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Lesion Size Is a Predictor of Clinical Outcomes After Bone Marrow Stimulation for Osteochondral Lesions of the Talus

A Systematic Review

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Background: The critical lesion size treated with bone marrow stimulation (BMS) for osteochondral lesions of the talus (OLTs) has been 150 mm² in area or 15 mm in diameter. However, recent investigations have failed to detect a significant correlation between the lesion size and clinical outcomes after BMS for OLTs.

Purpose: To systematically review clinical studies reporting both the lesion size and clinical outcomes after BMS for OLTs.

Study Design: Systematic review.

Methods: A systematic search of the MEDLINE and EMBASE databases was performed in March 2015 based on the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines. Included studies were evaluated with regard to the level of evidence (LOE), quality of evidence (QOE), lesion size, and clinical outcomes.

Results: Twenty-five studies with 1868 ankles were included; 88% were either LOE 3 or 4, and 96% did not have good QOE. The mean area was 103.8 ± 10.2 mm² in 20 studies, and the mean diameter was 10.0 ± 3.2 mm in 5 studies. The mean American Orthopaedic Foot and Ankle Society score improved from 62.4 ± 7.9 preoperatively to 83.9 ± 9.2 at a mean 54.1-month follow-up in 14 studies reporting both preoperative and postoperative scores with a mean follow-up of more than 2 years. A significant correlation was found in 3 studies, with a mean lesion area of 107.4 ± 10.4 mm², while none was reported in 8 studies, with a mean lesion area of 85.3 ± 9.2 mm². The lesion diameter significantly correlated with clinical outcomes in 2 studies (mean diameter, 10.2 ± 3.2 mm), whereas none was found in 2 studies (mean diameter, 8.8 ± 0.0 mm). However, the reported lesion size measurement method and evaluation method of clinical outcomes widely varied among the studies.

Conclusion: An assessment of the currently available data does suggest that BMS may best be reserved for OLT sizes less than 107.4 mm² in area and/or 10.2 mm in diameter. Future development in legitimate prognostic size guidelines based on high-quality evidence that correlate with outcomes will surely provide patients with the best potential for successful long-term outcomes.

Keywords: talar osteochondral lesion; bone marrow stimulation; lesion size; systematic review

Traditional surgical procedures for osteochondral lesions of the talus (OLTs) include both reparative and replacement techniques.²⁴ Bone marrow stimulation (BMS) is a reparative procedure and is commonly performed, predominantly as a primary procedure in smaller lesions.³⁴ One systematic review reported that BMS had an 85% to 88% clinical success rate in the short term and midterm in treating

OLTs.⁴⁹ In the athletic population, nearly 90% of athletes returned to their preinjury level.³⁷ However, despite good short- and medium-term outcomes, there is growing concern over the longevity of fibrocartilaginous infill at the defect site produced by BMS. Clinically, Ferkel et al¹⁷ have shown 35% deterioration in a subset of patients over 5 years after BMS. Moreover, Lee et al³⁰ have reported that only 35% of fibrocartilage had integrated with the surrounding cartilage at 1 year after arthroscopic surgery, while Becher et al³ have shown that 100% of cases treated with BMS for OLTs had fibrillation at the repair site at 5 years on magnetic resonance imaging (MRI).

Lesion size has been accepted widely as the most commonly used predictor of clinical outcomes after BMS for OLTs.^{11,12,34} In this regard, the critical sized lesion treated with BMS has been assessed based on both the lesion area and diameter. In a series of 120 ankles, Choi et al¹¹ concluded that 150 mm² is a critical defect area beyond which clinical scores after BMS for OLTs decreased significantly. Chuckpaiwong et al¹² found that 15 mm was the critical diameter beyond which BMS was associated with a greater likelihood of failure. These 2 investigations form the basis of current treatment paradigms for OLT treatment strategies. However, despite the evidence presented in the abovementioned studies, recent investigations have failed to detect a significant correlation between the lesion size and clinical outcomes after BMS.^{8,15,23,27-30,44,46,47} This has led to some confusion as to whether there is a true critically sized defect beyond which BMS will perform poorly.

The purpose of this study was to systematically review published literature reporting the lesion size after BMS for OLTs to establish whether sufficient evidence exists to support current prognostic size guidelines.

METHODS

Search Strategy

Two independent reviewers performed a systematic review of the PubMed/MEDLINE and EMBASE databases in March 2015 based on the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines, and all references by both reviewers were included.³³

The search strategies for MEDLINE and EMBASE were the following: (microfracture OR microdrilling OR drilling OR drill OR bone marrow stimulation OR marrow stimulation OR BMS OR abrasion chondroplasty OR arthroscopy OR arthroscopic) AND (talus OR talar OR ankle) AND (cartilage OR osteochondritis dissecans OR chondral OR osteochondral OR transchondral OR osteochondral lesion OR OCL OR OCD). In addition to electronic searches, citations and references of all articles and relevant studies were also screened. The inclusion and exclusion criteria are shown in

TABLE 1
Inclusion and Exclusion Criteria^a

Inclusion criteria
Therapeutic clinical studies evaluating both lesion size of OLTs and outcomes in patients who underwent BMS
BMS includes microfracture, drilling, and abrasion
All patients included had >6-month follow-up
Published in a peer-reviewed journal
Published in English
Full-text version available
Exclusion criteria
Cadaveric studies
Animal studies
Case reports
Review articles
Technique articles
Articles with unseparated results if >1 technique was described
Inadequate description of surgical technique
Use of scaffolds
Errors in reported data

^aBMS, bone marrow stimulation; OLT, osteochondral lesion of the talus.

Table 1. No time limit was given to the publication date so as to incorporate all studies relating to the search terms.

The titles and abstracts were reviewed by applying the aforementioned criteria, and the full text of potentially relevant studies was then selected. BMS includes more than 1 technique: microfracture, drilling, and abrasion. Studies that included more than 1 surgical procedure¹⁸ or a subgroup of patients with different follow-up times⁴² were included in the data set by analyzing only patients who underwent BMS at a minimum follow-up time of 6 months. Differences between reviewers were discussed until agreement was achieved, and the senior author (J.G.K.) was consulted in the event of persistent disagreement.

Assessment of Level of Evidence

Two independent reviewers evaluated each study and created a classification based on the level of evidence (LOE) using previously published criteria.³²

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Assessment of Quality of Evidence

The quality of evidence (QOE) of the included studies was assessed using the Modified Coleman Methodology Score (MCMS) (Table 2). The Coleman Methodology Score¹³ was initially described to evaluate the quality of studies investigating the treatment of tendinopathy. This score includes part A (primarily evaluates baseline study characteristics; 0-60) and part B (primarily evaluates outcome criteria and recruitment rates; 0-40) and was subsequently modified by Jakobsen et al²² for the assessment of cartilage repair. The current authors have further modified the score for the current review on OLTs in the categories of “diagnostic certainty” and “description of postoperative rehabilitation” in part A and “outcome criteria” in part B (Table 2). With respect to “diagnostic certainty,” the authors analyzed the percentage of patients who underwent diagnostic MRI preoperatively. Under “description of postoperative rehabilitation,” “well described” was defined as reporting 3 characteristics: weightbearing status in the postoperative period, range of motion allowed in the postoperative period, and timing of return to sport. In terms of “outcome criteria,” there are no validated scoring systems available for the assessment of OLTs. Therefore, this section was modified to reassign 6 points to further specify the type of outcomes utilized in each study, including objective, subjective, and imaging criteria.

Two independent reviewers determined the MCMS for each study. If any discrepancy existed, the senior author evaluated all available data, and a consensus was reached. Excellent studies were considered those that scored 85 to 100, good studies scored 70 to 84, fair studies scored 55 to 69, and poor studies scored less than 55.²²

Statistical Analysis

All statistical analyses were performed using a commercially available statistical software package (SAS 9.3; SAS Institute Inc). Descriptive statistics were calculated for each study and parameters analyzed. For each variable, we calculated the number and percentage of studies that reported the variable. Variables were reported as the weighted mean ± weighted SD where applicable.

RESULTS

After a full-text review, 25 studies including 1868 ankles were identified for inclusion in the current study (Figure 1).^{##} The weighted mean follow-up was 46.1 months (range, 6-146 months), with only 5 studies reporting a follow-up time of ≥5 years. Patient characteristics are shown in Table 3.

Level of Evidence

There were 3 studies of LOE 2,^{18,28,39} 9 of LOE 3,^{1,7-11,14,25,42} and 13 of LOE 4.^a Although 1 study¹⁸ was described as LOE

TABLE 2
Modified Coleman Methodology Score^a

	Score
Part A: Only 1 score to be given for each section	
1. Number of study patients	
>60	10
41-60	7
20-40	4
<20, not stated	0
2. Mean follow-up, mo	
>24	5
12-24	2
<12, not stated or unclear	0
3. Number of different surgical procedures included in each reported outcome	
1	10
>1, but >90% of patients undergoing the 1 procedure	7
Not stated, unclear, or <90% of patients undergoing the 1 procedure	0
4. Type of study	
Randomized controlled trial	15
Prospective cohort study	10
Retrospective cohort study	0
5. Diagnostic certainty (on MRI)	
In all	5
In >80%	3
In <80%	0
6. Description of surgical procedure	
Adequate (technique stated and necessary details of that type of procedure provided)	5
Fair (technique only stated without elaboration)	3
Inadequate, not stated, or unclear	0
7. Description of postoperative rehabilitation	
Well described (ROM, WB, and sport)	10
Not adequately described (2 items between ROM, WB, and sport)	5
Protocol not reported	0
Part B: Scores may be given for each option in each of the 3 sections if applicable	
1. Outcome criteria	
Outcome measures clearly defined	2
Timing of outcome assessment clearly stated (eg, at best outcome after surgery or follow-up)	2
Objective, subjective, and imaging criteria	6
2 items between objective, subjective, and imaging criteria	4
Objective, subjective, or radiological criteria	2
2. Procedure for assessing outcomes	
Patients recruited (results not taken from surgeons' files)	5
Investigator independent of surgeon	4
Written assessment	3
Completion of assessment by patients themselves with minimal investigator assistance	3
3. Description of patient selection process	
Selection criteria reported and unbiased	5
Recruitment rate reported	
>80%	5
<80%	3
Eligible patients not included in study satisfactorily accounted for or 100% recruitment	5

^aMRI, magnetic resonance imaging; ROM, range of motion; WB, weightbearing.

^{##}References 1, 4, 7-12, 14, 15, 18, 21, 23, 25, 27-31, 39, 42, 44-47.

^aReferences 4, 12, 15, 21, 23, 27, 29-31, 44-47.

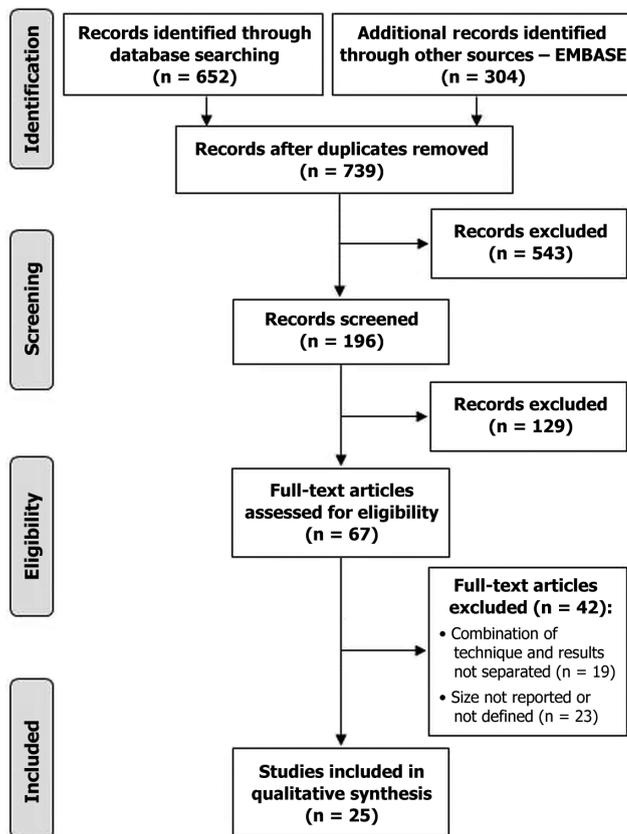


Figure 1. PRISMA flowchart outlining the systematic review.

1 in the published journal, this article was reassigned as LOE 2 in the current study based on the previously published criteria (Table 4).

Quality of Evidence

The weighted mean MCMS of the overall population of the studies was 57.6 ± 10.2 of 100 points. The weighted mean MCMS in part A and part B were 37.9 ± 8.1 and 20.0 ± 6.0 , respectively. Only 1 (4%) study²⁸ was classified as excellent quality. There were 16 studies (64%) of fair quality^b and 8 (32%) of poor quality^{4,9,14,15,23,29,42,47} (Table 4 and Figure 2).

Lesion Size

In the 25 available studies, the overall lesion size was calculated by either weighted lesion area or weighted lesion diameter. In 20 studies,^c the weighted mean lesion area was $103.8 \pm 10.2 \text{ mm}^2$, and the weighted mean lesion diameter was $10.0 \pm 3.2 \text{ mm}$ in the remaining 5 studies.^{1,11,12,21,44} Two studies^{1,27} also included volume measurements, and 3 studies^{1,11,47} included depth measurements.

^bReferences 1, 7-9, 12, 18, 21, 25, 27, 30, 31, 39, 42, 44-46.

^cReferences 1, 4, 7-11, 14, 15, 18, 23, 28-31, 39, 42, 45-47.

TABLE 3
Patient Demographics and Clinical Characteristics

Studies, n	25
Ankles, n	1868
Sex, male/female/unknown, n	918/504/446
Age, y, weighted mean (range)	33.8 (12-78)
Duration of symptoms, mo, weighted mean (range)	19.5 (1-240)
Follow-up, mo, weighted mean (range)	46.1 (6-146)

TABLE 4
Level and Quality of Evidence of Included Studies^a

	Studies, n (%)
Level of evidence	
1	—
2	3 (12)
3	9 (36)
4	13 (52)
Quality of evidence	
Excellent (MCMS ≥ 85)	1 (4)
Good (MCMS 70-84)	—
Fair (MCMS 55-69)	16 (64)
Poor (MCMS < 55)	8 (32)

^aMCMS, Modified Coleman Methodology Score.

For those studies assessing the lesion area, 8 studies used MRI,^{1,4,7,9,10,27,46,47} 3 used arthroscopic surgery,^{23,31,39} and 2 used both MRI and arthroscopic surgery.^{11,25} The methods utilized to calculate the lesion area varied among these studies. In the 10 studies utilizing MRI, 7 studies used an ellipse formula ($area = ab\pi = coronal \text{ length} \times sagittal \text{ length} \times 0.79$),^{7,9-11,25,46,47} 2 used an ellipsoid formula ($area = \pi \times [coronal \text{ diameter}/2] \times [sagittal \text{ diameter}/2]$),^{1,27} and 1 study⁴ used manual region of interest analysis. Of the 3 studies using arthroscopic measurement methods, Jung et al²³ used an oval formula ($area = \pi \times [longitudinal \text{ diameter}/2] \times [transverse \text{ diameter}/2]$), whereas the other studies^{31,39} did not report the method to calculate the lesion area.^{11,25,31,39}

Lesion diameter was evaluated on MRI in 3 studies,^{1,11,44} and 3 studies used arthroscopic surgery.^{11,12,21} van Bergen et al⁴⁴ used computed tomography, MRI, or radiography to evaluate the lesion diameter.

The timing for the assessment of the lesion size also varied in the included studies. Of the 10 studies using MRI for measurements, 9 studies measured preoperatively,^{1,7,9-11,25,27,46,47} and 1 measured postoperatively.⁴ Of the 7 studies using arthroscopic measurements, 1 study³¹ assessed the lesion size before debridement of the cartilage flap, 2 assessed after debridement,^{23,39} and 4 were unclear as to when measurements were made.^{11,12,21,25}

Clinical Outcomes

Clinical outcomes were evaluated using a number of different scoring systems for OLTs (Table 5). The American Orthopaedic Foot and Ankle Society (AOFAS) score was the most frequently utilized.²⁶ Of the 22 studies that

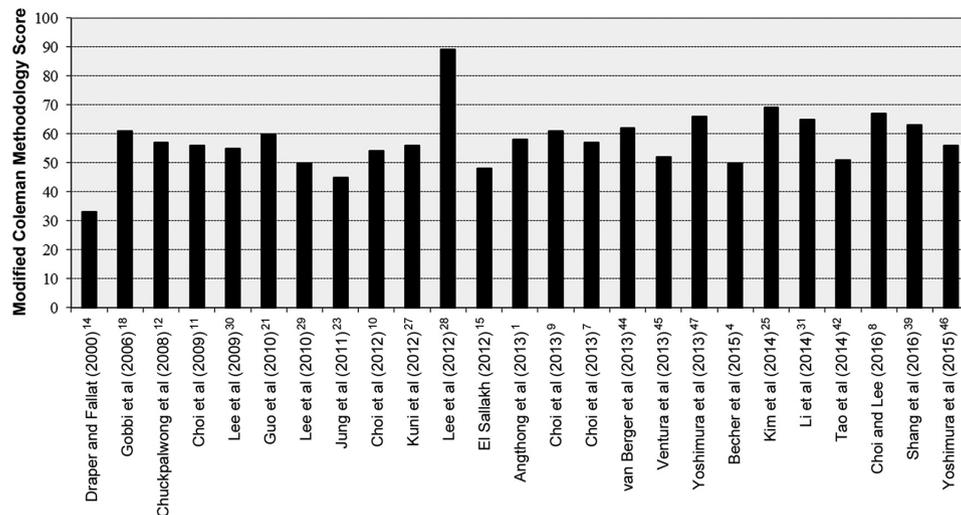


Figure 2. Modified Coleman Methodology Score of included studies.

used the AOFAS score,^d 14 studies investigated both pre-operative and postoperative scores at a mean follow-up of longer than 24 months, among which the weighted mean AOFAS score improved from 62.4 ± 7.9 preoperatively to 83.9 ± 9.2 at a weighted mean 54.1-month follow-up.^e In addition, 10 of these studies reported that 864 of 1053 patients (82.1%) had a successful outcome at a weighted mean 56.0-month follow-up.^{8-11,15,23,28,29,31,47} A weighted mean rate of return to sport was 76.5% in 3 studies.^{14,29,44}

In this systematic review, 5 studies reported sequential clinical outcomes at ≥2 postoperative time points.^{9,11,18,28,31} Three of these found temporal improvement in the AOFAS score over the first 2 years of postoperative follow-up.^{18,28,31} In contrast, 2 studies demonstrated that the number of clinical failures increased over time.^{9,11}

Correlation

Of the 16 studies that reported a correlation between the lesion size and clinical outcomes,^f 14 studies with a mean follow-up of more than 24 months were included in the analysis (Table 6).^g

With regard to the lesion area, a significant correlation was found in 3 studies with a weighted mean area of 107.4 ± 10.4 mm².⁹⁻¹¹ In contrast, no significant correlation was reported in 8 studies with a weighted mean area of 85.3 ± 9.2 mm².^{2,1,8,15,23,28,29,46,47}

The lesion diameter was significantly correlated with clinical outcomes in 2 studies with a mean diameter of 10.2 ± 3.2 mm,^{11,12} whereas no significant correlation was found in 2 studies with a mean diameter of 8.8 ± 0.0 mm.^{1,44}

^dReferences 4, 7-12, 15, 18, 21, 23, 25, 27-31, 39, 42, 44, 45, 47.
^eReferences 7-11, 15, 18, 23, 25, 28, 29, 31, 45, 47.
^fReferences 1, 8-12, 15, 21, 23, 27-30, 44, 46, 47.
^gReferences 1, 8-12, 15, 23, 27-29, 44, 46, 47.

TABLE 5
Clinical Outcome Scores Utilized in Included Studies^a

Score	Studies, n (%)
AOFAS	22 (88)
VAS	12 (48)
SF-36	3 (12)
AAS	3 (12)
Berndt and Harty outcome question	3 (12)
JSSF	2 (8)
AHS	2 (8)
HSS	1 (4)
Roles and Maudsley score	1 (4)
Loomer rate	1 (4)
SANE	1 (4)
NPI	1 (4)
Ogilvie-Harris score	1 (4)
Karlsson-Peterson score	1 (4)
Saxena criteria	1 (4)

^aAAS, Ankle Activity Score; AHS, Ankle-Hindfoot Score; AOFAS, American Orthopaedic Foot and Ankle Society; HSS, Hannover Scoring System; JSSF, Japanese Society for Surgery of the Foot; NPI, Numeric Pain Intensity; SANE, Subjective Assessment Numeric Evaluation; SF-36, Short Form-36 Health Survey; VAS, visual analog scale.

DISCUSSION

This systematic review demonstrated that there is a lack of supporting data to justify current prognostic size guidelines to treat OLTs. Fundamentally, high-level clinical evidence is necessary to treat patients according to the principles of evidence-based medicine.³⁶ While the number of LOE 1 and 2 studies have increased in the clinical sports medicine literature in recent years,²⁰ greater than 80% of foot and ankle surgery literature remains as having low LOE.^{2,48} In the current study, 88% of included studies in which BMS was performed for OLTs were classified as

TABLE 6
Correlation Between Lesion Size and Clinical Outcomes^a

Size	Studies, n (%)	Lesion Size, Weighted Mean	No. of Ankles	Sex, Male/Female, n	Age, y, Weighted Mean	AOFAS Score, Weighted Mean		Coefficient Correlation	MCMS, Weighted Mean	Reference No.
						Preoperatively	Last Follow-up			
Significant correlation between lesion size and clinical outcomes										
Area	3 (12)	107.4 mm ²	692	201/89 ^b	37.3 ^b	61.6	85.4	$r = -0.843^{11}$	57.0	9-11
Diameter	2 (8)	10.2 mm	225	153/69 ^b	37.4	63.0 ^c	85.1 ^c	$r = -0.642, -0.676^{11}$	57.0	11, 12
Depth	2 (8)	5.4 mm	170	100/67 ^b	35.3	— ^c	— ^c	$R^2 = 0.14^1, r = -0.344^{11}$	57.0	1, 11
No significant correlation between lesion size and clinical outcomes										
Area	8 (32)	85.3 mm ²	394	233/110 ^b	34.9	66.8 ^c	89.7 ^c	$r = -0.04^{46}, r = 0.10^{47}$	57.6	1, 8, 15, 23, 28, 29, 46, 47
Diameter	2 (8)	8.8 mm	100	50/50	34.0	— ^c	— ^c	— ^d	60.0	1, 44
Depth	1 (4)	4.7 mm	50	22/28	35.0	74.0	90.0	$r = -0.386^{47}$	66.0	47
Volume	2 (8)	254.2 mm ³	72	32/40	33.5	— ^c	— ^c	— ^d	57.0	1, 27

^aAOFAS, American Orthopaedic Foot and Ankle Society; MCMS, Modified Coleman Methodology Score.

^bData are not clear/complete in the studies.

^cThe AOFAS score was not used in all the studies.

^dNot reported.

poor LOE. In addition, almost all included articles (24/25) could not be classified as good methodological quality. These findings suggest that it is necessary to re-evaluate the evidence upon which current treatment paradigms and prognostic indicators are based.

Although lesion size has been the standard cutoff criterion for utilizing BMS as a treatment strategy for OLTs, the current systematic review revealed that a variety of assessment methods for the lesion area exist. This variation in measurement techniques underscores the difficulty of meaningfully comparing such data. Choi et al¹⁰ originally developed an assessment method for the lesion area using an MRI formula and suggested 150 mm² as the cutoff line for BMS for OLTs. Subsequent studies associated with the lesion area used not only the Choi et al method^{7,9-11,25,46,47} but also their own methods.^{1,23,27,31,39,44} Caution is necessary when interpreting the ways in which the lesion size is represented in these studies. Intuitively, different mathematical formulas used to calculate the lesion area can produce different areas even if the lesion diameter is the same. In addition, although several studies used arthroscopic surgery to evaluate the lesion area,^{11,23,25,31,39} previous literature suggests that the lesion size measured by arthroscopic surgery is often different from that by MRI.^{6,11,19,25,41,43} Uniform measurement techniques and area representation would therefore be useful to standardize across the literature and may result in a more statistically valid correlation between the OLT size and treatment outcomes.

OLTs with diameters of 15 mm represents a widely followed metric whereby OLTs below this measurement would be treated with BMS and those above this measurement would be treated by replacement therapies. The current systematic review revealed that reported measurement methods for the lesion diameter varied among the included studies^{1,10,11,21,44} and that the timing for the assessment of the lesion size was not reported.^{11,12,21} Debridement for unstable cartilage lesions and necrotic bone is a common and recommended step before BMS,⁴⁰ which inherently changes the

lesion size. Furthermore, arthroscopic lesion assessment has poor interobserver reliability,³⁵ and this was not evaluated in the included studies. The inconsistency that exists between MRI and arthroscopic measurements^{6,11,19,25,41,43} cannot be overlooked and must be considered when evaluating the available evidence. Similar to the representation of the lesion area, uniform measurement techniques for the diameter should also be standardized, thereby allowing investigators to speak a common language.

Clinical outcomes were evaluated using the AOFAS score in the majority of studies that were reviewed. To date, however, there remains no validated scoring system for OLTs. Moreover, discrepancy between clinical outcomes and imaging outcomes currently exists. Several studies have suggested that clinical outcomes may improve over time,^{18,28,31} whereas others have reported deterioration in outcome scores over time.^{9,11,17} Notably, while van Bergen et al⁴⁴ reported that initial success of BMS for OLTs was maintained at a mean follow-up of 141 months, one-third of patients increased by 1 grade of arthritis on standard radiographs. A potential reason for these discrepancies or lag in sensitivity of clinical outcome data may be the invalid clinical evaluation methods after OLT surgery.

This systematic review demonstrates that lesion sizes greater than 107.4 mm² in area and 10.2 mm in diameter are significantly correlated with poorer clinical outcomes. This supports previous literature that suggests an inverse relationship between defect size and outcomes after BMS.^{11,12,18} However, the size of the lesion that correlated with poorer outcomes is smaller both in volumetric and diametric size than was previously believed.

It has been well documented that the reparative fibrous cartilage after BMS is mechanically inferior to hyaline cartilage^{5,16} and will deteriorate over time.^{17,30} Size analysis in the current study may therefore indicate the lesion size beyond which fibrocartilage has the capacity to withstand repetitive biological and mechanical insults after BMS for OLTs.

There are several limitations to our review and analysis. First, we were unable to determine if the lesion was

a contained or noncontained lesion.^{10,47} This has previously been implicated as an important prognostic factor in OLT treatment; however, few articles included these data in their studies.^{7,9,46} Additionally, the differences in clinical outcomes among the laterality of OLTs have not been reported in the studies evaluated. Previous clinical studies have implicated that laterality may have an effect on outcomes^{12,37,38}; however, more recent investigations have shown that the laterality of the OLT does not affect clinical outcomes.^{9,11} Further studies may be required. Another limitation was that we were unable to differentiate between cystic and noncystic lesions, which we consider to be another potentially important outcome variable. Despite these limitations, the current analysis of available literature to evaluate size guidelines for BMS for OLTs presents compelling data that hopefully promote further work as to defining accurate and reliable prognostic factors for managing OLTs.

CONCLUSION

Despite the good to excellent results reported in numerous studies over the short term, no standardized method of lesion analysis or outcome evaluation continues to persist. Assessment of currently available data does suggest that BMS may best be reserved for OLT sizes of less than 107.4 mm² in area and/or 10.2 mm in diameter. Nonetheless, the future development of legitimate prognostic size guidelines based on high-quality evidence that correlates with a clinical assessment will provide patients with the best potential for successful long-term outcomes after the surgical management of OLTs.

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