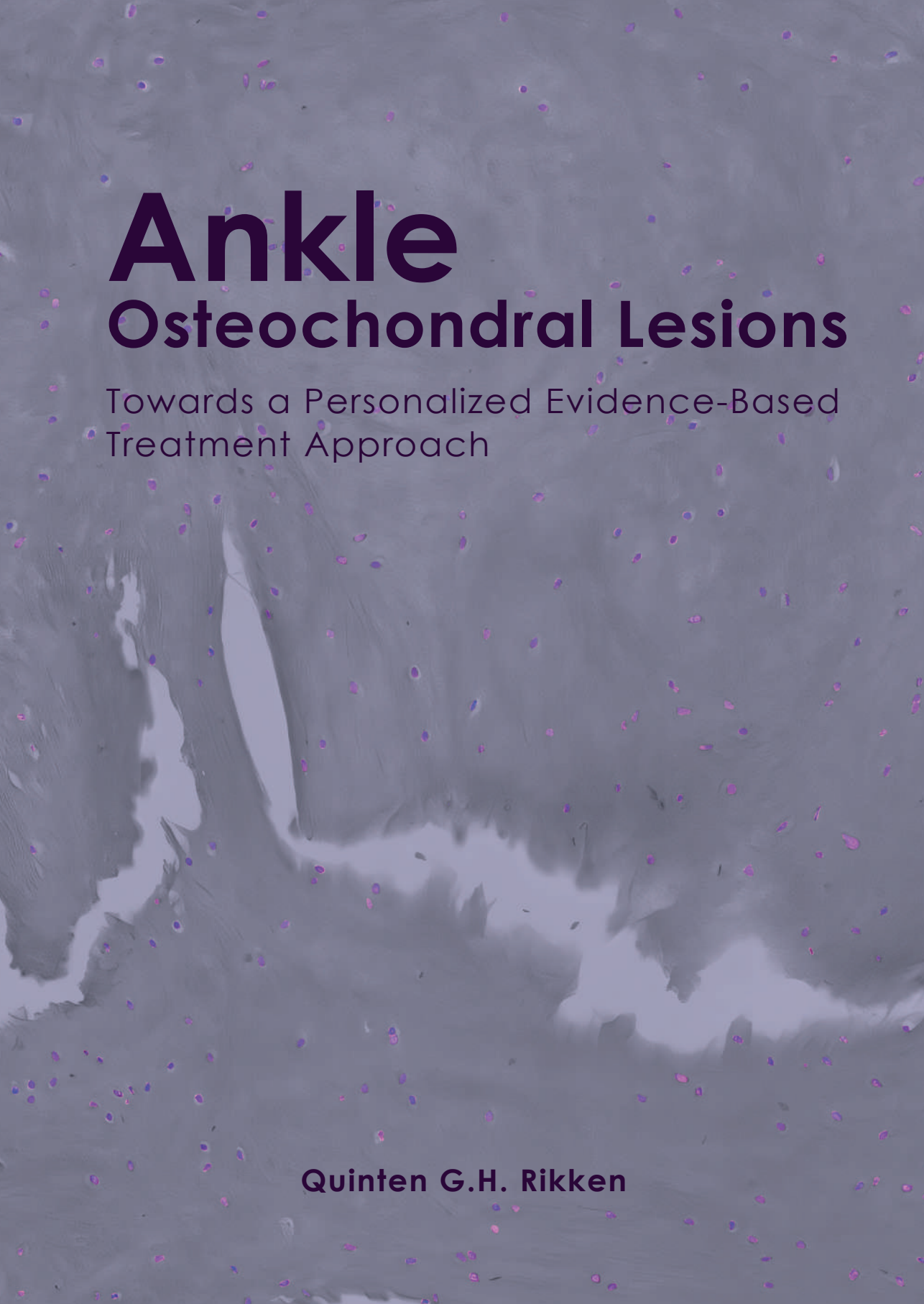

Ankle Osteochondral Lesions

Towards a Personalized Evidence-Based Treatment Approach

Quinten G.H. Rikken

Stellingen behorend bij het proefschrift getiteld
"Ankle Osteochondral Lesions: Towards a Personalized Evidence-Based Treatment Approach"

1. Arthroscopische beenmerg stimulatie resulteert in acceptabele klinische resultaten op de langer termijn met een 10- jaars overleving van 83% - *Dit proefschrift*

2. Herhaalde beenmerg stimulatie voor OLT resulteert in een verbetering in klinische uitkomsten op de korte- tot midden-termijn, maar mogelijk tot inferieure uitkomsten ten opzichte van een primaire procedure - *Dit proefschrift*

3. Open fixatie van osteochondraal fragmenten van de talus middels 'Lift-Drill-Fill-Fix' (LDFF) is technisch haalbaar, resulteert in goede 2-jaars klinische uitkomsten, en leidt tot genezing van het fragment in 91% van de patiënten - *Dit proefschrift*

4. Arthroscopische fixatie van osteochondraal fragmenten van de talus middels 'Lift-Drill-Fill-Fix' resulteert in houdbare lange termijn uitkomsten - *Dit proefschrift*

5. Patiënten met overgewicht hebben mogelijk minder lang profijt van een arthroscopische beenmerg stimulatie procedure en hebben een grotere kans op non-union na fixatie - *Dit proefschrift*

6. De niet-operatieve behandeling van patiënten met een OLTP is veilig maar resulteert in een marginale verbetering in klinische uitkomsten - *Dit proefschrift*

7. Arthroscopische beenmerg stimulatie voor OLTP resulteert in acceptabele pijn scores en functionele uitkomsten in activiteiten van het dagelijks leven, maar in matige uitkomsten bij sportactiviteiten - *Dit proefschrift*

8. Een osteotomie en vullen met eigen bot van een mediaal of centraal gelokaliseerde OLTP is technisch haalbaar en een mogelijke optie voor complexe laesies, maar de klinische uitkomsten en veiligheid moet onderzocht worden - *Dit proefschrift*

9. The optimal treatment of ankle OCLs is à la carte, using patient- and lesion factors as the ingredients – *This thesis*

10. Sometimes it's all about the win, sometimes it's about the skiing – *Bode Miller*

11. You can't always get what you want – *The Rolling Stones*

Quinten G.H. Rikken
April, 2026
Amsterdam, the Netherlands

Ankle Osteochondral Lesions:
Towards a Personalized Evidence-Based Treatment Approach

Quinten G.H. Rikken

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Ankle Osteochondral Lesions: Towards a Personalized Evidence-Based Treatment Approach

ACADEMISCH PROEFSCHRIFT

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in het openbaar te verdedigen in de Aula der Universiteit
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Faculteit der Geneeskunde

Voor Mam en Pap

Table of Contents

Part 4. Management of Osteochondral Lesions of the Tibial Plafond

Part 5. General Discussion and Appendices

Part 1

Introduction

Chapter 1
General Introduction

Osteochondral Lesions of the Ankle: Etiology

The ankle joint is comprised of the talar, tibial and fibular bones, is lined with articular cartilage, and filled with synovial fluid (Figure 1). The articular cartilage is supported by the underlying subchondral bone, and together these form the 'osteochondral unit'. The articular cartilage is a smooth and elastic tissue that is mainly made of specialized collagen and water-rich proteoglycans. The subchondral bone is a dense and rigid structure, comprised of cortical and spongious bone. The function of the osteochondral unit is to absorb forces under load and to facilitate near frictionless motion, which are critical for efficient joint functioning. When the structure of the cartilage and its underlying bone is compromised or damaged, for example due to an ankle sprain or fracture, it is called an osteochondral lesion (OCL).[46] In the ankle such lesions are known as osteochondral lesions of the talus (OLT) or as osteochondral lesions of the tibial plafond (OLTP).

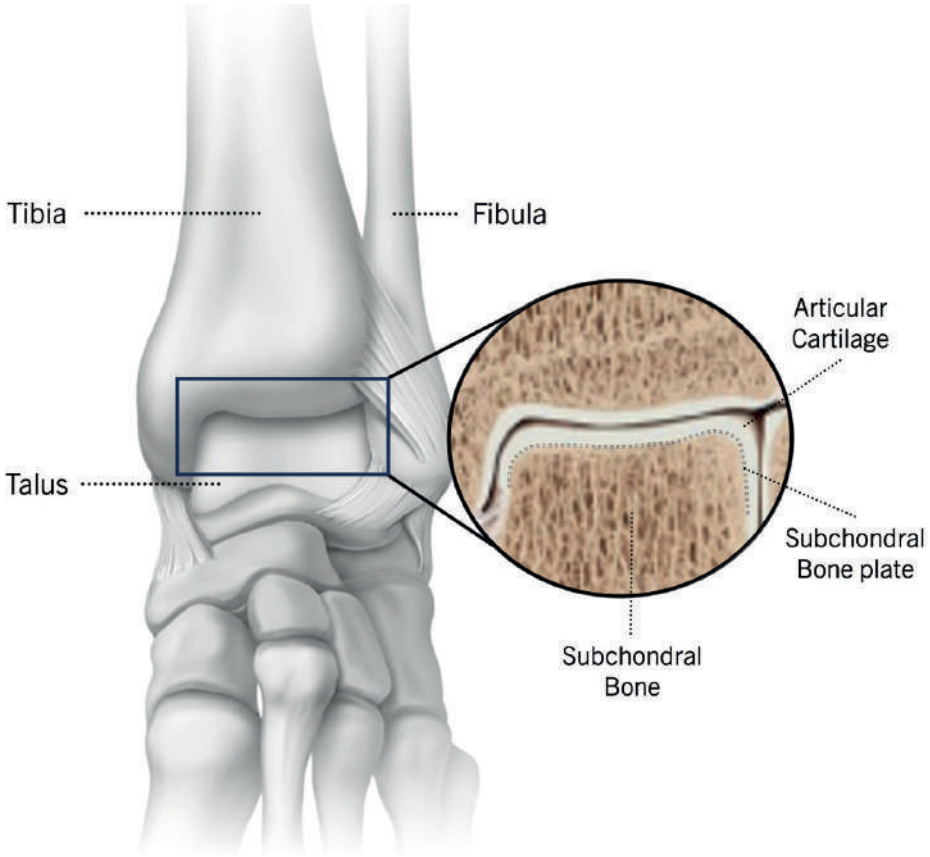

Figure 1. General anatomy of the normal ankle joint (left ankle viewed from the front) and close-up of the 'osteochondral unit' comprised of articular cartilage and subchondral bone (plate).

The primary cause of ankle OCLs is a traumatic event, such as a sprain or fracture, in up-to 70% of patients.[29,30] In such cases it is thought that the direct impact or the shearing of the talar dome into the tibial plafond causes injury to the articular cartilage and the underlying subchondral bone (Figure 2).

Such injuries can be severe (in cases of osteochondral or intra-articular fractures), considerable (cartilaginous tissue involved), or not detectable (i.e., cartilage micro-cracks). Patients typically present 6-12 months after the initial trauma, meaning there is a run-up phase before the OCL becomes clinically symptomatic, and this suggests that such lesions are not present at initial injury. Blom et al.[5] found that a single-impact load on carpine ankle joints did not cause macro- or micro-damage of the joint but did result in 'invisible injuries' which altered the whole-joint biomechanics after impact. Herein, the hypothesis of the 'cartilage-cascade' has been proposed by Dahmen et al.[17], which postulates that from the initial injury a 'cascade' of subsequent biomechanical and biochemical changes occur in the ankle joint which leads to the incremental development of an (symptomatic) OCL. An alternate theory is that of 'hydrostatic loading', which states that after initial injury to the articular cartilage synovial fluid can protrude through 'micro-cracks' of the cartilage and subchondral bone during joint loading (for example during walking), resulting in the development of an OCL.[21] Aside from the theories based on a traumatic origin of the lesions, it is thought that OCLs could have a genetic, developmental, or vascular origin. For example, in a study reporting on bilateral OLT, present in 15% of OLT patients, 1 in 3 patients was bilaterally symptomatic.[51]

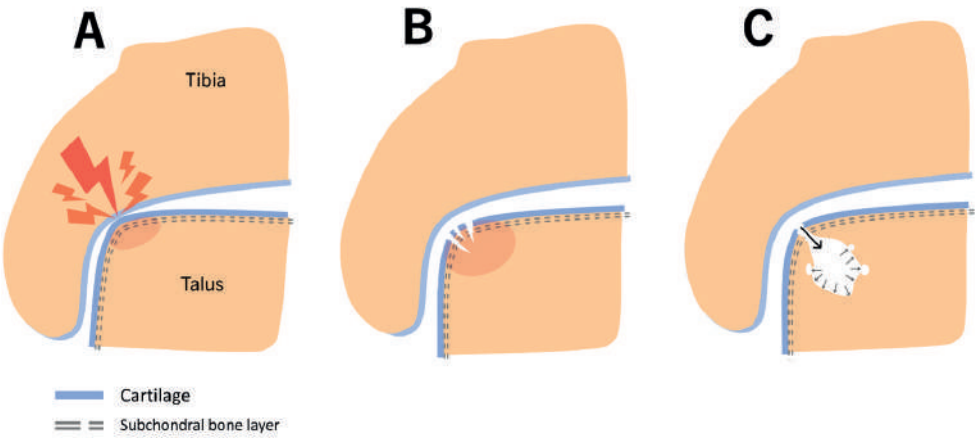

Figure 2. Schematic depiction of OCL formation on the talus due to trauma which forms after direct impact trauma between talus and tibia (a), as a result micro-crack form (b), which allow for hydrostatic loading and cyst formation (c). *Adopted from Rikken QGH, Kerkhoffs GMMJ. Osteochondral Lesions of the Talus: An Individualized Treatment Paradigm from the Amsterdam Perspective. Foot Ankle Clin. 2021;26(1):121-136 (CC BY-NC-ND 4.0).*

It is thought that a period of localized avascularity of the talar dome (such as related to trauma) or talar vascular malformations could hamper the development of the subchondral bone and/or articular cartilage during skeletal growth, resulting in a fragmentous OCL (Figure 3), commonly referred to as 'osteochondritis dissecans'.[51] Additionally, congenital factors could also play a role in these lesions.[26,28,57]

Epidemiology

Osteochondral lesions are found throughout human joints, most frequently affecting the ankle, knee, and elbow.[60] Recent studies showed that ankle OCLs are a frequent co-pathology among common ankle injuries. These systematic reviews found an OCL to be present in up-to 45% of patients which sustain an ankle fracture, 32% of patients with chronic lateral ankle instability, and 20% of patients with syndesmotic instability.[16,38,61] Even though such high rates of ankle OCL incidences are reported, the prevalence of these lesions is considered rare, with an incidence rate of 2.1 cases per 100.000 person years reported in the United States.[60] To date, it remains unknown which patients are at risk of developing a symptomatic ankle OCL. One hypothesis is that such lesions can naturally heal, or that local and non-local biological factors including biomechanics contribute in its development towards a symptomatic lesion. There is no information to-date on the 'natural' incidence of asymptomatic OCLs in the general population. As such, the clinical presentation and work-up of a patient with an OCL of the ankle is paramount for its optimal treatment.

Clinical Presentation

As previously stated, most OCLs are thought to originate from a trauma to the ankle. Patients typically present to a doctor with complaints 6 to 12 months following injury.[46] The cardinal symptom is pain, most notably deep ankle pain during activities such as walking or sports.[46] This pain may also radiate towards other areas of the ankle (referred pain). Other symptoms may include joints swelling, locking of the ankle, a sensation of instability, or a decreased range of motion.

A physical examination of the ankle should be performed when suspecting an ankle OCL.[4] This examination should also include assessment of ankle alignment, range of motion testing, neuromuscular status, balance, and instability testing. Upon specific examination for an OLT a recognizable pain may be palpated on the talus with the ankle in full plantar flexion.[46] For OLTP this is difficult to assess as the lesion may be unreachable. Additionally, grinding, clicking, locking or popping of the ankle can be observed during range of motion examination with axial load and may point to a loose body or displaced cartilaginous tissue impingement. Concomitant pathology may also be present, either congenitally (such as malalignment of the foot and ankle) or acquired through trauma, and should be assessed thoroughly. If there is a clinical

suspicion for an ankle OCL, advanced imaging with computed tomography (CT) scanning or magnetic resonance imaging (MRI) should be obtained as these hold the highest non-invasive diagnostic value.59

Radiological examination of ankle OCLs in our center is preferably performed by means of CT (Figure 3 and Figure 4), as it has been found to yield more accurate measurements of lesion dimensions.[20,62] However, MRI is of added value in cases of associated soft-tissue injuries or sole cartilaginous injuries.4 Additionally, a bilateral standing radiograph or weightbearing CT-scan can be obtained to assess malalignment of the foot and ankle. On advanced imaging the lesion morphology, size, and location are assessed.[4,20] These are important parameters on which treatment choice is largely based.[46] From the information obtained from the patient's history, physical examination, and imaging studies a patient-specific treatment plan is advised based on patient and lesion characteristics and is discussed with the patient in a shared-decision manner.[46]

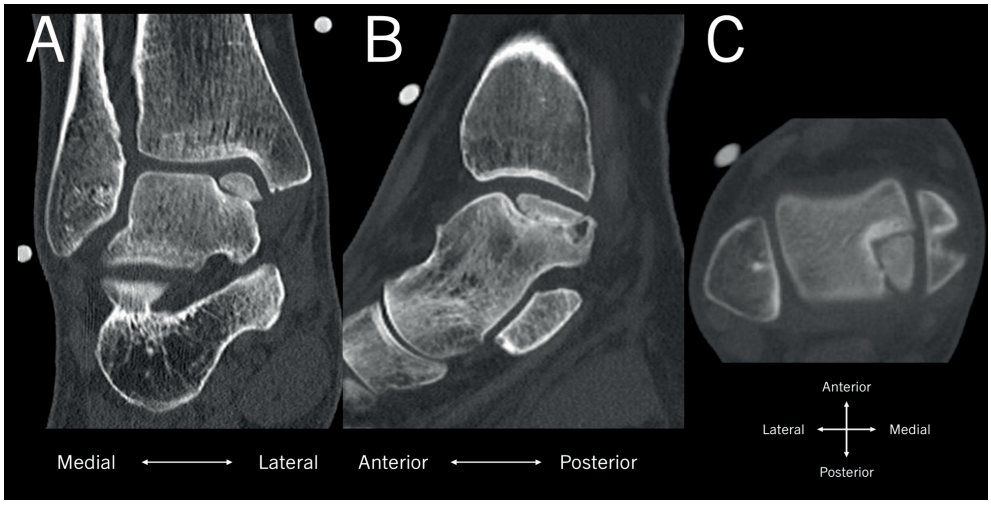

Figure 3. CT-scan of the ankle joint showing an osteochondral fragment on the posteromedial talus, as depicted from the coronal view (A), sagittal view (B), and axial view (C).

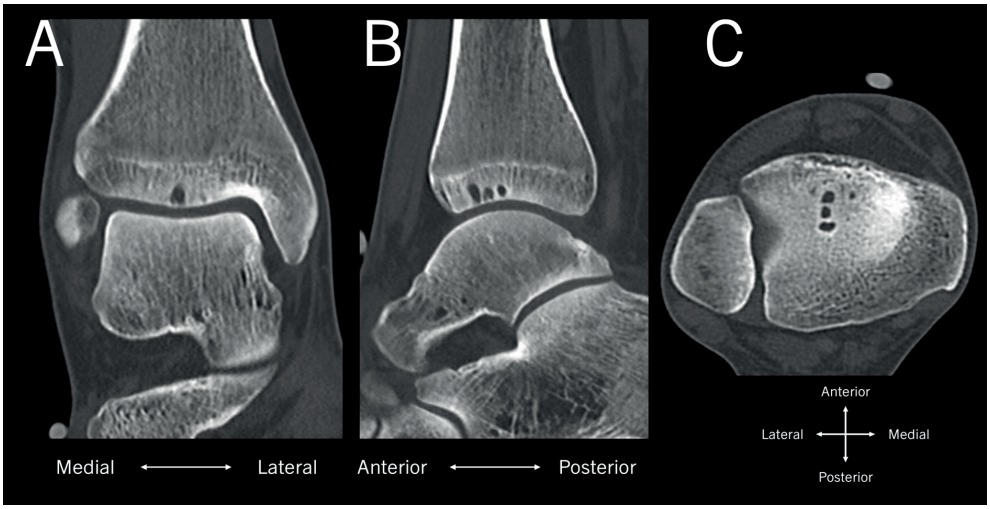

Figure 4. CT-scan of the ankle joint showing an OLTP on the anterocentral tibial plafond, as depicted from the coronal view (A), sagittal view (B), and axial view (C).

Treatment of Talar Lesions

OLT can be treated non-operatively or operatively.[6,18,37,46] Non-operative management consists of the following treatments: supervised neglect, insoles or shoe modifications, physical therapy (which includes a personalized rehabilitation program for improving muscle strength, balance, and range of motion), weight-loss and other life style recommendations, a period of non-steroid anti-inflammatory drugs (NSAIDs), or intra-articular injections.6,46 Even though non-operative treatment is known to benefit patients, up-to 55% of patients have persisting complaint, resulting in a majority of patients undergoing surgery.[6] To date, no gold-standard surgical treatment for OLT exists, while the number of treatment options has risen over the years.[18,37] The current literature for the surgical treatment of OLT can be considered of low-level evidence due to the limited number of patients per study, heterogenous samples of patients and lesions, and relatively few comparative prospective studies and randomized clinical trials (RCT).[18,37] However, a growing body of evidence shows that treatments yield reproducible results in specific sub-groups of patients.[1,3,9–12,14,25,35,41–43,46,47,54,56,63] These studies have identified prognostic factors for outcomes following surgery in OLT patients and could provide a pathway towards improving outcomes. As such, the current literature recognizes that these patient and lesion specific factors should guide treatment choice, in an individualized approach.[46] An overview of such a treatment algorithm, from the Amsterdam perspective, is provided in Figure 5.

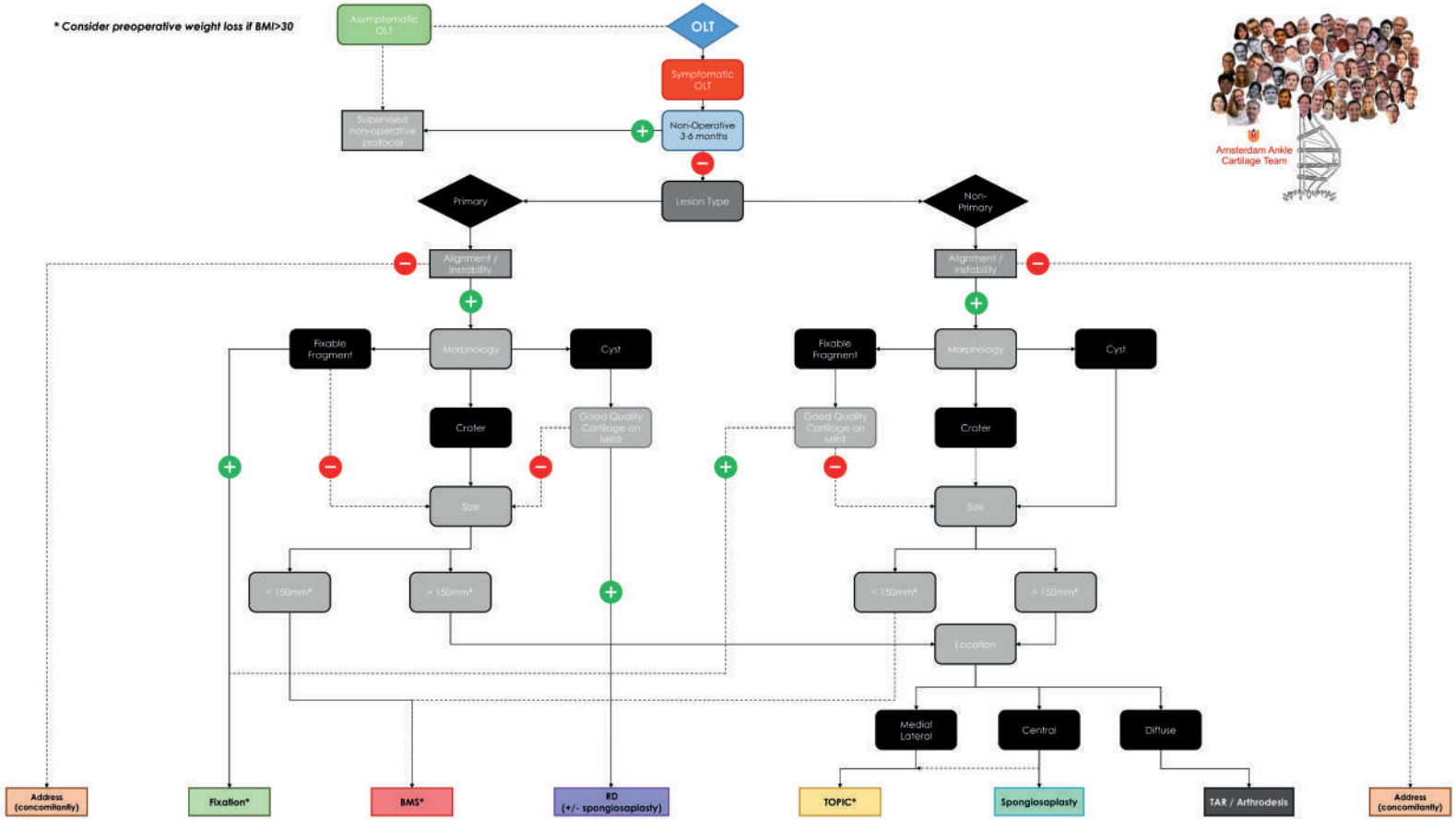

Figure 1. Flowchart of the Amsterdam Ankle Cartilage Team for the treatment of OLT. *Adopted from Pijnacker et al. Tratamiento de las lesiones osteocondrales del astrágalo mediante artroscopia anterior del tobillo Rev Esp Artrosc Cir Articul 2025;32(2):109-16, under public licence (CC BY-NC-ND 4.0)*

Rationale and Aims of this Thesis

Controversy remains on the optimal treatment algorithm for ankle OCLs, encompassing the diagnosis, treatment selection, and factors influencing treatment outcomes in these patients.[4,13,19,22,23,27,32,33,39,44,52,55] Current clinical practice consists of a treatment approach that includes patient- and lesion factors. The main goal of this thesis was to improve the evidence-based treatment algorithm for patients with an OCL of the ankle. This thesis aimed to do so by evaluating existing treatment strategies and aimed to identifying factors for patient selection. The focus of this thesis was on bone marrow stimulation and fixation for OLT, and the treatment of OLTP.

Part 2. Bone Marrow Stimulation for Osteochondral Lesions of the Talus

Bone marrow stimulation (BMS) is the most common surgical treatment for small (<150mm^2), primary, OLT.[18] The treatment provides good early to mid-term clinical results and is less costly and less technically demanding compared to other surgical options.[18,58] It is usually performed through an arthroscopic approach, which results in less morbidity compared to open procedures.[31] BMS aims to remove the defective cartilage and subchondral bone, stimulating the subchondral bone by drilling, thereby yielding a healing response of the lesion.[40] This healing response forms a fibrin clot which, with the help of mesenchymal stem cells, initiates the formation of fibrocartilage. The properties of fibrocartilage result in inferior wear characteristics compared to native cartilage.[53] This has led to the hypothesis that patients who underwent BMS are susceptible to recurrence of the OLT, the development of ankle osteoarthritis, and long-term treatment failure. To study this hypothesis, we aimed to investigate the clinical outcomes, radiological outcomes, and revision rates of patients who underwent BMS for an OLT at long-term follow-up. In Chapter 2 a systematic literature review was conducted to assess the current evidence available. Chapter 3 assessed the 10-year revision free survival rate following arthroscopic BMS in 262 patients and evaluated the influence of baseline patient and lesion characteristics on survival.

Another controversy regarding BMS is whether patients can benefit from repeating the surgery.[27] The current evidence is poor and shows mixed results, while selecting the right patients for such a procedure could lower costs and shield patients from more invasive surgery.[1,15] Chapter 4 and Chapter 5 evaluate the outcomes of patients who underwent BMS for an OLT that failed prior surgical treatment and compared these to patients who underwent BMS for the first time.

Part 3. Fixation for Osteochondral Lesions of the Talus

One specific lesion morphology is the OLT with an osteochondral fragment (Figure 3), which may result from trauma or could be developmental in origin.[50,51] Such osteochondral fragments are amendable for fixation if they are symptomatic.[44,50] The theoretical benefits of fixation are the retainment of the native hyaline cartilage, immediate stabilization of the fragment, and restoration of the joint congruency.[50] Clinically, an advantage is that other surgical options remain available if fixation fails. The outcomes of fixation are reported to be excellent, with 9 out of 10 patients achieving union of the fixed fragment.[45] In 2016, Kerkhoffs et al.[34] proposed the Lift-Drill-Fill-Fix (LDFF) technique, which aims to add a high-quality subchondral bone repair in chronic lesions, and as such can be seen as an intra-articular non-union repair. The LDFF procedure can be performed through an open or arthroscopic approach.[34,49] The safety and outcomes of open LDFF remain to be studied, while the arthroscopic LDFF has shown excellent early and mid-term results, but no long-term outcomes have been studied.[34,36] This thesis therefore aimed to fill these research gaps. Chapter 6 describes the surgical technique of the open LDFF procedure, and Chapter 7 reports its prospective 2-year clinical and radiological results. Chapter 8 assesses the long-term results of arthroscopic LDFF.

Part 4. Management of Osteochondral Lesions of the Tibial Plafond

OLTP are considered rare as only 1 occurs for every 14 to 24 OLT.[7,24] Their lower incidence is thought to be due to the stronger cartilage of the tibial plafond and larger surface area compared to the talus, which makes tibial cartilage less susceptible to injury.[2] Treatment strategies for OLTP currently lack patient- and lesion factors to guide management, and the treatment strategies are by and large copied from talar lesions.[48] The management of OLTP is therefore an open question, with outcomes reported in small and low-evidence case-series, without any evidence on non-operative treatment.[8,13,48] This clear lack of evidence leads us to come up with the first steps towards an evidence-based treatment approach for OLTP in order to improve outcomes for our patients.[13]

In Chapter 9 the current evidence in the literature for the treatment of OLTP was summarized. Chapter 10 explores the 2-year safety and patient-reported efficacy of non-operative treatment for OLTP in a prospective cohort. Chapter 11 assesses the clinical outcomes of a retrospective patient cohort that underwent arthroscopic BMS, at mid- to long-term follow-up. Chapter 12 describes a novel surgical technique for medial and central OLTP which might benefit from an osteotomy of the distal tibia and bone grafting of the lesion.

In Part 5 the findings of this thesis will be discussed and compared to the literature. The discussion section aims to provide clinical recommendation and visualizes these recommendations in a treatment algorithm flow-chart.

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Part 2

Bone Marrow Stimulation for Osteochondral Lesions of the Talus

Chapter 2

Satisfactory Long-Term Clinical Outcomes after Bone Marrow Stimulation of Osteochondral Lesions of the Talus

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Abstract

Purpose: The purpose of the present study was to evaluate the clinical and radiological outcomes of arthroscopic bone marrow stimulation (BMS) for the treatment of osteochondral lesions of the talus (OLTs) at long-term follow-up.

Methods: A literature search was conducted from the earliest record until March 2021 to identify studies published using the PubMed, EMBASE (Ovid), and Cochrane Library databases. Clinical studies reporting on arthroscopic BMS for OLTs at a minimum of 8-years follow-up were included. The review was performed according to the PRISMA guidelines. Two authors independently conducted the article selection and conducted the quality assessment using the Methodological index for Non-randomized Studies (MINORS). The primary outcome was defined as clinical outcomes consisting of pain scores and patient-reported outcome measures. Secondary outcomes concerned the return to sport rate, reoperation rate, complication rate, and the rate of progression of degenerative changes within the tibiotalar joint as a measure of ankle osteoarthritis. Associated 95% confidence intervals (95%-CI) were calculated based on the primary and secondary outcome measures.

Results: Six studies with a total of 323 ankles (310 patients) were included at a mean pooled follow-up of 13.0 (9.5 – 13.9) years. The mean MINORS score of the included studies was 7.7 out of 16 points (range: 6 – 9), indicating a low to moderate quality. The mean postoperative pooled American Orthopaedic Foot & Ankle Society (AOFAS) score was 83.8 (95%-CI: 83.6-84.1). 78% (95%-CI: 69.5 – 86.8) participated in sports (at any level) at final follow-up. Return to preinjury level of sports was not reported. Reoperations were performed in 6.9% (95%-CI: 4.1 – 9.7) of ankles and complications related to the BMS procedure were observed in 2% (95%-CI: 0.4 – 3.0) of ankles. Progression of degenerative changes was observed in 28% (95%-CI: 22.3 – 33.2) of ankles.

Conclusion: Long-term clinical outcomes following arthroscopic BMS can be considered satisfactory even though one in three patients show progression of degenerative changes from a radiological perspective. These findings indicate that OLTs treated with BMS may be at risk of progressing towards end-stage ankle osteoarthritis over time in light of the incremental cartilage damage cascade. The findings of this study can aid clinicians and patients with the shared decision-making process when considering the long-term outcomes of BMS.

Keywords: OLT; Osteochondral; Bone Marrow Stimulation; Talus; Long-term

Introduction

Osteochondral lesions of the talus (OLTs) are characterized by damage to the articular cartilage and the underlying subchondral bone. Patients typically present with pain during or after weightbearing 6 to 12 months after trauma, such as an ankle sprain or ankle fracture.[31] Initial treatment generally consists of non-operative management. Non-operative treatment fails in up to 55% of patients with symptomatic OLTs.[41] Operative treatment is therefore needed to address symptoms in the majority of these cases.

Operative management depends on lesion characteristics and patient preference in the context of shared-decision making.[16,31] Arthroscopic bone marrow stimulation (BMS) is the most commonly performed first-line operative treatment for OLTs, and should ideally be considered for smaller (<150mm^2) lesions.[8,29] During BMS, the damaged cartilage is removed and the subchondral bone plate debrided, after which microfracturing can be performed. The goal of BMS is to initiate the formation of fibrocartilage by the release of mesenchymal stem cells and local growth factors.[24] Multiple literature studies have found that short- to mid-term outcomes of BMS could be considered acceptable and show relatively consistent clinical outcomes over time.[8,39] However, there are conflicting outcomes of BMS concerning the clinical efficacy and clinical sustainability at long-term follow-up. The inferior quality and biomechanical properties of fibrocartilage, rather than the native hyaline cartilage, and poor subchondral bone health have been mentioned as possible reasons for the progression of osteoarthritic changes and subsequent deterioration of clinical results over time.[21,30,33] However, it is currently unknown on a larger group level what the long-term clinical and radiological outcomes are of arthroscopic BMS as no synthesis of the current clinical evidence nor consensus regarding its clinical efficacy exists.

It is therefore the purpose of the present study to assess the clinical and radiological outcomes of BMS for the treatment of OLTs at long-term follow-up. The findings of this study can improve guidance for clinicians as well as patients during the shared-decision making process.

Methods

A systematic review of the literature was conducted. The methodology of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) was followed for the conception of this study.[20]

Search Strategy

The PubMed, EMBASE (Ovid), and Cochrane Library databases were searched for eligible articles. Studies from the earliest record until March 2021 were retrieved.

Backwards citation chaining (i.e., reference screening) was applied during full-text screening. The full search strategy is available in the Appendix.

Eligibility Criteria and Study Selection

All studies reporting clinical outcomes of arthroscopic BMS (i.e., debridement and/or microfracturing) for OLTs at long-term follow-up were included. The inclusion and exclusion criteria are listed in Table 1. The definition of short- to long-term follow-up is subjective in clinical research, as the cut-offs vary throughout the literature.[11,18,26,27,39] Defining a cut-off for "long-term" follow-up depends on the pathology, treatment, and patient population.[1] Long-term follow-up was therefore defined as a minimum of 8-years in the present study, as previously reported in the literature.[4] Two authors (Q.R. and J.D.) independently conducted the title and abstract screening, as well as the full-text screening, using Rayyan.[25] When no consensus on inclusion could be reached, the senior author (G.K.) was decisive.

Table 1. Inclusion- and Exclusion Criteria

Inclusion Criteria	Exclusion Criteria
- Clinical studies reporting outcomes of arthroscopic BMS (debridement and/or microfracturing) for OLTs	- Less than five patients - No separate data for arthroscopic BMS patients available
- Minimum of 8-years follow-up	- Review-, cadaver-, and animal studies
- Level I-IV peer-reviewed studies	- Patient overlap
- Full-text articles available in English	- Asymptomatic lesions - Level V evidence

Methodological Quality

The Methodological Index for Non-Randomized Studies (MINORS) criteria were used to evaluate the methodological quality of the included studies.34 Assessment of methodological quality was performed by two independent reviewers (Q.R. and J.D.). In case of disagreement, the senior author (G.K.) was decisive.

Data Extraction

Data extraction was performed by two independent reviewers (Q.R. and J.D.) using a pre-designed extraction form. Data was extracted for study characteristics (author, publication date, level of evidence, and number of patients and ankles), patient characteristics (patient age, gender, body mass index (BMI), history of trauma, duration of symptoms, follow-up time, and BMS technique (i.e., debridement or, debridement with microfracturing or drilling)), and lesion characteristics (size, lesion location, presence of cysts, and primary nature - i.e., first time surgical treatment). Additionally, clinical- and radiological outcomes at baseline and at follow-up were extracted. As part of the clinical outcomes, return to sport was defined according to Ardern et al.[2] as return to any level of sports and return to preinjury level of sports.

If lesion location was reported according to a 9-grid scheme,[28] localization was categorized according to the following distribution: medial (zone 1, zone 4, and zone 7), central(zone 2, zone 5, and zone 8), or lateral (zone 3, zone 6, and zone 9) location. To assess signs of postoperative ankle osteoarthritis within the tibiotalar joint, a modified classification system was used, in which the Takakura et al.[38] and van Dijk et al.[9] classifications were pooled (see Table 2). The degenerative progression rate was defined as the proportion of patients who progressed with a minimum of one stage of the aforementioned modified classification system (e.g., grade 0 to grade 1 and/or grade 1 to grade 2 or higher).

Table 2. Modified Classification of Degenerative Changes in the Tibiotalar Joint

Grade	Classification	
	Takakura[38]	**van Dijk**[9]
Grade 0	*undefined*	Normal joint or subchondral sclerosis (van Dijk grade 0)
Grade 1	No joint-space narrowing but early sclerosis and osteophyte formation (Takakura grade 1)	Osteophytes without joint space narrowing (van Dijk grade 1)
Grade 2	Narrowing of the joint space medially (Takakura grade 2)	Joint space narrowing with or without osteophytes (van Dijk grade 2)
Grade 3	Obliteration of the joint space with subchondral bone contact medially (Takakura grade 3) and, Obliteration of the whole joint space with complete bone contact (Takakura grade 4)	(Sub)total disappearance or deformation of the joint space (van Dijk grade 3)

Statistical Analysis

The primary outcome was defined as clinical outcome measures consisting of pain scores, patient-reported clinical outcome measures, or physician reported clinical outcome measures. Secondary outcomes concerned the return to sport rate, reoperation rate, complication rate, and the rate of progression of degenerative changes within the tibiotalar joint. Descriptive variables were displayed as means with ranges for continuous variables and absolute numbers and frequencies for categorical variables. Due to the limited number of comparative studies and between study heterogeneity, a formal meta-analysis could not be performed. A simplified pooling method was therefore used to pool baseline characteristics and clinical outcome scores, whereby pooled means and proportions were weighted by the number of ankles per study. 95% Confidence intervals (95%-CI) were calculated for pooled clinical outcome scores. 95%-CI were additionally calculated using the Wilson score method (without continuity correction) for the return to sport rate, reoperation rate, complications rate, and the degenerative progression rate. Ranges from the reported pooled means and proportions include the lowest and highest mean values from the

included studies. Time units were converted to either weeks or months depending on the variable analysed. Lesion area was calculated in squared millimetres (mm^2). If lesion diameter was reported, lesion size was converted into surface area using the following formula: Area lesion= $\pi \times ((\text{lesion diameter})/2)^2$. Data analysis was performed in Stata 15 (StataCorp LP, College Station, TX).

Results

A total of 2,169 records were found trough the literature search, of which six studies were included for final analysis (see figure 1).[3,4,7,17,27,32] Consensus was reached for all included articles. There were two prospective cohort studies[27,32] and four retrospective

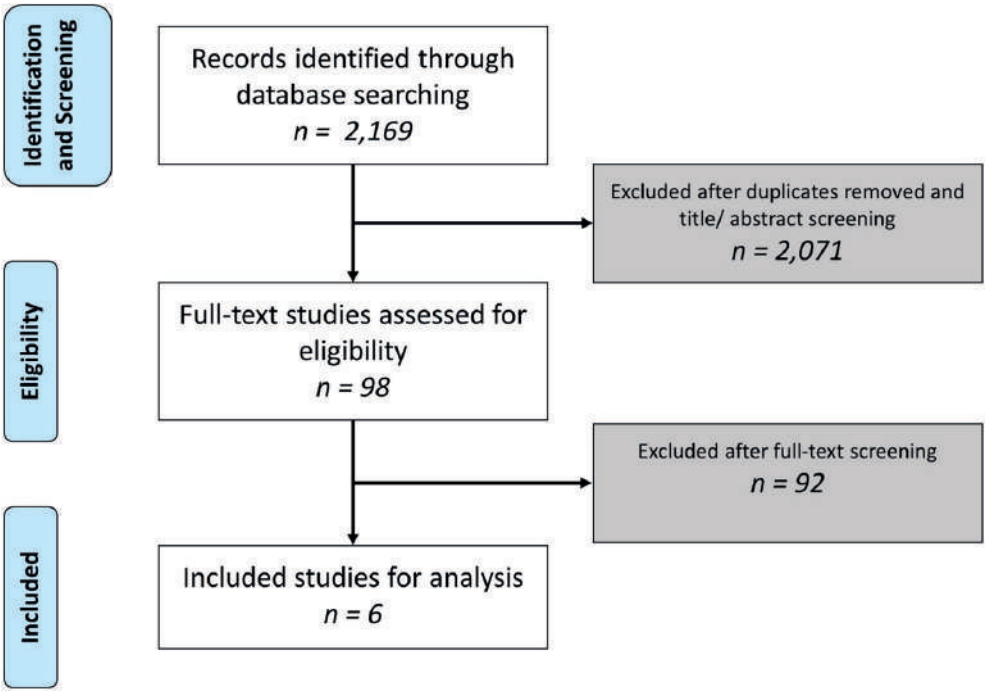

Figure 1. PRISMA flowchart of the study selection.

Methodological Quality

Consensus was reached on the MINORS score for all included articles. The average MINORS score of the included studies was 7.7 points out of 16 (range: 6 – 9). The MINORS score per individual study can be appreciated in the Appendix.

Patient- and Lesion Characteristics

From the six included studies, outcomes for a total of 310 patients (323 ankles) were reported. A full overview of the pooled baseline patient and lesion characteristics can be appreciated in Table 3.

Table 3. Baseline Patient- and Lesion Characteristics†

Patient Characteristics		*Percentage Reported**
Patients, n	310	100%
Ankles, n	323	100%
Sex, males/females, %	65% / 35%	100%
Age, years (range)	37.0 (24.7 – 39.2)	100%
Body mass index, kg/m^2 (range)	24.7 (24.3 – 26.4)	69%
History of trauma, %	60%	86%
Duration of symptoms, months (range)	10.2 (17.0 – 28.1)	84%
Follow-up, years (range)	13.0 (9.5 – 13.9)	100%
Method of BMS, n (%) - Debridement and microfracturing or drilling - Debridement alone	 312 (97%) 11 (3%)	100%
Lesion Characteristics, n (%)		
Primary, %	96%	94%
Non-primary, %	4%	94%
Presence of cyst, n (%)	24%	63%
Lesion Size		
Area, mm^2 (range)	100.1 (74.2 – 105.3)	78%
> 150 mm^2 *< 150 mm^2*	21% 79%	63%
Depth, mm (range)	7.1 (NA)	15%
Lesion Location, n (%)		
Medial	229 (71%)	99%
Central	10 (3%)	99%
Lateral	83 (26%)	99%

† Data are presented as weighted means (range of means) and percentages.
*Percentage frequency of reporting by number of ankles.
Abbreviations. n: number, BMS: bone marrow stimulation, mm: millimetre.

Clinical Outcomes

A complete overview of the clinical outcomes from the included studies is provided in Table 4. The weighted mean postoperative American Orthopaedic Foot & Ankle Society (AOFAS) score for 252 cases was 83.8 out of 100 points (95%-CI: 83.6 – 84.1). Return to sport was reported in two studies.[4,7] 68 out of 87 reported patients (78%, 95%-CI: 69.5 – 86.8) returned to any level of sports at follow-up. No specific outcomes on preinjury level of sports return were reported in any of the included studies.

Table 4. Postoperative Clinical Outcomes

Author, Year	Ankles (n)	Follow-Up (years)	Ogilvie-Harris	Berndt & Harty	AOFAS
Baker et al. 1999	12	11.8	NA	Excellent: 5, Good: 5, Fair: 1, Poor: 1	NA
van Bergen et al. 2013	50	10.1	Good: 37, Fair: 10, Poor: 3	Excellent: 10, Good: 29, Fair: 11, Poor: 0	88.0 (range: 64.0 - 100)
Corr et al. 2021	45	11.6	NA		NA
Hunt et al. 2003	8	11.8	NA	Good: 4, Fair: 4, Poor: 0	NA
Park et al. 2021	202	13.9	NA	NA	Preop: 58.2 (± 13.6) Postop: 82.8 (± 11.7)
Schuman et al. 2002	6	9.5	Excellent: 1, Good: 4, Fair: 1, Poor: 0	NA	NA

Abbreviations: n: number of ankles, NA: not available, AOFAS: American Orthopaedic Foot & Ankle Society score, VAS: Visual Analogue Scale, FAOS: Foot and Ankle Outcome Score, SF-36: Short-Form 36 questionnaire, FAAM-ADL: Foot And Ankle Mobility measure - Activities of Daily Living, FAAM-Sports: Foot And Ankle Mobility measure - sports, SANE: Single Assessment Numeric Evaluation (SANE) question, ADL: Activities of Daily Living, QoL: Quality of Life

VAS-Pain	FOAS	Other
NA	NA	NA
NA	NA	SF-36: Vitality component: 71.0 (± 16.0) Emotional component 94.0 (± 22.0)
14.0 out of 100 (range: 0-75.0)	NA	FAAM-ADL: 90.3 (range: 31.0-100) FAAM-Sports: 82.0 (range: 12.5-100)
NA	NA	Martin score: Good: 4, Fair: 1, Poor: 3 SANE score: Excellent: 2, Good: 3, Fair: 2, Poor: 1
Preop: 7.1 out of 10 (±1.7) Postop: 1.99 out of 10 (±1.7)	Pain: 83.0 (± 14) Symptoms: 82.0 (± 14.6) ADL: 83.5 (± 11) Sports: 79.3 (± 11.6) QoL: 78.7 (± 12.4)	NA
NA	NA	NA

Reoperations and Complications

Reoperations for OLTs were reported in five studies.[3,4,7,17,27] for a total of 317 patients. At final follow-up, 22 ankles required revision surgery (6.9%, 95%-CI: 4.1 – 9.7). Reoperations following BMS consisted of repeat BMS (n = 12), autologous osteochondral transplantation (n = 6), and total ankle arthroplasty (n = 1). The specific type of surgical re-operation was not reported for three patients.

Complications related to the BMS procedure were reported for 260 cases in a total of three studies.[4,17,27] Among the reported group of cases four complications were observed (2%, 95%-CI: 0.4 – 3.0), all the complications were due to neurological complications related to arthroscopy.

Radiological Outcomes

Three studies reported radiological outcomes at final follow-up.[4,27,32] All studies assessed postoperative degenerative changes within the tibiotalar joint using radiographs. Two studies[4,32] used the van Dijk score[9] and one study[27] reported the Takakura score.[38] From the 256 ankles assessed at final follow-up, the following osteoarthritic stages were reported: grade 0 in 168 ankles (66%), grade 1 in 77 ankles (30%), grade 2 in 8 ankles (3%), grade 3 in 1 ankle (1%). Progression of degenerative changes was reported for 71 out of 256 ankles, with a corresponding degenerative progression rate of 28% (95%-CI: 22.3 – 33.2).

Discussion

The most important finding of the present study is that long-term clinical outcomes of arthroscopic BMS for primarily smaller (<150mm^2) lesions are satisfactory. This important outcome is necessary to evaluate in the light of limited data due to heterogenous reporting of data and low level-of-evidence. Progression of degenerative changes was found in approximately one out of three patients.

Clinical outcomes of BMS for OLTs have been reported to be good to excellent at short- to mid-term follow-up.[8,39] Toale et al.[39] - who reviewed the literature on clinical outcomes of 858 ankles treated with BMS for primary OLTs at mid-term follow-up - found that clinical outcomes remain adequate. The aforementioned study reported a pooled AOFAS score of 89.9 points and a reoperation rate of 6% at a mean 6 years follow-up. Previously, no specific study had pooled evidence for long-term clinical outcomes of BMS. When comparing the clinical results of the present study to the findings of Toale et al.[39], a slight decrease in AOFAS score though comparable revision rate can be observed. The rationale for specifically investigating outcomes at long-term follow-up lies in the hypothesis that BMS may not be a sustainable treatment option for all OLTs.[4,11,22,39] This may be due to the development of degenerative changes within the repair tissue and tibiotalar joint.[4,22,39] A number of reasons for

the degeneration of repair tissue after BMS and consecutive clinical failure have been proposed in the literature. Firstly, it is known that lesion filling by fibrocartilage shows inferior wear characteristics compared to the native hyaline cartilage.[15,23] Fibrocartilage predominantly consists of type-1 collagen which is biomechanically inferior to type-2 collagen that is primarily expressed in hyaline cartilage.[23] This hypothesis may be substantiated by findings from second-look arthroscopy, which show a poor quality of the cartilage repair tissue.[19] Secondly, fibrocartilage may not be able to sufficiently protect the underlying subchondral bone, which is an important structure for cartilage health and the load-bearing capacity of the talus, and thus plays an important role in the development of osteoarthritis.[22,37] Reilingh et al.[30] found that 74% of patients show a depressed subchondral bone plate at one-year after the initial surgery. Moreover, Shimozono et al.[33] found that the subchondral bone degradation is associated with lower clinical outcomes after BMS at mid-term follow-up. These findings drive the hypothesis that repair tissue degradation and osteoarthritis formation play an important role in deteriorating clinical outcomes. When assessing the incidence of degenerative changes as a measure for ankle osteoarthritis in the present study, one in three patients were found to show radiographic degenerative changes at final follow-up. However, it should be mentioned that the majority of these patients showed osteophyte formation or minimal degenerative changes, and a limited proportion of patients presented with joint space narrowing and/or total joint obliteration (i.e., late-stage ankle osteoarthritis). Caution should be warranted for the interpretation of these findings as this study concerns a low number of patients. The findings of degenerative changes observed in the present study concur with previous studies on long-term outcomes of OLT treatment in which a high rate of early-stage degenerative changes were observed but a low proportion of patients was found to have end-stage ankle osteoarthritis.[10,12,40] When examining long-term outcomes of cartilage lesions in the knee, a high degree of patients is observed to develop osteoarthritis after sustaining a cartilage lesion and undergoing BMS.[13,14,35] The progression of degenerative changes in the knee is associated with poor clinical outcomes following BMS.[13,14]

Inferior wear characteristics of talar fibrocartilage and poor subchondral bone health may be exacerbated by an increased lesion size.[22] It has been well established that lesion size is an important factor for the clinical success of BMS in OLT treatment. Current evidence from clinical studies shows that the optimal cut-off for clinical outcomes after BMS is between 110mm2 and 150mm2 (10mm to 15mm diameter).[5,6,29] When specifically considering this in the context of long-term follow-up as assessed in the present study, it becomes clear that 160 out of 202 (79%) available patients were reported to have an OLT smaller than 150mm^2. These data were available for a single study, by Park et al.[27] The aforementioned study reported that a lesion size area of ≥ 150mm^2 and a BMI of ≥ 25 was associated with a significantly higher reoperation rate

for the 12 (out of 202) failed procedures. In contrast, van Bergen et al.[4] and Corr et al.[7] did not find a significant association between lesion size and clinical outcomes. This may be attributable to the lower number of patients included in both studies. The findings of the present study show large long-term (prognostic) database studies are highly needed to elucidate the influence of prognostic factors such as lesion size on the survivability of BMS procedures.

When assessing the sports participation rate of patients included in the present study it is important to note that no return to sport participation level (i.e., return to preinjury- or any level of sports[36]) nor preinjury level of sports (i.e., recreational, competitive, or professional athlete) was reported. All patients were therefore classified as having returned to any level of sports. Lambers et al.[18] found that 90% of patients participated at any level of sports after BMS at a mean 6.4 years follow-up. However, it was noted in the aforementioned study that 53% of patients were able to return to their preinjury level of sports. Steman et al.[36] observed that patients treated with BMS were able to return to any level of sports in 88% of the cases and to a pre-injury level of sports in 79% of the cases. It may therefore be the case that sports participation after BMS decreases over time, especially when considering preinjury level of sports. However, the results of the present study are limited to a low number of cases and are at risk of bias. More research on long-term sports participation after BMS is therefore highly necessary. It is crucial that future studies report sport outcomes based on the level of preinjury and any level of sport participation. These outcomes are of importance for assessing the long-term effects of any OLT treatment and for the shared-decision making between physicians and patients.

The present study is not without its limitations. First, the included articles were of low-level of evidence. Additionally, a limited number of patients were available for analysis and data was heterogeneously reported. Moreover, the study by Park et al.[27] made up the majority of included patients assessed from the included studies, which could introduce bias. Due to the underreporting and heterogenous reporting of outcomes it was challenging to pool clinical outcomes. The only clinical outcome which could be pooled was the AOFAS score. The AOFAS score is however regarded as a subjective scoring system and is not validated for the use in patients with an OLT. Future studies should therefore focus on including validated clinical outcome measures. Secondly, the present study included both primary and non-primary lesions as well as differing lesion morphologies (i.e., lesion area, lesion depth, and the presence of cysts which could affect outcomes and introduce bias. The outcomes of the present study therefore concern a heterogenous patient group, and caution is warranted when interpreting the findings of this study. A strength of the present study was that the presence of degenerative changes in the tibiotalar joint was assessed

prospectively in all available studies.[4,27,32] It is highly necessary to prospectively follow-up patients at predetermined time points in order to increase the level of evidence for BMS outcomes at long-term follow-up and optimize the treatment indication.

The clinical relevance of this study concerns the clinical and practical summary of current available evidence for BMS and the conclusion that BMS yields satisfactory clinical outcomes at long-term follow-up. The findings of the study can aid clinicians and patients in the shared decision-making process when considering the long-term outcomes of BMS in the context of an individualized treatment plan. Another clinical application of the present study is the identification of a clear research gap within OLT treatment and recommendations for future research concerning the long-term clinical outcomes of BMS.

Conclusion

Long-term clinical outcomes following arthroscopic BMS can be considered satisfactory even though one in three patients show progression of degenerative changes from a radiological perspective. These findings indicate that OLTs treated with BMS may be at risk of progressing towards end-stage ankle osteoarthritis over time in light of the incremental cartilage damage cascade. The findings of this study can aid clinicians and patients with the shared decision-making process when considering the long-term outcomes of BMS.

Appendix

The appendix information can be accessed at: https://doi.org/10.1007/s00167-021-06630-8

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Chapter 3

Ten-Year Survival Rate of 82% in 262 Cases of Arthroscopic Bone Marrow Stimulation for Osteochondral Lesions of the Talus

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Abstract

Background: The long-term sustainability of arthroscopic bone marrow stimulation (BMS) for osteochondral lesions of the talus (OLT) remains a matter of debate. The primary aim of the present study was to assess the 10-year survival free from revision in ankles that had undergone arthroscopic BMS for an OLT. The secondary aim was to evaluate the influence of baseline patient and lesion characteristics on survival.

Methods: Patients who underwent arthroscopic BMS for a symptomatic OLT and had a minimum follow-up of 10 years were included to assess procedure survival. The primary outcome, the 10-year cumulative survival rate, was analyzed by the Kaplan-Meier survival method. Secondary outcomes were the median time to revision and the effects of baseline factors (lesion size, primary or non-primary lesion type, preoperative cysts, and obesity as defined by a body mass index [BMI] of ≥30 kg/m2) on survival, analyzed with a Cox regression model and reported using hazard ratios (HRs).

Results: The 262 included patients had a mean follow-up of 15.3 ± 4.8 years. The 10-year cumulative survival rate of the arthroscopic BMS procedures was 82% (95% confidence interval [CI]: 77% to 87%). At 15 years of follow-up, the cumulative survival rate was 82% (95% CI: 76% to 86%). The median time to revision was 2.4 years (interquartile range: 1.3 to 5.1 years). Of the baseline factors, obesity (HR: 3.0 [95% CI: 1.44 to 6.43], $p < 0.01$) was associated with decreased survival. Lesion size (HR: 0.9 [95% CI: 0.5 to 1.8], $p = 0.8$), non-primary lesion type (HR: 1.8 [95% CI: 0.9 to 3.4], $p = 0.1$), and the presence of preoperative cysts (HR: 1.0 [95% CI: 0.6 to 1.9], $p = 0.9$) were not significantly associated with survival.

Conclusion: At a minimum follow-up of 10 years, the survival rate of arthroscopic BMS for OLT was 82%. At 15 and 20 years of follow-up, survival appeared to remain stable. Obesity (BMI ≥ 30 kg/m2) was associated with a higher likelihood of revision surgery. This risk factor should be incorporated into the treatment algorithm for OLT when counseling patients regarding surgery.

Introduction

Osteochondral lesions of the talus (OLT) are lesions of the articular cartilage and the underlying subchondral bone. Symptomatic OLT typically result in pain and can be debilitating for patients, especially for those involved in physical activities and sports. Up to 75% of OLT are the sequelae of trauma, such as a sprain or fracture, and the lesions may initiate the cascade toward end-stage ankle osteoarthritis.[11,18,43]

Nonoperative treatment is the first-line treatment for OLT, but it fails in up to 55% of patients, meaning that the majority of patients require surgical treatment.[6,15] In smaller (<150 mm^2) primary lesions, the preferred surgical treatment for OLT to date is arthroscopic bone marrow stimulation (BMS).[12,17] The advantages of arthroscopic BMS over other treatments are its relative minimal invasiveness, low cost, technical feasibility, and wider availability in less-resourced health-care systems.[17,34] Moreover, arthroscopic BMS has shown good and reliable results up to mid-term follow-up.[23,41] There is a concern in the literature, however, that clinical results may deteriorate and/or ankle osteoarthritis may progress over time because biomechanically inferior fibrocartilage is formed after BMS.[5,23,25,26,35] This may result in recurrent symptoms and the need for subsequent revision surgery.[24]

The current literature on long-term outcomes following BMS for OLT can be considered limited.[35] As such, the long-term sustainability of BMS for OLT, with a specific focus on survival outcomes, is understudied and there is sparse evidence on baseline patient and lesion factors that may influence long-term survival free from revision.35 The primary aim of the present study was therefore to assess the 10-year survival following arthroscopic BMS for OLT. The secondary aims were to evaluate the median time to revision and the influence of baseline patient and lesion characteristics on survival. These outcomes are of critical importance for patients and physicians during patient counseling and shared decision-making, and could aid in optimizing patient outcomes.[24,30]

Methods

This was a single-center retrospective cohort study. Our institution is an academic tertiary referral hospital that specializes and is (inter)nationally accredited in the treatment of ankle cartilage injuries. This study was approved by the institutional review board (MEC 08/326) and performed in accordance with the Declaration of Helsinki.

Patient Selection

All patients who underwent arthroscopic BMS for a symptomatic OLT and had a minimum of 10 years of follow-up (i.e., were treated before January 2013) were

eligible for inclusion. BMS was defined as arthroscopic debridement with or without microfracture. Patients who underwent treatment had a symptomatic OLT with pain and/or associated clinical symptoms (swelling, locking, etc.) and failure of initial nonoperative management.[34] BMS was performed in accordance with previously published techniques.[13,33] Patients were identified, according to the inclusion and exclusion criteria, from an existing historical database of patients with a computed tomography (CT)-confirmed OLT.[36] After patients were identified, they were contacted by phone for their participation in the study. If patients could not be reached by phone, 2 subsequent emails and/or letters were sent. If no response was received or if the patient had died, they were considered lost to follow-up (i.e., nonresponders). The exclusion criteria are outlined in Table 1.

Table 1. Exclusion Criteria

Exclusion criteria
- Revision surgery due to postoperative infection related to the index procedure, requiring surgical debridement of the ankle
- No preoperative CT scan or MRI available
- Coexisting osteochondral lesion of the tibial plafond (OLTP) on preoperative CT or MRI
- Preoperative advanced tibiotalar joint osteoarthritis, defined as severe joint-space narrowing or Kellgren-Lawrence grade ≥3
- Objection to study participation

Outcome Measures

The primary outcome of this study was the 10-year cumulative survival rate, defined as the proportion of ankles that had not undergone revision surgery at 10 years after the index procedure. The index procedure in patients with multiple arthroscopic BMS procedures was defined as the procedure that had the longest follow-up at our institution. Revision surgery was defined in accordance with the definition established by the International Consensus Meeting on Cartilage Repair of the Ankle.[24] More specifically, the present study defined revision surgery as any surgical procedure for a recurrent OLT after the index procedure, according to the OLT treatment categories defined by Dahmen et al.[12], or tibiotalar joint arthrodesis, total ankle replacement, amputation, or ankle realignment surgery.

The secondary outcomes of this study were the time to revision, 15 and 20-year revision rates, and associations of predictive baseline patient and lesion factors with revision surgery. According to the statistical principles of survival analysis, a 10:1 ratio of the number of failures to the number of predictive baseline factors was considered acceptable.[28] Therefore, before the start of the study, a hierarchy of possible dichotomous predictive factors was defined according to the current evidence-based literature in order to determine which factors were to be analyzed.[2,8,10,16,21,22,27,32]

The following hierarchy was established: (1) lesion size (≤100 versus >100 mm^2), (2) a primary versus non-primary lesion (i.e., following failed primary surgery), (3) the presence versus absence of subchondral cysts on preoperative imaging, (4) a body mass index (BMI) of ≥30 versus <30 kg/m^2, and (5) sex.

Data collection

Baseline patient, lesion, and treatment characteristics were collected from the patient electronic health records. Patient characteristics included sex, age at the time of surgery, BMI, laterality, etiology (traumatic or non-traumatic), the presence of ankle instability (defined as patient-reported recurrent spraining and/or subjective ankle instability, laxity during physical examination, or as concluded by the physician in the clinical report[36]), and previous ankle surgeries. Lesion characteristics included primary or non-primary lesion type as well as radiographic characteristics. Treatment characteristics included follow-up time (in years), lesion debridement with or without microfracture, anterior or posterior arthroscopy, and any concomitant procedures.
Outcome measures were collected from the patient electronic health records as well as by phone interview to confirm whether patients had or had not undergone revision surgery. If a revision surgery had been performed, the following data were collected: type of revision surgery (according to the previously described categorization of surgical procedures for the OLT), revision surgery date, and reason for revision surgery.

Radiographic Evaluation

Preoperative lesion characteristics were collected by 2 independent raters (Q.G.H.R. and M.B.A.) on CT scans (n= 254). If no preoperative CT scan was available, magnetic resonance imaging (MRI) was utilized (n = 8). The following lesion characteristics were collected: lesion size (anterior-posterior and medial-lateral directions as well as depth) measured in millimeters and converted to the area as described by Choi et al.[7] and to the volume as described by Angthong et al.1, dominant lesion morphology as described by Rikken et al.[36], the presence of cysts, and the location according to a 9-gird scheme.[31] A consensus meeting was held in case of disagreement on the lesion characteristics between the 2 raters, and if no agreement could be achieved, a third rater (J.D.) made the decision.

Statistical Analysis

Data analyses were conducted using Stata (version 15; StataCorp). A 2-sided p value of <0.05 was considered significant. Baseline dichotomous and categorical data are reported as counts with percentages, and continuous data are reported as means with standard deviations. Data were visually assessed for normality using histograms. The primary outcome, namely the cumulative 10-year survival rate, was analyzed by means of the Kaplan-Meier survival method and reported with the 95%

confidence interval (CI). Patients who were lost to follow-up were censored for the primary outcome at the time of their latest follow-up visit. No power analysis was performed for the primary outcome, as this study involved an observational outcome in a single cohort. The median time to revision surgery was calculated along with the interquartile range (IQR). The effects of baseline predictive factors on survival were determined using univariate Cox regression analysis and reported as hazard ratios (HRs) with 95% CIs. All variables that were significantly associated with revision in the univariate analyses (at an adjusted significance level of 0.1) were entered into a multivariable Cox regression model. Backward selection was used to identify the factors that remained predictive of revision (at a significance level of 0.05). Multiple imputation was performed for missing data (BMI for 74 ankles [28%] and lesion size for 1 ankle [0.4%]), under the assumption that data were missing at random. All model variables and 2 auxiliary variables (age, sex) were used for imputation of the missing data. Five data sets were created, and pooling of the outcome was performed according to the Rubin rules.[29] A sensitivity analysis was also performed by means of complete-case analysis. A description of further subanalyses as well as interrater and intrarater reliability measurements are provided in the Appendix.

Results

At the time of final follow-up, at a mean of 15.3 ± 4.8 years postoperatively, 262 cases were eligible for inclusion; the patient was reached in 217, and the other 45 were censored at a mean of 1.8 ± 3.4 years (Figure 1). One patient had a bilaterally treated OLT (i.e., 2 cases).

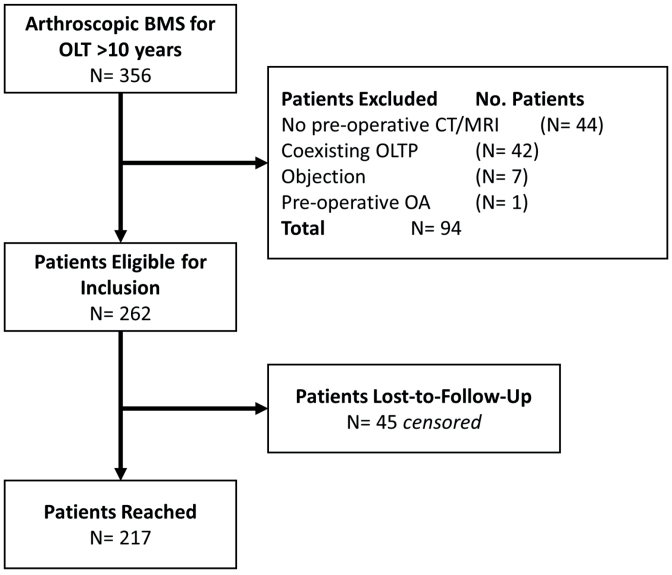

Figure 1. Flowchart of patient selection. OLTP = osteochondral lesion of the tibial afond, and OA = osteoarthritis.

An overview of the baseline patient, treatment, and lesion characteristics is shown in Table 2. There were no significant differences in baseline characteristics between the patients who were reached and those who were censored, except for a longer follow-up time for censored patients (i.e., nonresponders). The outcomes of the interrater and intrarater reliability measurements are shown in the Appendix.

Table 2. Baseline Patient, Treatment, and Lesion Characteristics*

	All Cases (N = 262)		Responders (N = 217)		Nonresponders (N = 45)		P-Value
	Value	% with Data	Value	% with Data	Value	% with Data	
Sex: male	162 (62%)	100	130 (60%)	100	32 (71%)	100	0.2
Age *(yr)*	32.3 ± 11.7	100	32.1 ± 11.6	100	33.0 ± 12.2	100	0.8
Time to event† *(yr)*	10.9 ± 7.3	100	12.8 ± 6.4	100	1.8 ± 3.4	100	NA
Follow-up time‡ *(yr)*	15.3 ± 4.8	100	14.9 ± 4.6	100	17.1 ± 5.3	47	**<0.01**
BMI *(kg/m²)*	25.7 ± 4.4	72	25.5 ± 4.2	77	26.8 ± 5.5	100	0.2
Laterality: right	137 (52%)§	100	113 (52%)	100	24 (53%)	100	0.9
Lesion etiology		93		93		93	0.8
Non-traumatic	64 (26%)		53 (26%)		11 (26%)		
Traumatic	180 (74%)		149 (74%)		31 (74%)		0.1
Ankle instability	50 (20%)	93	40 (20%)	94	10 (25%)	89	
Treatment characteristics							
Arthroscopic approach		97		97		98	0.8
- Anterior	197 (77%)		162 (77%)		35 (80%)		
- Posterior	58 (23%)		49 (23%)		9 (20%)		
Microfracture		99		99		98	0.5
- Debridement only	35 (13%)		31 (14%)		4 (9%)		
- Debridement with microfracture	225 (87%)		185 (86%)		40 (91%)		
Concomitant surgery#		100		100		100	0.1
No. of ankles	107 (41%)		84 (39%)		23 (51%)		
Total no. of procedures	129		99		30		
- Resection of osseous impingement	55 (43%)		41 (41%)		14 (47%)		
- Resection of soft-tissue impingement	13 (10%)		11 (11%)		2 (7%)		
- Removal of loose body	39 (30%)		32 (32%)		7 (23%)		
- FHL release	11 (9%)		7 (7%)		4 (13%)		
- Resection of os trigonum	8 (6%)		6 (6%)		2 (7%)		

Table 2. Continued

Lesion characteristics	All Cases		Responders		Nonresponders		P Value
	Value	% with Data	Value	% with Data	Value	% with Data	Value
Primary lesion	212 (81%)	100	173 (80%)	100	39 (87%)	100	0.4
Presence of cyst	139 (53%)	100	113 (52%)	100	26 (58%)	100	0.5
Lesion morphology		100		100		100	0.6
- Cyst	127 (48%)		102 (47%)		25 (56%)		
- Crater	85 (32%)		73 (34%)		12 (27%)		
- Fragment	50 (19%)		42 (19%)		8 (18%)		
Lesion location		100		100		100	0.4
- Zone 1	19 (7%)		16 (7%)		3 (7%)		
- Zone 2	1 (0.4%)		1 (0.4%)		0 (0%)		
- Zone 3	10 (4%)		7 (3%)		3 (7%)		
- Zone 4	87 (33%)		75 (35%)		12 (27%)		
- Zone 5	4 (2%)		3 (1%)		1 (2%)		
- Zone 6	29 (11%)		23 (11%)		6 (13%)		
- Zone 7	63 (24%)		52 (24%)		11 (24%)		
- Zone 8	6 (2%)		3 (1%)		3 (7%)		
- Zone 9	43 (16%)		37 (17%)		6 (13%)		
Lesion size (mm)							
Anterior-posterior	10.7 ± 4.0	99	10.8 ± 4.0	99	10.4 ± 4.6	100	0.5
Medial-lateral	7.8 ± 3.3	100	7.8 ± 3.2	100	7.7 ± 3.4	100	0.5
Depth	6.5 ± 2.9	100	6.5 ± 3.0	100	6.2 ± 2.5	100	0.5
Lesion area (mm^2)	73.1 ± 49.8	99	73.4 ± 49.8	99	71.8 ± 64.8	100	0.4
Lesion volume (mm^3)	367.8 ± 385.5	99	369.4 ± 357.9	99	360.0 ± 502.1	100	0.4

* The values are given as the mean ± standard deviation or as the count with the percentage in parentheses. All percentages are of the number of cases with available data for the variable except for the individual concomitant procedures, which are of the total number of concomitant procedures. NA = not applicable, FHL = flexor hallucis longus, ATFL = anterior tibiofibular ligament.
† The time to event is the time from the index surgery to censoring (i.e., including the observation time with or without loss to follow-up) or to revision surgery.
‡ The follow-up time is from the index procedure to the time of inclusion.
§ 1 case had bilaterally treated OLT.
# This is the total number of procedures; a patient may have had >1 concomitant procedure.

Survival Analysis

The 10-year cumulative survival rate of arthroscopic BMS in the 262 cases available in this cohort was 82.3% (95% CI: 76.6% to 86.7%). The Kaplan-Meier survival curve is shown in Figure 2. The median time to revision was 2.4 years (IQR: 1.3 to 5.1 years). A subanalysis revealed no significant differences in baseline patient and lesion characteristics between patients who underwent revision early (<2.5 years of follow-up) or late (>2.5 years of follow-up) revision (see the Appendix). At 15 and 20 years of follow-up, the cumulative survival rate was 81.6% (95% CI: 75.8% to 86.1%, n = 62) and 77.7% (95% CI: 68.5% to 84.0%, n = 33), respectively.

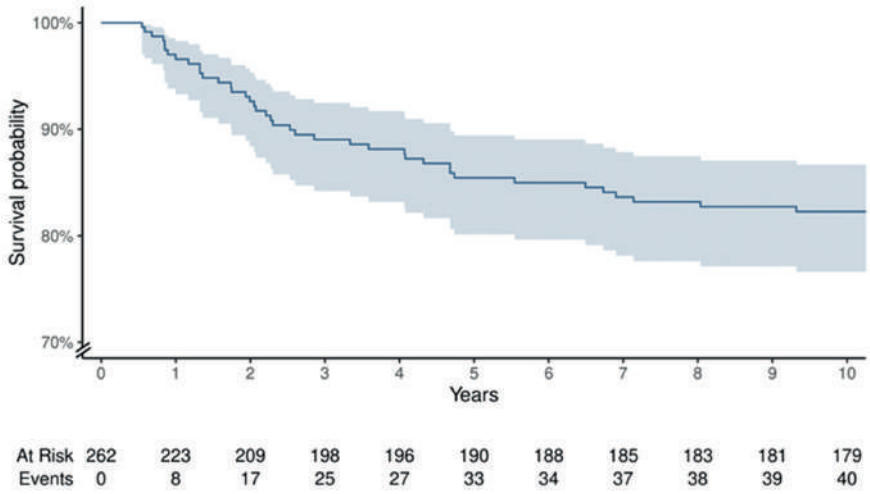

Figure 2. Kaplan-Meier survival curve at up to 10 years of follow-up. Of note: The survival rate is shown using a y axis from 70% to 100%; shading represents the 95% CI. The number of patients at risk and the cumulative number of events at each given time are listed below.

Baseline Factors and Survival Outcomes

As 44 events occurred in the study population, 4 of the 5 predetermined baseline factors (selected according to the prospectively established hierarchy) were analyzed for their association with survival. Table 3 shows the hazard ratio for each variable. The Kaplan-Meier curves for all variables are shown in the Appendix.

A baseline BMI of ≥30 kg/m^2 was significantly associated with a higher likelihood of revision following BMS (HR: 3.0 [95% CI: 1.44 to 6.43], $p < 0.01$) (Figure 3) A comparison of baseline characteristics is shown in the Appendix. The complete-case analysis, which is shown in the Appendix, found results comparable to those of the primary analysis.

Table 3. Cox Regression Analysis of Baseline Factors Associated with Failure*

Analysis and Variable	HR (95% CI)	P Value
Univariate		
Lesion size		
≤100 mm^2	Reference	
>100 mm^2	0.93 (0.47-1.83)	0.82
Lesion type		
Primary	Reference	
Non-primary	1.78 (0.93-3.41)	0.08
Presence of cyst		
No	Reference	
Yes	1.02 (0.57-1.85)	0.94
BMI		
<30 kg/m^2	Reference	
≥30 kg/m^2	3.04 (1.44-6.43)	**<0.01**
Sex †		
Male	Reference	
Female	0.60 (0.33-1.08)	**0.09***
Multivariable		
Lesion type		
Primary	Reference	
Non-primary	1.57 (0.83-3.03)	0.18
BMI		
<30 kg/m^2	Reference	
≥30 kg/m^2	2.82 (1.30-6.1)	0.01
Final model		
BMI		
<30 kg/m^2	Reference	
≥30 kg/m^2	3.04 (1.44-6.43)	**<0.01**

*After multiple imputation. HR = hazard ratio, CI = confidence interval.
†Sex was not included in the formal analysis because of underpowering, as described in the Materials and Methods section. However, it is shown here to support the secondary analysis and should be interpreted as such.

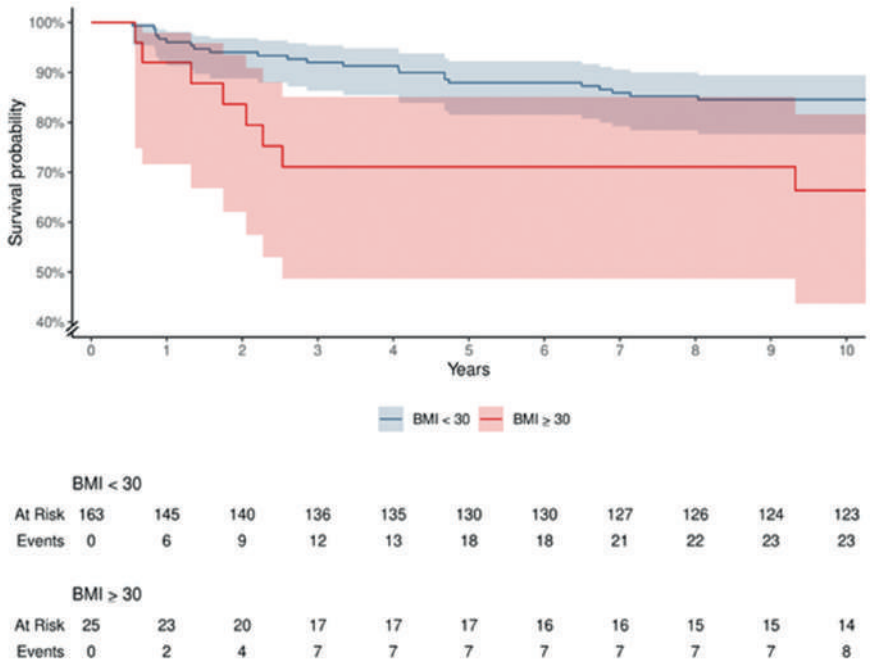

Figure 3. Kaplan-Meier survival curve comparing the survival of patients with and without obesity. Of note: The survival rate is shown using a y axis from 40% to 100%; shading represents the 95% CI. The number of patients at risk and the cumulative number of events at each given time are listed below for each group.

Discussion

The most important finding of this study is that 82% of ankles that underwent arthroscopic BMS procedures for an OLT remained free from revision at 10 years of follow-up. At 15 and 20 years of follow-up, the cumulative survival rate was 82% and 78%, respectively. Furthermore, this study found that obesity (BMI ≥ 30 kg/m^2) may be associated with a higher likelihood of revision surgery.

Survival in orthopaedics is a dynamic outcome that incorporates functional outcomes, pain, complications, return to sports and work, and mental aspects, as well as a patient's experience and expectations.[20,30,39] Outcomes in 1 or more of these domains must reasonably be below the level of satisfaction in order for a patient to consider revision surgery. In contrast to arthroplasty studies, few studies to date have specifically focused on survival outcomes in joint preservation surgery for osteochondral lesions of the ankle.[27,38,44] This study sought to evaluate the long-term clinical survival after arthroscopic BMS for OLT and observed a high rate of survival that was sustained over time. When comparing the outcomes of this study

with the literature, it should be noted that a limited number of studies on the long-term outcomes following BMS for OLT have been published, with even fewer assessing its survival.[3,5,9,19,27,35,37] A recent systematic review found an overall survival rate of 93% in 317 ankles from 5 studies with long-term outcomes.[35] The study by Park et al.[27] was the largest contributor, with 202 of the 317 ankles. That study found a survival rate of 94% at a mean of 14 years of follow-up and good clinical outcomes. The second largest study, by van Bergen et al.[5], included 50 patients with primary OLT at a mean follow-up of 10 years; it found a survival rate of 90% and excellent to good Berndt and Harty scores in 78%. It can be hypothesized that the 10% higher survival rate reported in the literature compared with the present study is due to patient selection.[35] First, the aforementioned systematic review included almost exclusively (96%) primary lesions[35], whereas the present study includes 19% non-primary lesions. Even though the association of a non-primary lesion type with decreased survival did not reach significance, the inclusion of the relatively high proportion of non-primary lesions could have impacted the survival rate, as there is evidence that these lesions may result in inferior patient-reported outcome measures (PROMs) compared with primary lesions.[2] Second, the present study was performed in a cohort of patients from a tertiary referral hospital recognized as an (inter)national expert center in the diagnosis and treatment of OLT. Thus, the patients may have been inherently more challenging to treat because of the presence of more risk factors or higher patient expectations. However, it should be noted that an 82% to 94% survival rate at 10 years is to be expected following arthroscopic BMS, according to the literature and the findings of this study.[3,5,9,19,27,35,37] Moreover, this study also calculated survival rates at 15 and 20 years of follow-up, and survival appeared nearly stable beyond 10 years, which is an encouraging finding for the practice of BMS for OLT.

It has been hypothesized that BMS fails over time due to the progression of osteoarthritis, and 28% of cases reported in the literature showed radiographic progression of degenerative changes; however, only 4% of cases were reported to have actual joint-space narrowing.[35] Radiographic follow-up was not included in the present study, as our treatment protocol does not include long-term radiographic evaluation of patients who are doing well clinically. Thus, we believe that including the available radiographic studies of the patients who returned for re-evaluation of their ankle would not have been representative of the cohort as a whole, may have overestimated the progression of osteoarthritis due to selection bias, and could therefore have resulted in incorrect conclusions. The revisions in this cohort included only 5 procedures (2% of all cases) that consisted of tibiotalar arthrodesis or arthroplasty, suggesting that the rate of symptomatic end-stage osteoarthritis was low or that its onset would present outside the time window of this study.

Baseline Factors Associated with Survival

Our findings suggest that patients with obesity (BMI ≥ 30 kg/m^2) have a decreased survival rate. The effect of BMI on clinical outcomes remains debated. A recent study by Koh et al.[22] reported that a BMI of ≥25 kg/m^2 was not associated with decreased outcomes at 2 years of follow-up in 252 patients who underwent arthroscopic BMS. Indeed, the aforementioned authors found that a higher BMI appeared to be weakly associated with improved outcomes. In contrast, several studies found that BMI was associated with poorer PROMs[4,14] and decreased survival.[27] Based on these reports and the findings of the present study, advising weight reduction can be recommended as best practice when counseling obese patients regarding surgery. It could be hypothesized that an association between obesity and poorer survival outcomes is present because the elevated BMI exaggerates the biomechanical stress on fibrocartilage or surrounding hyaline cartilage and subchondral bone in the highly congruent tibiotalar joint, leading to treatment failure. On the other hand, we hypothesize that obesity may also represent a variable that encompasses a multifactorial risk profile, such as lower social economic status, general health, or mental health, which could affect PROMs.[40,42] Additionally, we note that it is important to consider the statistical frailty due to the relatively small number of patients with obesity in this study, which precludes definitive conclusions regarding the relationship between BMI and survival.

Among the other baseline factors assessed, the associations of long-term survival with the lesion size, a non-primary lesion type, the presence of preoperative cysts, and patient sex did not reach the level of significance. These findings are not in line with previous studies finding a relationship between these baseline characteristics and PROMs[2,8,10,16,21,22,27,32], which may be because the outcome of survival free from revision incorporates not only PROMs but also mental health, physical functioning, work and sport activities, etc. However, we did observe a nonsignificant trend toward poorer survival for non-primary OLT and for female patients the (see Appendix). These trends could show a significant association in larger samples, which would be highly clinically relevant, and both factors should therefore be investigated further.

Limitations and Strengths

The results of this study should be interpreted in the context of its design, and it is not without limitations. First, it was performed retrospectively using a single-center cohort. Additionally, it did not include clinical and radiographic follow-up data, but instead focused on revision outcomes. In our institution, a recurrent OLT is treated according to shared decision-making using a stepwise approach before revision surgery is chosen. As such, recurrent lesions are first treated with a period of nonoperative treatment and any concomitant pathology is addressed. Second, 17% of patients could not be contacted; however, that is to be expected in long-term follow-up studies and

is in line with prior studies.[27] Furthermore, no differences in baseline characteristics were observed between responders and nonresponders. Third, statistical frailty and overfitting of the models for assessing the effects of baseline characteristics on survival may be present, given the small number of patients per group. However, we sought to limit this effect by prospectively establishing a hierarchy for assessing these variables.

The strengths of this study are its focus on survival outcomes in what we believe to be the largest cohort of patients with long-term follow-up after BMS for OLT to date and its predetermined statistical plan for the evaluation of prognostic baseline factors. Moreover, the data extraction and radiographic measurements were performed by 2 authors and their results showed excellent interrater and intrarater reliability. We recommend future studies to substantiate our findings regarding the survival rate and risk factors for failure as well as osteoarthritis by utilizing large (international) multicenter cohorts of patients with long-term follow-up following BMS for OLT.

Conclusions

At a minimum follow-up of 10 years, the survival rate free from revision was 82% after arthroscopic BMS for OLT. At 15 and 20 years of follow-up, survival appeared to remain stable. Obesity (BMI ≥ 30 kg/m^2) was associated with a higher likelihood of revision surgery. This risk factor should be incorporated into the treatment algorithm for OLT when counseling patients regarding surgery.

Appendix

The appendix information can be accessed at: http://dx.doi.org/10.2106/JBJS.23.01186

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Chapter 4

Outcomes of Bone Marrow Stimulation for Secondary Osteochondral Lesions of the Talus equal Outcomes for Primary Lesions

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Abstract

Purpose: To compare clinical, sports, work, and radiological outcomes between primary and secondary OLTs (<15mm) treated with arthroscopic BMS.

Methods: Secondary OLTs were matched to primary OLTs in a 1:2 ratio to assess the primary outcome measure; the Numeric Rating Scale (NRS) during activities. Secondary outcomes included the pre- and one-year postoperative NRS at rest, American Orthopaedic Foot and Ankle Society score, Foot and Ankle Outcome Score (FAOS) subscales, and the EQ-5D general health questionnaire. The rates and time to return to work and sports were collected. Radiological examinations were performed preoperatively and at final follow-up using computed tomography (CT).

Results: After matching, 22 and 12 patients with small (<15 mm) OLTs were included in the primary and secondary group, respectively. The NRS during activities was not different between primary cases (median: 2, IQR: 1 – 4.5) and secondary cases (median: 3, IQR: 1 – 4), P= 0.5. Both groups showed a significant difference between all pre- and postoperative clinical outcome scores, but no significant difference between BMS groups postoperatively. The return to sport rate was 90% for primary cases and 83% for secondary cases (P= 0.6). All patients returned to work. Lesion filling on CT was complete (67% - 100%) in 59% of primary cases and 67% of secondary cases (P= 0.6).

Conclusion: No differences in outcomes were observed between arthroscopic bone marrow stimulation in primary and secondary OLT at one-year follow-up. Repeat BMS may therefore be a viable treatment option for failed OLTs in the short term.

Key Terms: Osteochondral Lesion; OLT; Bone Marrow Stimulation; Microfracture; Secondary Treatment.

Introduction

Arthroscopic bone marrow stimulation (BMS) is the most frequently performed operative treatment for primary osteochondral lesions of the talus (OLT).[6] The aim of BMS is to reduce pain, improve clinical outcomes, and allow patients to resume physical activities and sports.[6,13] Previous studies have reported that up to 82% of patients treated with primary BMS show successful clinical outcomes.[6,18] Additionally, the return to preinjury level of sports has been found to be 79% following BMS.[36] Arthroscopic BMS is exempt from the disadvantages of other more invasive secondary defect treatments, such as donor-site morbidity, the need for an osteotomy, and would still allow for additional surgical options if treatment fails.[17,24]

The use of arthroscopic BMS in secondary – i.e. repeat BMS after failed primary surgery – OLT is less frequent compared to primary cases.[6,18] This can be attributed to the relatively inferior clinical results of secondary BMS reported in the literature.[18,29,33] However, the number of studies with accompanying clinical evidence is limited and of low methodological quality including a low number of patients. Additionally, no consensus exists on the effect of secondary BMS on sports outcomes, nor do studies directly compare clinical outcomes between primary- and secondary BMS. This warrants further exploration of the efficacy of secondary BMS treatment on pain reduction, clinical outcomes, and the resumption of sports.

The primary objective of this study was to compare the one-year postoperative Numeric Rating Scale (NRS) pain scores during activity between primary and secondary OLTs treated with arthroscopic BMS. It was hypothesized that no difference in postoperative NRS scores during activities would be observed between the two groups. The secondary aim was to compare the clinical-, sports-, work-, and radiological outcomes between primary and secondary treatment groups.

Methods

Approval by the local medical ethics committee at Amsterdam UMC, location AMC, was obtained prior to the start of this study (Reference Number: MEC 08/326)) and the study was performed in accordance with the Declaration of Helsinki. Patients were selected from a database constructed for a previously published randomized control trial (RCT), which was conducted between 2009 to 2014.[27] The respective RCT investigated pulsed electromagnetic fields (PEMF) compared to a placebo as adjuvant treatment for BMS, and included 36 patients in the PEMF group and 32 patients in the placebo group. The aforementioned study did not find statistically significant differences in clinical nor radiological outcomes between the PEMF- and placebo group at one-year follow-up, and therefore both groups were merged into the database for the present study. The operative technique and postoperative

rehabilitation protocol were previously described in detail.[27]

Patient Selection

Patients who underwent arthroscopic debridement and bone marrow stimulation (i.e. microfracturing) for either a primary or failed primary lesions (<15 mm in all dimensions as measured per computed tomography scan) were included (Figure 1). The frequency of previous BMS procedures did not preclude inclusion. Exclusion criteria were set by the study from Reilingh et al.[27] Patients who underwent repeat BMS (secondary group) were matched to patients who underwent primary BMS (primary group) as a control in a 1:2 ratio.[38] Matching was based on the following prognostic variables; 1) lesion size as measured (in anterior-posterior, medial-lateral, and depth) per computed tomography (CT) scan, 2) age, 3) body mass index (BMI), and 4) sex, as these factors have been shown to correlate with clinical outcomes following BMS.[4,5]

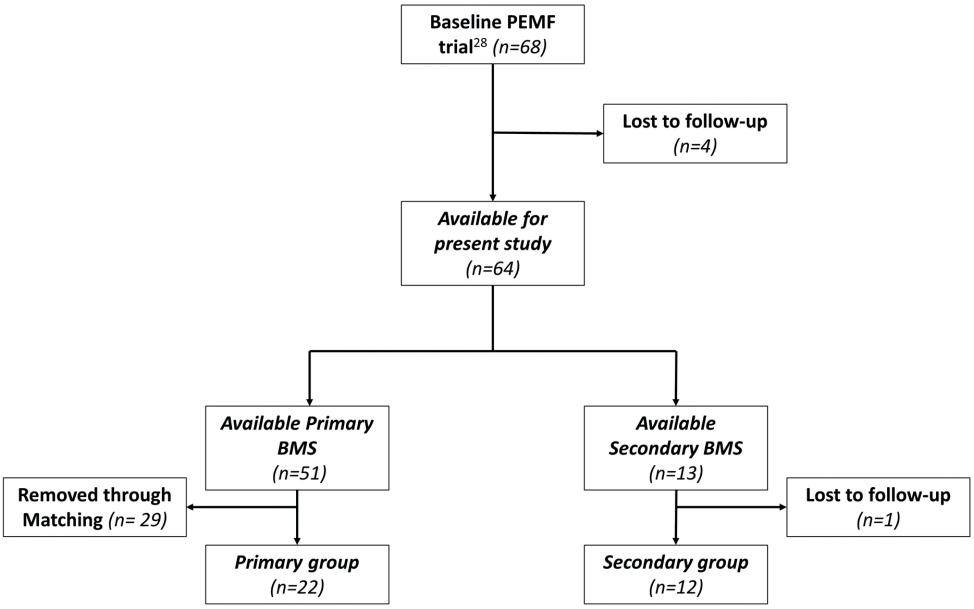

Figure 1. Flowchart of patient selection with in- and exclusion criteria.

Clinical Evaluation

Primary Outcome Measure

The primary outcome was defined as the difference of postoperative Numeric Rating Scale (NRS)10 during activities between the two groups. The NRS is a subjective pain scale from 0 (no pain) to 10 (worst pain imaginable).

Secondary Outcome Measures

Clinical outcomes were evaluated preoperatively and at one-year follow-up. Secondary clinical outcomes concerned both pre- and postoperative comparisons in each respective treatment group, as well as a comparison between groups postoperatively, and included; the NRS at rest, American Foot and Ankle Outcome Society (AOFAS) score, the Foot and Ankle Outcome Score (FAOS), and the EQ-5D general health questionnaire. The AOFAS is a 100-point, physician administered, clinical outcome scale.[19] Its subcategories consist of pain (40 points), function (50 points), and alignment (10 points). The FAOS is a patient-reported outcome measure consisting of 42 questions distributed over five subscales; symptoms, pain, activities of daily living, sport, and quality of life.[30,35] The EQ-5D is a general health questionnaire, which reports the overall health of an individual on a 0 to 100% scale.[8]

Sports and Work Evaluation

Pre-operatively, the type of sport and athletic level (i.e. amateur, competitive, or professional) were recorded. Postoperatively, the evaluation consisted of the return to sports (RTS) rate in percentages and RTS time in weeks, type of sport, and level of activities. Return to sports was defined as the resumption of any sport at a minimum of pre-symptomatic level of sports, minus 1 point on the ankle Activity Score[12] (AAS), maintained for a minimum of 30 days.[27] Similarly, the pre- and postoperative occupation of patients, and time to return to work were collected. Return to work was defined as resumption of work with normal activities without any deficits in work quality.[27]

Radiological Evaluation

Radiological evaluation was performed by means of a CT scan preoperatively, at two weeks postoperatively, and one year postoperatively. A standardized imaging protocol concerned axial slices with 0.3mm increment and 0.6mm thickness, and multidirectional (coronal and sagittal) reconstructions of 1mm.[28] On preoperative imaging, lesions were graded according to the Berndt and Harty classification[3] and localization of the lesion was determined using a 9-grid scheme from Elias et al.[26] Furthermore, lesion dimensions were measured in anterior-posterior, medial-lateral, and cranial-caudal (depth) directions, and the morphological aspects of the lesion were assessed (such as the presence of cysts). Subchondral bone plate characteristics (flushed or depressed) and the level of lesion filling (difference in lesion dimensions between two weeks postoperative and one-year postoperative scans) were assessed on final follow-up imaging. Reilingh et al.[27] previously established the intra-observer reliability for the radiological outcomes assessed to be excellent.

Statistical Analysis

A sample size calculation for the primary outcome using a level of significance (α) of 0.05 and a two-sided, two group Wilcoxon rank-sum test was performed with nQuery advisor 7.0 (Statistical Solutions Ltd., Boston, MA). The minimally clinical important difference (MCID) in the Numeric Rating Scale (NRS) for pain during activities of 2.0 (± 1.3) between the primary- and secondary group with a power of 80% was chosen, as it correlates with a "much better" improvement in pain.[9,23,31] Therefore, a minimum of 10 patients per group were needed. [27]

Patient baseline characteristics were summarized using descriptive statistics with absolute numbers and percentages for categorical variables and means with standard deviations for continuous variables. Data was assessed for normality using a Shapiro-Wilk test and inspected visually with histograms and box plots. Baseline characteristics and outcome variables were compared using a Fisher's exact test for dichotomous variables and a Chi-square test for ordinal variables. For continues outcomes, a Wilcoxon signed rank test was used for comparing pre- and postoperative outcomes per treatment group, and a Wilcoxon rank sum test for comparing pre- an postoperative outcomes between treatment groups. A univariate linear regression analysis was used to investigate the influence of covariates on clinical outcome scores. A two-sided level of $P < .05$ was considered significant. Data analysis was performed using Stata 15 (StataCorp LP, College Station, TX).

Results

Patient Selection and Demographics

A total of 22 primary BMS patients and 12 secondary BMS patients were included for analysis after matching (Figure 1). No significant differences in baseline patient- and lesion characteristics between the primary and the secondary group were present (Table 1).

Primary Outcome

The median postoperative NRS during activities for the primary and secondary group was 2 (IQR: 1 – 4.5) and 3 (IQR: 1 – 4), respectively, and did not show a significant difference (P= 0.46). Preoperatively, the NRS in rest (P= 0.09) and NRS during activities (P= 0.47) were not significantly different between both groups. Both treatment groups showed significantly lower pain scores during activity at final follow-up compared to the pre-operative assessment (Table 2).

Table 1. Patient and Lesion Characteristics at Baseline

Patient Characteristics	Primary Group (n = 22)	Secondary Group (n = 12)	P-Value
Sex, n (% male)	12 (56%)	8 (67%)	n.s.
Age (years), mean ± SD	30.5 ± 8.3	31.3 ± 7.5	n.s.
BMI (kg/m^2), mean ± SD	24.1 ± 2.4	24.8 ± 2.6	n.s.
Smoking, n (%)	3 (14%)	4 (33%)	n.s.
Laterality, n (% right side)	7 (32%)	5 (42%)	n.s.
Previous ankle trauma, n (%)	19 (86%)	8 (67%)	n.s.
Previous ankle fracture, n (%)	3 (14%)	0 (0)	n.s.
Sports, n (%)	22 (100%)	12 (100%)	n.s.
Sports Level, n (%) - Professional - Competitive - Recreational	 3 (14%) 12 (54%) 7 (32%)	 1 (9%) 7 (58%) 4 (33%)	n.s.
Previous BMS procedures, mean (range)	-	1.4 (1-3)	n.a.
Time since previous BMS procedure (months), mean ± SD	-	31.9 ± 22.8	n.a.
Lesion Characteristics			
Brendt and Harty, n (%)	Stage 2: 1 (5%) Stage 3: 3 (13%) Stage 4: 1 (5%) Stage 5: 17 (77%)	Stage 1: 1 (8%) Stage 2: 2 (17%) Stage 5: 9 (75%)	n.s.
Presence of Cyst, n (%)	11 (50%)	7 (58%)	n.s.
Size (mm), mean ± SD			
Anterior-Posterior	11.1 ± 2.7	11.3 ± 2.6	n.s.
Medial-Lateral	9.2 ± 2.5	9.1 ± 2.3	n.s.
Depth	7.0 ± 2.0	7.5 ± 1.4	n.s.
Location per zone†, n (%)			n.s.
Anteromedial (zone 1)	5 (23%)	1 (8%)	
Anterocentral (zone 2)	5 (23%)	2 (18%)	
Anterolateral (zone 3)	5 (23%)	3 (24%)	
Centeromedial (zone 4)	0	1 (8%)	
Centerocentral (zone 5)	3 (13%)	2 (18%)	
Centerolateral (zone 6)	4 (18%)	1 (8%)	
Posteriomedial (zone 7)	0	1 (8%)	
Posteriocentral (zone 8)	0	1 (8%)	
Posteriolateral (zone 9)	0	0	

†: all zones not significant, zone distribution according to Elias et al.[26]
Abbreviations: n: number, SD: standard deviation, BMI: body mass index, BMS: bone marrow stimulation

Table 2. Clinical Outcomes for the Primary and Secondary BMS Group

	Primary Group (n= 22)			Secondary Group (n= 12)			Between Groups†
	Pre-operative	**1 Year Postopera-tively**	**P-Value**	**Pre-operative**	**1 Year Post-operatively**	**P-Value**	**P-Value**
NRS, median (IQR)							
Pain (activties)	8 (6 -10)	2 (1 – 4.5) N=20	**<0.01**	8.5 (8 – 10)	3 (1 – 4) N=11	**<0.01**	n.s.
Pain (rest)	2 (0 – 4)	0 (0)	**<0.01**	4 (2 – 4.5)	1 (0 – 2)	n.s.	n.s.
Satisfac-tion	-	7 (5- 8)	n.a.	-	7 (6.5 -8)	n.a.	n.s.
AOFAS, median (IQR)	72 (49 – 75)	90 (85 – 100)	**<0.01**	67 (46 – 69)	87 (79.5 – 100)	**<0.01**	n.s.
FAOS, median (IQR)							
Symp-toms	58.9 (53.6 – 71.4)	75 (64.3 – 89.3)	n.s.	60.7 (50 – 71.4)	67.9 (48.2 – 82.1)	**0.03**	n.s.
Pain	63.9 (52.8 – 75)	91.6 (73.6 – 94.4)	**<0.01**	52.8 (45.8 – 66.7)	81.9 (63.9 – 91.7)	**0.01**	n.s.
ADL	69.1 (54.4 – 80.9)	95.6 (91.2 – 100)	**<0.01**	69.1 (47.8 – 87.5)	94.9 (72.8 – 98.5)	**0.02**	n.s.
Sport	42.5 (25 – 50)	80 (50 – 85)	**<0.01**	27.5 (20 – 52.5)	70 (42.5 – 75)	**0.01**	n.s.
QOL	34.4 (18.8 – 43.8)	53.1 (37.5 – 75)	**<0.01**	25 (18.8 – 28.1)	46.9 (28.1 – 68.8)	**0.01**	n.s.
EQ-5D, median (IQR)	78% (69.3 – 80.7)	84% (77.5 – 100)	**<0.01**	78% (29.8 – 77.5)	87% (79.3 – 100)	**<0.01**	n.s.
AAS, median (IQR)	5.5 (4 – 9)	7.5 (4 – 9)	n.s.	7.5 (4 – 9) n=19	5 (4 – 8) n=11	n.s.	n.s.

†: Comparison of postoperative outcomes between primary and secondary group.
Abbreviations. NRS: Numeric Rating Scale, AOFAS: American Orthopaedic Foot and Ankle Society score, FAOS: Foot and Ankle Outcome Score, ADL: Activities of Daily Living, QOL: Quality Of Life, EQ-5D: EQ-5D general health questionnaire, AAS: Ankle Activity Scale, N.A. not applicable

Secondary outcomes

Clinical outcomes

Preoperatively, no clinical outcome scores were significantly different between groups. Most secondary outcomes significantly improved in both groups at final follow-up in comparison to preoperatively, but did not show a significant difference between treatment groups at final follow-up (see Table 2).

Patient age, sex, BMI, lesion size, the presence of cysts, or laterality did not significantly correlate with the primary and secondary clinical outcome scores. At final follow-up, no major or minor complications were recorded. One patient from the secondary group was re-operated with a HemiCAP prosthesis for persistent pain complaints.

Resumption of Sport and Work

No statistically significant differences in sports outcomes were found between the two groups (Table 3). Patients returned to work at a median 5 weeks and 7 weeks for primary and secondary cases, respectively. Resumption of work was 100% in both groups.

Table 3. Sports and Work resumption

	Primary group	Secondary group	P-Value
Return to sports rate, n (%)	20 (91%)	10 (83%)	0.6
Time to return to sports, median (IQR)	14 weeks (8 – 23)	19 weeks (13 – 26)	0.16
Return to work, n (%)	22 (100%)	12 (100%)	1.0
Time to return to work, median (IQR)	5 (2 – 6)	7 (5 – 11)	0.1

Abbreviations: IQR; inter-quartile range

Radiological Outcomes

The baseline radiological lesion dimensions and characteristics are displayed in Table 1. At one-year follow-up, CT scans were available for all patients except one patient from the secondary group. The subchondral bone plate status and filling were not significantly different (Table 4).

Table 4. CT findings at one-year follow-up

	Primary group	Secondary group	P-Value
Subchondral bone plate status, n (%)			0.6
Depressed	17 (77%)	10 (91%)	
Flushed	5 (23%)	1 (9%)	
Subchondral bone plate filling, n (%)			0.62
Complete (67 – 100%)	13 (59%)	8 (73%)	
Partially Complete (34 – 66%)	5 (23%)	1 (9%)	
Incomplete (0 – 33%)	4 (18%)	2 (18%)	

Discussion

The main finding of this study is that no differences in clinical outcomes were observed between patients treated with primary and secondary bone marrow stimulation. Both treatment groups showed a significant and clinically relevant benefit from the intervention when compared to the preoperative situation. Moreover, similar return to sport and work rates were observed in both groups.

Clinical Outcomes

On average, pain outcomes -in particular during activities- improved above the MCID threshold[31] of 2 points in both treatment groups at one-year follow-up. This threshold corresponds to a "much better" improvement in pain. Postoperative pain plays a major role in the limited success of repeat BMS, as reported by other authors.[32,37] This finding is of clinical relevance as our findings do not fully coincide with the available literature, which shows poor results for patients treated with secondary BMS.[29,33,37] However, when comparing the observed pain outcomes of the present study to the available literature one is constrained by the underreporting of the exact measure of pain. This study investigated pain scores during activities, while others did not report the circumstances of the perceived pain by study participants.[22,32,37] It is therefore challenging to accurately compare these findings.

Clinical outcome scores, however, are universally reported, though limited.[18] Yoon et al.[37] found a mean Visual Analog Scale (VAS) for pain of 5.3 out 10 and a mean AOFAS score of 70 at 48 months follow-up in their study comparing repeat BMS to osteochondral autograft transplantation. In the aforementioned study 32% of lesions treated with secondary BMS were larger than 150mm^2 which was in turn correlated with decreased clinical outcomes, a finding supported by the literature.[4,37] However, the authors noted clinical outcomes - most notably the VAS pain score – for secondary BMS cases to decline over time, and reported a clinical failure rate (defined as persistent pain or recurrent symptoms, repeat surgery, or AOFAS <80) of 53%.On the other hand, our findings concur with Savva et al.[32], who similarly concluded that secondary BMS yields good postoperative outcomes. Their retrospective case study found similar AOFAS scores for 12 patients at a mean follow-up of 6 years. In contrast, their study excluded cystic lesions as these have been associated with decreased clinical outcomes.[29,32] In the present study 50% of primary lesions and 58% of secondary lesions included a cystic morphology, which did not significantly correlate with clinical outcomes.

From these findings an interesting question arises; why do patients treated with secondary BMS not show successful outcome after initial surgery? An explanation to the aforementioned question could be that during the initial procedure the

lesion site was not amply debrided. During BMS it is key that full debridement of the lesion site and/or possible (subchondral) cysts takes place.[15] Hereafter, adequate perforation of the sclerotic bone until bleeding needs to be achieved in order to facilitate sufficient bone filling and fibrocartilage formation.[15,16] Another reason for BMS failure could be the inadequate healing of the subchondral bone plate, which has been seen as a crucial structure for cartilage regeneration.[25,34] In the present study 77% and 91% of primary and secondary patients, respectively, were found to have a depressed subchondral bone plate at one-year follow-up. This may lead to decreased fibrocartilage vitality over time and could lead to failure of the procedure at mid- to long-term follow-up. Preoperative and postoperative imaging, utilizing CT-scans, is useful to determine lesion characteristics, arthroscopic access, and follow-up of the subchondral bone plate over time.[2,21] Moreover, even though arthroscopic BMS is considered a simple procedure, surgeons should be mindful that lesion location (especially posteriorly located lesions) and morphology can impact the surgical access and level of difficulty of arthroscopic BMS procedures.

Possible augmentation with adjunct therapies such as autologous platelet rich plasma (PRP) or bone marrow aspirate concentrate (BMAC) could further increase the clinical outcomes of BMS and might thereby increase the outcomes of repeat BMS cases.[11,14] This could increase its indication in the future as small OLTs may not warrant more invasive surgical treatments.

Return to Sports and Work

The return to sports rate for repeat BMS patients ranges from 38% to 67%, but is rarely reported.[22,32] This is in contrast to a systematic review by Steman et al.[36] which found 78% of patients treated with mostly primary BMS to return to pre-injury level of sports, while 18% had some limitations in sporting activities. The present study found a higher RTS rate for both primary and secondary cases. When considering the return to sports time the present study observed no statistical difference, but did find a clinically relevant sooner return to sports for primary cases. A possible hypothesis for the longer RTS time could be the increased rehabilitation time after a more extensive repeat arthroscopy due to increased synovitis and scar tissue formation from previous arthroscopic ankle procedures. From the available literature it is not evidently clear what the impact of repeat BMS is on return to sports compared to a primary procedure. All patients returned to work in this study. This is in accordance to findings from Ogilvie-Harris et al.[22], who reported a similar return to work time for all patients.

Radiological Outcomes

The subchondral bone plate has been identified to play an important role in osteochondral lesion healing as pain from an OLT arises from bony structures.[7] In the present study a high rate of subchondral bone plates were found to be depressed.

This was also the case for a number of patients who reported high NRS pain scores (during activities) pre- and postoperatively, and could thus be considered failed cases. Inferior healing or an irregular bone plate morphology may increase the likelihood for the development of osteoarthritis.[20] Additionally, deterioration of clinical outcomes over time because of the development of osteoarthritis - due to inferior wear characteristics of fibrocartilage - is a concern in the literature.[1,20,32] Further research into the long-term effect of both primary- and secondary BMS is needed to clearly establish the rate- and prognostic factors for osteoarthritis after an OLT.

Treatment Indication

Careful patient selection and education is critically important when considering secondary BMS for the treatment of OLTs as prognostic factors for successful outcome and long-term results have not yet been investigated. First, treatment indications for secondary BMS are similar to primary cases and are led by lesion- and patient factors.13 Thus, lesions under 15mm in diameter, non-cystic lesions, and non-fixable lesions should preferably be treated with secondary BMS.[13] Secondly, repeat BMS is a feasible option for patients with pain complaints and inability to work or participate in sports, who would benefit from surgical intervention but do not wish to undergo a more invasive procedure due to the risk of (long-term) complications and a relatively longer rehabilitation period. A personalized, evidence-based, approach is therefore needed when advising patients for the treatment of OLTs.[28]

Methodological Considerations

The results of this study should be interpreted in the context of its design. The present study included a limited number of patients as matching was based on secondary BMS cases. However, matching primary and secondary BMS cases ensured no significant patient- or lesion differences between groups were present in order to limit the effect of confounding covariates. Furthermore, the present study included a sufficient number of participants according to our power analysis. It must be stated, however, that this assumption cannot be made for the secondary outcome measures. Secondly, even though data was prospectively collected it was retrospectively analyzed. The results of the present study should therefore be interpreted carefully and in the context of the study design. Lastly, the present study had a follow-up of 1 year. As seen in previous literature, it may be that outcomes decrease over time.[37] It is therefore of interest to further follow-up these patients.

Clinical Relevance and Future Perspectives

The present study shows surgeons can consider repeat BMS for small OLTs and patients who do not wish to undergo a more invasive procedure. The treatment indication for failed primary OLTs may therefore increase in the context of individualized patient care. However, future research with larger sample sizes in a randomized controlled

setting or prospective cohort are highly needed, as limited evidence for secondary BMS exists.[18] The MCID in NRS can be used as a benchmark for further comparative research. Furthermore, studies assessing the effect of adjunct therapies and long-term follow-up outcomes are needed.

Conclusion

No differences in postoperative pain scores during activities at one year follow-up for primary (median NRS: 2) and secondary OLTs (median NRS: 3) treated with arthroscopic bone marrow stimulation were observed. Similarly, no significant differences in secondary clinical, sport, work, and radiological outcomes were found between both groups. Repeat BMS may therefore be a viable treatment option for, small (<15mm), failed OLTs. The indication for secondary BMS should be considered carefully by patients and surgeons.

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Chapter 5

Arthroscopic Bone Marrow Stimulation for Non-Primary Osteochondral Lesions of the Talus Yields Limited Improvements in Patient Reported Outcomes Compared to Primary Lesions: A Prospective 2-Year Follow-Up Study

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Abstract

Purpose: Our aim in this study was to prospectively assess the patient-reported clinical outcomes of arthroscopic bone marrow stimulation (BMS) for non-primary osteochondral lesions of the talus (OLT) and to compare these with primary cases at 2-year follow-up. The secondary aims were to assess the association of baseline factors with outcomes and the occurrence of adverse events.

Methods: Patients who underwent arthroscopic BMS were prospectively included and assessed up-to 2-years follow-up and were grouped according to non-primary (i.e., failed previous OLT surgery) or primary BMS. Patient-reported outcomes were collected at baseline and 2-years follow-up and included the Numeric Rating Scale (NRS) for pain and the foot and ankle outcome score (FAOS) questionnaires. The primary outcome was the improvement in NRS pain during walking, with a minimally clinical important difference (MCID) of 2.0. Adverse events concerned reoperations and complications during the study period.

Results: Forty-four patients were included, 25 patients in the primary group and 19 in the non-primary group. Both groups showed a statistically significant improvement in pain and functional outcomes from preoperatively to 2-years follow-up. The improvement in the primary outcome was significantly higher in the primary group (median 3 [IQR: 1 – 5] out of 10) compared to the non-primary group (median 1 [IQR: 1 – 3] out of 10), P= 0.01. Moreover, 68% (95%-CI: 46% - 85%) reached the MCID compared to 32% (95%-CI: 13% - 57%) in the non-primary group, which was statistically significant (P= 0.03). Baseline variables showed no consistent association with the primary outcome, except for a moderate correlation with age and lower improvements for patients who received concomitant surgery in the primary group. None of the changes in the FAOS sub-scales showed a statistically significant difference between the two groups. Two revision procedures (non-primary group: 11% [95-CI: 1% - 33%] versus 0% primary group, P=0.2) occurred in the non-primary group. During the study period 1 case (non-primary group: 5% [1% - 26%] versus primary group: 0%, P= 0.4) had a complication.

Conclusion: The most important finding of this prospective study is that arthroscopic BMS for non-primary OLT yields a significant improvement in patient-reported outcomes compared to baseline, but an inferior improvement compared to primary OLT at 2-year follow-up. On average, approximately two-thirds of BMS-treated primary OLTs reached the MCID compared with one-third in the non-primary group.

Keywords: Osteochondral Lesion Talus, OLT, Bone Marrow Stimulation, BMS, Non-primary

Introduction

Arthroscopic bone marrow stimulation (BMS) is the most common surgical treatment for small (<150mm^2), primary, osteochondral lesion of the talus (OLT).[8] Its advantages over other surgical options are its relatively less invasive nature, faster return to weightbearing and sporting activities, lower costs, no donor site morbidity, and technical simplicity.[11,14,26] The clinical results of arthroscopic BMS up-to mid-term follow-up are good and appear satisfactory at long-term follow-up.[8,20,27] Despite these positive results, a number of controversies surrounding BMS remain.

One such controversy is the use of BMS in non-primary OLT (i.e., failed prior surgical treatment).[1,10] Previous studies reported varying results from non-primary BMS, while (osteo)chondral replacement or chondrogenesis inducing techniques have reported good outcomes in non-primary lesions.[13,28] These techniques can be costly and relatively more invasive, however. Clinically, non-primary BMS may be an option in previously inadequately treated lesions and patients may benefit from its less-invasive nature and lower costs. A recent systematic review on non-primary BMS found only small improvements in patient outcomes, however, but the current literature consists of small (retrospective) non-comparative case-series.[1,13,19,23] There is, therefore, insufficient data to make an evidence-based statement on the indication and efficacy of arthroscopic BMS for non-primary OLT. Moreover, studying non-primary BMS could identify patients who may benefit from the procedure, thus expanding the treatment options for OLT patients.

The present study, therefore, aimed to prospectively assess the patient-reported clinical outcomes of non-primary BMS for OLT and to compare these with primary BMS cases at 2-year follow-up. The secondary aims were to assess the association of baseline factors with outcomes and the occurrence of adverse events. It was hypothesized that primary BMS would results in superior outcomes compared to non-primary BMS.

Methods

The present study is a prospective comparative study performed at a tertiary academic referral hospital specialized in the treatment of cartilage lesions in the ankle. The study was approved by the local medical ethics committee (reference number: W14_237#14.17.0288) and is in accordance with the declaration of Helsinki.

Patient Selection

Patients who underwent arthroscopic BMS (debridement and/or microfracturing) between March 2018 to July 2022 were prospectively assessed and included for the study according to the inclusion and exclusion criteria as reported in Table 1. Patients

were eligible for arthroscopic BMS in case of a symptomatic OLT unresponsive to non-operative treatment for a minimum of 3 – 6 months and counseled for surgery in a shared-decision making process. All patients provided consent before inclusion.

Table 1. Inclusion and Exclusion Criteria

Inclusion Criteria	Exclusion Criteria
- Patient who underwent arthroscopic BMS for a symptomatic OLT AND - CT-scan before surgical treatment	- Ankle osteoarthritis (> Cohen grade 2) at baseline on CT-scan - Concomitant osteochondral lesion of the tibial plafond - Systemic disease affecting the ankle; including rheumatoid arthritis and hemophilic arthropathy - Ankle fracture at baseline - Not able or willing to participate - Lost-to follow-up

Abbreviations: BMS = bone marrow stimulation, OLT, osteochondral lesion of the talus, CT = computed tomography.

Data Collection

Baseline demographic and surgical information was extracted from the electronic patient records using a predefined extraction form using CASTOR®. Baseline demographics included: sex, age, body mass index (BMI), traumatic injury etiology, smoking status, and any prior foot or ankle surgery. Treatment characteristics included arthroscopic approach (anterior, posterior, both), type of BMS (debridement alone or with microfracturing), any concomitant surgical intervention, and postoperative rehabilitation protocol.

Clinical Outcomes

Patient-Reported Outcome Measures

All patient-reported outcome measures (PROMs) were prospectively collected using the online CASTOR®-portal by a researcher not involved in clinical care. The primary outcome of this study concerned the improvement of the numeric rating scale (NRS) for pain during walking from baseline to 2-year follow-up. The NRS for pain ranges from 0 (no pain) to 10 (worst imaginable pain). Furthermore, the proportion of patients exceeding the minimal clinically important difference (MCID) of the primary outcome in both groups was calculated. The secondary PROMs concerned the NRS for pain during rest, running, and stairclimbing. Additionally, the foot and ankle outcomes score (FAOS) was collected. The FAOS is a functional outcome score and measures from 0 (lowest) to 100 (highest) and consists of 42 questions distributed among five subscales: symptoms, pain, activities of daily living, sport, and quality of life.

Adverse Events

Any postoperative complication or reintervention were prospectively collected in the electronic patient health records and reviewed. Reoperation was divided into revision surgery (any surgical intervention affecting the OLT) and reoperation for any other reason. Non-surgical interventions in the postoperative period were reported separately.

Radiological Assessment

Computed tomography (CT) scans were available for all patients at baseline and were assessed by two independent raters (Q.R. and J.D.) for lesion characteristics. The baseline assessment consisted of lesion size measurements (anterior-posterior direction, medial-lateral direction, and depth), lesion location according to Raikin et al.[15], and lesion morphology according to Rikken et al.[21] A pre-operative CT-based evaluation of ankle osteoarthritis grading was conducted according to Cohen et al.[5]

Statistical Analysis

A power analysis for the primary outcome indicated a minimum sample size of 13 cases was needed to detect a minimally clinical important difference (MCID) of 2.0 out 10 points (NRS during walking), assuming a standard deviation of 1.5 using a Wilcoxon rank-sum test with a 2-sided 0.05 significance level and 80% power (nQuery advisor 8.5.1, Statistical Solutions Ltd., Boston, MA).[22,28] To correct for a potential loss to follow-up of 20% the required minimum sample size for the present study was 16 cases. All data analyses were conducted using Stata 17 (StataCorp LP, College Station, TX). A two-sided level of $P < .05$ was considered significant. Baseline characteristics were reported in absolute numbers with percentages for dichotomous and categorical variables, and medians with inter-quartile ranges (IQR) for continues values. Normality of data was visually assessed and with a Shapiro-Wilk test. A Fishers' exact test and Mann-Whitney U test were used to compare baseline characteristics between the primary and non-primary groups. Patient-reported outcomes, including the primary outcome, were analyzed with a Mann-Whitney U test between the primary and non-primary groups. A Wilcoxon signed rank test was used when comparing baseline values to 2-year postoperatively within each group. The difference in proportions of MCID reached (including revision surgery as a failure) per group for the primary outcome, as well as the rate of adverse events, was assessed using a Fishers' exact test. A Wilson score method (without continuity correction) was used to calculate 95% confidence intervals (95%-CI) for these proportions. To assess the association of covariates with the primary outcome a spearman's rho test was used. The Spearman's rho was interpreted according to Schober et al.[25] Sub-analyses were performed on the primary outcome for non-continuous baseline variables in both groups, using a Fishers' exact test for binary variables and Kruskal Wallis test for ordinal variables > 2 groups.

Results

At final follow-up, 47 eligible patients were included in the study (Figure 1). Of these, 44 (94%) patients had a complete follow-up, and 25 patients were included in the primary group and 19 patients in the non-primary group. There were no significant differences in baseline patient and treatment characteristics (Table 2). In terms of lesion characteristics there was a significant difference in lesion morphology as well as the osteoarthritis grading between the two groups, see Table 3. Lesion localization is depicted in Figure 2.

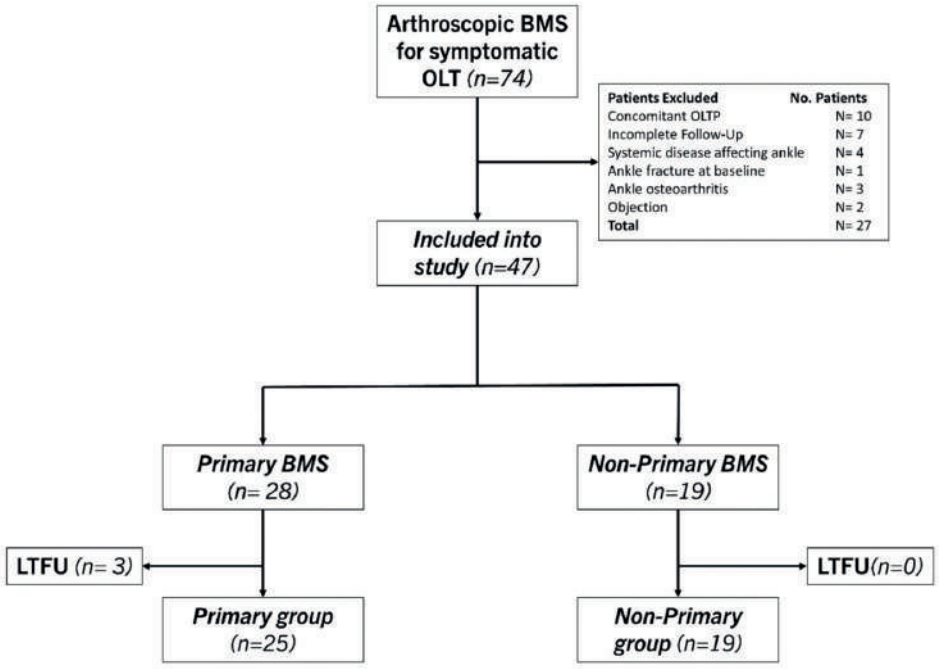

Figure 1. Flowchart of patient selection.

Table 2. Baseline Patient and Treatment Characteristics

Patient Characteristics	Primary Group (N= 25)	% reported	Non-Primary Group (N= 19)	% reported	P-Value
Sex, n (% male)	10 (40%)	100	12 (63%)	100	0.2
Age (years), median (IQR)	25.6 (19.0 – 36.5)	100	28.0 (23.8 – 33.6)	100	0.3
BMI (kg/m^2), median (IQR)	23.8 (21.6 – 24.5)	100	24.2 (21.2 – 26.6)	100	0.5
Smoking Status, n (%)		88		95	0.4
- Non-Smoker	20 (91%)		14 (78%)		
- Active Smoker	2 (9%)		4 (22%)		
Previous ankle trauma, n (%)		96		68	0.4
- Yes	20 (82%)		9 (69%)		
- No	4 (18%)		4 (31%)		
Specified (% of total no. trauma)					
- Sprain	13 (65%)		5 (56%)		
- Axial impact or fall from height	2 (10%)		0		
- Direct impact trauma	2 (10%)		0		
- Fracture	1 (5%)		1 (11%)		
- Mechanism Unknown	2 (10%)		3 (33%)		
Number of previous OLT procedures, n	N.a.		25	100	n.a.
Per patient, median (IQR)			1 (1 – 2)		
Specified in procedures (% of total)	N.a.				
- Arthroscopic BMS			21		
- Open BMS			1		
- Fixation			1		
- Autologous bone grafting			2		

Abbreviations: IQR: interquartile range, N: number of, BMS: bone marrow stimulation, BMI: Body mass index, N.a.: not applicable, OLT: osteochondral lesion of the talus, ATFL: anterior talofibular ligament, FHL: flexor hallucis longus.

Table 2. Continued

Treatment Characteristics	Primary Group (N= 25)	% reported	Non-Primary Group (N= 19)	% reported	P-Value
Surgical Approach, n (%)		100		100	0.4
- Anterior	23 (92%)		15 (79%)		
- Posterior	1 (4%)		1 (5%)		
- Both	1 (4%)		3 (16%)		
BMS technique, n (%)		100		100	0.9
- Debridement only	2 (8%)		1 (5%)		
- Debridement with microfracturing	23 (92%)		18 (95%)		
Concomitant Surgery, n (%)	14 (56%)	100	10 (53%)	100	0.9
Total no. of Specified per procedure (% total no. of)	16		12		
- Impingement removal – bony	6 (39%)		7 (58%)		
- Impingement – soft-tissue	1 (6%)		1 (8%)		
- Removal free body	4 (25%)		0		
- Duquenoy (open)	1 (6%)		1 (8%)		
- ATFL-repair (arthroscopic)	1 (6%)		0		
- Tightrope syndesmosis	1 (6%)		0		
- FHL-release	1 (6%)		1 (8%)		
- Excision posterior talar process	0		1 (8%)		
- Removal os trigonum	1 (6%)		1 (8%)		

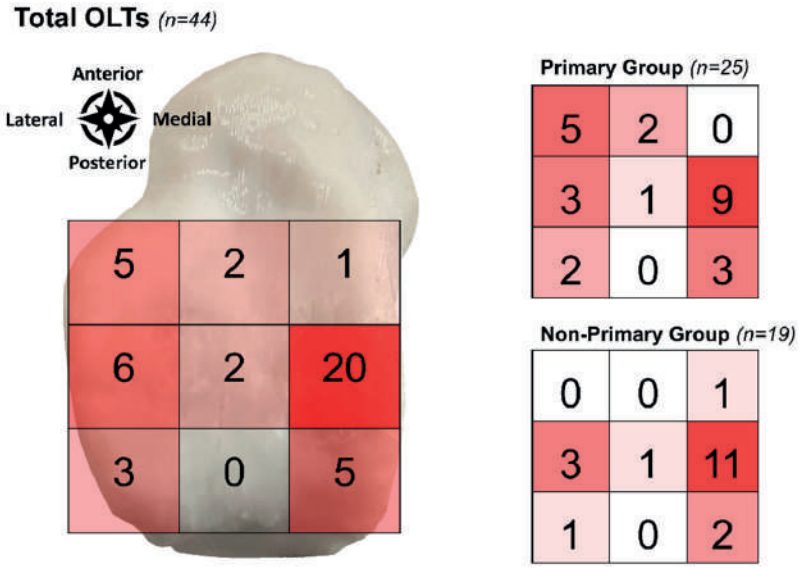

Figure 2. Lesion localization according to a 9-grid scale

Table 3. Baseline Lesion Characteristics

Lesion Characteristics	Primary Group (N= 25)	Non-Primary Group (N= 19)	P-Value
Morphology, n (%)			
- Cystic	9 (36%)	4 (21%)	**0.03**
- Crater	6 (24%)	12 (63%)	
- Fragment	10 (40%)	3 (16%)	
Size (mm), median (IQR)			
Anterior-Posterior	12 (8 – 15)	12 (9 – 15)	0.7
Medial-Lateral	8 (7 – 11)	8 (7 – 10)	0.4
Depth	6 (5 – 8)	5 (4 – 6)	0.3
Area (mm^2)	77.4 (50.6 – 113.8)	78.2 (66.4 – 123.2)	0.4
Pre-operative Ankle Osteoarthritis Stage[15]			
Median [IQR]	1 (0 – 1)	1 (0 – 1)	
Stage, n (%)			
- Stage 0	10 (40%)	2 (11%)	**0.04**
- Stage 1	12 (48%)	16 (84%)	
- Stage 2	3 (12%)	1 (5%)	
- Stage 3	-	-	
Osteophytes present, n (%)	15 (60%)	17 (89%)	**0.04**

Abbreviations: N: number of, mm: millimeters, IQR: inter-quartile range

Clinical Outcomes

The primary outcome, the NRS during walking, significantly improved from baseline to 2-years postoperatively in the primary group (median 5 [IQR: 3 – 7] to 1 [IQR: 0 – 2], P= <0.01) and the non-primary group (median 6 [IQR: 3 – 8] to 4 [IQR: 1 – 6], P= <0.01). The improvement of the primary outcome was significantly higher in the primary group (median 3 [IQR: 1 – 5] out of 10) compared to the non-primary group (median 1 [IQR: 1 – 3] out of 10), P= 0.01), Figure 3. Moreover, in the primary group 68% (95%-CI: 46% - 85%) reached the MCID compared to 32% (95%-CI: 13% - 57%) in the non-primary group, was statistically significant (P= 0.03).

In the analysis of association between baseline variables and the primary outcome it was observed that there was a moderate correlation ($\rho = 0.4$, $P = 0.04$) of age with the primary outcome in the primary group (see the Appendix). In the sub-analysis of the primary group there was a significant difference in the primary outcome for patients who had received concomitant surgery (see the Appendix). There were no other baseline variables associated with the primary outcome in both groups.

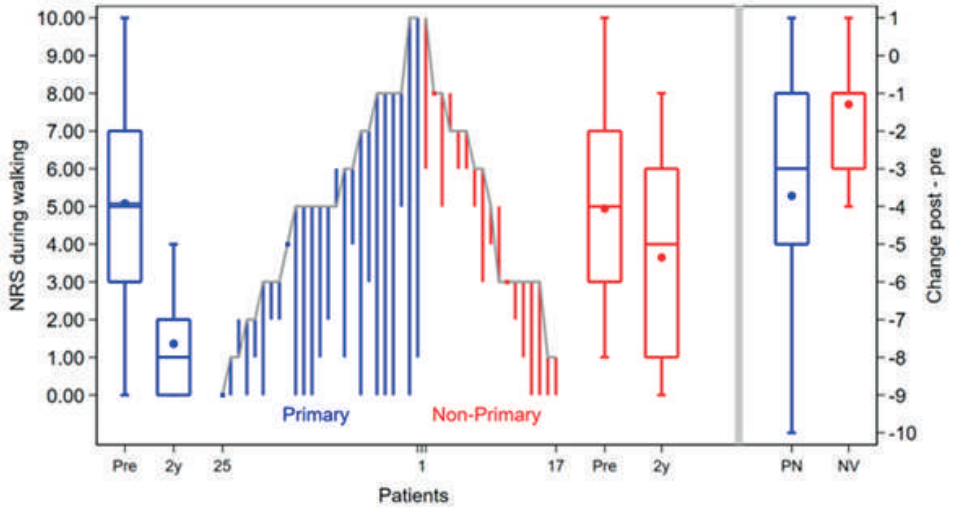

Figure 3. Depiction of the per case change of the NRS during walking from preoperatively to 2-year postoperatively for primary group (blue) and non-primary group (red). Boxplots depict the preoperative (pre) and 2-year postoperative (2y) outcomes on a group level (IQR indicated by a box with line as median value, mean is depicted as a dot in the box, and whiskers depict the absolute values). On the right the change on a group level from preoperative to 2-years postoperatively is depicted per group.

With respect to the secondary outcome measures, there was a statistically significant difference in the improvement of the NRS during stairclimbing, with the primary group (median: 4 [IQR: 1.5 – 7.5]) showing a higher improvement than the non-primary group (median 1.5 [IQR: -0.5 – 3.5], P= 0.04). None of the changes in the FAOS sub-scales from pre-operatively to 2-years postoperatively showed a statistically significant difference between the primary and non-primary groups. An overview of all PROMs is available in Table 4.

Adverse Events

During the study period a total of 3 reoperations occurred. From these 3 reoperations, 2 revision procedures (non-primary group: 11% [95-CI: 1% - 33%] and 0% primary group, P=0.2) occurred in the non-primary group. From these 2 revision surgeries, 1 case underwent an autologous osteoperiostic grafting from the iliac crest (TOPIC) procedure and 1 case had an autologous bone grafting procedure. There was 1 reoperation (nonprimary group 0% and primary group: 4% [1% - 20%], P=0.9) not pertaining to the OLT, which was the placement of an additional tightrope for symptomatic residual instability of the syndesmosis.

In the study follow-up period 1 case (non-primary group: 5% [1% - 26%] and primary group: 0%, P= 0.4) had a complication. This patient presented 2 weeks postoperatively with a blister from the pressure bandage which resolved uneventfully. Secondly, this patient had persistent pain from the saphenous nerve for which a multi-disciplinary pain treatment was undertaken, and the patient underwent bi-annual pulsed radiofrequency (PRF) treatment to alleviate symptoms. All other non-surgically related adverse events were reported in the Appendix in detail.

Table 4. Comparison of Clinical Outcomes for the Primary and Non-Primary BMS Group

	Primary Group (n= 25)			
	Preoperative	**2-Year Postoperatively**	**Improvement**	**P-Value**
NRS, median (IQR)				
Pain during walking	5 (3 – 7)	1 (0 – 2)	3 (1 – 5)	**<0.01**
Pain in rest	2 (1 – 4)	0 (0 – 1)	2 (0 – 4)	**<0.01**
Pain during running	7 (5.5 – 9.5) N=24	3 (0 – 5.5) N=24	3 (2 – 6) N=23	**<0.01**
Pain during stairclimbing	5.5 (3 – 8) N=21	0.5 (0 – 3) N=24	4 (1.5 – 7.5) N= 20	**<0.01**
FAOS, median (IQR)				
Symptoms	63 (44 – 79) N=24	68 (54 – 79) N=23	4 (-10 – 29) N= 23	0.1
Pain	63 (43 – 71) N=24	83 (69 – 94) N=23	22 (6 – 36) N= 23	**<0.01**
ADL	98 (97 – 100) N=24	100 (100-100) N=23	0 (0 – 2) N= 23	**<0.01**
Sport	45 (30 – 55) N=24	65 (55 – 95) N=23	25 (10 – 50) N= 23	**<0.01**
QOL	31 (19 – 41) N=24	53 (38 – 75) N= 22	19 (13 – 31) N= 22	**<0.01**

† Comparison of postoperative outcomes between primary and secondary group.
*2 patients underwent reoperation and were thus not included, otherwise a complete sample is available or a deviation mentioned in cursive text

Non-Primary Group (n= 19)				Between Groups†
Preoperative	**2-Year Postoperatively***	**Improvement***	**P-Value**	**P-Value**
6 (3 – 8)	4 (1 – 6)	1 (1 – 3)	**<0.01**	**0.01**
3 (2 – 5)	2 (0 – 3)	1 (0 – 3)	**<0.01**	0.4
7 (5 – 10) N=15	5 (2 – 10)	2 (0 – 5) N= 14	**<0.01**	0.2
5.5 (3 – 7) N=16	3.5 (0 – 6) N=14	1.5 (-0.5 – 3.5) N=12	0.1	**0.04**
46 (43 – 61)	54 (39 – 64)	4 (-7 – 11) N= 17	0.6	0.6
52 (42 – 69)	67 (56 – 89)	11 (3 – 19) N= 17	**0.03**	0.1
98 (97 – 98)	98 (98 – 100)	0 (0 – 0) N= 17	0.4	0.1
30 (15 – 45)	45 (35 – 60)	10 (0 – 30) N= 17	**<0.01**	0.2
31 (19 – 44) N= 18	38 (25 – 69)	6 (0 – 34) N= 16	**0.04**	0.2

Abbreviations: NRS: Numeric Rating Scale, AOFAS: American Orthopaedic Foot and Ankle Society score, FAOS: Foot and Ankle Outcome Score, ADL: Activities of Daily Living, QOL: Quality Of Life

Discussion

The most important finding of this study is that non-primary BMS for OLT yields a significant improvement in patient-reported outcomes compared to baseline, but a smaller improvement compared to primary BMS at 2-year follow-up. On average, approximately two-thirds of BMS-treated primary OLTs reached the MCID compared to one-thirds in the non-primary group. Revision procedures were infrequent in both groups; within the limitations of the sample size, we did not detect a clear difference in revision rates between primary and non-primary BMS.

Clinical Outcomes of Non-Primary BMS

The use of BMS for non-primary OLT is a topic of debate.[1,7,10] Recent systematic reviews have shown that BMS for non-primary OLT likely results in inferior clinical outcomes.[1,7] A limitation outlined in these studies is the level of evidence of these studies, which mostly consist of retrospective non-comparative case-series.[1,7] The largest study on non-primary BMS is the retrospective study by Yoon et al.[28], which compared clinical outcomes of 22 ankles that underwent non-primary BMS with 22 ankles that underwent autologous osteochondral transplantation (AOT) at 4.2-years follow-up. The authors of the aforementioned study reported significant improvements in pain (VAS) and functional (AOFAS) outcomes up-to 1-year follow-up but reported a deterioration of the results to baseline level outcomes at final follow-up. These results do not represent the findings of the present study. This difference may be explained by the inclusion of 32% large (>150mm^2) lesions in the study by Yoon et al., which all required revision surgery, and only 41% of cases being treated with microfracturing.[28] It could be hypothesized that the reasons for the reported limited outcomes following non-primary BMS are insufficient fibrocartilage formation or progressive degeneration, subchondral bone damage, and inherent (yet unknown) patient- or lesion factors that would preclude a successful result regardless of primary or non-primary BMS. Moreover, another reason could be that patients with pre-existing degenerative changes could benefit less from non-primary arthroscopic BMS. In this study the classification of pre-operative degenerative changes was not associated with lower PROM in the non-primary group, though these patients overall had a higher grade compared to the primary group. Current long-term literature does not support the progression to end-stage osteoarthritis following BMS in the majority of patients.[20] However, the grade of degenerative changes could be a predictive factor for the success of repeat BMS and should be studied further.

When directly comparing the outcomes of non-primary BMS to other surgical options for non-primary OLT, such as replacement or regenerative therapies, it is known from the limited literature that non-primary BMS may result in inferior outcomes.13,28 However, the associated morbidity, rehabilitation time, and costs of replacement and

regenerative therapies should be taken into account when considering the surgical options in non-primary OLT.[11,24,28] As such, non-primary BMS may be a beneficial treatment option in selected cases. First, non-primary BMS could reasonably be considered for small (< 150mm^2) OLT in patients who do not wish, or are not able, to undergo more invasive surgery (such as an autograft or allograft procedure), in healthcare systems where alternative options are not (financially) available, in cases of inadequate previous BMS, or in cases where other treatment options are contra-indicated. Second, physicians should incorporate the prognostic lesion- and patient characteristics currently known in the literature (e.g. as lesion size and location, the presence of cysts, smoking status, alignment, instability, and BMI) in their algorithm in order to evaluate the indication for non-primary BMS on an individual basis.[4,6,9,10,12,16–18] As such, the indication for non-primary BMS can be embedded in a patient-centered shared-decision treatment algorithm. Further prospective comparative studies with homogenous patient groups should evaluate the efficacy and longevity of non-primary BMS compared to replacement or regenerative treatment options. Clinically, a non-primary BMS procedure is considered it is paramount for physicians to clearly inform patients on the expected outcomes, where one could reasonably state that there is a limited improvement in pain and functional outcomes following BMS for a non-primary OLT based on the current literature.[1,7]

Another important aspect of the interpretation of the PROMs in the present study is whether patients sufficiently achieved the minimally clinically important difference (MCID). Although no formal MCID is available for the NRS (or VAS) in OLT patients, one could state that a MCID of 2 points on the NRS scale coincides with a "much better" improvement in pain.[22] When critically examining the results of this study, this change was observed in the majority of primary cases but not in the non-primary cases. A number of non-primary patients may be able to achieve this MCID, though limited evidence is available on prognostic factors which could predict achieving this threshold. Moreover, changing patient expectations and mental health outcomes could also affect this threshold. The expected outcomes for a patient could reasonably change within the setting of a 'simple' primary procedure compared to a recurrent OLT, where pain catastrophizing and patients' sports and/or work demands may change. This could also be a source of bias when comparing primary to non-primary cases.

Importance of Baseline Factors

One of the aims of this study was to investigate the association of baseline factors with clinical outcomes. Except for a moderate correlation between age and the primary outcome, and concomitant surgery showing better improvements, in the primary group it was found that no baseline patient- and lesion factors were correlated. The external validity of these findings is likely low due to underpowering and the findings

possibly being due to statistical chance. To date, there is no clear correlation between age and outcomes of BMS for OLT reported in the literature nor a clinically relevant cut-off.[2,10]

From the literature as a whole, it is reported by Yoon et al.[28] that there is a significant association between baseline lesion size and postoperative clinical outcomes. This is in alignment with numerous prior studies on BMS in primary OLT, establishing a relationship between lesion size and postoperative outcomes.[3,16] Another finding of interest is that we did not observe an association between the number of previous OLT surgeries and the amount of improvement in pain outcomes. The authors hypothesize that there may be a critical threshold for the number repeat BMS procedures for it to be clinically effective, and that these deteriorate over the number of subsequent procedures. An important note for the observed influence of baseline factors in this study, and the literature in general, is that there is likely underpowering of studies for the assessment of such factors.[1] Future efforts should, therefore, include larger sample sizes and possibly include (inter)national collaborative efforts to better identify patients who may benefit from repeat BMS.

Adverse Outcomes

The present study assessed the 2-year revision rate and observed that 2 cases (11%) in the non-primary group required revision surgery. Arshad et al.[1] reported a 34% (26 out of 77 cases reported) revision rate in their systematic review of non-primary BMS at a weighted average follow-up of 52 months (range of means: 12 – 154). The studies of Chuckpaiwong et al.[4] and Yoon et al.[28] largely (21 out 26 revision cases) contributed to this revision rate, which may be due to the prognostically poorer lesions characteristics included in both studies. In a recent study by Rikken et al.[18], which investigated the 10-year revision rate in 262 BMS cases (19% non-primary lesions), no increased revision risk for non-primary OLT was observed. In general, caution is warranted with the interpretation of the findings of this study and the present literature due to the relatively short follow-up and risk of bias, considering the variation in patient characteristics and study designs, respectively. Further evaluating the mid-term to long-term revision risk in non-primary OLT cases may assist in assessing its safety and clinical usefulness. When assessing the complications it was observed that 1 case had a nerve injury with persistent complaints. Nerve injuries are one of the most common complications following ankle arthroscopy and are often transient.[1,11] Additionally, 1 case required a reoperation not pertaining to the OLT. In general, it could be stated that in terms of safety non-primary BMS is not inferior to primary BMS.[1]

Methodological Considerations

This study has several strengths and limitations. First, it is a prospective comparative study that includes comparable patient groups. Second, a prospective sample size calculation was conducted for the primary outcome measure. Third, the lesion size measurements were conducted by two independent reviewers.

The limitations of this study are the loss to follow-up of 3 cases (6%), possibly including bias and a number of incomplete questionnaires, limiting the power of the analysis for the non-primary outcome measures. Secondly, the results of the secondary outcome measures and sub-analysis should be interpreted with caution, as the present study included a relatively low number of patients and may therefore be underpowered for these outcome measures. Third, there were several heterogeneities in the patient baseline factors, as well as varying concomitant surgical procedures which could have affected the outcomes. Fourth, the present study did not include an imaging analysis at follow-up.

Conclusions

The most important finding of this study is that arthroscopic BMS for non-primary OLT yields a significant improvement in patient-reported outcomes compared to baseline, but an inferior improvement compared to primary OLT at 2-years follow-up. Approximately one-third of BMS-treated primary OLTs reached the MCID compared to two-third in the non-primary group. The indication for non-primary BMS can be embedded in a patient-centered shared-decision treatment algorithm, where it is paramount for physicians to clearly inform patients on the expected outcomes.

Appendix

The appendix information can be accessed at: https://doi.org/10.1177/10711007251405240

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Part 3

Fixation for Osteochondral Lesions of the Talus

Chapter 6

Open Lift-Drill-Fill-Fix for Medial Osteochondral Lesions of the Talus: Surgical Technique

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Abstract

Objective: Osteochondral lesions of the talus (OLT) with a fragment on the talar dome, that fail conservative treatment and seek surgical treatment, can benefit from in situ fixation of the OLT. The advantages of OLT fixation include preservation of the native cartilage, high quality subchondral bone repair, and restoration of the joint congruency by immediate stabilization of the fragment. To improve the chance of successful stabilization an adequate lesion exposure is of critical importance, especially in difficult to reach lesions located on the posteromedial talar dome. In this study we describe the open Lift, Drill, Fill, Fix technique (LDFF) for medial osteochondral lesions of the talus with an osteochondral fragment. As such, the lesion can be seen as an intra-articular non-union that requires debridement, bone-grafting, stabilization, and compression. The LDFF procedure combines these needs with access through a medial distal tibial osteotomy.

Indications: Symptomatic osteochondral lesion with a fragment (≥10mm diameter and ≥3mm thick as per computed tomography scan) situated on the medial talar dome which failed 3-6 months conservative treatment.

Contraindications: Systemic disease, including active bacterial arthritis, hemophilic or other diffuse arthropathies, rheumatoid arthritis of the ankle joint, and malignancies. Neuropathic disease. End stage ankle osteoarthritis or Kellgren and Lawrence score 3 or 4.4 Ipsilateral medial malleolus fracture less than 6 months prior. Relative contra-indication: posttraumatic stiffness with ROM <5 degrees. Children with open physis: do not perform an osteotomy as stabilization of the osteotomy may lead to early closure of the physis, potentially resulting in symptomatic varus angulation of the distal tibia. In these cases, only an arthrotomy can be considered.

Surgical Technique: The OLT is approached through a medial distal tibial osteotomy, for which the screws are pre-drilled and, the osteotomy is made with an oscillating saw and finished with a chisel in order to avoid thermal damage. Hereafter, the joint is inspected and the osteochondral fragment is identified. The cartilage is partially incised at the borders and the fragment is then lifted as a hood of a motor vehicle (Lift). The subchondral bone is debrided and thereafter drilled to allow a thorough bone marrow stimulation (Drill) and filled with autologous cancellous bone graft from either the iliac crest or the distal tibia (Fill). The fragment is then fixated (Fix) in anatomical position, preferably with two screws to allow additional rotational stability. Finally, the osteotomy is reduced and fixated with two screws.

Postoperative Management: Casting includes 5 weeks of short leg cast non-weight bearing and 5 weeks of short leg cast with weightbearing as tolerated. At 10 week follow-up a CT-scan is made to confirm fragment and osteotomy healing, and patients start personalized rehabilitation under the guidance of a physical therapist.

Keywords: Osteochondral lesion; Talus; OLT; Fixation; Open

Introductory Remarks

Osteochondral lesions of the talus (OLTs) concern lesions of the articular cartilage in combination with the subchondral bone. Patients with a symptomatic OLT typically present with deep ankle pain, especially during or after weightbearing, and are not limited to swelling, range of motion restrictions, and locking of the ankle.[18] These complaints can have a significant impact on patients' ability to participate in sports and quality of life.[7] The first-line treatment for OLTs consists of conservative management, however, in up to 55% of patients conservative treatment fails and, ultimately, operative treatment is warranted.[1]

When considering surgical treatment for OLTs it is crucial to follow a patient individualized approach, incorporating patient and (morphological) lesion characteristics in determining the optimal treatment method.[18] In primary, non-cystic, lesions up to 10-15 mm in diameter, arthroscopic debridement and bone marrow stimulation is the preferred treatment method.[16] Alternatively, for larger (>15 mm diameter) and/or cystic lesions, autografting, scaffolding techniques, or allografting are available.[14,18] In case of an OLT with osteochondral fragment, fixation can be considered.[17] The theoretical benefits of fixation include the preservation of the native cartilage, high quality subchondral bone repair, and restoration of the joint congruency by immediate stabilization of the fragment.[6,15,17] Previously, the arthroscopic Lift, Drill, Fill and Fix (LDFF) technique was described as a promising fixation method and showed excellent results up to long-term follow-up.[6,17,19] OLTs that can be treated arthroscopically are usually located anteriorly.[9] However, even though lesions can be reached arthroscopically, incomplete access may impede the ability to effectively reduce and fixate the osteochondral fragment with perpendicular screw placement, which can lead to treatment failure.[12] Even more so, lesions located posteriorly are challenging to reach and fixate by means of anterior ankle arthroscopy, and it is known that more than half of OLTs are located on the posteromedial and centromedial zones.[3] In these lesions, an open technique could provide an alternative approach and excellent exposure to the talar dome, which is crucial for an effective reduction of the osteochondral fragment and prevention of union complications.[6,13,21] To date, however, the open LDFF approach for medially located OLTs has not yet been described and previous studies reporting on other means of open fixation of OLTs have not specifically focused on this surgical technique.[8–11,20] A clear surgical description for fixation of OLTs will aid surgeons in expanding their treatment options tailored to individualized cases. The purpose of the present surgical technique paper is to therefore describe the open LDFF surgical technique for symptomatic medial fragmentous osteochondral lesions of the talus.

Surgical Principles and Objectives

Primary acute and chronic osteochondral lesions of the talus with a fragment with a minimum diameter of 10 millimeters (mm) and 3mm depth on computed tomography (CT-scan) are suitable candidates for fixation with this technique, as it allows for immediate stabilization of the fragment and restoration of the talar congruency, preservation of the native hyaline cartilage, and the initiation of subchondral bone plate healing.[6,17] The four step *Lift-Fill-Drill-Fix* approach aims to provide both biological healing by the introduction of marrow cells as well as stable biomechanical fixation to allow for optimal union of the fragment and subchondral bone plate healing. In essence, the LDFF can be seen as an intra-articular non-union repair with debridement, bone-grafting, which provides stability and compression. Access to the talar dome can be obtained for lesions located medially through a medial distal tibial osteotomy, which allows for adequate working space and correct screw placement.

Advantages

- Preservation of the hyaline cartilage.
- High quality subchondral bone repair by bone marrow stimulation and additional cancellous bone grafting.
- Excellent exposure.
- No harvest site complications with distal tibia grafting, minimal harvest site complications in iliac crest grafting.
- Other surgical salvage options remain possible in case of failed fixation

Disadvantages

- Access through distal tibia osteotomy.
- Potential hardware complications which may lead to the need for hardware removal procedure.

Indications

- Symptomatic osteochondral lesion with a fixable fragment situated on the medial talar dome with a minimum size of >10mm diameter and 3mm in depth measured on CT-scan.[17]

Contraindications:

- Systemic disease, including active bacterial arthritis, hemophilic or other diffuse arthropathies, rheumatoid arthritis of the ankle joint, and malignancies.
- Neuropathic disease.
- End stage ankle osteoarthritis or Kellgren and Lawrence[4] score 3 or 4.
- Ipsilateral medial malleolus fracture less than 6 months prior.
- Relative contra-indication: posttraumatic stiffness with ROM <5 degrees.
- Children with open physis: do not perform an osteotomy as stabilization of

the osteotomy may lead to early closure of the physis potentially resulting in symptomatic varus angulation of the distal tibia. In these cases only arthrotomy can be considered.

Patient Information

- Surgical risks include infection, hematoma, thromboembolic events, wound healing problems, and transient or permanent nerve damage leading to hypaesthesia of the saphenous nerve.
- Non-weightbearing cast for 5 weeks, followed by a walking boot for another 5 weeks. Hereafter, patient individualized rehabilitation 3-6 months after cast removal guided by a physical therapist .
- Late or early screw discomfort requiring removal after consolidation.
- Adverse treatment events include fragment delayed- or non-union, or osteotomy delayed- or non-union.

Preoperative Work-Up

- Clinical evaluation, including patient history and physical examination is performed for all patients at the outpatient clinic in order to assess symptoms befitting an OLT. Additionally, care is taken to assess any relevant coexisting pathologies of the foot and ankle which may warrant treatment, such as symptomatic ankle instability which is frequently encountered in patients with OLT.[2,22]
- Radiological assessment of the lesion is preferably carried out through a pre-operative computed tomography (CT) scan to assess the three-dimensional lesion and fragment size, lesion location, as well as the lesion and fragment morphology.
- Additionally, the CT-scan is used for pre-operative planning in order to determine the surgical approach and osteotomy orientation based on the lesion location as well as to assess the need for additional debridement and filling of possible cysts situated below the osteochondral fragment. In case additional cancellous bone is required in order to fill the lesion site before fixation cancellous bone grafts can be obtained from the distal tibial metaphysis after osteotomy, or the iliac crest as described in a previously published surgical technique.[5]
- Lastly, clinical and radiographic work-up by means of weightbearing x-ray should be conducted in cases of suspected hindfoot malalignment as it may be necessary to address these concomitantly.[18]

Instruments and Implants

- Standard orthopaedic set
- Hohman retractors
- Bone rongeur
- Oscillating saw

- Chisel set (including thin blades)
- 2.0mm Kirschner wires
- 2.0mm drill
- Coagulation knife
- 3.5mm cortical screws or a headless alternative
- Large Weber clamps
- Screw or biomaterials for fragment fixation, not limited to, but options including depending on fragment size and surgeon preference:
  - » Bio-Compression screw 2.7mm (Arthrex Inc., Naples, USA) or poly-L-lactide pins (GRAND FIX, Depuy)
  - » Autologous bone pegs harvested from the distal tibia
  - » (multiple) chondral darts 1.3mm (Arthrex Inc., Naples, USA), to be used only as an anti-rotational post, a dart will not give sufficient compression in itself.
  - » Self-tapping 2.0 or 2.7mm cortical screw (Johnson & Johnson, New Brunswick, USA)

Anaesthesia and Positioning

- General or spinal anaesthesia.
- Patients are placed in a supine position with a thigh tourniquet ipsilaterally.
- Preoperative antibiotic prophylaxis with two grams (or adjusted to weight) of Cefazolin is administered intravenously.

Surgical Technique

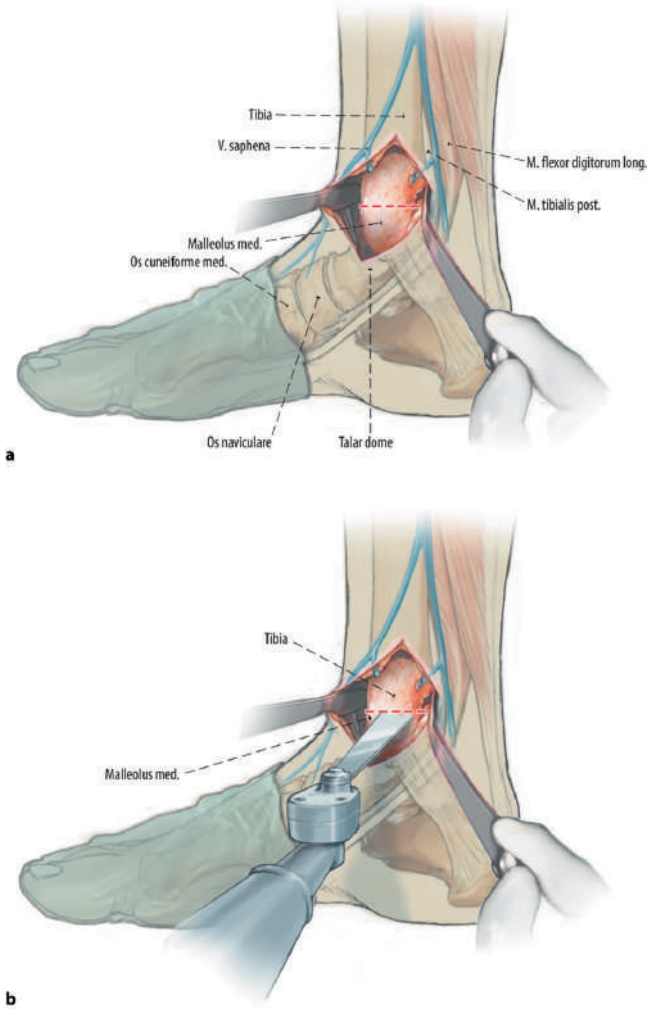

Figure 1. After patient positioning, the work field is carefully prepared by sterile draping of the ankle. The first step is the medial distal tibial osteotomy: an incision is centered over the medial malleolus of approximately 7 cm and lightly curved anteriorly. The large saphenous vein is identified and protected. The arthrotomy is performed anteromedially with a partial resection of the anteromedial joint capsule. In case any anterior distal tibial or anterior medial malleolar osteophytes are present, these are resected using a bone rongeur. Thereafter, the posterior retinaculum of the posterior tibial tendon is released, which is then retracted posteriorly to allow for a limited posteromedial capsule resection. Hohmann retractors are placed both anteriorly and posteriorly of the medial malleolus to protect the tendons and neurovascular

structures (a). A rolled sterile surgical gown is placed underneath the distal tibia, to allow for the neurovascular structures to move dorsally in order to protect these when performing the osteotomy. Next, when there is good visualization on the extent of the medial distal tibial osteotomy, two cortical lag screw (3.5 mm) holes are predrilled in divergent bicortical manner and measured in anatomical position. Afterwards, the osteotomy is performed with an oscillating saw (b). As previously stated, the direction and extent of the osteotomy is determined by the location and size of the osteochondral lesion during preoperative planning. The osteotomy is performed up to around 3 mm from the joint surface and finalized with a broad chisel to avoid (thermal) damage to the surrounding cartilage of the tibial plafond.

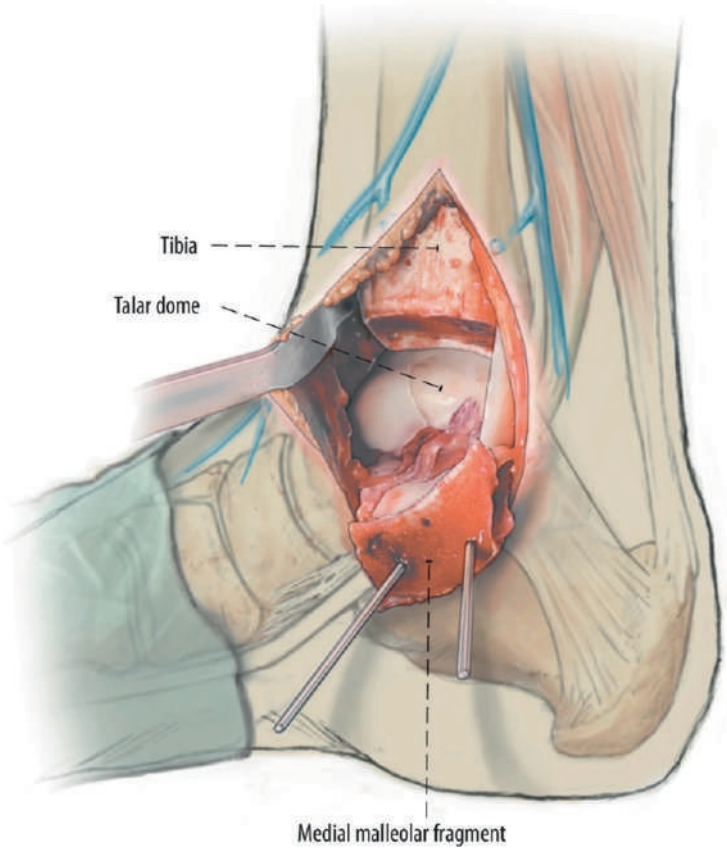

Figure 2. When the osteotomy is completed, the osteotomy site is opened by dislocating the distal tibial fragment of the medial malleolus and fixating it in a plantar and medial direction on the talar body with one or two 2.0 mm Kirschner wires providing stable access to the medial and central talar dome. The Kirschner wires are placed through the drill holes of the osteotomy fixation screws.

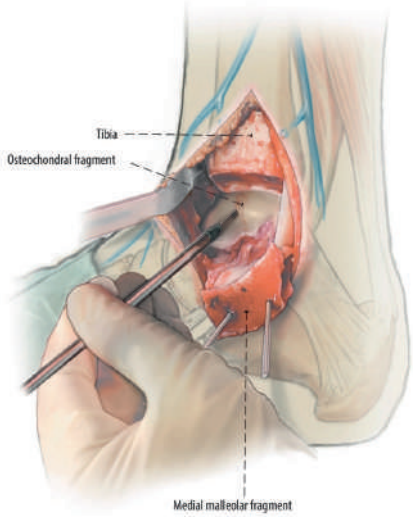

Figure 3. After the osteochondral lesion is identified and inspected, a sharp incision in the cartilage is preferably created with a beaver knife because this allows nice round corners (or any other scalpel to the surgeon's preference) and a clean lift of the fragment. A semilunar incision is made around the defect, leaving the posterior side of the osteochondral fragment intact if possible. Leaving the posterior side intact provides additional rotational stability and facilitates using only 1 screw in smaller fragments. Of note: in case a fully detached fragment is present, this step is not relevant.

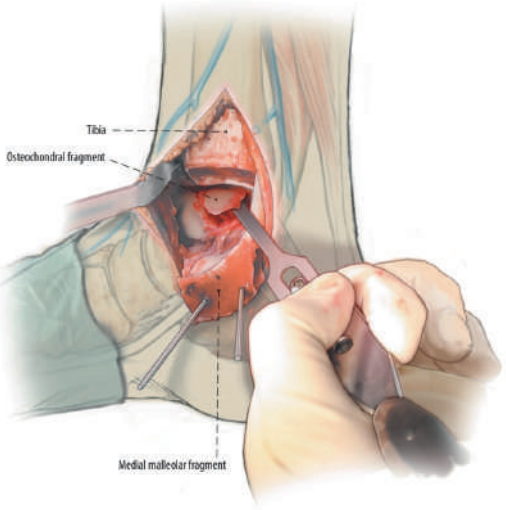

Figure 4. The flap can now be lifted (lift) from anteriorly with the use of a chisel. In case the fragment is completely detached in situ before the semilunar incision it is carefully excised and preserved.

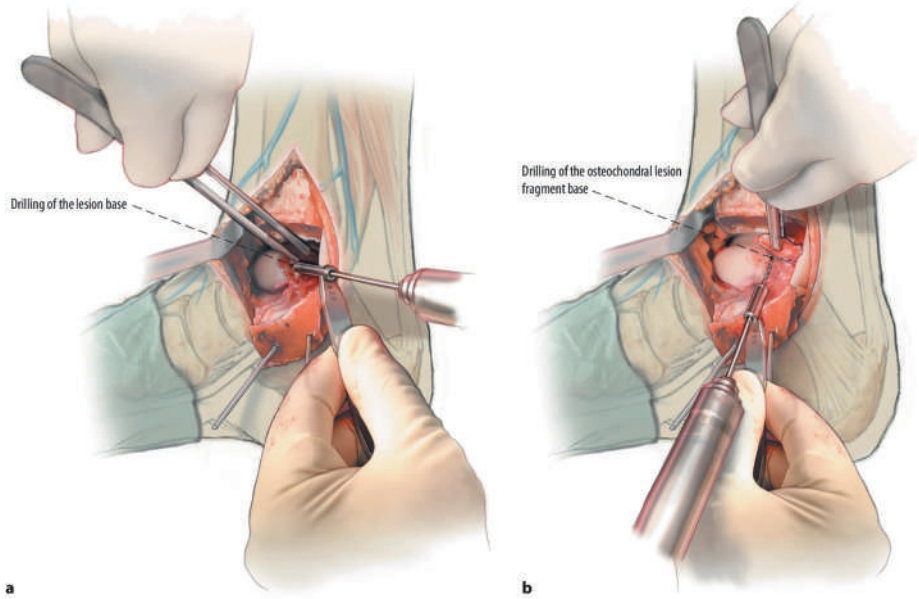

Figure 5. a,b; After lifting or excision of the osteochondral fragment, the subchondral bone is inspected. Promotion of revascularization is key for the surgery to succeed, so all osteosclerotic areas should be diligently debrided, any subchondral cysts should be circumferentially curetted, and the bottom of the surface of the cyst as well as the bony part of the osteochondral talar fragment should be drilled (drill) to stimulate underlying bone marrow.

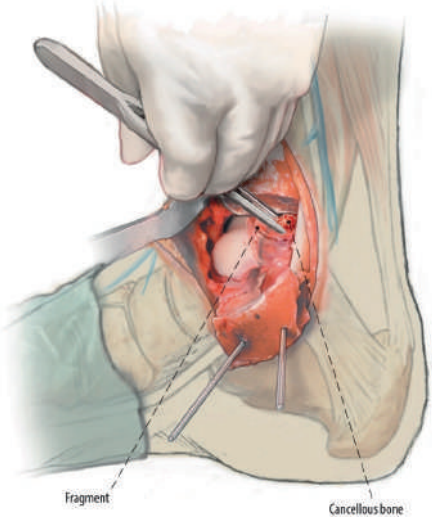

Figure 6. The remaining lesion site after debridement and drilling is filled (fill) with autologous cancellous bone harvested from the (exposed) distal tibial metaphysis with a chisel or the iliac crest as described in a previously published surgical technique.[5]

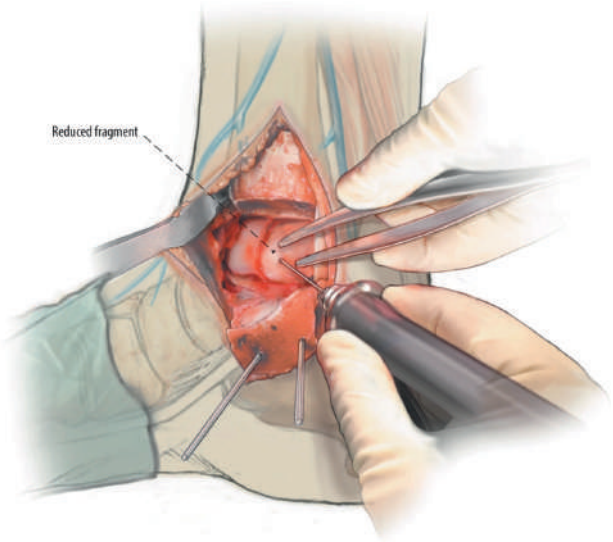

Figure 7. After filling of the defect, the osteochondral flap is reduced to its original position and fixated (fix) with a bio-compression screw (Arthrex Inc., USA), poly-L-lactide pins (GRAND FIX, Depuy, USA), or a self-tapping 2.0 or 2.7 mm cortical screw (Johnson & Johnson, USA). Chondral darts (Arthrex Inc.) or bone pegs can be considered in the case of a smaller fragment, or multiple smaller fragments, amendable for fixation.

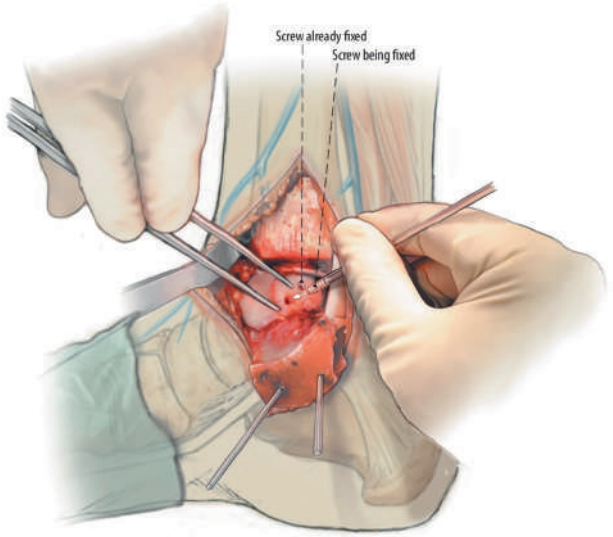

Figure 8. In case of smaller fragments (i.e., < 15 mm diameter), a single screw, centred with adequate compression for good stabilization of the fragment, is placed centrally of the fragment and perpendicular to the lesion site axis. In case of a larger fragment multiple screws can be considered in similar perpendicular orientation to the lesion axis in order to provide rotational stability of the fragment as well

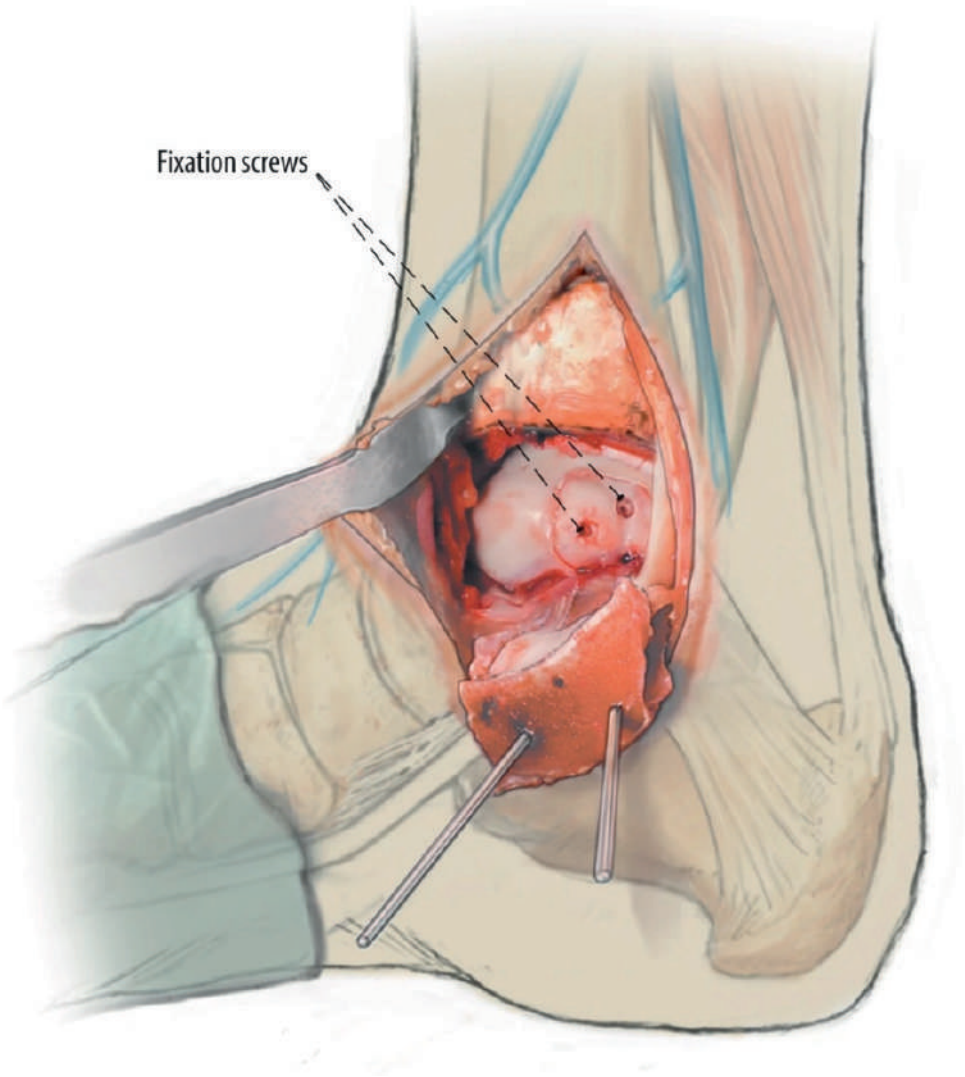

Figure 9. It is important to let the fragment sink discretely (0.5 mm to 1 mm) under talar articular cartilage and to place the fixation screws under this surface to prohibit damage by the screws or darts on the distal tibial articular surface. If a stable fragment reduction and fixation is achieved the joint is carefully inspected and flushed using saline.

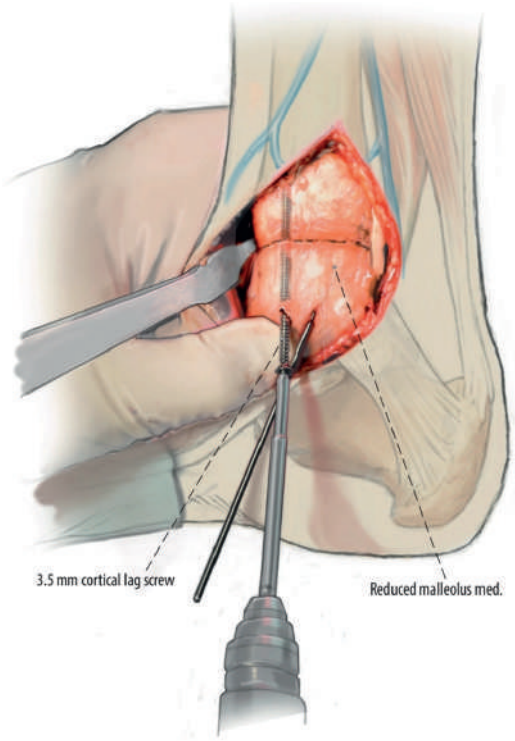

Figure 10. Finally, closure of the osteotomy site is performed. The Kirschner wires are removed, and the medial malleolus is placed in anatomical position and reduced. The two premeasured 3.5 mm cortical lag screws are divergently placed to fixate the osteotomy site and to allow distal tibial bone grafting from the tibial proximal between the two screws. If a large osteotomy was performed, an additional anti-glide plate (1/3 tubular plate) can be added to provide additional rotational and translational stability of the osteotomy. An alternative to the anti-glide plate could be a third cortical lag screw placed transversely in the proximal apex of the osteotomy for additional shear stability. The reduction of the medial distal tibial osteotomy is assessed by means of fluoroscopy.

Special Surgical Considerations

Osteotomy

The authors would like to note that osteotomy choice is surgeon specific and may also include a lateral directed chevron-like osteotomy.

Grafting

During the filling of the OLT this surgical technique describes the usage of autologous cancellous bone harvested from the ipsilateral distal tibia osteotomy site or iliac crest in case a larger quantity of cancellous bone is needed to a large defect site. Graft choice is surgeon specific.

Postoperative management

- A short leg cast is applied with non-weightbearing for 5 weeks postoperatively and antithrombotic prophylaxis is prescribed for this period. All casts are set in neutral flexion and hindfoot position. One to two weeks postoperatively the non-weightbearing casts consists of a splint to allow for swelling, followed by a circular cast for the remaining time of immobilization. The sutures are removed at two weeks postoperatively combined with a change of the short leg cast.
- At 5 weeks postoperatively the non-weightbearing cast is exchanged for a short leg walking cast and weightbearing is allowed as tolerated. This cast is applied for 5 weeks.
- Radiographic follow-up with conventional AP and lateral X-rays is performed at 5 weeks postoperatively before protected weight- bearing is commenced to reaffirm positioning of the osteotomy. At 10 weeks and 1-year postoperatively a CT-scan is performed in order to assess osteotomy, fragment consolidation and cyst formation or onset/progression of osteoarthritis (Figure 11).
- After casting, a patient centered rehabilitation protocol is started, guided by a physical therapist in order to regain range of motion and muscle strength of the ankle, as well as a normal gait pattern.
- Clinically, the patient is assessed postoperatively. We recommend a follow-up visit at two, six, and twelve weeks postoperatively for casting, wound healing, and osteotomy / fragment union consolidation, as well as 6 months and 1 year postoperatively for physical follow-up.

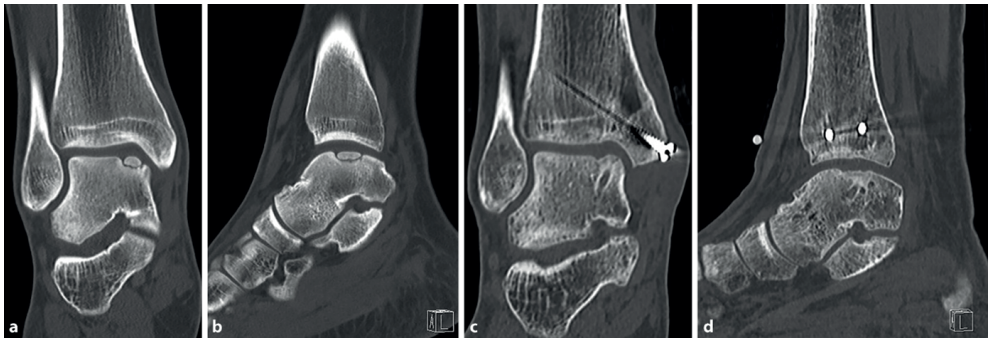

Figure 11. Preoperative (a,b) and 1-year postoperative (c,d) CT scan of LDFF in a large OCL with a fragment. Two bioabsorbable screws were used to achieve a stable fragment fixation as a whole. At 1-year postoperatively, good union of the fragments and consolidation of the osteotomy had occurred. Of note, the postoperative radiolucency below the fragment is the bioabsorbable screw.

Errors, Hazards, Complications

Preoperative Planning:

- No available CT-scan within 1 year of surgery could yield inadequate information regarding the morphology or size of the OLT and osteochondral fragment.
- Surgical Technique:
- Inadequate exposure.
- No perpendicular screw fixation leading to shallow insertion angle and inadequate compression of the fragment; leading to a higher chance of delayed- or non-union.
- Screw size unfit for the fragment size; causing the fragment to break in smaller fragments requiring a salvage procedure (i.e., other OLT surgical treatment) or inadequate compression in larger fragments.
- Fragment stabilization too proud (i.e., above the articular cartilage); leading to (early) wear of tibiotalar cartilage.

Postoperatively:

- Weightbearing too early postoperatively leading to higher risk of osteotomy or fragment non-union or pseudoarthrosis; possibly requiring revision surgery with a non-union repair of the osteotomy.
- No 10-week postoperative CT-scan to assess union of the fragment and osteotomy, which could lead to too early weightbearing and a higher risk of non-union.

Post-operative complications:

- Infection, hematoma, thromboembolic events, wound healing problems, and transient or permanent nerve damage leading to hypaesthesia of the saphenous nerve, delayed- or non-union of the osteotomy or fixed fragment.

Results

This study was approved by the local medical ethics committee of the University of Amsterdam (Reference number: 08/326). All patients who underwent an open LDFF procedure with a medial distal tibial osteotomy for a symptomatic primary OLT with an osteochondral fragment from January 2017 until January 2021 were prospectively followed up until 2-years. Fourteen patients with a total of 15 ankles (one bilateral case) were eligible and included at a mean age of 24 (range: 14 – 46) years. 7 patients were male and 7 were female. Pre- and postoperative outcome assessment was performed with the Numeric Rating Scale (NRS) for pain during rest and walking as well as with the American Orthopaedic Foot and Ankle Society (AOFAS) Ankle-Hindfoot score. Radiological assessment was done with a 3 months CT-scan to assess osteotomy union and 1-year follow-up CT-scan to assess fragment union. Lastly, post-operative complications, reoperations, and revision surgeries were assessed.

At final follow-up, 13 out of 14 patients (with 14 out of 15 ankles) were available, and one patient was lost to follow-up. The baseline NRS for pain at rest significantly improved from a median 4 out of 10 (IQR: 3 – 5) to 0 out of 10 (IQR: 0 – 2) at 2-year follow-up (P= <0.05). Moreover, the NRS during walking improved from a baseline median 7 out of 10 (IQR: 6 – 7) to 1 out of 10 (IQR: 0 – 4) (P= <0.05). The AOFAS score improved from a median 61 out of 100 (IQR: 48 – 68) at baseline to 95 out of 100 (IQR: 76 – 100) at follow-up (P= <0.05). All osteotomies showed union at follow-up CT scans. 14 out of 15 ankles showed union of the osteochondral fragment on 1-year CT scans. At 2-years follow-up, 9 patients had undergone a reoperation, of which 8 patients underwent removal of medial distal tibial screws, with two patients additionally undergoing an osteophyte removal and soft-tissue impingement, respectively. One patient had a revision procedure by means of a TOPIC autologous bone grafting for recurrent OLT and non-union of the fragment.[5] Apart from the one patient who had a non-union of the osteochondral fragment no postoperative complications were noted.

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Chapter 7

Open Lift, Drill, Fill and Fix For Chronic Osteochondral Lesions of the Talus: Favorable Two-Year Clinical Outcomes

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Abstract

Background: In the presence of an osteochondral fragment with sufficient subchondral bone thickness fixation is considered to be an effective treatment method for osteochondral lesions of the talus (OLT). One such a fixation technique is the Lift-Drill-Fill-Fix (LDFF) procedure, which has shown reliable long-term results in an arthroscopic approach, however, the outcomes in cases treated through an open approach are unknown.

Purpose: To assess the 2-year outcomes following open LDFF for chronic OLTs.

Study Design: Prospective Case-Series

Methods: Thirty-four patients who underwent an open LDFF procedure for chronic (>6 weeks) OLT were prospectively followed for 2-years. The primary outcome concerned the comparison in numeric rating scale (NRS) (0 no pain – 10 most severe pain) of pain during walking between the preoperative score to the 2-year postoperative follow-up score. The association of baseline factors with the change in the primary outcome between baseline and 2-year follow-up was assessed. Secondary patient-reported outcome measures (PROMs) were the Foot and Ankle Outcome Score (FAOS) and Short-Form (SF)-36. The fragment union rate on 1-year follow-up computed tomography (CT) scans and the influence of possible baseline factors on union was assessed. Adverse events, including revision surgery and complications were assessed and documented.

Results: The primary outcome significantly improved from a median of 6 (IQR: 4 – 7) out of 10 preoperatively to 1 (IQR: 0 – 3) out of 10 at final follow-up, P= <0.01. There was no association between baseline factors (sex, age, body mass index (BMI), smoking status, lesion size, and location) and change in primary outcome between baseline and 2-year follow-up. All other PROMs significantly improved, except for the SF-36 mental component scale. The fragment union rate was 91% [95%-CI: 76 – 98]. BMI ≥ 30 kg/m2 was significantly associated with fragment non-union (OR: 1.39 [95%-CI: 1.04 – 1.84], P=0.02). Three patients underwent revision surgery while 2 complications (1 case of delayed superficial wound healing and 1 case of complex regional pain syndrome) were observed.

Conclusions: Open LDFF results in favorable patient-reported outcomes for chronic OLT up-to 2-year follow-up. The procedure achieves a 91% fragment union rate while patients with obesity showed a higher risk of fragment non-union.

Introduction

Osteochondral lesions of the talus (OLT) concern a disruption of the articular cartilage and the underlying subchondral bone. Such lesions may cause complaints of pain during activities such as sports.[25] The current treatment of symptomatic OLT is based on a patient- and lesion-specific treatment algorithm and consists of non-operative and operative treatment options.[25] Important factors for the treatment decision are the lesion morphology and size.[21,25]

A distinct morphological OLT type is the presence of an osteochondral fragment.[28] In such lesions with an osteochondral fragment the articular cartilage can be intact, though the subchondral bone is compromised.[15] Fixation techniques were developed to exploit this opportunity as they aim to retain the native hyaline cartilage, stabilize the osteochondral fragment through direct fixation, and restore the joint congruency.[22,28] A recent systematic review found that fixation techniques for OLT show good clinical results, with high union rates and low revision rates.[24]

One such fixation technique is the Lift-Drill-Fill-Fix (LDFF) technique. This technique is tailored to chronic lesions, which can be seen as an intra-articular non-union. They require subchondral bone repair through drilling of the lesion site, autologous bone grafting and subsequent fixation (compression).[9,12,27] The LDFF technique was initially introduced as an arthroscopic technique, which showed good mid-term results that were retained up-to long-term follow-up.[12,26] A limitation of the arthroscopic technique is the accessibility to centrally and posteriorly located OLT, especially on the medial side, or lesions too large to fix arthroscopically. A difficult to reach or inaccessible lesion may lead to inappropriate screw placement, peri-screw cysts, and insufficient stability following fixation.[9,17] Moreover, it is known that the majority of OLT are located on the central or posterior medial talar dome.[5] Therefore, an open version of the LDFF technique was developed, which showed promising clinical results in a sample of 13 patients.[27] The mid-term outcomes of the open LDFF technique remains to be elucidated, however.

As such, the primary aim of the present study was to assess the 2-year prospective patient-reported clinical outcomes following open LDFF for chronic OLT with an osteochondral fragment. Secondarily, this study evaluated the radiological outcomes and adverse events. It is hypothesized that the open LDFF technique leads to an improvement in 2-year patient-reported outcomes with a high union rate of the fixed fragment.

Methods

Study design

This study is a prospective, single-center, case series with 2-year follow-up. The study was approved by the local Medical Ethics Committee at Amsterdam UMC, location AMC with reference number W14_237#14.17.0288, and was performed in accordance with the current ethical standards (Declaration of Helsinki).

Patient selection

All prospectively followed patients who had a symptomatic chronic OLT with osteochondral fragment, confirmed per CT-scan, and who were treated with LDFF through an open approach from July 2015 to July 2022 were assessed for the inclusion and exclusion criteria (Table 1). The indication for an open medial LDFF procedure is a symptomatic chronic osteochondral fragment of the medial or central talus, eligible for in-situ fixation (≥10mm diameter and ≥3mm thick as per CT-scan), that fails 3-6 months of non-operative treatment.[27] The contra-indications were previously described.[27] Laterally located OLT treated by LDFF adhered to the same indication criteria, except for the omitted contra-indication of open physis. The decision for an open approach was made on surgeon discretion and based on pre-operative planning (ankle range of motion and evaluation of the lesion [size and location] and bony structures on CT-scan) to establish if an open approach was necessary for sufficient access to the lesion for successful fixation. The study site concerned a tertiary academic referral hospital which is recognized as an expert center in the diagnosis and treatment of OLT.

Table 1. Inclusion- and Exclusion Criteria

Inclusion criteria	Exclusion criteria
- Symptomatic chronic osteochondral fragment of the talus, eligible for in-situ fixation[27], failing of 3-6 months non-operative treatment	- Patients presenting with a symptomatic acute lesion (<6 weeks after clearly identifiable trauma) requiring immediate fixation - Concomitant ankle or hindfoot fracture at the time of the LDFF surgery - Severe developmental disorder of the foot and ankle - Patients unwilling or unable to participate

Abbreviations: AP=anterior-posterior; LDFF=Lift, Drill, Fill and Fix; ML=medial-lateral; OLT = osteochondral lesion of the talus

Surgical technique

The surgical technique for the open LDFF procedure was previously described in detail for medial or centrally located OLT.[27] In summary, the joint is accessed either through a medial arthrotomy or distal tibial osteotomy. In case of a lateral OLT, an anterolateral arthrotomy was performed where it was necessary to release the anterior talofibular ligament (ATFL) or perform an osteotomy of the distal fibula in order to achieve good visualization of the affected part of the talus, as previously described.[4] After identification of the osteochondral fragment the articular cartilage around the fragment is partially incised to allow of lifting of the fragment (Lift). The subchondral bone is debrided and drilled for marrow stimulation (drill), whereafter the autologous bone graft from the distal tibia (osteotomy) or iliac crest used to fill the site (fill). Hereafter, the fragment is anatomically fixed and compression and rotational stability is provided by preferable two screws (and/or darts). In the initial experience the senior authors utilized metallic screws but based on clinical experience opted to later use headless bio-absorbable screws and/or chondrodarts. This was chosen to reduce the risk of screw migration and cartilage wear on the opposing distal tibial articular surface.

Postoperative management

Postoperatively, patients were immobilized in a non-weightbearing lower leg cast for 5 to 6 weeks and were provided crutches. At 2 weeks postoperatively a cast change, wound assessment, and removal of stiches was performed. After the initial 5 to 6 weeks of non-weightbearing casting the patient was moved to a walking cast for another 5 to 6 weeks with gradual build-up of loading as tolerated up-to 100% of body weight. The total 10 weeks of casting was later introduced in the study based on expert-opinion and previous experience of the treating surgeons.[7] This protocol was applied in the last 6 consecutive patients. The previous patients from the start of the study all underwent a total of 12 weeks of casting. All patients underwent a CT-scan following the 10 or 12 weeks of casting to assess consolidation of the medial malleolus osteotomy and fragment union. Additionally, all patients were referred to a physiotherapist for a rehabilitation program. Such a program concerned a phased and personalized rehabilitation protocol. This means that patients first had to regain range of motion, a normal walking pattern, neuromuscular control and joint stability. Hereafter, patients progressed to strength and further stability training, and to sports/ activity specific training with the eventual goal to return to a desired level of activities.

Data Collection

Patient and treatment characteristics at baseline were collected from the hospital electronic patient records. Data extraction was performed by using a pre-defined excel extraction format. Baseline patient characteristics included: sex, age, body mass index (BMI), smoking status, previous injury circumstances (traumatic or non-

traumatic), and previous foot and ankle surgery. Treatment characteristics collected were primary or non-primary (i.e., failed previous surgical treatment) nature of the lesion, surgical approach (medial or lateral), osteotomy use and location (medial malleolar or distal fibular), type of fixation (bio-absorbable screw, chondral dart, or metal screw), and any concomitant procedures at index surgery.

Patient Reported Outcome Measures

Patient reported outcome measures (PROMs) were collected electronically using CASTOR® in a prospective manner. The primary outcome of this study was the comparison in numeric rating scale (NRS) (0 no pain – 10 most severe pain) of pain during walking between the preoperative score to the 2-years postoperative follow-up score. The NRS of pain is an 11-point Likert scale ranging from 0 (no pain) to 10 (worst imaginable pain). Other PROMs collected were the NRS of pain during rest, during running, and during stairclimbing, as well as the foot and ankle outcomes score (FAOS), and the short form-36 (SF-36). The FAOS is a validated questionnaire for OLT and consists of 42 questions distributed over five subscales: symptoms, pain, activities of daily living, sport, and quality of life, and is measured from 0 (lowest) to 100 (highest).[2] The SF-36 is a general health questionnaire with two subscales, the physical component scale (PCS) and mental component scale (MCS).

Complications and Reoperations

When patients presented at the outpatient clinic during the 2-year study period the presence of any complications or reoperations were prospectively assessed and recorded in the electronic patient-records. Reoperations were divided into revision surgery (i.e., reoperation for recurrent OLT) and reoperation of the index foot or ankle for any other reason.

Radiological Outcome Measures

Baseline CT-scans were assessed for all patients by two measurers independently (Q.R. and J.D.). Baseline radiological data consisted of the maximum diameter of the lesion and fragment in anterior-posterior direction, medial-lateral direction, and depth. The location of the lesion was reported according to a 9-grid scheme.[19] Additionally, the presence of preoperative cysts, regardless of size, was evaluated.

Follow-up CT-scans 1-year after LDFF were assessed for union of the osteochondral fragment by two measurers independently (Q.R. and J.D.). CT-scans were available for 33 out of 34 patients. The definition of fragment union was modified from Choi et al.[20]; and defined as: union (75% bony healing), partial union (75% - 25% bony healing), or non-union. The union rate was calculated as union and partial-union over the total number of ankles

Statistical analysis

A sample size calculation for the primary outcome, the NRS during walking from preoperatively to 2-years postoperatively, indicated that 26 ankles were needed to detect a difference in means of 1.5 out of 10, assuming a standard deviation of 2.5 using a Wilcoxon signed-rank test with a 2-sided 0.05 significance level and 80% power (05 (nQuery advisor 8.5, Statistical Solutions Ltd., Boston, MA).[29] To correct for a potential loss to follow-up of 25% the required minimum sample size for the present study was 33 cases.

Statistical analysis was performed using Stata 17 (StataCorp LP, College Station, TX). A two-sided level of P< 0.05 was considered significant. Baseline characteristics were depicted as means with standard deviations for continuous variables if normally distributed, and frequencies with percentages for dichotomous and categorical outcomes. Data normality was assessed visually with boxplots and histograms. The preoperative and 2-year postoperative PROMs, including the primary outcome, were compared with a Wilcoxon signed-rank test. The change in PROMs was reported as 'improvement' due to the different effect directions of the outcome measures. A sub-analysis was performed for the association of baseline variables with the change in primary outcome from baseline to 2-years follow-up, for which a Mann-Whitney U test was performed for dichotomous variables, Kruskal-Wallis for categorical variables, and Spearman's Rho test for continuous variables. For the union rate 95% confidence-intervals (95%-CI) were calculated using the Wilson score method (without continuity correction). A logistic regression was used to assess the influence of baseline variables on the risk of non-union. Lastly, a sub-analysis on baseline characteristics of included patients and patients which had an incomplete follow-up or were lost-to-follow-up was performed.

An inter-observer reliability assessment for the lesion size and fragment size measurements was conducted with a 2-way mixed effects interclass correlation coefficient (ICC) model with absolute agreement. ICC analysis outcomes were interpreted as; 0.41-0.60 fair agreement, 0.61-0.80 moderate agreement, and 0.81-1.00 substantial agreement.[31] A Cohen's Kappa analysis was used to assess the reliability of union assessment and the novel descriptive morphological classification. Agreement for the Cohen's kappa test was interpreted as substantial if k=0,61-0,8, and near perfect if k>0,81.[13]

Results

In total, 51 patients were assessed for inclusion, of which 34 patients (34 ankles) were assessed for the primary outcome and/or secondary outcomes (Figure 1).

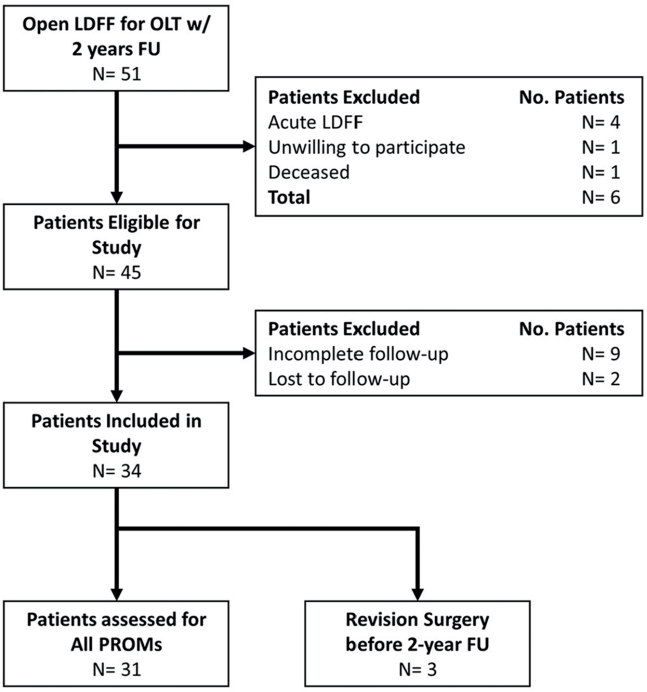

Figure 1. Flowchart of the patient selection process.

A detailed overview of all patient and treatment characteristics is available in Table 2 and lesion characteristics in Table 3. The sub-analysis on baseline characteristics of included patients and patients which had an incomplete follow-up or were lost-to-follow-up did not show any significant differences (Appendix).

Table 2. Overview of Patient and Treatment Characteristics

Patient Characteristics, N= 34	Value	% Reported
Sex, N male (%)	18 (53%)	100
Age, Years (SD)	19.3 ± 5.1	100
Smoking Status, N (%) active	6 (19%)	94
BMI (SD)	24.1 ± 5.5	100
Previous Traumatic Etiology, N (%)		100
- No previous described trauma	14 (41%)	
- Inversion/eversion	13 (38%)	
- Distortion	4 (12%)	
- Fall from height	2 (6%)	
- Other	1 (3%)	
Prior Ankle Surgery, N (%)*		100
- Ankles	8 (24%)	
- Total no. prior procedures	13	
Detailed, N (% of total no. prior surgeries)		
- Previous fixation	1 (8%)	
- Open	3 (23%)	
- Arthroscopic		
- Arthroscopic BMS	1 (8%)	
o Other OLT	1 (8%)	
o OLT treated with LDFF		
- Hardware removal	1 (8%)	
o Open (osteotomy screws)	1 (8%)	
o Arthroscopic (removal of 1 fixation screw)	2 (15%)	
- Retrograde drilling	1 (8%)	
- Clubfoot correction	1 (8%)	
- Achilles tenotomy	1 (8%)	
- Excision of Os Trigonum		

Abbreviations: N: number of, SD: standard deviation, mm: millimeters
*A patient could have had more than one previous surgical procedure. $: combination of bioscrew with chondral dart

Table 2. Continued

Treatment Characteristics	Value	% reported
Approach, N (%)		100
- Medial	20 (59%)	
- Lateral	14 (41%)	
Osteotomy, N (%)	20 (59%)	100
Detailed, N (% of total no. osteotomies)		
- Medial Malleolar	19 (95%)	
- Fibular	1 (5%)	
Screw, mean no. per patient	1.4	100
Detailed, N (%)		
- Bioscrew	22 (65%)	
- Metal screw	6 (17%)	
- Chondral dart	1 (3%)	
- Combination$	5 (15%)	
Bone grafting, N (%)		100
- Distal Tibia	28 (82%)	
- Iliac Crest	5 (15%)	
- None	1 (3%)	

Table 3. Overview of Lesion Characteristics

Characteristics (N=34)	Value
Primary lesion, N (%)	28 (82%)
Presence cyst, N (%)	20 (59%)
Lesion Location, N (%)	
- Zone 1 (anteromedial)	0 (0%)
- Zone 2 (anterior-central)	0 (0%)
- Zone 3 (anterolateral)	7 (20%)
- Zone 4 (central-medial)	6 (18%)
- Zone 5 (central)	1 (3%)
- Zone 6 (central-lateral	3 (9%)
- Zone 7 (posteromedial)	15 (44%)
- Zone 8 (posterior-central)	0 (0%)
- Zone 9 (posterolateral)	2 (6%)
Lesion Size, mm (SD)	
- Anterior-Posterior	18.7 ± 4.3
- Medial-Lateral	12.0 ± 2.4
- Depth	8.5 ± 2.5
- Lesion Area, mm2	178.3 ± 57.1

Abbreviations: N: number of, SD: standard deviation, mm: millimeters

Patient Reported Outcome Measures (PROMs)

The primary outcome, the NRS pain during walking, significantly improved from a median of 6 (IQR: 4 – 7) out of 10 preoperatively to 1 (IQR: 0 – 3) out of 10 at final follow up, P= <0.01 (Figure 2).

There was no association between baseline factors and change in primary outcome between baseline and 2-years follow-up (Appendix). All other PROMs significantly improved compared to the preoperative situation, except for the MCS of the SF-36 (Table 4).

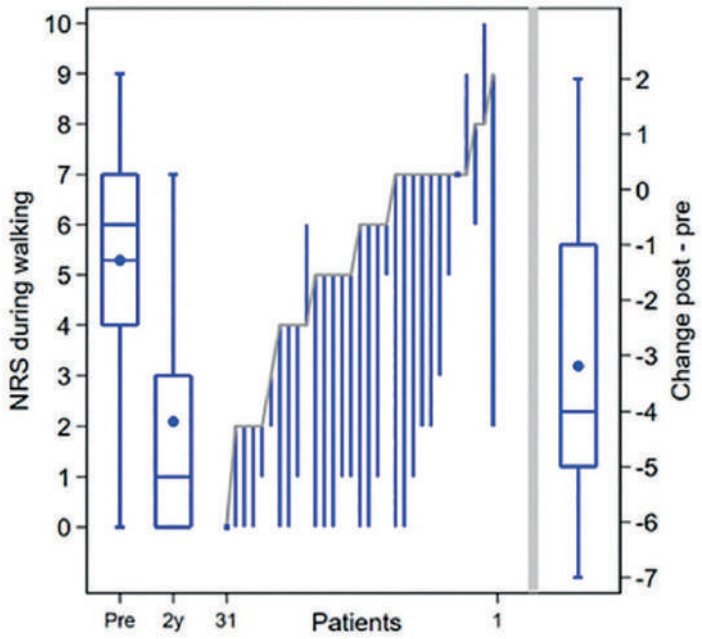

Figure 2. Preoperative to 2-year postoperative change in NRS during walking; depicted per individual patient. On the left side the boxplots depict the preoperative and 2-year postoperative outcomes on a group level (IQR indicated by a box with line as median value, mean is depicted as a dot in the box, and whiskers depict the absolute values). On the right the change on a group level from preoperative to 2-years postoperatively is depicted.

Table 4: Secondary Patient Reported Outcome Measures

Outcome, N= 31	Pre-Operative	2-Years Follow-Up	P-Value
NRS pain during, Median (IQR)			
Rest	3 (1 – 4)	0 (0 – 2)	**< 0.01**
Walking	6 (4 – 7)	1 (0 – 3)	**< 0.01**
Running N= 29	8 (7 – 10)	3 (0 – 6)	**< 0.01**
Stair Climbing N= 29	5 (2 – 7)	1 (0 – 3)	**< 0.01**
FAOS, Median (IQR), N=30			
Symptoms	50 (39 – 61)	64 (50 – 79)	**<0.01**
Pain	53 (42 – 64)	86 (69 – 97)	**< 0.01**
ADL	66 (54 – 85)	96 (88 – 100)	**< 0.01**
Sport	33 (20 – 45)	73 (55 – 85)	**< 0.01**
QoL	38 (31 – 50)	56 (50 – 69)	**< 0.01**
SF-36, Median (IQR), N= 29			
PCS	37.4 (32.6 – 41.7)	47.8 (38.1 – 52.2)	**< 0.01**
MCS	49.8 (35.7 – 58.1)	53.3 (46.3 – 57.8)	0.2

Abbreviations: NRS: Numeric Rating Scale, IQR: inter-quartile range, FAOS: Foot and Ankle Outcome Score, ADL: activities of daily living, QoL: Quality of Life, SF-36: short-form 36, PCS: Physical Component Scale, MCS: Mental Component Scale

Radiological Outcomes

On 1-year follow-up CT-scans a union rate of 91% [95%-CI: 76 – 98] was observed. Patients which showed union had full union in 27 (90%) cases and partial union in 3 (10%). Two case examples are shown in Figures 3 and 4. BMI by ≥ 30 kg/m^2 was significantly associated with fragment non-union (OR: 1.39 [95%-CI: 1.04 – 1.84], P=0.02), and all cases of non-union had a BMI >30. The fragment area (OR: 0.99 [95%-CI: 0.98 – 1.02], P= 0.9) or depth (0.90 [95%-CI: 0.41 – 1.96], P=0.8) was not associated with union. The osteotomy healed uneventfully in 100% of the cases. The outcomes of the inter-observer analysis for the measurement of lesions size are available in the Appendix.

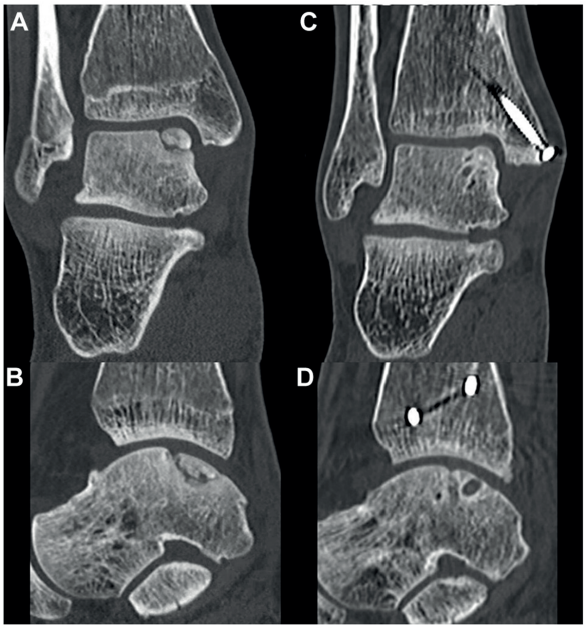

Figure 3. Pre-operative coronal (a) and sagittal (b) and 2-year postoperative (c and d) CT-scan images of an 18-year-old male with a posteromedial osteochondral fragment of the talus, who underwent open LDFF with one bioscrew. The postoperative radiolucency on the talus is the bioscrew in-situ.

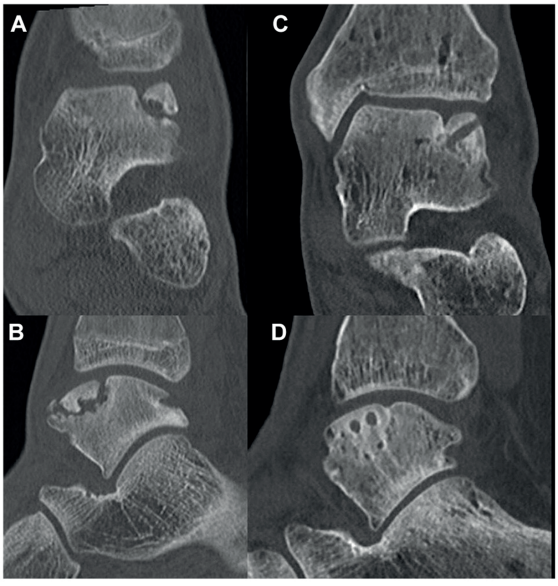

Figure 4. Pre-operative coronal (a) and sagittal (b) and 1-year postoperative (c and d) CT-scan images of a 16-year-old male with an anterolateral osteochondral fragment of the talus, who underwent open LDFF with two bioscrews. The postoperative radiolucencies on the talus are the bioscrew in-situ.

Complications, Revision Surgery, and Reoperations

In this cohort 2 (6%) complications were observed. Of these, 1 patient presented with delayed superficial wound healing without signs of infection, which required an additional cast change at 4 weeks postoperatively, and thereafter resolved uneventfully. Additionally, 1 patient developed a complex regional pain syndrome (CRPS) postoperatively for which a multi-disciplinary pain rehabilitation treatment was started.

When considering revision surgery, 3 (9%) patients underwent revision surgery at an average 13.7 (range: 10 – 16) months follow-up, all due to a symptomatic non-union of the fragment. Of these 3 patients, 1 patient underwent arthroscopic bone marrow stimulation, and 2 patients underwent talar osteoperiostic grafting from the iliac crest (TOPIC).[3] All achieved adequate results and did not require additional surgery afterwards. A detailed overview of the patient characteristics for revision cases is presented in the Appendix. In addition to the revision surgeries, a total 9 patients underwent additional surgery following the LDFF procedure within the study period, which was osteotomy hardware removal in 6 out of 9 patients (Appendix). None required screw removal used in fixation of the lesion.

Discussion

The main finding of this study is that open LDFF for chronic OLT with an osteochondral fragment results in a favorable pain reduction and patient-reported outcomes at 2-years follow-up. Moreover, 91% of patients showed union of the fragment at 1-year CT evaluation, and it was found that BMI is associated with a significantly increased risk of non-union. The revision rate was 9% and reoperation rate 24% (majority symptomatic hardware removal). These findings show that open LDFF is a clinically effective treatment method for chronic OLT with an osteochondral fragment amenable for fixation. Moreover, these findings may allow surgeons for a wider range of treatment options for specific lesion types.

The indication for fixation is debated. A 2019 consensus statement from experts in the field stated that osteochondral lesions with an osteochondral fragment require a bony stock of at least 10 millimeters in diameter and 3 millimeters depth to be eligible for fixation.[22] However, recent work by Nakasa et al.[16] has shown that even in smaller (<100mm2) lesions fixation yields good clinical and union outcomes. The indication for fixation of OLT therefore seems to be expanding. A recent systematic review and meta-analysis, including 241 ankles among 10 studies, observed a pooled treatment success rate of 91%, which was based on cut-off values for commonly used patient- or physician-reported outcome measures.[24] From these studies, 88% of cases reported outcomes of fixation through an open approach and 44% of cases reported the use of screw or pin fixation.[24] From the present literature, Nakasa et al.[16] reported the

largest case series of 36 ankles fixed with poly-L-lactide pins. The authors reported an improvement of the AOFAS score from 71.1 (SD: 2.6) preoperatively to 97.2 (SD: 4.3) at a mean 23 months postoperatively. Moreover, the aforementioned study found post-operative clinical scores of fixation to be statistically significantly higher compared to arthroscopic bone marrow stimulation. Haraguchi et al.[6] reported the largest cohort of patients fixed using a bone-peg in 45 ankles and reported an improvement of the JSSF from 63.5 (SD: 17.9) preoperatively to 93.0 (SD: 6.6) at a mean 43.2 months postoperatively. Moreover, the outcomes observed in the present study concur with these improvements in clinical outcomes and, similarly, with prior findings of the arthroscopic LDFF procedure.[12] The present study found no baseline factors to be associated with the improvement of pain outcomes during walking (primary outcome). Similarly, no baseline factors have been found to correlate with postoperative PROMs in previous studies on fixation for OLT.[6,10,16,20] This may be due to underpowering for such an analysis in these studies as well as the current study and should be investigated in a larger cohort.

Although sports outcomes were not formally assessed in the present study, pain scores during running and the FAOS sports sub-scale showed a statistically and clinically relevant improvement, albeit with residual pain during running and a moderate to fair improvement in the FAOS sport score. These outcomes may suggest that fixation could, similarly, result in good sport outcomes. Nakasa et al.[16] reported that in their series of 36 patients the ankle activity scale (AAS) remained stable from preoperatively 6.5 (SD 2.2) to 6.3 (SD: 2.2) at an average 23 months follow-up, and was found to be superior compared to BMS. Schuh et al.[30] reported in their retrospective evaluation of 20 ankles treated with K-wire fixation of the osteochondral fragment that all patients returned to their preoperative sports and work but did not define return to sports per level or specific sport. In the cases included in the present study it was the clinical experience of the authors that the main goal for patients to undergo surgical intervention was either a pain reduction during activities of daily living, such as walking, or a pain reduction during sports or work. Additionally, the use of the 10–12-week immobilization period could affect the sport outcomes due to prolonged immobilization. Current trends are to decrease the immobilization period for open OLT surgery as it shows safe outcomes.[7,8] In the fixation literature no consensus is reached on the appropriate immobilization period for OLT fixation healing, with non-weightbearing periods of 4 – 6 weeks being reported, and subsequent partial weightbearing either protected or unprotected.[1,6,9,11,18,20,22] The authors acknowledge that during the course of this study the immobilization period was shortened and no adverse outcomes were noted, while to date commonly using a walker boot during weightbearing immobilization in compliant patients. Consensus should be reached on the adequate immobilization period for fixation of OLT.

Radiological outcomes

The fragment union rate observed in the present study was 91%. This concurs with the literature, where the aforementioned systematic review on fixation observed union in 91% of ankles.[24] The present study found that an increased body mass index (BMI) by ≥ 30 kg/m^2 was associated with an increased risk for non-union. The authors hypothesize that obesity may result in increased peak forces during early weightbearing, thereby increasing the risk of (subtle) fragment instability and inadequate bone healing, leading to a delayed- or non-union of the fragment. Clinically, it can be considered to include these findings when counseling patients for surgery. Moreover, in the elective setting it can be considered to aim for optimal weight-reduction pre-operatively for obese (BMI ≥ 30) patients, or to extend the postoperative partial weightbearing period of the ankle (for example with a walking boot). The authors do warrant caution when interpreting the findings of this analysis due to the relatively low number of patients in the present cohort and statistical fragility. Further studies in large cohorts should assess the effect of BMI and other patient factors on union outcomes for fixation of OLT. Additionally, it was observed in the present study that no osteotomy non-unions occurred. This concurs with the literature, where similarly, no osteotomy non-unions have been reported in fixation cases.[24] Although the aim should be to approach the lesion in the most minimally invasive method possible, a concomitant osteotomy during fixation of OLT seems to be safe and is therefore justified in case the access to the lesion is otherwise limited. Moreover, further research will have to elucidate whether the open approach results in similar outcomes as an arthroscopic approach for fixation of OLT, and what the impact of osteotomy use is on patient outcomes.

Complications, Revision Surgery, and Reoperations

In the present study 2 complications were recorded. Of these, 1 case had persistent complaints of complex regional pain syndrome requiring further treatment, a complication which is seen in up-to 4% of foot and ankle surgery cases.[23]

The revision rate for fixation reported in the literature is 6%.[24] Among these, Choi et al.[20] and Kramer et al.[10] both reported 5 revision cases in 26 and 18 ankles, respectively. Choi et al.[20] reported that all had a symptomatic non-union as the reason for revision surgery, which was conducted through removal of the fragment and bone grafting from the lateral calcaneus. This concurs with the findings in this study, where it was observed that up-to 2-years follow-up all 3 patients underwent revision for non-union. Kramer et al.[10] did not report the reason for revision, however. Although not observed in the present cohort, there is a mismatch in the literature[24] regarding the revision rate (6%) and non-union rate (9%), which suggests some patients may have a non-symptomatic non-union. With caution, it could be stated that there are patients who do not achieve union but do not present with clinically relevant complaints. As such, it is critical to thoroughly evaluate a patient with a non-union after fragment

fixation, and to consider watchful neglect with radiological follow-up in case of a non-symptomatic case.

The reoperation rate in the present study (24%) was higher compared to the literature (9%)[24] and arthroscopic LDFF (0%).[12] The authors hypothesize that this is largely due to the symptomatic hardware removal following osteotomy of 67% in this cohort. This is supported by the 72% hardware removal rate reported by Meisterhans et al.[14] in their series of 67 ankles who underwent open surgery for an OLT. The present literature on fixation shows an osteotomy rate of 45%[24], compared to the 59% reported in this study, which could be a contributing factor to the reoperation rate observed in this study. Our experience shows that most medially located lesions require an osteotomy to gain access to the joint while most lateral lesions did not. As previously discussed, access to the lesion is paramount in optimal screw placement during fixation, thus requiring an osteotomy. As such, the authors believe that it is important to counsel patients on these findings and to only remove hardware in case of complaints. Future studies may further compare the morbidity and success of medially versus laterally fixed OLT, where factors such as the necessity to remove hardware may play a role in outcomes.

Strengths and Limitations

The strengths of this study are its prospective design, the inclusion of a prospective sample size calculation for the primary outcome, and multiple measurers for the radiological data collection with a moderate to excellent inter-observer reliability. However, the present study is not without limitations. First, this study concerns a non-comparative case series. Second, 24% of patients had an incomplete follow-up or were lost-to-follow-up. From these, the majority were patients who failed to complete a baseline questionnaire. Furthermore, no significant differences in baseline characteristics among excluded and included patients were observed, suggesting that their exclusion may not have changed the primary findings of the study. Thirdly, the authors warrant caution in the interpretation of the sub-analyses performed in this study, as these may be underpowered. Fourth, one patient was not included in the prospective CT-evaluation at 1-year follow-up as they did not undergo the examination, which could have had an impact on the union rate and its sub-analyses.

Conclusion

Open LDFF results in a favorable pain reduction and good clinical outcomes for chronic OLT up-to 2-year follow-up. The procedure achieves a 91% fragment union rate while patients with obesity may be at a higher risk of fragment non-union. The revision rate was 9% and reoperation rate 24% (majority symptomatic hardware removal). These findings show that open LDFF is a clinically effective treatment method for chronic OLT with an osteochondral fragment amenable for fixation.

Appendix

The appendix information can be accessed at: https://doi.org/10.1177/23259671251356700

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Chapter 8

Sustained Clinical Success at 7-Years Follow-Up After Arthroscopic Lift-Drill-Fill-Fix (LDFF) of Primary Osteochondral Lesions of the Talus

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Abstract

Purpose: To describe the long-term clinical results of arthroscopic fragment fixation for chronic primary osteochondral lesions of the talus (OLT), using the Lift-Drill-Fill-Fix (LDFF) technique.

Methods: Eighteen patients (20 ankles) underwent fixation for a primary OLT with an osteochondral fragment using arthroscopic LDFF and were evaluated at a minimum of 5-years follow-up. Pre- and postoperative clinical assessment was prospectively performed by measuring the Numeric Rating Scale (NRS) of pain at rest, during walking and when running. Additionally, the change in Foot and Ankle Outcome Score (FAOS) and the procedure survival (i.e., no reoperation for the OLT) at final follow-up was assessed.

Results: At a mean follow-up of 7 years the median NRS during walking significantly improved from 7 (IQR: 5 - 8) pre-operatively to 0 (IQR: 0 – 1.5) at final follow-up ($p = <0.001$). This result was sustained from 1-year follow-up to final follow-up. The NRS during running significantly improved from 8 (IQR: 6 - 10) to 2 (IQR: 0 – 4.5) ($p < 0.001$) and the NRS in rest from 2.5 (IQR: 1 - 3) to 0 (IQR: 0 - 0) ($p = <0.001$). The median FAOS at final follow-up was 94 out of 100 for pain, 71 for other symptoms, 99 for activities of daily living, 80 for sport and 56 for quality of life. The FOAS remained significantly improved post-operatively on all subscales, except for the symptoms subscale. The procedure survival rate is 87% at final follow-up.

Conclusion: Arthroscopic LDFF for fixable chronic primary OLTs results in excellent pain reduction and improved patient reported outcomes, with sustained results at long-term follow-up. These results indicate that surgeons may consider arthroscopic LDFF as treatment of choice for fragmentous OLT.

Keywords: Osteochondral Lesion, OLT, Fixation, LDFF, Surgery

Introduction

Osteochondral lesions of the talus (OLT) affect the articular cartilage and its underlying subchondral bone. Treatment of these lesions is challenging as no superior treatment is available to date.[2] Treatment of OLTs should be based on lesion and patient characteristics in a patient individualized, evidence-based, shared-decision making process.[20] Choosing between surgical options is mainly directed by lesion morphology.[19] Patients presenting with an osteochondral fragmentous lesion may benefit from fragment fixation both in the acute (< 6 weeks after trauma) or chronic phase.

The theoretical advantage of fixation over other surgical techniques is the preservation of native hyaline cartilage, immediate stabilization of the fragment and restoration of the talar dome congruency, as well as facilitating subchondral bone healing.[8,18] One such a fixation technique for OLTs is "Lift-Drill-Fill-Fix" (LDFF).[8] The LDFF technique is indicated for primary fragmentous OLTs with ≥10mm in diameter and ≥ 3mm thickness.[8,18] In the case of a chronic OLT, the LDFF procedure can be considered an intra-articular non-union repair by means of subchondral bone drilling, autologous bone grafting, and compression. LDFF can be performed both open and arthroscopically, with previous studies reporting excellent short- to mid-term clinical outcomes.[8,10] In general, mid-term outcomes of fragment fixation for OLTs are promising.[6,9,10,17,23] The durability and longevity of such fixation procedures remain a matter of debate however.[3,9]

The primary aim of the present study is therefore to evaluate the long-term patient reported outcome of arthroscopic LDFF. The hypothesis is that the results of arthroscopic LDFF results are maintained over time. The secondary aims of this study are to investigate the survival rate and complications.

Methods

Approval for this study was obtained from the Medical Ethical Committee of Amsterdam UMC, Location AMC (reference number: MEC 08/326). The present study is in accordance with the Medical Research Involving Human Subjects Act (WMO) and the principles of the Declaration of Helsinki.

Patient Selection

The present study is a long-term follow-up of a cohort of consecutive patients who underwent arthroscopic fixation by means of LDFF for a primary chronic (> 6 weeks after trauma or start of symptoms) OLT and minimum of 6 months conservative treatment before surgery.[10,20] Fragmentous OLTs, with a preferred minimum diameter of 10 millimetres (mm), 3mm of fragment thickness, and reachable by arthroscopy

were considered fixable.[10,19] The exclusion criteria as well as the surgical technique and postoperative rehabilitation protocol for arthroscopic LDFF were described by Lambers et al.[10] Additionally, patients who were lost to follow-up, patients who declined to participate, patients who underwent surgery of the lower extremity within 6 months before final follow-up, and patients with less than 5-years follow-up were excluded in the present study. Patients were identified and included in a cross-sectional manner after applying the inclusion and exclusion criteria.

Outcome Measures

Outcomes were collected in a prospectively at the preoperative, one- and two years follow-up, and at a minimum of 5-years postoperatively at the cross-sectional final follow-up.[10] At final follow-up, patients were contacted by phone in order to obtain informed-consent for the present study.

Clinical Outcomes

In order to obtain patient reported outcome measures (PROMs) online questionnaires were distributed via the Castor© electronic data capture system. The primary outcome measure for the present study was the Numeric Rating Scale (NRS) of pain during walking, which is a patient reported pain scale from 0 (no pain) to 10 (most pain imaginable).[5] The NRS contained two additional subscales in the present study, namely, the NRS in rest, and the NRS during running. Secondary patient reported outcome measures collected were; the Foot and Ankle Outcome Score (FAOS) and the Short Form Health Survey (SF-36).[1,25]

By phone, and from the electronic patient records, any reoperation of the ankle was recorded. Revision surgery was defined as any reoperation of the OLT after the arthroscopic LDFF procedure. The survival rate was defined as the proportion of the number of ankles which did not undergo revision surgery from the total number of ankles included at final follow-up. Postoperative complications were extracted from the hospital electronic patient records.

Radiological Outcomes

All patients received a preoperative and one-year postoperative radiological assessment of the OLT by means of a computed tomography (CT) scan. The aforementioned study by Lambers et al.[10] previously assessed the osteochondral fragment union rate and the subchondral bone plate appearance at one-year follow-up, these outcomes were therefore not included in the present study. Radiological lesion baseline characteristics included: lesion size (as measured in millimetres from three planes - anterior-posterior (AP), medial-lateral (ML) directions, and depth), the number of lesions per ankle, the presence of cysts, and the lesion location according

to Raikin et al.[16] CT measurements were performed by two independent measurers (Q.R. and J.N.A.), in case of disagreement a third assessor (J.D.) was decisive. Lesion size is reported as the mean lesion size from the two independent assessors.

Data Collection

Baseline patient- and treatment characteristics were extracted from the hospital electronic patient records. Patient characteristics included sex, laterality, age at surgery, body mass index (BMI), participation in sports and level of sports participation (i.e., none, amateur, competitive, or professional), injury circumstances (i.e., traumatic - fracture or sprain - or non-traumatic onset), and concomitant injuries. Treatment characteristics collected were the follow-up time, screw type used for fixation (i.e., bio-absorbable screw, chondral dart, or cortical screw), and any concomitant procedures at index surgery.

Statistical Analysis

Before the start of the present study a sample size calculation for the primary outcome was performed with a Wilcoxon signed rank test, using a level of significance (α) of 0.05 (nQuery advisor 7.0, Statistical Solutions Ltd., Boston, MA). A minimally clinical important difference (MCID) of the NRS pain during walking 2.0 points between the preoperative and postoperative situation, with a standard deviation of 2.5 points and a power of 80% was chosen, as previous studies observed a much better improvement in pain.[4,10,14,22] A minimum of 16 patients were needed.

Descriptive analysis was performed to summarize the baseline characteristic variables, which are presented with frequencies and percentages for categorical variables and means with standard deviations and ranges for continuous variables. Data was assessed visually for normality and with a Shapiro-Wilk test. Wilcoxon signed-rank test was used to compare clinical outcomes preoperatively with postoperatively. Specifically for the primary outcome, a comparison of the NRS during walking between the final follow-up with 6-months follow-up, 1-year follow-up, and 2-years follow-up was made using the Wilcoxon signed-rank test. In order to test inter-rater reliability of the lesion size measurements and the lesion localization 2-way mixed effects interclass correlation coefficient (ICC) model with absolute agreement and Cohen's Kappa analysis were used, respectively. ICC analysis outcomes were interpreted according to Shrout et al.[24] with 0.41-0.60 being a fair agreement, 0.61-0.80 moderate agreement, and 0.81-1.00 substantial agreement. The agreement on the Cohen's kappa test was interpreted as substantial if k=0.61-0.8, and almost perfect if k>0.81.[11] A two-sided level of $P < .05$ was considered significant. All data analysis were conducted using Stata 15 (StataCorp LP, College Station, TX).

Results

From the 25 eligible patients 20 patients were included with a total of 23 ankles. 5 patients were excluded, as outlined in Figure 1. Two patients underwent revision surgery for a total of 3 ankles (one bilateral case) and the PROMs were therefore analyzed for a total of 18 patients with 20 ankles at final follow-up.

The baseline patient and lesion characteristics are available in Table 1. In terms of prior or concomitant surgical procedures to the ankle, one patient underwent an anterior arthroscopy for debridement of anteromedial soft-tissue impingement and a chondral lesion of the medial tibial plafond 12 months prior to the LDFF procedure and one patient received an additional Duquennoy procedure at the time of LDFF due to lateral ankle instability.

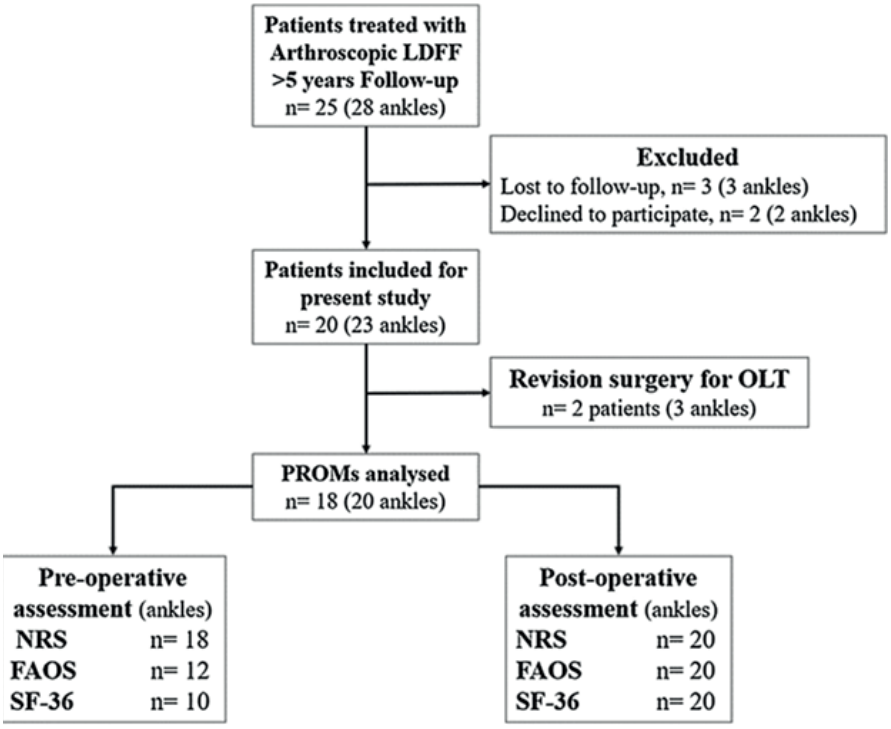

Figure 1. Flowchart of patient selection according to inclusion and exclusion criteria. Of note: pre-operative clinical outcome measures were not available for all patients.

Table 1. Baseline Patient- and Lesion Characteristics*

Patient Characteristics	**Total N = 18**
Sex, n (% male)	9 (50%)
Age (years), mean ± SD (range)	24.2 ± 15.2 (11.3 - 62.2)
FU (months), mean ± SD (range)	82.9 ± 9.3 (71.4 - 96.4)
BMI (kg/m2), mean ± SD (range)	22.9 ± 3.7 (19.4 - 36.5)
History of smoking, n (%)	3 (17%)
Laterality, n (%) Right / Left / Bilateral	9 (50%) / 7 (39%) / 2 (11%)
Previous ankle trauma, n (%)	10 (56%)
Previous ankle fracture, n (%)	1 (6%)
Sports participation, n (%) Yes / No / Unknown	14 (78%) / 3 (17%) / 1 (5%)
Sports Level, n (%)	
- Professional	0 (0%)
- Competitive	9 (64%)
- Recreational	4 (29%)
- Unknown	1 (7%)
Concomitant Procedures, n (%)	
- Open lateral ligament repair	1 (5%)
Lesion Characteristics	**Total N = 20**
Presence of Cyst, n (%)	6 (30%)
Size (mm), mean ± SD (range)	
Anterior-Posterior	13.8 ± 2.9 (10.0 – 20.0)
Medial-Lateral	9.4 ± 2.5 (5.2 – 14.0)
Depth	7.0 ± 2.2 (4.0 – 11.5)
Lesion Volume, mean ± SD	
Location per zone†, n (%)	
Anteromedial (zone 1)	1 (5%)
Anterocentral (zone 2)	0
Anterolateral (zone 3)	2 (10%)
Centeromedial (zone 4)	15 (70%)
Central (zone 5)	0
Centerolateral (zone 6)	1 (5%)
Posteromedial (zone 7)	2 (10%)
Posterocentral (zone 8)	0
Posterolateral (zone 9)	0

Please note that the patient characteristics are given for the total number of patients (n = 18) who underwent post-operative clinical assessment (i.e., no failure casus), and that lesion characteristics are given for the total number of ankles (n = 20).
† one ankle had two lesions and was thus counted double.
Abbreviations: n: number of, SD: standard deviation, FU: follow-up, BMI: body mass index, mm: millimeters.

Clinical Outcomes

The primary outcome, the NRS pain during walking, significantly improved at mean 6.9 years follow-up (median: 0 out of 10 (IQR: 0-1.5)) compared to preoperatively (median: 7 out of 10 (IQR: 5-8), P= <0.01), as well as for the other NRS subdomains (Table 2). The NRS during walking did not significantly change from 1-year postoperatively compared to the 2-year and long-term follow-up time points (Figure 2). An overview of the PROMs is available in Table 2.

Reoperations, Revision Surgery, and Complications.

A total of two patients underwent surgery to the ankle unrelated to the OLT after LDFF. From these two patients, one had an anterior ankle arthroscopy for anteromedial soft-tissue impingement debridement and one had a gastrocnemius release at another institution at 18 and 86 months after the LDFF procedure, respectively. Additionally, two patients underwent surgery of the ipsilateral lower extremity not involving the ankle (one anterior cruciate ligament reconstruction and one biplanar chevron osteotomy for a symptomatic hallux valgus).

From the 20 patients with 23 ankles available in this study, two patients with a total of three ankles (13%) underwent revision surgery. This corresponds to a procedure survival rate of 87% (Figure 3). The baseline demographics and treatment characteristics, including reason for revision surgery, of these patients are provided in the Appendix. No complications were recorded in this cohort.

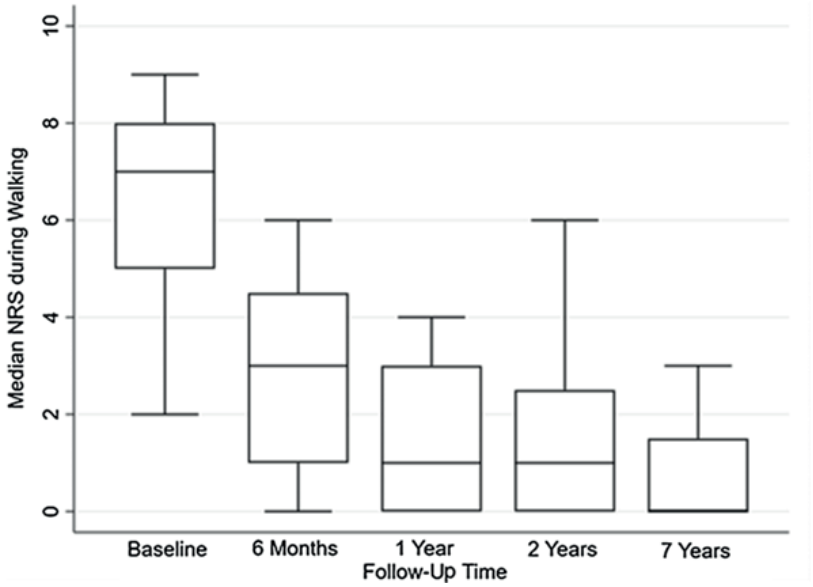

Figure 2. Boxplots of median NRS pain during walking over time, Of note: the following number of ankles available for analysis at certain time points; baseline n=18, 6 months n=12, 1-year n= 15, 2-years n=20, 7 years n=20

Table 2. Preoperative and Final Follow-up Patient Reported Clinical Outcome Scores

Outcome	Preoperative n= 18	Final Follow-up n = 20	P-Value
NRS, median (IQR)			
Pain (rest)	2.5 (1.0 – 3.0)	0.0 (0.0– 0.0)	**<0.01**
Pain (walking)	7.0 (5.0 – 8.0)	0.0 (0.0 – 1.5)	**<0.01**
Pain (running)	8.0 (6.0 – 10.0) n=13	2.0 (0.0 – 4.5)	**<0.01**
FAOS, median (IQR)	n= 12		
Symptoms	69.5 (52.0 – 75.0)	71.4 (57.1 – 84.0)	n.s.
Pain	66.5 (54.0 – 79.5)	94.4 (83.3 – 100)	**<0.01**
ADL	90.5 (74.5 – 97.0)	98.5 (97.1 – 100)	**0.02**
Sport	40.0 (27.5 – 60.0)	80.0 (60.0 – 100)	**0.01**
QoL	22.0 (13.0 – 34.5)	56.3 (50.0 – 68.8)	**0.02**
SF-36, median (IQR)	n= 10		
PCS	43.3 (35.8 – 51.1)	45.1 (41.8 – 47.8)	n.s.
MCS	57.1 (53.5 – 60.8)	37.4 (35.4 – 39.5)	**<0.01**

Abbreviations: n= number of ankles, NRS= Numeric Rating Scale, IQR= Inter Quartile Range, ADL= Activities of Daily Living, QoL= Quality of Life, SF-36= Short Form-36, PCS= Physical Component Summary, MCS= Mental Component Summary, n.s.= non-significant.

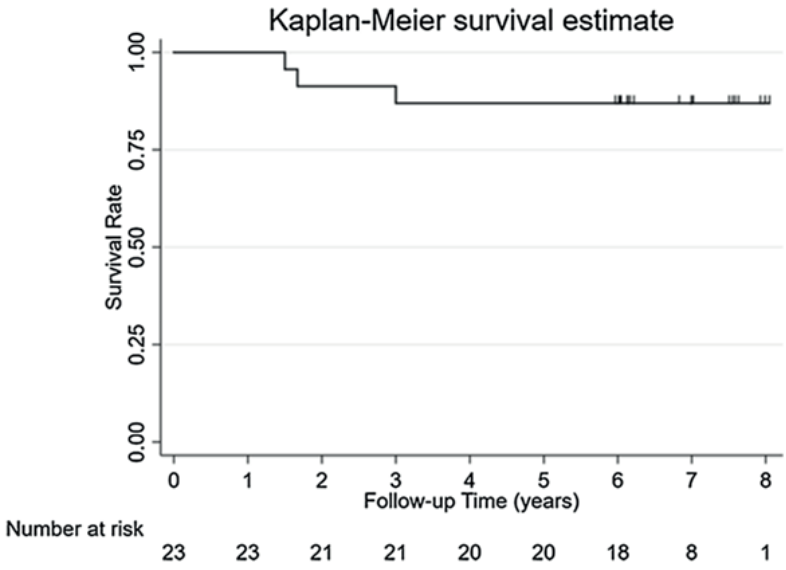

Figure 3. Kaplan-Meier survival curve for procedure survival over time, Of note: patients were censored starting at 5-years follow-up due to no long follow-up.

Radiological Assessment

One-year postoperative CT-scans were performed for all ankles. The baseline lesion characteristics are reported in Table 1. The inter-rater reliability was observed to be substantial for the AP (ICC: 0.88), ML (ICC: 0.91), and depth (ICC: 0.82) lesion size measurements. The Cohens' kappa for the inter-rater reliability of the lesion location was 0.71 (substantial).

Discussion

The principal finding of this study is that clinical outcomes remain excellent at long-term follow-up in patients who underwent fixation of a chronic primary fragmentous OLT by means of arthroscopic LDFF. Moreover, the procedure survival rate is 87% at mean 7 years follow-up. These results indicate that outcomes of arthroscopic LDFF stand the test of time and that fixation may be considered for primary OLTs which are amendable for fixation.

To the knowledge of the authors this is the first study reporting on the long-term clinical outcomes of arthroscopic fixation for OLTs. When comparing the outcomes of the present study to the literature it is clear that, although fixation outcomes are reported, long-term outcomes and results from arthroscopic fixation are rare.[3,6,9,10,12,15,17] Overall, patient reported clinical outcomes after open fixation available in the literature can be considered excellent and fragment union is seen from 77% in up-to 100% of cases.[6,9,12,15,17,23] To date, two studies reported on the long-term outcomes of open fixation. Kumai et al.[9] reported good Berndt and Harty scores in 16 and fair 3 in patients with more than 5-year follow-up. Dunlap et al.[3] observed a mean postoperative AOFAS score of 86, and good Berndt and Harty scores in 4 out of 5 patients at a mean 12 years follow-up.

The advantage of fixation over other surgical treatment options for fragmentous OLTs is the preservation of the native hyaline cartilage, immediate stabilization of the fragment and restoration of the talar dome congruency, as well as facilitating subchondral bone healing.[8,18] The LDFF procedure complements this by subchondral drilling and autologous bone grafting, essentially qualifying it as an intra-articular non-union repair. The superior subchondral bone healing following LDFF is supported by findings from Reilingh et al.[18], who observed that the subchondral bone healing after fixation is superior compared to bone marrow stimulation (BMS), the most frequent surgical treatment for OLTs.[2] However, when interpreting the revision rate of 7% reported in the literature for BMS at long-term follow-up[21], one can argue this can be considered comparable to the survival rate reported in the present study. Data concerning surgical treatment for fragmentous OLTs is too scarce, however, to make any direct comparison on long-term procedure survival and clinical outcomes between BMS and fixation. The authors consider LDFF the first-line surgical treatment

in case of a symptomatic fragmentous OLT amendable for fixation which is not responding to conservative therapy. This is case as other surgical treatment options remain available in case of treatment failure.[20] According to the senior author, the reason for failure of the 3 revised ankles (in two patients) is partial non-union of the osteochondral fragment. This raises a clinical question what baseline patient and lesion factors may influence union and warrants further investigation.

Fixation for OLTs can only be considered in specific cases in order to be amendable for fixation, with a fragment of sufficient dimensions and good cartilage coverage.19 It should be stated that arthroscopic fixation of OLTs can be technically demanding and that it to be reserved for experienced arthroscopists. In addition to the previously described LDFF technique the authors note a supplemental technique recommendation.[8] In order to gain sufficient access to the lesion and to achieve an adequate perpendicular compression force on the fragment a third portal may be necessary for fixation. A portal 1-2cm superiorly from to the standard working portals, depending on the lesion location, can be made for this purpose. Combined with the ankle in full plantar flexion (for anterior and central lesions) or dorsiflexion (for posterior lesions) optimal access and a perpendicular screw insertion angle can be achieved, which is important for fragment union and limiting the chance for osteolytic changes without the need for an additional osteotomy.[13]

To the knowledge of the authors, this is the first study reporting long-term clinical outcomes following arthroscopic fixation of OLTs. All patients were treated at a single centre which is accredited as an (inter)national expert centre for the diagnosis and treatment of ankle cartilage injuries. Patients were prospectively followed and data was collected by independent investigators not involved in patient care in order to limit observer bias. All radiological measurements were conducted by two independent raters with excellent inter-rater reliability.

The present study is not without its limitations. First, 20% of eligible ankles were lost to follow-up. Lost to follow-up is a known problem in long-term follow-up studies.[7] It could be interpreted as a good sign, that patient need no further care for their ankle, nevertheless they might as well have looked for care elsewhere. Second, as previously described by Lambers et al.[10], it should be noted that clinical outcome measures were not available for all patients at every follow-up moment due to a historical change in the outcome measures used for the clinical assessment. Third, the present study did not include a long-term radiological follow-up in order to assess the presence of degenerative changes in the tibiotalar joint. Fourth, the present study included a limited number of patients, limiting the statistical power.

The present study addresses the paucity of literature concerning the long-term clinical outcomes as well as the clinical sustainability of the procedure. Fixation of fragmentous OLTs should always be considered by the treating physician and should be made in the context of an individualized treatment algorithm which includes patient and lesion characteristics.[20] This study underlines the need for prospective research assessing clinical outcomes of fixation techniques, both open and arthroscopically, with sufficient statistical power in order to provide further evidence for its clinical efficacy in OLT treatment as well as to assess prognostic factors associated with treatment success.

Conclusions

Arthroscopic LDFF for fixable chronic primary OLTs results in a long-term procedure survival rate of 87%. Clinically, excellent and sustained pain reduction and patient reported outcomes were observed. These results indicate that surgeons may consider arthroscopic fixation for a fragmentous OLT.

Appendix

The appendix information can be access at: https://doi.org/10.1007/s00167-022-07243-5

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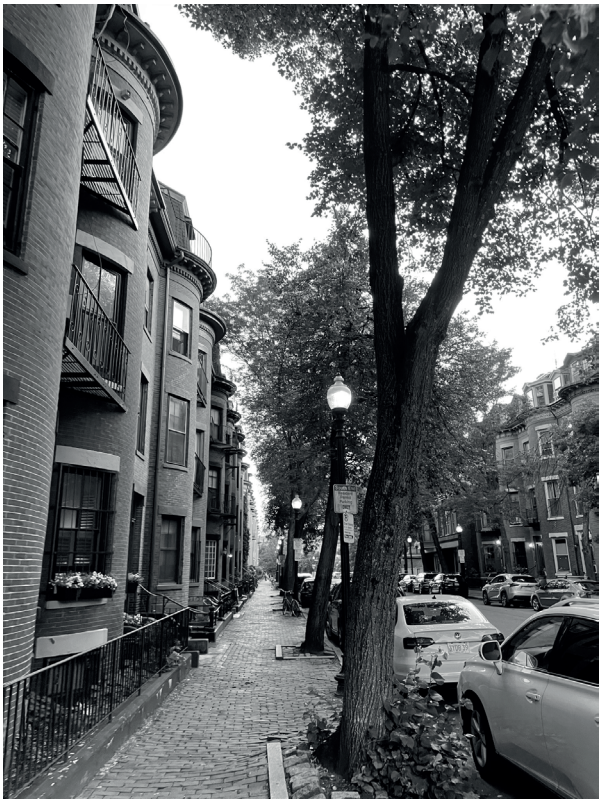
Part 5

Management of Osteochondral Lesions of the Tibial Plafond



Chapter 9

Surgical Treatment of Osteochondral Lesions of the Tibial Plafond: A Systematic Review and Meta-Analysis

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Abstract

Purpose: The literature on osteochondral lesions of the tibial plafond (OLTPs) is sparse. The aim of this study was therefore to provide an overview of clinical and radiological outcomes following treatment of OLTPs.

Methods: We performed a systematic search of the MEDLINE, Embase, and Cochrane library databases. The review was performed in accordance with the PRISMA (Preferred Reporting Items for Systematic reviews and Meta-Analyses) guidelines and included all original articles on treatment outcomes for OLTPs. The methodological quality of the articles was assessed using the Methodological Index for Non-Randomized Studies (MINORS). Baseline patient and lesion characteristics were pooled and weighted according to the number of lesions per study. The primary outcome was any clinical or patient-reported outcome measure pooled by treatment method when separable data were available. Secondary outcomes were complications, reoperation rates, radiological outcomes, and sport outcomes.

Results: The search yielded 2,079 articles, of which 10 studies (1 prospective case series, 1 retrospective comparative study, and 8 retrospective case series) with a total of 175 patients were included. The overall methodological quality of the studies was low. All patients were treated surgically; 96% of the lesions were primary cases (i.e., first-time surgery) and 58% were solitary tibial lesions (i.e., no opposing talar lesion). Arthroscopic bone marrow stimulation was the most frequently used treatment strategy (51%), followed by cartilage transplantation (17%), chondrogenesis-inducing techniques (11%), osteochondral transplantation (3%), retrograde drilling (3%), and mixed (i.e., inseparable) treatments (15%). The clinical outcomes of the different surgical therapies were considered to be moderate to good. The pooled postoperative AOFAS (American Orthopaedic Foot & Ankle Society) score for bone marrow stimulation and osteochondral transplantation was 54.8 (95% confidence interval [CI], 49.5 to 85.0) (n = 14) and 85.3 (95% CI, 56 to 100) (n = 3), respectively. Overall, complications and reoperations were rarely reported. The pooled complication and reoperation rates could only be calculated for bone marrow stimulation and were 5% and 7%, respectively.

Conclusion: Surgical interventions for OLTPs appear to yield moderate to good clinical outcomes. Bone marrow stimulation resulted in a moderate AOFAS score. Complications and reintervention rates were found to be low. The current evidence in the literature is limited because of the underreporting of clinical, radiological, and sport data and the heterogenous outcome scores reported.

Introduction

An osteochondral lesion of the tibial plafond (OLTP) is defined as damage to the articular cartilage of the distal part of the tibia and its subchondral bone. The lesion can be caused by an ankle sprain or fracture.[20,21] Although the exact incidence of the injury is not known, it is stated that 1 tibial lesion is found for every 14 to 24 osteochondral lesions on the talar dome, thereby making it a rare ankle injury.[7,16] The treatment of OLTPs is considered to be challenging for the orthopaedic surgeon and necessitates an evidence-based approach in order to yield optimal outcomes.

There is a paucity of research focusing on clinical, radiological, and sport outcomes in the treatment of OLTPs, as current literature concerns a number of studies with a low level of evidence.[2,7] Because of this, clinical practice is based on expert opinion and evidence from the treatment of osteochondral lesions of the talus (OLTs).[12] A summary of the current literature on OLTPs could help surgeons toward evidence-based treatment strategies and could subsequently improve clinical outcomes. It was therefore our primary aim with the present report to provide an overview of clinical outcomes of surgical treatment of OLTPs. A secondary aim was to assess treatment complications, reoperations, radiological outcomes, and sport outcomes.

Methods

The PRISMA (Preferred Reporting Items for Systematic reviews and Meta-Analyses) statement was used as a guideline for the present study.30 The study protocol was prospectively registered in the PROSPERO registry (reference number: CRD42020152822).

Search Strategy

Studies from the earliest record to October 2019 were retrieved from PubMed, Embase (Ovid), and the Cochrane library. Additionally, a backward-citation-chaining technique (i.e., reference screening) was applied during full-text screening in order to find additional eligible studies. The full search strategy is shown in the Appendix.

Eligibility Criteria and Study Selection

All studies investigating treatment outcomes of OLTPs were included. The exclusion criteria are listed in Table 1.

Table 1. Exclusion Criteria

Exclusion Criteria
- No separate treatment outcome data for tibial or bipolar lesions available from a cohort of ankle osteochondral lesions
- Patient overlap
- Study with <3 patients with OLTPs per study
- No clinical outcomes
- Review articles. conference abstracts, technique reports, or trial registry
- Animal studies
- Language other than English, French, German, or Dutch

An independent evaluation of the articles and a subsequent discussion were conducted by 2 reviewers (Q.R. and J.D.) after title and abstract screening as well as full-text reading. In the event of a disagreement after discussion, the senior author (G.K.) was consulted for the deciding opinion. If ≥2 studies with overlapping cohorts were included, the study with the highest number of patients was included. When separate outcome data for tibial or bipolar lesions (i.e., an osteochondral lesion of the tibial plafond with a corresponding talar lesion) were unavailable from a cohort of ankle osteochondral lesions or when it was unclear whether distal tibial lesions were present in a cohort, the authors were contacted through email to clarify certain methodological points or to request data. Authors were also contacted when additional data were needed for inclusion or when incomplete data were available. If no response was received, 2 subsequent reminder emails were sent, after which a study was excluded if there was no response and the study remained ineligible.

Methodological Quality

Methodological quality was assessed using the Methodological Index for Non-Randomized Studies (MINORS).[36] Studies were graded by 2 independent reviewers (Q.R. and J.D.) after which any conflicting outcomes were resolved by a discussion. When disagreement persisted, the senior author (G.K.) was consulted for a deciding opinion.

Data Extraction

An extraction form was specifically designed for this study and piloted prior to usage with Excel 2017 (Microsoft). The collected baseline characteristics were as follows: author names; year of publication; number of patients and ankles; patient age, sex, and body mass index (BMI); follow-up duration; duration of symptoms; specific type of treatment; lesion location (according to Elias et al.[16]), solitary tibial lesion or bipolar lesion (i.e., osteochondral lesion of the tibial plafond with an opposing talar lesion); size (medial-lateral, anterior-lateral, and depth); and primary (i.e., first-time surgery) or nonprimary nature of the lesion (i.e., failed primary surgical treatment). Primary

outcome measures retrieved were any clinical scoring system and/or patient-reported outcome measure(s) (PROMs). Secondary outcomes collected were the occurrence of complications and/or reinterventions, the rate and time of return to sport at any level and the preinjury level, and any radiological outcome or osteoarthritis score.

Statistical Analysis

A simplified pooling method was used to analyze data. Baseline characteristics were pooled and weighted according to the number of lesions per study. The same method was used to pool baseline characteristics of patients stratified by treatment method. In order to evaluate clinical outcome, corresponding clinical outcome scores were similarly pooled per treatment method. Continuous variables were reported as weighted means with the corresponding range of means. Categorical variables were reported as frequencies with percentages. Time units were converted either to weeks or months, depending on the outcome variable. Mean lesion size and depth were calculated in square millimeters (mm^2) and millimeters (mm), respectively. If lesion size was reported as the diameter, it was converted into surface area using the formula for a circle: Lesion Area= $\pi \times ((\text{lesion diameter})/2)^2$. When the lesion coronal and sagittal length were given, the formula by Choi et al.[8] was used to calculate lesion size. Median values were transformed to mean values according to the formula proposed by Hozo et al.[22]

Results

Article Selection

After duplicate removal, a total of 2,079 articles were identified from the literature search and backward citation chaining (Figure 1). After screening the titles and abstracts, 105 articles were included in the full-text review. Ninety-five were ineligible for inclusion, leaving 10 studies in the final analysis.[2,3,9,11,23,29,31,33,35,40] Authors of 6 eligible articles and 4 ineligible articles were contacted to provide additional data or separate data.[2,3,9,10,18,26,29,32,33,35] One author did not wish to provide data, and 9 authors did not reply. Consequently, the eligibility did not change for the articles of contacted authors.

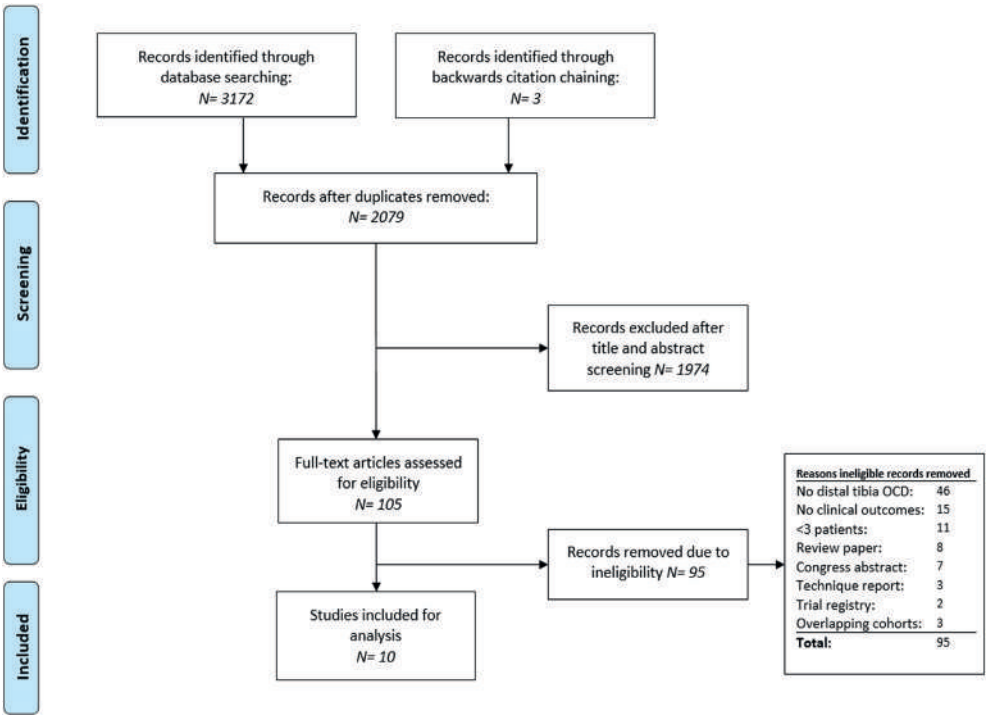

Figure. 1. Flowchart of article selection. OLTP = osteochondral lesion of the tibial plafond.

Baseline Characteristics

A total of 175 OLTPs in the same number of patients were identified. Of these 175 lesions, 73 (41.7%) were bipolar. From the available lesion data, 96% of the lesions were primary and 4% were secondary. Table 2 shows the pooled baseline data and lesion characteristics. Table 3 shows an overview of the pooled lesion dimensions. Figure 2 shows the localization of the lesions, subdivided by tibial lesions and bipolar lesions according to a 9-zone scheme developed by Elias et al.[16]

Methodological Quality

One prospective case series, 1 retrospective comparative study, and 8 retrospective case series were included. Consensus for the MINORS score was reached for all individual studies. Nine noncomparative studies had an average score of 11.4 (range, 9 to 14) of a possible total of 16 points.[2,3,9,11,23,29,33,35,40] The 1 comparative study was found to have a MINORS score of 16 of 24 points.[31] The individual MINORS score per study can be found in the Appendix.

Treatment Strategies

In the 10 included studies, 5 different treatment groups were identified (Figure 3). No nonoperative treatment strategies were reported in any of the studies

Table 2. Pooled Baseline Characteristics for All Patients*

Patients/ankles (no.)	175/175
Sex (% male/% female)	53%/47%
Age† (yr)	38.2 (13.5-43.5)
Body mass index† (kg/m^2)	32.4 (NA)
Duration of symptoms† (mo)	28.8 (12.7-40)
Follow-up† (mo)	43.8 (14.7-72)
Lesion characteristics (no. [%])	
Primary	107 (96%)
Nonprimary	5 (4%)
Unknown	63
Solitary	102 (58.3%)
Bipolar	73 (41.7%)

*Not all data were uniformly reported; percentages were therefore calculated with available data. †The values are given as the weighted mean, with the range of means in parentheses.

NA = not available.

Table 3. Pooled Lesion Dimensions*

	All Lesions	Solitary Lesions	Bipolar Lesions
Size (mm^2)	90.9 (38-180)	172.3 (143.1-180), n = 34	53.1 (38-65.2), n = 73
Depth (mm)	4.2 (2.3-4.4)	4.2 (2.3-4.4), n = 30	NA

*Lesion dimensions not available for all studies or subgroups.
The values are given as the weighted mean, with the range of means in parentheses.
NA = not available.

Clinical Outcomes

An overview of the study characteristics and pooled baseline characteristics per treatment method can be seen in Table 4. A summary of the clinical outcomes per individual study is presented in Table 5. Additionally, an overview of clinical outcome measures reported by the included studies can be found in the Appendix.

Bone Marrow Stimulation

Seven studies reported the clinical outcomes following bone marrow stimulation for a total of 90 patients.[9,11,23,29,31,35,40] An overview of study and pooled patient characteristics following bone marrow stimulation is presented in Table 4. The American Orthopaedic Foot and Ankle Society (AOFAS) score was pooled for 14 cases from 2 studies[11,40] (not regarding tibial or bipolar lesion localization), corresponding to a pooled score of 54.8 (95% confidence interval [CI]: 49.5 to 85.0). An overview of clinical outcomes following bone marrow stimulation can be found in Table 5.

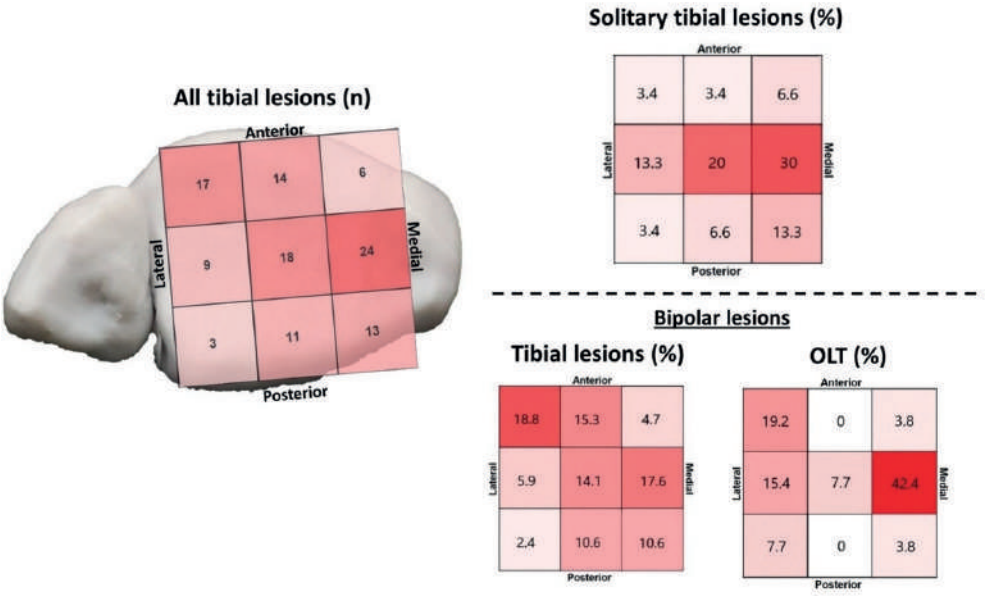

Figure 2. Heat map of the OLTP distribution using a grid scheme as described by Elias et al.[16]. *Left panel: Location of all lesions found in this study. Upper-right panel: Percentage of solitary tibial lesions by location. Lower-right panel: Percentage of bipolar tibial lesions by location and lesion type (tibial or talar [OLT]). Localization data available for 115 OLTPs (42 tibial and 73 bipolar lesions) and 26 OLTs. Bipolar data are for solitary lesions unable to be extracted separately from reported data.*[18]

Cartilage Transplantation

Two studies on cartilage transplantation were found.[5,15] Clinical outcomes of cartilage transplantation were reported in 1 of the studies[3] for 27 patients, while the other study[2] only separately reported radiological and sport outcomes for 3 patients. Table 4 shows the study and pooled baseline characteristics of these patients. Following bone-marrow-derived stem cell therapy (BMDCT), Baldassarri et al.[3] reported a mean AOFAS score of 80.6 at 72 months of follow-up.

Chondrogenesis-Inducing Technique

One study reported clinical outcomes following matrix-associated stem cell transplantation (MAST) as the chondrogenesis-inducing technique for 19 patients.[33] The study and baseline characteristics are shown in Table 4. Richter et al. reported a mean Visual Analog Scale Foot and Ankle (VAS FA) of 89.8 at 2 years of follow-up.[33]

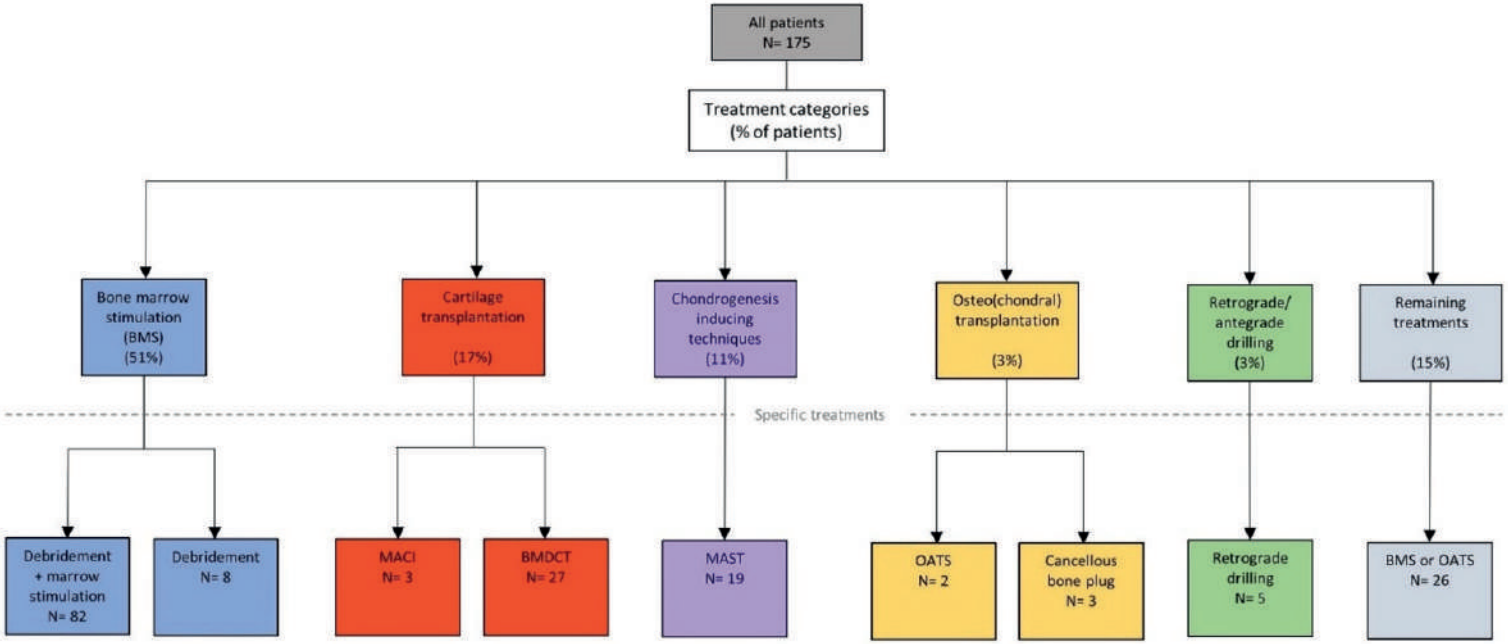

Figure 3. Flowchart of OLTP treatment with the corresponding number of patients reported. The "Remaining treatments" group includes 26 patients from a single study treated either with BMS (bone marrow stimulation) or OATS (osteochondral autograft transfer system).[23] MAST = matrix-associated stem cell transplantation, MACI = matrix-associated chondrocyte implantation, and BMDCT = bone-marrow-derived cell transplantation.

Table 4. Overview of Study, Patient, and Lesion Characteristics per Treatment*

	Study Characteristics		Patient Characteristics†			Lesion Characteristics†					
Treatment	No. of Studies	Type of Study (%)	No. Ankles	FU‡ (mo)	Age‡ (yr)	P (no. [%]	NP (no. [%])	S (no. [%])	B (no. [%]	Size‡ (mm^2)	Depth‡ (mm)
BMS	7[9,11,23 29,31,35,40]	RCS (85.7%) RC (14.3%)	90	38.3 (14.7-48.5)	37.0 (24.5-42.1)	77 (96)	3 (4)	39 (56)	31 (44)	52.1 (38.0-165.1)	NA
Cartilage transplantation	2[2,3]	RCS (100%)	30	67.2 (24.3-72.0)	37.7 (24.0-39.2)	NA	1 (NA)	30 (100)	0 (0)	174.7 (126.7-180.0)	4.2 (2.3-4.4)
Chondrogenesis-inducing techniques	1[33]	PCS (100%)	19	NA	NA	NA	NA	19 (100)	0 (0)	NA	NA
Osteo(chondral) transplantation	4[11,23, 31,40]	RCS (100%)	5	34 (24-54)	30.3 (24.5-42)	4 (80)	1 (20)	5 (100)	0 (0)	143.1 (NA)	NA
Retrograde drilling§	1[31]	RCS (100%)	5	44.0 (NA)	38.0 (NA)	NA	NA	NA	NA	NA	NA

*Some studies reported multiple treatment modalities. †Data available for a limited number of patients. ‡Data are presented as the weighted mean, with the range of means in parentheses. §Age and follow-up data also include other treatments, as no separate data for drilling were available.[22.]

Abbreviations: P= Primary, NP= Non-primary, S= Solitary, B = Bipolar. FU = follow-up, BMS = bone marrow stimulation, RCS = retrospective case series, RC = retrospective comparative, NA = not available, and PCS = prospective case series.

Osteo(chondral) Transplantation

Osteo(chondral) transplantation was reported separately in 3 studies[11,31,40] for a total of 5 patients and combined with results of bone marrow stimulation in 1 study with 26 patients.[11] The study characteristics and pooled baseline characteristics are presented in Table 4. The AOFAS score could be pooled for 3 cases with solitary lesions from 2 studies.[11,311] The mean pooled AOFAS score was 85.3 (95% CI, 56 to 100). A full overview of clinical outcomes for osteo(chondral) transplantation is found in Table 5.

Retrograde Drilling

Clinical outcomes for retrograde drilling were reported in 1 study for a total of 5 patients.[31] However, clinical outcomes were not separately available for retrograde drilling. The study and baseline characteristics are shown in Table 4, and the clinical results are shown in Table 5.

Complications and Revision Surgery

Six studies reported on the occurrence of complications in a total of 107 patients following surgical treatment.[2,3,11,29,31,35] Complications per treatment were reported for 90 patients in 5 studies.[2,3,11,29,35] From these, 60 had been treated with bone marrow stimulation, 27 with BMDCT, and 3 with matrix-associated chondrocyte implantation (MACI). Three complications (1 subchondral cyst, 1 deep venous thrombosis, and 1 superficial peroneal nerve dysesthesia) were found for bone marrow stimulation in 1 study[35], corresponding to a pooled complication rate of 5%. One case of ankle rigidity (4%) following BMDCT was noted as a complication by the authors but resolved by extending the rehabilitation protocol.[3] Mologne and Ferkel[31] noted 2 neurological complications (12%) in a case series involving multiple treatments for 17 patients and attributed these to tourniquet use. Except for 1 case of saphenous neurapraxia, none of the complications were reported to be long-term. Revision surgery was reported in 3 studies with a total of 36 patients.[11,29,31] A total of 4 patients underwent revision surgery. One study reported 3 revisions; 2 of the patients were initially treated with bone marrow stimulation, and 1 had been treated with use of an allograft bone plug.[11] One patient initially treated with transmalleolar drilling underwent revision surgery in the cohort of Mologne and Ferkel.[31] The pooled revision rate could be calculated for a total of 28 cases with bone marrow stimulation and corresponded to 7%. An overview of complications and reoperations per study can be seen in Table 5.

Table 5. Clinical, Radiological, and Sport Outcomes per Individual Study

Study	Treatment	N	FU (SD, Range) (mo)	Location	Clinical Outcomes
Chuckpaiwong et a.[9] (2008)	BMS	19	NA	Tibia and talus	Clinical success rate: 6 of 19 (31.6%)
Cuttica et al.[11] (2012)	BMS	4	14.7 (8.7-23.9)	Tibia and talus	AOFAS: preop: 37 (28-49)/postop: 49.5 (44-55) (n = 2) Time to full activities: 23.8 wk (± 11.7, range: 12-39 wk)
	BMS (microfracture and drilling)	8	48.5 (14-100.5)	Tibia	AOFAS: preop: 34.6 (24-45)/postop: 49.9 (33-58)†
	Allograft bone plug	1	54 (NA)	Tibia	AOFAS: preop: 33/postop: 56†
Lee et al.[29] (2019)	BMS	16	29.8 (± 13.2, 12-54)	Tibia and talus (n = 4)	VAS pain score preop: 8.3 (± 1.2)/ post-op: 1.8 (± 1.2) FAAM: daily pre-op: 57.6 (± 21.2)/ daily postop: 84.3 (± 14.3) SF-12 PCS preop: 36.3 (± 10.7)/post-op: 46.0 (± 10.3) SF-12 MCS preop: 41.3 (± 18.1)/ postop: 52.6 (± 9.2)
Mologne and Ferkel31 (2007)	Combined‡	11	Total: 44 (24-99)	Tibia	AOFAS preop: 55.0 (median)/post-op: 87.0 (median)
		6		Tibia and talus	AOFAS preop: 48.5 (median)/post-op: 87.5 (median)

†AOFAS score includes 1 nonprimary lesion.

Abbreviations: FU = follow-up, SD = standard deviation, BMS = bone marrow stimulation, NA = not available, AOFAS = American Orthopaedic Foot and Ankle Society score, RTS = return to sports, OATS = osteochondral autograft system, SF-12 = Short-Form 12, PCS = physical component summary, MCS = mental component summary, FAOS = Foot and Ankle Outcome Score, , and VAS FA = visual analog scale foot and ankle.

Radiological Outcomes	Complications	Reoperation	Sport Outcomes
NA	NA	NA	NA
NA	None	0	For all patients, RTS (unspecified level): 9 (81.8%) of 11 available
NA	None	2 (BMS, OATS)	
NA	None	1 (BMS)	
NA	None	0	FAAM sport preop.: 34.5 (± 26.0) FAAM sport postop.: 65.2 (± 30.2) Sports impact level preop: low (12.5%), mid (56.25%), and heavy (31.25%) impact Sports impact level postop: low (62.5%), mid (18.75%), and heavy (18.75%) impact
van Dijk grade (for 15 patients): normal: n = 7, grade1: n = 6, grade 2: n = 2	All patients: 1 sciatic nerve neurapraxia, 1 saphenous neurapraxia		NA
		1 (defect filling from iliac crest)	

‡Combined therapy consisting of arthroscopy with curettage for all patients with additional transmalleolar drilling (n = 5), microfracturing (n = 2), or OATS (n = 2).

FAAM = Foot and Ankle Ability Measure , MOCART = magnetic resonance observation of cartilage repair tissue, DVT = deep venous thrombosis, ICRS = International Cartilage Repair Society, MRI = magnetic resonance imaging, BMDCT = bone marrow-derived cell transplantation, MACI = matrix-associated chondrocyte implantation.

Table 5. Continued

Study	Treatment	N	FU (SD, Range) (mo)	Location	Clinical Outcomes
Ross et al.[35] (2014)	BMS	31	44 (24-72)	Tibia, and talus (n = 14)	FAOS preop: 50.5 (17-75)/postop: 74.2 (47-92) SF-12 preop: 38.7 (3-57)/postop: 59.5 (16-89)
Takao et al.[40] (2010)	BMS (ante-grade drilling)	2	24	Tibia	AOFAS preop: 58.5 (58-59)/postop: 85.0 (80-90) ICRS: 5, 1-yr FU
	Bone plug	2	24	Tibia	AOFAS preop: 64.5 (64-65)/postop: 100 ICRS: 11, 1-yr FU
Irwin et al.[23] (2018)	Combined§	26	32	Tibia and talus	FAOS preop: 49.4 (± 18.6)/postop: 83.8 (± 14.7)
Baldassarri et al.[3] (2018)	BMDCT	27	72	Tibia	AOFAS: preop: 52.4/postop: 80.6
Aurich et al.[2] (2011)	MACI	3	24.3 (11-38)	Tibia	NA
Richter et al.[33] (2017)	MAST	19	24	Tibia	VAS FA postop: 89.8

§Combination of microfracture or autologous osteochondral transplantation with bone marrow aspirate.

Radiological Outcomes	Complications	Reoperation	Sport Outcomes
MOCART: 69.4 (10-95) (n = 23)	1 subchondral cyst, 1 superficial peroneal nerve dysesthesia, 1 DVT	NA	Time to return to activity: 27.4 wk (range: 8.7-95.7 wk)
MRI: mean subchondral lesion diameter reduction: 7 mm MRI: mean subchondral lesion diameter reduction: 13.5 mm	NA	NA	NA
NA	NA	NA	NA
van Dijk grade: all normal MOCART: defect filling: 68%, subchondral intact: 72%	1 ankle rigidity	NA	NA
MOCART: 50 (range: 45-60)	None	NA	RTS: 1 same level, 1 lower level, 1 no return Level: recreational
NA	NA	NA	NA

Radiological Outcomes

Three studies[2,3,35] reported radiological outcomes by means of the magnetic resonance observation of cartilage repair tissue (MOCART) score. Two studies[3,31] reported osteoarthritic changes according to the van Dijk grade.[15] Among patients treated with bone marrow stimulation, Ross et al.[35] found a mean MOCART score of 69.4 at 44 months follow-up, while Mologne and Ferkel[31] found osteoarthritic changes in 53% at a mean follow-up of 44 months for patients primarily treated with debridement and retrograde drilling. Grade 1 and 2 osteoarthritic changes were seen in 40% and 13% of these patients, respectively. Aurich et al.[2] reported a mean MOCART score of 50 at 24 months for patients treated with MACI. Baldassarri et al.[3] found osteoarthritic changes in no patient at 72 months of follow-up in their cohort treated with BMDCT. However, in this study, patients with severe osteoarthritis (van Dijk grade 3 or higher) were excluded. This study only reported the subscores and not the total MOCART score. Complete defect filling and an intact subchondral bone layer were observed in 68% and 72% of the patients, respectively.

Sport-Related Outcomes

Sport-related outcomes were reported in 4 studies.[2,11,29,35] The return-to-sport rate (any and pre-injury level) was reported in 3 studies[2,11,29] for a total of 28 patients. One study[35] reported the time to return to activity for 31 patients. Cuttica et al.[11] reported that 82% of available patients (primarily treated with bone marrow stimulation) returned to their preoperative sports or activities, but did not specify at which level. Lee et al.[29] found that 63% of patients treated with bone marrow stimulation engaged in a low level of impact sport activity postoperatively compared with 13% preoperatively. This study also found that the Foot and Ankle Ability Measure (FAAM) sports subscale score significantly increased, from 35 preoperatively to 65 postoperatively. Ross et al.[35] reported that the mean time to return to activities following bone marrow stimulation was 27.4 weeks. Among the 3 patients treated with MACI, Aurich et al.[2] found that 33% of the patients returned to their preoperative level of sports and 66%, to any level of sports.

Discussion

To the best of our knowledge, this is the first systematic review of OLTPs and provides a comprehensive overview of the available evidence. The most important finding of this systematic review is that, overall, surgical treatment of OLTPs appears to yield moderate to good clinical outcomes regardless of treatment, given the limited and heterogenous data available. The current evidence in the literature is limited, however, because of the heterogeneity and underreporting of data, thus not allowing a formal comparison of OLTP treatments. Most lesions were primary in nature and treated with bone marrow stimulation.

Studies showed great diversity in both treatment strategies and clinical outcomes. When compared with results from surgical treatment of OLTs in the literature, OLTPs show lower clinical outcome scores.[13,27]

Lesion Location and Size

Lesion location was reported according to an anatomical grid as proposed by Elias et al.[16] in 6 studies.[2,3,11,23,29,35] The results showed solitary lesions to be most often located in the central-medial area and bipolar lesions to be located anterolaterally. The location of solitary lesions could be explained by the compressive forces of the talus on the tibial cartilage during ankle inversion injuries, as was hypothesized by Baldassarri et al.[3] Furthermore, the higher incidence of anterolateral localization for bipolar lesions has been hypothesized to be associated with a combination of predisposing lateral ankle stability and a history of ankle trauma.[23] The number of lesions with combined traumatic etiology and lateral ankle instability could not be determined in the present study because of inseparable data. A second explanation for the localization of bipolar lesions could be the cartilaginous properties of tibial cartilage; tibial cartilage has been demonstrated to be stiffer in the posteromedial and anterolateral regions.[1] Consequently, when the talus impacts the tibia, a higher force is needed to damage the tibial cartilage, thereby forming a lesion on both the tibia and the talar dome.

Lesion size was substantially higher for solitary lesions than for bipolar lesions. Of the available data, bipolar lesions were primarily treated with bone marrow stimulation. Bone marrow stimulation is generally considered a good indication for surgery for smaller lesions.[19] Due to this reason, the lower lesion size of bipolar lesions could be biased. Only Irwin et al.[23] explicitly stated that they treated lesions of <150 mm with bone marrow stimulation. In contrast, solitary lesions were predominantly treated with cartilage transplantation or osteo(chondral) transplantation, which is generally considered for larger lesions.[13,19] The treatment indication for solitary and bipolar lesions might have differed.

Clinical and Radiological Outcomes

Because of the heterogeneity of the included studies and the underreporting of data, limited pooling of data could be performed. Our findings are therefore limited as the level of evidence of the included studies as well as the number of included patients were low. We can thus primarily give an overview of the clinical outcomes after treatments for OLTPs as a whole. Clinical outcomes can be considered heterogenous concerning the clinical efficacy, even among analogous treatment modalities. The pooled AOFAS score for bone marrow stimulation was lower compared with previous systematic reviews on OLTs.[13,27] However, the pooled AOFAS score for osteo(chondral) transplantation was comparable.[13,27]

The treatment of OLTPs is based on lesion morphology and size and should best be conducted on a patient-specific basis. Even though corresponding treatment principles are applied, OLTPs seem surgically more challenging than talar lesions and therefore might yield inferior results, as stated by experts in the field.[3,31] First, tibial lesions occur less often than talar lesions, therefore allowing fewer surgeons to gain experience in their treatment. The low incidence of OLTPs has been hypothesized to be due to the concave shape of the distal part of the tibia, thereby resulting in a better distribution of axial forces than with the talus.[16] Therefore, referring patients with OLTPs to an experienced arthroscopist is advised. Moreover, the technical difficulty concerning the arthroscopic accessibility of the ankle joint is evident, especially because of the inability to maneuver the tibia to gain better access as is possible for the talus.[6] Moreover, surgeons should be mindful of the translatability of conventional talar treatment methods and their limitations.

Regarding radiological outcomes, one can state that postoperative magnetic resonance imaging (MRI) assessment of the filled defect was reported with the MOCART score in 3 studies[2,3,35], of which 2 studies presented a mean total outcome. The MOCART scores of patients treated with BMS were higher than for those treated with MACI, possibly because of the longer follow-up duration (44 versus 24 months), allowing for greater filling of the defect. Osteoarthritic changes were reported in 2 studies.[3,31] However, only short to mid-term outcomes were available, and it is therefore likely that degenerative changes did not present on radiographs at the reported follow-up times of the included studies. Long-term radiological follow-up is needed to examine the rate and onset of degenerative osteoarthritic changes in the ankle joint after OLTP treatment as posttraumatic osteoarthritis develops in later stages of the disease.[4]

Complications and Revision Surgery

Few complications were noted in a considerably small number of patients; 6 of 10 studies reported on the occurrence of complications associated with treatment of OLTPs. The predominant complications reported were neurological problems attributed to tourniquet use, which can be considered a relatively minor complication from the common use of tourniquets in foot and ankle surgery.[14,44]

Revision procedures were reported in 3 studies with a low number of included patients. Overall, the reintervention rate found in this study can be considered moderate. The pooled revision rate of OLTPs treated with bone marrow stimulation can be considered comparable with previously reported revision rates for OLTs.[41] However, OLTPs were predominantly treated as primary lesions in the present study, and we speculate that these lesions would be likely to have higher rates of clinical reintervention over a longer period of follow-up. The clinical reintervention rate may therefore be higher

when longer follow-up times are assessed. Consequently, additional studies with longer follow-up times and transparent reporting of reinterventions are necessary.

Sport Outcomes

Sports-specific outcomes for OLTPs are sparsely reported in the literature. In the present study, we found 4 studies that reported sport-specific outcomes, for a total of 59 patients. Only 1 study reported the type of sport that patients participated in, and 1 reported sports impact level.[2,29] Moreover, Lee et al.[29] reported the pre- and postoperative sports impact level but not the level of sports. It is therefore difficult to compare their findings with those of other authors. The return-to-sport rates reported for patients with OLTPs are considerably lower than the return-to-sport rates that were found in a recent systematic review by Steman et al.[38] assessing sport outcomes after treatment of talar osteochondral lesions.

In the present study, sport results were reported for patients undergoing additional surgical procedures in 2 studies[11,29], which makes it difficult to assess the sport outcomes of OLTP treatment independently of these additional procedures. Surgeons should therefore carefully inform patients about the rehabilitation and expectations for return to sports in comparison to talar lesions as the return-to-sport rates for OLTPs may be lower and evidence for OLTPs is limited.[12]

Bipolar Versus Solitary Lesions

Talar involvement can be seen as a possible factor of a clinically inferior outcome compared with solitary tibial osteochondral lesions.[12,23] Chuckpaiwong et al.[9] noted a lower rate of clinical success for bipolar lesions. However, tibial lesions were predominantly larger than 20 mm in diameter, which was found to be a predictor of worse clinical outcomes. Additionally, all patients were treated with BMS—a surgical intervention that has been demonstrated to result in inferior clinical outcomes in larger lesions.[8] Studying both solitary and bipolar lesions, Cuttica et al.[11] found similar postoperative AOFAS scores but a significantly quicker return to activities in cases of solitary tibial lesions, albeit with clinical data from only 4 patients, which limits the ability to extrapolate this finding.

Comparison with Talar Lesions

In this study, we found that the predominant treatment for OLTPs was bone marrow stimulation, a finding similar to that for primary, small, non-fragment type OLTs.[13] The pooled AOFAS score demonstrated a moderate result for OLTP, which is a finding in contrast to good clinical outcomes for OLT.[13,27] Bone marrow stimulation might be less effective in the relatively less common tibial lesions, potentially because of the more technically challenging access to the lesion site compared with that of talar lesions. Studies on talar lesions treated with bone marrow stimulation have noted

unfavorable long-term outcomes due to the progression of osteoarthritis over time. It is possible that these factors have less effect on tibial lesions because of the more concave shape of the tibial articulating surface.[5,16,17,28] However, a large portion of tibial lesions in the present review were bipolar and might therefore not be exempt from this line of thought. Moreover, the long-term outcomes of OLTPs have been sparsely studied, and it is unknown how clinical outcomes of the treatment of OLTPs change over time, as opposed to clinical outcomes after surgery for OLTs.[24,41,43] When comparing the osteoarthritic changes reported by the 2 included studies in this review to those of talar lesions reported in the literature, it seems that tibial lesions show similar results.[5] However, the number of patients was too low and distributed among multiple treatments to make an accurate comparison.

Methodological Considerations

The results of this systematic review have to be interpreted in the context of its design. First, a high proportion of retrospective case series with low methodological quality were included in this study. The MINORS score of the body of included articles further exemplifies this point. The findings presented in this study should therefore be interpreted with adequate caution. Second, clinical results were, in the majority of the cases, not able to be separated by treatment modality according to lesion location and the effect of talar involvement. Moreover, no uniform clinical outcome measure was used in the included studies, making a formal statistical comparison between treatment options methodologically inappropriate. As a consequence, we chose to perform a simplified pooling method.

The strengths of the present study were the inclusion of primary and secondary tibial lesions, the wide and thorough article selection process by 2 independent investigators, and the quality assessment of the body of included articles. Additionally, we performed a corresponding-author contact protocol in order to include additional articles and to ensure the included articles met the inclusion and exclusion criteria. We advocate wider use of such a protocol.

Future Perspectives and Clinical Relevance

The results of this review suggest that treatment for patients with an osteochondral lesion of the tibial plafond yields moderate to good outcomes and may be clinically inferior compared to the outcomes of OLTs reported in the literature. To provide the most appropriate care and better clinical outcomes for patients with an osteochondral lesion of the tibial plafond, as well as to determine the optimal treatment strategy, there is a need for high-quality, prospective, comparative studies of treatment options. Moreover, the present study shows the need for an evidence-based, personalized treatment approach for individual patients that incorporates patient and lesion characteristics. In order to reach this goal, it is essential to thoroughly

follow patients with OLTPs and to be transparent about the treatment strategy and results. The findings from the present study can aid surgeons and patients during the shared clinical decision-making process.

The clinical relevance of this systematic review is in its overview of lesion and patient characteristics and clinical outcomes, which can aid surgeons and patients in the clinical decision-making process. This study also highlights the importance of the involvement of surgeons experienced in the treatment of these type of lesions.

Conclusions

Given the limited and heterogenous data available, surgical interventions for OLTPs appear to yield moderate to good clinical outcomes. Bone marrow stimulation and osteo(chondral) transplantation resulted in moderate and good AOFAS scores, respectively. Complication and reintervention rates were found to be low. The current evidence in the literature is limited because of the heterogeneity and underreporting of data, thus not allowing a formal comparison of OLTP treatments. Our findings highlight the need for further high-level research with larger sample sizes and uniformly comparable outcome measures for patients treated for OLTPs.

Appendix

Appendix 1. Search Strategy

#	PubMed	EMBASE (Ovid)	Cochrane library
1	"Osteochondritis Dissecans"[MeSH] OR osteochondritis dissecans[tiab] OR osteochondrosis dissecans[tiab] OR osteochondrolysis[tiab] OR OCD[tiab] OR OLT[tiab]	osteochondritis dissecans/	MeSH descriptor: [Osteochondritis Dissecans] explode all trees
2	(osteochondral[tiab] OR chondral[tiab] OR transchondral[tiab] OR cartilage*[tiab]) AND (defect*[tiab] OR lesion*[tiab])	(osteochondritis dissecans or osteochondrosis dissecans or osteochondrolysis or OCD or OLT).ti,ab,kw.	(osteochondritis dissecans or osteochondrosis dissecans or osteochondrolysis or OCD or OLT):ti,ab,kw
3	#1 OR #2	((osteochondral or chondral or transchondral or cartilage*) and (defect* or lesion*)).ti,ab,kw.	((osteochondral or chondral or transchondral or cartilage*) and (defect* or lesion*)):ti,ab,kw
4	"Tibia"[Mesh] OR "Ankle"[Mesh] OR distal tibia*[tiab] OR OLTP[tiab] OR ankle[tiab]	1 or 2 or 3	#1 or #2 or #3
5	#3 AND #4	exp distal tibia/ or exp ankle/ or (distal tibia* or OLTP or ankle).ti,ab,kw.	(distal tibia* or OLTP or ankle):ti,ab,kw
6	"Letter" [Publication Type] OR "Comment" [Publication Type] OR "Editorial" [Publication Type] OR "Congress" [Publication Type] OR letter[ti] OR comment[ti] OR editorial[ti]	4 and 5	#4 and #5
7	#5 NOT #6	letter/ or editorial/ or (letter or comment or editorial).ti.	
8	(("Animals"[Mesh] OR "Animal Experimentation"[Mesh] OR "Models, Animal"[Mesh] OR rat[tiab] OR rats[tiab] OR mice[tiab] OR mouse[tiab] OR dog[tiab] OR dogs[tiab] OR pig[tiab] OR pigs[tiab] OR cow[tiab] OR cows[tiab] OR monkey[tiab] OR monkeys[tiab]) NOT ("Humans"[Mesh] OR human*[tiab]))	6 not 7	
9	#7 NOT #8	(exp animal/ or exp animal experiment/ or exp animal model/ or (rat or rats or mice or mouse or dog or dogs or pig or pigs or cow or cows or monkey or monkeys).ti,ab,kw.) not (human/ or human*.ti,ab,kw.)	
10		8 not 9	

Appendix 2. Minors criteria of included studies									Additional criteria comparative research				
Study	A clearly stated aim	Inclusion of consecutive patients	Prospective collection of data	Endpoint appropiate to the aim of the study	Unbiased assesment of the study endpoint	Follow up period appropiate to the aim of the study	Lost of follow up less than 5%	Prospective calculation of study size	An adequate control group	Contampory group	Baseline equivalent of groups	Adequate statistical analysis	Total
Aurich, 2011	2	2	2	2	2	2	2	0					14/16
Baldassarri, 2018	2	2	0	2	1	2	2	0	-	-	-	-	11/16
Chuckpaiwong, 2009	2	2	2	2	1	2	2	0	-	-	-	-	13/16
Cuttica, 2012	2	2	0	2	1	2	1	0					10/16
Irwin, 2018	2	2	0	2	2	2	1	0					11/16
Lee, 2019	2	2	0	2	1	2	1	2	-	-	-	-	11/16
Mologne, 2007	1	2	0	1	1	2	1	0	1	2	2	2	16/24
Richter, 2017	2	2	2	2	1	2	1	0	-	-	-	-	12/16
Ross, 2014	2	2	0	2	2	2	2	0	-	-	-	-	12/16
Takao, 2010	2	2	0	1	1	2	1	0	-	-	-	-	9/16

Appendix 3. Summary of clinical outcome measures reported in the included studies

Outcome measure	No. reported
American Orthopaedic Foot and Ankle Society (AOFAS) ankle and hindfoot score	5
Foot and Ankle Outcome Score (FAOS)	2
Short-Form 12 questionnaire	2
International Cartilage Repair Society (ICRS) score	1
Visual Analog Scale- Foot and Ankle (VAS-FA)	1
Visual Analog Scale pain	1

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Chapter 10

Non-Operative Management for Osteochondral Lesions of the Tibial Plafond Results in Minor Improvements of Patient-Reported Outcomes: A 2-Year Prospective Follow-Up Study

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Abstract

Purpose: Osteochondral lesions of the tibial plafond (OLTP) are considered rare, and to date the treatment for these lesions has solely focussed on operative management. The aim of this study was to prospectively assess the 2-year patient-reported outcomes, radiological outcomes, and adverse outcomes for the non-operative treatment of patients with a symptomatic OLTP.

Methods: Eighteen patients with a symptomatic OLTP that underwent non-operative treatment were prospectively assessed. The primary outcome concerned the numeric rating scale (NRS) for pain during weightbearing from baseline to 2-years follow-up. Secondarily, the patient-reported outcomes (PROMs) NRS during rest, running, and stairclimbing, as well as the Foot and Ankle Outcome Score (FAOS) and short-form-36 (SF-36) questionnaires were assessed. CT-scans at median 2 years (IQR: 1.5 – 2) follow-up were reviewed for changes in lesion volume or signs of lesion healing. Return to sports and work rates were evaluated. The conversion to surgery rate and any complications were assessed.

Results: The NRS during weightbearing improved (non-significantly) from a median of 5 (IQR: 3 – 7) out of 10 at baseline to 2 (IQR: 1 – 6) out of 10 at 2-years follow-up, P=0.06. The other NRS subscales, FAOS subscales, and SF-36 did not significantly improve at final follow-up. The follow-up CT-evaluation showed that lesion volume did not change (219 (IQR: 79 – 890) mm3) compared to baseline (226 (IQR: 79 – 890) mm3), P= 0.2. In 10 (77%) out of 13 cases signs of lesion filling or no change was observed. At final follow-up, 93% (13/14) of patients returned to any level of sports, 54% (7/13) of patients returned to preinjury level of sports, and 94% (15/16) of patients returned to work. No adverse events were observed, and 1 (6%) case converted to surgery.

Conclusions: Non-operative management for OLTP resulted in minor improvements of patient-reported pain and functional outcomes up-to 2-years follow-up. The conversion to surgery rate was 6%. Radiologically, lesion size and filling were found to remain stable at CT follow-up. Moreover, on average 9 out of 10 patients were able to participate in sport and could return to, or remain at, their preinjury work activities.

Keywords: Ankle; Tibia; OLTP; Cartilage; Non-operative

Introduction

Osteochondral lesions of the Tibial Plafond (OLTP) are considered rare, with an incidence ratio of 1 OLTP to 14-24 osteochondral lesions of the talus (OLT).[4,8] Patients with an OLTP may present after an ankle trauma, such as a sprain or fracture, with complaints of (deep) ankle pain during weightbearing, joint swelling, and/or locking.[10,18]

To date, the treatment of OLTP is largely based on the rationale and algorithm for talar lesions, and primarily consists of operative treatment options.[11] Recent systematic reviews found that the outcomes of these operative treatments can be considered moderate to good, but a severe limitation of the current literature is its low-quality evidence.[5,11] It is known from the OLT literature that up-to 45% of patients show satisfactory clinical outcomes following non-operative treatment, which recedes the need for surgical treatment. Moreover, surgical treatment entails inherent surgical risks, and possibly higher costs and a longer time-off from work and sports.[2] Even though its use is considered standard practice before commencing with operative treatment in cartilage lesions of the ankle, no literature is currently available on the non-operative management for OLTP.[6,7,11] Therefore, no evidence-based (shared-decision) discussion can be held between patient and physician on the safety and efficacy of non-operative treatment for OLTP.

The present study, therefore, primarily aimed to prospectively assess the 2-year patient-reported outcomes for the non-operative treatment of patients with a symptomatic OLTP. Secondarily, the study assessed radiological outcomes, return to sport- and work rates, as well as adverse events and the conversion to surgery rate These results can aid in patient counseling and expectation management, while providing physicians with evidence for patient-specific treatment guidance.

Methods

This study is a prospective, single-center, case-series with 2-year follow-up. Ethical approval for this study was obtained from the local Medical Ethics Committee Amsterdam UMC, location AMC (reference number W14_237#14.17.0288).

Patient Selection

All patients presenting with a symptomatic OLTP at our institution between November 2019 and July 2022 were screened for eligibility. A symptomatic OLTP was defined as a radiologically confirmed OLTP with deep ankle pain (during or after weightbearing) arising from the lesion with or without joint swelling or mechanical symptoms (such as locking or catching), and corroborative findings on physical examination (such as palpation pain of the lesion). The inclusion and exclusion criteria for participation in

the study are listed in the Appendix. Patients with a OLTP and coexisting talar lesion (OLT) were eligible for inclusion. Our institution is a tertiary academic referral hospital that is recognized as an expert center in the diagnosis and treatment of cartilage lesions of the foot and ankle.

Non-Operative Treatment

Non-operative treatment consisted of, or the combination of, the following treatments during the follow-up period: supervised neglect, insoles or shoe modifications, physical therapy, weight-loss recommendations, or intra-articular injection with hyaluronic acid or corticosteroids (2 injections with a 2-week interval). The choice for a specific treatment was made on an individual basis, in a shared decision-making process, and was thus not standardized.

Data Collection

Baseline demographic and treatment information were extracted from the hospital electronic patient records. Baseline demographics included: sex, age, body mass index (BMI), injury circumstances, laterality, hindfoot alignment, and prior foot or ankle surgery. Treatment characteristics were primary or non-primary (i.e., failed previous surgical treatment) lesion type, any concomitant diagnosis at initial clinical evaluation, and the specific non-operative treatments utilized as previously described.

Patient-Reported Outcome Measures

All patient-reported outcome measures (PROMs) were collected through the online CASTOR®-portal and prospectively collected by a researcher not responsible of clinical care. The PROMs that were collected concerned the numeric rating scale (NRS) of pain (during rest, during walking, during running, and during stairclimbing), the foot and ankle outcomes score (FAOS), and the Short Form-36 (SF-36). The NRS of pain is a Likert pain scale that ranges from 0 (no pain) to 10 (worst imaginable pain). The FAOS measures from 0 (lowest) to 100 (highest) and consists of 42 questions distributed among five subscales: symptoms, pain, activities of daily living, sport, and quality of life. The SF-36 is a general-health questionnaire with two subscales, the physical component scale (PCS) and mental component scale (MCS).

At baseline, the type of sport and athletic level (i.e. amateur, competitive, or professional) were recorded. At 2-years follow-up a patient-reported sports evaluation consisted of the return to sports (RTS) rate in percentages and RTS time in weeks, type of sport, and level of activities. Return to sports level was defined as according to Ardern et al.1 In a similar fashion, the baseline and 2-year postoperative patient-reported work activities and return to work time were collected.

Radiological Assessment

Baseline CT-scans were available for all patients and were assessed by two independent measurers (Q.R. and J.D.) for lesion characteristics. The baseline assessment consisted of lesion size (anterior-posterior direction, medial-lateral direction, and depth), lesion location according to a 9-grid scheme[8], the presence of cysts, and lesion morphology according to a general morphological classification for OLT.[13]

CT-scans at final clinical follow-up were assessed by two independent measurers (Q.R. and J.D.) The assessment included lesion size measurements and signs of lesion healing (subjective increased lesion filling compared to baseline) or deterioration (subjective increased cyst formation).

Statistical Analysis

A sample size calculation for the primary outcome, the NRS during walking from preoperatively to 2-years postoperatively, indicated that a minimum of 16 ankles were needed to detect a difference in means of 2.0 out of 10, assuming a standard deviation of 2.5 using a Wilcoxon signed-rank test with a 2-sided 0.05 significance level and 80% power (nQuery advisor 7.0, Statistical Solutions Ltd., Boston, MA). A difference of 2 points was chosen as this corresponds to a "much better" improvement in pain.[9,15] To correct for a potential loss to follow-up of 10% the required minimum sample size for the present study was 18 cases.

Statistical analysis was performed using Stata 17 (StataCorp LP, College Station, TX). A two-sided level of $P < .05$ was considered significant. Data normality was assessed using a Shapiro-Wilk test. Continuous baseline variables distributed normally were reported as means with standard deviations and as median with inter-quartile ranges (IQR) if distributed non-normally. Dichotomous and categorical variables were reported in frequencies and percentages. The comparison of the primary outcome and other PROMs was conducted by means of a Wilcoxon signed-rank test. Additionally, a sub-analysis for the improvement in the primary outcome was examined for patients who were classified as 'responders' or 'non-responders'. A patient was classified as a 'responder' if a change of ≥ 2 out of 10 the NRS during walking from baseline to 2-year follow-up was achieved, as this was previously described as a 'much better improvement in pain', and no conversion to surgery had occurred.[15] Moreover, the baseline characteristics for responders and non-responders were comparing with a Mann-Whitney U test for continuous variables and Fishers' exact test for dichotomous variables. To test the between-group difference within each follow-up point (i.e., baseline, 6 months, 1 year, and 2-years) an adjusted P-value was used (0.05/4 = 0.0125). Lastly, a sub-analysis was conducted by comparing the change in PROMs from baseline to 2-year follow-up of patients with a solitary OLTP compared to bipolar (i.e., OLTP with coexisting OLT) lesions with a rank-sum test. An inter-observer intra-

observer (with a minimum 2 months interval) reliability assessment for the lesion size measurements was performed with a 2-way mixed effects interclass correlation coefficient (ICC) model with absolute agreement. The ICC analysis was interpreted by the following cut-offs: 0.41-0.60 fair agreement, 0.61-0.80 moderate agreement, and 0.81-1.00 substantial agreement.

Results

During the study period 22 patients were assessed for eligibility, of which 18 were included. An overview of the patient selection process is available in Figure 1. An overview of the baseline patient characteristics is available in Table 1, the treatment characteristics in Table 2, and the lesion characteristics in Table 3. Lesion localization is depicted in Figure 2.

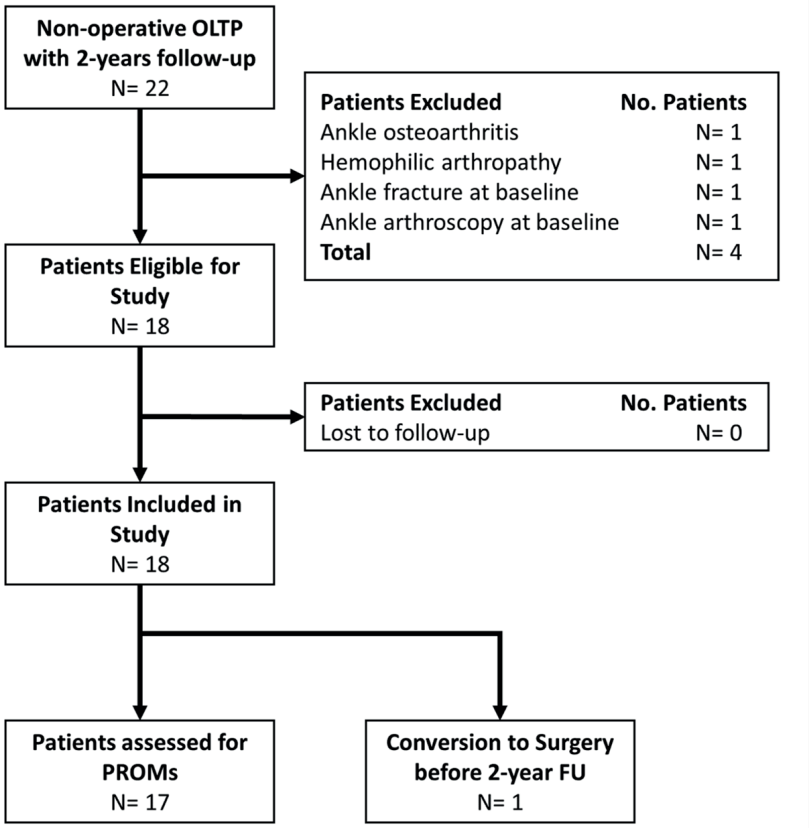

Figure 1. Flowchart of patient selection.

Table 1. Baseline Patient Characteristics

Variable	Value	% Reported
Sex, N male (%)	12 (67%)	100
Age, Years (SD)	35.8 ± 11.4	100
BMI (SD)	24.3 ± 3.6	100
Traumatic Etiology, N (%)		95
- No trauma	4 (24%)	
- Ankle fracture	7 (41%)	
- Inversion/eversion or distortion	5 (29%)	
- Other	1 (6%)	
Sports Participation, N (%)	14 (78%)	100
Detailed, N (% of participating)		
- Fitness	2 (14%)	
- Cycling or mountain biking	4 (29%)	
- Walking/hiking	2 (14%)	
- Racket sport (tennis, padel, badminton)	2 (14%)	
- MMA/kickboxing	2 (14%)	
- Other	2 (14%)	
Prior Ankle Surgery*, N (%)		100
- Ankles	9 (50%)	
- Total no. prior procedures	20	
Detailed, N (% of total no. prior surgeries)		
- External fixation ankle fracture	2 (10%)	
- ORIF ankle fracture	4 (20%)	
- Hardware removal	5 (25%)	
- Ankle arthroscopy		
o BMS OLTP	3 (15%)	
o BMS OLT	1 (5%)	
o Diagnostic arthroscopy	2 (10%)	
o Removal bony impingement	1 (5%)	
- OATS OLT (open)	1 (5%)	
- Malunion correction calcaneus	1 (5%)	

*One ankle could have had more than one prior surgery for the OLTP.
Abbreviations: N: number of, BMI: body mass index, BMS: bone marrow stimulation, OLTP: osteochondral lesion of the tibial plafond, OATS: osteochondral autograft transplantation system, OLT: osteochondral lesion of the talus, SD: standard deviation

Table 2. Treatment Characteristics

Variable	Value	% Reported
Number of Non-Operative Treatments*, Mean (SD)	2.3 ± 1.1	100
Specified per Treatment, N (% of total)		
- Physical Therapy	13 (31%)	
- Supervised Neglect	5 (12%)	
- Injection hyaluronic acid	9 (21%)	
- Weight-loss advise	2 (5%)	
- Insole	9 (21%)	
- Brace or immobilizer		
o Brace during exercise	3 (7%)	
o 6 weeks of NWB cast	1 (3%)	
Concomitant diagnosis*, N (%)		
- Ankles	10 (56%)	
- Total no. concomitant diagnosis	13	
Specified (% by no. concomitant diagnosis)		
- Anterior bony impingement	6 (45%)	
- Anterior soft-tissue impingement	1 (8%)	
- Sinus tarsi syndrome	2 (15%)	
- Hardware irritation	1 (8%)	
- Lateral ankle instability	1 (8%)	
- Posterior tibial tendon tendinitis	1 (8%)	
- Malunion distal fibula	1 (8%)	

*One ankle could have had more than one concomitant diagnosis, and more than one non-operative treatment for the OLTP. **Abbreviations:** N: number of, SD: standard deviation, NWB: non-weightbearing

Table 3. Baseline Lesion Characteristics

Variable	Value	% Reported
Primary OLTP lesion, N (%)	16 (89%)	100
Coexisting talar lesion, N (%)	7 (39%)	100
Presence cyst, N (%)	13 (72%)	100
Lesion Morphology, N (%)		100
- Cystic	12 (67%)	
- Crater	5 (28%)	
- Fragment	1 (5%)	
OLTP Lesion Size, median (IQR)*		100
- Anterior-Posterior	10 (7 – 15)	
- Medial-Lateral	10 (6 – 14)	
- Depth	7.5 (5 – 10)	
Coexisting OLT Size, median (IQR)*		100
- Anterior-Posterior	5 (3 – 15)	
- Medial-Lateral	5 (4 – 12)	
- Depth	4 (3 – 9)	

Abbreviations: N: number of, OLTP: osteochondral lesion of the tibial plafond, mm: millimeters, OLT: osteochondral lesion of the talus. *data not distributed normally, therefore represented with as median with interquartile ranges (IQR)

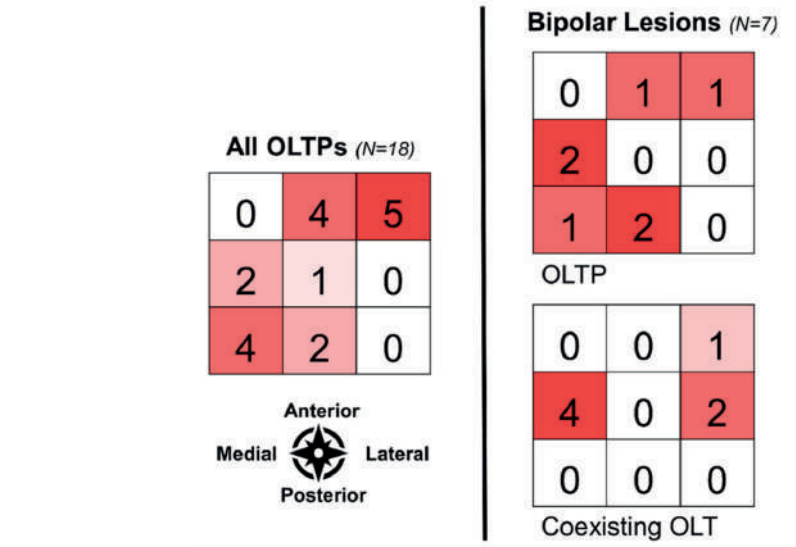

Figure 2. Heatmap of OLTP localization and bipolar OLTP with a coexisting OLT

Patient-Reported Outcomes

The primary outcome, the NRS during walking, did not significantly change from a median of 5 (IQR: 3 – 7) at baseline to 2 (IQR: 1 – 6) at 2-years follow-up, P=0.06. The primary outcome did not significantly change from 6 months to 1-year or 2-year follow-up (Figure 3). All NRS subscales, the FAOS, and SF-36 subscales did not significantly change (Table 4).

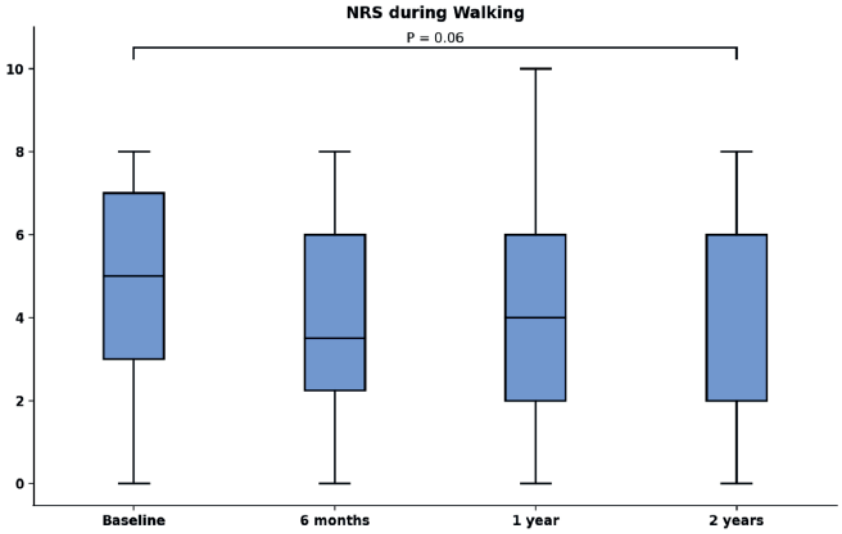

Figure 3. NRS during walking over time, of note, the outcome was not available for 3 patients at 6 months follow-up.

Table 4. Patient-Reported Outcome Measures at Baseline and 2-Years Follow-Up

	Baseline	2-Years Follow-up	P-Value
NRS pain during, Median (IQR)			
Walking	5 (3 – 7)	2 (2 – 6)	0.1
Rest	2 (1 – 4)	1 (0 – 3)	0.2
Running	7 (4.5 – 8.5) N=16	5 (3 – 9) N= 15	0.2
Stair Climbing	5 (4 – 7) N=16	2 (1.5 – 6.5) N= 16	0.1
FAOS, Median (IQR)		N=14	
Symptoms	64 (50 – 71)	59 (50 – 75)	0.7
Pain	64 (53 – 72)	67 (44 – 89)	0.7
ADL	98 (97 – 98)	98 (97 – 100)	0.8
Sport	40 (15 – 50)	43 (10 – 95)	0.1
QoL	31 (19 – 38)	41 (13 – 56)	0.4
SF-36, Median (IQR)		N= 13	
PCS	38.0 (35.7 – 42.0)	41.0 (37.5 – 44.1)	0.6
MCS	32.0 (30.5 – 36.8)	31.3 (29.2 – 39.8)	0.6

Abbreviations: NRS: numeric rating scale, FAOS, foot and ankle outcome score, IQR: inter-quartile range, ADL: activities of daily living, QoL: quality of life, SF-36: short-form 36, PCS: physical component scale, MCS: mental component scale.

When examining the sub-analysis for responders compared to non-responders, we observed that 10 (55%) patients were classified as responders. Responders had a significantly lower NRS for pain during walking (median 2 [IQR: 1 – 2]) at final follow-up compared to non-responders (median 7 [IQR: 3 – 8]) P= <0.01), and a different clinical course (Figure 4). Additionally, we observed there were no significant differences in baseline characteristics (Appendix). Moreover, there were no significant differences in change of PROMs from baseline to follow-up when comparing solitary OLTP to bipolar lesions (Appendix).

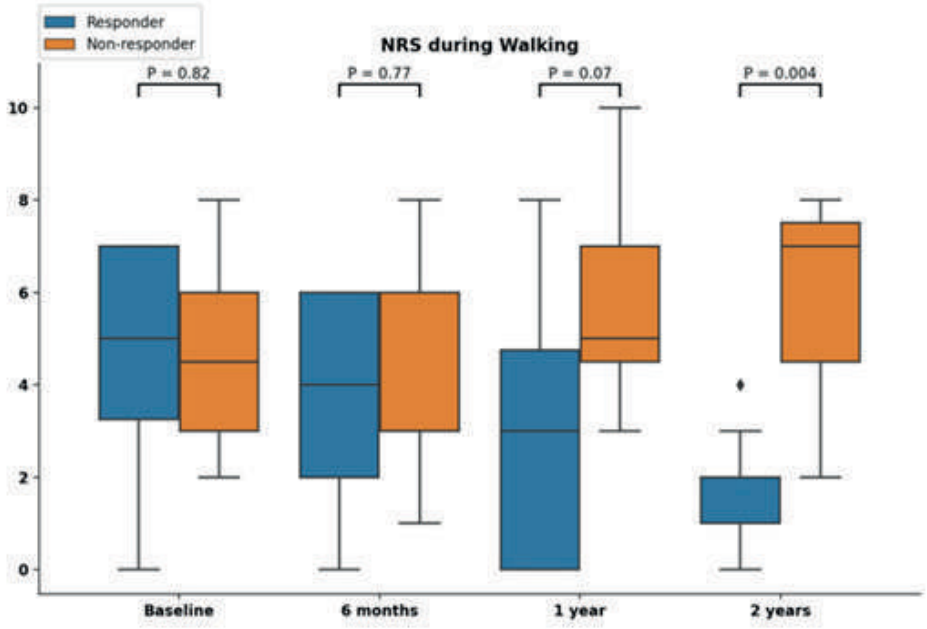

Figure 4. NRS during walking categorized according to 'responder' or 'non-responder' to treatment

Radiological Outcomes

At median 2 years (IQR: 1.5 – 2) follow-up CT-scan examination was available for 13 patients. Median lesion volume did not significantly change at final follow-up (219 (IQR: 75 – 552) mm^3) compared to baseline (226 (IQR: 79 – 890) mm^3), P= 0.2. In 4 (31%) cases a stable lesion was observed, in 6 (46%) cases lesion healing was observed, and in 3 (23%) cases deterioration was observed. A qualitative description of lesion healing is provided in the Appendix. The ICC measurements all showed substantial (>0.81) agreement and are available in the Appendix.

Sports and Work Outcomes

Of the patients who participated in sports at baseline 93% (13/14) returned to any level of sports. Of these, 54% (7/13, 1 case unknown) returned to preinjury level of sports. Of the 4 patients who did not participate in sports at baseline, 1 (25%) patient started sporting activities (fitness). At baseline 16 patients worked and 2 patients were unemployed. Of the employed patients, 15 (94%) returned to work or remained working. Of these, 14 patients remained at their preinjury occupation and 1 patient returned to a part-time non-physically demanding occupation. A detailed overview of the return to sports and work outcomes per patient is provided in the Appendix.

Treatment Failure and Adverse Outcomes

In this cohort 1 (6%) patient underwent a surgical intervention of the ankle within the study period at 7 months after initiating non-operative treatment due to ongoing symptoms. The patient underwent an osteotomy and filling with an autologous bone grafting procedure. At 2-year follow-up this patient achieved satisfactory pain levels and functional outcomes in activities of daily living and returned to sports (tennis) at any level. No adverse events in any of the included patients were observed during the study period.

Discussion

The principal finding of this study was that non-operative management for OLTP results in minor improvements of patient-reported pain and functional outcomes up-to 2-years follow-up. In this cohort, 1 patient (6%) required conversion to surgical treatment. Radiologically, lesion size and filling were found to remain stable at CT follow-up. Moreover, on average, 9 out of 10 patients were able to participate in sport and could return to, or remain at, their preinjury work activities.

Patient-Reported Outcomes

When comparing the results of the present study to the literature on non-operative OLT management it can be stated that these largely concur, in the sense that non-operative management shows limited success.[2,3] Although the OLT literature on non-operative management is larger than compared to OLTPs it should be stated that it, too, is limited as it mainly consists of retrospective studies which may overestimate treatment effects due to selection bias (e.g., not including patients who converted to surgery in their PROMs assessment).[2] Concerning the observed patient-reported outcomes in the present study, the authors note that these do not point to a substantial clinically relevant improvement and that minor improvements in pain and functional outcomes were obtained. This should be considered when counseling patients with an OLTP, as from the present results it cannot reasonably be expected that most patients achieve substantial improvements in clinical outcomes. It is therefore important to further study which patients with an OLTP may benefit from non-operative management. We observed that 55% of cases could be considered a 'responder' (i.e., improvement of 2 points NRS during walking) to non-operative management. Such patients showed a different clinical pathway in terms of pain outcomes compared to 'non-responders', with continued improvement up-to 2-year follow-up. We could not identify any differences in baseline characteristics between responders and non-responders. It should be noted, however, that this sub-analysis contains a low number of patients and that a 'response', as defined in this study, should not necessarily mean treatment success for a patient. In clinical practice, it is therefore critical to assess the effect of non-operative management on an individualized level. Moreover, we assessed whether a concomitant OLTP would affect clinical outcomes

in a sub-analysis, which is hypothesized in BMS for OLTP with a concomitant OLT.[12,14] This analysis found no differences but was likely underpowered.

Another point to consider from the findings of this study is that patient-reported outcomes and radiological outcomes on a group level did not deteriorate, meaning that it can be considered a safe treatment alternative, as was previously observed in OLT.[16,17] When counseling patients for the treatment of an OLTP the pros and cons of non-operative management versus surgery should be weighed. On the one hand non-operative management could reasonably be used as a first-line treatment for OLTP as it appears safe, possibly avoiding the need for surgical intervention, as is the clinical recommendation in OLT.[2,7] Moreover, the effects of non-operative management could be assessed at 6 months follow-up due to no significant improvements being observed thereafter. On the other hand, it could be recommended that surgical intervention can be considered at 6 months of treatment if complaints deteriorate or are at an unacceptable level for patients. It should be stated, however, that the reliability of surgical treatment results remains limited due to the current limited low level of evidence literature.[5,11]

Radiological Examination

We observed no significant change in lesion volume, and 77% of lesions showed either no change or a healing tendency of the OLTP at follow-up CT-evaluation. A systematic review by Buck et al.[2], assessing non-operative management for OLT among 30 studies evaluated lesion deterioration on CT for 131 ankles. The authors observed deterioration of the OLT in 11% of patients, while the lesion was found unchanged in 76% on CT and 83% on magnetic resonance imaging (MRI).[2] Although not wholly comparable to the present study, as these findings solely concern OLT, one could state that these findings concur with the present study. This suggests that lesions remain stable over time, showing no clear adverse effects from non-operative treatment on lesion size and filling based on these data. Moreover, the authors advocate the use of follow-up CT-scan examinations in symptomatic OLTP cases where non-operative management is started.[2] It could be argued that this is required in all cases as, up to this point in time, little is known about the natural history of OLTP. Routine CT-evaluation can assist in clinical decision making by early detection of clinically significant lesion change (e.g., size increase or cyst formation) and assists with informing patients as well as expectation management. However, there is no evidence on the timing and cost-effectiveness of routine CT-examination in OLTP and its use should, therefore, be considered in a case-based and shared-decision making manner.

Sport and Work Outcomes

Sport outcomes reported for the operative management of OLTP range from 63% to 83% return to any level of sports.[11] The present literature on sports outcomes for OLTP concerns a low number of patients, among heterogenous treatment groups, and lacks clear definitions of return to sport, such as postulated by Ardern et al.[1] Moreover, in the present study we observed that several patients did not stop with their sporting activities during treatment, for example as would be common following surgery. This makes defining clear end-points difficult, and we thus focused on sports-participation based on any-level or pre-injury level of sports.[1]

With regards to the work outcomes, it was observed that 94% of patients returned to work or remained at their occupation. Moreover, of those patients who remained at their occupation 4 patients initiated some kind of work modification, which were primarily focused on reducing weightbearing activities. Future studies should assess the impact of OLTP on work outcomes as these are important outcome measures for patients.

Conversion to Surgery and adverse outcomes

A notable finding was that 1 (6%) patient converted to a surgical intervention within the study period. This is comparatively low to what is reported in OLT literature (46%, evaluated in 400 ankles).[2] This could be explained by the tertiary academic referral setting of our institution and shared decision-making process at initial clinical consultation. As a tertiary referral center for ankle cartilage lesions most patients had already undertaken a period of non-operative management before presenting at our institution and could therefore have been more inclined to undergo surgery. As such it could be hypothesized that the patients in this cohort were less inclined to convert to a surgical intervention as they initially chose to commence non-operative treatment. The present cohort may, therefore, be subject to selection bias. On the other hand, patient expectations, treatment goals, and pain coping may have changed during the study period, which could influence the decision to convert to surgery. Such factors were not measured in the questionnaires. Implementing a standard period of up-to 6 months of non-operative management in initially diagnosed OLTP cases and prospectively examining these could elucidate the conversion rate of non-operative management in the general OLTP population.

Strengths and Limitations

The strengths of this study are its prospective design with 2-year follow-up, clinical relevance through its novelty with regards to non-operative treatment for OLTP, sample size calculation, and use of multiple assessors for the radiological outcomes. Moreover, there was a 100% follow-up rate for the primary outcome measure, and patients were assessed through a wide spectrum of outcomes.

The present study is not without its limitations. First, patients underwent a heterogenous number of treatments within non-operative management and timing of these treatments. The effect of these specific sub-treatments could not be assessed as there was insufficient power, which should be further investigated in larger cohort studies. Second, patients presented with a number of concomitant diagnoses besides the OLTP, including concomitant OLT. The authors excluded all cases of asymptomatic OLTP, but it could be argued that such concomitant diagnoses were in-part responsible for the complaints and treated during the 2-year study period, and as such, the present study did not wholly assess the effect of non-operative management on OLTP alone. Lastly, the present study did not have a complete follow-up of 1-year CT-scans and a number of patients did not fully complete the questionnaires, resulting in a number of incomplete secondary patient-reported outcome measures which could have introduced bias.

Conclusions

Non-operative management for OLTP resulted in minor improvement of patient-reported pain and functional outcomes up-to 2-years follow-up. In this cohort, 1 patient (6%) required conversion to surgical treatment. Radiologically, lesion size and filling were found to remain stable at CT follow-up. Moreover, on average, 9 out of 10 patients were able to participate in sport and could return to, or remain at, their preinjury work activities.

Appendix

The appendix information can be accessed at: https://doi.org/10.1177/19476035251376180

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Chapter 11

Bone Marrow Stimulation for Osteochondral Lesions of the Tibial Plafond Yields Good Patient Reported Outcomes in Daily Living But Moderate Outcomes in Sports Activities at 2 to 22-Years Follow-up

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Abstract

Purpose: The purpose of this study was to assess the patient reported outcomes, as well as the revision- and complication rates, of patients who underwent arthroscopic bone marrow stimulation (BMS) for an OLTP.

Methods: Patients with an OLTP treated with arthroscopic BMS at a minimum follow-up of 2 years were cross-sectionally included from a historical database. The primary outcome was the Numeric Rating Scale (NRS) during walking. Secondary outcomes included the NRS in rest and during running, and the Foot and Ankle Outcome Score (FAOS). Additionally, the association of baseline patient and lesion demographics with follow-up PROMs was assessed with spearman rank correlation test. A sub-analysis was performed for PROMs in patients with or without a coexisting talar (i.e., bipolar) lesion. Finally, the revision surgery (i.e., repeat surgery for the OLTP) - and complication rates were assessed.

Results: Fifty-one patients were included at a mean 8.8 (SD: 5.7, range: 2 - 22) years follow-up. 73% of patients had a solitary OLTP and 27% had a coexisting talar (bipolar) lesion. Males had a significantly higher rate of bipolar lesions compared to females (P= <0.01), and patients with a bipolar lesion had a significantly larger OLTP lesion diameter (P= 0.02) and volume (P= 0.04). At final follow-up, the mean NRS during walking was 1.9 (SD: 2.3) out of 10. Anterior-posterior OLTP size (r= 0.36; P= <0.01) was significantly associated with a higher NRS pain score during walking, though the presence of bipolar lesions did not result in inferior clinical outcomes. At final follow-up, 6% of patients underwent revision surgery. Minor complications were observed in 12% of patients.

Conclusion: Arthroscopic BMS for OLTP results in favourable patient-reported outcomes at mid- to long-term follow-up, though moderate outcomes were observed in sports activities. Lesion size was associated with increased pain scores while bipolar lesions did not result in inferior patient reported outcomes. 6% of patients required revision surgery and 12% of patients had minor complications postoperatively.

Keywords: Osteochondral Lesion Tibial Plafond, OLTP, Tibia, OCL, Bone Marrow Stimulation, BMS

Introduction

An osteochondral lesion of the tibiotalar joint is characterized by damage to the articular cartilage and subchondral bone. Osteochondral lesions of the ankle are by and large situated on the talus but can also be present on the tibial plafond with a 1:14-24 ratio compared to talar lesions reported in the literature.[4,10] These cartilage injuries are particularly debilitating for active patients and can result in long-term joint degeneration[3,18] The clinical presentation and treatment of osteochondral lesions of the tibial plafond (OLTP) has not been well described, which may be due to their low incidence.[4,10]

In case non-operative treatment fails, surgical treatment for OLTPs should be considered.[19] To date, surgical treatments for OLTPs are largely based on conventional treatment strategies for osteochondral lesions of the talus (OLT), and clinical outcomes are only reported in a low number of case-series.[7,19] Bone marrow stimulation (BMS) is the most frequently performed operative procedure to treat OLTPs according to a recent systematic review.[19] The aforementioned study found that clinical outcomes for BMS of OLTPs could be considered varying. The reported success rates of BMS for OLTPs could be considered sub-optimal compared to OLTs.[8,19] Due to the paucity of clinical outcomes in the literature and relatively low incidence of OLTP patients there is limited concensus in the management of OLTPs and their treatment is largely based on expert-opinion.[7,19]

In order to strengthen the evidence-based treatment of OLTPs, as well as to improve outcomes for patients, a better understanding of clinical outcomes and prognostic factors is imperative. It was therefore the purpose of this study to assess the patient reported outcomes, as well as the revision- and complication rates, of patients who underwent arthroscopic bone marrow stimulation (BMS) for an OLTP. It was hypothesized that BMS yields adequate patient reported outcomes in OLTPs at mid- to long-term follow-up.

Methods

Ethical approval for this study was granted by the Medical Ethical Committee of the Amsterdam UMC, location AMC, with reference number: 08/326. The present study is in accordance with the medical Research Involving Human Subjects Act (WMO) and the principles of the Declaration of Helsinki.

Patient Selection

All consecutive patients who underwent arthroscopic bone marrow stimulation (BMS) for a symptomatic primary or non-primary (i.e., failed primary surgical treatment) OLTP at our institution between 1999 and 2021 with a minimum 2-year follow-up

were eligible for this cross-sectional follow-up study and were selected from a large historical database of more than 1000 ankle cartilage patients with CT-proven osteochondral lesions of the ankle.[20] Our institution concerns a large academic tertiary referral centre specialized and (inter)nationally accredited in the treatment of osteochondral lesions of the ankle with two consultant fellowship-trained foot and ankle surgeons. Arthroscopic BMS was indicated if a minimum 6 months period of conservative management did not improve symptoms resulting from the lesion. The exclusion criteria are listed in Table 1. Arthroscopic BMS was defined as debridement and/or microfracturing of the OLTP.

Table 1. Exclusion Criteria for Patient Selection

Exclusion Criteria
- Less than 24 months follow-up
- Any surgery or severely debilitating injury of the lower extremity requiring treatment within 12 months of assessment
- No preoperative radiological assessment with CT or MRI
- Patient with preoperative advanced (≥ grade 3)9 tibiotalar joint osteoarthritis
- Active rheumatological disease
- Re-operation for OLTP at another institution
- Lost to follow-up

Operative Technique and Postoperative Protocol

All arthroscopic BMS procedures were carried out under spinal or general anaesthesia according to standardized operative protocols.[9,17] The ankle was elevated by use of a small cushion with the patient in a supine position in case of anterior arthroscopy - or placed over the edge of the table with the patient in a prone position in case of posterior arthroscopy - to allow full range of motion of the tibiotalar joint during the procedure. Procedures were performed using a lower limb tourniquet pressurized to 250mmgh. Standard medial and lateral portals were created. Visualization of the joint was obtained using a standard - 4mm, 30 degrees - arthroscope with auto-regulated pressurized 0.9% NaCl irrigation fluid. If needed, non-invasive distraction of the ankle was used in order to improve access and visualization. After identification of the OLTP with a probe, the joint was fully inspected. All unstable and necrotic cartilage or bone was removed until healthy bone was reached using a curette and bone cutter shaver. The subchondral bone was subsequently perforated using a microfracture awl or 1.5mm K-wire until bleeding or fatty droplets were visualized. Any concomitant intra-articular pathological findings such as of loose bodies or soft-tissue and/or bony impingement were similarly addressed intraoperatively. In case of a coexisting talar lesions (i.e., bipolar lesions) a BMS procedure for the OLT was only performed if the OLT was considered symptomatic (during preoperative work-up) or instable. Hereafter,

any concomitant procedure (e.g. lateral ligament reconstruction) was undertaken. After finishing all steps and removing the surgical instruments full ankle range of motion and stability was tested. A pressure bandage was applied at the end of the procedure.

Post-operative rehabilitation was not uniform in all patients due to the cross-sectional design of the study (i.e., varying post-operative protocols over time) and multiple surgeons involved. Generally, patients were encouraged to start range of motion exercises as soon as tolerated. Full weightbearing was allowed at either immediately or 6 weeks postoperatively, depending on the treating surgeon. Concurrently, patients were advised to undergo personalized physical therapy to build-up strength and stability of the ankle with the goal to return to daily activities and sports.

Outcome Measures

Patients were contacted by phone in order to obtain informed-consent. Online questionnaires were distributed via the CASTOR© portal in order to obtain patient reported outcome measures (PROM).

Patient Reported Outcome Measures

The primary outcome measure was the Numeric Rating Scale (NRS) during walking, which is a patient reported pain scale from 0 (no pain) to 10 (most pain imaginable).11 The NRS is a PROM and contained three additional subscales in the present study, namely, the NRS in rest, the NRS during running, and the NRS when climbing stairs. Secondary patient reported outcome measures collected were; the Foot and Ankle Outcome Score (FAOS), and use of pain medication. The FAOS consists of 42 questions distributed over five subscales; symptoms, pain, activities of daily living, sport, and quality of life, and is validated in ankle osteochondral lesions.[2,24]

Revision Surgery, Reoperations, and Complications.

By phone and from the patient electronic records any reoperation of the ankle was recorded. Revision surgery was defined as any reoperation after index surgery specifically of the OLTP. Index surgery was defined as the latest arthroscopic BMS procedure performed at our institution. In case patients underwent a repeat arthroscopic BMS procedure at our institution the first procedure was considered the index surgery for the revision surgery outcome only, and PROM were assessed according to the most recent BMS procedure of the OLTP. Post-operative complications were extracted from the hospital electronic patient records and were defined as major (i.e., infection, deep vein thrombosis, bleeding, persistent neurological damage) or minor (i.e., any other complication) within 6 months postoperatively.

Data Collection

Patient Demographics

Patient demographics at baseline were extracted from the hospital electronic patient records and included sex, age, body mass index (BMI), participation in sports and at what level (i.e., none, amateur, competitive, or professional), injury circumstances (i.e., traumatic - fracture or sprain - or sudden onset), time from injury to treatment, and concomitant injuries. Treatment characteristics collected were; primary or non-primary (i.e., failed prior surgical treatment) lesions. If patients underwent revision surgery of the OLTP by means of repeat arthroscopic BMS at our institution, demographic and lesion characteristics were extracted from the most recent procedure.

Lesion Characteristics and Radiological Assessment

Baseline lesion characteristics were assessed either through imaging studies. Radiological assessment was performed by two raters (Q.R. and J.D.). In case of disagreement a discussion was held, and if disagreement persisted the senior author (G.K.) was decisive. The following lesion characteristics were assessed through imaging (preferred computed tomography (CT) and if not available by magnetic resonance imaging (MRI), N=2); lesion size as measured in millimetres (mm) from three planes - anterior-posterior (AP), medial-lateral (ML) directions, and depth -, lesion volume according to Angthong et al.[1] in cm^3, the presence of cysts and lesion location as proposed by Elias et al.10 and the presence of a coexisting talar lesion.

Statistical Analysis

Descriptive statistics are presented as means with standard deviations for continuous variables, and absolute numbers and percentages for dichotomous and categorical variables. Data normality was assessed visually and by means of a Shapiro-Wilk test. A subgroup analysis was performed for patients with a coexisting talar lesion (bipolar group) or solitary OLTP (solitary group). In order to compare the baseline demographic characteristics and PROMs between groups a Fisher's exact test was used for dichotomous variables and a Wilcoxon rank-sum test was used for continuous variables. The Spearman rank correlation test was used to investigate the relationship between covariates (age, sex, BMI, follow-up time, OLTP size in AP, ML, depth, and volume) and the primary outcome for all OLTP patients. The correlation coefficient was interpreted according to Schober et al.[22] Significantly correlated variables were further assessed using a linear regression analysis. Additionally, a sensitivity analysis was performed by comparing baseline demographic characteristics for included and patients lost-to-follow-up. No power analysis was performed for the primary outcome due to its retrospective cross-sectional design with descriptive observational outcomes wherein the goals was to include as many patients as possible.19 Inter-rater and intra-rater reliability for lesion size measurements was determined with a subset of 10 lesion by two independent raters (Q.R. and J.D.). Intra-rater reliability

was assessed by repeating the measurements at a 2-week interval. Inter-rater and intra-rater reliability of lesion size measurements were analyzed using the intraclass correlation coefficient (ICC) analysis and interpreted according to Shrout et al.[23], wherein 0.61–0.80 corresponds with a moderate agreement, and 0.81–1.00 with substantial agreement. A two-sided level of P< .05 was considered significant. All data analysis were conducted using Stata 15 (StataCorp LP, College Station, TX).

Results

At final follow-up, 79 patients were eligible, of which a total of 51 patients were included and 28 patients were excluded. The patient selection procedure and reasons for exclusion are outlined in Figure 1. The baseline demographics of the included patients are shown in Table 2. An overview of the localization and anatomical distribution of lesions according to the 9-grid scheme is available in Figure 2. The sensitivity analysis showed no difference in baseline demographics of the included patients and patients lost-to-follow-up, except for a longer follow-up time in the lost to follow-up group (see Appendix).

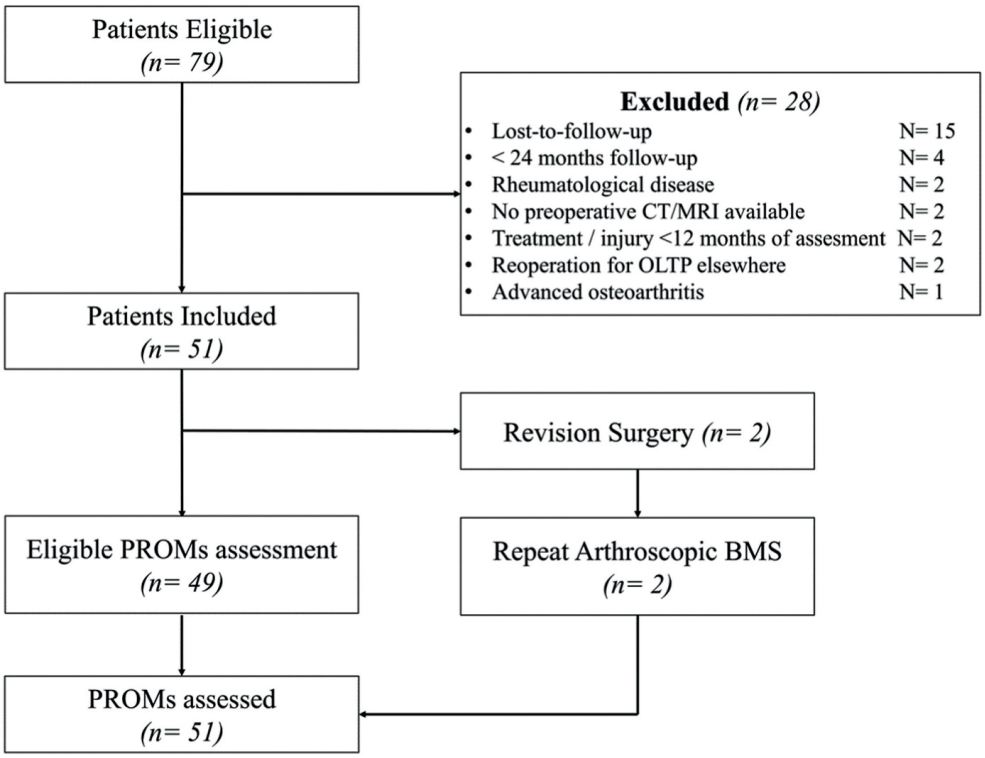

Figure 1. Flowchart of patient selection.

Table 2. Baseline Patient Demographics and Lesion Characteristics

Patient Characteristics (N= 51)	
Sex, n (% male)	36 (71%)
Age (years), mean ± SD	33.0 ± 13.1
Follow-up (years), mean ± SD	8.8 ± 5.7
BMI (kg/m2), mean ± SD*	24.8 ± 3.9
Laterality, n (% right side)	30 (59%)
Participation in Sports, n (%)	
- Yes	33 (64%)
- No	9 (18%)
- Unknown	9 (18%)
Professional Athlete, n (%)	
- Yes	2 (4%)
- No	40 (78%)
- Unknown	9 (18%)
Traumatic Injury Aetiology, n (%)	
- Yes	38 (74%)
- No	8 (16%)
- Unknown	5 (10%)
Lesion Characteristics	
Primary Lesion, n (%)	44 (86%)
Non-primary Lesion, n (%)	7 (14%)
Localization, n (%)	
- Solitary Tibial Lesion	36 (71%)
- Bipolar Lesion	15 (29%)
Kissing Lesion (from total number of bipolar lesions)	5 (33%)
Morphology, n (%) Presence of Cyst	35 (69%)
Lesion Size (mm) Tibial Lesions, mean ± SD	
Anterior-Posterior	7.3 ± 3.5
Medial-Lateral	7.4 ± 3.4
Depth°	5.6 ± 2.5
Lesion Volume (cm3) Tibial Lesions, mean ± SD°	0.22 ± 0.27
*Lesion Size (mm) Talar Lesion, mean ± SD***	
Anterior-Posterior	8.6 ± 4.4
Medial-Lateral	6.2 ± 2.7
Depth	5.7 ± 3.8
Lesion Volume (cm3) Talar Lesions, mean ± SD**	0.24 ± 0.29

*N=48, BMI missing in 3 patients. °N=48, not available for 3 ankles, only axial scans available. **N= 14, lesion not visible on imaging in 1 ankle, though observed during arthroscopy. † the number depicted concerns the total number of concomitant procedures, patients could have had more than one concomitant procedure.
Abbreviations: BMI: body-mass index, SD: standard deviation, n: number of, cm: centimeters, mm: millimeters, FHL: flexor hallucis longus, OLT: osteochondral lesion of the talus.

Table 2. Continued	
Treatment Characteristics	
Arthroscopic Approach, n (%)	
- Anterior	31 (61%)
- Posterior	18 (35%)
- Both	2 (4%)
Concomitant Surgery, n (%)	
Patients who underwent concomitant procedures	35 (69%)
Per procedure (arthroscopic, or if stated otherwise):	51 procedures†
- Nettoyage bony impingement	15 (28%)
- Nettoyage soft-tissue impingement	10 (20%)
- FHL-release	9 (18%)
- Removal of loose body	9 (18%)
- BMS of OLT	4 (8%)
- Hardware removal (open)	1 (2%)
- Sliding calcaneal osteotomy (open)	1 (2%)
- Nettoyage symptomatic os trigonum	1 (2%)
- Nettoyage symptomatic elongated talar process	1 (2%)

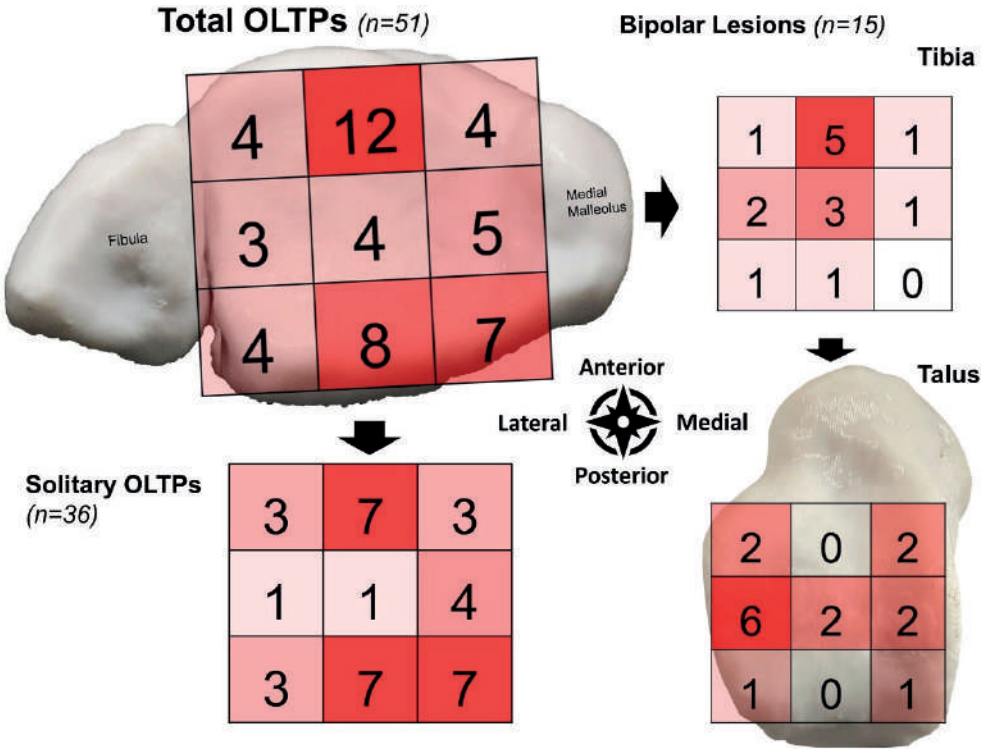

Figure 2. Distribution of lesions according to their anatomical location

Patient Reported Outcomes Patient Reported Outcomes

At a mean 8.8 (SD: 5.7, range: 2 – 22) years follow-up the mean NRS during walking was 1.9 (SD: 2.3) out of 10 for the total group of OLTP patients. The NRS during running was 3.9 (SD: 3.1) out of 10.A full overview of the PROM is available in Table 3.

Table 3. Patient Reported Clinical Outcomes, and separated by lesion localization

	All Patients (n= 51)	Solitary Group (n = 36)	Bipolar Group (n = 15)	P-Value
NRS, mean (SD)				
Pain (rest)	1.1 ± 2.0	1.0 ± 2.0	1.1 ± 2.1	0.73
Pain (walking)	1.9 ± 2.3	1.8 ± 2.3	2.2 ± 2.7	0.55
Pain (running)	3.9 ± 3.1 n = 46	3.9 ± 3.1 n = 32	4.1 ± 3.2	0.83
Pain (stairs)	2.4 ± 2.6 n = 47	2.3 ± 2.7 n = 33	2.6 ± 2.6	0.58
FAOS, mean (SD)	n= 50	n = 35		
Symptoms	68.1 ± 20.9	69.1 ± 21.7	66.0 ± 19.3	0.63
Pain	79.5 ± 17.3	80.2 ± 17.9	78.0 ± 16.3	0.67
ADL	99.2 ± 1.3	99.3 ± 1.3	99.1 ± 1.4	0.58
Sport	62.6 ± 28.6	63.9 ± 29.5	60.0 ± 27.0	0.62
QoL	56.3 ± 28.0	58.6 ± 26.6	50.8 ± 31.1	0.33

Abbreviations: NRS; numeric rating scale, FAOS: foot and ankle outcome score, ADL: activities of daily living, QoL: quality of life, n.s.: non-significant.

From the analysis of the relationship between covariates and the primary outcome it was observed that anterior-posterior OLTP lesion diameter (r= 0.36; P= <0.01) was significantly associated with increased NRS pain scores during walking. Regression analysis found a beta-coefficient of 0.24 ([95%-CI: 0.07 – 0.42], P= 0.01). An overview of the spearman correlation analysis is available in the Appendix. The use of pain medication related to the ankle complaints was reported by 4 patients (8%). Of these four patients, all reported either using paracetamol or a non-steroid inflammatory drug (NSAID) and none used opioids.

Solitary versus Bipolar Lesions

Out of 51 OLTP patients, 71% presented with a solitary OLTP (solitary group) and 29% presented with a coexisting talar lesion (bipolar group). A significantly higher rate of males was found to have a bipolar lesion compared to patients with a solitary OLTP (P= <0.01). Additionally, OLTPs which presented with a coexisting OLT were found to be significantly larger in AP (P= 0.02) diameter and presented with a larger lesion volume (P= 0.04).

An overview of the baseline patient demographics and lesion characteristics for the solitary and bipolar groups is available in the Appendix. Lesion location for both groups is available in Figure 2. No significant difference in the mean NRS during walking between the solitary group (NRS during walking 1.8 ± 2.3) and the bipolar group (NRS during walking 2.2 ± 2.7, P= 0.55) were found. Additionally, no significant differences were observed between the solitary and bipolar group for the remaining NRS sub-scales (rest, running, stair climbing) as well as the FAOS subscales (Table 3).

Reoperations, Revision Surgery, and Complications

In total, 6 (12%) of patients received surgery after their index BMS surgery. 3 of these reoperations were not revision surgeries of the OLTP. Of these, 2 patients received an arthroscopic subtalar arthrodesis and 1 patient received an ankle arthroscopy to remove a loose body. Of the patients who underwent revision surgery 2 patients (4%) underwent repeat arthroscopic BMS at 9 and 48 months postoperatively. At final follow-up at 22 and 10 years post re-BMS patients reported an NRS during walking of 0 and 1, respectively, and reported participating in a competitive level of sports (cycling and krav maga, respectively). Lastly, 1 patient underwent relook arthroscopy for recurrent OLTP, which showed good fibrocartilaginous filling, which was subsequently treated with hyaluronic acid injections.

No major complications were noted in this cohort. A total of 6 (12%) minor complications were reported. Of these, 3 patients had soft-tissue impingement and 1 patient had anterior bony impingement which was managed with physiotherapy and heel inlay in all cases. 1 patient had a symptomatic thickening of the PTFL. Lastly, 1 patient reported transient hypoesthesia of the superficial peroneal nerve.

Interobserver Agreement

The inter-rater and intra-rater reliability analysis showed a substantial level of agreement for all domains except the depth measurements and ML measurements of rater 2, respectively (Table 4).

Table 4. Inter- and Intra-reliability measurements

	AP	ML	Depth
Inter-rater reliability	0.97	0.97	0.78
Intra-rater reliability rater 1	0.94	0.98	0.67
Intra-rater reliability rater 2	0.94	0.78	0.58

Abbreviations: AP: anterior-posterior, ML: medial-lateral

Discussion

The most important finding of this study is that arthroscopic BMS for OLTPs yields good patient-reported outcomes in activities of daily living at mid- to long-term follow-up, though moderate outcomes were observed in sports activities. The findings of patient-reported outcomes in this study may represent a best-case scenario due to its cross-sectional design. Lesion size and depth were weakly associated with inferior clinical outcomes. The procedure can be considered safe and results in a low failure rate. These findings can aid both physicians and patients in their evidence-based treatment decision making as well as expectation management. Additionally, this study highlights areas of interest for further research, which may improve outcomes for patients in the future.

Clinical Outcomes in the Literature

When examining the clinical outcomes of BMS for OLTPs in the literature it can be noted that these, by and large, concur with the outcomes observed in the present study.[19] Ross et al.[21], with the largest cohort of OLTP patients to date, reported clinical and radiological outcomes for 31 patients who underwent BMS at a mean 44 months postoperatively. The authors reported a mean postoperative FAOS score of 72 and MOCART score of 69. The aforementioned study, found a negative correlation between clinical outcomes and age, although sex, lesion size, and the presence of a bipolar lesion were not. Lee et al.[14] reported the Visual Analogue Scale (VAS) for 16 OLTP patients treated with BMS at a mean 30 months postoperatively. The aforementioned authors found a mean VAS pain score improvement from 8.3 preoperatively to 1.8 postoperatively but did not report the circumstances VAS was recorded (e.g., VAS during rest or VAS during running).

Coexisting Talar Lesions

As outlined by prior studies, coexisting talar lesions may be a prognostic factor for inferior clinical outcomes following BMS of OLTPs.[5,6,13] Cuttica et al.[6] and Irwin et al.[13] found no association between clinical outcomes and the presence of bipolar lesions in their cohorts of 13 and 26 patients, respectively. On the other hand, Chuckpaiwong et al.[5] noted a lower clinical success rate for bipolar lesions in their study of 19 patients. It should be stated, however, that most OLTPs included in the aforementioned study could be considered large (>20mm diameter), which was observed to be predictive factor for inferior clinical outcomes.[5] The present study found no difference between clinical outcomes for solitary and bipolar OLTPs. Bipolar lesions were found to have a larger lesions size, however. This may be due to the higher peak forces needed to create a bipolar lesion, and clinically may correlate to inferior clinical outcomes after BMS, as described in talar lesions and the aforementioned study of Chuckpaiwong et al.[5,16] The authors wish to note that the current literature and the present study may

be underpowered to examine the influence of outcomes from OLTP patients treated by means of BMS with or without coexisting talar lesions.

Revision Surgery and Complications

The rate of revision surgery observed in this study can be considered low and concurring with the current literature that reads a pooled revision rate of 7% following BMS of OLTPs.[19] The aforementioned also found that this outcome was underreported in the literature. From the two available studies that reported revision cases it could be noted that cystic lesions were reoperated in 50% of revision cases.[6,15] From our series it was observed that all cases that underwent revision had a preoperative cystic lesion morphology. Although our data did not allow for a formal analysis of the presence of a cyst on revision surgery it could be hypothesized that cystic OLTPs may be less amendable for BMS due to inadequate fibrocartilage filling. Additionally, it should be acknowledged that the present study excluded two cases of revision surgery as these were treated at another institution as these could not be assessed for the primary outcome and their records could not be accessed, the revision rate should therefore be interpreted in the context of the study design.

This study did not observe any major complications, though did observe a 12% minor complication rate. The aforementioned systematic review found a complication rate of 5% reported in surgical treatment for OLTPs in general.[19] When comparing the observed complication rate in the OLT literature this can be considered corresponding to the rate observed in BMS procedures for OLTs.[12] In the present study we observed a low rate of nerve complications, though these are the most frequently encountered after arthroscopic surgery of the ankle.[12] In this context it is important to note that, due to the retrospective design, transient complications such as temporary nerve damage or wound healing problems were not observed and thus not included because they did not require additional treatment.

Limitations

The present study is not without limitations. First, patients were retrospectively selected from a large historical database with CT-proven OLTPs treated at a specialized centre for ankle osteochondral lesions. The present study included a heterogenous patient population and did not exclude patients based on lesion size, bipolar lesions, or non-primary nature of the lesion, and debridement with or without microfracture. Second, due to the cross-sectional follow-up design the rate of patients lost-to-follow-up (19%), and absence of preoperative outcomes, it could be that the clinical outcomes observed in the present study may represent a best-case scenario. Baseline characteristics did not differ between the patients lost to follow-up and included patients. Third, even though the present study includes a relatively high number of patients compared to the literature19, its statistical power may be limited

due to a low number of available patients. Fourth, radiological follow-up outcomes were not uniformly available as the protocol of the authors' institution only prescribes postoperative imaging in symptomatic patients more than 2 years postoperatively. As such, the authors believe that including the available radiological studies of the patients who returned for re-evaluation would not be representative of the cohort as a whole, could overestimate the progression of osteoarthritis or lesion deterioration due to selection bias, and therefore reach incorrect conclusions. Due to the abovementioned reasons caution is warranted when interpreting the findings of this study.

Conclusion

Arthroscopic BMS for OLTP results in favourable patient-reported outcomes in activities of daily living at mid- to long-term follow-up, though moderate outcomes were observed in sports activities. Lesion size was associated with increased patient reported pain outcomes, while bipolar lesions did not result in inferior patient pain outcomes. 6% of patients required revision surgery and 12% of patients had minor complications postoperatively.

Appendix

The appendix information can be accessed at: https://doi.org/10.1016/j.arthro.2023.07.038

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Chapter 12

Osteotomy and Bone Grafting for Osteochondral Lesions of the Tibial Plafond: Surgical Technique

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Revision Submitted

Abstract

Objective: Symptomatic large - cystic or crater-like - primary and non-primary (i.e., failed prior surgical treatment) osteochondral lesions of the tibial plafond (OLTP) are challenging entities to treat as bone marrow stimulation likely result in poor outcomes and few other surgical options are available. In the present manuscript we describe the surgical technique by means of an intra-articular osteotomy of the distal tibia and cancellous bone grafting which aims to overcome these issues. The procedure provides surgeons a lesion specific treatment alternative for such complex OLTPs.

Indications: Symptomatic large primary cystic or crater-like, and non-primary (i.e., failed prior surgical treatment), osteochondral lesions of the medial and central tibial plafond which failed to respond to a minimum 6 months of nonoperative treatment.

Contraindications: Systemic diseases including malignancies, active bacterial arthritis, hemophilic or other diffuse arthropathies, and rheumatoid arthritis. Severe ankle osteoarthritis (Kellgren and Lawrence score ≥ 3). .Fracture of the ipsilateral medial malleolus less than 6 months prior to treatment, unless the OLTP is caused by a mal-union or non-union. In skeletally immature patients with open growth plates the osteotomy cannot be performed as this can result in early closure of the physis, resulting in a symptomatic varus growth disorder of the distal tibia.

Surgical Technique: Symptomatic large - cystic or crater-like - primary and non-primary (i.e., failed prior surgical treatment), osteochondral lesions of the medial and central tibial plafond which failed to respond to a minimum 6 months of nonoperative treatment are eligible for osteotomy of the distal tibia with autologous cancellous bone graft filling. The procedure involves an oblique intra-articular distal tibia osteotomy which directly transects the lesion, curettage of the defective lesion tissue, filling with autologous cancellous bone from the ipsilateral iliac crest or from the osteotomy site, and refixation of the osteotomy. Bone grafts can also be taken from, or near, the osteotomy site if the post debridement lesions dimensions are not too large (otherwise resulting in inadequate filling). The osteotomy is transfixed with two diverging 3.5mm cortical lag screws and may also include a third horizontal screw for additional compression and stability.

Postoperative Management: Post-operatively, there is a period of 4-6 weeks in short leg cast non-weight bearing and 4-6 weeks of short leg cast with weightbearing as tolerated. After 12 weeks radiological assessment (by means of radiographs or CT-scan) confirms osteotomy union and graft incorporation. At this point the patient starts a personalized rehabilitation under the guidance of a physical therapist.

Keywords: Osteochondral lesion; Tibial Plafond; Tibia; OLTP; Filling; Open; Osteotomy

Introductory Remarks

Osteochondral lesions of the tibial plafond (OLTP) are a rare pathology of the ankle. In comparison, one OLTP occurs for every 14 to 24 osteochondral lesions of the talus (OLT).[2,8] These lesions affect the articular cartilage and the subchondral bone of the distal aspect of the tibia. Patients typically present with pain during or after weightbearing, originating deep from within the ankle, and may report a history of trauma prior to presentation.[4,10,12,15] Radiologically, patients commonly present with varying lesion sizes and morphologies, such as the presence of cysts.[8]

The treatment of OLTP can be non-operative or operative. To date, however, few studies with clinical outcomes of OLTP have been reported, and from these studies it be stated that the treatment options and outcomes are limited.[10] Moreover, there does not exist a consensus on the optimal operative treatment of OLTP.[6]

Most OLTP present on the medial or central aspect of the distal tibia and these lesions may present with a cyst or deep crater-like morphology.[3,8,10,11] OLTP are by-and-large treated by means of arthroscopic bone marrow stimulation, but outcomes of this treatment and other surgical treatments of OLTP seem to be less favorable than for OLT.[10] Moreover, it is known from the OLT literature that a cystic lesion morphology and lesion dimensions negatively affect clinical outcomes of BMS.[1,5,11] As such, lesions may clinically recur, and the articulating lesion size may increase following prior surgical treatment. In such select non-primary OLTP cases, and in large - cystic or crater-like - primary lesions, the surgical options may, therefore, be limited and can be described as unpredictable. To treat such complex OLTP, which are located on the medial or central tibial plafond, we developed a novel surgical technique that aims to overcome these shortcomings. This technique comprises of an intra-articular distal tibial osteotomy, which transects the lesion, and filling with an autologous bone graft. This surgical technique paper describes the indication, surgical technique, after-treatment, pearls-and-pitfalls, and the preliminary outcomes of the procedure.

Surgical Principles and Objectives

Symptomatic large - cystic or crater-like - primary and non-primary (i.e., failed prior surgical treatment), osteochondral lesions of the medial and central tibial plafond which failed to respond to a minimum 6 months of nonoperative treatment are eligible for osteotomy of the distal tibia with autologous cancellous bone graft filling. The procedure involves an oblique intra-articular distal tibia osteotomy which directly transects the lesion, curettage of the defective lesion tissue, filling with autologous cancellous bone from the ipsilateral iliac crest or from the osteotomy site, and refixation of the osteotomy. The choice for autologous bone from the iliac crest is preferred by the authors due to its high quality of growth factors and abundant availability in case

of large lesions.[13] Bone grafts can also be taken from, or near, the osteotomy site if the post debridement lesions dimensions are not too large (otherwise resulting in inadequate filling).[14] The osteotomy is transfixed with two diverging 3.5mm cortical lag screws and may also include a third horizontal screw for additional compression and stability.

Advantages

- Excellent exposure.
- High quality subchondral bone repair by means of autologous cancellous bone grafting.
- No harvest site complications with distal tibia grafting.

Disadvantages

- Potential hardware complications or complaints may lead to the need for a hardware removal procedure.
- Potential joint stiffness due to the arthrotomy and iatrogenic cartilage damage due to the intra-articular distal tibia osteotomy.

Indications

Symptomatic large primary cystic or crater-like, and non-primary (i.e., failed prior surgical treatment), osteochondral lesions of the medial and central tibial plafond which failed to respond to a minimum 6 months of nonoperative treatment.

Contraindications

- Systemic diseases including malignancies, active bacterial arthritis, hemophilic or other diffuse arthropathies, and rheumatoid arthritis.
- Severe ankle osteoarthritis (Kellgren and Lawrence score ≥3).
- Fracture of the ipsilateral medial malleolus less than 6 months prior to treatment, unless the OLTP is caused by a mal-union or non-union.
- In skeletally immature patients with open growth plates the osteotomy cannot be performed as this can result in early closure of the physis, resulting in a symptomatic varus growth disorder of the distal tibia.

Patient Information

- The surgical risks include infection, hematoma, venous thromboembolism, deficient wound healing, saphenous nerve damage leading to (temporary) hypaesthesia or hyperesthesia.
- Non-weightbearing cast for 4-6 weeks followed by a walking cast for another 4-6 weeks, after which the patient commences an individualized rehabilitation program of 3-6 months guided by a specialized physical therapist.

- Minimal harvest site complications in case of iliac crest grafting.[7]
- Screw discomfort requiring hardware removal, on the basis that adequate union of the osteotomy is achieved.
- Adverse events include osteotomy step-off or delayed- or non-union, bone graft resorption, recurrent symptomatic OLTP formation, and progressive osteoarthritis.
- Possible progression of osteoarthritis despite adequate filling and (after) treatment.

Preoperative Work-Up

All patients are preoperatively assessed clinically, where a history and physical examination is performed in order to establish the diagnosis of a symptomatic OLTP. Radiological assessment by means of advanced imaging (CT or MRI) is mandatory to assess the lesion location (on the tibia according to a 9-grid scale[8]), lesion size (in three-dimensional measurements), morphology (e.g., (multi)cystic, crater, combined, etc), and possible concomitant OLT. A second reason for obtaining a preoperative imaging is the surgical planning of the osteotomy and possible concomitant interventions necessary during the procedure (Figure 1 and 2).

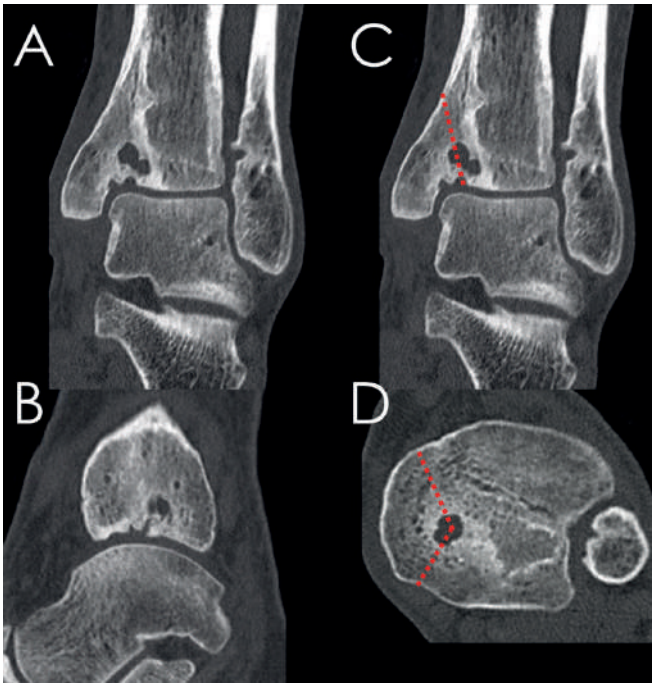

Figure 1. Preoperative coronal (A), sagittal (B), and axial (D) CT-scan of case 1. The case concerns a 40-year-old male, presenting with pain in activities of daily living 1 year after open-reduction and internal fixation for a closed bimalleolar ankle luxation fracture. Physical examination showed pain upon palpation of the OLTP and a similar range of motion to the contralateral side. CT-scan showed a large medial OLTP with large cyst formation. PET-CT and infectious blood lab results showed no signs of an active infection. The osteotomy is shown with a red-dotted line in a chevron configuration in C and D.

The authors prefer the use of CT imaging due to the bony morphology that is important for planning the osteotomy, as well as the risk of lesion size overestimation by MRI due to bone marrow oedema.[16] If the patient presents with a symptomatic OLTP unresponsive to nonoperative treatment and with appropriate lesion characteristics (as described in the indications section) the patient is counselled on the possible treatment options and, in a shared decision-making process, treatment is chosen. Two examples of patients eligible for the present technique and their planned osteotomy are outlined in Figure 1 and Figure 2.

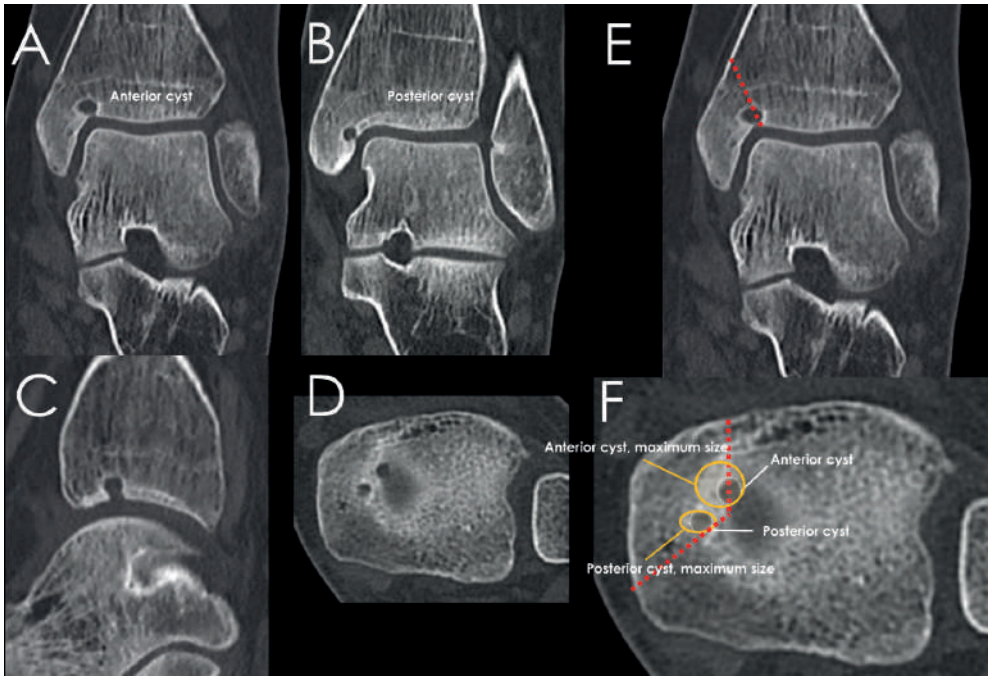

Figure 2. Preoperative coronal (A and B), sagittal (C), and axial (D) CT-scan of case 2. Case 2 concerns a 14-year-old female, presenting with sustained recognizable pain complaints deep within the ankle from a refractory OLTP, previously treated with arthroscopic debridement and bone marrow stimulation. CT-scan showed closed physes and an open multi-lobed cystic OLTP located on the border from the medial malleolus and medial plafond. The pre-operative planning of the planes for the chevron-type osteotomy is exemplified with a red-dotted line on coronal (E) and axial (F) images. The axial slide (F) illustrates the multi-level size differences of the cysts, for which the planned osteotomy aimed to account.

Instruments and Implants

- Standard orthopaedic set
- Coagulation knife
- Hohman retractors
- Bone rongeur
- Oscillating saw
- Chisel set
- 2.0mm Kirschner wires
- 2.0mm drill
- Impactor
- 3.5mm cortical screws or a headless alternative
- Large Weber clamps

Anaesthesia and Positioning

- General or spinal anaesthesia.
- Supine position with an ipsilateral thigh tourniquet.
- Antibiotic prophylaxis with two grams (or adjusted to weight) of Cefazolin preoperatively.

Surgical Technique

After positioning the patient in a supine position, the surgical field is disinfected with chlorohexidine and prepared by sterile draping. A rolled sterile surgical gown is placed under the ankle to accommodate improved surgical access and visualization during the procedure. Secondarily, this improves safety as the neurovascular bundle moves away from the surgical plane. The first step of the procedure is preparing the distal tibial osteotomy by means of surgical exposure, which has been described in detail in a previously published surgical technique paper.[9]

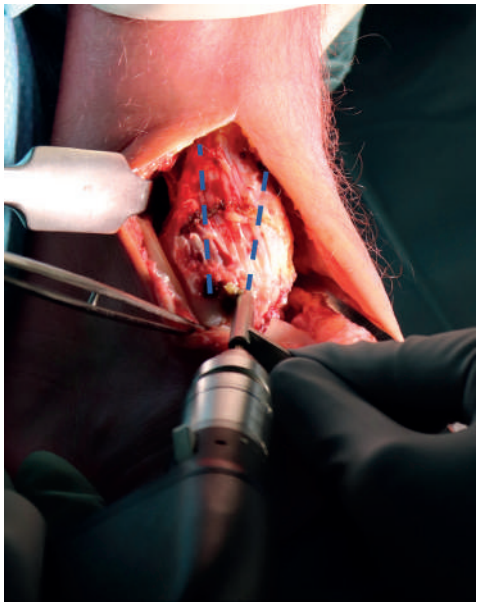

Figure 3. When there is visualization of the medial malleolus and most distal aspect of the tibia, two cortical lag screw holes are pre-drilled in a slight divergent and bi-cortical fashion and measured in anatomical position. It is important to achieve sufficient exposure of the medial malleolus and distal tibia to accommodate proper osteotomy angulation, which is critically important for transecting the lesion during osteotomy.

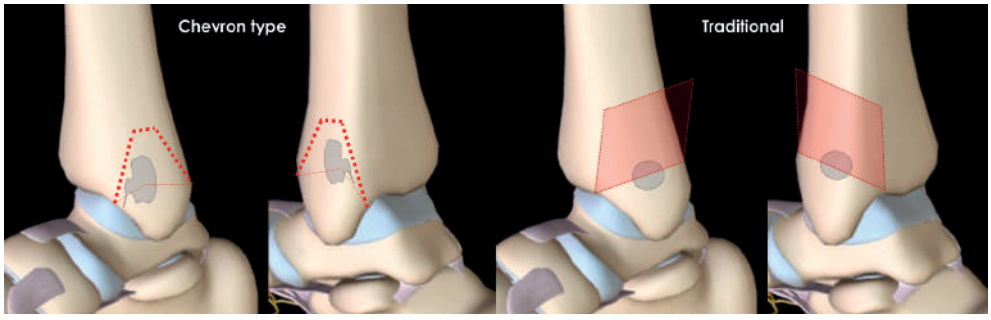

Figure 4a. When the osteotomy site is well visualized the osteotomy angle is decided. In order to angulate the osteotomy so that it will transverse the lesion the surgeon should make use of a preoperative CT-scan to determine the exact lesion location, size, and morphology (also see figure 1 and 2). These images can assist with angulation of the osteotomy intra-operatively. Additionally, the medial junction of the distal tibia and medial malleolus can aid in the identification of the anatomical position in the ankle joint and angulation. A schematic visualization of the intra-operative osteotomy, in both chevron-type and 'traditional' straight configuration, are outlined with red-dotted lines.

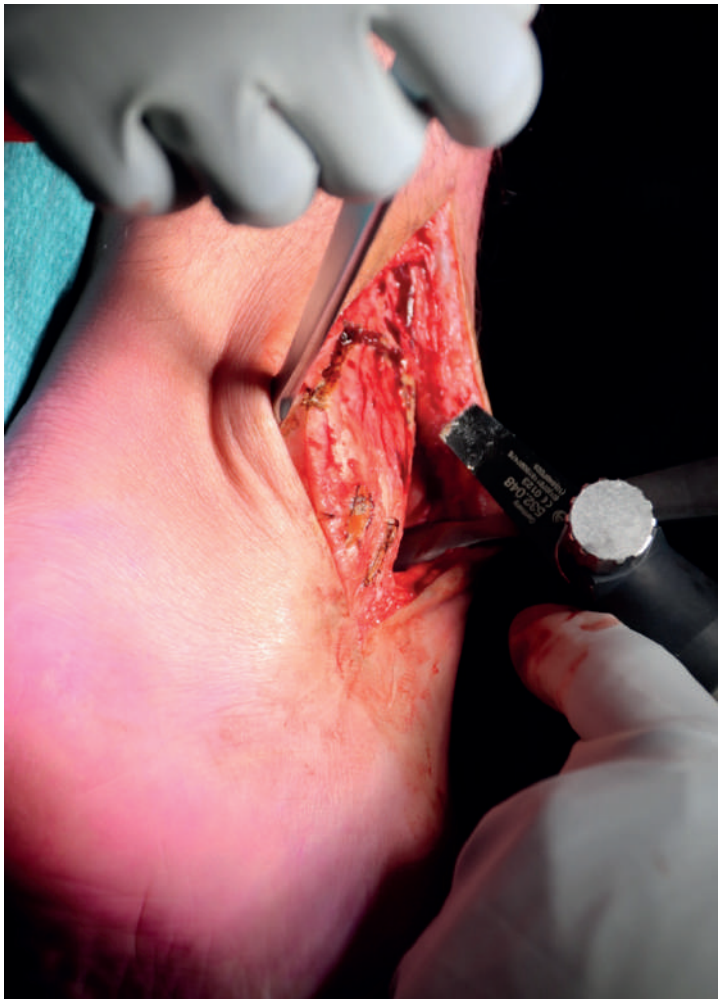

Figure 4b. If a satisfactory osteotomy position and angle is achieved the osteotomy is performed with an oscillating saw up to 3mm from the article surface of the ankle joint (where in this case a chevron type osteotomy is performed). The osteotomy is finalized with a broad chisel to avoid (thermal) damage to the surrounding cartilage of the tibia plafond.

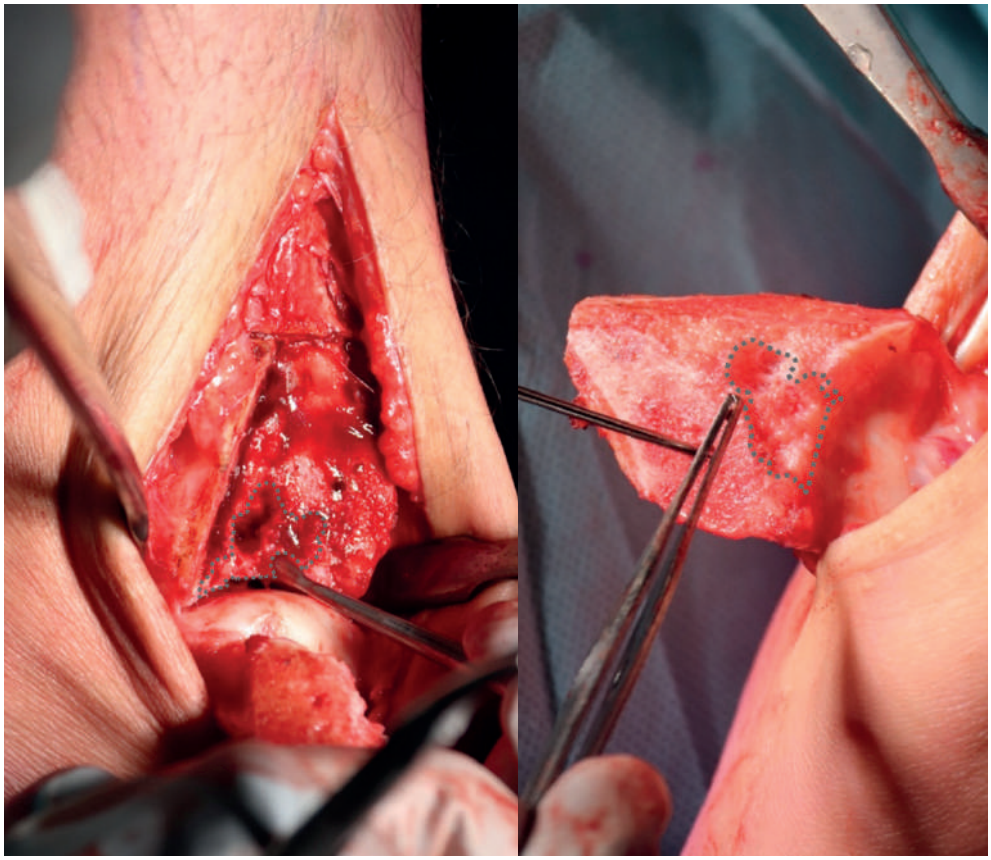

Figure 5a and 5b. With a completed osteotomy, the site is opened by dislocating the distal tibial fragment medially and distally. After dislocation the lesion is identified, and thus appropriate osteotomy angulation is confirmed. Hereafter, the tibia fragment is fixed in a plantar and medial direction onto the talar body with one or two 2.0mm Kirschner wire(s) to accommodate working space and stability of the distal tibial fragment for the next steps in the procedure. The ankle joint is inspected, paying attention to the articular cartilage of the tibia and the talus. Any concomitant intra-articular pathologies are addressed at this stage. Hereafter, the lesion is debrided using a curette, making sure all defective cartilage and subchondral bone are removed and until healthy bleeding bone is observed

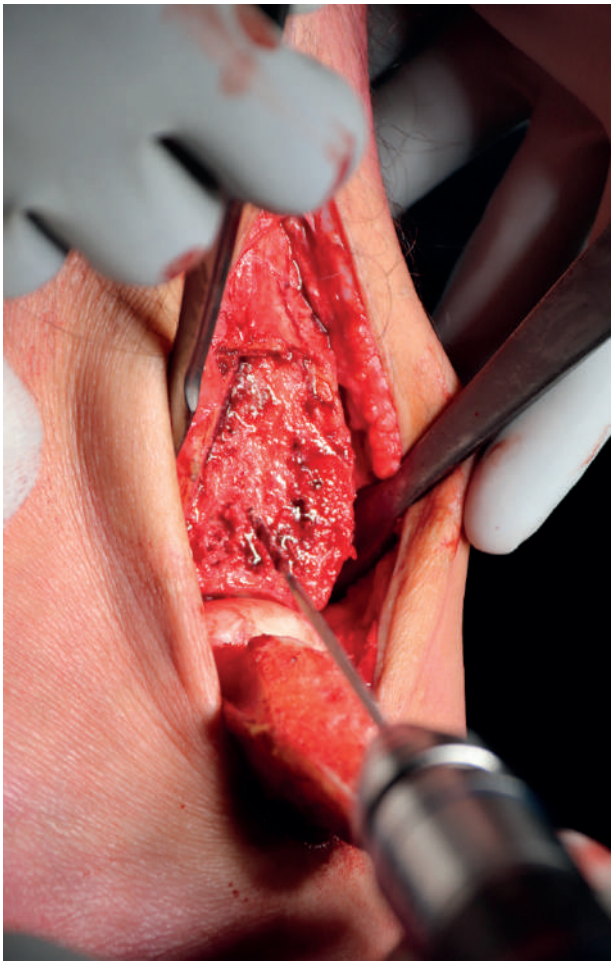

Figure 5c. In the case of (large) cysts attention is paid to debriding the cyst walls. Additionally, it can be decided to microfracture the debrided cysts walls in the distal tibia and distal tibial fragment in order to accommodate healing, using a microfracture awl or a 2mm burr. Next, attention is turned to harvesting the autologous cancellous bone graft. This can be either performed from the ipsilateral anterior iliac crest, as previously described[16], or proximal from the distal tibial osteotomy site. The choice of graft type depends on the expected amount of cancellous bone needed (with larger lesions more likely to need iliac crest grafting), patient and surgeon preference, and intra-operative findings (e.g., post-debridement more than expected bone graft needed). The authors prefer bone grafting from the iliac crest due to high quality and abundant amount of graft material available.[13]

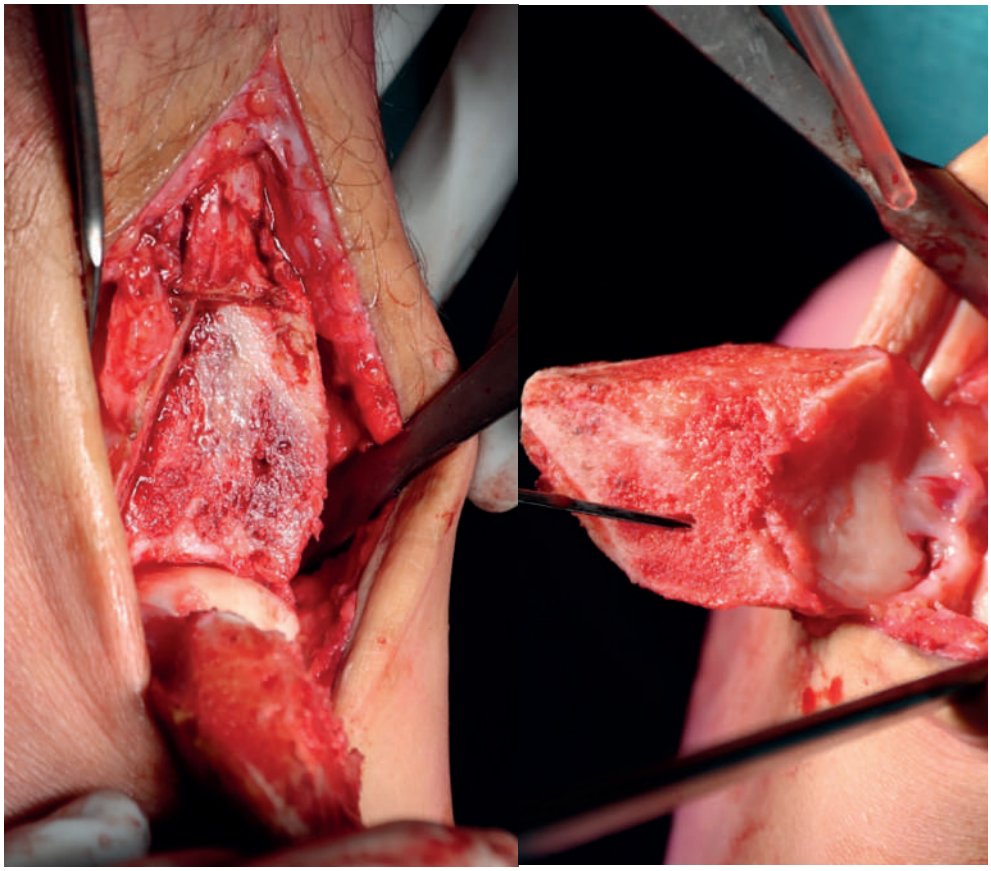

Figure 6a and 6b. In the next step the debrided lesion site is filled with autologous cancellous bone graft. The acquired bone graft is placed on both sides from the excised lesion site and the aid of a small impactor, making sure not to overfill the site.

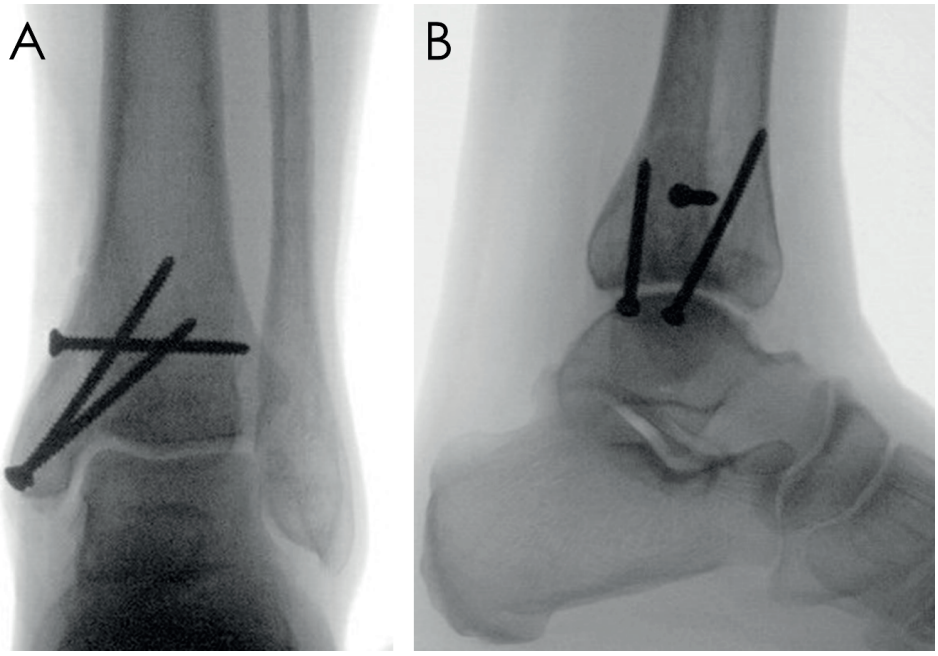

Figure 7a and 7b. After filling the lesion, the ankle is irrigated and the K-wire(s) holding the distal tibial fragment is removed. The distal tibial fragment is mobilized and reduced into its anatomical position to confirm no overstuffing or protrusion of bone grafting. Next, the distal tibial fragment is repositioned and assessed to make sure there is no intra-articular step-off or gapping of the osteotomy. To complete the closure of the osteotomy, and to apply compression of the bone grafting, fixation is performed with two pre-measured 3.5mm cortical lag screws in a slightly divergent manner as previously reported [9]. A third cortical screw can be placed transversely in the proximal apex of the osteotomy for additional shear / rotational stability if a large osteotomy was performed or by surgeon preference. Fluoroscopy is then used to confirm the correct placement of the screws and repositioning of the distal tibial osteotomy. Hereafter, hemostasis is acquired and the incision(s) is closed in layers.

Special Surgical Considerations

Osteotomy

Pre- and intra-operative planning for the osteotomy placement and angulation is imperative to achieve an osteotomy which transverses the OLTP, to ensure proper filling, compression and union, with a reduced risk of recurrence or osteotomy complications. A pre-operative CT-scans or MRI is, therefore, mandatory for preoperative planning of the osteotomy and filling of the lesion as these allow for morphological evaluation of both the lesion and the distal aspect of the tibia.

Postoperative management

Postoperatively, a non-weightbearing short backslap is applied for 2 weeks, followed by suture removal and a non-weightbearing circular cast for another 2-4 weeks. Antithrombotic prophylaxis is prescribed for this period. 4-6 weeks postoperatively the non-weightbearing cast is changed for a short leg weightbearing cast with weightbearing allowed as tolerated for another 4-6 weeks. Additionally, radiographic examination with anterior-posterior and lateral views are obtained at 4-6 weeks postoperative to confirm continued appropriate osteotomy position before commencing weightbearing activities. After the 8-12-week casting, a patient-centered rehabilitation protocol is started and guided by a physical therapist with the aim to regain range of motion and muscle strength of the ankle, as well as a normal gait pattern. The authors recommend minimal clinical follow-up visit at 2 and 8-12 weeks (depending on the 4+4, 5+5 or 6+6 regime) postoperatively for casting, wound healing, and osteotomy / fragment union consolidation assessment, as well as 1-year follow-up. Further visits are recommend on indication or for research purposes. Radiological follow-up is recommended at 12 weeks and 1-year postoperatively to assess the osteotomy union and bone graft filling (Figure. 8). The authors prefer the utilization of a CT-scan to accurately assess graft and osteotomy healing before commencing unprotected weightbearing and at 1-year follow-up to assess full healing of the lesion, also considering the natural course for OLTP is thus far understudied.[10] Further imaging studies should only be obtained on indication or for research purposes.

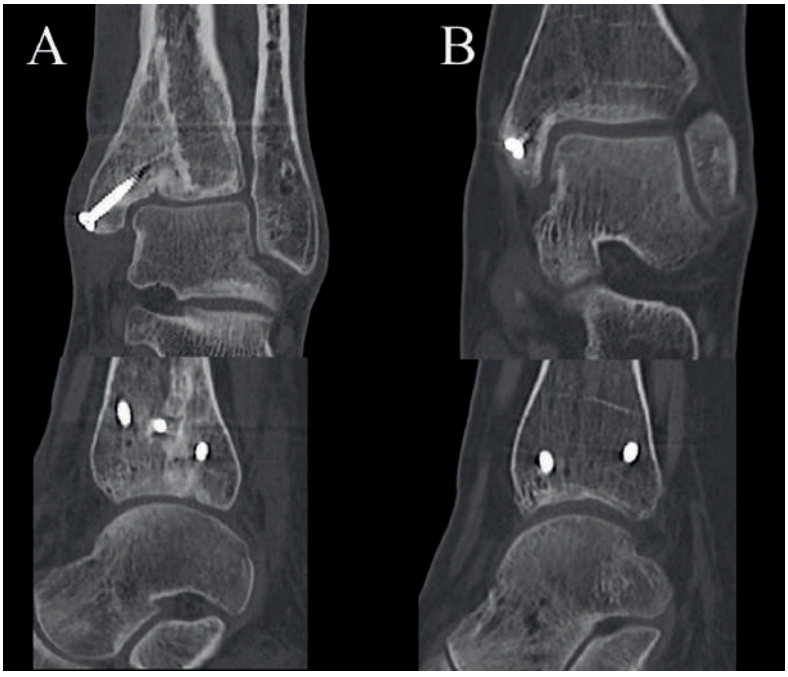

Figure 8. 1-year and 3-year postoperative CT-scan of the cases in figure 1 and figure 2, respectively.

Errors, Hazards, Complications

Patient Selection:

- Relevant comorbidities (e.g., smoking, obesity, diabetes) possibly leading to non-union of the osteotomy or outweighing the surgical risks.
- In skeletally immature patients with open growth plates, the osteotomy cannot be performed as this can result in early closure of the physis, resulting in a symptomatic varus growth disorder of the distal tibia.

Preoperative Planning:

- No preoperative advanced imaging (CT-scan or MRI) could result in improper aiming of the osteotomy and missing the lesion.
- No preoperative advanced imaging (CT-scan or MRI) <1-year of surgery could result in inadequate information regarding the OLTP size and its morphology (such as progressive lesion volume).

Surgical Technique:

- Improper osteotomy angulation (to shallow or steep) causing osteotomy to miss the OLTP with risk of reduced treatment effect by means of filling and compression
- Inadequate exposure
- Potential damage to saphenous nerve.
- Osteotomy closure step-off, possibly leading to osteoarthritis over time
- Autologous bone graft under- or over filling yielding improper filling with a higher risk of recurrence or non-anatomical reduction of the osteotomy, respectively

Postoperatively:

- Weightbearing earlier than recommended by health-care provider, leading to a higher risk of osteotomy delayed or non-union
- No 8-12-week postoperative radiological follow-up to assess osteotomy union in clinically painful patients with the possibility of too early weightbearing, aggravating a delayed- or non-union. In such cases it is advised to extend the period of partial weightbearing by means of a walker boot.

Results

The study was approved by the local medical ethics committee of the Amsterdam UMC, location AMC (Reference number: W14_237#14.17.0288). All patients who underwent an intra-articular distal tibia osteotomy and bone grafting for a symptomatic OLTP from September 2020 until November 2022 were prospectively followed up until 1-year. Four patients were eligible and included. Two patients were female and two were male, with a median age of 35 (inter-quartile range [IQR]: 27 – 41) years. Lesions were primary in 3 cases, and non-primary in 1 case. From a morphological perspective 3 cases were cystic lesions and 1 case showed a crater

morphology. 3 cases had bone grafting from the iliac crest and 1 case had bone grafting proximal from the osteotomy site. Preoperative and postoperative outcome assessment was performed with the Numeric Rating Scale (NRS) for pain during walking (primary outcome), rest, and running, as well as the Foot and Ankle Outcome Score (FAOS). Radiological assessment was done with a 10- or 12-week CT-scan to assess osteotomy union and 1-year follow-up CT-scan to assess graft incorporation. Lastly, post-operative complications, reoperations, and revision surgeries were assessed.

All patients were available at final follow-up. The baseline NRS for pain during walking non-significantly improved from 4.5 out of 10 (IQR: 3 – 4.5) to 2 out of 10 (IQR: 2 – 3) at 2-year follow-up (P= >0.05). The NRS in rest improved from 2.5 (IQR: 1.5 – 3.5) to 2 (IQR: 1 – 2.5; P= >0.05), and during running from 9 (IQR: 7.5 – 10) to 6 (IQR: 4 – 9; P= >0.05). The FAOS subscales of symptoms (54 out of 100 ([IQR: 43 – 79] to 66 out of 100 [IQR: 55 – 80], P = > 0.05), pain (54 [IQR: 44 – 60] to 68 [IQR: 58 – 75], P= > 0.05), activities of daily living (98 [IQR: 97 – 99] to 99 [IQR: 98 – 100], P= > 0.05), sports (25 [IQR: 25 – 38] to 43 [IQR: 40 – 53], P= >0.05), and quality of life (13 [IQR: 9 – 22] to 31 [IQR: 28 – 34], P= >0.05) all non-significantly improved. All osteotomies showed union at 10- or 12-week follow-up CT scans. Three patients showed full integration of the bone graft and 1 patient showed near-complete (> 75%) graft incorporation on 1-year follow-up CT scans. In terms of adverse events no complications were observed or any patients requiring revision surgery of the OLTP. One patient underwent hardware removal.

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Part 5

General Discussion and Appendices

Chapter 13
General Discussion

Controversy remains on several aspects of osteochondral lesions (OCL) of the ankle. These controversies encompass etiology, pathophysiology (biochemical and biomechanical), being a specific local problem or whole-joint disease, natural history, and optimal management with factors influencing outcomes. This thesis focused on several treatment outcomes and factors influencing those outcomes of patients with an OCL of the ankle. This was conducted by focusing on bone marrow stimulation (BMS) and fixation for osteochondral lesions of the talus (OLT), and the treatment for osteochondral lesions of the tibial plafond (OLTP) as a whole. This thesis thereby aims to improve the evidence-based treatment algorithm for ankle OCL. These findings can assist clinicians in their clinical decision making and aid patients by improving treatment outcomes.

Part 1. Bone Marrow Stimulation for Osteochondral Lesions of the Talus

Bone marrow stimulation is the most common surgical treatment for OLT.[23] Its practical benefits are its less invasiveness, lower costs, and shorter rehabilitation time compared to other surgical techniques for OLT. Studies consistently show good results in up-to 80% of patients.[23,76] This is contrary to evidence from the knee, which shows less favorable results for BMS.[30,31] The good results in combination with its practical benefits highlight its continued important role in the surgical toolbox for OLT. Though popular, several controversies surrounding BMS have gained attention in recent years. This thesis aimed to address two of those controversies.

The first clinical question considered in this thesis is whether arthroscopic BMS is sustainable at long-term (>10 years) follow-up. Historically, there is a leading hypothesis that BMS is at an inherent risk of failure over time due to the formation of fibrocartilage following the procedure.[51] Contrary to the native hyaline cartilage, fibrocartilage mainly consists of type-1 collagen (with inferior tensile strength), loss of proteoglycans (resulting in the loss of water from the extra-cellular matrix in the fibrocartilage and a reduction in the ability to withstand compressive forces) and fibroblasts.[51,65] Prior research has shown that fibrocartilage repair tissue exhibits less favorable biomechanical wear properties, lesser quality tissue on macroscopically evaluated second-look arthroscopy, and inferior subchondral bone plate healing compared to natively replaced cartilage grafts or cartilage substitutes.[32,54,77] It is thought that this could result in recurrent symptoms and further degeneration of the joint towards osteoarthritis, leading to treatment failure.[8] The satisfactory clinical outcomes and 7% revision rate observed in **chapter 2** contradict the hypothesis that BMS will fail over time. This may be due to the fact that the indication for BMS has shifted towards a smaller (<100mm^2 to <150mm^2) lesion size.[15,33,58] Such smaller OLT result in better outcomes from BMS or result in better outcomes in general. When examining the clinical literature, the 2021 study by Park et al. included 202 ankles (average lesion size 105 mm^2 ± 56) and was the largest contributor to the systematic

review described in **chapter 2**. Park et al. observed that patient-reported outcomes (PROMs) of pain and function remained stable up-to 3 to 6-years follow-up and deteriorated slightly from there to an average 14-years follow-up.[56] This deterioration was, on average, clinically irrelevant. Corr et al.[18], similarly, reported a high rate of patient satisfaction for 45 cases (average lesion size 74 mm^2, range: 20-270) at an average of 12-years follow-up. Another encouraging finding for BMS in **chapter 2** was the relatively low rate of patients that showed advanced osteoarthritis (4% with joint space narrowing or whole-joint osteoarthritis). One could hypothesize that there are critical lesion dimensions (size and volume) to which BMS may be effective in combination with other lesion factors (e.g., presence cyst and level of containment). Developing evidence is showing that, besides lesion size, that lesion depth could also be an important factor for outcome, albeit with no established consensus to date on the optimal depth.[1,2,13] These smaller lesion dimensions could mean that the fibrocartilage repair tissue may not be exposed to sufficient wear to lead to advanced joint degeneration or treatment failure over time. As a recommendation for further research, one could also hypothesize that these aforementioned lesion dimension cut-offs should be postulated on an individual level in the form of a size proportion relative to talar size. This could be a more accurate method to estimate treatment success and can be supported by the relative size differences of osteochondral lesions eligible for surgical treatment seen across joints measuring from <1cm^2 (ankle and elbow) up-to 8 cm^2 (hip).[38]

When examining the sustainability of BMS through the outcome of procedure survival, **chapter 3** showed that the 10-year survival free from revision rate for 262 arthroscopic BMS patients was 82%. This lower survival rate compared to the literature (93%) is thought to be due to patient selection (22% of non-primary lesions and tertiary referral setting) of the study.[63,67] Moreover, it was observed in **chapter 3** that the median time to revision was 2.4 years. This is supported by the literature, which reports that few patients fail surgery at long-term follow-up, as evidenced by the 1% increase in revision rate reported between systematic reviews on mid-term and long-term BMS (6% versus 7% revision rate, respectively).[67,76] This reported 'early failure' could be due to local (lesion factors such as size or morphology) or non-local (patient factors such as alignment, BMI, smoking status, or mental health) factors. On the other hand, this could be a blind spot, as underreporting for clinical failures could result from reporting / loss-to follow-up bias in the literature. Survival is a complex outcome which includes aspects of pain and functional outcomes, mental health, and patients' satisfaction and expectations. Although caution is warranted due to its complex nature, survival outcomes can be seen as a proxy for clinical success. To date, few studies have focused on survival for BMS in OLT and could be considered underpowered for examining prognostic baseline factors related to survival.[6,8,18,37,56,67,73] An advantage of survival studies is its ability to gather large pools of patients, and thus increase statistical power,

exemplified by (national) arthroplasty registry studies. These opportunities should be further explored for BMS cases, preferably in a (inter)national effort.

When considering the evidence-based treatment algorithm for BMS, several local and non-local factors are recognized as relevant for patient selection. Such factors include sex, ankle instability, hindfoot alignment, lesion dimensions, the presence of cysts, lesion containment, previous surgery, and bone marrow edema (BME).[3,16,19,21,29,33,43,56,58] In **chapter 3**, it was observed that a body mass index (BMI) above 30 is associated with poorer BMS survival. There is conflicting evidence in the literature regarding the effect of BMI on BMS outcomes, with studies showing both a protective and negative effect on PROMs.[7,26,45] We hypothesize that an increased BMI elevates peak-forces in the highly congruent ankle joint, resulting in accelerated wear of the fibrocartilage, and thereby lowering the threshold for failure of BMS.[63,75] Future large sample cohort studies should further identify and define the relevancy of baseline factors on treatment outcomes with validated outcome measures. Such efforts should also aim to include possible relevant factors such as postoperative rehabilitation (including strength and propriocepsis) and mental health.

Second, this thesis explored the question whether outcomes of arthroscopic BMS for a non-primary OLT (i.e., failed prior surgery) are comparable to BMS in primary cases. Over the last decade the clinical dogma has been that repeat BMS would result in inferior outcomes compared to primary BMS and other surgical options for non-primary OLT.[3,33,81] However, this is a poorly studied subject and patients could potentially benefit from non-primary BMS as it is a relatively less invasive surgery and likely less costly treatment compared to other surgical options for recurrent OLT. In **chapter 4**, 11 non-primary BMS patients were matched to 22 primary BMS patients. The clinical outcomes improved in both groups at 1-year follow-up compared to preoperatively, while no differences between the groups at final follow-up were observed. Arshad et al.[3], in their systematic review of 12 studies with 111 patients in total, concluded that non-primary BMS yielded inconsistent results, with improvements in PROMs generally near or below a minimally clinically important difference (MCID) used in foot and ankle patients, which may be inflated due to low-level of evidence literature analyzed in their review. To date, no PROM except for the Foot and Ankle Outcome Score (FAOS) has been validated for OLT, nor has a disease specific MCID been defined for OLT patients.[3,5,17] Moreover, Arshad et al.[3] reported that a wide range of MCID values across different pathologies of the foot and ankle were utilized. This leaves open an important research gap as no conclusions can be drawn based on these data. In **chapter 5**, 2-year prospective follow-up outcomes from 19 non-primary cases were compared to 25 primary cases. It was observed that non-primary BMS for OLT yielded a significant improvement in patient-reported pain and functional outcomes compared to baseline, but an inferior improvement compared to primary

BMS. In this study, non-primary BMS did not result in a statistically significant higher revision rate compared to primary BMS. When critically examining the results of this study, the majority of non-primary cases did not show a substantial improvement in outcomes compared to the primary cases, meaning they would be less likely to reach a (to be established) MCID threshold. A number of non-primary patients may be able to achieve this MCID, however, though limited evidence is available on prognostic factors which could predict achieving this threshold.

Another point of interest for clinicians treating non-primary OLT is the comparison of BMS to other surgical techniques commonly used (such as replacement or regenerative techniques). Previous studies suggest that such techniques result in superior outcomes compared to non-primary BMS.[70,74,81] Here, other factors such as cost-effectiveness and the morbidity of the more invasive surgeries may be relevant when weighing the usefulness of non-primary BMS and for establishing a consensus on treating non-primary OLT. Further prospective comparative studies that asses the clinical outcomes, adverse events, and cost-effectiveness of non-primary BMS compared to other surgical options for non-primary OLT should be conducted to establish this consensus as this thesis did not explore this comparison and the current literature is limited.

In terms of revision surgery for non-primary BMS, Arshad et al.[3] observed a 34% (26/77 cases reported) revision rate at a weighted average follow-up of 52 months (range of means: 12 – 154). This contradicts the finding in **chapter 3** that non-primary BMS was not associated with a significant increase in risk of revision at 10-year follow-up and **chapter 5** which showed that non-primary BMS did not result in a statistically significant higher revision rate compared to primary BMS at 2-year follow-up. This difference compared to the revision rate reported in the literature and **chapter 3 and 5** can potentially be explained by two factors. First, the studies of Chuckpaiwong et al.[16] and Yoon et al.[81] largely contributed (21 out 26 revision cases) to the revision rate reported by Arshad et al.[3], with these studies including lesions with prognostically poorer characteristics. Second, the inclusion of only case series or retrospective studies and no uniform reporting of revision outcomes across the included studies (7/12 studies) in the systematic review by Arshad et al.[3] possibly overestimated the revision rate.

Our abovementioned results seem to open the debate regarding the role of BMS for non-primary OLT, but a new question arises; why would repeat BMS work if it did not in the first place? Although no histological, biomechanical, or structural imaging (e.g., micro-CT) studies are available to investigate this question, several explanations can be proposed. First, the initial BMS procedure might have been technically insufficient, leading to an inadequate healing response and residual complaints.[46] Second, patients may have changed their expectations following the initial surgery, leading

to a decreased loading demand on the ankle (e.g., quitting a certain sport) and as a result a higher patient satisfaction from the relatively improved outcomes. On the other hand, these expectations might also work the other way around; meaning that patients could expect similar results as from a primary BMS procedure, leading to lower satisfaction rates. It, therefore, remains challenging to accurately compare primary to non-primary BMS, as the influence of the abovementioned factors have thus far not been evaluated.

As a *clinical recommendation from part 1*, it can be stated that the current evidence on long-term outcomes of BMS shows satisfactory clinical outcomes and low rates of advanced osteoarthritis. Moreover, a 82% to 94% 10-year procedure survival rate can be expected for BMS.[63,67] Clinically, patients with obesity should be counseled before surgery on the increased risk for long-term failure and interventions for improving patient body mass should be considered.

With respect to non-primary BMS, it can be stated that it is a possible treatment option for patients with a smaller (<150mm^2) non-primary OLT who do not wish or are not able to undergo more invasive surgery, in healthcare systems where alternative options are not (financially) available, or in cases where other treatment options are contra-indicated. Moreover, physicians are advised to incorporate the prognostic lesion- and patient characteristics recognized (e.g. lesion size and location, the presence of cysts, smoking status, and BMI) into their algorithm in order to evaluate the indication for non-primary BMS on an individual basis.[16,21,29,33,43,58,62,63] As such, the indication for non-primary BMS can be embedded in a patient-centered shared-decision treatment algorithm. It is paramount, however, for physicians to clearly inform patients when counseling for surgery, where one could reasonably state that it is expected that there is a less favorable improvement in pain and functional outcomes following BMS for a non-primary OLT. As it could be argued that non-primary BMS remains a treatment option further efforts should be made to improve patient selection and continued monitoring studies are needed to evaluate its effect and safety.

Part 2. Fixation for Osteochondral Lesions of the Talus

A distinct sub-type of OLT is the presence of an osteochondral fragment. Such lesions may be amendable for fixation in case of good cartilage quality and sufficient bone stock of the fragment.[59] The theoretical benefits of fixation are the retainment of the native hyaline cartilage, immediate stabilization of the fragment, and restoration of the joint congruency.[69] An additional benefit is that other surgical options remain available in case fixation fails. One such a fixation technique is the Lift-Drill-Fill-Fix (LDFF).[41,68]

The goal of this thesis was to evaluate the clinical efficacy and safety of open LDFF and to evaluate the long-term outcomes for arthroscopic LDFF. **Chapter 6** describes the step-by-step surgical technique for open LDFF through a medial approach. The LDFF technique was first proposed as an arthroscopic treatment in 2016.[41] The LDFF technique is aimed at treating chronic osteochondral fragments, which can be seen as an intra-articular non-union, that will benefit from debridement, bone grafting, and compression.[68] In addition to the arthroscopic technique, an open technique was developed as the majority of OLT are located on the posteromedial talus which is challenging to treat arthroscopically.[25,68]

In **chapter 7** the prospective 2-year patient-reported, radiological, and safety outcomes following open LDFF for chronic OLT in 34 cases were evaluated. It was found that pain, functional, and quality-of-life PROMs significantly improved, and that fragment union was achieved in 91% of cases. During the study period 3 (9%) revisions (all due to non-union) and 2 (6%) complications were observed. These results concur with the current literature, which shows good clinical outcomes in 9 out of 10 patients and a fragment union rate of 91%.[60] Another aim of **chapter 7** was to evaluate the influence of baseline demographic factors on postoperative outcomes in order to strengthen the evidence-based treatment algorithm. None were found to be correlated with PROMs, however, as is similar to the present fixation literature.[34,47,53,55] The lack of identifiable baseline factors associated with PROMs is likely due to underpowering. On the other hand, a novel finding in **chapter 7** is that obesity was associated with an increased risk for non-union following open LDFF. The authors hypothesize that this may be due to the higher peak-forces in the ankle, potentially leading to (micro) instability of the fragment and thus an increased risk for healing complications. However, metabolic and inflammatory factors may also play a negative role in bone healing in obese patients. Second, as there is limited data variability in the current fixation literature due to the successful outcomes it may be statistically more challenging to identify prognostic factors. We therefore advocate for (inter)national collaborative efforts to identify such factors and improve outcomes for patients.

When examining the factors involved in patient selection for fixation of OLT it can be argued that fragment size and the choice of fixation device (screw, bone-peg, or pin) are important aspects for fragment union. The current consensus on fragment size is an expert statement, defining 10-millimeter bony diameter and 3-millimeter bony depth as the minimum for fixation.[59] This threshold has recently been questioned by the study of Nakasa et al.[53], which showed favorable results in patients with fragments from 50 mm^2 fixed with bone-pegs, pointing towards the possibility to also fix smaller lesions.[69] The aforementioned study also underlines the role of fixation device choice in the fixation of (increasingly smaller) OLT. To achieve both rotational and axial stability

two devices are preferably used, which may necessitate surgeons to be proficient in multiple fixation techniques.[69] In the future, the optimal management of OLT fixation incorporates these aspects of fragment size and fixation device choice from an evidence-based perspective. Such an approach could be tailor made to a patient and could include biomechanical (optimal lesion/talus loading scans) and biological (biological adjuncts or personalized fixation device choice) aspects. From a clinical outcome perspective, it should be recognized that few prognostic factors are thus far identified to predict fixation healing, meaning that the optimal patient selection for the fixation of OLT still lacks a complete evidence-based approach.[60] The role of patient factors (BMI, smoking status, ankle alignment, ankle instability), lesion factors (size, presence of cysts, location), and treatment factors (open versus arthroscopic, fixation device, use of biological adjuncts) on outcomes remain unknown. Further study is therefore necessary to improve the evidence-based patient selection process for fixation and, in turn, the (long-term) clinical outcomes.

A less-invasive fixation technique is arthroscopic fixation. Although several surgical technique papers on arthroscopic fixation are available, little is known on the clinical outcomes of the procedure and its long-term outcomes.[41,42,52,60] **Chapter 8** evaluated the long-term (> 5-years) clinical outcomes of arthroscopic LDFF in 20 ankles. The study is a consecutive follow-up study of the 27-ankle cohort described by Lamberts et al.[48] published in 2020. Up-to an average 7-years follow-up, it was observed in **chapter 8** that patient-reported outcomes remained stable compared to the 2-year follow-up timepoint. In terms of revision surgery, we observed that 87% of cases were free from revision surgery. This is lower than what is reported in the literature (94%), and the 2-year study by Lambers et al. (96%).[48,60] However, the literature concerns an average follow-up duration of 40 (range: 12 – 98) months and may therefore not accurately reflect the long-term sustainability of the procedure.[60] A limitation of the study was the loss-to-follow-up of 20% of initially available cases, which may have introduced bias in the evaluation of the clinical outcomes and survival outcomes. As such, continued monitoring of this patient category remains important. Furthermore, an effort should be made by the orthopaedic community at large to report outcomes of arthroscopically treated patients who underwent fixation for an OLT, as the potential benefit for this less-invasive technique can be clinically important to patients but data is currently limited.[60] Moreover, the balance between optimal fixation (i.e., perpendicular screw placement) versus morbidity of the surgical approach should be examined in future studies, as fixable lesions are commonly located in the (postero)medial talus, thus requiring an open approach.[25,69] A prospective comparison of the outcomes and morbidity of open versus arthroscopic OLT fixation in matched cohorts could aid in this controversy.

As a clinical summary of part 2 of this thesis, it can be stated that open LDFF for the fixation of OLT is technically feasible. Open LDFF results in good mid-term PROM and safety outcomes with a 91% fragment union rate. In terms of patient selection for open LDFF, obese patients may be at a higher risk for non-union and should be counseled accordingly. For arthroscopic LDFF, the long-term clinical outcomes are sustained with an 87% free from revision rate at an average 7-years follow-up. These results point to the satisfactory long-term sustainability of arthroscopic LDFF. It can, therefore, be argued that LDFF is a reliable and evidence-based treatment option in the surgical toolbox for the management of fixable OLT.

Part 3. Management of Osteochondral Lesions of the Tibial Plafond

In the ankle joint, osteochondral lesions of the tibial plafond (OLTP) are located opposite to the talus. Though pathophysiologically similar to OLT, it its known that OLTP have a lower incidence; with one OLTP present for every 14 – 21 OLT.[11,28] There are multiple factors which are thought to be the reason for this lower incidence. Compared to the talus the shape of the distal tibial is concave which is thought to lead to a better load-distribution.[28,57] Moreover, the relatively thicker cartilage of the tibial plafond and its properties (higher tensile, compressive, and shear force properties) are hypothesized to make it less susceptible to injury. However, these assumptions are based on low-volume cadaveric studies.[4,57] In talar injuries, the relatively poor blood supply, especially to the posteromedial talus, is thought to be in-part responsible for OLT development.[36] In OLTP this theory has not been proposed, as the distal tibia is supplied by extra- and intra-osseus arteries and through the periosteum, without any clear (cadaveric) data showing a 'watershed' region of poor blood supply that would make it less prone to lesion healing.[72] It is to be concluded that little is known about the origin of OLTP and basic properties of tibial plafond cartilage.

The management of OLTP, in part due to its rarity, is considered difficult.[22] As to-date, the treatment of OLTP is largely mirrored from the treatment algorithm of OLT, while the natural history and clinical outcomes of OLTP are poorly understood. As no evidence-based treatment algorithm for OLTP exists it was the aim of this part of the thesis to study the current management of OLTP and to initiate a treatment algorithm for OLTP.

In **chapter 9,** the literature on OLTP treatment was summarized. In total, 10 studies with 175 cases were included. No studies reported outcomes of non-operative management. The outcomes following operative treatment were considered moderate to good. From a broader point of view, one could argue that the observed outcomes are inferior to those reported for similar treatment methods in talar lesions.[23,49] One can also hypothesize why this would be the case. From a clinical point of view this could be due to the relative inexperience of physicians with the injury, where one could argue that the current management is likely sub-optimal and that, with more experience

gained and prognostic factors identified, that these outcomes could be improved. There may also be biological and biomechanical factors that contribute to a lower treatment success. First, the dome shape of the talus allows for a near anatomical replacement of the defective osteochondral lesion in OLT (e.g. with osteochondral autografts), while this may be more challenging in OLTP where the concave shape is less easily reproduced. Moreso, due to the anatomy of the distal tibia, it may be more difficult to reach the OLTP without iatrogenic damage to the surrounding structures (e.g., need for osteotomy). On the contrary, one could hypothesize that the larger surface area of the distal tibia makes it less prone to wear due to the lower peak forces received, which could be a protecting factor for BMS and regenerative procedures. This is not seen in the scarce literature, however. Second, higher forces may be needed to create an OLTP due to the stiffer cartilage in comparison to talar cartilage, possibly meaning that such lesions are inherently more extensive than OLT, thus resulting in inferior outcomes for similar treatment strategies. When considering the present OLTP literature the major limitations are the heterogenous treatment modalities and low number of cases reported for each treatment modality, and inclusion of heterogenous patient- and lesion characteristics. Overall, the literature can be considered of poor methodological quality.[12] These shortcomings underline the absence of evidence-based clinical recommendations for OLTP and call for further study.

Generally, the layered treatment approach for ankle OCLs starts with a period of non-operative treatment in case of a symptomatic lesion.[22,27] However, as outlined in the systematic review in **chapter 9**, no studies reported outcomes on non-operative treatment.[64] As a result, in **chapter 10**, we aimed to investigate the 2-year prospective clinical, radiological, and sport- and work outcomes following the non-operative treatment of 18 cases with a symptomatic OLTP. No statistically significant change in PROMs and a 6% conversion to surgery rate was observed. Lesion size and lesion filling appeared stable at follow-up CT. Nine out of 10 patients were able to participate in sports and could return to, or remain at, their preinjury work activities. These initial results suggest that non-operative management is safe and is a reasonable first-line treatment for OLTP, while the expected clinical improvements can be considered limited. This is in line with the current understanding of non-operative treatment for OLT, which is clinically successful in 45% of cases.[9,10] When counseling patients for the treatment of an OLTP the pros and cons of non-operative management versus surgery should be weighed for each individual patient. In general, non-operative management could reasonably be used as a first-line treatment for OLTP, possibly avoiding the need for surgical intervention. This is line with clinical recommendations for OLT.[9,27,62] In our clinical judgement, we are of the opinion that patient education (on balance as well as foot - and calf muscle strength) and injury awareness at initial presentation, as well as a regular follow-up interval supported by imaging (to evaluate

lesion progression), are important aspects of a successful non-operative treatment regime for OLTP patients. Continued clinical and radiological monitoring is required, both from a physicians' and research perspective, as we are further investigating the natural history of symptomatic OLTP and long-term outcomes of non-operative management. Although not specifically addressed in **chapter 10**, it is of clinical importance for future studies to evaluate the natural history of asymptomatic and minimally symptomatic OLTP patients, as this can provide valuable information on the prognosis of such lesions and can be utilized in patient counseling. In OLT, previous studies found such patients, and patients who responded well to non-operative management, to not deteriorate over time clinicallly and radiologically.[44,79] These studies highlight that not all lesions are created equal, and that other factors besides lesion characteristics may be important for patient outcomes.

The most common surgical treatment for OLTP is arthroscopic BMS.[64] In **chapter 11,** a retrospective cross-sectional study was conducted for 51 cases who underwent arthroscopic BMS for an OLTP at an average 9 years (range: 2 - 22) follow-up. Pain and functional outcomes in daily living were considered satisfactory while outcomes in demanding activities, such as sports, were less successful. These PROMs can be considered similar to those reported in the OLTP literature[20,50,71,78], but inferior to outcomes reported for BMS of OLT.[23,76] The revision rate was 6% at final follow-up. To improve the evidence-based patient selection for BMS of OLTP it is important to investigate baseline patient and lesion characteristics. In OLT, lesion size is acknowledged as one of the most important predictive factors for treatment selection in BMS.[15,33,58] For OLTP, based the findings in **chapter 11** that lesion size is associated with postoperative PROMs, this seems to concur.[16,58,78] To date, no cut-off in OLTP size predictive for clinical outcome has been established, meaning clinicians could argue to utilize the maximum 150mm^2 determined for talar lesions as a threshold for BMS in OLTP.[15,58,62] Another important factor thought to influence outcomes of OLTP treated with BMS is the presence of a coexisting OLT. Although, to date, 1 study[16] has reported a negative influence coexisting OLT on outcomes, subsequent clinical studies and the analysis in Chapter 11 found no relationship.[20,39,66] All these studies are likely underpowered. It seems logical to assume that additional articular damage in the joint (by means of a coexisting talar and tibial lesion) would result in earlier wear and onset of osteoarthritis, and a higher chance of clinical failure over time. In such cases of OLTP with a coexisting OLT, it is advisable to concomitantly treat the OLT if symptomatic, and to inform patients on the possible inferior clinical course. However, further study is required to identify and further define the clinical relevancy of these baseline factors.

Further improving the treatment algorithm with OLTP specific lesion and patient factors is paramount in improving its outcomes, which is also a recurring trend in the OLT literature.[24,40,58,62,69] In **chapter 12**, a novel surgical treatment for OLTP located on the medial to central tibial plafond is described. Patients with a large - cystic or crater-like morphology - primary or non-primary OLTP would be eligble. The technique uses an osteotomy to directly transect the lesion, debride all defective tissue, and fill it with an autologous bone graft. This method was developed as, from our clinical experience and previous literature, it is known that complex lesions that are large, with a cystic or crater moprhology, as well as non-primary lesions, are less amendable to BMS.[2,14,58,66,74] Such an osteotomy and bone grafting procedure for an OLTP may well be reserved for complex cases due to the incurring iatrogenic damage to the joint. This procedure adds another layer to the toolbox for surgeons managing patients with an OLTP and may play a role in averting more rigorous surgery such as an ankle fusion or arthroplasty. The safety and clinical efficacy will have to be researched in future studies to validate the procedure.

As a clinical summary from Part 3 of this thesis one could derive a proposed treatment algorithm for OLTP wherein surgeons should consider the following lesion and patient factors in their treatment decision making; lesion location, size, morphology, coexisting talar lesions, ankle alignment and instability, and concomitant pathology.[11,22,28,35,50,61,64,66,71,80] A visualization of such a proposed algorithm is depicted in Figure 1. Most of these factors are established from expert-opinion recommendations and their clinical relevancy should be further investigated. Moreover, clinicians should be warranted that OLTP are rare and should not be managed in a 1 to 1 fashion as we treat OLT. As such, it could be advised to preferably treat these lesions in an expert center.

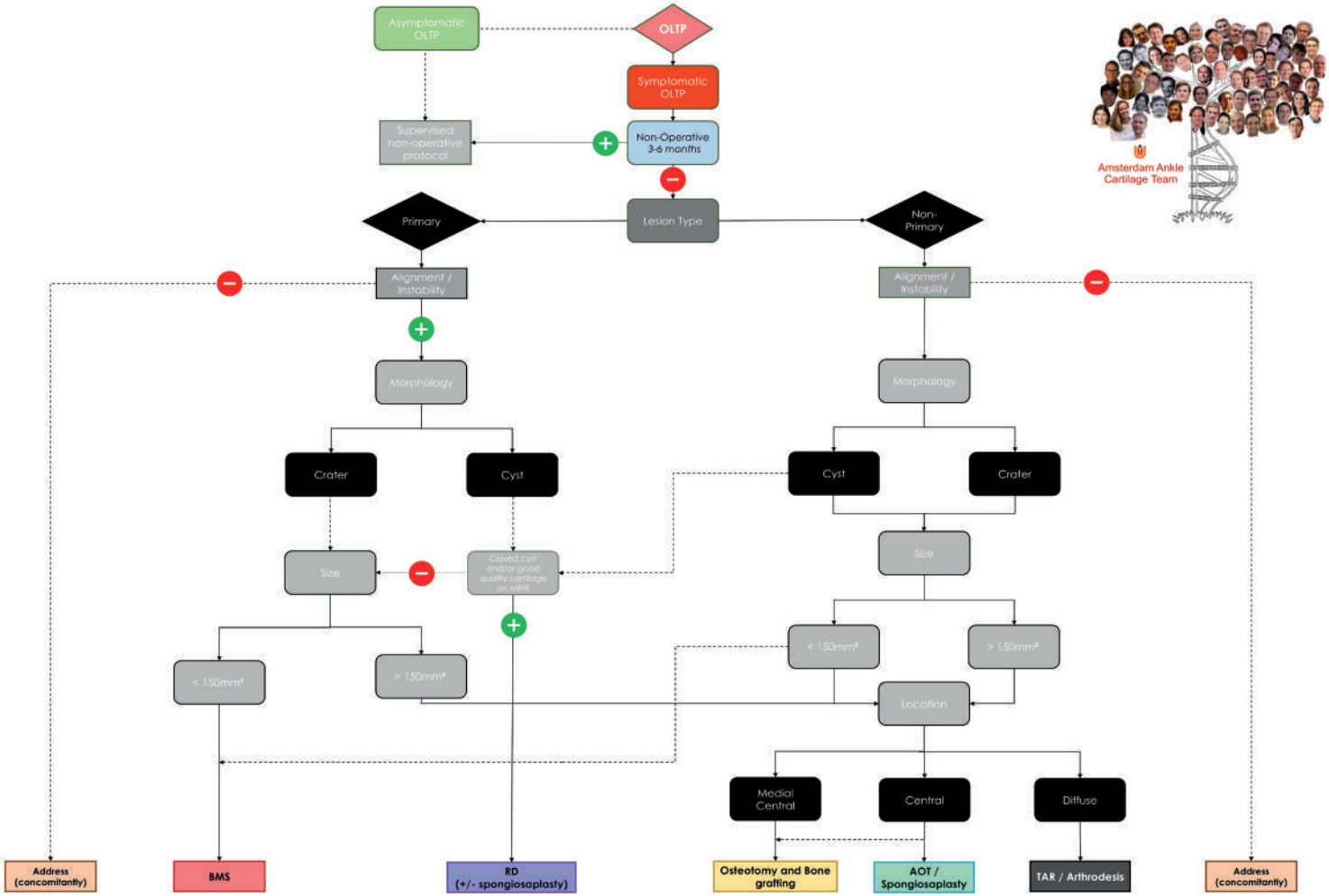

Figure 1. Flowchart of the Amsterdam Ankle Cartilage Team for the treatment of OLTP

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Appendices

Summary in English

Part 1. Introduction

Chapter 1 provides a general introduction into the etiology, epidemiology, clinical presentation, and treatment of osteochondral lesions (OCLs) of the ankle. As no gold-standard treatment has yet been identified for the treatment of ankle OCLs controversy remains on its optimal management. The main goal of this thesis was to improve the evidence-based treatment algorithm for patients with an OCL of the ankle. This thesis aimed to do so by evaluating existing treatment strategies and aimed to identify factors for patient selection. The focus of this thesis was on bone marrow stimulation and fixation for osteochondral lesions of the talus (OLT), and the treatment of osteochondral lesions of the tibial plafond (OLTP).

Part 2. Bone Marrow Stimulation for Osteochondral Lesions of the Talus

Bone marrow stimulation (BMS) is the most common surgical treatment for osteochondral lesions of the talus. While successful in 4 out of 5 patients up-to mid-term follow-up, less is known about its long-term clinical sustainability. Previous studies have cited the inferior wear characteristics of the substitute fibrocartilage, which is formed after BMS, as a reason for an increased risk of long-term issues, such as recurrent complaints, the (early) onset of osteoarthritis, and revision surgery.

Chapter 2 evaluates the current literature on the long-term clinical and radiological outcomes following arthroscopic BMS. We observed 323 ankles reported in 6 studies at a mean 13-year follow-up. As a pooled aggregate, it was observed that the American Orthopaedic Foot and Ankle Society (AOFAS) score at final follow-up was 84 out of 100 points, that 78% of patients participated in any level of sports, and that revision surgery occurred in 7% of cases. However, progression of degenerative changes was observed in 28% of ankles, with only a few cases of joint space narrowing or end-stage osteoarthritis. Notably, the quality of the literature was low- to moderate and included a heterogenous patient population. In **chapter 3** we conducted a survival analysis (free from revision surgery) for 262 patients that underwent arthroscopic BMS at a minimum 10-years follow-up. The 10-year cumulative survival rate was 82%. At 15 years of follow-up the survival rate was 82%. The median time to revision was 2.4 years. As a secondary analysis we analyzed if baseline patient- and lesion factors were associated with survival outcomes. It was found that obesity (a body mass index $\geq$ 30 kg/m^2) was associated with poorer survival. This factor should be incorporated into the treatment algorithm for patients with an OLT when counseling for surgery.

Another controversy regarding BMS is whether patients can benefit from repeating the surgery. The current evidence is poor and shows mixed results, while selecting the right patients for such a procedure could lower costs and shield patients from more invasive surgery. In the study described in **chapter 4**, patients with a non-primary OLT were matched to a primary OLT in a 1:2 ratio, and 1-year clinical outcomes were compared. 11 patients with a non-primary OLT were matched to 22 patients with a primary OLT. It was found that there were no significant differences between the groups in pain outcomes, functional outcomes, quality of life, return to sports and work, or lesion filling on 1-year CT. **Chapter 5** describes a prospective 2-year follow-up cohort of patients that underwent arthroscopic BMS. The aim was to assess the 2-year postoperative clinical outcomes in 19 patients with a non-primary OLT and compare these to 25 patients with a primary lesion. It was observed that both groups had a significant improvement in patient-reported pain and functional outcomes compared to baseline. However, patients with a non-primary OLT had less favorable improvements compared to primary BMS. Moreover, non-primary BMS did not result in a statistically significant higher revision rate compared to primary BMS.

Part 3. Fixation for Osteochondral Lesions of the Talus

Fixation for symptomatic OLT with an osteochondral fragment can be regarded as the current gold-standard treatment for such lesions as 9 out of 10 patients achieve a clinically successful outcome and union of the fragment. The procedure can be performed open or arthroscopically. For patients with a chronic lesion, which can be seen as an intra-articular non-union, the Lift-Drill-Fill-Fix (LDFF) technique was developed. Though the arthroscopic approach of the LDFF showed good early- to mid-term results, no studies have been conducted on the safety and clinical outcomes of open LDFF. Additionally, it remains to be elucidated what the long-term outcomes of arthroscopic LDFF are. As such, this thesis aimed to fill these research gaps.

Chapter 6 describes the step-to-step surgical technique of the open LDFF procedure. Moreover, the study provides an insight in the initial prospective results of the cohort, which were found to be promising. **Chapter 7** focused on the 2-year prospective patient-reported clinical outcomes and 1-year fragment union rate in 34 patients following open LDFF for chronic OLT with an osteochondral fragment. Patients reported significant improvements in pain, function, and a quality-of-life subscale. The fragment union rate was 91%, while its was found that obesity was associated with non-union. During the study period, 3 revision surgeries were performed for a symptomatic non-union of the fragment and 2 complications occurred. It was concluded that open LDFF leads to excellent 2-year outcomes and is a viable treatment for fragmentous OLT, while obesity may pose a risk for non-union of the fragment, and patients should be counseled accordingly.

Chapter 8 describes the long-term results of arthroscopic LDFF from a historic cohort consisting of 20 ankles (18 patients), which were evaluated at a mean 7-year follow-up. We observed that the patient-reported outcomes (which included reported pain, functional ability, and quality of life) remained stable over time, and that the survival free from revision surgery rate was 87% (18/20 ankles). Arthroscopic LDFF, therefore, seems to result in sustained long-term outcomes.

Part 4. Management of Osteochondral Lesions of the Tibial Plafond

Osteochondral lesions of the tibial plafond are located opposite to the talus and are considered rare. Treatment strategies for these lesions are largely copied from their use in talar lesions and lack patient- or lesion factors to guide management. The management of OLTP is therefore an open question, with outcomes reported in small and low-evidence case-series, without any evidence on non-operative treatment. This clear lack of evidence leads us to come up with the first steps towards an evidence-based treatment approach for OLTP in order to improve outcomes for our patients.

Chapter 9 summarizes the current literature on management of OLTP. No studies describing non-operative treatment were found. Six different surgical treatment options were among the 10 included studies (175 patients) with BMS being the most frequently reported among these. The patient-reported outcomes of surgical treatment for OLTP were considered moderate to good, while complications and reoperations were rarely reported. Moreover, the quality of evidence was considered low, and there was considerable underreporting of clinical, radiological, and sport outcomes, amongst a heterogenous patient population.

In **chapter 10** a 2-year prospective study among 18 patients who underwent non-operative management for a symptomatic OLTP assessed its safety and efficacy. Patient-reported outcomes, follow-up CT-scans, and conversion to surgery or any complications were assessed. No significant improvement of the primary outcome, the NRS during weightbearing, was observed. Similarly, no significant changes in the other NRS scales (in rest, during running, and stairclimbing), the FAOS functional outcome score, and SF-36 general health questionnaire were observed. CT-evaluation of 13 available cases showed that lesion size and volume did not change compared to baseline. In 10 (77%) cases signs of lesion filling or no change was found. 9 out of 10 patients returned to sports at any level and work. No complications and 1 case of conversion to surgery was observed. These results suggest that non-operative management for OLTP appears safe but yields marginal improvements in patient-reported pain and functional outcomes.

Chapter 11 describes a retrospective cross-sectional study of 51 patients who underwent arthroscopic BMS for OLTP at 2 to 22 years follow-up. We observed that pain outcomes and functional outcomes were good, but that patients reported higher levels of pain during running. Lesion size was found to correlate with worse pain scores. We did not find a coexisting talar lesion to influence outcomes in this cohort. Additionally, there was a low rate of revision surgeries and complications. These results point to favorable outcomes following BMS for OLTP in activities of daily living, but less so in more strenuous activities. Lesion size may be a factor to take in consideration when treating OLTP with BMS, though further studies should confirm this and determine a cut-off size.

Chapter 12 is a surgical technique study for a novel treatment of large medial and central OLTP, by means of an osteotomy directly transecting the lesion and filling it with autologous bone. This technique adds a new treatment layer for challenging and/or recurring OLTP. The safety and clinical efficacy will have to be investigated in future studies to validate the procedure.

Part 5. Discussion

In this section the findings of this thesis are discussed and compared to the literature. The discussion section provides clinical recommendations based on the work from this thesis. These recommendations are visualized in a treatment algorithm flow-chart.

Samenvatting in het Nederlands

Deel 1. Introductie

Hoofdstuk 1 betreft een algemene introductie over de etiologie, epidemiologie, klinische presentatie, en uitkomsten van de behandeling van osteochondraal laesies (OCLs) van de enkel. Er is geen gouden standaard voor de behandeling van enkel OCLs waardoor er controverse is over de optimale behandeling van deze laesies. Het doel van dit proefschrift is om de wetenschappelijk onderbouwde behandeling van enkel OCLs te verbeteren. Dit proefschrift poogt dit door huidige behandelstrategieën voor enkel OCLs te bestuderen en factoren te identificeren voor patiëntselectie. De focus van dit proefschrift was op beenmerg stimulatie en fixatie voor osteochondraal laesies van de talus (OLT), en de behandeling van osteochondraal laesies van het tibia plafond (OLTP).

Deel 2. Beenmerg Stimulatie voor Osteochondraal Laesies van de Talus

Beenmerg stimulatie (BMS) is de meest uitgevoerde operatie voor OLT. Ondanks dat op de korte tot midden-termijn de behandeling succesvol is bij 4 uit 5 patiënten, is er weinig bekend over de lange termijn houdbaarheid van de operatie. Eerdere studies hebben de slechtere slijtage karakteristieken van het na BMS gevormde fibrocartilaginueze weefsel benoemd als een reden voor problemen op de lange termijn, zoals de terugkeer van klachten, (beginnende) artrose, en revisie operaties.

Hoofdstuk 2 is een literatuurstudie naar de gerapporteerde klinische en radiologische lange termijn uitkomsten na arthroscopische BMS. 323 enkels werden geïncludeerd uit 6 studies, met een gemiddelde follow-up van 13 jaar. Als een gewogen gemiddelde zagen wij een gemiddelde American Foot and Ankle Society (AOFAS) score van 84 uit 100 punten bij follow-up, dat 78% van de patiënten sportte, en dat een revisie operatie bij 7% van de patiënten had plaatsgevonden. Degeneratieve veranderingen werden gezien in 28% van de geïncludeerde enkels, waarvan enkele patiënten ook gewricht spleet versmalling of gevorderde artrose hadden. Noemenswaardig is dat de kwaliteit van de literatuur laag- tot matig was en de geïncludeerde patiënten een heterogene populatie betrof.

In **hoofdstuk 3** hebben we een overlevingsanalyse (revisie vrij) uitgevoerd van de arthroscopische BMS operatie in 262 patiënten op minimaal 10-jaar na de operatie. De cumulatieve 10-jaars overleving was 82%. Op 15 jaar follow-up was het overlevingspercentage 82%. Als een secundaire analyse bekeken wij of patiënt- en laesie factoren bij de start van de operatie geassocieerd waren met de overlevinguitkomsten. Hieruit kwam dat obesitas (body mass index ≥ 30 kg/m^2) was geassocieerd met een slechtere overleving.

Deze factor dient meegewogen te worden in het behandel algoritme voor OLT patiënten wanneer een eventuele operatie wordt besproken.

Een andere controverse binnen de BMS is of patiënten baat zouden hebben bij het herhalen van de operatie. Het huidige bewijs hiervoor is slecht en laat wisselende resultaten zien, terwijl correct geselecteerde patiënten de kosten van een her-operatie zouden kunnen verlagen en patiënten een minder invasieve operatie hoeven te ondergaan.

In **hoofdstuk 4** werden patiënten met een niet-primair OLT gematched met een primair OLT met een 1:2 ratio, en de klinische uitkomsten vergeleken. 11 patiënten met een non-primair OLT werden gematched tegen 22 patiënten met een primair OLT. Er werden geen significante verschillen gevonden in pijn uitkomsten, functionele uitkomsten, kwaliteit van leven, terugkeer naar sport en werk, of laesie opvulling op 1-jaars CT tussen de beiden groepen.

Hoofdstuk 5 beschrijft een prospectieve 2-jaar follow-up cohort van patiënten die arthroscopische BMS hebben ondergaan. Het doel van de studie was om de 2-jaar postoperatieve klinische uitkomsten van 19 non-primaire OLT patiënten te vergelijken met 25 primaire OLT patiënten. Er werd gevonden dat beiden groepen een significante verbetering in patiënt gerapporteerde pijn en functionele uitkomsten hadden. Echter hadden patiënten met een niet-primair OLT een minder gunstige verbetering in deze uitkomsten dan primaire OLT patiënten. Niet-primaire BMS had niet een statistisch significante hoger revisie percentage dan primaire BMS.

Deel 3. Fixatie voor Osteochondraal Laesies van de Talus

Fixatie voor symptomatische OLT met een osteochondraal fragment kan gezien worden als de huidige standaard voor zulke laesie omdat 9 uit 10 patiënten een klinisch succesvol resultaat bereiken en fragment genezing laten zien. Fixatie kan open of arthroscopisch uitgevoerd worden. Voor patiënten met een chronische laesie, wat gezien kan worden als een intra-articulaire pseudartrose, werd de Lift-Drill-Fill-Fix (LDFF) techniek ontwikkeld. De arthroscopische LDFF heeft eerder goede korte- en middel termijn resultaten laten zien maar is er nog geen onderzoek gedaan naar de lange termijn uitkomsten. Verder is er nog geen onderzoek verricht naar de veiligheid en klinische uitkomsten van open LDFF. Daarom heeft dit proefschrift als doel deze onderzoek lacunes op te vullen.

Hoofdstuk 6 beschrijft de chirurgische techniek van de open LDFF procedure stap voor stap. Daarnaast geeft deze studie een eerste inzicht in de prospectieve resultaten van de operatie, welke veelbelovend waren.

Hoofdstuk 7 focust zich op de prospectieve 2-jaar patiënt gerapporteerde uitkomstmaten en 1-jaar fragment genezing in 34 patiënten die de open LDFF ondergingen voor een chronisch OLT met een osteochondraal fragment. Patiënten rapporteerde een significante verbetering in pijn, functionele uitkomsten, en kwaliteit van leven. De fragment genezing was 91%, terwijl gezien werd dat patiënten met obesitas een hoger risico op een non-union (pseudoartrose) hadden. Tijdens de studieperiode werden er 3 revisie operaties uitgevoerd voor een symptomatische pseudartrose van het fragment en waren er 2 complicaties. Er werd geconcludeerd dat de open LDFF resulteert in excellente 2-jaar uitkomsten en een goede behandeloptie is voor OLT met een osteochondraal fragment, terwijl obesitas een mogelijk risico factor is voor het krijgen van een non-union.

Hoofdstuk 8 beschrijft de lange-termijn resultaten van arthroscopische LDFF in een historisch cohort van 20 enkel (18 patiënten), welke werd opgevolgd op gemiddeld 7 jaar na de operatie. We zagen dat de patiënt-gerapporteerde uitkomsten (waaronder pijn, functionele uitkomsten, en kwaliteit van leven) stabiel bleven over de tijd en dat de overleving van de operatie 87% was. Arthroscopische LDFF lijkt daarom te resulteren in houdbare lange-termijn uitkomsten.

Deel 4. Behandeling van Osteochondraal letsels van het Tibia Plafond

Osteochondraal letsels van het tibia plafond (OLTP) bevinden zich in de enkel overliggend ten opzichte van de talus en worden beschouwd als zeldzaam. De behandeling van deze laesies wordt grotendeels gekopieerd van de behandeling voor OLT, en mist heden patiënt- en laesie karakteristieken om de behandeling te sturen. De behandeling van OLTP is daarom een open vraag, met uitkomsten momenteel gerapporteerd in kleine en laag niveau bewijs 'case-serie' studies. Daarnaast zijn de uitkomsten van non-operatieve behandelen bij OLTP onbekend. Deze hiaten in bewijs voor de behandeling van OLTP geeft de aanleiding om in dit proefschrift deze patiëntengroep te onderzoeken en een eerste stap te zetten richting een 'evidence-based' behandel algoritme om zo uitkomsten voor patiënten te verbeteren.

Hoofdstuk 9 vat de huidige literatuur naar de behandeling van OLTP samen. Geen studies beschreven een non-operatieve behandeling. Zes verschillende operatieve behandelingen beschreven in 10 studies (175 patiënten) werden geïncludeerd, waarvan BMS de meest voorkomende behandeling was. De patiënt gerapporteerde uitkomstmaten na de operatieve behandeling van OLTP kan gezien worden als matig tot goed, terwijl complicaties en her-operaties zeldzaam waren. De kwaliteit van het bewijs was laag, en er was onderrapportage van klinische, radiologische, en sport uitkomsten in een heterogene patiënt populatie.

In **hoofdstuk 10** wordt een prospectieve studie beschreven met 2 jaar follow-up naar de veiligheid en effectiviteit van een niet-operatieve behandeling voor een symptomatisch OLTP bij 18 patiënten. Hierin werd gekeken naar de patiënt-gerapporteerde uitkomstmaten, opvolg CT-scans, en conversie naar een operatie of complicaties. Er werd geen significante verbetering gezien in de primaire uitkomstmaat, de NRS voor pijn tijdens lopen. Daarnaast werd er ook geen significante verandering gezien in de andere NRS schalen (in rust, tijdens rennen, en traplopen), de FAOS functionele uitkomst score, en de SF-36 kwaliteit van leven score. De evaluatie van de CT-scans was beschikbaar in 13 patiënten en liet geen verandering in het grootte en het volume van de laesie zien ten opzichte van de start van de behandeling. Bij 10 (77%) patiënten waren er tekenen van laesie opvulling of geen verandering. 9 uit 10 patiënten keerde terug naar sport (ongeacht niveau) en werk. Er werden geen complicaties gezien en 1 patiënt converteerde naar een operatieve behandeling. Deze resultaten suggereren dat non-operatieve behandeling voor OLTP veilig is maar tot marginale verbetering in patiënt-gerapporteerde pijn en functionele uitkomsten leidt.

Hoofdstuk 11 betreft een retrospectief cross-sectionele studie naar 51 patiënten die arthroscopische BMS voor een OLTP hebben ondergaan met een follow-up duur van 2 tot 22 jaar. We observeerde dat de gerapporteerde pijn- en functionele uitkomsten goed waren, maar dat patiënten slechtere pijn uitkomsten rapporteerde tijdens rennen. Laesie grootte correleerde met een slechtere postoperatieve pijn score. Een additioneel overliggend OLT leek niet geassocieerd te zijn met uitkomsten in dit cohort. Er werd een laag revisie en complicatie percentage gezien. Deze resultaten wijzen op gunstige uitkomsten na BMS voor OLTP in dagelijkse activiteit, maar minder gunstige uitkomsten tijdens zwaardere activiteiten. Laesie grootte is een factor waar rekening mee moet worden gehouden wanneer een OLTP behandeld wordt met BMS, maar toekomstige studies dienen dit te bevestigen en een afkap waarde vast te stellen.

Hoofdstuk 12 is een chirurgische techniek studie naar een nieuwe behandeling voor grote mediaal en centraal gelegen OLTP. De behandeling maakt een osteotomie direct door de laesie en vult deze met autoloog bot. Deze techniek voegt mogelijk een nieuwe behandeling toe aan het palet voor uitdagende op terugkerende OLTP. De veiligheid en klinische effectiviteit dient in vervolgstudies onderzocht te worden.

Deel 5. Discussie

In dit deel worden de resultaten van dit proefschrift bediscussieerd en vergeleken met de literatuur. De discussie geeft daarnaast klinische aanbevelingen gebaseerd op het werk uit dit proefschrift. Deze aanbevelingen zijn grafisch weergegeven in een behandel algoritme stroomdiagram.

PhD Portfolio

General Courses:	**ECTS**	**Year**
Harvard Catalyst Course in biostatistics - Online	2.0	2019 - 2020
Seminars, Workshops, and Masterclasses:		
Amsterdam Elbow Course	0.5	2019
SICOT-AFAS-ESSKA PIONEER 'Acute Injuries and Return to Sport' we-binar		2020
Annual Knee Arthroscopy Practicum Bachelor. Students Medicine UvA	1.0	2019 - 2021
Annual Fracture Fixation Practicum Bachelor Students Medicine UvA	1.0	2019 - 2021
Poster Presentations:		
Harvard Orthopaedic Trauma Research Day (Boston, USA) – Virtual* (x2)	0.5	2020
ESSKA Congress 2020 (Milan, Italy) – Virtual* (x2)	0.5	2021
AOFAS Annual Meeting 2021 (Charlotte, NC, USA) - Virtual* (x6)	0.5	2021
NVA Lustrum Congress 2021 (Noordwijk, The Netherlands) (x3)	0.5	2021
AAOS Annual Meeting 2022 (Chicago, IL, USA) (x2)	0.5	2022
ICRS World Congress 2022 (Berlin, Germany) (x3)	0.5	2022
ESSKA Congress 2022 (Paris, France) (x5)	0.5	2022
ICRS World Congress 2023 (Sitges, Spain) (x3)	0.5	2023
ESSKA Congress 2024 (Milan, Italy)	0.5	2024
AAOS Annual Meeting 2025 (San Diego, USA) (x2)	0.5	2025
ISAKOS World Congress 2025 (Munich, Germany)	0.5	2025
ICRS World Congress 2025 (Boston, USA) (x3)	0.5	2025
ESSKA Congress 2026 (Prague, Czech Republic)	0.5	2026
Oral Presentations:		
NVA Lustrum Congress 2021 (Noordwijk, The Netherlands)	0.5	2021
NOV Jaar congress 2021 ('s-Hertogenbosch, The Netherlands) - Duo presentation	0.5	2021
ESSKA congress 2022 (Paris, France) (x2)	1.0	2022
Global Conference Ankle Surgery - Lift Drill Fill Fix (LDFF) in the Ankle: the gold standard?	0.5	2022
ISAKOS Congress 2023 (Boston, USA) (x4)	2.0	2023
ICRS World Congress 2023 (Sitges, Spain)	0.5	2023
SRATS Congress 2024 (Romania)	0.5	2024
ESSKA Congress 2024 (Milan, Italy) (x3)	1.5	2024
NOF/NOV Congress 2024 (Rotterdam, the Netherlands)	0.5	2024

AAOS Annual Meeting 2025 (San Diego, USA)	0.5	2025
ISCRA Consensus meeting 2025 (New York, USA) (x2)	1.0	2025
ISAKOS World Congress 2025 (Munich, Germany)	0.5	2025
ESSKA Congress 2026 (Prague, Czech Republic)	0.5	2026

(Inter)National Conferences:

AAOS Congress 2019 (Las Vegas, USA)	2019
Harvard Orthopaedic Trauma Research Day 2019 (Boston, MA, USA)	2019
Harvard Orthopaedic Trauma Research Day 2020 (Boston, MA, USA) – Print	2020
ICRS Cartilage Repair 2020 - Virtual	2020
ESSKA Congress 2021 (Milan, Italy) - Virtual	2021
AOFAS Annual Meeting 2021 (Charlotte, NC, USA) - Virtual	2021
NVA Lustrum Congress 2021 (Noordwijk, The Netherlands)	2021
NOV Jaar congress 2021 ('s-Hertogenbosch, The Netherlands)	2021
ICRS World Congress 2022 (Berlin, Germany)	2022
ESSKA Congress 2022 (Paris, France)	2022
NVA Jaar Congres 2022 (Apeldoorn, The Netherlands)	2022
ISAKOS Congress 2023 (Boston, USA)	2023
ICRS Congress (Sitges, Spain)	2023
ESSKA Specialty Days (Warsaw, Poland)	2023
ESSKA Congress 2024 (Milan, Italy)	2024
ISCRA Consensus meeting 2025 (New York, USA)	2025
ISAKOS World Congress 2025 (Munich, Germany)	2025
ICRS World Congress 2025 (Boston, USA)	2025
ACES Congress (Amsterdam)	2026
ESSKA Congress 2026 (Prague, Czech Republic)	2026

Lectures:

Friday Research Lecture Amsterdam Ankle Cartilage Team	1.5	2020 - 2025
IOC/ACHSS Amsterdam research meeting	0.5	2023

Tutoring / Mentoring:

Brent Beljaars – Long-term outcomes surgical treatment OLT	1.0	2020
Julian Hollander – MT5 stress fractures	1.0	2020
Emma Wijnhoud – Incidence of OCL in CLAI	1.0	2020
Elmer Petersson – MT5 return to sports	1.0	2020
Lisanne Wolsink – Incidence of bilateral OLT	2.0	2021
Elze Geurts – Return to sports TOPIC	2.0	2021
Carlijn Ter Laak Bolk – Return to sports elite athletes with OLT	2.0	2022

Margot Aalders – Long-term revision arthroscopic BMS of OLT	2.0	2022
Hayden Hartmann (USA) – Sex-differences in outcomes of BMS for OLT	0.5	2024
Isabelle Rustenburg - Long-term revision fixation of OLT	2.0	2026

Other:

Journal Club	2.0	2019 - 2021
FAST-course team (Amsterdam, The Netherlands)	-	2020 - 2021
Clinical researcher assisting in on-site cadaveric testing WaterDrill Jet	-	2020
Amsterdam Movement Sciences (AMS) annual meeting congress organizing committee: Jury Member 'Best Poster Award' AMS Meeting 2022	0.5	2021 - 2022

Editorial Duties:

Journal of Experimental Orthopaedics (JEO) - (web)editor	-	Since 2021
Arthroscopy – Editorial Board Member	-	Since 2022

Peer-Reviewing:

Knee Surgery, Sports Traumatology, Arthroscopy (KSSTA)	-	Since 2020
Journal of Bone and Joint Surgery (JBJS) - Case Connector	-	Since 2021
Injury	-	Since 2021
Journal of Experimental Orthopaedics (JEO)	-	Since 2021
Arthroscopy	-	Since 2022
American Journal of Sports Medicine (AJSM)	-	Since 2022
CARTILAGE journal	-	Since 2023
Journal of Bone and Joint Surgery (JBJS)	-	Since 2023

Parameters of Esteem

Van Walree grant, Koninklijke Akademie van Wetenschappen (KNAW) – ESSKA Congress 2020	2020
AMS Talent Call 2020 for Sustainable or Deteriorating? Ultra-Long-Term Clinical Success of Treatment for Cartilage Lesions in the Ankle	2020
ON/ESSKA Education Scholarships 2024	2023
ON Open Education Grant 2025	2025
ISCRA '30 under 30' award	2025

List of publications

Peer-Reviewed

1. Poor Mental Health in Patients with Symptomatic Osteochondral Lesions of the Talus. *Bone and Joint Journal (2026)*
   J.H.M. Pijnacker, K.Emanuel, I. Sierevelt, J.J. Hollander, J.A.H. Steman, Q.G.H. Rikken, J. Dahmen, N.O. Aygeman-Prempeh, B.F.P. Broekman, S.A.S. Stufkens, G.M.M.J. Kerkhoffs

2. Return To Sports After Talar OsteoPeriostic Grafting From the Iliac Crest for Large Osteochondral Lesions of the Talus. *Orthopaedic Journal of Sports Medicine (2026)*
   J. Dahmen, E.J. Geurts, Q.G.H. Rikken, S.A.S. Stufkens, G.M.M.J. Kerkhoffs

3. Return to Sport and Performance After Treatment of Osteochondral Lesions of the Ankle in Elite Athletes: A Retrospective Study. *Orthopaedic Journal of Sports Medicine (2026)*
   C.S. Ter Laak Bolk, J.J. Hollander, E.J. Geurts, K.R. Ramsodit, Q.G.H. Rikken, J. Dahmen, S.A.S. Stufkens, G.M.M.J. Kerkhoffs

4. Understanding Pain in Osteochondral Lesions of the Talus: A Cross-Sectional, CT-Based Analysis Showing Limited and Inconsistent Associations with Pain. *Foot and Ankle International (2026)*
   J.J. Hollander, I. Sierevelt, J.A. Steman, J.H.N. Pijnacker, K.S.Emanuel, G.M.M.J. Kerkhoffs, S.A.S. Stufkens, Amsterdam Ankle Cartilage Team (N.O. Agyeman-Prempeh, N.T.M. van Bergen, D.P. Borensztajn, J. Dahmen, Q.G.H. Rikken)

5. Isolated Intermediate Cuneiform Dislocation: A Case Report on the Surgical Considerations for a Rare Injury of the Foot. *Journal of ISAKOS (2026)*
   Q.G.H. Rikken, M. Roetman, R. Krips, P.A.J. de Leeuw

6. Eight Out of Ten Patients Participate at Their Desired Level of Sports After Talar OsteoPeriostic grafting from the Iliac Crest for Large Osteochondral Lesions of the Talus. *Orthopaedic Journal of Sports Medicine (2026)*
   J. Dahmen, E. Geurts, Q.G.H. Rikken, S.A.S. Stufkens, G.M.M.J. Kerkhoffs

7. Arthroscopic Bone Marrow Stimulation for Non-Primary Osteochondral Lesions of the Talus Yields Limited Improvements in Patient Reported Outcomes Compared to Primary Cases: A Prospective 2-Year Follow-Up Study. *Foot and Ankle International (2026)*
   Q.G.H. Rikken, J. Dahmen, J.J. Hollander, J.S. Steman, S.A.S. Stufkens, G.M.M.J. Kerkhoffs

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Alena, Leen, Moppie: Ik zal ze de rest besparen in het kader van PDA. Dit proefschrift hoort zondermeer ook jou toe. Je bent mijn onafscheidelijke steun en maatje. Samen genieten van alles wat het leven voor lekkers, moois, en sportiefs te bieden heeft maakt jou de allerfijnste om mee te zijn. Een krachtige vrouw met een heel groot hart en een eigenzinnige mening. Samen zijn en de wereld ontdekken is het mooiste wat er is. Ik kijk uit naar onze reis en de velen die komen gaan. Loveyou Major F!

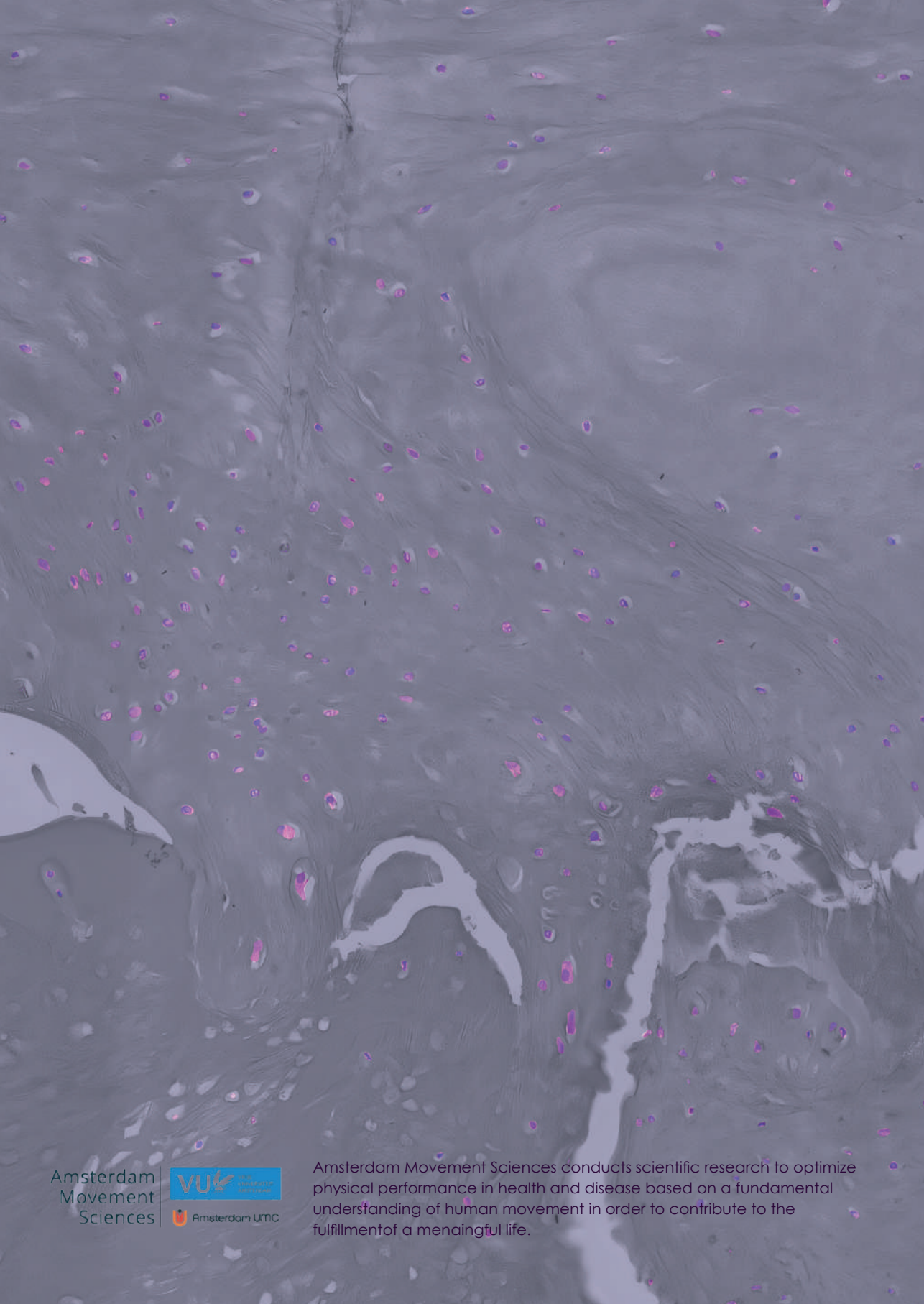
About the Author

Quinten Rikken (1996) was born and raised in Amsterdam by his parents Anita Meijssen and Enrique Rikken. Following graduation from Fons Vitae Lyceum (VWO), he studied Medicine at the Vrije Universiteit (VU) in Amsterdam, starting in 2015. During this period an unhappy accident led to his first encounter with orthopaedics, which sparked his scientific interests and brought him in contact with his later mentor prof. Gino Kerkhoffs. In 2019 this interest motivated him to pursue a scientific internship in the United States, at the Foot and Ankle service of Massachusetts General Hospital (MGH) in Boston, under the supervision of dr. DiGiovanni.

After his time in Boston, Quinten was welcomed in the Amsterdam Ankle Cartilage Team by prof. Gino Kerkhoffs and dr. Sjoerd Stufkens to pursue a PhD at the department of Orthopaedic Surgery and Sports Medicine of the Amsterdam University Medical Centers (AUMC). In 2022 he started his clinical rotations to complete his MD, which he combined with his work as PhD student. During his rotations he had the humbling opportunity to visit Pretoria, South Africa, for a general surgery internship at Steve Biko Academic Hospital.

In 2024, he completed his MD and started working as a resident not in training at the Orthopaedic Surgery department of the Flevoziekenhuis (Almere), under the guidance of dr. Rover Krips. Hereafter, he happily worked at the department of Orthopaedic Surgery at Spaarne Gasthuis (Hoofddorp) under the supervision of dr. Arthur van Noort and dr. Roel Hoogendoorn.

In 2026, Quinten will continue his orthopaedic career as a resident of orthopaedic surgery in the Amsterdam region. Outside of the hospital Quinten is most happy on skis in deep snow or on a bike in the Basque hills. He lives in Amsterdam with his partner Alena Wisse.



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