensuring there was an exact 1-1 match on skeletal maturity because open or closed growth plates were deemed to be the most important patient factor that influenced healing rates.

All patients in this study had surgery with the same senior surgeon (L.J.M.). With the patient in the supine position, a tourniquet was applied and inflated. An anterolateral portal was made, and an arthroscope inserted. A diagnostic arthroscopy was performed, and then an anteromedial portal was made under direct vision. The OCD lesion was identified and probed. Using a 0.45 mm K wire, multiple holes were placed through the cartilage lesion, as well as the subchondral bone below it. Care was taken to pass through the entirety of the OCD lesion, through cartilage, necrotic bone, and epiphyseal bone. Bleeding at drilling sites was confirmed. The exact number of holes was dependent on the size of the OCD lesion and surgeon judgement at the time of surgery but generally involved about 10 passes per centimeters squared. Arthroscopic lavage was done, and the portals were closed with 3-0 nylon suture. Bupivacaine epinephrine 0.25% was injected into portal sites. Sterile dressing was applied, as well as a Cryocuff and a Bledsoe brace. The Bledsoe brace was to be worn at all times after surgery and was placed in 0° to 30° flexion and locked in extension for ambulation. This was sequentially increased from 0°-30° to 0°-60°, and 0°-90° at subsequent follow-up. The patient was partial weightbearing for 6 weeks. The postoperative rehabilitation was the same for both groups.

The primary outcome measure was rate of healing as determined by MRI measurements of coronal and sagittal width and depth of the OCD lesions (Fig 1),

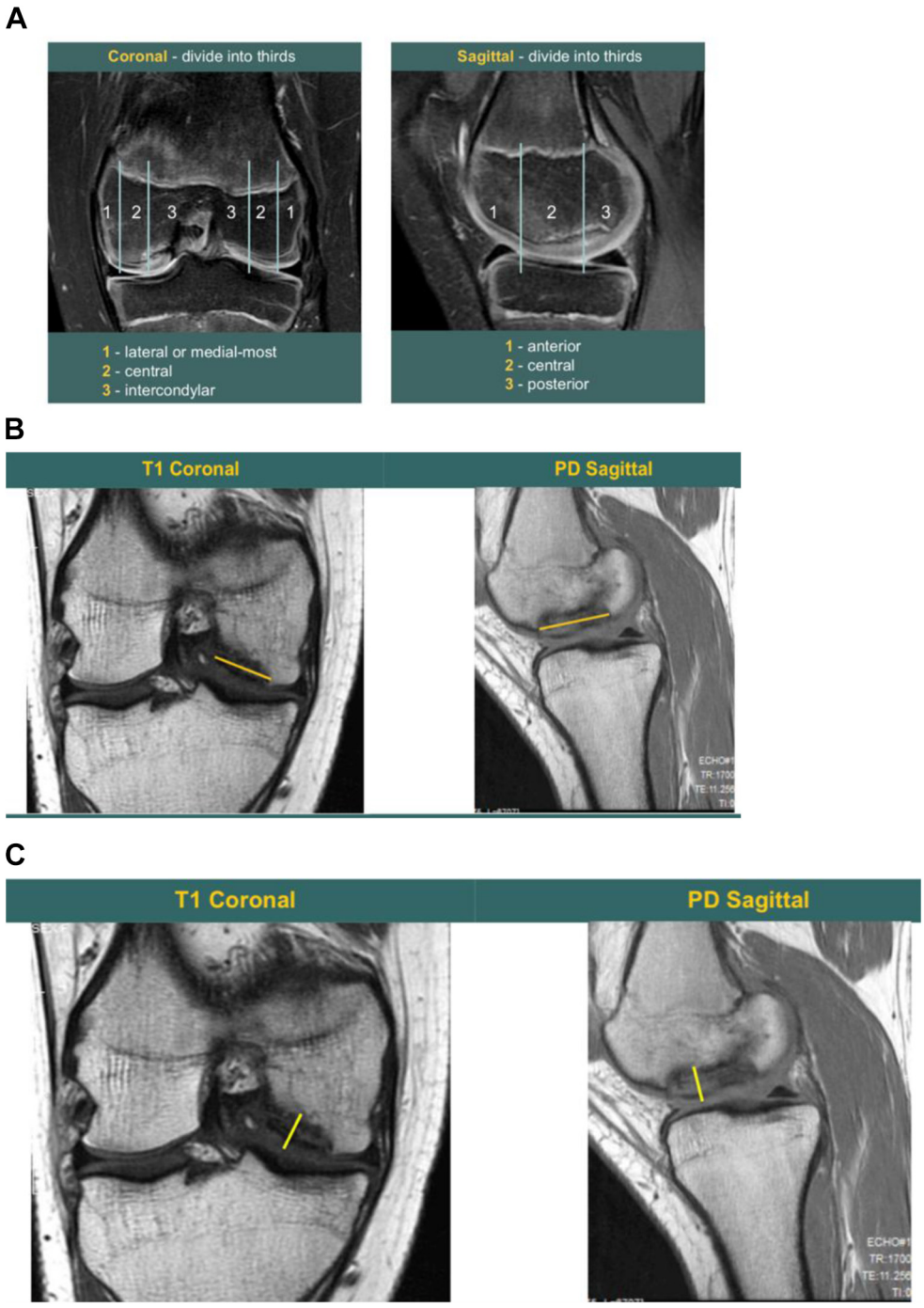

Fig 1. Magnetic resonance imaging measurement guide using left knee MRI as example. (A) Measure in thirds based on the width of the condyle (including bone and cartilage), if lesion spans more than one zone, indicate all zones in which the lesion resides on the coronal and sagittal. (B) Measure in millimeters (mm) the maximal width (coronal) or length (sagittal) of lesion from edge to edge where normal bright white fat containing marrow is lost. (C) Measure maximal depth of OCD lesion in mm from deep interface between black (sclerotic) bone and white marrow to articular cartilage surface. Figure used with permission from ROCK (Research in Osteochondritis Dissecans of the Knee) group.

taken before surgery and at 3 months after. These were measured on non-fat-suppressed coronal T1 and sagittal PD MRI images. Overall healing was subjectively assessed using an ordinal scale, from −1 (worse), 0 (same), to 1 (better), with any signs of reossification or decrease in lesion size considered healing. These were measured by a fellowship-trained, board-certified orthopaedic surgeon (M.D.M.) and 2 orthopaedic sports medicine fellows (S.T.M. and K.M.), and interrater reliability was measured.

The secondary outcome measures were collected using clinical information regarding complications and revision rate, clearance to weightbearing (surgeon judgement), clearance to sports (surgeon judgement), and time from surgery to discharge.

Statistical Analysis

Continuous variables were summarized using means ± standard deviations and ranges as needed. Categorical variables were summarized using counts and

Table 1. Patient Demographics and Magnetic Resonance Imaging Measurements

Characteristics	Bone Stimulator (n = 20)	No Bone Stimulator (n = 20)	*P* Value*
Male	15 (75.0%)	14 (70.0%)	1.0
Age at surgery†	13.2 ± 2.0 (10.9-16.7)	12.9 ± 2.0 (9.3-17.3)	.658
Skeletal maturity			1.0
Closed/Closing	5 (25.0%)	5 (25.0%)	
Open	15 (75.0%)	15 (75.0%)	
MFC	16 (80.0%)	19 (95.0%)	.342
LFC	4 (20.0%)	1 (5.0%)	
Coronal width of lesion (mm) †	−0.9 ± 1.8 (−5.7-1.6)	−0.8 ± 3.6 (−8.9 to 7.1)	.706
Coronal depth of lesion (mm) †	−0.1 ± 2.1 (−3.4 to 4.8)	0.4 ± 1.6 (−1.9 to 3.4)	.510
Sagittal width of lesion (mm) †	−2.2 ± 2.6 (−9.1 to 2.3)	−2.5 ± 4.4 (−11.5 to 3.2)	.729
Sagittal depth of lesion (mm) †	−0.2 ± 1.8 (−4.9 to 3.5)	−0.3 ± 1.6 (−3.7 to 2.2)	.798

MFC, medial femoral condyle; LFC, lateral femoral condyle.
*Based on Fisher's exact test or Wilcoxon rank sum test.
†Mean ± SD (Range).

percentages. Comparisons between groups for categorical variables were performed with Fisher's exact test. Comparisons for continuous variables were performed with independent Wilcoxon rank sum tests to address non-normality and the small size. Paired analyses were not needed because 1-1 matching was not possible, and the matching provided similar but independent groups. Interrater reliability for MRI measurements was measured using the intraclass correlation coefficients (ICC) with 95% confidence intervals (CIs). For the agreement on overall imaging healing at 3 months, pairwise Cohen's Kappa was used. All tests were 2-sided, and $P < .05$ was considered statistically significant. SAS (version 9.4; SAS Institute, Cary, NC) software was used.

Results

Fifty-five patients were identified according to the inclusion and exclusion criteria. There were only 5 skeletally mature patients in the no bone stimulator group (NBSTIM), so 5 of the closest matching skeletally mature patients from the bone stimulator group (BSTIM) based on location of lesion, sex, and closest age were selective. This meant that 13 skeletally mature patients from the BSTIM group had to be excluded. Two patients were removed from the BSTIM skeletally immature patients based on location of lesion (only 1 LFC lesion in the NBSTIM group) and age (with the oldest patient in the cohort of BSTIM patients with an LFC lesion removed). This left 20 of the 35 bone simulator (BSTIM) patients, who were then closely matched to the 20 patients with no bone simulator (NBSTIM) and were subsequently included for analysis.

Demographic data

Demographic data is summarized in Table 1. The ratio of male to female patients was 15:5 in the BSTIM group and 14:6 in the NBSTIM group. Mean age for BSTIM at surgery was 13.2 years ± 2.0 (range, 10.9-16.7), and mean age for NBSTIM at surgery was 12.9 years ± 2.0 (range, 9.3-17.3) ($P = .658$). Both groups were matched for skeletal maturity with 75% open physes. Most OCD lesions involved the MFC (80% and 95%, respectively) with no significant difference found between the 2 groups ($P = .342$).

Primary outcome measures

The primary outcome measure was the decrease in coronal and sagittal measurements of the OCD lesions, as determined by MRI at 3 months. These data are summarized in Table 1. The average reduction in the

Table 2. Overall Healing Osteochondritis Dissecans and Inter-Rater Reliability

Measurement	ICC (95% CI)	Closed/Closing (n = 8)	Open (n = 29)	*P* Value*
Coronal width of lesion	0.72 (0.51, 0.86)			
Coronal depth of lesion	0.57 (0.20, 0.80)			
Sagittal width of lesion	0.47 (0.20, 0.71)			
Sagittal depth of lesion	0.31 (0.02, 0.60)			
Overall imaging healing				.158
−1 (worsening)		2 (25.0%)	3 (10.3%)	
0 (unchanged)		2 (25.0%)	3 (10.3%)	
1 (improved)		4 (50.0%)	23 (79.4%)	

ICC, Intraclass correlation coefficient; CI, confidence interval.
Interpretation cutoff (30): slight 0.0-0.20; fair, 0.21-0.40; moderate, 0.41-0.60, substantial, 0.61-0.80; almost perfect, 0.81-1.0.
*Based on Fisher's exact test.

Table 3. Clinical Outcome Data

Characteristics	Bone Stimulator (n = 20)	No Bone Stimulator (n = 20)	*P* Value*
Complications	2 (10.0%)	2 (10.0%)	1.0
Reoperation	2 (10.0%)	2 (10.0%)	1.0
Time from surgery to full weightbearing (wk)†	6.4 ± 1.5 (5.2-12.3)	5.8 ± 1.0 (1.9-6.5)	.684
Time from surgery to clearance for sports (mo)†	4.6 ± 1.9 (2.5-8.3)	4.0 ± 1.3 (2.6-6.5)	.627
Time from surgery to discharge (mo)†	10.0 ± 8.3 (2.8-27.6)	8.1 ± 4.7 (2.8-19.6)	.945

*Based on Fisher's exact test or Wilcoxon rank sum test.
†Mean ± SD (Range).

coronal width of the lesion was 0.9 mm ± 1.8 (range, −5.7 to −1.6) for BSTIM and 0.8mm ± 3.6 (range, −8.9 to −7.1) for NBSTIM ($P = .706$). No significant difference was found between the BSTIM and NBSTIM groups in the coronal and sagittal measurements of the OCD lesions at 3 months, indicating no statistically significant difference in the rate of healing. Table 2 illustrates inter-rater reliability among the 3 raters; there was moderate to good reliability for measuring the coronal width of the lesions (ICC, 0.72; 95% CI, 0.51-0.86) and poor agreement with sagittal width (ICC, 0.31; 95% CI, 0.02-0.60). The pairwise Cohen's Kappa for overall healing evaluation using the ordinal scale was 0.71 (0.33-1) between STM and KM, 0.13 (−0.14 to 0.39) between STM and MDM and 0.13 (−0.14 to 0.39) between STM and KM. Table 2 also demonstrates the overall imaging healing based on MRI and rated on an ordinal scale of −1, 0, and 1, as previously discussed. Sixty-three percent of the BSTIM group and 78% of the NBSTIM group demonstrated overall improved healing at 3 months ($P = .272$).

Secondary outcome measures

The secondary outcome measures are summarized in Table 3. Ninety percent of patients in both groups went on to clinical healing at 2 years after surgery. Two patients (10%) in each group suffered postoperative complications requiring reoperations. Two of the lesions failed to heal, one in each group, resulting in either excision of lesion and microfracture (BSTIM) or redrilling and fixation (NBSTIM). The other BSTIM patient reinjured his knee 1.5 years after surgery when the lesion became loose, requiring excision and microfracture, and the other NBSTIM patient suffered from pain and mechanical symptoms after operation and underwent a synovectomy 10 months later, which was successful.

Mean time from surgery to full weight bearing was 6.4 ± 1.5 weeks in BSTIM group and 5.8 ± 1.0 weeks in NBSTIM group ($P = .684$). Mean time from surgery to clearance for sports was 4.6 ± 1.9 months in BSTIM group and 4.0 ± 1.3 months in NBSTIM group ($P = .627$). Mean time from surgery to discharge was 10.0 ± 8.3 months in BSTIM group and 8.1 ± 4.7 months in NBSTIM group ($P = .945$).

Table 4 summarizes the pooled clinical outcomes data by skeletal maturity and sex. Those with open physes exhibited superior outcomes compared to closed physes, with a significantly shorter time from surgery to discharge ($P = .005$) and reduced complication rates ($P = .042$). There was no significant difference between the pooled male and female data; however, there was a nonsignificant trend toward male patients having a shorter time from surgery to clearance for sports ($P = .063$), time from surgery to discharge ($P = .057$) and lower complication rate ($P = .056$).

Discussion

The most important finding of this study is that adjuvant bone stimulation using LIPUS did not cause accelerated bone healing in stable OCD lesions managed with antegrade drilling in pediatric and adolescent patients. No clinically relevant differences were found between the bone stimulator and control groups as determined by our radiographic or clinical outcomes.

Table 4A. Osteochondritis Dissecans Outcomes Based On Skeletal Maturity

	Closed/Closing (n = 10)	Open (n = 30)	*P* Value*
Clinical characteristics based on skeletal maturity			
Time from surgery to full weightbearing (d)†	6.2 ± 2.5 (1.9 -12.3)	6.1 ± 0.4 (5.3-6.9)	.913
Time from surgery to clearance for sports (mo)†	5.0 ± 1.3 (2.8-6.5)	4.1 ± 1.7 (2.5-8.3)	.127
Time from surgery to discharge (mo)	18.3 ± 8.8 (8.7-27.6)	7.0 ± 3.8 (2.8-17.0)	.005
Complications	3 (30.0%)	1 (3.3%)	.042
Reoperation	3 (30.0%)	1 (3.3%)	.042

*Based on Fisher's exact test or Wilcoxon rank sum test.
†Mean ± SD (Range).

Table 4B. Osteochondritis Dissecans Outcomes Based on Sex

Clinical Characteristics based on sex	Male (n = 29)	Female (n = 11)	*P* Value*
Time from surgery to full weight bearing (d)†	6.1 ± 1.5 (1.9-12.3)	6.1 ± 0.4 (5.6-6.9)	.693
Time from surgery to clearance for sports (mo)†	4.0 ± 1.4 (2.5-7.0)	5.5 ± 2.0 (2.7-8.3)	.063
Time from surgery to discharge (mo)†	7.8 ± 5.7 (2.8-27.6)	13.4 ± 8.0 (5.7-25.8)	.057
Complications	1 (3.4%)	3 (27.3%)	.056
Reoperation	1 (3.4%)	3 (27.3%)	.056

*Based on Fisher's exact test or Wilcoxon rank sum test.
†Mean ± SD (Range).

Our demographic data was in keeping with previous studies on OCD[8]; the average age was 13 years, and most patients were male with an OCD lesion on the MFC. In their descriptive epidemiological study of OCD lesions of the knee, Kessler et al.[19] noted a 3.3-fold increase in knee OCD incidence in patients between 12 to 19 years compared to 6 to 11 years, a 3.8-fold increase in OCD incidence in male patients compared to female, and 63.6% of lesions involved the MFC, with subsequent studies reporting a higher incidence of MFC OCD location.[20]

Studies have previously investigated the use of LIPUS in OCD of the capitellum.[21,22] Maeda et al.[22] conducted a histopathological evaluation of the effect of LIPUS on OCD of capitellum, using samples from 15 adolescent OCD patients treated surgically, of which 7 had received LIPUS for 15 days before surgery. Although the subchondral and cartilage bone findings did not differ significantly, they did note a significantly higher expression of osteopontin, a matrix protein known to play a pivotal role in bone formation.[23] In a study of 43 patients who were randomized to either receive conservative treatment only or LIPUS for capitellum OCD, Kusano et al.[21] noted that the LIPUS group went on to radiographic healing significantly quicker than those who received conservative treatment only; importantly, however, all patients who underwent surgery were excluded. It could be hypothesized that surgery provides better or sufficient bone stimulation alone to heal OCD lesions, which could explain the results seen in our study; however, larger randomized studies will need to be conducted before causality can be established.

Other types of bone stimulation have also been attempted as an adjunct or primary treatment in OCD. In a study investigating whether ESWT can enhance OCD healing in 20 skeletally immature rabbit knees, Lyon et al.[24] found that ESWT application resulted histologically in more mature bone formation and better healing on the treated side and radiographically in an increase in bone density. Conversely, a randomized controlled trial of 68 patients investigating the effect of pulsed electromagnetic fields as an adjunct to arthroscopic microfracture of OCD of the talus found no significant difference to placebo.[25] Thiele et al.[26] investigated ESWT therapy for OCD of both the knee and talus and found superior outcomes for knee OCD, attributing this to ease of targeting the ESWT to the lesion at the knee compared to the ankle. These studies highlight that the clinical efficacy of other modalities of bone stimulation is unclear, despite encouraging biochemical studies, and higher-powered studies are needed to investigate any effect.

The measurement of coronal width continues to be the most reliable measurement when measuring OCD lesions. Fabricant et al.[27] reviewed the MRI scans of 42 OCD lesions were evaluated by 10 fellowship-trained orthopaedic surgeons and, similar to our study ICC of 0.72, the most concordant agreement was in coronal width with an ICC of 0.77, providing an argument for purely focusing on this radiological parameter for future studies.

Adjuvant LIPUS use did not seem to influence revision/complication rate, with 2 patients from each group undergoing revision surgery and 90% of patients going on to heal without complication. Rates of healing with arthroscopic drilling range from 82% to 98% in the literature,[3] with healing time ranging from 6 weeks to 2 years. Our pooled data found a significant number, 30% (n = 3), of those with closed physes required revision surgery compared to their skeletally immature counterparts. This is reflected in the literature, with Anderson et al.[28] reporting 90% healing post-transarticular drilling for OCD in their skeletally immature group but only 50% healing in their skeletally mature group. This is believed to be due to the decreased healing potential of the bone once the physis is closed and skeletal maturity is often quoted as one of the most important factors in deciding treatment options for OCD lesions.[3,8,29,30]

Limitations

Our study had some limitations. With the healing measures used and the small sample size, there is a risk of beta error. Using the study result of the average reduction in the coronal wide of the lesion being 0.9mm ± 1.8 for BSTIM and a 0.1 difference (0.8 mm) with NBSTIM in a post hoc sample size calculation, a sample size of over 5000 would be needed in each group to achieve 80% power to reject the null

hypothesis of equal means. The analysis of the MRI was done at 3 months compared to the 1- to 2-year follow-up, which would have highlighted a higher healing rate. Fifteen out of 35 patients of the LIPUS group were excluded from this study, which could lead to selection bias. The study would have benefited from the reporting of patient reported outcome measures, which were not collected. It was not possible to constantly monitor patient compliance with the bone stimulator over a 3-month period or to check correct positioning of the device at home. Because our controls were determined by insurance status rather than random sampling, it does introduce the possibility of socioeconomic status as a source of bias, which was not a factor that was measured in this study. The conclusions from the study are limited to OCD treatment using antegrade drilling, we did not include OCDs requiring screw or other device fixation. Finally, this was a single center, single surgeon study, which limits the generalizability of the findings.

Conclusion

In antegrade drilling of stable knee OCD lesions in pediatric and adolescent patients, adjuvant bone stimulator use did not appear to improve radiographic or clinical healing.

References

1. Vancea A, Serban O, Fodor D. Relationship between osteopontin and bone mineral density. *Acta Endocrinol (Buchar)* 2021;17:509-516.
2. Kocher MS, Tucker R, Ganley TJ, Flynn JM. Management of osteochondritis dissecans of the knee: current concepts review. *Am J Sports Med* 2006;34:1181-1191.
3. Edmonds EW, Polousky J. A review of knowledge in osteochondritis dissecans: 123 years of minimal evolution from König to the ROCK study group. *Clin Orthop Relat Res* 2013;471:1118-1126.
4. Mohr B, Baldea JD. *Knee osteochondritis dissecans. StatPearls. Treasure Island (FL)*. StatPearls Publishing, 2021.
5. Andriolo L, Crawford DC, Reale D, et al. Osteochondritis dissecans of the knee: Etiology and pathogenetic mechanisms. A systematic review. *Cartilage* 2020;11:273-290.
6. Hevesi M, Sanders TL, Pareek A, et al. Osteochondritis dissecans in the knee of skeletally immature patients: Rates of persistent pain, osteoarthritis, and arthroplasty at mean 14-years' follow-up. *Cartilage* 2020;11:291-299.
7. Edmonds EW. Editorial commentary: Osteochondritis dissecans of the knee: The great confounder. *Arthroscopy* 2020;36:795-796.
8. Chau MM, Klimstra MA, Wise KL, et al. Osteochondritis dissecans: Current understanding of epidemiology, etiology, management, and outcomes. *J Bone Joint Surg Am* 2021;103:1132-1151.
9. Baghdadi S, Isaacs D, Chan CT, Wells L, Ganley TJ, Lawrence JTR. Arthroscopic drilling for stable juvenile osteochondritis dissecans of the knee is safe and patients reliably return to daily activities by 3 months. *Arthrosc Sports Med Rehabil* 2022;4(2):e645-e651.
10. Heyworth BE, Edmonds EW, Murnaghan ML, Kocher MS. Drilling techniques for osteochondritis dissecans. *Clin Sports Med* 2014;33:305-312.
11. Yonetani Y, Tanaka Y, Shiozaki Y, et al. Transarticular drilling for stable juvenile osteochondritis dissecans of the medial femoral condyle. *Knee Surg Sports Traumatol Arthrosc* 2012;20:1528-1532.
12. Santana-Rodríguez N, Clavo B, Llontop P, et al. Pulsed ultrasounds reduce pain and disability, increasing rib fracture healing, in a randomized controlled trial. *Pain Med* 2019;20:1980-1988.
13. Elvey MH, Miller R, Khor KS, Protopapa E, Horwitz MD, Hunter AR. The use of low-intensity pulsed ultrasound in hand and wrist nonunions. *J Plast Surg Hand Surg* 2020;54:101-106.
14. Bhan K, Patel R, Hasan K, et al. Fracture nonunions and delayed unions treated with low-intensity pulsed ultrasound therapy: A clinical series. *Cureus* 2021;13(8):e17067.
15. Caliogna L, Medetti M, Bina V, et al. Pulsed electromagnetic fields in bone healing: Molecular pathways and clinical applications. *Int J Mol Sci* 2021;22:7403.
16. Harrison A, Alt V. Low-intensity pulsed ultrasound (LIPUS) for stimulation of bone healingrange: A narrative review. *Injury* 2021;52:S91-S96 (Suppl 2).
17. Meng J, Hong J, Zhao C, et al. Low-intensity pulsed ultrasound inhibits RANKL-induced osteoclast formation via modulating ERK-c-Fos-NFATc1 signaling cascades. *Am J Transl Res* 2018;10:2901-2910.
18. Khormaee S, Kramer DE, Yen YM, Heyworth BE. Evaluation and management of patellar instability in pediatric and adolescent athletes. *Sports Health* 2015;7:115-123.
19. Kessler JI, Nikizad H, Shea KG, Jacobs JC Jr, Bebchuk JD, Weiss JM. The demographics and epidemiology of osteochondritis dissecans of the knee in children and adolescents. *Am J Sports Med* 2014;42:320-326.
20. Cruz AI Jr, Shea KG, Ganley TJ. Pediatric knee osteochondritis dissecans lesions. *Orthop Clin North Am* 2016;47:763-775.
21. Kusano H, Furushima K, Mitsui Y, et al. Usefulness of low-intensity pulsed ultrasound (LIPUS) for the treatment of osteochondritis dissecans (OCD) of the humeral capitellum. *J Orthop Trauma* 2016;30(8):S3-S4.
22. Maeda S, Tsuda E, Mizukami H, et al. Histological evaluation of low-intensity pulsed ultrasound on osteochondritis dissecans of the humeral capitellum. *Asia Pac J Sports Med Arthrosc Rehabil Technol* 2015;2:56-62.
23. Si J, Wang C, Zhang D, Wang B, Zhou Y. Osteopontin in bone metabolism and bone diseases. *Med Sci Monit* 2020;26:e919159.
24. Lyon R, Liu XC, Kubin M, Schwab J. Does extracorporeal shock wave therapy enhance healing of osteochondritis dissecans of the rabbit knee? A pilot study. *Clin Orthop Relat Res* 2013;471:1159-1165.
25. Reilingh ML, van Bergen CJ, Gerards RM, et al. Effects of pulsed electromagnetic fields on return to sports after arthroscopic debridement and microfracture of osteochondral talar defects: A randomized, double-blind, placebo-controlled, multicenter trial. *Am J Sports Med* 2016;44:1292-1300.

26. Thiele S, Thiele R, Gerdesmeyer L. Adult osteochondritis dissecans and focussed ESWT: A successful treatment option. *Int J Surg* 2015;24:191-194 (Pt B).
27. Fabricant PD, Milewski MD, Kostyun RO, et al. Osteochondritis dissecans of the knee: An interrater reliability study of magnetic resonance imaging characteristics. *Am J Sports Med* 2020;48:2221-2229.
28. Anderson AF, Richards DB, Pagnani MJ, Hovis WD. Antegrade drilling for osteochondritis dissecans of the knee. *Arthroscopy* 1997;13:319-324.
29. Heyworth BE, Kocher MS. Osteochondritis dissecans of the knee. *JBJS Rev* 2015;3(7):e1.
30. Landis JR, Koch GG. The measurement of observer agreement for categorical data. *Biometrics* 1977;33:159-174.