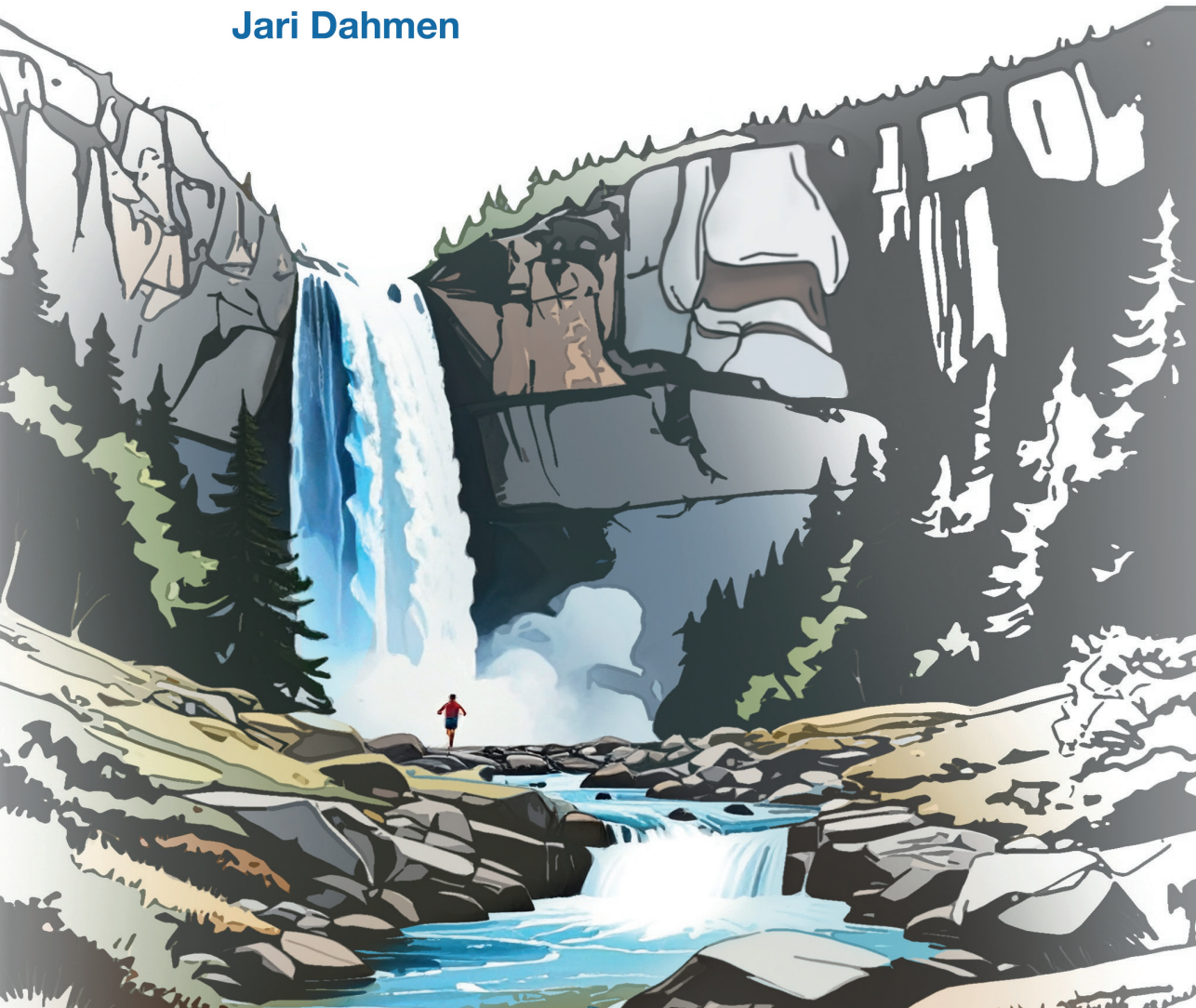
Incremental Cartilage Damage of the Ankle:

Steps Towards an Evidence-Based Personalized Approach

Jari Dahmen



STELLINGEN

behorende bij het proefschrift getiteld

Incremental Cartilage Damage of the Ankle:
Steps Towards an Evidence-Based Personalized Approach

1. **"Understanding ankle cartilage damage as a progressive cascade rather highlights the need for early recognition and tailored intervention"**
   This thesis
2. **"When it comes to revision surgery for surgically failed osteochondral lesions of the talus, no single surgical technique clearly outperforms the rest"**
   This thesis
3. **"Talar OsteoPeriostic grafting from the Iliac Crest (TOPIC) offers a press-fit solution for large and complex talar osteochondral lesions, with promising two-year clinical outcomes"**
   This thesis
4. **"Return to desired level of sport after TOPIC surgery was achieved in 8 out of 10 patients, based on self-reported attainment of their own performance goals"**
   This thesis
5. **"Osteochondral lesions of the talus are not all the same; like geological formations, they vary in morphology, depth, and behavior"**
   This thesis
6. **"The post-operative (re-)occurrence of cysts highlights an unresolved biological response, with pathophysiological mechanisms and clinical significance yet to be clearly defined"**
   This thesis
7. **"Cartilage is found where it is an advantage that the solid framework should be pliable and glutinous for the benefit of the flesh that surrounds them"**
   Aristotle (384–322 n.Chr.)
8. **"Wanneer men wil genezen, is men reeds half gezond"**
   Seneca (4 v.Chr. – 65 n.Chr.)
9. **"De beste manier om iets te leren is er les in te geven"**
   Seneca (4 v.Chr. – 65 n.Chr.)
10. **"Tough times never last, only tough people last"**
    Mr Demi Demi

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Incremental Cartilage Damage of the Ankle: Steps Towards an Evidence-Based Personalized Approach

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PART I

Introduction, aetiology, incidence, and phenotypes of cartilage damage in the ankle

Chapter 1

General introduction

Setting the scene

Ankle sprains remain one of the most frequent injuries in sporting activities.[20,21,63] A number of decades ago, ankle sprains were assumed to be injuries that were not associated with harm. However, the last twenty years have shown that they are not as harmless as previously thought, resulting in the following statement: '*There is no simple lateral ankle sprain*'.[30,31] One possible entity of this harm can be the development of cartilage lesions following an ankle sprain. The process of cartilage degradation in the ankle following an ankle injury can resemble a waterfall or cascade.[14] Each stage sets up or "pours down" into the next stage of cartilage damage in the ankle joint (Figure 1.1).

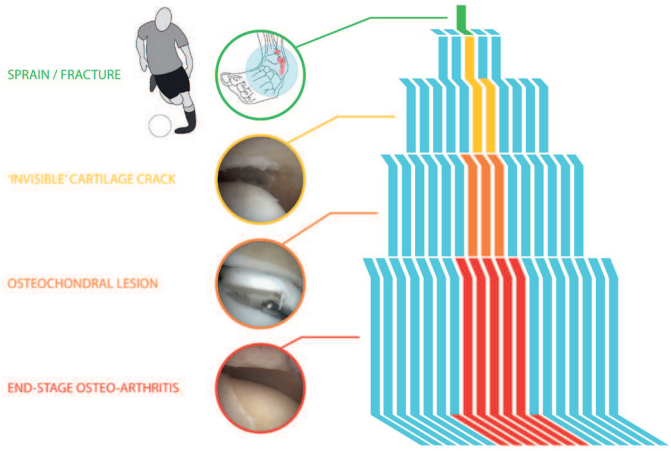

Figure 1.1: Cascade or waterfall analogy, from sprain to end-stage osteo-arthritis (reprint permission from Springer Nature License, published in KSSTA).

The first stage in this process, represented by an invisible cartilage crack, is preceded by a trauma such as an ankle fracture or sprain.[4,5] The invisible cartilage crack, which is often asymptomatic due to the aneural nature of cartilage, is referred to as the subclinical phase. Over time, this phase may progress to the following stage: an osteochondral lesion of the ankle.[19,47,54,55] This stage, which can develop months to years after the initial trauma, involves damage to the cartilage and to its underlying subchondral bone.[37] Patients with symptomatic osteochondral lesions of the ankle typically complain of deep ankle pain during weight-bearing activities such as walking, stair-climbing and sporting activities. This may substantially limit their level of physical activity and participation in work and sports.[23,61] Although reactive swelling or stiffness is often present, absence of the aforementioned swelling, locking or catching does not completely rule out an

osteochondral lesion of the ankle. Patients can also experience undefined pain on walking or experience giving way. Rather typical is the tenderness on palpation often recognized when the osteochondral lesion is palpated with the foot in maximal plantarflexion.[45] The symptoms of patients with an osteochondral lesion of the ankle can severely impact their quality of life [36]. When setting the scene in this perspective, it is important to mention that cartilage and osteochondral lesions of the ankle are most commonly located on the talar dome with exact proportions regarding distribution on the talar dome versus the distal tibia being not exactly known. However, some studies mention that 1 tibial lesion is found for every 19 talar dome lesions.[9,22,44] When observing the cascade once more, one can appreciate that the last stage of the cascade is the onset of (end-stage) osteoarthritis (OA) after the previous stages. End-stage OA of the ankle is a debilitating condition associated with substantial direct and indirect costs as well as an inferior mental and physical quality of life as compared with matched controls from the general population.[25,41,43] This short description of the ankle cartilage cascade may be a simplified overview – cartilage cracks, osteochondral lesions, and osteoarthritis – it also exposes several unanswered scientific questions regarding the etiology and causality, the difference between symptomatic and asymptomatic cartilage and osteochondral lesions, the pathophysiological mechanism behind the cascade, and as such representing a grand data-gap.

Present issues in the management of cartilage and osteochondral lesions of the ankle are characterized by a lack of comprehensive understanding of their etiology, exact incidence, as well as phenotypic variability. Furthermore, there remains an absence of evidence-based treatment frameworks, particularly for large, secondary osteochondral lesions following failed previous (surgical) intervention(s). The general aim of this thesis is investigating the prevention of large lesions progressing to osteoarthritis by personalized (surgical) treatment methods. This thesis systematically addresses several key issues briefly introduced below. The focus of **Part I** is on the aetiology, incidence, and phenotypic presentations of (osteo)chondral injuries of the ankle. **Part II** consists of chapters on the (after)treatment of large osteochondral lesions of the talus that have failed prior surgical intervention(s). **Part III** finalizes the thesis with a general discussion and a summary.

Part I: Aetiology, incidence, and phenotypes of cartilage damage of the ankle

The first part of the present thesis focuses on the etiology, incidence and phenotypic presentation of (osteo)chondral injuries of the ankle. **Chapter 2** describes the progression of incremental cartilage damage in the ankle joint as stages of the cartilage cascade analogy. **Chapter 3**: it is known that there is a vast diversity amongst different phenotypic presentations of osteochondral lesions of the talus as observed on baseline Computed Tomography (CT) scans and Magnetic Resonance Imaging (MRI) scans, ranging from fragmentous to cystic and crater-type lesions (Figure 1.2).[46] Crater-type lesions may be specifically observed after a prior bone marrow stimulation procedure. We aim to categorize and describe these osteochondral lesions of the talus based on radiological phenotypic presentations from an orthopedic and geologist's perspective. As mentioned above, a cartilage lesion, and subsequently an osteochondral lesion, can occur after a trauma. From a classical point of view, the incidence of cartilage damage in ankle injuries is likely to be severely underestimated. This observation forms the basis for conducting a systematic review of a specific type of ankle injury where cartilage damage has historically been underreported, namely syndesmotic injuries. These injuries are often challenging to identify, lack effective preventive strategies, and highlight the importance of improved recognition, diagnosis, and treatment. It is currently unknown what the exact incidence is of cartilage injuries in both acute and chronic isolated syndesmotic injuries.[12] As such, **Chapter 4** evaluates the incidence of (osteo)chondral lesions of the ankle in patients with acute and chronic isolated ligamentous syndesmotic injuries.

Part II: Surgical treatment for large, complex, and secondary osteochondral lesions of the ankle

The second and largest part of this thesis aims to improve our understanding of the outcomes of surgical treatment for large, complex, and secondary osteochondral lesions of the talus (OLT). Over the years, most research projects have focused on studying (the efficacy of) conservative and operative treatment options for small (usually referred to as < 1.5 cm in diameter), non-complex, primary OLTs.[16] To a lesser extent researchers have focused on OLTs that are either large, and complex and/or have failed prior surgical intervention(s), that is, non-primary or secondary OLTs.[48,65] Currently, there is a great variety in surgical treatment options for osteo-

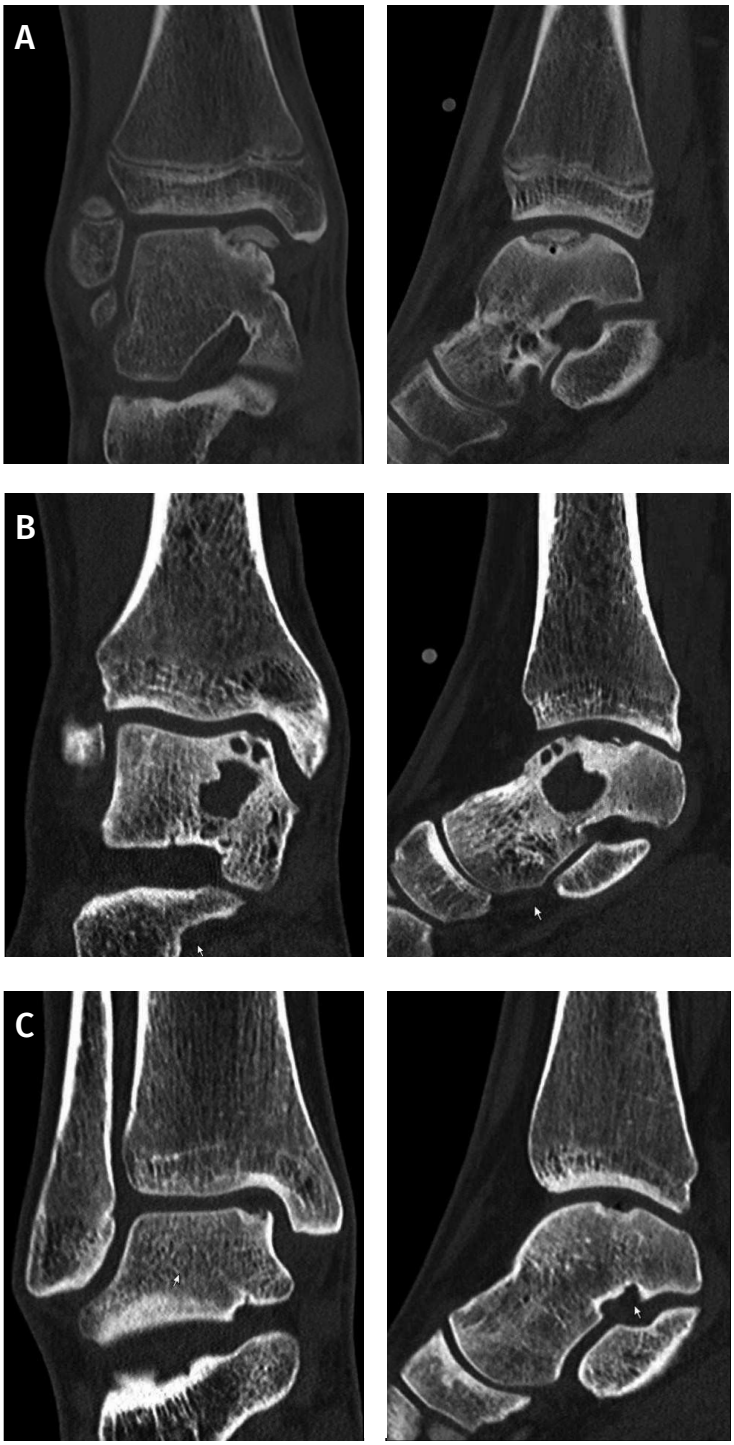

Figure 1.2: Morphological classification into three groups: (A) fragmentous, (B) cystic, (C) crater-type.

chondral lesions of the talus that have failed prior surgery to the osteochondral lesion. However, a clear overview on the clinical efficacy of different surgical treatment options for non-primary OLTs has not been presented yet. As such, an overview of the existing literature is necessary, to highlight the different surgical therapies as well as provide a comparison of their clinical efficacy. **Chapter 5** focuses on the question whether a superior surgical treatment can be identified from past and present literature for managing secondary osteochondral defects of the talus. Building upon Chapter 5, a different, more detailed systematic review and meta-analysis is presented in **Chapter 6** in which the specific bone marrow stimulation treatment is assessed regarding its efficacy as a surgical treatment strategy for patients with osteochondral lesions of the talus who have failed a prior surgical intervention.

Invasive surgical interventions may be necessary to address the patients' complaints in the case of symptomatic, large, non-primary OLTs.[33,40] These interventions range from transplantation techniques such as (osteo)chondral transplantation, including the classical osteochondral autograft transfer system (OATS) and the chondrocyte implantation techniques.[56] Alternatively, metal implantation and bulk talar allografting are used.[2,49,51,58-60,64] These treatment options show short- and medium-term adequate efficacy regarding clinical success rates, however, it can be stated that each of these surgical techniques are associated with specific downsides. For example, the OATS procedure can cause knee donor-site morbidity incidence rate ranging from 11% to 35%.[15,27] Alternatively, a specific downside for allografting can be non-union of the graft, whereas specifically for cartilage implantation techniques financial costs can be also regarded a downside.[1,6,18] Regarding the usage of metal implantation for resurfacing of the medial or lateral side of the talar dome for large osteochondral lesions of the talus can be erosion of the distal tibia through wear and tear of the cartilage, incongruency of the resurfacing implant regarding curvature and fitting. An alternative graft can be the usage of an autologous osteoperiosteal graft harvested from the iliac crest. The usage of cylindrical osteoperiosteal grafts from the iliac crest has been previously described by Hu et al.[27] and Chen et al.[11] and yielded clinically effective outcomes. A downside of the usage of cylindrical grafts is that the size of the cylinder autograft is static and determined pre-operatively.[57] In order to overcome the aforementioned downsides, a novel technique for the treatment of large talar osteochondral lesions had recently been developed in Amsterdam; The *Talar Osteo-Periostic grafting from the Iliac Crest (TOPIC)*. This procedure uses an en-bloc ipsilateral iliac crest autograft including the overlying periosteum func-

tioning as a layer to induce articular cartilage-like tissue regeneration.[29,38,42] From previous research, we know that around 60% of all osteochondral lesions of the talus are located on the combined posteromedial and centromedial zone of the talar dome, while 24% of the lesions are located on the lateral talar dome.[32,34,52,62] This is why the TOPIC technique has been developed in an inclusive manner, both medial and lateral lesions. In **Chapter 7**, the Talar OsteoPeriostic grafting from the Iliac Crest (TOPIC) procedure is described for osteochondral lesions residing on the medial talar dome. Conversely, in **Chapter 8**, the new Talar OsteoPeriostic grafting from the Iliac Crest (TOPIC) procedure will be described for osteochondral lesions residing on the lateral talar dome. The aims of Chapter 7 and 8 are to describe the surgical technique and to present the reader with specific tips and tricks regarding the technical details when performing this technique including pitfalls. **Chapter 9** focuses on describing the prospective two-year clinical and radiological outcomes for large, complex, medial talar osteochondral lesions that have been operated on with the TOPIC procedure.

We are well aware that there is a gender gap regarding the description of clinical efficacies that asks for an evaluation.[3,24,35] Building on the foundation laid in the previous chapters in this thesis, **Chapter 10** aims to close this knowledge gender gap in the field of osteochondral lesions of the talus by analyzing whether there are sex-specific differences in clinical and radiological outcomes after Talar OsteoPeriostic grafting (TOPIC) for large osteochondral lesions of the talus. Another research gap that has been understudied is the aftertreatment and postoperative rehabilitation after surgery for osteochondral lesions of the talus.[8,13] A clinically relevant scientific question on this matter that is frequently asked by patients is whether it is possible to reduce the number of weeks of immobilization and casting after osteochondral autograft transplantation being performed through a medial malleolar osteotomy. As such, **Chapter 11** aims to answer the following question: Is there a difference in outcomes between 5 and 6 weeks of non-weight bearing after osteochondral grafting with medial malleolar osteotomy for medial talar defects? Although the TOPIC procedure showed satisfactory clinical outcomes up to 2-years follow-up, it is currently unknown what the sports outcomes are in this group of patients having received this relatively new surgical treatment option.[17,53] **Chapter 12** aims to answer this question by researching what the (return to) sports outcomes at one and two years of follow-up are in patients having undergone Talar OsteoPeriostic grafting (TOPIC) for large, complex talar osteochondral lesions.

A significant number of surgical interventions for large and non-primary OLTs make use of an osteochondral autograft or allografts.[2,10,28,51] These grafts need to be fitted perfectly into the excised osteochondral lesion of the talus in order to match the size, morphology and curvature of the talar dome ensuring appropriate fitting and prevent the prone positioning of the grafts. This appropriate restoration of the talar surface is required for an adequate contact area and pressure distribution in the ankle, as well as sufficient joint space and medial clear space which are important biomechanical properties to consider.[7] It is currently unknown to what extent the surface curvature of the medial talar dome matches with the surface curvature of the ipsilateral iliac crest. **Chapter 13** aims to answer this question through the description of the development of an automated curvature matching technique.

A potential complication which is observed at follow-up after treating osteochondral lesions of the talus through an autografts or allograft procedure, is the development of cysts within or around a transplanted graft.[26,27,39,50] It is unclear what the exact incidence rate is of the occurrence of these cysts at follow-up after autograft and allograft transplantation, and, additionally, it is unclear whether a certain transplantation technique produces a significantly higher or lower rate of cystic development over time. Moreover, it is unclear if the post-operative presence of cysts actually affects clinical outcomes. **Chapter 14** will delve into this topic, aiming to assess and compare cystic occurrence after autografting, allografting and osteoperiosteal grafting for osteochondral lesions of the talus, and explore the presence of correlations of clinical outcomes with the presence of postoperative cysts.

A novel surgical treatment strategy for large mostly single osteochondral lesions of the lateral or medial talar dome was described in this PhD thesis. However, whenever there are multiple, secondary, cystic osteochondral lesions including the whole surface of the talus, there is a sparse variety of surgical treatment options possible with most of them being in the form of an ankle arthrodesis or total ankle replacement, thereby limiting the choice for a joint-sparing alternative for orthopedic surgeons. In the Addendum section of this PhD thesis, the technique and 2-year prospective outcomes of a novel bone- and joint sparing hemi-prosthesis surgery, the Ankle Spacer, for treating multiple secondary osteochondral lesions of the talus is described.

Part III: General discussion and appendix

Chapter 15 puts the findings of this thesis into perspective through the discussion of thoughts. Hereafter, the most important conclusions are made based on the findings of the present thesis.

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Chapter 2

The ankle cartilage cascade: incremental cartilage damage in the ankle joint

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Ankle sprains remain the most frequent injuries in sporting activities.[7,8,36] A few decades ago, ankle sprains were assumed to be injuries that were not associated with any substantial harm. However, the last twenty years have shown that they are not as harmless as thought, as depicted in the March Issue of the year of 2016 in this Journal: '*There is no simple lateral ankle sprain*' (Figure 2.1).[13,14] The development of cartilage lesions following an ankle sprain is certainly food for thought, thus sparking the idea of the current Editorial. The process of cartilage degradation in the ankle following an ankle injury resembles a waterfall or cascade. Each stage sets up or "pours down" into the next stage of cartilage damage in the ankle joint.

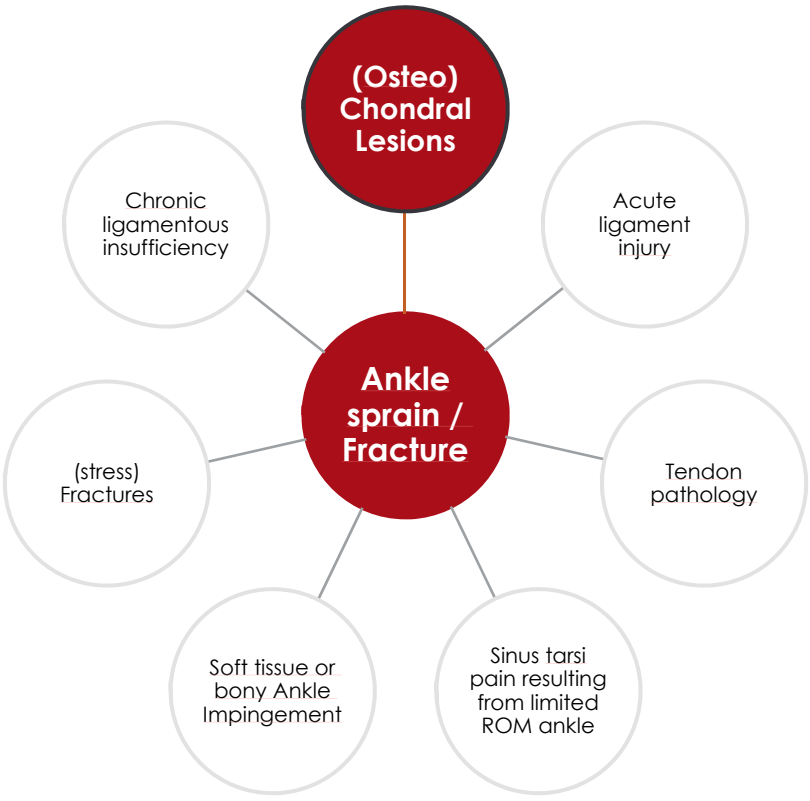

Figure 2.1: Sequential pathologies after an ankle fracture or sprain.

Asymptomatic superficial cartilage lesions

An asymptomatic cartilage lesion of the ankle, not involving any damage to the subchondral bone plate, may arise from a traumatic event, such as an ankle sprain or fracture.[3] Microscopic cartilage lesions are mostly referred to as inert, and it is believed that these lesions will not progress into an osteochondral

lesion neither end-stage osteoarthritis, nor will they become symptomatic due to the fact that cartilage is avascular and a-neural tissue.[16,17,28] As concluded by Mankin et al. in 1974, if superficial lacerations of articular cartilage are limited in size and depth, they will '*neither heal nor progress to more serious disorders*'.[16,17] This statement can be substantiated by a recent meta-analysis that showed that although the incidence of reported (osteo)chondral damage after ankle sprain or fracture was high (namely 45%) the proportion that may result in poor clinical outcomes (as a consequence of osteochondral damage or end-stage osteoarthritis) can be considered relatively low.[5,19,26,33,37] This finding has further been described by several studies reporting good patient-reported mid- to long-term outcomes following ankle trauma (sprains and fractures).[11,12] It must however be acknowledged that although Mankin et al. refer to the superficial lacerations as being relatively harmless or inert, it may well be the case that these superficial lesions contain microscopic cracks potentially inducive of the cartilage cascade as described and shown below.[3]

Posttraumatic cartilage cracks with damage to the subchondral bone and post-traumatic chondrocyte apoptosis

Cartilage lesions may become symptomatic after a traumatic event when (microscopic) cartilage cracks progress into the subchondral bone.[3] Consequently, these lesions will induce bleeding[4,10,16-18,21] after which the lesion will either heal or fail to heal. The failed healing induces a cascade of events as highlighted in Figure 2.2. The first stage entails a cartilage crack with subchondral bone plate damage with an insufficient repair response, that subsequently leads to an osteochondral lesion, with the potential of leading to end-stage osteo-arthritis, either localized or of the whole joint.[6,27,32,34] The most interesting research question remains: why do some of the above-mentioned lesions heal while others do not? Another entrance into the cascade is via chondrocyte apoptosis following, for example, intra-articular fractures.[2,15,20] A recent study by Blom et al. supports the theory of the *Incremental Cartilage Damage* (Figure 2.2) in the ankle as part of the cascade.[3] In this study, Blom et al. investigated the presence of chondral damage after incremental single axial impact loads in ex-vivo ankle joint caprine models. After these single axial impact loads, the damage was assessed microscopically as well as through a contrast-enhanced high-resolution micro-computed tomography scan. Furthermore, whole-joint biomechanics were assessed. Although no (osteo) chondral damage was visible through the micro-CT-scan nor on the microscopic tests, changes were observed in the biomechanical behaviour of the joint following

a single axial impact load. These changes can be a result of the alteration of the specific relative and absolute compositions and balance between proteoglycans, glycoproteins, (sulphated) glycosaminoglycans (sGAGs), and water content in the joint. Such biomechanical alternations as a result of impact load have also been observed in the knee.[3,9,22,25,38]

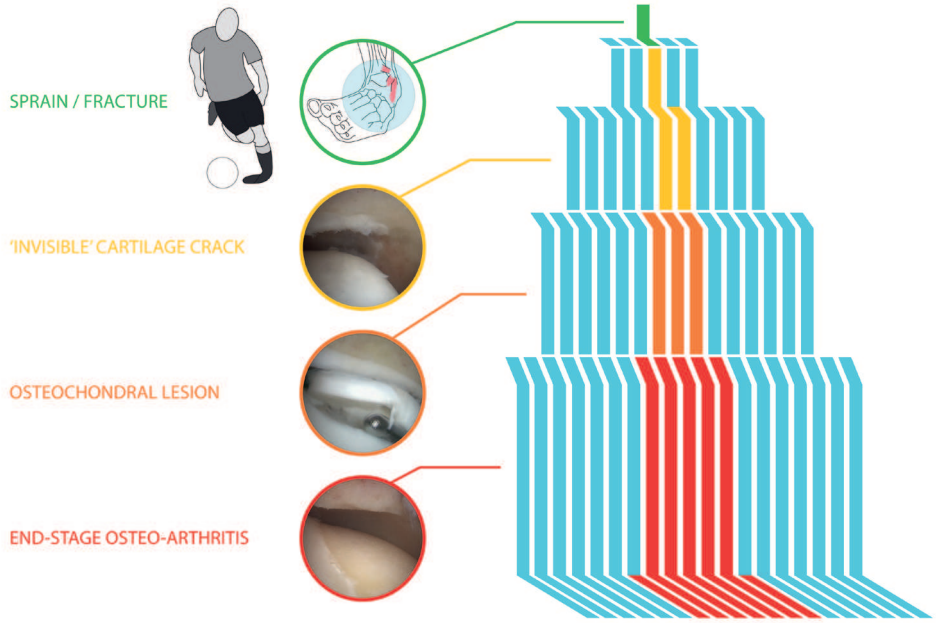

Figure 2.2: Cascade analogy, from sprain to end-stage osteo-arthritis.

Large superficial or erosive cartilage lesion due to a post-traumatic status or biomechanical problem

Another potential pathophysiological pathway is a large acute superficial or erosive chronic cartilage lesion caused by trauma or an underlying biomechanical problem in or around the ankle, such as malalignment, malunion after fracture or (chronic) ligament laxity. Altered pressure distribution, edge-loading and chronic erosion of the cartilage are related to repeated microtrauma due to chronic ligament laxity and may ultimately result in a deep cartilage lesion, as a result leading to subchondral plate damage (and subsequent bleeding). A large lesion may have an insufficient repair response leading to scar tissue and fibrocartilage formation. This structure may potentially progress in size and volume, ultimately leading to degenerative changes in the entire joint. This process is different from the previously described cascade event, as its' mechanism is more "delayed".

These degenerative processes have a latency time and it may take decades before symptoms become disabling.[35]

Chondrolysis after intrasynovial hemorrhage

Last, but not least, a separate entity is the cascade of chondrolysis after repeated intrasynovial hemorrhage or intra-articular bleeding. This might occur due to mechanical injury (ligament injury/laxity or capsular tears) or hemophilia. The repeated hemorrhages within the joint may lead to alterations in the cartilage matrix, more specifically leading to superficial and deep erosions where the proteoglycan concentration is low and the synthetic activity of the chondrocytes is depressed.[39] Enhanced chondrolysis can progress into damage of the subchondral bone and, thereafter, to degradation of the entire joint.[16,17] This process might be catalyzed by chronic ligament laxity. Intra-articular bleedings may also play a role in the prior cascades where deep lesions give no guarantee of healing. It is possible that there may exist a subtle tipping point where repetitive bleeding from the subchondral bone, instead of healing the joint, erodes the cartilage and maintains a chronic synovitis.

Take to work from the ankle cartilage cascade

Related to the description of the idea on the abovementioned cascades and the underestimated incidence rates of posttraumatic (osteo)chondral lesions, there might be different pathophysiological pathways that can induce cartilage damage and potentially lead to osteoarthritis of the ankle joint. Hence, more focus should be put on early detection and primary individualized preventive interventions to prevent cartilage damage in the earliest step of the cascade: the subclinical phase. This approach could allow for an early delay or even stop to the cartilage crack that leads to the waterfall of degeneration, and could prevent the development of osteochondral lesions and end-stage OA; two conditions with severe symptoms that affect the quality of life of the patient.[1,24] Moreover, from a societal perspective, one can also state that this is a paramount undertaking, as we know from previous literature that end-stage OA is associated with high direct and indirect costs.[12,23] In order to accomplish such goals as mentioned above, we need novel, sophisticated imaging tools[29-31] as well as innovations to cushion the joint so that we are able to diagnose and treat the cartilage damage at the early subclinical phase.[29-31] Through presentation of the Ankle Cartilage Cascade, we hope to encourage future research to focus on the subclinical phase after ankle

trauma, ultimately stalling the ongoing cascade in this phase in order to work towards prevention of end-stage ankle osteo-arthritis.

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Chapter 3

The geologist's perspective: morphological description of phenotypic osteochondral lesions of the talus

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Abstract

Purpose: This study aims to categorize and describe osteochondral lesions of the talus based on radiological phenotypic presentations from a geologist's perspective, elucidating the morphological characteristics and potential mechanisms underlying lesion formation.

Methods: Nineteen representative computed tomography (CT) scans of a broad range of osteochondral lesions of the talus were analyzed and categorized into different groups by two independent geologists based on distinct morphological features observed in radiological images. Variations within these categories were identified and discussed. The sequence of events leading to lesion formation was examined, particularly focusing on the interplay between mechanical and chemical factors. Consensus meetings were held to validate geological categorizations, involving peer review by orthopedic experts. Descriptive statistics and qualitative analyses were conducted to elucidate lesion characteristics across geological categories.

Results: The analysis revealed five main categories of osteochondral lesion morphology: brittle deformation, ductile deformation, damage zone/cratering, dissolution, and abrasion. Each category was described in detail in a qualitative manner including a provision of exemplary CT scans. Examples exhibiting characteristics of multiple categories underscored the complexity of lesion formation processes. Two potential sequences of events — fracture or fault preceding cyst formation, and cyst formation preceding fracture or fault — were identified, though ambiguity persisted in some cases.

Conclusion: This study presents a morphological description of radiological phenotypic presentations of osteochondral lesions of the talus from a geologist's perspective. Five groups were identified each illustrating distinct characteristics of deformation processes: brittle deformation (Category 1), ductile deformation (Category 2), damage zone/cratering (Category 3), dissolution (Category 4), and abrasion (Category 5). Applying and understanding the morphological characteristics and potential etiological mechanisms underlying lesion formation from a geologic lens is essential for elucidating the complex interplay between (bio)mechanical and chemical factors in lesion development, and this cross-pollination with geological models opens up new insights into forming hypotheses on the underlying etiological processes of osteochondral lesions or other bone-related injuries. This can then, ultimately, guide the development of personalized preventive treatment options.

Introduction

Osteochondral lesions of the talus are predominantly caused by traumatic events, being lateral ankle sprains, syndesmotic injuries, or fractures of the ankle and cause deep ankle pain generally during weight-bearing.[7, 8, 20, 30] However, a substantial percentage of the lesions are also of non-traumatic origin.[3, 26] Currently, there is no best treatment option for lesions that have not been operated on before (primary lesions) nor lesions that have failed prior surgical intervention(s) (non-primary lesions).[9, 16, 19] As such, treatment considerations and choices are based on individualized patient characteristics, such as – but not limited to – Body Mass Index (BMI), age, sporting activities, concomitant injuries, as well as radiological factors.[10, 29] These radiological factors are usually based on baseline Magnetic Resonance Imaging (MRI) or Computed Tomography (CT) images and include lesion size (diameter, volume and/or surface), lesion location, and lesion morphology.[21-23, 34] Lesion morphology can be classified in three main phenotypic groups, being cystic, fragmentous and crater(like), as previously described.[30]

Besides the fact that it is currently not fully clear what the exact etiological mechanism is behind the development of each type of cartilage and osteochondral lesion of the ankle, another research gap concerning osteochondral lesions of the talus lies in the abovementioned oversimplified categorization of lesion morphology into solely the three abovementioned groups. Although this approach provides a basic, easily applicable, framework for classification, it fails to capture the full spectrum of morphological variations observed in daily clinical practice.[17] Through limiting the categorization to solely three groups, important nuances and subtleties in lesion morphology may be overlooked. Furthermore, the categorization may hinder the identification of new phenotypic subtypes or variations that could have distinct pathophysiological mechanisms and clinical implications beyond the abovementioned groups. Another shortcoming of the classification is that it does not take into account the etiological, pathophysiological mechanisms why certain lesions progress over time. As such, we can conclude that there is a need for a more comprehensive, broad description encompassing a broader range of morphological descriptors, allowing for a more accurate and clinically relevant characterization of osteochondral lesions of the talus.

Addressing this research gap requires a multidisciplinary and cross-disciplinary approach integrating principles outside of orthopedic research into the study of osteochondral lesions of the talus. While the pathogenesis of OLT is multifactorial,

involving mechanical and chemical factors, the inclusion of geological perspectives may offer unique insights into the structural and mechanical properties of bone and cartilage and their interplay. By applying geological concepts and science to radiological phenotypic presentations, researchers can discern morphological features indicative of underlying pathophysiological deformation processes. This interdisciplinary collaboration holds promise for advancing our understanding of lesion morphology and formation mechanisms, ultimately leading to more effective diagnostic and treatment strategies for osteochondral lesions of the talus.

As such, it is our primary aim to categorize and describe osteochondral lesions of the talus based on radiological phenotypic presentations from a geologist's perspective, elucidating the morphological characteristics and potential mechanisms underlying lesion formation. The underlying aim is to provide novel insights into the pathophysiological mechanisms behind the etiology of cartilage damage of the ankle in order to work towards a personalized preventive treatment option through future research endeavors.

Materials and methods

This present study concerns a cross-disciplinary qualitative study encompassing a collaboration between the Department of Orthopedic Surgery and Sports Medicine of the Amsterdam UMC and the Faculty of Science, Geology and Geochemistry (Department of Earth Sciences) of the Vrije Universiteit Amsterdam.

Ethical considerations

This study adhered to ethical guidelines governing research involving human subjects and medical data. All patient information was anonymized to protect confidentiality. Computed Tomography (CT) scans of patients with osteochondral lesions of the talus were selected from a database without any Patient Reported Outcome Measures (PROMs) or additional data being taken, or subject to any additional procedures. Approval from the medical ethical committee was therefore not deemed necessary per the guidelines of the local medical ethical committee (Amsterdam UMC, University of Amsterdam).

Commencement of collaboration

The collaboration commenced by reaching out to two experienced geologists through the university network. An in-person introductory meeting was organized at the Vrije Universiteit Amsterdam to facilitate mutual acquaintance and foster knowledge exchange between the orthopedic and geological disciplines. During this meeting, participants engaged in discussions aimed at bridging the knowledge gap between orthopedic science and geological science. Orthopedic colleagues provided an overview of the symptomatology, diagnostics, and treatment modalities for osteochondral lesions of the ankle. Several examples of morphologies derived from CT scans of the ankle were presented. Following the introduction and exchange of foundational knowledge, the geological scientists gained insights into the orthopedic aspects of (i.e. diagnosis, symptomatology, radiology as well as treatment associated with) osteochondral lesions, enabling them to approach the subsequent analysis from a comprehensive perspective encompassing both disciplines. This interdisciplinary collaboration enriched the methodology by integrating geological expertise with orthopedic understanding, enhancing the depth and breadth of the investigation. A second in-person meeting was organized in which, again, the geological scientists as well as the orthopedic researchers/surgeons met in order to further intensify the collaboration; in this meeting, ten to fifteen representative examples of CT scans of a diverse range of osteochondral lesions of the talus were presented and interactively discussed from the orthopedic as well as the geological perspective.

Sample selection

Thereafter, nineteen computed tomography (CT) scan samples of osteochondral lesions of the talus were chosen to provide a broad representation of osteochondral lesions of the talus. These examples were selected to encompass a representative spectrum of different morphological lesion types ensuring a comprehensive coverage of the pathology. It was chosen to mix different morphological presentations, primary and non-primary lesions, medial and laterally located lesions, as well as smaller and larger lesions. High quality coronal, sagittal as well as axial slices of the CT scans were provided including an interactive video (MP4) so that the geologists could independently evaluate the CT scans. Each CT scan was anonymized to maintain patient confidentiality.

Categorization through a geological analysis

Each example was examined, freely described, and, thereafter categorized into distinct geological domains/groups based on distinct radiological morphological features from the geologist's perspective. Each geologist categorized the lesions according to their expertise and geological knowledge. The categories were developed to encompass a wide range of morphological variations observed in osteochondral lesions of the talus. In cases where examples exhibited characteristics of multiple categories, careful consideration was given to the predominant features to assign the most appropriate category. Schematic drawings and geological photographs were included and provided to supplement the categorizations, aiding in the visualization and comprehension of the findings.

Consensus meeting and validation process

Following the independent evaluations, the two geologists convened to discuss and reconcile their findings. During this consensus meeting, they collaboratively reviewed their respective categorizations, aiming to reach agreement on the geological categories of the deformation structures. Discrepancies or uncertainties were addressed through discussion and further examination of the CT scan examples. The agreed-upon geological categories of the deformation structures were interpreted and documented in a geological context, considering principles and terminology relevant to geology. The categories were: brittle deformation, ductile deformation, damage zone/crater, karst/dissolution and abrasion. This approach facilitated a systematic and standardized analysis of the osteochondral lesions, ensuring consistency and accuracy in the categorization process. The categorized lesions and their geological interpretations were subsequently reviewed by two researchers from the orthopedic and sports medicine department of Amsterdam UMC and two orthopedic surgeons specializing in foot and ankle injuries. This peer review process provided additional validation and refinement of the geological categorizations, enhancing the robustness of the findings.

Statistical analysis

Qualitative analyses were employed to elucidate the distribution and characteristics of the osteochondral lesions across the geological categories.

Results

A total of nineteen computed tomography (CT) scan samples were analyzed. The geologists categorized the osteochondral lesions into five main groups, each exhibiting distinctive morphological features indicative of different geological processes. Several examples demonstrated characteristics that could fit into multiple categories, which necessitates a nuanced understanding of the sequential occurrence of geological processes. Here, we discuss each category, along with the clinical analogies.

Group 1: Brittle deformation

Brittle deformation is a type of deformation that occurs in solid materials, including rocks, when they break or fracture under stress without significant ductile deformation. Unlike ductile deformation, during which materials deform in a viscous manner without breaking of atomic bonds on a macroscopic scale, brittle deformation involves the development of fractures or faults, which are planar discontinuities along which atomic bonds have been broken on a macroscopic scale. This type of deformation is common in rocks at low temperatures and subjected to high deviatoric stresses, and is typically associated with deformation at shallow depths (< 10 km) near the Earth's surface where earthquakes occur.[2] There are generally two groups of brittle deformation structures, faults and fractures.[13] Faults are planar discontinuities along which displacement has occurred (Figure 3.1a-c). Fractures are discontinuities along which no or negligible displacement has occurred (Figure 3.1d). There are three main types of faults in geological settings: (1) normal faults, which often have a dip angle of ~60 degrees and which are characterized by a hanging wall (material above the fault plane) that has moved downward along the fault plane with respect to the footwall (material below the fault plane) (Figure 3.1a); (2) thrust faults, which often have a dip angle of ~30 degrees and which are characterized by a hanging wall that has moved upward along the fault plane with respect to the footwall (Figure 3.1b); strike-slip faults, which often have a (sub)vertical dip angle and which are characterized by horizontal motion of material on either side of the fault in opposite directions (Figure 3.1c).

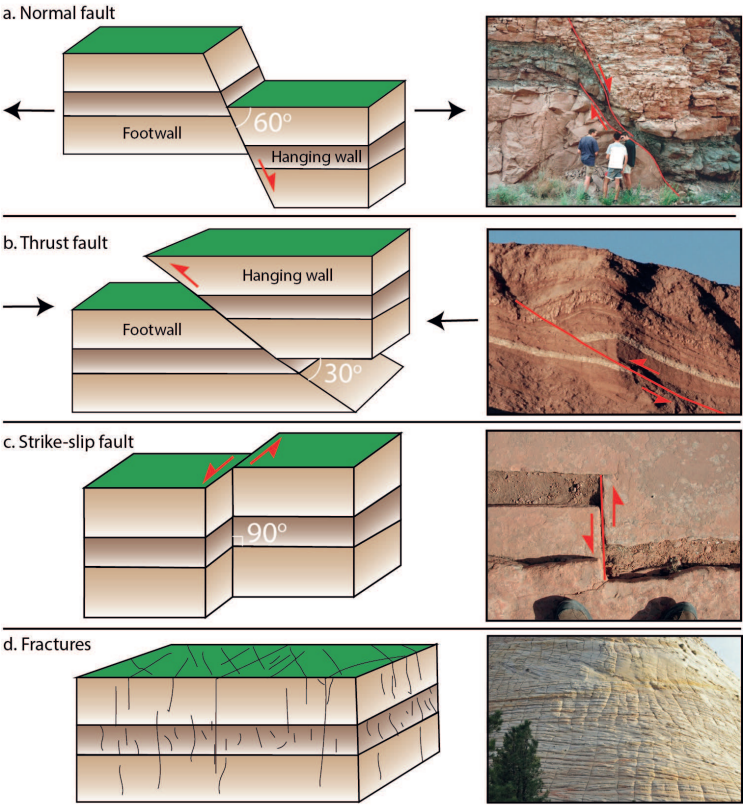
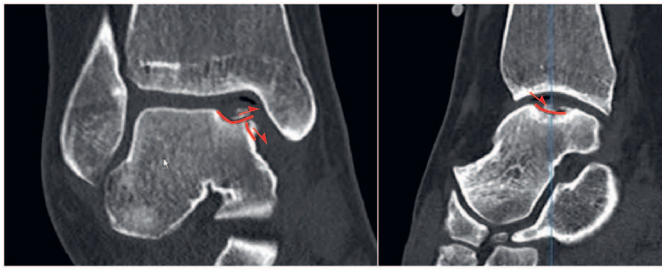


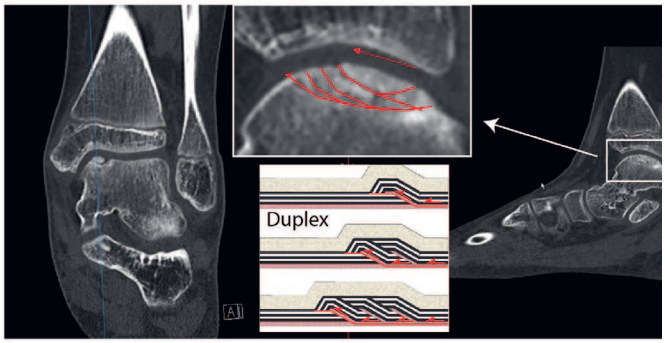
Figure 3.1: Brittle structures in geology. (a) a normal fault is characterized by a 'hanging wall' that has moved downward along a fault plane with respect to the footwall, **(b)** a thrust fault is characterized by a hanging wall that has moved upwards along a fault plane with respect to the footwall, **(c)** a strike-slip fault is characterized by a (sub-)vertical faultplane along which horizontal motion of material occurred in opposite directions on either side of the fault plane, **(d)** fractures in rock layers without or with neglible displacement along fracture planes. Modified after Fossen.[13]

Fault

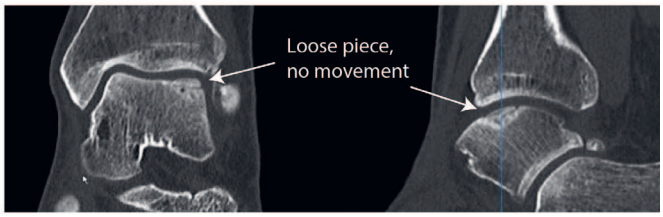
Examples exhibiting sharp or irregular surfaces with material displacement were categorized into normal faults (Figure 3.2a) or thrust faults (Figure 3.2b). In the 'normal' fault example (Figure 3.2a) there appears to be a displacement of a bone fragment along a sharp surface. The displacement has led to a depression in the underlying bone, implying that the fragment has moved downwards along a relatively sharp contact. From an orthopedic perspective, the presence of a small fragment as observed in Figure 3.2a may have been due to the development of a (potentially) bilateral osteochondral fragmentous lesion, that can have dissolved in the majority over time. The process of dissolution may have been accelerated by a traumatic event which could have induced osteolysis.



a. Normal fault



b. Thrust fault with 'Duplex'-structure



c. Fracture

Figure 3.2: Examples of brittle structures/osteochondral lesions in the talus. (a) normal displacement of material, **(b)** thrust displacement of material with internal smaller faults, **(c)** fracture without displacement of material.

The thrust fault example (Figure 3.2b) shows structure that is observed at the front of the fault zone. An interpretation has been drawn (middle of the image). It appears that there are numerous small faults within the damaged zone, with the damage zone perhaps extending all the way through to the back. As the scan is examined, the fragmented piece remains somewhat attached to the main bone at the back the whole time, but there is a dent in the back-end of the bone that implies movement might have occurred throughout the bone. Currently, the fault is only disconnected at the front. This could imply that there was some distributed or ductile deformation at the back due to oblique impact with more pressure from behind than in front, causing the fragment at the back of the

ankle to be completely pressed onto the underlying bone and allowing space for material to be transported forward. The structure depicted is referred to as a "duplex"-structure,[24] allowing different flakes/fragments ('nappes') of material to slide over each other. In some locations, these fragments appear completely detached from one another, for instance, in the initial frame of the video, where it seems as though there are two separate pieces, one large on top and a smaller one just below.

Fracture

Lesions characterized by sharp or irregular surfaces without material displacement were classified as fractures (Figure 3.2c). The fracture example (Figure 3.2c) shows a weakness in the bone, but the fragment appears not to have moved with respect to the underlying bone. Below the fragment, some cyst have formed, which could be the result of the fracture that allowed fluids to enter the bone tissue. From an orthopedic perspective, this could be a traumatic osteochondral fracture of the lateral talar dome that could have been formed after an ankle sprain or fracture, in which the osteochondral fragment was slightly detached, but not fully loose.

Clinical lesson(s) learnt

The formation of osteochondral fragments with depression can be compared to the process of brittle deformation (either in the form of fracturing or faulting), and, through the comparative description, one can explain the slow process of formation of cysts around fragments with depression. One could state that the degree of instability of the fragment can cause symptomatology of the osteochondral lesion due an active process being present, better explaining why larger (slowly) moveable fragments can be symptomatic. Symptomatology is important from a clinical relevance point of view as pain sensations during weightbearing is the most common symptom for patients suffering from an osteochondral lesion of the ankle.[8]

Group 2: ductile deformation

Ductile deformation is another type of deformation that occurs in materials, such as rocks or metals, when they are subjected to stress over time.[11] Unlike brittle deformation, where materials break or fracture, ductile deformation involves the gradual and permanent change in shape of the material without the breaking of atomic bonds on a macroscopic scale. In ductile deformation,

the material undergoes permanent deformation without rupturing or breaking apart. Permanent deformation, also known as plastic deformation, is referred to when something irreversibly deforms or changes shape due to higher stresses. For instance, if a piece of paper is torn in half, it will never return to its original state; some degree of deformation will always be evident, even when it is taped back together. Elastic deformation, on the other hand, occurs when a material temporarily deforms due to higher stresses but subsequently returns to its original state. For example, when a beach ball is forcefully pressed, it becomes flattened, but upon releasing the pressure, the ball regains its round shape. Excessive pressure, however, causes the ball to burst, resulting in plastic deformation. In rocks, ductile deformation typically occurs under high temperatures and pressures, such as those found deep within the Earth's crust. It results in features like folding, stretching, and shearing (Figure 3.3), where the rock layers change shape but remain intact.[13] In metals, ductile deformation is what allows them to be shaped through processes like forging, rolling, or extrusion without breaking.

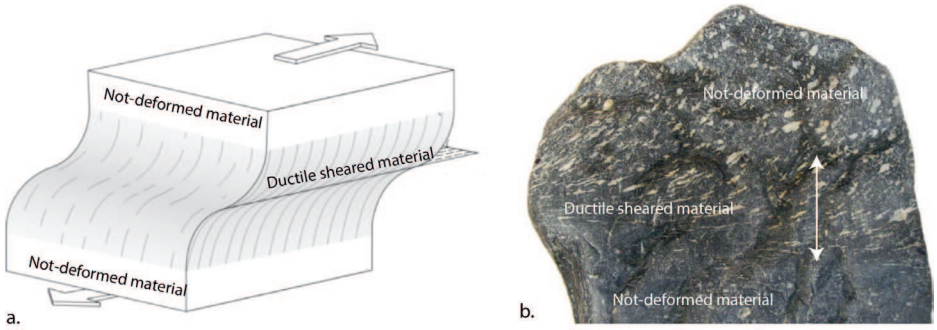


Figure 3.3: Ductile structures in geology. (a) Schematic representation of a zone with ductile deformation, **(b)** example of ductile sheared material in a rock. Modified after Fossen.[13]

Lesions displaying broader zones of material deformation without sharp edges were categorized as ductile shear zones (Figure 3.4). In those lesions, there is no clear contact along which movement as occurred, nor were there cavities that weakened the bone. It is possible that in this example a fracture or fault happened before, which welded together again. If that was the case, the interface that accommodated all the stresses, could be referred to as a 'damage zone' (Figure 3.5).

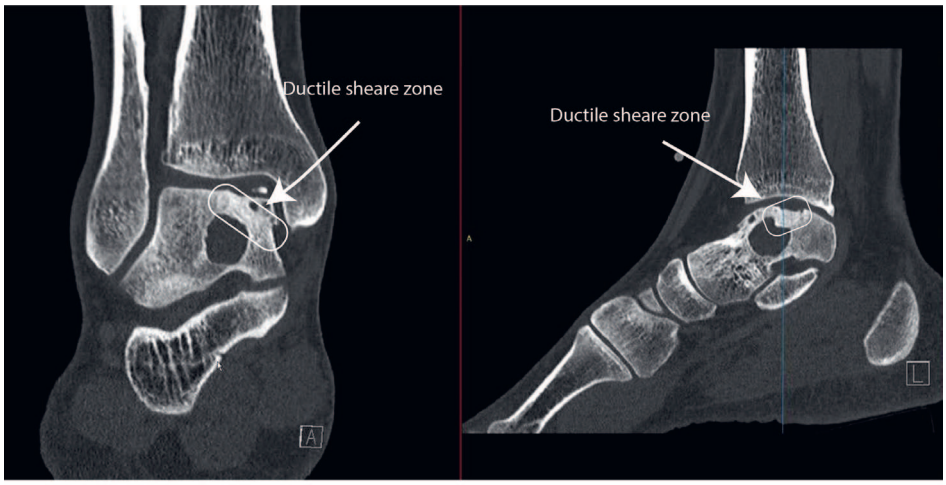


Figure 3.4: Example of ductile structures/osteochondral lesions in the talus.

Clinical lesson(s) learnt

When assessing the category ductile deformation from a clinical perspective, we can refer to the example in Figure 3.4 that has been described above. However, it must be admitted that when carefully considering ductile deformation, this geological perspective on this morphological category is not something that we fully recognize in osteochondral lesions of the ankle that we see on daily basis. It may rather be more consistent with a phenomenon known as chondrolysis (rare but relatively acute cartilage necrosis or degradation) during which the cartilage layer has been subjected to stress over time and then can form a shearing or folding pattern in which the cartilage can be separated from the subchondral bone.

Group 3: damage zone/cratering

Lesions without clear fracture planes are characterized by a broad zone of deformation (fractures, faults, cysts). Such a zone does not coincide precisely with the plane of the fracture itself (Figure 3.5) but extends slightly into the bone. In geology, this zone is called the damage zone and is often characterized by a heavily deformed core (the fault core, Figure 3.5 a, b) surrounded by a damage zone that still hosts large pieces of host rock, but which can be fractured and sheared to various degrees (Figure 3.5b). A damage zone can also occur when material has suffered from an impact (Figure 3.5c), for example a meteorite impact (Figure 3.5d). In such a case, the material that was directly in contact with the body that impacted, will be broken up and might, over time, weld together again

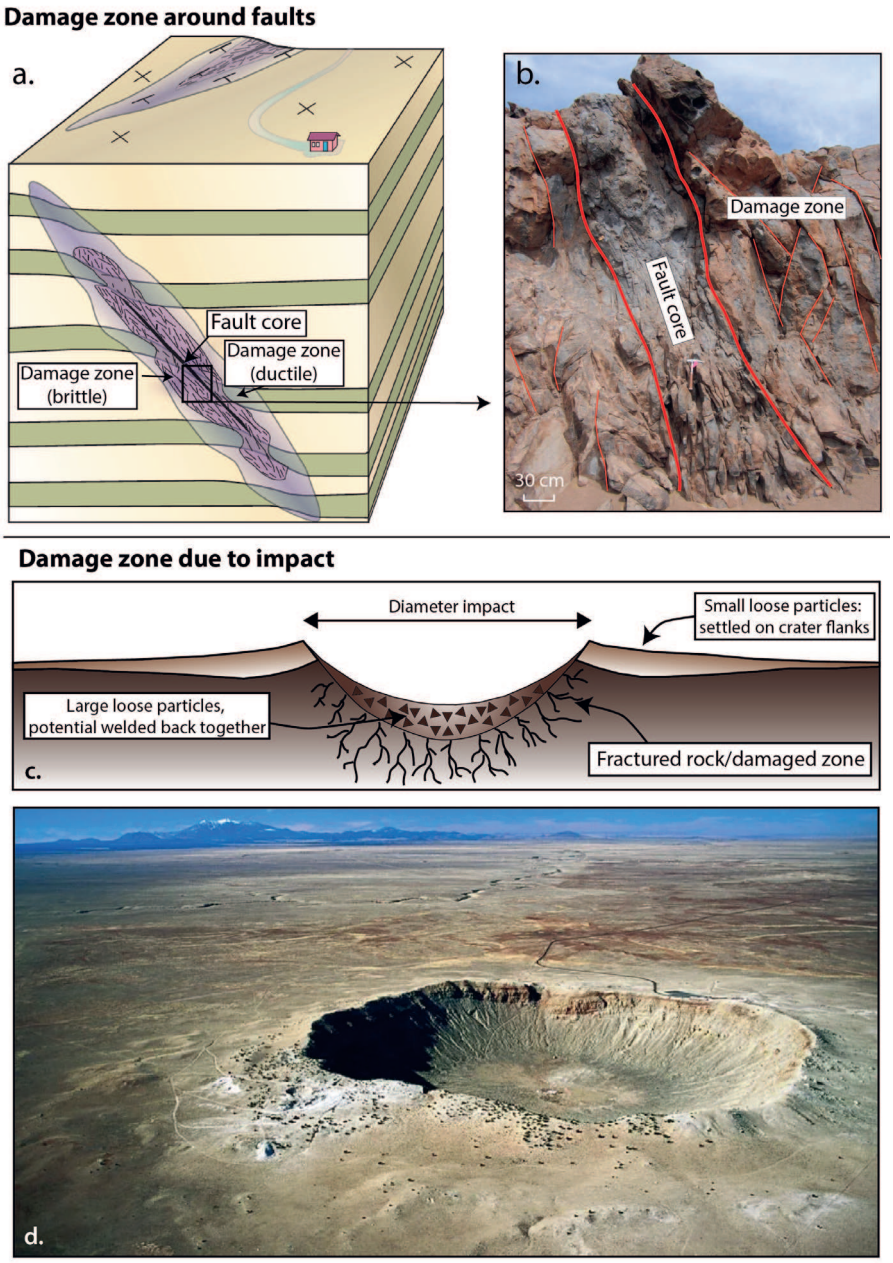


Figure 3.5: (a) Schematic representation of the damagezone of a geological structure (after Fossen).[13] **(b)** Example of a fault with a damage zone. The center of the fault (picture from the Chilean Altiplano near Salar de la Isla is completely damaged, but within a certain distance the rock is also affected by deformation, although not as intense as the core of the fault (picture from https://www.geological-digressions.com/geofluids-the-permeability-of-faults/). **(c)** When material is locally impacted by a body, for example a meteorite, the host rock will develop a crater which is surrounded by broken up material that might have been welded together again through the precipitation of minerals. Below this zone, the host rock maybe be fractured and weakened. **(d)** An example is the Barringer Meteor crater in Arizona, USA.

when minerals precipitate. Below the directly impacted material, the host rock will also have suffered from higher stresses, leading to fractures and damage of the host material.

This damage-zone-type of deformation can present a mixture of multiple phenotypic representations (Figure 3.6a). In the talar bone itself, there are no large cavities, only directly beneath the fracture. This suggests that initially, the bone experienced severe stresses, leading to a fracture. The fragment itself appears crushed, and at the discontinuity between the broken fragment and the main bone, the 'damage zone' is created where fluids can enter, causing small cysts through chemical dissolution/weathering. The damage zone might be larger entering the main bone, as evidenced by the whitish material within the bone. What would be of interest to a geologist if this were a rock, is to determine whether the fracture occurs first and then the cyst, or vice versa. Because the cysts here are so small compared to the size of the damage (the breaking off of the bone fragment), it would be more obvious that the cyst is caused by the presence of a significant injury.

Figure 3.6: (a) Example of a damage zone in osteochondral lesions in the talus. A larger zone consisting of smaller bone fractures with a lighter-coloured rim in the 'healthy' bone tissue. **(b)** Example of a lesion with a circular depression in the talar bone. Very small cysts close to the damagezone, light-coloured rim, and loose fragments are observed.

The crater-type example (Figure 3.6b) shows a defined domain consisting of loose fractures with small black spots (possibly recognizable as cysts) that is identified as a 'damage zone'. It appears that an impact on this ankle resulted in the shattering of a section of the bone. The potential cysts are hypothesized to have formed post-impact, as they are relatively small compared to the total surface area of the deformed domain and are located only on the surface and not as deep into the bone as seen in Figures 3.4 and 3.8. If explained geologically, it is suggested that an initial impact damaged and possibly broke off pieces of an otherwise robust-looking main bone at the edges, creating irregularities on the surface. Subsequently, fluids could have infiltrated these irregularities, aiding the dissolution of the bone. Thus, it is hypothesized that mechanical weathering occurred first, followed by chemical weathering.

Clinical lesson(s) learnt

The clinical lesson that we can take to work from describing this group of osteochondral lesions from the geologist's perspective is that this group is relatively undefinable, residual group in which a mixture of deformation processes take place from the geological perspective. Translating this to a clinically relevant identifiable morphological osteochondral group, we could state that crater-type lesions (Figure 3.6b) can resemble a lesion that has been treated with surgery (for example bone marrow stimulation) before as such forming a damage zone (crater zone) which can explain the rough irregularities visible at the level of the subchondral bone.

Group 4: dissolution

Dissolution is a phenomenon that takes place when water interacts with rocks. Culshaw and Cooper[6] defined dissolution as follows; "*The process by which soluble rocks such as limestone (predominantly calcium carbonate), chalk (also calcium carbonate), dolomite (magnesium calcium carbonate), gypsum (hydrated calcium sulfate), and halite/"rock-salt" (sodium chloride) are dissolved by the passage of water or weakly acidic water either over the rock surfaces or through fractures and pores in the rock.*" There are generally two types of dissolution phenomena, chemical dissolution and pressure solution. In chemical dissolution, acidic fluids will react with calcareous rocks under normal pressures and temperatures (Figure 3.7a). Calcareous rocks consist of $CaCO_3$ that will react with CO_2 and H_2O, the acidic fluid. The most important equation for this process is: $CaCO_3 + CO_2. + H_2O$

→ $Ca(HCO_3)_2$ This reaction may lead to very large caves and caves systems in the subsurfacethat have the potential to collapse, creating sink holes (Figure 3.7a).

For dissolution of material under higher pressures, the calcareous material will dissolve and then either precipitate on the sides of the dissolved grain that are not under pressure, or the dissolved minerals will remain diffused in the fluid that fills the pores in between the solid grains (Figure 3.7b).

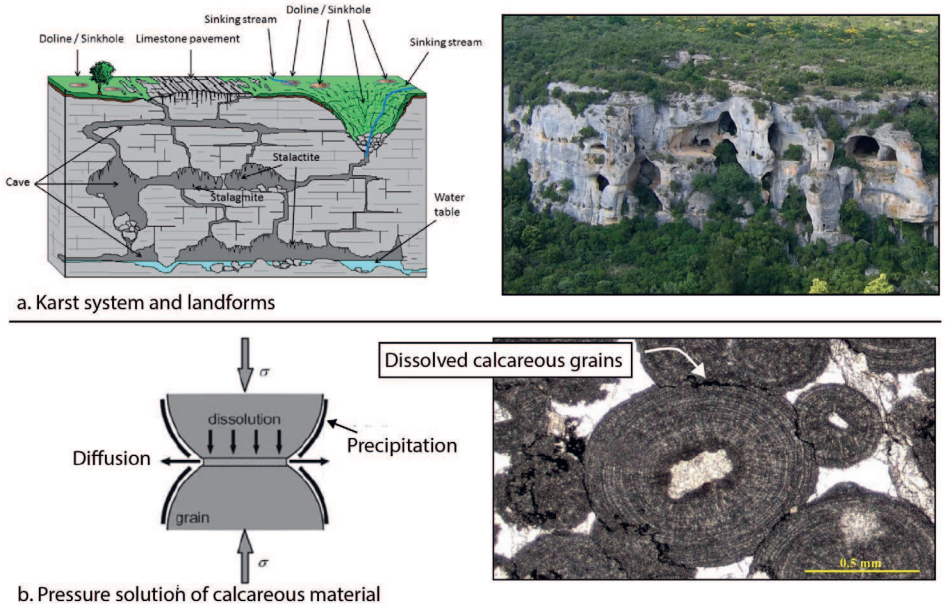


Figure 3.7: Karst and dissolution of carbonaceous material in rocks. (a.1) Schematic representation of karst-systems in the subsurface leading to hollows in the subsurface and sinkholes in the surface (courtesy of the Geological Survey of Ireland, Government of Ireland). **(a.2)** Natural example of a karst system (Minerve Hérault, France) (source: Hugo Soria GNU Free Documentation License Version 1.2). **(b.1)** Schematic representation of pressure solution on micro-scale between individual calcareous grains. On the plane on which pressure is exerted, the material will dissolve and move through diffusion after which it can precipitate again in areas with no pressure.[36] **(b.2)** Example of dissolved calcareous grains leading to irregular surfaces (image credit: https://pet.gns.cri.nz/result_list.jsp - N. Mortimor).

Karst or chemical dissolution was defined as lesions featuring cavities or voids, potentially filled with fluids, and exhibiting organic shapes were classified as karst formations (e.g., Figure 3.8b and 3.8c).

Lesions with apparent cavities and voids exhibiting organic shapes in various sizes are often observed in ankle injuries (Figure 3.8). When no bone fragment has broken off, no mechanical (brittle or ductile) deformation has occurred (Figure 3.8 a, b, c). Instead, the predominant process appears to be chemical weathering

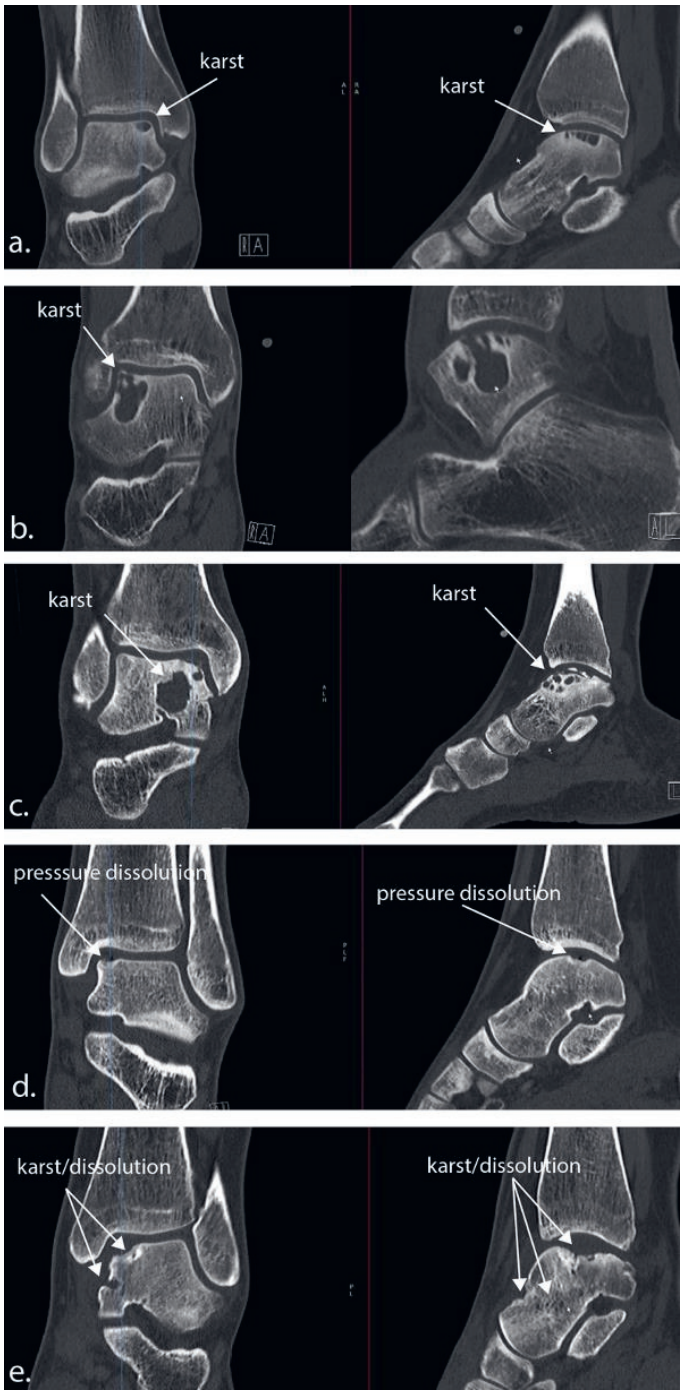


Figure 3.8: Examples of karst osteochondral lesions in the talus. (a), (b), (c) Examples showing hollow cavities with different sizes and shapes in the bone, **(d)** and **(e)** examples of lesions with depressions in the bone either a result of pressure solution (d) or a caved-in karst system (e).

or dissolution. In some cases (Figure 3.8 d, e), the cavities (cysts) do not occur as deep within the bone as in other examples, they remain rather shallow. This could represent a form of 'pressure solution' (or dissolution due to pressure.[15] In geological terms, this means the following: there is direct contact between different grains or minerals, but spaces (pores) exist between these grains and minerals, within which water or other fluids are present. When these contacting minerals are subjected to relatively high pressure/stress, material at the contact points can dissolve in the surrounding water through 'diffusive mass transfer' (diffusion). This primarily occurs when rock is under compaction, indicating increasing pressure on the system, such as when sediments are continuously deposited in a basin.[15] The sediments at the bottom will experience increasing pressure, and diffusion of material can eventually take place.

With chemical weathering, it is possible to maintain the original shape of the bone (Figure 3.8 a, b), while the bone is significantly affected by the chemical weathering. The precise original geometry of the ankle's surface, which should be smooth, is unclear; it is unknown whether it should be straight or exhibit a curvature. For instance, a fragment of bone seems to be detached at the surface forming a distinct arch, which, disregarding the local ruggedness, can be traced from the front to the back. On the right side, at the same location, the bone fragment appears detached from the main bone, with a noticeable step or difference in height. This might indicate an impact that caused the fragment to break off from the main bone, resulting in brittle faulting or fracturing of the bone. However, if this arch reflects the ankle's original geometry, then the fragment may not have moved significantly and could have detached due to the dissolution of the underlying material, potentially from a cyst. It is possible that chemical weathering initially weakened the bone from below, leaving a thin, fragile layer still attached to the main bone, which subsequently broke off due to an impact. The presence of a cyst suggests ongoing chemical weathering of the bone, weakening its structure before an impact caused the brittle fracture.

In some cases (Figure 3.8c), large cavities have developed with organic shapes, while the surface of the bone keeps its original shape. Those cavities are found interconnected by smaller channels. No signs of brittle or ductile deformation are observed. The accompanying deformation process appears to be dominated by a chemical reaction that dissolves the bone, known as chemical weathering. Were this to be rock, it would be referred to as chemical weathering, a process where materials are decomposed through chemical reactions, often due to

the presence of fluids (water) containing chemical elements in contact with the stone.[5] For instance, acidic fluids can dissolve calcareous rocks. When this occurs underground, karst systems may form, which may consist of cavities and networks of channels created by the dissolution of rock through chemical weathering. In example 8, the bone surrounding these cavities appears weakened. For example, small black spots surrounded by very light material are visible, which is an indication for a cyst, which can be a sign of weakened. These small black spots are presumed to be cysts, indicating that the bone has dissolved, and the white material, severely weakened, is interspersed among the black spots and is considered 'weak' relative to the surrounding tissue. Despite the inherent strength of the material itself, its overall integrity is compromised due to the surrounding cysts. Several types of chemical weathering are described below:

1. Dissolution: The rock (or bone) dissolves through a reaction with chemical components in fluids. If the fluid later disappears, the dissolved material precipitates again. This process is reversible; an example is salt dissolving in water and reappearing when the water evaporates.
2. Hydrolysis: The addition of water weakens the chemical bonds of a mineral, potentially breaking them and leading to the formation of new minerals. A well-known example in geology is the weathering of feldspar into clay minerals.[25] This reaction is irreversible.
3. Hydration: During hydration, water molecules are actively incorporated into the mineral structure, binding to the crystal. This generally also weakens the mineral.[14]
4. Oxidation: In oxidation, free oxygen molecules integrate into the crystal structure. This oxidation often reacts with iron-containing minerals in the rock, for example pyrite,[4] giving the stones a rust-brown/red/orange hue.

The second group within dissolution is pressure solution: Areas where material dissolution occurred due to high compressive stresses, resulting in irregular surface features, were categorized as pressure solution zones (Figure 3.8 d, e). Lesions without any loose material can have a significant amount of weakened bone, light coloured with black spots, which is found beneath the crater (cysts). This weakening is caused by the presence of cysts, which can lead to the bone deforming plastically (irreversibly) when subjected to high stresses (pressure solution). Alternatively, brittle deformation may occur initially in the form of small fractures or cracks, weakening the ankle and facilitating the movement of fluids, resulting in the gradual dissolution of the bone (chemical weathering).

Clinical lesson(s) learnt

A current challenge in clinical practice is the differentiation between an ongoing active or passive process causing the damage to the cartilage and mainly the underlying subchondral bone. Does acidity play a role particularly for the active processes? Are pressure processes potentially passively or indirectly linked to intra-articular synovial fluid pressures? These are questions that need to be answered in future studies. Active processes may involve ongoing acid-mediated dissolution processes which can impact the quality of the calcium due to active secretion of acid by the osteoclasts. Consequently, this active process may need a relatively fast medical intervention to prevent further bone degradation – potentially in the form of reversing acidity in some manner. In contrast, passive processes might represent a historical event with no current (clinical) activity, potentially requiring a different, more conservative (wait and see) management approach. Recognizing the fundamental differences in morphology between chemical and erosive dissolution, along with an awareness of the role of water pressure and chemical processes, is crucial for giving us leads towards improving diagnostic accuracy and more tailored (preventive) therapeutic approaches.

Group 5: abrasion

As defined by Fairbridge,[12] abrasion is "*the physical process of rubbing, scouring, or scraping whereby particles of rock (usually microscopic) are eroded away by friction*" (Figure 3.9). In lesions where bone fragments break off, they might move around the ankle. This moving around of bone fragments may lead to scraping or scratching of loose bone material on the underlying talus. It may also lead to polishing of the surface of the talus. Lesions exhibiting surface scratches, abrasions, or polishing indicative of mechanical processes were categorized as abrasions (Figure 3.10). Here, a main bone that appears completely intact without internal weakening due to cysts or fractures is exhibited by this ankle fracture. A large piece has been broken off, with small fragments (resembling gravel) seen hanging off the front of the foot. No damage zone developed in the main bone of this fracture. A very acute, hard impact appears to have caused a piece of bone to be knocked off through mechanical (brittle) deformation. The broken piece of bone has subsequently been displaced. The surface of the main bone is rough, but no cysts are visible, suggesting that there likely hasn't been enough time (yet) for chemical weathering (dissolution) of the bone to occur.

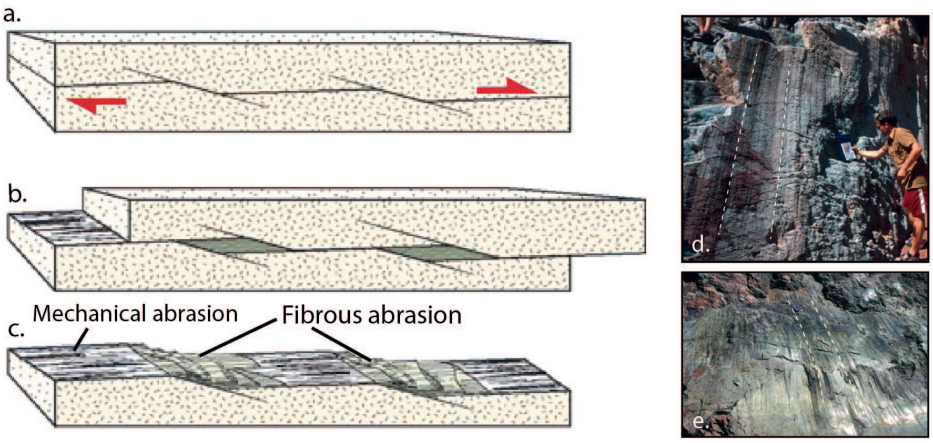


Figure 3.9: Examples of abrasion in geology. (a), (b) and **(c)** Schematic representation of mechanical abrasion **(d)** which creates lineations when materials with different strengths are put under stress, leading to scratches and lineations on the stronger material and fracturing and crumbling of the weaker material, and fibrous abrasion **(e)** during which lineations develop when new minerals precipitate. Modified after Fossen.[13]

Clinical lesson(s) learnt

The clinical lesson that we can take to work from describing this group of osteochondral lesions from the geologist's perspective is that the process of abrasion is most probably not a relatively long-existing process during which damage can be developed due to either an applied force (Figure 3.10b) in which the analogy is that an acute osteochondral fracture of the ankle resembles an acute fracture in a stone due to an applied force. Subsequent longer-existing mechanical processes degrade the cartilage and the underlying subchondral bone through abrasion. Non-cartilaginous materials can scrape the cartilage until a bare area develops in which the bone may get exposed. These materials can be osteophytes on the distal tibial side, however, loose fragments, longer-existing loose bodies as well as focal implants (such as metal implants) are also among the examples causing abrasion of the cartilage. A specific example that has been described is the so-called tram track lesion in the ankle joint, which is a narrow longitudinal articular cartilage defect due to the mechanical impingement of one or multiple large osteophyte(s) projecting form the anterior distal tibia.[18, 32] Another example is the abrasion (wear) on the distal tibia due to a proudly placed focal medial talar implant (Figure 3.10b).

Figure 3.10: (a) Example of abrasion in which a piece of bone that has broken off, has moved around the bone. **(b)** An example of abrasion of the distal tibia (medial malleolus) due to a proudly placed metal implant.

Complex lesions

There are lesions that show characteristics of multiple deformation categories. They have for example considerable cyst formation beneath the broken piece (Figure 3.11). The geometry of the 'fault planes,' the discontinuity between the broken piece and the main bone, seems quite symmetrical with almost vertical edges on either side forming a kind of depression) in which the piece rests. This is observed in both the frontal and lateral views. Here, it appears as if the broken piece has been somewhat pressed into the main bone. It is possible that chemical weathering occurred first, with material being dissolved in the main bone. If there

is then insufficient support, an impact could cause the piece still attached to the main bone at the sides to break off and slide into the depression. There does not appear to have been much horizontal displacement along the fault, but there has been vertical displacement, because there is a clear offset or a step visible between the main bone and the broken piece. In geological terms, this would be described as a 'sinkhole' or 'caldera collapse', where material is removed underground, forming a cavity. This can occur due to chemical dissolution, but underground flows of water and fluids can also carry material away.

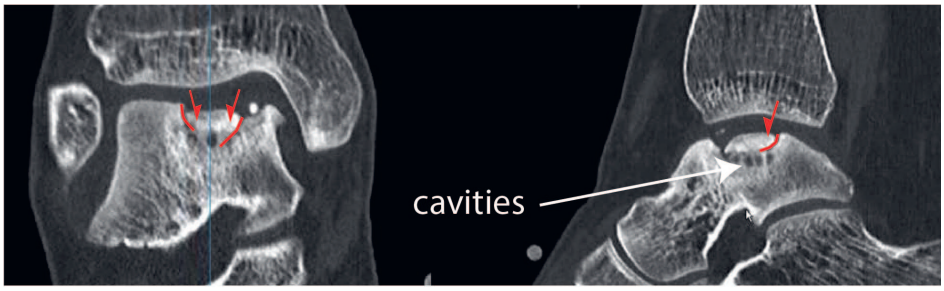


Figure 3.11: Examples of complex osteochondral lesions in the talus in which multiple characteristics are observed. Cavities (karst) in the bone tissue appear caved in along brittle normal faults.

Discussion

This cross-disciplinary qualitative study conducted through a collaboration between the Department of Orthopedic Surgery and Sports Medicine of the Amsterdam UMC and the Department of Earth Sciences of Vrije Universiteit Amsterdam yielded novel terminologies for osteochondral lesions of the talus through geological pattern recognition of different morphologies. Our principal finding is that through the geological lens, five main phenotypic groups of osteochondral lesions of the talus could be identified, being: brittle deformation (category 1), ductile deformation (category 2), dissolution (category 3), damage zone/cratering (category 4), and abrasion (category 5). A logical consequence of aiming to categorize these lesions through pattern recognition in a more uniform approach is improved understanding, and hence, due to the improved understanding an improvement of the quality of care for patients with (osteo)chondral lesions can be achieved.

Etiology

We can state that the observed results from this investigation introduces a novel out-of-the-box understanding of the radiological presentation of osteochondral lesions through the lens of a geologist. Through the categorization of examples based on different morphological characteristics, one can note that we have established hypotheses shedding new light on the complex etiology of these lesions based on geological processes. Both the categorization and identification of various types of deformation, dissolution, damage zones, and abrasion underscores the multifactorial nature of osteochondral lesion formation, implicating both (bio)mechanical and chemical factors playing a role in the etiology, progression and prognosis of these lesions. Specifically, the observation of brittle and ductile deformation patterns highlights the interplay between mechanical forces and tissue integrity. In more detail, one could state that osteochondral lesions of the talus consisting of a chronic fragmentous morphology may be subject to the analogy of geological processes such as faulting and/or fracturing on the basis of the fragment, indeed creating a separate slightly displaced osteochondral unit, potentially from the formation or closure of the epiphyseal plate onwards.[1]

A crucial question remains whether dissolution is an active process, potentially mediated by osteoclasts secreting acid, leading to cyst formation, or a passive process where acid dissolves calcium. If the process is passive, it might suggest an apoptotic mechanism, where cell death due to the contact with synovial fluid leads to localized acid production and subsequent bone dissolution. Additionally, the role of acidic solutions in a solid medium as an erosive force in the formation of large cavities, similar to karst processes in geology, offers a new perspective on the formation of subchondral cysts in osteochondral lesions without the involvement of pressure.

Overall, the presence of dissolution features underscores the role of chemical and acidity-related (rather than pressure-related) processes in lesion development which can, on its turn give us more information on the formation and progression of subchondral cysts in primary osteochondral lesions of the talus, but also in lesions that have been treated with an allograft or autografting procedure.[27, 28, 33] One can state that by applying geological models (cross-pollination) to damages concerning osteochondral lesions or other bone-related injuries in general opens up new insights with regards to forming a hypothesis on what the underlying etiological processes are. Consequently, for future studies on this topic, one could start researching the testing of the in this paper described hypotheses.

Classification systems

Through the insights gained from the present study, one can aim to work towards an evidence-based geologically inspired development of classification systems for osteochondral lesions of the talus, enabling standardized terminology and criteria for lesion characterization, including lesion size, localization as well as morphology (phenotypic description). By categorizing lesions inspired by their geological feature as described in this study, being for example as brittle deformation, ductile deformation, dissolution, damage zones, and abrasion, clinical classification systems can provide a comprehensive framework for describing lesion morphology and pathophysiology. Through the inclusion of geological concepts and methodologies, classification systems are able to capture the nature of talus lesions and accommodate variations in lesion presentation and progression over time as such dynamically describing the lesion's etiology. A classification system that has reached consensus can thus aim to facilitate effective and streamlined communication among healthcare providers treating osteochondral lesions of the talus, enhances consistency in lesion reporting and documentation, and supports comparative research and outcome analysis across different (international) clinical settings.[35]

Future studies

Looking towards the future, further research can focus on diving deeper into researching the underlying pathophysiological mechanisms of osteochondral lesion formation and progression, factors that can also be related to natural history, prognostics around treatment outcomes.[30, 31] Longitudinal prospective studies that contain sufficiently-powered follow-up radiological assessments are necessary to unravel the natural trajectory of these lesions and elucidate the factors influencing their evolution over time.

Limitations and strengths

While this study offers valuable insights into the geological categorization of osteochondral lesions of the talus, several limitations should be acknowledged. Firstly, although a broad spectrum of different phenotypic morphologic presentation of osteochondral lesions of the talus were used, the sample of the CT scan samples may potentially have limited the generalizability of the findings. A larger sample size inclusive of a higher number of CT scans and an (even) broader spectrum of lesion types and severities could provide a more comprehensive understanding

of lesion morphology and formation mechanisms. Additionally, the reliance on CT scans for lesion characterization may overlook subtle morphological features that could be alternatively elucidated through other imaging modalities, such as an MRI scan. Despite these limitations, this study has several strengths contributing to its significance and validity. The cross-disciplinary collaboration between orthopedic and geological disciplines enriches the methodology and enhances the depth of investigation. As mentioned, the detailed examination and categorization of lesions based on geological principles offer novel insights into the complex interplay between orthopedic and geological factors in defining lesion characteristics.

Conclusion

This study presents a morphological description of radiological phenotypic presentations of osteochondral lesions of the talus from a geologist's perspective. Five groups were identified each illustrating distinct characteristics of deformation processes: brittle deformation, ductile deformation, dissolution (Category 3), damage zone/cratering (Category 4), and abrasion (Category 5). Applying and understanding the morphological characteristics and potential etiological mechanisms underlying lesion formation through a geologic lens is essential for elucidating the complex interplay between (bio)mechanical and chemical factors in lesion development, and this cross-pollination with geological models opens up new insights into forming hypotheses on the underlying etiological processes of osteochondral lesions or other bone-related injuries. This can then, ultimately, guide the development of personalized preventive treatment options.

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Chapter 4

Incidence of (osteo)chondral lesions to the ankle in isolated syndesmotic injuries: a systematic review and meta-analysis

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Abstract

Objective: To determine and compare the incidence of (osteo)chondral lesions of the ankle in patients with acute and chronic isolated syndesmotic injuries.

Design: A literature search was conducted in the PubMed (MEDLINE) and EMBASE (Ovid) databases from 2000 to September 2021. Two authors independently screened the search results and risk of bias was assessed using the MINORS (Methodological Index for Non-Randomized Studies) criteria. Studies on acute and chronic isolated syndesmotic injuries with pre-operative or intra-operative imaging were included. The primary outcome was the incidence rate with corresponding 95% confidence intervals (CI) of (osteo)chondral lesions of the ankle in combined and separate groups of acute and chronic syndesmotic injuries. Secondary outcomes were anatomic distribution and mean size of the (osteo) chondral lesions.

Results: Nine articles (402 syndesmotic injuries) were included in the final analysis. Overall (osteo)chondral lesion incidence was 20.7% (95% CI 13.7–29.9%). This rate was 22.0% (95% CI 17.1–27.7) and 24.1% (95% CI 15.6–35.2) for acute and chronic injuries, respectively. 95.4% of the lesions were located on the talar dome and 4.5% of the lesions were located on the distal tibia. (Osteo)chondral lesion size was not reported.

Conclusions: Isolated syndesmotic injuries are (21%) associated with (osteo)-chondral lesions of the ankle. No difference in incidence rate was found between the different syndesmotic injury types and the majority of lesions are located on the talar dome.

PROSPERO registration number: CRD42020176641.

Keywords: Ankle · Osteochondral lesion · Meta-analysis · Isolated syndesmotic injuries · Incidence rate

Introduction

Syndesmotic injuries are usually caused by external rotation and combined hyperdorsiflexion of the ankle.[1,45] During this high-force injury mechanism external rotational forces are being impacted on the distal tibia and talar dome potentially resulting in intra-articular pathologies, such as damage to the osteocartilaginous unit. There is also a growing body of evidence documenting a high incidence of intra-articular injuries following acute ankle fractures. Martijn et al.[19] published a recent meta-analysis having shown that osteochondral lesions in the ankle were frequently seen in patients with acute ankle fractures with a high incidence rate around 45%. Two different studies by D'Hooghe et al.[7] and Rellensmann et al.[26] found cartilage damage of the talar dome in patients with isolated unstable syndesmotic injuries was present in 23% to 48% of cases. Left untreated, cartilage damage to the talus may have severe impact on the quality of life and function, emphasizing the necessity to create awareness among care providers as to the potentially high incidence rate of intra-articular (osteo)chondral lesions ((O)CL) in isolated syndesmotic injuries and acute ankle fractures.[42] From the current literature, it is unclear what the exact incidence rate is of (O)CLs in both acute (< 6 weeks from trauma to diagnosis) and chronic (> 6 weeks from trauma to diagnosis) isolated syndesmotic injuries as well is it unclear whether the incidence rate is higher in the chronic isolated syndesmotic group versus the acute isolated syndesmotic group. Moreover, lesion size and anatomic distribution of potentially present (O)CLs remain unknown. Understanding the incidence of (O)CLs in patients with isolated syndesmotic injuries will aid clinicians in the early recognition and treatment of these intra-articular pathologies and may prevent the progression of lesion size as well as cysts, the deterioration of subchondral bone, and, as such, may improve clinical outcomes. Moreover, the presence of (O)CLs in patients with syndesmotic injuries can justify the necessity for earlier diagnostic measures and the application of adjuvant (minimally invasive) arthroscopy for patients with isolated syndesmotic injuries undergoing a stabilization procedure in order to address concomitant complaints and prevent further deterioration of damage.

It is therefore the primary aim of the present systematic review to determine and compare the incidence of (O)CLs in the ankle in patients with acute and chronic isolated syndesmotic injuries. The secondary aim of this study is to assess the size and the anatomic distribution of the (O)CLs in such injuries. Our primary hypothesis is that (O)CLs frequently occur in all types of isolated syndesmotic injuries irrespective of acuteness of the injury. Our secondary hypothesis is that lesion

size is heterogeneous and that most lesions are located in the anterolateral talar dome which is known to be a more common location for post-traumatic (O)CLs.[38]

Materials and methods

The PRISMA statement (Preferred Reporting Items for Systematic reviews and Meta-Analyses) was used as a guideline for the present study.[21] The protocol for our systematic review and meta-analysis was prospectively registered in the PROSPERO register with registration number CRD42020176641.[6]

Search strategy

PubMed (Medline) and EMBASE databases were used for a systematic search of the literature from 2000 to September 2021. A backward citation chaining strategy was used to identify additional eligible studies. The full literature search is provided in Appendix 4.1.

Eligibility criteria and study selection

Clinical studies investigating the treatment or diagnosis of acute and chronic isolated syndesmotic injury and concomitantly reporting findings of potential presence of (O)CLs of the ankle were included. Isolated syndesmotic injuries were defined as purely ligamentous injuries, as suggested by the ESSKA-AFAS consensus statement by van Dijk et al.[39] Remaining in- and exclusion criteria are described in Table 4.1. Independent screening of the title/abstract and full-text of included articles was carried out by two reviewers (JD and SJ). If the reviewers disagreed, the two reviewers discussed the matter and aimed to come to a decision. However, if the disagreement remained, the judgement of a third investigator (GK) was decisive. Studies were not blinded for author, affiliation or source, and no limitation was put on publication status.

Table 4.1: Inclusion and exclusion criteria

Inclusion criteria	Exclusion criteria
- All clinical studies investigating patients with isolated stable or unstable syndesmotic injuries (acute and/or chronic) - Necessity to mention whether pre-operatively or intra-operatively, a diagnosis of concomitant ankle (osteo)chondral injury is assessed - All ages of the patients - Studies published in English	- < 5 patients included - Patient overlap in different studies - Full-text article unavailable - Level V evidence / review studies - Animal studies - Cadaveric studies - Conference abstracts - Studies published before the year of 2000

Methodological quality assessment

The methodological quality of studies was assessed with the Methodological Index for Non-Randomized Studies (MINORS) tool and was scored by two independent reviewers (JD and SJ).[30] The MINORS tool consists of 8 or 12 items for noncomparative or comparative nonrandomized studies, respectively. Maximum scores are 16 for non-comparative nonrandomized studies and 24 for comparative nonrandomized studies. An item was scored with a “0” when not reported, a “1” when inadequately reported, and a “2” when adequately reported. After independent evaluation, all disagreements were solved through discussion between the two independent reviewers. If the disagreement remained, the judgement of a third investigator (GK) was decisive.

Data extraction

Data of included studies were extracted using Microsoft Excel (version 2020, macOS CATALINA) by one reviewer (JD) and cross-checked by a second author (SJ). Standard study characteristics were retrieved, as well as, the following patient characteristics: number of patients and ankles, sex, age at operation, method of diagnosis (magnetic resonance imaging (MRI), computed tomography (CT), arthroscopy, other), number of (O)CLs, type of cartilage lesion (osteochondral or purely chondral), size of (O)CLs (diameter, surface area or volume), type of syndesmotic injury (acute, chronic) and associated grading system when available (e.g. West Point Grading System[7,18,42]), and reported (in)stability of the syndesmotic injury. Additionally, anatomic distribution of (O)CLs was extracted.

Terminology

Many derivatives and combinations of chondral, cartilage, defect, lesions and injury are currently used in the literature. Therefore, all reported osteochondral and purely cartilaginous lesions were considered an (O)CLs and were referred to as an (osteo)chondral in the results whenever not reported in sufficient detail, unless studies used an osteochondral classification system focusing separately on a subdivision of chondral versus osteochondral damage or studies that specifically qualitatively reported on a subdivision of chondral versus osteochondral damage.[19] When cartilage damage was per-operatively assessed using arthroscopy, a lesion of the cartilage was defined as an (O)CL, because visualization of the subchondral bone is not always possible nor accurate during the arthroscopy. Injuries were categorized into two groups based on the time period between initial trauma and diagnosis; 1) acute isolated syndesmotic up to six weeks after trauma, and 2) chronic injuries diagnosed 6 weeks after the trauma.[9,28,37] If the article in question did not mention the time from the injury to the time of diagnosis, it was chosen not to categorize the injury and it was marked as unknown: the incidence rate of (O)CLs in this subgroup was pooled as part of the overall incidence rate of (O)CLs in all types of isolated syndesmotic injuries, that is, acute and chronic combined (*see statistical and data analysis below*).

Statistical and data analysis

Concerning demographic data, in the case of categorical data, frequencies and percentages were calculated. In the case of continuous data, weighted averages were calculated with the associated ranges of these averages. The primary outcome of the present study is the incidence rate of (O)CLs of the ankle in acute and chronic isolated syndesmotic injuries. Reported (O)CL incidence rates after syndesmotic injury were extracted from the original articles and pooled. If no (O)CL incidence percentage was reported, we calculated the (O)CL incidence by dividing the total number of (O)CLs by the total number of ipsilateral syndesmotic injuries reported in the article in question. Firstly, an overall incidence rate in all isolated syndesmotic injury groups (that is, acute and chronic together) was calculated, and subsequently, a sub-analysis was performed to calculate the incidence rate of (O)CL in the acute isolated syndesmotic group and the chronic syndesmotic group. A log transformation was applied in order to calculate 95% confidence intervals for the incidence rates by means of random-effects model with inverse-variance weighting.[4] Subgroups with < 5 observations (total included number of patients in one sub-group) were excluded due to a potential inclusion

of a bias. Comparisons were made between the different groups in terms of time from injury to diagnosis and tested by use of Q-tests. Heterogeneity was quantified among studies (overall incidence group and separate analyzed subgroups) with the I^2 statistic.[12] We chose an $I^2 < 25\%$ to represent low heterogeneity and a value > 75% to indicate high heterogeneity.[12]

Secondary outcomes were anatomical location distribution of the (O)CLs in the ankle joint and lesion size of the (O)CL. Anatomical location distribution of (O) CLs was described and classified according to the anatomical osseous location (i.e., talus or distal tibial plafond or lateral malleolus). If possible and reported, location was specified to more specified exact locations; e.g., anterior, medial, posterior or lateral, and if possible subdivided into anterolateral, anteromedial, posterolateral or posteromedial, or if possible in the 9-grid scale developed by Raikin et al.[24] In the case of lesion size reporting, lesion size was calculated by extracting individual diameter (antero-posterior, medio-lateral, and depth), surface area or volume of the separate lesion. Secondary outcomes were analyzed in a descriptive manner (numeric presentation and percentage presentation) and no between-group comparisons were made due to heterogeneity of reporting of data. Data analysis was conducted using Microsoft Excel (version 2020, macOS CATALINA)and R version 3.2.3 (R Foundation for Statistical Computing, Vienna, Austria) using the metaphor package.[40]

Results

Search results

The selection of studies is shown in the PRISMA flow diagram (Figure 4.1). The literature search provided 1,213 results. After screening the articles on title and abstract, and full-text screening, nine articles were included.[7,11,13,22,26,27,29,35,46]

Methodological quality

For all cases, there was full agreement between the first two authors on the assessment of methodological quality of the studies. The overall methodological quality of the studies with the separate MINORS scores are to be appreciated in Table 4.2. There was one comparative study, Han et al.,[11] and its MINORS score was 14 out of 24 (Table 4.2).

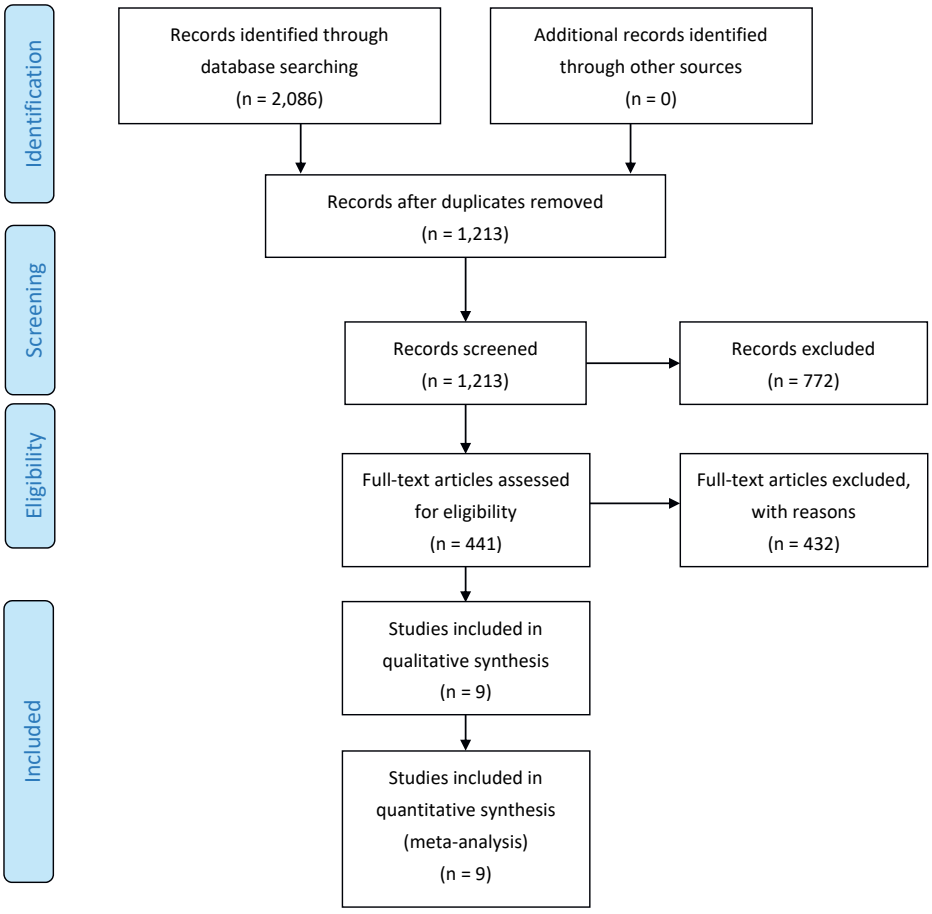

Figure 4.1: Literature selection algorithm – preferred reporting items for systematic reviews and meta-analyses (PRISMA).

Evaluation of characteristics of included studies

Articles included for final analysis totaled 402 syndesmotic injuries. The average age of the included patients was 26.9 (range of reported means, 24.0–33.7) years. 52.4% of the affected ankles were on the right side, while 47.6% was on the left side. Of the reported and extracted data, 94.0% was male and 6.0% was female. Pre-operatively, all patients underwent magnetic resonance imaging (MRI) of their injury. Other study, patient, outcomes characteristics can be appreciated in Table 4.2 and 4.3.

Table 4.2: Study characteristics and patient demographic characteristics

Authors Year of publication, Journal	No. of patients	Study design	% male	Mean age	Pre-operative radiology used	Grading system	Stable / unstable	Author definition of acute / chronic definition	Minors score
D'Hooghe et al.[7] 2018, BJSM	110	Retrospective	100%	24.9	MRI	West-Point IIB: 75, III: 35	All unstable (West-Point IIB and III)	All acute (< 6 weeks from injury to diagnosis)	10/16
Han et al.[11] 2007, FAI	20	Prospective	55%	32.0	MRI	N.R.	N.R.	Unclear definition of chronic syndesmotic injuries	14/24
Kent et al.[13] 2020, KSSTA	116	Retrospective	N.R.	N.R.	MRI	West-Point IIB: 204	All unstable (5.0 mm blader through syndesmosis, all West-Point IIB)	Combination of acute and chronic (separate data available)	7/16
Mollon et al.[22] 2019, OJSM	21	Retrospective	100%	24.0	MRI	N.R.	N.R.	Combination of acute and chronic (no separate data available))	7/16
Rellensmann et al.[26] 2020, KSSTA	18	Retrospective	78%	33.7	MRI	West-Point IIB: 13, III: 5,	All unstable (West-Point IIB and III)	Combination of acute and chronic (no separate data available))	8/16
Roemer et al.[27] 2014, AJSM	53	Prospective	N.R.	N.R.	MRI	N.R.	N.R.	All acute (< 6 weeks from injury to diagnosis)	8/16
Sikka et al.[29] 2012, FAI	36	Retrospective	100%	N.R.	MRI	Own system I: 4, II:5, III: 24, IV: 3	N.R.	All acute (< 48 hours from injury to diagnosis)	10/16
Takao et al.[35] 2005, AJSM	17	Retrospective	N.R.	N.R.	MRI	N.R.	N.R.	All chronic (> 4 months from injury)	9/16
Zamzami et al.[46] 2008, FAS	11	Retrospective	100%	31.5	MRI	N.R.	N.R.	All chronic (> 2 years from injury)	10/16

No., number; MINORS, methodological index for non-randomized studies; NR, not reported; MRI, magnetic resonance imaging.

Table 4.3: (Osteo)chondral assessment

Authors Year of publication, Journal	No of patients	Diagnostic method of (osteo)chondral damage assessment	(Osteo) chondral or osteochondral definition	Classification system used for (osteo)chondral assessment	No of (O)CLs (incidence rate and 95% CI)	Anatomical location reported (Y/N), if yes, where	Size reported (Y/N), if yes how large
D'Hooghe et al.[7] 2018, BJSM	110	Arthroscopy	(Osteo)chondral	N.R.	23 (20.9% 95% CI: 14.3–29.5)	Y: all talar (not further sub-specification on location)	N
Han et al.[11] 2007, FAI	20	Arthroscopy	(Osteo)chondral	N.R.	3 (15.0% 95% CI: 4.9–37.6)	Y: all talar (not further sub-specification on location)	N
Kent et al.[13] 2020, KSSTA	116	Arthroscopy	(Osteo)chondral	N.R.	22 (19.0% 95% CI: 12.8–27.1)	Y: all talar (not further sub-specification on location)	N
Mollon et al.[22] 2019, OJSM	21	MRI	Osteochondral	N.R.	1 (4.8% 95% CI: 0.7–27.1)	N	N
Rellensmann et al.[26] 2020, KSSTA	18	Arthroscopy	(Osteo)chondral	ICRS (8 grade II, 3 grade IV)	11 (61.1% 95% CI: 37.9–80.2)*	Y: talar and tibial (9-grid scheme by Elias et al.[28] and Raikin et al.[19]): 8 talar (1,2,3,1,1 lesions for zone 1, 2, 3, 4 and 6, respectively) and 3 tibial lesions (1 medial, 1 lateral, 1 anterior)	N
Roemer et al.[27] 2014, AJSM	53	MRI	Osteochondral	N.R.	4 (7.5% 95% CI: 2.9–18.4)	Y: all talar (not further sub-specification on location)	N
Sikka et al.[29] 2012, FAI	36	MRI	Chondral	N.R.	9 (25.0% 95% CI: 13.6–41.5)	N	N
Takao et al.[35] 2005, AJSM	17	MRI and arthroscopy	Osteochondral	Pritsch et al.[29] (no separate scores available)	3 (17.6% 95% CI: 5.8–42.7)	N	N
Zamzami et al.[46] 2008, FAS	11	Arthroscopy	(Osteo)chondral	N.R.	3 (27.3% 95% CI: 9.0–58.6)	Y: all talar (not further sub-specification on location)	N

LOE, level of evidence; MQOE, mean quality of evidence; NR, not reported; MRI, magnetic resonance imaging; ICRS, international cartilage repair society score.
* Subgroups not analysed due to < 5 observations.

Overall pooled incidence rate

The overall pooled incidence rate of (osteo)chondral lesions in the ankle joint in all isolated syndesmotic injuries – acute and chronic group – was 20.7% (95% CI 13.7–29.9%) as there were 79 reported lesions in a total of 402 patients (I^2 = 65%)[7,11,13,22,26,27,29,35,46] (Figure 4.2).

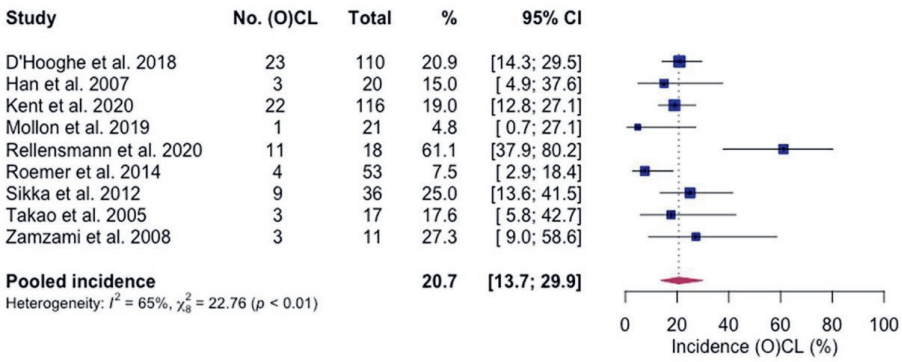

Figure 4.2: Forest plot of overall summarized incidence rate of (O)CLs of the ankle in all types of isolated syndesmotic injuries.

Anatomical location was reported in six studies[7,11,13,26,27,47] (Table 4.3). There were 63 talar lesions (95.4%) and 3 tibial lesions (4.5%). One study[5] reported on a specified sub-localization distribution of the lesions on the distal tibial plafond and the talar dome, and these results can be appreciated in Table 4.3. Lesion size was not reported in any of the studies.

A classification system for cartilage assessment was reported in two studies,[26,35] comprising of the International Cartilage Repair Society score (ICRS) and the Pritsch et al.[23] classification system. Separate data on these lesions were extractable for the ICRS scores. Rellensmann et al.[26] concluded that there were 8 grade II and 3 grade IV lesions.

A subgroup analysis on the distribution of chondral versus pure osteochondral injuries was not feasible due to the underreporting and heterogeneity of this outcome.

Acute group

In the acute isolated syndesmotic group, there were five study groups included.[7,13,26,27,29] Fifty-six (O)CLs in a total of 271 patients were found, having an associated (O)CL incidence rate of 22.0% (95% CI 17.1–27.7%) (I^2 = 78%) (Figure 4.3).

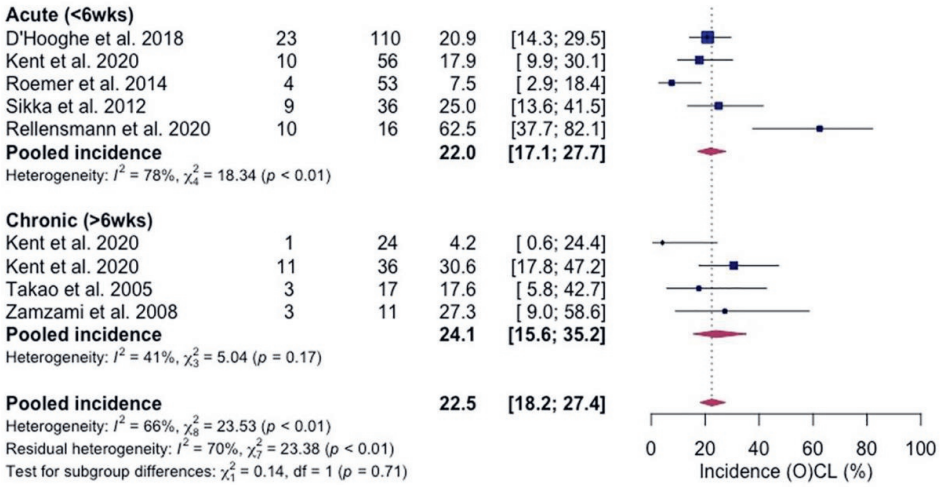

Figure 4.3: Forest plot of the separate incidence rates of (O)CLs of the ankle in acute and chronic isolated syndesmotic injuries.

Four studies reported on anatomical location reporting of the lesions.[7,13,26,27] The majority was located on the talar bone (94%), while a minority was located on the distal tibial bone (6%). Rellensmann et al.[26] used the 9-grid scheme by Elias et al.[8] and Raikin et al.[24] to describe the sub-localization distribution of the lesions on the distal tibial plafond and the talar dome. Seven lesions were found on the talus (1, 2, 2, 1, 1 lesions for zones 1, 2, 3, 4 and 6, respectively) and three on the tibia (1 medial, 1 lateral, 1 anterior).

A subgroup analysis on the distribution of chondral versus pure osteochondral injuries was not feasible due to the underreporting and heterogeneity of this outcome.

Chronic group

In the sub-group three studies and four study groups were included,[13,35,46] totaling 88 patients with 18 (O)CLs (incidence rate of 24.1%; 95% CI 15.6–35.2) (I^2 = 41%) (Figure 4.3). Two studies[13,46] reported the specific location distribution: All lesions were located on the talar dome.

A subgroup analysis on the distribution of chondral versus pure osteochondral injuries was not feasible due to the underreporting and heterogeneity of this outcome.

Subgroup comparisons

(O)CLs were not significantly more common in acute versus chronic isolated syndesmotic injuries (p = 0.71) (Figure 4.3).

Discussion

The present study shows that (O)CLs of the ankle are present in 21% of the patients with isolated syndesmotic injuries. The incidence rates of (O)CLs of the ankle were 22% in the acute group and 24% in the chronic isolated syndesmotic injuries group. These findings are of high clinical importance as it aids clinicians in the early recognition and treatment of these intra-articular pathologies and may prevent the progression of a lesion. Furthermore, the present study raises awareness amongst clinicians to (O)CLs in patients with acute and chronic syndesmotic injuries.

The prevalence of (O)CLs among patient with isolated syndesmotic may be due to the position of the ankle mortise at the time of syndesmotic injury. The most likely mechanism is external rotation movement through the foot and the ankle with the ankle in dorsiflexion and the foot being pronated.[10,45] Another mechanism that may cause a syndesmotic injury is a combination of external rotation and supination.[15] During both injury mechanisms, the axial load in combination with the previously described rotatory component of the injury may cause damage to the (osteo-)cartilaginous unit of the ankle joint. This is the same principle as the mechanism of osteochondral injury in acute lateral ankle sprains or ankle fractures.[3,14,36,43] This evidence is further underscored with a recent article by Tampere et al.[36] comparing the ankle syndesmosis pivot shift to the trauma mechanism of the Anterior Cruciate Ligament.

The incidence rate of 21% found in this study may be an underrepresentation of the actual incidence rate as not all included publications in this meta-analysis used arthroscopy to assess the (osteo)chondral damage. Three studies[22,27,29] included in our analysis used magnetic resonance imaging (MRI) with a combined intra-operative arthroscopic assessment of concomitant (osteo)chondral damage. The intra-operative arthroscopic assessment of (osteo)chondral damage may have a higher sensitivity and specificity rate in comparison to the sole usage of MRI.[3,41] Furthermore, the majority of the studies did not assess the incidence of (O)CLs as their primary outcome, but rather reported these as concomitant injuries during

surgical procedures for isolated syndesmotic injuries. It may therefore be that the pooled incidence of ankle (O)CLs found in the present study underestimates the true incidence of (O)CLs, as exemplified by the high incidence found by Rellensmann et al.[26] having accurately and thoroughly performed the inspection of the total ankle joint with a specific focus on identifying the presence of intra-articular pathologies. In this context, it is not surprising that the incidence rate may be comparable to a recently published systematic review by Martijn et al.[19] on the incidence of (O)CLs in acute ankle fractures which reported[19] an incidence of 45% from a total of 1,707 patients with acute ankle fractures directly after trauma. This is a similar incidence to the present meta-analysis.

It was found that there were no significant differences between the O(CL) incidence rates of the acute isolated syndesmotic (less than six weeks) injury group, and the chronic isolated syndesmotic (more than six weeks) injury group (Figure 4.3). It was hypothesized that chronic isolated syndesmotic injuries would yield a higher incidence of (O)CLs as in the acute isolated syndesmotic injury group. Chronic insufficiency together with concomitant deltoid insufficiency may lead to a talar shift thereby causing a decrease of the tibiotalar contact surface subsequently causing cartilaginous damage to the ankle joint.[2,16,17,20,25,33,44]

Due to the heterogeneity of reported incidence rates, it was not possible to compare incidence rates between stable and unstable isolated syndesmotic injuries. D'Hooghe et al.[7] included solely unstable isolated syndesmotic ankle injuries in male professional football players and found that cartilage injury was significantly more common in West-Point Grade III syndesmotic injuries versus West-Point Grade IIB injuries (40% versus 12%, respectively).[5] Future research should study the relation between higher grades and the severity of cartilage damage in the ankle joint (lesion size, osteochondral nature versus solely cartilaginous nature, and relation to localization). This is in line with the previously published study by Martijn et al.[19] having demonstrated higher incidence rates in rotational type ankle fractures than non-rotational type ankle fractures.

Increased incidence of cartilage damage or osteochondral damage in the ankle in those patients with higher grades of injury or when associated with specific trauma mechanisms may introduce specific profiles for 'high-risk' patients that have an increased chance of a concomitant injury to the (osteo)chondral unit in the ankle. This is a highly clinically relevant topic of discussion being of interest for future research as well as clinical interventions as it may introduce a cost-

effective manner of concomitant (osteo)chondral damage assessment in 'high-risk' profiles with immediate (evidence-based) treatment in the acute setting. Future applications and developments that may be suitable for this include the use of minimally invasive smaller arthroscopy techniques. A 2-mm bendable needle arthroscope has recently been developed, and in a recent study it was concluded that this novel system can safely and effectively be utilized for the visualization and surgical reach of the ankle joint thereby holding the potential to make ankle arthroscopy less invasive and more accessible.[31,32] These novel innovations may be effective in helping to provide both a diagnostic and therapeutic protocol for high-risk patients with syndesmotic injuries to the ankle who could potentially have intra-articular (O)CLs present in the ankle joint.

With regards to the distribution of anatomical location of (O)CLs in the ankle joint, we conclude there was inadequate reporting of the anatomic localization of the lesions among included studies. The present study shows that for the summarized isolated syndesmotic injury group the majority of the lesions were located on the talar bone (i.e., 95%), as opposed to 5% for the distal tibial bone. A more extensive in-depth analysis of anatomical location distribution of the (osteo)chondral damage in the isolated syndesmotic injury group was not reported nor performed in the included studies with the exception of Rellensmann et al.[26] specifically focusing on the distribution of the (osteo)chondral damage among the ankle joint. This study reported on the distribution of the lesions on the distal tibial plafond and the talar dome. The 9-grid scheme by Elias et al.[8] and Raikin et al.[24] was used and the study concluded that the majority of the lesions were located on the anterior talar dome with a higher incidence rate on the anterolateral talar dome. This finding is in contrast to the findings of a recently performed meta-analysis by van Diepen et al.[38] who found that 59% of the osteochondral lesions of the talus were located on the posterior side of the talar dome with the most commonly reported anatomical location being the centromedial zone (31%). As the publication by van Diepen et al.[38] consisted of mostly chronic osteochondral lesions and because of the fact that there is evidence that (antero)lateral lesions are potentially predominantly caused by traumatic events it can be stated that the finding of the anteriorly located (O)CLs in the isolated syndesmotic injury group follows the specific evidence currently available on location distribution. The size of the lesions was not reported in any of the included studies. Further research projects may focus on accurately reporting concomitant (O)CLs in patients with isolated syndesmotic injuries, their distribution and localization, lesion characteristics, and lesion size.

This is the first study to assess the incidence rate of (O)CLs in ankles with acute and chronic isolated syndesmotic injuries. A strength of this study was the strict in- and exclusion criteria and the thorough selection of articles concerning the selection process. Specifically, articles were only included if assessment of intra-articular (O)CLs was performed and specifically reported in the methods section. Another strength of the present study is the usage and application of a random-effects model with an inverse variance weight statistic for pooling the data as this was chosen to be the most appropriate statistical method to summarize the results. This was chosen because the true effect size varied from study to study within the present meta-analysis thereby obviating the need for a random-effect model.[4]

This study is however not without its limitations. Firstly, the level of evidence of the included studies are considered of moderate quality as shown by the MINORS scores and it should be stated that considerable heterogeneity was summarized. No sub-analyses were possible to compare the incidence rates of stable versus unstable isolated syndesmotic injuries, nor was it possible to compare the incidence rates of (O)CLs amongst different West-Point Grades. It was not possible to compare the incidence rates of osteochondral versus purely chondral lesions amongst the different isolated syndesmotic injury groups. Another limitation of the present study is that it was not reported whether the (O)CLs were symptomatic.

Conclusion

This meta-analysis shows (O)CLs of the ankle are associated with isolated syndesmotic injuries as the overall incidence of (O)CLs in the ankle joint was 21%. There was no significant difference in the incidence rate between the acute isolated syndesmotic injuries (22%) and the chronic isolated syndesmotic (24%). These findings are of high clinical importance as it aids clinicians in the early recognition and treatment of these intra-articular pathologies and may prevent the progression of a lesion. Furthermore, the present study raises awareness amongst clinicians to (O)CLs in patients with acute and chronic syndesmotic injuries.

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Appendix 4.1

MEDLINE (OVID)

Database(s): Ovid MEDLINE(R) and Epub Ahead of Print, In-Process & Other Non-Indexed Citations

Search strategy:

#	Searches
1	(syndesmos* or syndesmotic or tibiofibular* or tibio fibular* or high ankle or AITFL or PITFL).ti,ab,kw. and ("Sprains and Strains"/ or Rupture/)
2	((syndesmos* or syndesmotic or tibiofibular* or tibio fibular* or high ankle or AITFL or PITFL) adj3 (injur* or sprain* or instabilit* or unstable or rupture* or disruption* or tear* or torn)).ti,ab,kw.
3	1 or 2
4	letter/ or editorial/ or comment/ or (letter or editorial or comment).ti.
5	3 not 4

EMBASE (OVID)

Database(s): Embase Classic+Embase

Search strategy:

#	Searches
1	(syndesmos* or syndesmotic or tibiofibular* or tibio fibular* or high ankle or AITFL or PITFL).ti,ab,kw. and (exp sprain/ or ankle instability/ or rupture/)
2	((syndesmos* or syndesmotic or tibiofibular* or tibio fibular* or high ankle or AITFL or PITFL) adj3 (injur* or sprain* or instabilit* or unstable or rupture* or disruption* or tear* or torn)).ti,ab,kw.
3	1 or 2
4	limit 3 to conference abstract status
5	3 not 4
6	letter/ or editorial/ or comment/ or exp conference paper/ or (letter or editorial or comment).ti.
7	5 not 6

PART II

Surgical treatment for large, complex, and secondary osteochondral lesions of the ankle

Chapter 5

No superior surgical treatment for secondary osteochondral defects of the talus

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Abstract

Purpose: The purpose of this systematic review was to identify the most effective surgical treatment for talar osteochondral defects after failed primary surgery.

Methods: A literature search was conducted to find studies published from January 1996 till July 2016 using PubMed (MEDLINE), EMBASE, CDSR, DARE, and CENTRAL. Two authors screened the search results separately and conducted quality assessment independently using the Newcastle-Ottawa scale. Weighted success rates were calculated. Studies eligible for pooling were combined.

Results: Over twenty-one studies a total of 299 patients with 301 talar OCDs that failed primary surgery were investigated. Eight studies were retrospective case series, twelve were prospective case series and there was one randomized controlled trial (RCT). Calculated success percentages varied widely and ranged from 17–100%. Because of the low level of evidence and the scarce number of patients, no methodologically proper meta-analysis could be performed. A simplified pooling method resulted in a calculated mean success rate of 90% [CI 82–95%] for the osteochondral autograft transfer procedure, 65% [CI 46–81%] for mosaicplasty, and 55% [CI 40–70%] for the osteochondral allograft transfer procedure. There was no significant difference between classic autologous chondrocyte implantation (success rate of 59% [CI 39–77%]) and matrix-associated chondrocyte implantation (success rate of 73% [CI 56–85%]).

Conclusions: Multiple surgical treatments are used for talar OCDs after primary surgical failure. More invasive methods are administered in comparison to primary treatment. No methodologically proper meta-analysis could be performed because of the low level of evidence and the limited number of patients. It is therefore inappropriate to draw firm conclusions from the collected results. Besides an expected difference in outcome between the autograft transfer procedure and the more extensive procedures of mosaicplasty and the use of an allograft we could not demonstrate clear or significant differences between treatment options. The need for sufficiently powered prospective investigations in a randomized comparative clinical setting remains high. This present systematic review can be used in order to inform patients about expected outcome of the different treatment methods used after failed primary surgery.

Level of evidence: Level IV.

Keywords: Osteochondral defects · Talus · Failed primary surgery · Surgical treatment · Success rate

Introduction

For the treatment of talar osteochondral defects (OCD) a wide variety of treatment strategies have been reported in the literature. These strategies can be divided into a number of treatment groups: conservative treatment, bone marrow stimulation (BMS), retrograde drilling, osteo(chondral) transplantation, cartilage implantation and chondrogenesis-inducing therapies (CIT). In general, the different surgical treatments of talar osteochondral defects have good results but although the great majority of defects improve after surgical treatment, a minority of lesions will fail first-line surgical treatment and therefore remain symptomatic.[30,40,63] This was exemplified by studies conducted by Yoon et al.[62] and Choi et al.,[11] in which 11% of 399 patients and 6.7% out of 120 ankles respectively, required revision surgery. These numbers indicate that secondary surgical treatment for talar OCDs is not uncommon.

Although these patients generally represent a therapeutic challenge to the orthopaedic surgeon, most research in the past decades has focused on the treatment of primary talar OCDs. To a lesser extent, researchers in the orthopaedic field have attempted to identify promising surgical treatment options for non-primary lesions.[62] Systematic reviews aspiring to determine the most effective treatment option for talar OCDs so far include patient populations of both primary and non-primary lesions.[30,40,63] To our knowledge no previously published systematic review has exclusively investigated the clinical effectiveness of different surgical treatment options for talar OCDs that have failed primary surgery. Hence, the aim of the present systematic review is to identify the most effective surgical treatment for talar OCDs after failed primary surgery.

Materials and methods

Search strategy

We prospectively registered our systematic review at the PROSPERO register.[10]

Electronic databases PubMed (MEDLINE), EMBASE, CDSR, DARE, and CENTRAL were screened from January 1996 till July 2016 for potential articles of interest (Appendix 5.1). Since not all titles or abstracts in these databases clearly describe if the OCD surgery was primary or secondary the authors deliberately did not use narrower terms such as “secondary”, “tertiary” or “failed primary” in our search

as this would potentially exclude eligible studies. In addition to this, a backward citation chaining strategy was used by scanning the literature lists of suitable studies.

Eligibility criteria and study selection

All studies that assessed the effectiveness of different surgical treatment strategies for previously failed surgical intervention of talar OCDs were included in the systematic review. The criteria for exclusion was primary OCDs, a study cohort of < 5 patients, aged < 16 (the age around which ephiphyseal fusing take place), concomitant distal tibial lesions and a follow-up of less than six months. When necessary, authors were contacted via email to provide separate data for those patients with non-primary lesions only and/or for patients ≥ 16 years old and/or to exclude concomitant tibial lesions. When no reply was received from an author, contact was attempted once more by a second email. In the cases of further lack of response a third email was sent. Ultimately, if no response was recorded from the corresponding author, then their specific article was excluded. Independent evaluation of the articles were conducted and then discussed by two reviewers (JD and KL). In cases of disagreement between the reviewers, the opinion from an independent third investigator (GK) was found to be decisive. Studies were not blinded for author, affiliation or source and no limitations were put on language and publication status of screened articles.

Quality assessment

To assess the quality of the included studies we used a Newcastle-Ottawa Scale (NOS) modified for talar OCD.[58] This scale assesses the methodological quality of nonrandomized studies (Appendix 5.2). Each included study was graded on methodological quality by two independent reviewers (JD and KL).

Data extraction

The following study and patient characteristics were retrieved: age, gender, number of patients and ankles, symptom duration, location, side, size and stage of the defect, type of surgery, clinical scoring system utilized, history of ankle trauma reported, follow-up duration and the OCD classification staging system reported. Pre-operative and post-operative clinical outcome scores were extracted. Clinical values of the last recorded follow-up were used. The treatment strategy in question

was defined to be successful when a good or excellent result was reported at follow-up in combination with an accepted scoring system such as the AOFAS (American Orthopaedic Foot and Ankle Society) Ankle/Hindfoot scale, the FAOS (Foot and Ankle Outcome Score) or the Hannover Scoring System. For clarification, an ankle was considered to be successfully treated when at the last follow-up there was a post-operative AOFAS score of 80 or above.[27] When the FAOS (Foot and Ankle Outcome Score) was used, a score of also 80 or above was regarded to be a successful treatment.[50] When the original ankle score by Mazur et al.[35] was used we considered a score of 70 or higher to be successful treatment. In one case, a modified Mazur score was used, which had a 100 point scale. In this case a score of 80 or higher was considered successful treatment.[26]

Statistical analysis

Since a formal meta-regression was not methodologically possible for the included studies (i.e. studies were included with highly different methodological study types and small numbers), we decided to present our results per study by means of a forest plot. A simple pooling method was used to combine data from different studies that had similar methodologies. We calculated 95% binomial proportion confidence intervals for the success percentages of each study with the Wilson score interval and included these in the forest plot (CIA, Confidence Interval Analysis for Windows, version 2.2.0).[8] To compare between groups with categorical variables a Fisher exact test was used (SPSS version 23.0, IBM Corp.). All reported p values are two-sided and statistical significance was set at $p < 0.05$.

Results

Search results

The literature search in the selected databases yielded 1,273 articles. After the application of the eligibility criteria to the titles and abstracts, potentially suitable articles were included for full-text review while ineligible articles were deleted. Subsequently, full-text articles were obtained and the eligibility criteria was applied again. After screening and discussion between the first two authors there was overall consensus in most cases except for two where disagreement persisted, these were resolved via discussion with the senior author. In the end, a total of 21 studies were included (Figure 5.1).

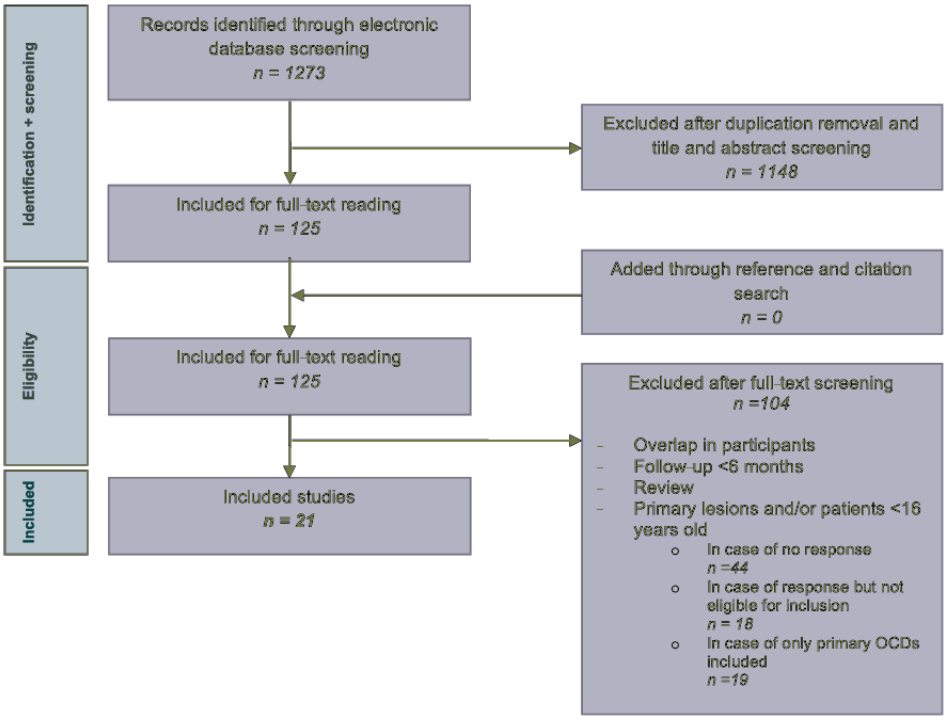

Figure 5.1: Literature selection algorithms – Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA).

Characteristics of included studies (Tables 5.1, 5.2 and 5.3)

A total of 299 patients with 301 talar OCDs who failed primary surgery were included. The average age of the patients was 35 (range 18–57) and the percentage of females and males in our study sample was 35% and 65% respectively. The right ankle was involved in 47% of the cases and the left ankle in 53%. The percentages of medial, lateral, central and combined medial and lateral location involvement were 64%, 19%, 15% and 2% respectively. Size of the lesion or surface diameter was rarely described or impossible to extract and was therefore not incorporated into our review. The most frequently used clinical scoring system and osteochondral damage classification system were the American Orthopaedic Foot and Ankle Society Score (AOFAS) and the Berndt and Harty/Loomer Classification system.[6,27] In total we found that 17 different scoring systems[3,9,13,14,21,25,27,33,38,42,50,56,57,61] and ten different osteochondral damage classification systems[2,6,7,15,23,31,32,36,43,48] were used (Table 5.2 and Table 5.3). It was only possible to extract Berndt and Harty stages for 80 ankles: there were 0 (0%), 9 (11%), 21 (26%), 26 (33%) and 24 (30%) Berndt and Harty/Loomer[6] stage I, II, III, IV and V cases respectively. In 87 of the 299

Table 5.1: Demographics

Number of patients	299
Number of described OCDs	301
Mean age (range)	35 (18–57)
% Right / Left	47 / 53
% Male / Female	65 / 35
% Location (Medial / Lateral / Central / Combined)	65 / 19 / 15 / 2
% With history of trauma	76
Mean follow-up (range)	40 (12–66)

All described calculations are weighted.

Table 5.2: Clinical scoring systems utilized for treatment of talar OCDs

Clinical scoring system	No. of studies
American Orthopaedic Foot and Ankle Society score (AOFAS)	17
Visual Analogue Scale (VAS)	7
Hannover Scoring System	3
Modified ankle grading system of Mazur, Schwartz and Simon	3
Short Form-36	3
Foot and Ankle Outcome Score (FAOS)	2
Patient based satisfaction score (*developed by authors*)	2
Short Form-12	1
Numeric Rating Scale (NRS)	1
Foot Function Index (FFI)	1
Modified Cincinnati rating scale score	1
EQ-5D	1
Ogilvie-Harris score	1
Ankle Activity score (AAS)	1
AAOS Foot and Ankle Module Score	1
Ankle Osteoarthritis Scale (AOS) score	1
Subjective Ankle Hindfoot Score (AHS)	1

Some studies utilized > 1 scoring system.

Table 5.3: Systems utilized for osteochondral staging

Bone/cartilage classification systems	No. of studies
Berndt and Harty Classification System	8
International Cartilage Repair Society (ICRS)	3
Outerbridge classification	2
MOCART	2
Revised classification based on MRI appearances by Hepple et al.	1
Cheng-Ferkel grading system	1
International Cartilage Repair Society II (ICRS II)	1
Anderson's modified MRI based classification system	1
Mintz staging system	1
OsScore	1

Some studies utilized > 1 classification system and others did not utilize or describe a classification system.

patients, a history of ankle trauma was reported. If divided through the number of treated ankles in the articles that report on history of trauma this corresponds with 76.3%. The mean follow-up was 40 months [range 12–66].

Methodological quality

Of the 21 studies included, eight were retrospective case series, twelve were prospective case series and there was one randomized controlled trial (RCT). Full consensus was reached between the reviewers regarding the grading of methodological quality. Seventeen studies described that their research was conducted according to protocol. In fourteen studies the described cohort was truly or somewhat representative to a talar OCD patient sample/population in the other seven studies the group was either selected by an orthopedic surgeon or there was no description of the cohort. In all studies, outcome was assessed through independent blind assessment or record linkage. In nine articles the follow-up was complete or the loss to follow-up was reported to be smaller than 5%. In the other twelve articles the percentage loss to follow-up was either more than 5% or the follow-up rate was not stated.

Treatment strategies

We divided the treatment strategies into the four previously indicated treatment groups: bone marrow stimulation (debridement and/or drilling), osteo(chondral) transplantation (autograft transfer, allograft transfer and mosaicplasty), cartilage implantation (MACI and ACI) and chondrogenesis-inducing techniques (AMIC) (Figure 5.2). Two studies did not correspond to any of these groups and are presented separately at the end of the results section. All calculated success percentages with their respectively confidence intervals are also visually presented in a forest plot (Figure 5.3). The calculated success percentages of the pooled groups are shown in an additional forest plot (Figure 5.4).

Bone marrow stimulation (BMS)

Two studies described the outcome of BMS as a secondary treatment for a total of 25 treated ankles.[47,51] One of these studies (Savva et al.) solely reported the results of repeat arthroscopic treatment.[51] The authors used the Berndt and Harty classification to grade the OCDs but excluded cystic lesions as their treatment type (debridement) had been demonstrated to have poor outcomes.[49] The second study by Reilingh et al. is an RCT investigating the effects of pulsed electromagnetic fields (PEMF) on

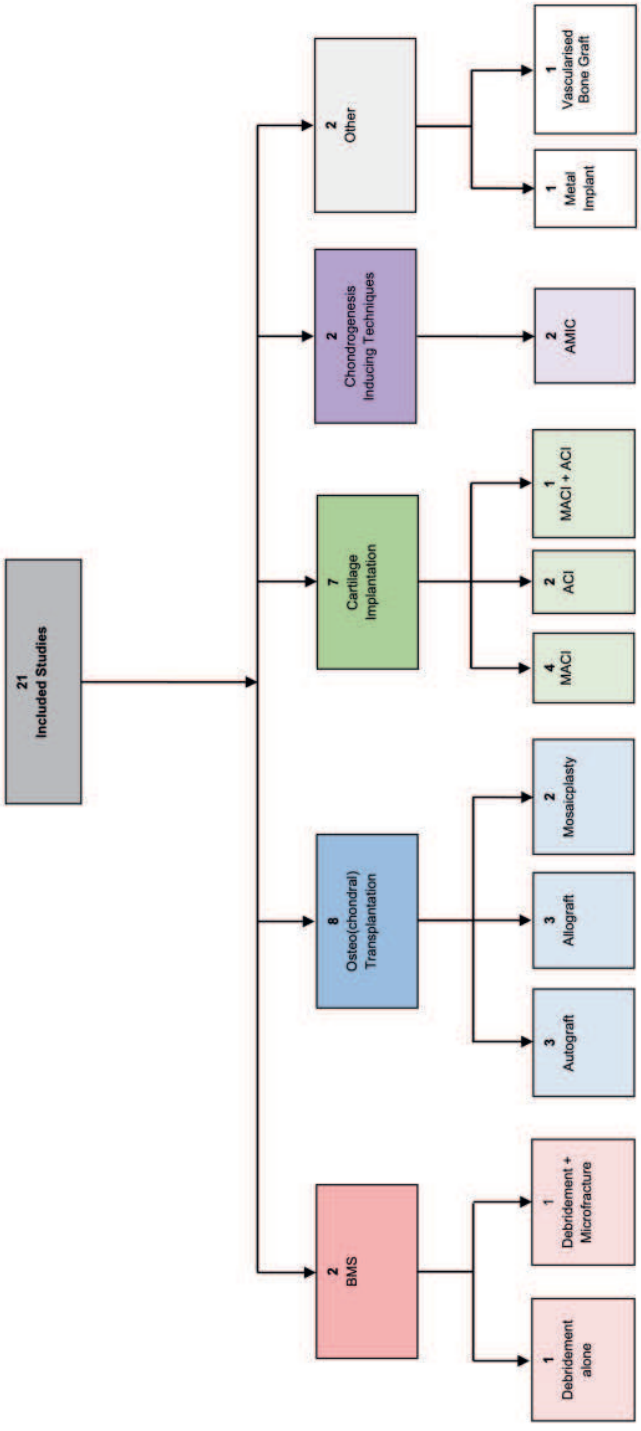

Figure 5.2: Flow chart of study inclusion and different treatment groups. ACI, autologous chondrocyte implantation; AMIC, autologous-matrix induced chondrogenesis; BMS, bone marrow stimulation; MACI, matrix-associated chondrocyte implantation.

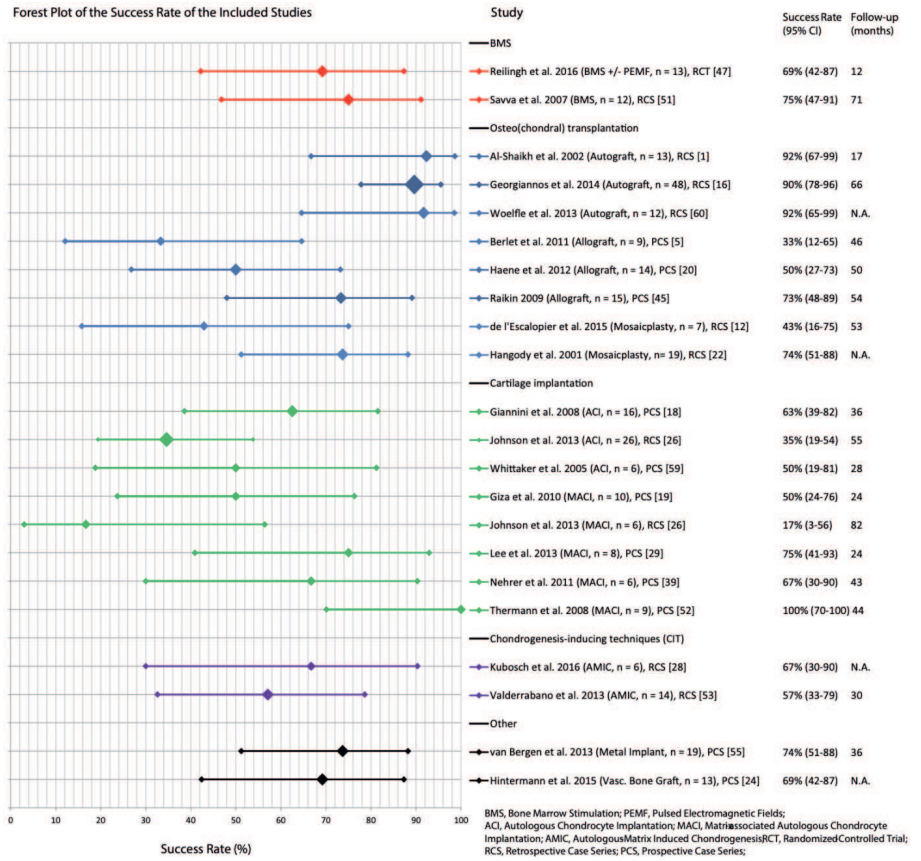

Figure 5.3: Forest plot of all included studies with the success rates per separate study sorted on treatment strategy and alphabetical order accompanied by number of ankles and follow-up duration. The size of the diamond representing the success rate is categorically adjusted for number of ankles included in the publications.

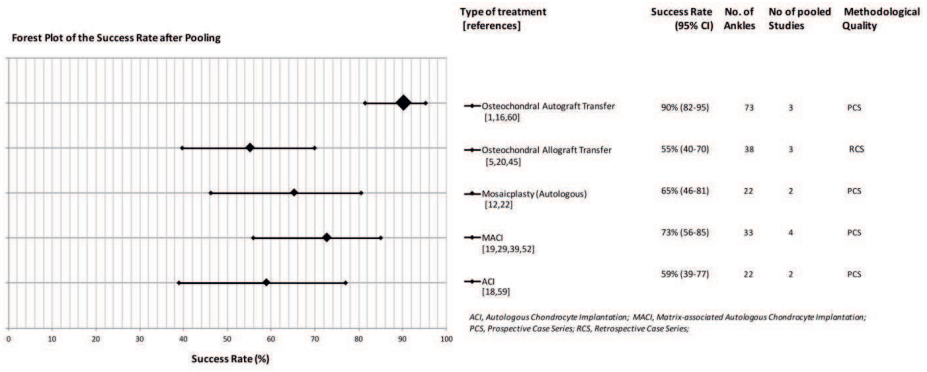

Figure 5.4: Forest plot of the success rates after pooling sorted on treatment strategy accompanied by the number of included studies, the success rate with confidence interval and the total number of ankles per group. The size of the diamond representing the success rate is categorically adjusted for the number of ankles included.

debridement and microfracture.[47] Due to the fact that the authors indicated that there was no significant difference between the randomized treatment groups, we included patients from both groups. In this study, cystic lesions were not excluded. The two studies describe a post-operative AOFAS of 81% and 80%. Success percentages of 75% (debridement alone) and 69% (debridement and microfracture) were calculated with confidence intervals of 47–91% and 42–87%, respectively.

Osteo(chondral) transplantation

Osteochondral transplantation was the most commonly described procedure after failed primary surgery as eight studies were identified describing 135 patients corresponding to 137 treated ankles.[1,5,12,16,20,22,45,60] Five of these studies were retrospective in design and the other three were prospectively described case series. The mean follow-up for these studies was calculated to be four years (range, 17 months – 5.5 years). The included studies described different osteo(chondral) transplantation techniques. Three articles investigated a procedure with a classic osteochondral autograft transfer system (OATS).[1,16,60] Two studies described a (autogenous) mosaicplasty procedure, which is similar to OATS technique but uses multiple grafts creating a mosaic pattern.[12,22] Three other studies described an allograft procedure.[5,20,45] A calculated success rate for all osteochondral transplantation techniques combined is not possible since the study designs were not similar enough for all studies. However, coincidentally all studies describing the allograft procedure were of the same level of evidence (retrospective case series) and all studies describing the autograft procedure and the two describing the mosaicplasty procedure were of the same level of evidence (prospective case series). We therefore were able to use a simplified pooling method to combine data from these groups (Figure 5.4). The autograft group after simple pooling consisted of 73 treated ankles and the allograft group of 38 treated ankles. This gave a calculated mean success rate for the autograft procedure of 90% [CI 82–95%] and a calculated mean success rate of 55% [CI 39.7–69.9%] for the allograft procedure. The success rate of the two studies describing a mosaicplasty procedure which was autogeneous in nature for both studies were 65% [CI 46.2–80.6%]. A Fisher's Exact Test showed no difference between mosaicplasty or the allograft transfer procedure ($p = 0.449$). We did not perform a comparison between these two groups and the aforementioned autograft group since a mosaicplasty or an allograft procedure are often used for larger OCDs and a direct comparison would not be appropriate.

Cartilage implantation

In total seven suitable studies were found that described a form of cartilage implantation after failed primary surgery.[18,19,26,29,39,52,59] The two major groups were the classic autologous chondrocyte implantation (ACI) and the more recently developed matrix-associated chondrocyte implantation (MACI). In total four studies described a MACI procedure[19,29,39,52] and two described an ACI procedure.[18,59] One study described both an ACI and a MACI procedure.[26] The latter was retrospective in design. All other studies in the cartilage implantation group were prospective which allowed a simplified pooling method for both the MACI and ACI group. Eighty-seven ankles were included in the cartilage implantation group as a whole and 39 of those received a MACI procedure and 48 received an ACI procedure. When data the ankles from the studies methodologically suitable for pooling, we found 33 ankles in the MACI group and 22 in the ACI group. The calculated success rates were 72% [CI 56–85%] and 59% [CI 39–77%] for the MACI and ACI groups, respectively. A Fisher's Exact Test showed no significant difference between these two groups ($p = 0.382$).

Chondrogenesis-inducing techniques (CIT)

We identified two studies that investigated the effects of a chondrogenesis-inducing technique.[28,53] Both are retrospective in design and performed an autologous matrix induced chondrogenesis (AMIC) procedure. The study by Kubosch et al. describes a procedure where the proximal tibia was used as a harvest site.[28] The study by Valderrabano et al. describes the iliac crest as a site to obtain the cancellous bone.[53] In total 21 patients with 21 treated ankles were described in the two included studies. Both Kubosch and Valderrabano report high mean post-operative AOFAS scores of 91 and 86 points respectively. The corresponding calculated success rates were 67% [CI 30–90.3%] and 57% [CI 32.6–78.6%] respectively. Both articles also included pre- and postoperative VAS scores for pain, which decreased from 8 and 5.5 to 1.7 and 2 respectively.

Other

Two studies described a specific technique that could not be incorporated into any of the groups. The first article describes a novel metal implant in 20 patients after failed previous treatment.[55] Almost all lesions (18 out of 20) were classified as type V (cystic) lesions.[6] The defect was debrided after which the metal implant was introduced into the defect, and this occurred two years (mean) after

the last failed surgical treatment. The median AOFAS score improved from 62 points pre-operatively to 87 points post-operatively. Of the nineteen patients fourteen were successfully treated according to the AOFAS resulting in a success percentage of 74% [CI 51–88%]. The second study included in this group was a transplantation method using a bone graft.[24] As the bone graft was vascularized the authors decided not to include this study in the previously described osteochondral transplantation group. For the vascularized bone graft, they identified the medial condyle of the femur as an ideal site to harvest since it is sufficiently large and solid and has a contour similar to the talar surface. We obtained data solely on the non-primary lesions, which included thirteen patients. The mean VAS for pain decreased from 5.8 to 1.7. The mean AOFAS hind foot score increased from 66 points pre-operatively to 81 points post-operatively. Nine of the thirteen patients scored good to excellent according to the AOFAS which resulted in a success rate of 69% [CI 42–87%].

Discussion

To the best of our knowledge, this is the first systematic review investigating the effectiveness of treatment options for talar osteochondral defects after failed primary surgical treatment. This is in contrast to previous reviews that focused either solely on primary or both primary and non-primary talar OCDs.[30,40,63] The differences in treatment approach for non-primary treated OCDs often differ and are mainly based on expert opinion since evidence is limited. By means of the present review, we aimed at giving an evidence-based insight into the most effective surgical treatment option.

One of the major differences compared to studies focused solely on primary talar OCDs is that the most described treatment option is different. As for the healing of articular cartilage injuries, O'Driscoll postulated that the treatment options of these defects can be grouped according to four principles. It can be restored, replaced, relieved, or resected.[41] It is generally expected that the first-line surgical treatment should at least incorporate restoration of the cartilage which is normally accomplished by enhancing the intrinsic capacity of this cartilage and subchondral bone to heal itself. In a previous review on primary OCDs, BMS (including retrograde drilling) was the most described treatment method. Not unexpectedly, we found that the most frequently described treatment method for secondary talar OCDs was not BMS but a type of replacement strategy.

In the literature numerous treatment recommendations are given considering failed primary surgery, for example that patients with failures of previous arthroscopic treatment should be treated with osteochondral transplantation.[17] The recommendations are however not based on any concrete data. In this review the success rates of BMS as a revision surgery were found to be 69% and 75% which seems acceptable and lies within the success rate ranges found in primary OCD surgery. It however lies below the confidence interval after pooling of eleven retrospective studies describing primary surgery in 317 ankles which yielded an overall BMS success rate of 82% [CI 78–86%]. In the present review, only 25 ankles treated with BMS were evaluated. The calculated success rate is however still promising and since BMS is a relatively non-invasive and inexpensive treatment it should still be considered for certain patients with small secondary defects or at least be included in the shared decision process with the patient when discussing further treatment options after a previously failed primary operation.[46] It should also be noted that a study by Yoon et al.[62] – which was not included in the present review – described a clinically inferior outcome which corresponded to a calculated success rate of 32%. In this study, the authors compared repeat arthroscopy to an osteochondral autograft procedure with the latter obtaining a success rate of 82%; however, in this patient populations were also ankles included with concomitant tibial lesions (5% in the osteochondral transplantation group and 14% in the repeat arthroscopy group). Since an associated tibial lesion was part of the exclusion criteria and despite of multiple requests, we were unable to obtain the separate data and therefore this article had to be excluded. Another remark that has to be made in light of the study by Yoon et al.[62] is that the authors included talar OCDs with subchondral cysts (up to an incidence of 64% in the repeat arthroscopy group), while in the study by Savva et al.[51] subchondral cysts were deliberately excluded. As stated above, an underlying cyst is associated to inferior outcomes and this could therefore be a plausible reason for the difference observed in the success rates. Thus, when considering performing a BMS procedure after failed previous surgical treatment, the presence of a cyst should be taken into account when choosing the optimal treatment strategy.

Most of the studies described a more invasive osteochondral or cartilage transplantation method as a subsequent procedure for a previously unsuccessfully treated OCD. In the pooled group, the OATS procedure with an autograft showed the highest success rate. Interesting enough, the pooled success rate of this OATS group which combined 73 treated OCDs resulted in a 90% success rate which was

significantly higher than the 77% success rate in our review about primary treated OCDs (p = 0.0296). The observed difference was a little unexpected and might be explained by differences in size of the treated lesions and concomitant damage to the cartilage of the rest of the ankle joint which were not stated in most studies. Differences in outcome expectancy from the patients can also play a role since the used outcome scores (AOFAS) have a subjective component. Finally, it must be noted that the pooled success rates in the review about primary surgery were all retrospective case series which we compared to three prospective case series in this review. It is therefore not possible to say whether the difference is due to a clinical or methodological difference.

A difference was found in the autograft versus the allograft procedure with success rates of 90% and 55% respectively. Differences in these procedures have been previously highlighted in the literature.[4,34,35,44] Since an allograft procedure is typically used for larger defects, it is to be expected that a difference in success percentage was likely to be found. The substantial difference underlines the recommendation that, if possible, an autograft procedure deserves preference over an allograft procedure. The same is the case for the mosaicplasty procedure, in most cases autogenous in nature but also used for larger defects. If we compared the allograft procedure with mosaicplasty, we did not find a significant difference and therefore could not say whether one has superiority in treating larger defects.

One of the major strengths of our systematic review is the contacting with the authors of included studies with the goal of acquiring separate data. This however also resulted in a limitation: almost half of the extracted data concerning outcome and success percentages was acquired through the direct approach of the authors which made it virtually impossible to collect all the variables which we initially desired to collect in our constructed data set, such as complications reported, lesion size, or classification systems used.

As for pooling of the data, it was not possible to perform a formal meta-regression, that is, utilizing mixed-effects logistic regression in order to compare treatment groups. This is because the number of patients in the studies we included was substantially lower than required to obtain stable parameters estimates for this type of analysis.[37] Instead, the authors decided to pool data through a simplified manner where different patients from the same treatment group were added and a new success percentage was calculated. This means that the results presented in the review need to be interpreted with caution. When comparing two different

treatment groups, one cannot with certainty state that the difference observed was based on clinical differences or on methodological differences. For example, since the allograft technique is mainly used for the larger defects it will consequently give a worse outcome.

As for the outcome measurements, the AOFAS score was the most frequently used scoring system. This score as with all the other scores used for success percentage calculation are not officially validated for the clinical evaluation of the treatment of talar OCDs as such. Subsequently, the calculated success percentages have to be interpreted with care. This is clearly exemplified by the outcome reported by the study of Johnson et al.[26] The adjusted Mazur score was unsatisfactory in the majority of patients which resulted in a rather low success percentage. However, they found a high average subjective patient based satisfaction score. This again brings up the question to what extent we should rely on these questionnaires.

The majority of the included studies were of low methodological quality. As long as no randomized comparative clinical trials are conducted (such as mosaicplasty versus allograft transplantation or OATS versus AMIC) data will remain insufficient to draw any firm conclusions. These results should therefore not be used in making decisions about technique but rather for prediction of outcome. In clinical practice this review can be used to illustrate the different treatment techniques and to give patients an indication about the expected success percentages of the different treatment methods for talar OCDs after failed primary surgery.

Conclusions

In conclusion, multiple diverse surgical treatment options are used for talar OCDs in the case of primary surgical failure. As expected, relatively more invasive methods are administered in comparison to primary treatment. Because of the low level of evidence and the scarce literature reporting on solely non-primary surgery, no methodologically proper meta-analysis could be performed and it is therefore inappropriate to draw firm conclusions. Besides an expected difference in outcome between the autograft transfer procedure and the more extensive procedures of mosaicplasty and the use of an allograft we could neither demonstrate a clear nor a significant difference between treatment options. The need for sufficiently powered prospective investigations in a randomized comparative clinical setting remains substantially high.

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Appendices

Appendix 5.1: Full electronic search strategy used in this systematic review

#	Searches	Results
1. PUBMED		
1	("Osteochondritis Dissecans"[Mesh] OR osteochondritis dissecans[tiab] OR osteochondrosis dissecans[tiab] OR osteochondrolysis[tiab] OR ((osteochondral[tiab] OR chondral[tiab] OR transchondral[tiab] OR cartilage*[tiab]) AND (defect*[tiab] OR lesion*[tiab])) OR OCD[tiab] OR OLT[tiab]) AND ("Talus"[Mesh] OR talus[tiab] OR talar*[tiab] OR ankle[tiab])	Total number of results 1996–2016: 986 hits
2. EMBASE (OVID)		
1	(osteochondritis dissecans/ or (osteochondritis dissecans or osteochondrosis dissecans or osteochondrolysis or OCD or OLT).ti,ab,kw. or ((osteochondral or chondral or osteochondral or transchondral or cartilage*) adj3 (defect* or lesion*)).ti,ab,kw.) and (talus/ or (talus or talar* or ankle).ti,ab,kw.)	1,351
2	limit 1 to yr="1996-Current"	1,097
3. COCHRANE LIBRARY		
1	MeSH descriptor: [Osteochondritis Dissecans] explode all trees	8
2	osteochondritis dissecans or osteochondrosis dissecans or osteochondrolysis or OCD or OLT:ti,ab,kw (Word variations have been searched)	1,117
3	(osteochondral or chondral or transchondral or cartilage*) and (defect* or lesion*):ti,ab,kw (Word variations have been searched)	305
4	#1 or #2 or #3	1,410
5	MeSH descriptor: [Talus] explode all trees	27
6	talus or talar* or ankle:ti,ab,kw (Word variations have been searched)	4,866
7	#5 or #6	4,866
8	#4 and #7, Publication Year from 1996 to 2016, in Cochrane Reviews (Reviews and Protocols), Other Reviews and Trials	23

Appendix 5.2: Quality Assessment Scale Utilized

NEWCASTLE - OTTAWA QUALITY ASSESSMENT SCALE
NONRANDOMIZED STUDIES ADJUSTED FOR CASE SERIES

Note: A study can be awarded a maximum of one star for each numbered item within the Selection and Outcome categories.

Study design

1. Type of study
   a. Prospective*
   b. Retrospective
   c. Other
   d. Not described

2. Set-up
   a. According to protocol*
   b. Without protocol
   c. No protocol described

Selection

3. Representativeness of the exposed cohort
   a. Truly representative of the average talar osteochondral defect patient (after failed previous surgery) in the community*
   b. Somewhat representative of the average talar osteochondral defect patient (after failed previous surgery) in the community*
   c. Selected group of patients by orthopaedic surgeon
   d. No description of the derivation of the cohort

Outcome

4. Assessment of outcome
   a. TIndependent blind assessment*
   b. TRecord linkage*
   c. TSelf-report
   d. TNo description

4. Adequacy of follow-up of series
   a. Complete follow-up – all patients accounted for*
   b. Subjects lost to follow-up unlikely to introduce bias – small number lost (< 5%)*
   c. Follow-up rate < 95% and no description of those lost
   d. No statement

Number of assigned stars

Study (*title, author, year*)	Study design	Selection	Outcome

Each included study was graded on methodological quality by two independent reviewers utilizing adjusted version of the Newcastle Ottawa Scale which is included above. Categories of study design, selection of patients, and outcome were scored by means of a scoring system using quantitive amounts of stars, and respectively for each category a maximum of 2 stars 1 star, and 2 stars could be obtained (maximum is 5 stars).

Chapter 6

Evidence-based treatment of failed primary osteochondral lesions of the talus: a systematic review on clinical outcomes of bone marrow stimulation

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Abstract

Purpose: The purpose of this study is to systematically review the literature and to evaluate the outcomes following bone marrow stimulation (BMS) for non-primary osteochondral lesions of the talus (OLT).

Methods: A literature search was performed to identify studies published using PubMed (MEDLINE), EMBASE, CDSR, DARE, and CENTRAL. The review was performed according to the PRISMA guidelines. Two authors separately and independently screened the search results and conducted the quality assessment using the Methodological Index for Non-Randomized Studies (MINORS). Studies were pooled on clinical, sports, work and imaging outcomes, as well as revision rates and complications. The primary outcome was clinical success rate.

Results: Five studies with 70 patients were included in whom non-primary OLTs were treated with secondary bone marrow stimulation. The pooled clinical success rate was 61% [95% CI, 50–72]. The rate of return to any level of sport was 83% [95% CI, 70–91], while the return to pre-injury level of sport was 55% [95% CI, 34–74]. The rate of return to work was 92% [95% CI, 78–97], and the complication rate was assessed to be 10% [95% CI, 4–22]. Imaging outcomes were heterogeneous in outcome assessment, though a depressed subchondral bone plate was observed in 91% of the patients. The revision rate was 27% [95% CI, 18–40].

Conclusions: The overall success rate of arthroscopic bone marrow stimulation for non-primary osteochondral lesions of the talus was 61%, including a revision rate of 27%. Return to sports, work and complication outcomes yielded fair to good results.

Level of evidence: Level IV.

Keywords: Osteochondral lesions · Talus · Meta-analysis · Bone marrow stimulation · Microfracture · Revision · Non-primary

Introduction

Osteochondral lesions of the talus (OLT) are a common injury in athletes and often result from acute ankle sprains, fractures, or chronic ankle instability. The initial non-operative management of OLT consists of physical therapy, immobilization, and for example the usage of non-steroidal anti-inflammatory drugs or other painkillers.[5,12,31] Once conservative treatment fails, surgical treatment, including bone marrow stimulation (BMS) for primary lesions up to 15 mm in diameter can be considered.[3,4,9,18,22,38] The ideal sized lesion treated with BMS is considered to be up to 10 mm in diameter and results in the formation of a bone-marrow filling of the defect, later differentiating in bone and fibrocartilage on top and this treatment can produce good results in the majority of patients at short- and mid-term follow-up.[13,15,38] However, there is concern that the fibrocartilage and the associated clinical outcomes may deteriorate over time and require revision treatment, thereby yielding worse outcomes at longer-term follow-up.[8,25,38]

When examining the evidence, it is clear that the majority of the literature focuses on BMS for primary OLTs.[5,6,10,14] A recent systematic review on primary lesions by Dahmen et al.[5] found that 82% of the primary OLTs treated with BMS resulted in successful outcomes. It is assumed that BMS for non-primary lesions results in worse outcomes in comparison to primary arthroscopic treatment; however, there is a clear paucity of clinical data and thus limited knowledge on the efficacy of BMS for non-primary OLTs.[9,27-29] The purpose of this study is to systematically review the literature and to evaluate the outcomes following BMS for non-primary OLTs. The hypothesis was that BMS in revision surgery would result in better outcomes than primary treatment due to the centralization of more complex cases.[12]

Materials and methods

The systematic review was prospectively registered at the PROSPERO register under number CRD42018082150.[2]

Search strategy

A systematic review was performed by two independent blinded reviewers (JD and EH) according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. The MEDLINE, EMBASE and The Cochrane Library databases were searched from January 1996. This time frame was chosen

by the authors as the arthroscopic techniques for treating osteochondral lesions of the talus were developed and established by 1996 in the orthopaedic field.[39] The search algorithm that was used for the search is presented in Appendix 6.1. Backward citation chaining strategy was applied as an additional search technique.

Eligibility criteria and study selection

The inclusion and exclusion criteria of the present study are presented in Table 6.1. The titles and abstracts were screened by two reviewers (JD and EH) using the inclusion and exclusion criteria. Subsequently, full texts of potentially relevant studies were then reviewed. The references of all of the studies receiving full text review were screened for additional articles that were not identified through our search strategy. Studies were included for further analysis with the agreement of both independent reviewers, instances of disagreement were settled in consultation with a third author (GK). When necessary, authors were contacted to ask the nature of the defect (primary or non-primary) and to separate data on solely non-primary lesions. When no reply was reported, contact was sought via two reminder e-mails. If no response was recorded, the article in question was excluded. Studies were not blinded for author, affiliation or source.

Table 6.1: Inclusion and exclusion criteria

Inclusion criteria	Exclusion criteria
- Clinical studies reporting outcomes of arthroscopic BMS for non-primary talar OCLs - Level I-IV clinical studies - 5 or more patients included - Peer-reviewed studies - Full-text available studies published in the English language	- Data not interpretable - Combination of patient/treatment groups and/or no separate data per group - Follow-up period < 6 months - Patient overlap in different studies - Treatment option inappropriately described - Asymptomatic lesions - Level V evidence - Animal studies / cadaveric studies

Assessment of level and quality of evidence

The level of evidence (LOE) of the included studies was evaluated based on the criteria from The Oxford Centre for Evidence-based Medicine. The methodological quality of evidence (MQOE) was evaluated by two independent investigators (JD and EH) using the methodological index for non-randomized studies (MINORS) tool.[36] The MINORS tool consists of eight non-randomized or twelve items for comparative non-randomized studies. Maximum scores are 16 for non-comparative non-randomized studies and 26 for comparative non-randomized studies. Instances

of discrepancy were resolved by consensus, and if any disagreement persisted, a senior author (GK) was consulted and a consensus was reached.

Data extraction

The data of each study was extracted using a standardized data sheet consisting of the pre-determined list of information required. All available data on patient characteristics were retrieved due to the scarcity of the literature on the particular topic. Pre-operative and post-operative clinical outcome scores were extracted on mean scores, subjective satisfaction and number of patients treated successfully. Pre-operative and post-operative imaging outcomes were also included in the study. All clinical and sports outcomes reported were evaluated. Wherever possible, the number of successfully treated lesions were also assessed. The surgical intervention was defined as successful when a good or excellent result at follow-up was reported with any accepted associated clinical scoring system (American Orthopaedic Foot and Ankle Score (AOFAS) at or above 80, Foot and Ankle Ability Measure (FAAM) at or above 80, or any other clinical scoring system rating the outcome as good or excellent post-operatively).[11,17] Mean post-operative clinical scores were pooled whenever possible.

Statistical and data analysis

Weighted means and ranges of original data were used in case of descriptive values. Success rates as well as return to sports and work rates were calculated per study with a 95% binomial proportion confidence interval, and – whenever possible – pooled success rates were be calculated with the Wilson score interval (CIA, Confidence Interval Analysis for Windows, version 2.2.0).[1] The overall pooled clinical success rate was regarded as the primary outcome for the present study. All other outcomes were classified as secondary outcomes. The remaining statistical analyses were performed using Microsoft Excel and SPSS (IBM Corp. Released 2013. IBM SPSS Statistics for Macintosh, Version 22.0. Armonk, NY: IBM Corp.).

Results

Overall, 1,810 studies were initially identified from the literature. No additional studies were added through reference and/or citation searches. In total, eleven author groups were contacted to request data according to our inclusion and exclusion criteria. After application of inclusion and exclusion criteria, 5 studies reporting 70 ankles were included in the final analysis (Figure 6.1).[19,26,29,30,41]

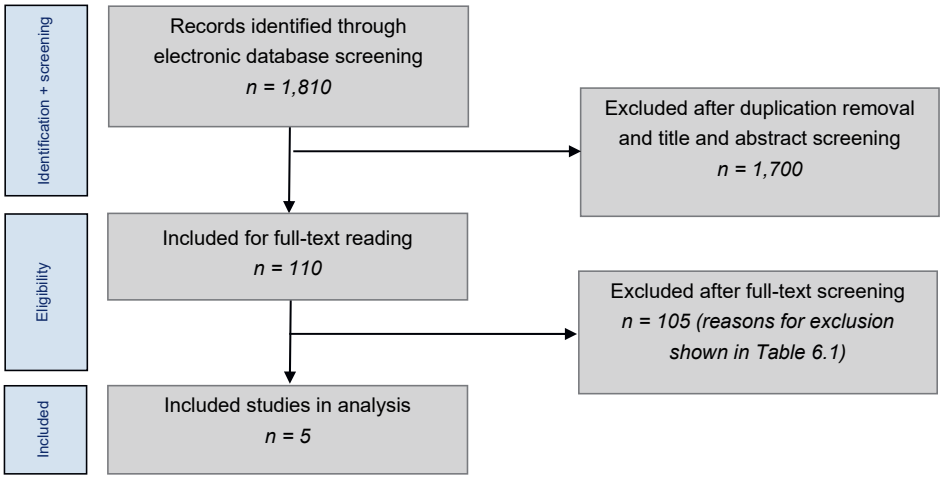

Figure 6.1: Literature selection algorithms – Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA).

Evaluation of the characteristics of included studies

A total of 70 patients were included; the average age was 33 years and 63% were male. A history of trauma was reported in 65% of cases, and further characteristics are shown in Table 6.2. The procedure before the non-primary BMS was noted as removal of an osteochondral fragment in 21 cases and open or arthroscopic BMS in 50 cases. The time between the previous surgery and current arthroscopic surgery was reported in 3 studies[19,26,29] and the weighed mean was 28 months [8–108]. The mean weighted follow-up was 49 months [13–71].

Nature of radiological lesion morphology, concomitant procedures/lesions and adjunct procedures

In two studies, information on the presence or absence of pre-operative cysts were not present. One study excluded lesions with cysts, while in the group studied by Reilingh et al.[26] there was solely one cyst included of the 12 (8%), and in the study by Yoon et al.[41] 14 out of the 22 (64%) patients had pre-operative cyst morphology. The study of Yoon et al.[41] mentioned whether lesions had uncontained or contained nature, of which 3 (14%) were contained lesions and 19 (86%) were uncontained.

Concerning concomitant procedures performed or concomitant diagnoses mentioned, Savva et al.[29] revealed that in the index procedure in 3 of 12 patients received a stabilization procedure for concomitant ankle instability and one of the patients received an arthroscopic debridement in the ankle. Schuman et al.[30]

and Ogilvie et al.[19] did not mention whether there were patients included with concomitant lesions or with concomitant procedures having been performed. By comparison, Yoon et al.[41] only included patients without ankle instability but did include 3 patients with tibial chondral lesions, 14 patients with soft-tissue impingement and 10 patients with loose bodies. Reilingh et al.[26] excluded patients with concomitant lower-extremity diseases.

The study by Reilingh et al.[26] included two study groups – an interventional group and a control group studying the addition of hyaluronic acid to arthroscopic BMS. Due to the fact that no differences were found in clinical outcomes, the secondary OLT patients from both groups were merged. The other studies did not include any additional (biological) adjuncts.

Methodological quality

Three studies were retrospective, and two were prospective. There were two comparative studies and three non-comparative studies. The average MINORS score of the non-comparative studies was 6.3 (range 3–9) out of a possible 16 points. The two comparative studies had an average MINORS score of 20.5 (range 20–21) out of a possible 24 points.

Clinical outcomes

The mean success rates ranged from 32 to 88% [95% CI, 16–98], and the overall pooled success rate was 61% [95% CI, 50–72]. The AOFAS was the most frequently used clinical scoring system,[26,29,41] and the weighted mean improved from 50 [42–58] pre-operatively to 76 [70–81] post-operatively. All mean pre-operative and post-operative clinical scores can be found in Table 6.3 and Table 6.4.

Sports and work outcomes

Sports outcomes were assessed in four of the five studies.[19,26,29,30] Return to sport time was only reported by Reilingh et al.[26] and was calculated to be 19 weeks [range 5–49 weeks]. Return to any level of sports rate was 83% across the four studies [95% CI, 70–91]. In two studies[19,29] return to pre-injury level of sports rate was reported, and the mean RTS to pre-injury level rate was assessed to be 55% [95% CI, 34–74]. Return to work was reported in three studies[19,26,30] and the mean rate of return to work was 92% [95% CI, 78–97]. Return to work time was reported by in two studies[19,26] and the mean return to work time was 7 weeks [range 2–14].

Table 6.2: Study characteristics and patient demographic characteristics

Authors, year	Patients, n	Prospective or retrospective	Treatment	LOE	MQOE	Male/ female	Side R/L	Mean age, yr [range]	Mean follow-up, months [range]	Mean pre-operative size mm^2/ mm^3 [range]	Location	Pre-operative radiology (system) used
Ogilvie-Harris et al.[19] 1999	8	Retrospective	Arthroscopic Debridement	IV	3/16	4/4	4/4	33 [22–42]	38 [24–63]	N.A.	4 PM, 4 AL	Radiographs (Berndt and Harty)
Reilingh et al.[26] 2016	12	Prospective	Arthroscopic Microfracture	I	21/14	8/4	7/5	32 [20–41]	13 [12–20]	102 mm^2 [60–196] / 782 mm^3 [360–1,764]	1AM, 2CM, 3PM, 1 AL, 2 CL, 1PL, 1AC, 1CC	CT (Berndt and Harty)
Savva et al.[29] 2007	12	Retrospective	Arthroscopic Debridement	IV	9/16	7/5	N.A.	31 [20–41]	71 [18–133]	72 mm^2 [25–120] / N.A.	6 medial, 6 lateral	Radiographs and MRI (Berndt and Harty)
Schuman et al.[30] 2002	16	Prospective	Arthroscopic Debridement and drilling	IV	7/16	7/9	N.A.	24 [16–38]	64 [29–129]	N.A / N.A.	12 medial, 4 lateral	Radiographs and CT (Berndt and Harty)
Yoon et al.[41] 2014	22	Retrospective	Arthroscopic Microfracture or abrasion arthroplasty	III	20/24	18/4	N.A.	42 [NR]	50 [24–116]	139 mm^2 [NR] / NR	6 anterior, 8 central, 8 posterior of which: 18 medial and 4 lateral	Radiographs MRI (Berndt and Harty)

N, number; LOE, level of evidence; MQOE, methodologic quality of evidence; yr, year; NA, not available; AC, anterocentral; CM, centromedial; AM, anteromedial; PM, posteromedial; CL, centrolateral; PL, posterolateral; AL, anterolateral; CC, centrocentral; CT, computed Tomography; MRI, magnetic resonance imaging.

Table 6.3: Pre-operative clinical scores

Authors, year	Pre-operative Ogilvie-Harris	Pre-operative AOFAS [range]	Pre-operative VAS/NRS [range]	Pre-operative FAOS [range]	Pre-operative EQ-5D [range]	Pre-operative AAS [range]	Pre-operative Tegner score [range]
Ogilvie-Harris et al.[19] 1999	Pain: 3 poor, 4 fair, 1 good. Swelling: 1 poor, 4 fair, 3 good. Stiffness: 0 poor, 4 fair, 4 good. Limp: 1 poor, 5 fair, 2 good. Activity: 2 poor, 5 fair, 1 good.	N.A.	N.A.	N.A.	N.A.	N.A.	N.A.
Reilingh et al.[26] 2016	N.A.	58 [42–72]	Rest: 3.3 [0–6] Running: 8.0 [4–10]	Symptoms: 61 [14–89] Pain: 56 [31–89] ADL: 65 [44–97] Sport: 37 [15–90] QoL: 26 [0–56]	0.6 [0.2–0.9]	6.8 [4–9]	N.A.
Savva et al.[29] 2007	N.A.	42 [28–67]	N.A.	N.A.	N.A.	N.A.	N.A.
Schuman et al.[30] 2002	Pain: 7 poor, 8 fair, 1 good, 0 excellent. Swelling: 2 poor, 7 fair, 0 good, 7 excellent. Stiffness: 0 poor, 6 fair, 5 good, 5 excellent. Limp: 2 poor, 4 fair, 2 good, 8 excellent. Activity: 5 poor, 11 fair, 0 good, 0 excellent.	N.A.	N.A.	N.A.	N.A.	N.A.	2.7 [N.A.]
Yoon et al.[41] 2014	N.A.	50 [N.A.]	General VAS: 6 [N.A.]	N.A.	N.A.	N.A.	N.A.

NA, not available; AOFAS, American Orthopaedic Foot and Ankle Score; VAS, visual analogue scale; NRS, numeric rating scale; FAOS, Foot and Ankle Outcome Score; ADL, activities of daily living; QoL, quality of life; EQ-5D, EuroQol; AAS, ankle activity scale (values are presented in means).

Table 6.4: Post-operative clinical scores

Authors, year	Post-operative Ogilvie-Harris	Post-operative AOFAS [range]	Post-operative VAS/NRS [range]	Post-operative FAOS [range]	Post-operative EQ-5D [range]	Post-operative satisfaction	Post-operative AAS [range]	Post-operative Tegner score [range]	RTW rate [95% CI] and time in weeks [range]	RTS rate [95% CI] and time in weeks [range]	Success rate [95% CI]
Ogilvie-Harris et al.[19] 1999	Pain: 0 poor, 1 fair, 4 good, 3 excellent. Swelling: 0 poor, 1 fair, 4 good, 3 excellent. Stiffness: 0 poor, 1 fair, 2 good, 5 excellent. Limp: 0 poor, 1 fair, 4 good, 3 excellent. Activity: 0 poor, 1 fair, 2 good, 5 excellent.	N.A.	N.A.	N.A.	N.A.	N.A.	N.A.	N.A.	- 100% [67–100] - time: 6 weeks [2–14]	- any level: 88% [55–98] - pre-injury level: 38% [14–69] - time: N.A.	88% [53–98]
Reilingh et al.[26] 2016	N.A.	81 [43–100]	Rest: 1.1 [0–4] Running: 3.4 [0–7] Satisfaction: 6 [0–10]	Symptoms: 66 [32–100] Pain: 80 [50–92] ADL: 89 [69–100] Sport: 58 [0–100] QoL: 50 [6–81]	0.8 [0.3–1]	See NRS	6 [4–9]	N.A.	- 100% [76–100] - time: 8 weeks [2–13]	- any level: 83% [55–95] - pre-injury level: N.A. - time: 19 weeks [5–49]	75% [47–91]
Savva et al.[29] 2007	N.A.	81 [36–95]	N.A.	N.A.	N.A.	11 satisfied, 1 dissatisfied	N.A.	N.A.	N.A.	- any level: 92% [65–99] - pre-injury level: 67% [39–86] - time: N.A.	67% [39–86]
Schuman et al.[30] 2002	Pain: 2 poor, 1 fair, 7 good, 6 excellent. Swelling: 1 poor, 2 fair, 4 good, 9 excellent. Stiffness: 2 poor, 2 fair, 7 good, 5 excellent. Limp: 1 poor, 2 fair, 3 good, 10 excellent. Activity: 2 poor, 1 fair, 5 good, 8 excellent.	N.A.	N.A.	N.A.	N.A.	N.A.	N.A.	5.6 [N.A.]	- 81% [57–93] - time: N.A.	- any level: 75% [51–90] - pre-injury level: N.A. - time: N.A.	75% [51–90]
Yoon et al.[41] 2014	N.A.	70 [N.A.]	5 [N.A.]	N.A.	N.A.	N.A.	N.A.	N.A	N.A.	N.A.	32% [16–53]

NA, not available; AOFAS, American Orthopaedic Foot and Ankle Score; VAS, visual analogue scale; NRS, numeric rating scale; FAOS, Foot and Ankle Outcome Score; ADL, activities of daily living; QoL, quality of life; EQ-5D, EuroQol; AAS, ankle activity scale; RTW, return to work; RTS, return to sports (values are presented in means); CI, confidence interval.

Imaging assessment

Imaging outcomes were reported in 3 studies.[19,26,30] Two studies[19,30] reported post-operative degenerative osteo-arthritic changes, while Reilingh et al.[26] reported CT scans in 11 patients at one-year follow-up in whom the subchondral bone plate quality (level and filling) and filling of the defect was assessed. In the study of Ogilvie-Harris,[19] there were no osteo-arthritic changes as assessed by the Kellgren and Lawrence scale at final follow-up. In the study of Schuman et al.[30] 6% of patients developed degenerative changes at a follow-up 10 years after the surgery as assessed with postoperative radiographs. The level of subchondral bone plate was depressed in 91% of the patients in the study by Reilingh et al.[26] while it was flush in 9% of the patients. Concerning subchondral bone plate filling, 55% of the patients showed incomplete filling while 45% of the patients showed fully complete or almost fully complete filling of the subchondral bone plate. Filling of the defect was reported to be between 0–33%, 34–66%, and 67–100% of the initial volume in 18%, 9%, and 73% of the patients, respectively.

Complications and revision surgery

For three studies[19,26,41] it was possible to extract data on complications as the other two studies either did not report on complications or it was not possible to extract separate data on complication occurrence. The complication rate was 10% [95% CI, 4–22] with 4 complications reported (1 temporary hypoesthesia of the dorsum of the foot in the 1st webspace, 1 paraesthesia of the foot, 1 delayed wound healing, and one persistent deep ankle pain after a novel distortion at 4-month follow-up). Revision or reoperation surgery was reported in 4 studies.[26,29,30,41] The revision rate was calculated to be 27% [95% CI, 18–40], with 1 HemiCap® implantation, 2 re-operations of unknown nature, and 14 osteochondral autograft transplantations.

Discussion

The most important finding of the present study is that the overall success rate of arthroscopic bone marrow stimulation for non-primary OLTs was low at 61% [95% CI, 50–72], and the re-revision rate was high. Furthermore, return to sports and work outcomes yielded moderate results. To the best of our knowledge, this is the first systematic review investigating the clinical outcomes of non-primary bone marrow stimulation for failed primary talar OCLs.

This study demonstrated that 61% of the patients showed successful clinical outcomes following bone marrow stimulation for secondary osteochondral lesions of the talus, collecting data from five different studies. When comparing this to a recent systematic review[5] on solely primary lesions, this percentage is relatively low. Dahmen et al.[5] found that the clinical success rate for primary lesions was 82% with a 95% confidence interval ranging from 78 to 86% with mean follow-up time of 38 months (ranging from 10 to 143 months). A potential explanation for this lower percentage may be that patients who did not respond to a primary BMS procedure as an index procedure may not respond well to a secondary procedure, potentially due to inherently poor biology particularly. Furthermore, in most lesions following microfracture the lesion size increased after the index procedure secondary to poor bone and cartilage healing. This finding is supported by clinical evidence,[7,13,15] as larger lesions do not respond well to bone marrow stimulation.[22] Another potential explanation of the lower clinical success percentage may be the unknown individual patient factors, such as stem cell characteristics, and may as well be the longer follow-up time in the present study versus the previous study performed by Dahmen et al.[5] on solely primary lesions (49 months vs. 38 months, respectively). However, this difference may be considered marginal, so large differences in clinical success rates may not be expected. Moreover, the success rate of 61% may be considered low due to the influence of the inclusion of the study by Yoon et al.[41] – this study had the lowest success rates of all the included studies with the highest number of patients included (n = 22, success rate = 32% [95% CI, 16–53]). A potential explanation for this calculated success rate may be the fact that the authors included a high percentage of cystic (64%) and uncontained (86%) lesions; both cystic uncontained lesions have been previously found to be negatively associated with clinical outcomes after bone marrow stimulation.[9,27,42]

Yoon et al.[41] stated in their study that worse outcomes were observed in larger lesions separating lesions smaller and larger than 150 squared millimetres. The authors found that patients with small defects demonstrated clinical failure in 53% of the patients with small lesions, versus 100% of the patients with large lesions. Another explanation for this finding may be that the subchondral bone plate may have resulted in inferior quality.[23-25,32,33,35] This theory is supported by the findings of Reilingh et al.[26] in the present study showing that 91% of the secondary lesions showed a depressed subchondral bone plate. Multiple studies have shown that the subchondral bone plate and the subchondral bone itself play a vital role in overall cartilage health and repair.[16,20,21] A recent study by Shimozono et al.[34] showed

that after bone marrow stimulation the subchondral bone was not restored at mid-term follow-up when assessing 42 patients. Moreover, the authors observed a significant decrease of overall subchondral bone health scores over time, and found that these subchondral bone health scores were positively corrected with clinical outcomes. It is therefore hypothesized that impairments to the subchondral bone may irreversibly alter the joint-loading support, resulting in fibrocartilage degradation over time and increased wear and tear of the joint.[23,25]

An opposing explanation for the fact that 6 out of 10 patients responded clinically well to the secondary bone marrow stimulation procedure, it may be hypothesized that the lesions had not been fully debrided during the index procedure, potentially because of inferior visualization of the defect during the arthroscopic index procedure. However, Savva et al.[29] found that in their study population this may not have been the case as otherwise a more dramatic subsequent increase in lesion size was to be expected at the secondary arthroscopic BMS. Additionally, they found that at repeat arthroscopy the lesions that were operated on showed low quality detached fibrocartilage. This finding is in line with other studies on second-look arthroscopic findings, such as the study by Lee et al.[13] in which the authors showed that 40% of the lesions had incompletely healed with fibrocartilage. Moreover, Yang et al.[40] recently concluded that 36% of the patients were incompletely healed and had inferior quality of repair tissue in comparison to native cartilage at a mean follow-up of 3.6 years. While our study found that 61% of the patients had successful outcomes after secondary BMS, it must be stated that the study with the longest follow-up time, the study by Yoon et al.,[41] showed the lowest individual success rate: 32% [95% CI, 16–53]. This is an important clinical topic of interest, as approximately 4 out of 10 patients will demonstrate progression of osteo-arthritis of the ankle at longer follow-up times.[8,38]

When assessing the sports outcomes in the present review, it was found that 83% of the patients returned to any level of sport and 55% of the patients were able to return to a pre-injury level of sport. Comparing these analyses to the findings of a recent systematic review by Steman et al.,[37] return to any level of sports is comparable; 83% for solely non-primary lesions after repeat arthroscopic BMS, versus 88% for mostly primary lesions. However, the return to pre-injury level of sports rate for the secondary lesions in our analyses showed that 55% of the patients were able to return to this level, while another study[37] revealed that 79% of the patients were able to return after arthroscopic BMS. The possible differences for these discrepancies in rates of return to sport are not yet fully understood.

The clinical relevance of this systematic review is that the pooled outcomes of secondary bone marrow stimulation for non-primary osteochondral lesions of the talus can be used to inform patients about which outcomes are to be expected concerning clinical success rates, sports and work outcomes, revision and complication as well as radiological outcomes. This may ameliorate the shared decision-making process between patients and physicians, making the decision between a repeat arthroscopy or a form of (osteo)chondral transplantation for the individual patient more evidence-based.

Limitations

The present study has to be interpreted in light of its strengths and limitations. Firstly, it can be observed that the majority of the studies were of low methodological quality, except for the study of Reilingh et al.[26] which can be regarded a high-quality publication in the form of an RCT. Additionally, one can appreciate that the mean defect size was below 150 mm^2. This finding, in combination with a lack of comparative (prospective) studies reporting the differences between repeat arthroscopic BMS versus a different treatment strategy within the same surgical indication (namely size of lesion, patients' complaints, and lesion morphology), made it impossible to perform a formal meta-analysis utilising mixed-effects logistics regression in order to compare between treatment groups, which can consequently be regarded as a limitation of the study. Another statement that should be made in this limitation section is that the included studies used scoring systems, such as the AOFAS score, which are not officially validated for the clinical evaluation of the treatment of OLTs – future studies should focus on developing validated outcome measures for the outcomes of treatment of OLTs. The strengths of this review are the inclusion of solely non-primary lesions having undergone bone marrow stimulation, thereby purely focusing on a highly selected group of lesion types and patients which yields novel insights into the clinical effectiveness of this surgical intervention. Other strengths that need to be mentioned are the extensive corresponding author contact protocol, the thorough reference selection and the quality assessment of the included studies.

Conclusion

The overall success rate of arthroscopic bone marrow stimulation for non-primary osteochondral lesions of the talus was low at 61% and was accompanied by a high revision rate of 27%. Return to sports and work outcomes yielded fair to good results.

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Appendix 6.1

Pubmed	
#	Searches
1	"Osteochondritis Dissecans"[Mesh]
2	Osteochondritis dissecans[tiab] OR osteochondrosis dissecans[tiab] OR osteochondrolysis[tiab] OR OCD[tiab] OR OLT[tiab]
3	(osteochondral[tiab] OR chondral[tiab] OR transchondral[tiab] OR cartilage*[tiab]) AND (defect*[tiab] OR lesion*[tiab])
4	#1 OR #2 OR #3
5	"Talus"[Mesh]
6	talus[tiab] OR talar*[tiab] OR ankle[tiab]
7	#5 OR #6
8	#4 AND #7

EMBASE (Ovid)	
#	Searches
1	(osteochondritis dissecans/ or (osteochondritis dissecans or osteochondrosis dissecans or osteochondrolysis or OCD or OLT).ti,ab,kw. or ((osteochondral or chondral or osteochondral or transchondral or cartilage*) adj3 (defect* or lesion*)).ti,ab,kw.) and (talus/ or (talus or talar* or ankle).ti,ab,kw.)

COCHRANE LIBRARY	
#	Searches
#1	MeSH descriptor: [Osteochondritis Dissecans] explode all trees
#2	(osteochondritis dissecans or osteochondrosis dissecans or osteochondrolysis or OCD or OLT):ti,ab,kw (Word variations have been searched)
#3	((osteochondral or chondral or transchondral or cartilage*) and (defect* or lesion*)):ti,ab,kw (Word variations have been searched)
#4	#1 or #2 or #3
#5	MeSH descriptor: [Talus] explode all trees 34
#6	(talus or talar* or ankle):ti,ab,kw (Word variations have been searched)
#7	#5 or #6

Chapter 7

Talar OsteoPeriostic grafting from the Iliac Crest (TOPIC) for large medial talar osteochondral defects: operative technique

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Abstract

Objective
Provision of a natural scaffold, good quality cells, and growth factors in order to facilitate the replacement of the complete osteochondral unit with matching talar curvature for large medial primary and secondary osteochondral defects of the talus.

Indications
Symptomatic primary and secondary medial osteochondral defects of the talus not responding to conservative treatment; anterior–posterior or medial–lateral diameter > 10 mm on computed tomography (CT); closed distal tibial physis in young patients.

Contraindications
Tibiotalar osteoarthritis grade III; multiple osteochondral defects on the medial, central, and lateral talar dome; malignancy; active infectious ankle joint pathology.

Surgical technique
A medial distal tibial osteotomy is performed, after which the osteochondral defect is excised in toto from the talar dome. The recipient site is microdrilled in order to disrupt subchondral bone vessels. Then, the autograft is harvested from the ipsilateral iliac crest with an oscillating saw, after which the graft is adjusted to an exact fitting shape to match the extracted osteochondral defect and the talar morphology as well as curvature. The graft is implanted with a press-fit technique after which the osteotomy is reduced with two 3.5 mm lag screws and the incision layers are closed. In cases of a large osteotomy, an additional third tubular buttress plate is added, or a third screw at the apex of the osteotomy.

Postoperative management
Non-weight bearing cast for 6 weeks, followed by another 6 weeks with a walking boot. After 12 weeks, a CT scan is performed to assess consolidation of the osteotomy and the inserted autograft. The patient is referred to a physiotherapis.

Results
Ten cases underwent the TOPIC procedure, and at 1 year follow-up all clinical scores improved. Radiological outcomes showed consolidation of all osteotomies and all inserted grafts showed consolidation. Complications included one spina iliaca anterior avulsion and one hypaesthesia of the saphenous nerve; in two patients the fixation screws of the medial malleolar osteotomy were removed.

Osteoperiostale Beckenkammtransplantation (TOPIC) für große Defekte der medialen Talusrolle

Zusammenfassung

Operationsziel
Wiederherstellung des natürlichen Knochengerüsts mit gesunden Zellen und Wachstumsfaktoren zur Rekonstruktion von großen primären und sekundären Knochendefekten an der medialen Talusrolle, mit Einsatz einer kompletten osteochondralen Einheit mit passendem Radius entsprechend der Talusrolle.

Indikationen
Symptomatische primäre und sekundäre mediale osteochondrale Defekte am Talus nach fehlgeschlagener Physiotherapie; anteroposteriorer und/oder mediolateraler Durchmesser > 10 mm in der Computertomographie (CT); bei jüngeren Patienten: geschlossene Wachstumsfuge der distalen Tibia.

Kontraindikationen
Generalisierte Osteoarthrose im gesamten Sprunggelenk; multiple Osteochondraldefekte; aktive Infektion; Malignität.

Operationstechnik
Zunächst wird eine mediale Osteotomie der distalen Tibia durchgeführt, anschließend der Osteochondrale Defekt vollständig aus dem Talus entfernt. Der Defekt wird angebohrt, um die subchondralen Blutgefäße zu öffnen. Das Transplantat wird am ipsilateralen Beckenkamm mit der oszillierenden Säge entnommen und in den Defekt unter Beachtung der korrekten Wiederherstellung von Form und Radius der Talusrolle eingepasst. Dann wird das Transplantat mittels Press-Fit-Technik fixiert. Anschließend erfolgen die Reposition der Tibiaosteotomie und die Fixation mit zwei 3,5-mm-Zugschrauben sowie der Wundverschluss.

Weiterbehandlung
Unbelastete Mobilisation im Unterschenkelgips für 6 Wochen, danach Vollbelastung in einer Unterschenkelorthese (Walker) für weitere 6 Wochen. Nach 12 Wochen Kontroll-CT zur Analyse der Knochenheilung sowohl der medialen Tibiaosteotomie als auch der Integration des Transplantates in den Talus. Danach beginnen mit Physiotherapie.

Ergebnisse
In einer prospektiven Studie wurden 10 konsekutive Patienten mit der TOPIC-Technik behandelt. Nach einem Nachuntersuchungszeitraum von 12 Monaten verbesserten sich alle klinischen Werte der Patienten. Als Komplikationen sind bisher eine Avulsionsfraktur der Spina iliaca anterior und eine Hypästhesie des N. Saphenus aufgetreten. Bei 2 Patienten traten leichte Druckschmerzen über dem medialen Malleolus auf, die nach Entfernen der Zugschrauben wieder verschwanden.

Introductory remarks

Osteochondral defects of the talus are defined as damage to the talar articular cartilage and its subchondral bone. The origin of this injury may be due to ankle fractures and ankle sprains, an avascular episode, and possibly a genetic predisposition.[1,15,25,50] The injuries have a severe impact on the quality of life of active patients, due to deep ankle pain during weight-bearing and sporting activities.[4,5,22]

Primary management of these defects is conservative; surgery is considered in cases of persistent symptoms.[52] For small primary defects, common first-line surgical management options consist of (arthroscopic) bone marrow stimulation and retrograde drilling.[11-13,30,43] For fixable defects, arthroscopic and open internal fixation procedures are amenable options and have proven to be effective for pediatric and adult patient populations.[28,29,31,45,46] In case of large defects or in case of failure of first-line surgical treatment, more extensive and invasive surgery can be considered a necessary step in the management process.[30] The more common treatment strategies currently include osteochondral allograft procedures, osteochondral autograft transfer system (OATS) procedures, and classic and matrix-associated chondrocyte implantation (ACI, MACI).[20,21,32,39,55,56] Even though the OATS procedure is regarded as an effective surgical management option with a 90% success rate reported in the literature, donor-site morbidity has been reported to occur relatively frequently with incidence rates ranging from 11 to 35% when the graft was harvested from the ipsilateral femoral condyle.[13,16,19,23,24,26,44,57] As an alternative to an OATS procedure harvesting the graft from the knee, an autologous osteoperiosteal cylinder graft can be harvested from the iliac crest. This technique has been described by Hu et al.[26] and Chen et al.[10] This surgical treatment yielded highly promising results with good clinical follow-up scores and radiological outcomes. However, both author groups utilized cylindrical grafts, thereby compromising optimal individualized treatment for large talar osteochondral defects as it is known that that the size of the cylinder autograft is static and determined preoperatively.

In order to overcome the aforementioned disadvantages, we developed a new surgical technique for the treatment of large talar osteochondral defects or secondary lesions: the Talar OsteoPeriostic grafting from the Iliac Crest (TOPIC) procedure. This technique utilizes the ipsilateral iliac crest with its overlying periosteal layer as a harvesting location for the autograft. The use of the periosteum has been shown to have potential concerning articular cartilage-like tissue

regeneration.[35,40] The chondrogenic potential of this technique arises because the cambium layer of periosteum contains chondrocyte precursor cells.[27,37] A bone-periosteal transplant for bone–cartilage repair meets the three requirements for tissue engineering: a source of cells, a scaffold, and local growth factors.[2,18,34,47,54] In addition, the curvature of the iliac crest is highly similar to the curvature of the talar bone, and the harvested graft can be exactly fitted to the excised defect from the talus.[38] The goal of the present surgical technique description is to describe the surgical technique of the newly developed TOPIC procedure and evaluate potential pearls and pitfalls.

Surgical principle and objective

A large primary or secondary osteochondral defect to the talus is a challenging problem in the orthopedic clinic. Multiple techniques exist to treat these defects, ranging from a cartilage implantation technique to an OATS procedure as well as an allograft procedure. These techniques have their individual advantages and disadvantages — such as donor-site morbidity, poor quality subchondral bone repair and low clinical efficacy. The current paper describes a new surgical technique for the treatment of large primary and secondary medial talar osteochondral defects. The technique comprises a medial distal tibial osteotomy and a talar autograft transplantation from the ipsilateral iliac crest. The technique has the main advantage of providing a natural scaffold, good quality cells, and growth factors, facilitating the replacement of the complete osteochondral unit — a triad considered important in the treatment of these defects.

Advantages

- No expensive planning software required
- Single-stage technique
- Limited operation time
- Cost-effective
- Surface geometry talus and curvature crest[38]
- Iliac crest graft provides a scaffold, cells, and growth factors.[2,18,34,47,54]

Disadvantages

- Access to talar dome through an osteotomy
- Potential complaints of discomfort of the inserted screws and/or plate
- Complications specifically for the harvest site, the iliac crest, and hyp(er) aesthesia of the skin[14]

Indications

- General: painful osteochondral defect with a clear episode of deep ankle pain not responding to conservative treatment
- Anterior–posterior or medial–lateral diameter should exceed 10 mm on computed tomography (CT)
- The depth of the defect is no limitation for this procedure
- Both primary and secondary surgical lesions are treated with a TOPIC
- Closed distal tibial physis in young patients
- If concomitant instability is present, a stabilizing procedure will be considered
- In case of malalignment, a corrective osteotomy will be considered.

Contraindications

- Tibiotalar osteoarthritis grade III
- Multiple osteochondral defects on the medial, central, and lateral talar dome
- Active infectious ankle joint pathology
- Malignancy

Patient information

- Usual surgical risks include infection, hematoma, thromboembolic event, wound healing problems
- Transient or permanent nerve damage leading to hypaesthesia of the saphenous nerve
- Late or early screw and or plate discomfort requiring removal after consolidation
- Nonweight bearing cast for 6 weeks, followed by a walking boot for another 6 weeks

Preoperative work up

The Department of Orthopedic Surgery of the Amsterdam UMC, Location AMC has been officially recognized as an expert center for the treatment of osteochondral defects of the ankle and foot. All patients are screened with a careful patient history and physical examination of both lower legs. During the physical examination there is special attention for recognizable pain on palpation over the site of the talar osteochondral defect with the foot in plantar flexion to be sure that the patients' deep ankle pain indeed arises from the osteochondral defect and not from any other pathology. Special emphasis is also put on the range of motion of the ankle joint, especially plantar flexion. This is done in order to determine whether an osteotomy will be necessary or whether the total defect can be reached without an osteotomy.

For confirmation of the diagnosis and as a preoperative sizing and planning tool, an additional CT scan is made. All talar osteochondral lesions are scanned for defect size, location, shape, and morphology. In addition, the lesion's preoperative shape is classified according to the modified Berndt and Harty's staging system with added stage V by Scranton and McDermott.[7,51]

Instruments and implants

- Hohman retractors
- Oscillating saw and/or chisel with thin blades
- Beaver knife
- 2.0 mm Kirschner wires
- 2.0 mm drill
- Coagulation knife
- Hemostatic gelatin sponge (Spongostan®)
- Impactor
- 3.5 mm cortical screws or a headless alternative
- Standard orthopedic set
- Chisel set
- Large Weber clamps

Anesthesia and positioning

- General or spinal anesthesia
- Supine position with a tourniquet applied around the thigh
- Antibiotic prophylaxis (cefazolin 2 g intravenous injection) is administered to each patient

Surgical technique

Figures 7.1, 7.2, 7.3, 7.4, 7.5, 7.6 and 7.7.

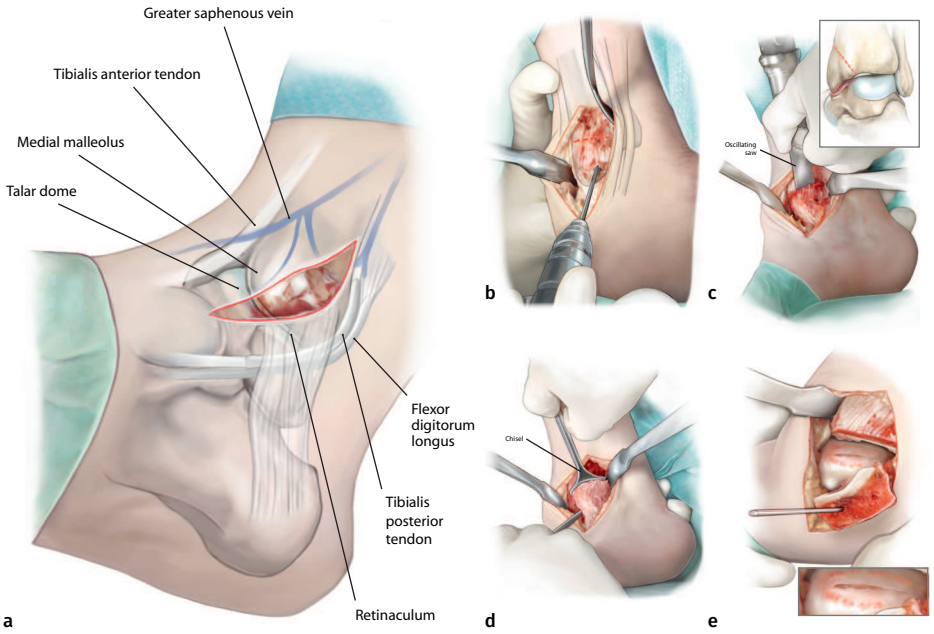


Figure 7.1: Medial distal tibial osteotomy. After prepping and draping, a slightly curved incision of approximately 7 cm is made over the medial malleolus **(a)**, the large saphenous vein is identified and protected. An anteromedial arthrotomy is performed with a partial resection of the anteromedial joint capsule. Posterior from the medial malleolus, the retinaculum of the posterior tibial tendon is opened and the tendon is retracted to allow a subtle posteromedial capsular resection. Anterior and posterior Hohman retractors are placed in order to protect the neurovascular structures and the tendons. Then, an osteotomy is first prepared by predrilling the lag screw holes **(b)**. Thereafter, the osteotomy is performed with an oscillating saw **(c)**. In order to prevent thermal damage to the cartilage, the last 3 mm of the osteochondral zone of the distal tibial plafond is finished with a chisel **(d)**. The extent of the osteotomy is decided based on the exact localization of the defect, as well as the sagittal and the coronal diameter of the defect. After finishing the osteotomy, the osteotomized distal tibia part is dislocated in both medial and plantar direction and this position is secured with the use of 1 (or 2) 2.0 mm Kirschner wire(s). This facilitates full exposure of the medial to central talar dome **(e)**.

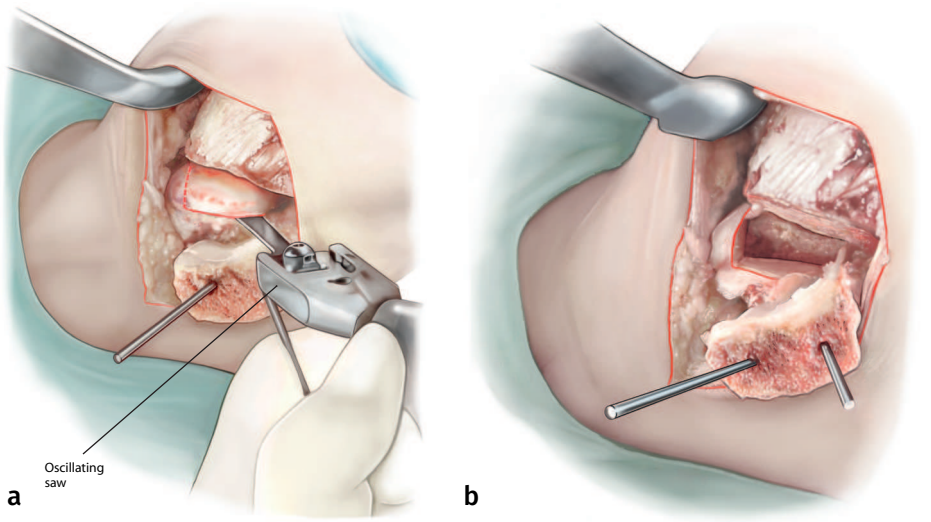


Figure 7.2: Excision of the diseased osteochondral defect. After the identification and exposure of the defect, a rectangular incision of the cartilage is made to preserve as much healthy cartilage as possible and to prevent the cartilage from rupturing in the next steps of the procedure **(a)**. All cystic and necrotic bone is removed in total with the use of either an oscillating saw or a chisel with thin blades or both. The end result should be a total removal of the pre-measured talar diseased osteochondral defect, deep enough so that healthy bone can be observed **(b)**.

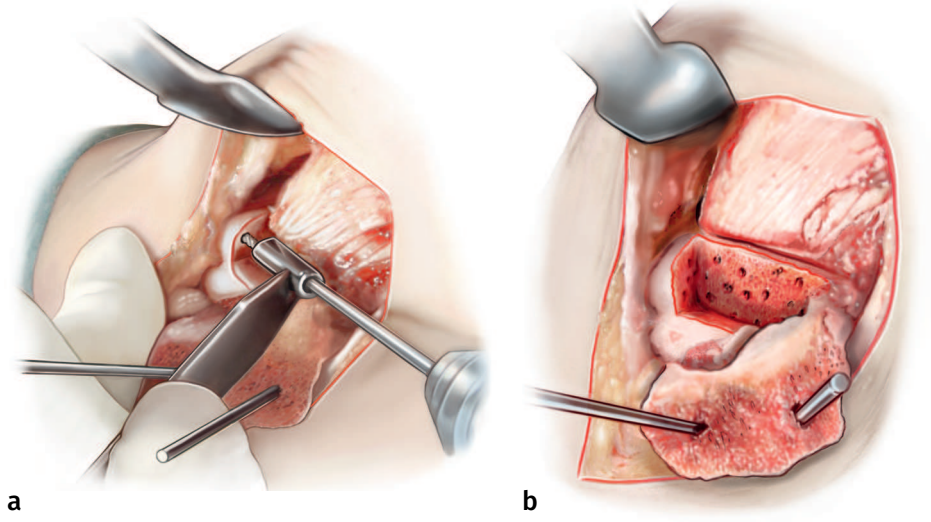


Figure 7.3: Drilling of the recipient's subchondral bone base. As the defect has been excised beyond the subchondral bone plate, the base of the autograft recipient can be freely (micro)drilled for bone marrow stimulation using a 2.0 mm drill **(a)**. This step of the procedure disrupts intraosseous vessels so that blood and bone marrow cells are introduced into the yet empty defect. **(b)** End result after drilling of the subchondral bone.

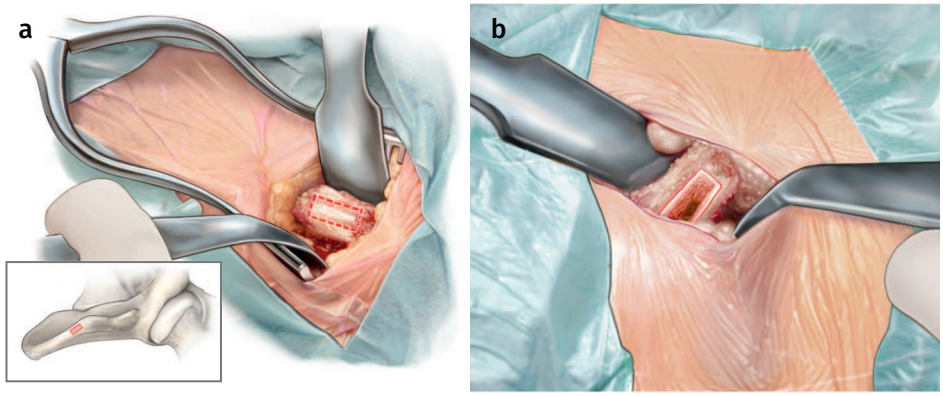


Figure 7.4: Measuring and harvesting the donor autograft from the iliac crest. After having drilled the subchondral bone of the talus, the graft harvest is started. The first step is to exactly measure the size of the excised block, so that a correct approximation of the donor autograft can be performed—the graft should be 1 mm larger in all directions (anteroposterior and mediolateral diameter as well as depth). Approach the iliac crest through a horizontal incision of approximately 3.5 cm. Take care not to use the coagulation knife in order to keep the periosteum nicely intact and attached. Expose part of the iliac crest by means of two retractors **(a)**. Then, a monocortical, bicortical, or tricortical osteoperiosteal autograft from the ipsilateral iliac crest is harvested with an oscillating saw and chisel **(b)**. The combination of the size of the graft needed and the width of the crest dictates the choice for monocortical, bicortical, or a tricortical graft. A hemostatic gelatin sponge (Spongostan®) can be left in the iliac crest after harvesting the autograft.

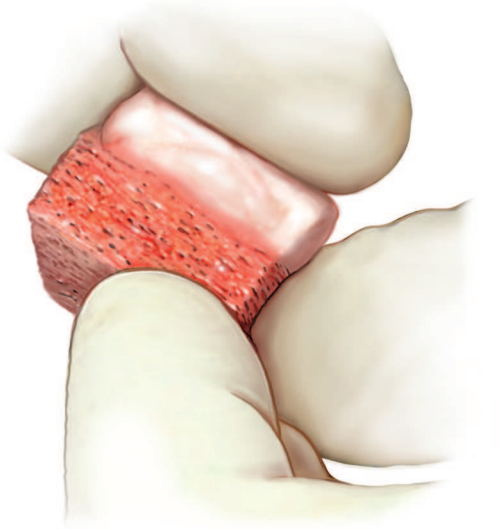
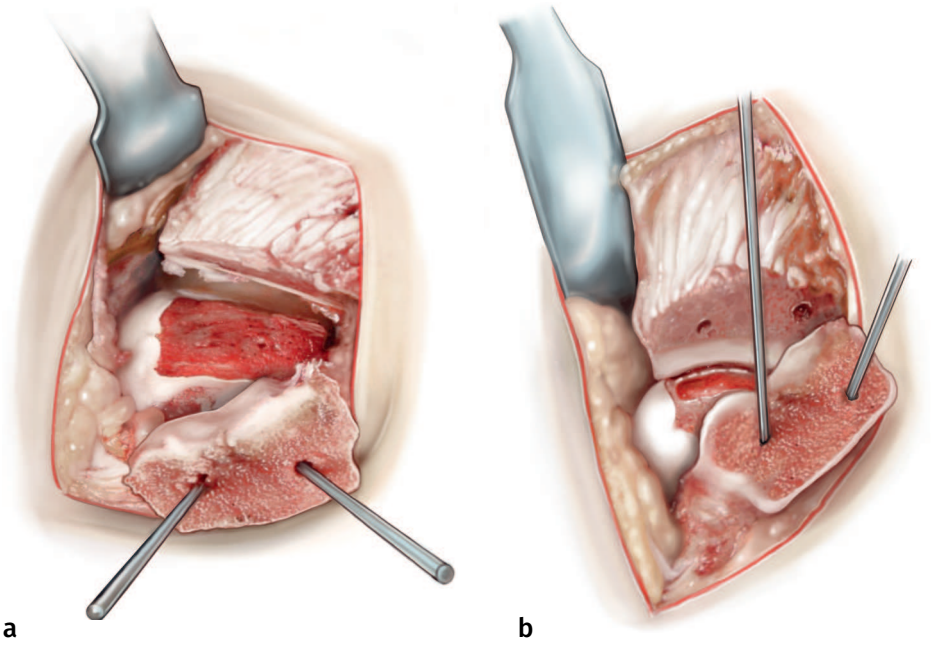


Figure 7.5: Adjusting the fitting shape of the autograft. The graft can be further fine-tuned to optimally fit curvature, size, and depth of the talar defect. Take care that graft is not too proud: 1–2 mm under the talar cartilage level at all sides seems best in order to prevent over-stuffing. The graft should be placed press-fit, which means 1 mm should be added on all dimensions of the excised defect, as mentioned in Figure 7.4. Take time to perform this correctly as it will facilitate the step of executing a press-fit insertion technique. Comparing the graft to the excised talar defect may ameliorate the similarity of the autograft.



a b

Figure 7.6: Implanting the graft through a press-fit technique. Once the optimal fitting shape has been reached, the autograft is transported and placed into the host site **(a)**. By means of an impactor the inserted autograft can be fitted exactly 1–2 mm underneath the level of the talar cartilage. The curvature of the iliac crest accurately matches the talar curvature **(b)**. As this is a press-fit technique, no additional screws are necessary in order to fixate the autograft. In case of graft instability, the option of using one or two screws to stabilize the graft always remains.

Special surgical considerations

- A preoperative CT scan is used to measure the bony dimensions of the osteochondral defect (anteroposterior diameter, mediolateral diameter and depth)
- The last part of the distal tibial osteotomy is done with a chisel to prevent thermal damage to the osteochondral unit
- Both the distal tibial osteotomy and iliac crest autograft transplantation can be customized for every patient
- In case a larger distal tibial osteotomy is indicated, an extra antiglide plate can be used to prevent rotation and proximal translation
- Press-fit autograft transplantation allows for quick rehabilitation without need for intra-articular screw removal
- Theoretically, an optimal graft to replace an osteochondral unit has the following characteristics: natural scaffold, good quality cells, and growth factors[36,41,42,48,53]

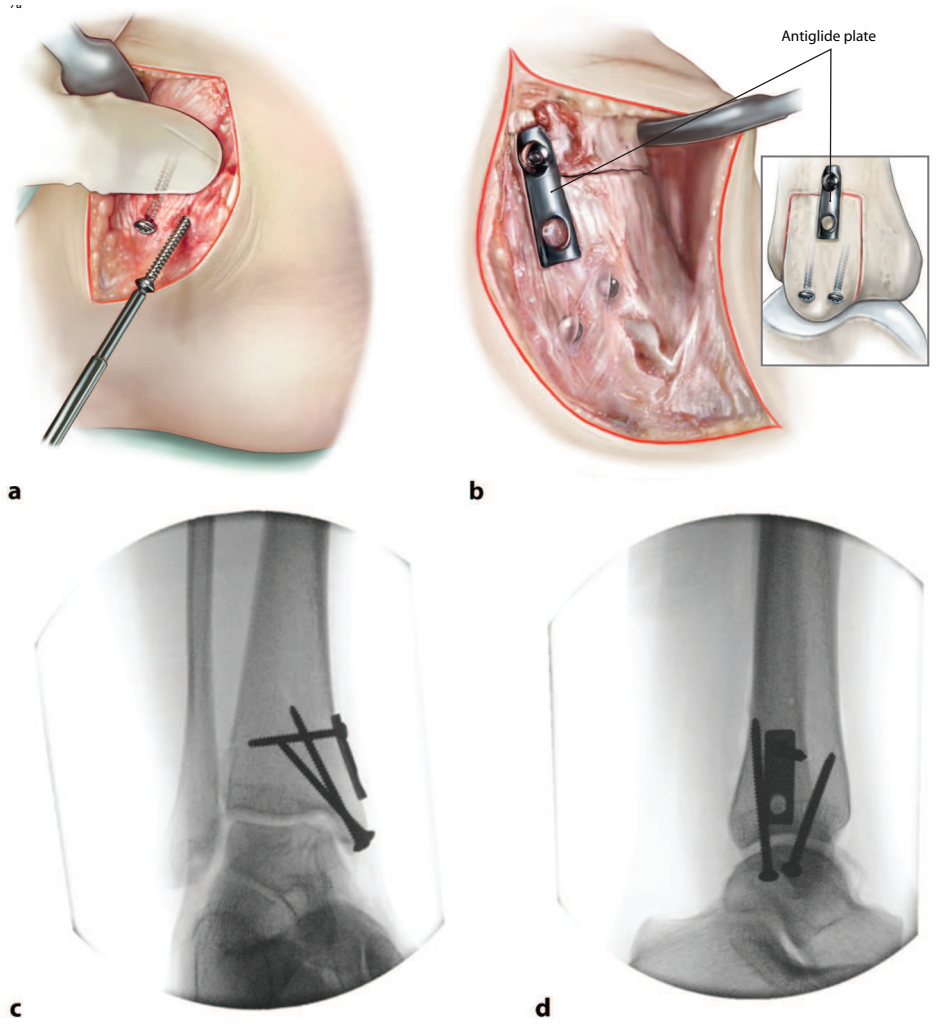


Figure 7.7: Closure of the distal tibial osteotomy and incision layers. The distal tibial osteotomy is closed and fixated by means of two 3.5 mm lag screws in case of a standard small medial malleolar osteotomy. We aim for two divergent bicortical screws **(a)**. In case of a larger distal osteotomy we opt for two bicortical medial screws perpendicular to the osteotomy and an antiglide plate to prevent rotation and proximal translation of the osteotomy **(b–d)**. Sometimes a third screw at the apex of the osteotomy is also a suitable option. Rinsing and closure in layers follows.

Postoperative management

Directly after surgery a lower leg splint is provided for the first 24 h. Surgery is performed as a 1-day admission as this allows for adequate pain management and application of a fresh circular nonweight bearing lower leg cast applied for 2 weeks. After 2 weeks, the stitches are removed and the patient is allowed an hour

of dorsoplantar ankle flexion motion in order to prevent stiffness and possibly enhance the stimulation of progenitor cells from the periosteum to produce an optimal chondral layer following stimulation through ankle joint motion.[8,9,33]

The non-weight bearing period is 6 weeks with regular cast changes in order to allow an hour of ankle joint motion. At the 6-week follow-up, a walking boot is applied for another 6 weeks. At the 12-week follow-up, a computed tomography (CT) scan provides information on consolidation of the distal tibial osteotomy as well as the autograft. At this visit we also do a clinical assessment of the patient and provide an individualized guideline for the next 3 months of rehabilitation. The patient is referred to a physiotherapist to guide and stimulate clinical progress and aid in the rehabilitation process. Additional follow-ups are performed at 6 months and 1 year postoperatively in order to closely assess progress of the patient, also concerning return to work, sports, and performance.

Errors, hazards, complications

At every follow-up, patients are checked for potential complications, such as crest pain, hyp(er)aesthesia in the crest and ankle joint region, infections, ankle joint synovitis, and postoperative pain. A radiograph is obtained 6 weeks postoperatively to assess consolidation of the osteotomy. A CT scan is made at 3 and 12 months after surgery to assess consolidation, ingrowth, and talar remodeling of the transplant. Potential pitfalls include the following:

- Cartilage damage to ankle joint if not enough attention is paid to the distal tibial osteotomy
- Neurovascular or posterior tibial tendon damage if Hohman retractors are not placed properly
- Avulsion or fracture of the iliac crest when harvesting the graft too close to the anterior superior iliac spine
- Proudness of the autograft might give a kissing lesion or chondral wear to distal anteromedial corner of the ankle joint
- Graft failure
- Non- or malunion of the osteotomy
- Ankle joint stiffness
- Persistent ankle pain because of progressive osteoarthritis (OA)
- Impingement of the medial gutter if the graft has slight overhang or in case of presence of an osteophyte or multiple osteophytes

Results

The present study was approved by the local Medical Ethics Committee at the University of Amsterdam and performed in accordance with the current ethical standards (Declaration of Helsinki, reference number MEC 14/237 #14.17.0288). All patients undergoing a TOPIC procedure were assessed preoperatively and at 1 year postoperatively. Ten patients underwent the TOPIC procedure. Mean age was 36.1 years (standard deviation [SD] 17.9). The mean follow-up for the patients was 12 months (SD 1.0). Pre- and postoperative assessment included the Foot and Ankle Outcome Score (FAOS) subcales, the American Orthopaedic Foot and Ankle Society (AOFAS), Short-Form 36 (SF-36) Mental Component Scale (MCS) and Physical Component Scale (PCS), and the Numeric Rating Scales (NRS) of pain at rest and during walking and stair-climbing. Dual energy CT scans were taken preoperatively and at the 1 year follow-up. All patients were available for follow-up. The AOFAS significantly improved from 50 to 83 ($p = 0.02$). The NRS during rest improved from 2.4 to 1.0 ($p = 0.072$), during walking from 4.6 to 2.3 ($p = 0.009$), during stairclimbing from 4.3 to 1.8 ($p = 0.011$), and during running from 7.1 to 2.6 ($p = 0.0011$). The SF-36 PCS improved from 36 to 48 ($p = 0.001$) and the MCS from 47 to 56 ($p = 0.132$). All Foot and Ankle Outcome Score (FAOS) subscales improved significantly, except for the symptoms subscale. On the postoperative CT scans, all osteotomies and grafts showed consolidation (Figure 7.8). Complications included one spina iliaca anterior avulsion and one temporary loss of sensitivity of the saphenous nerve; in two patients the medial malleolar screws were removed.

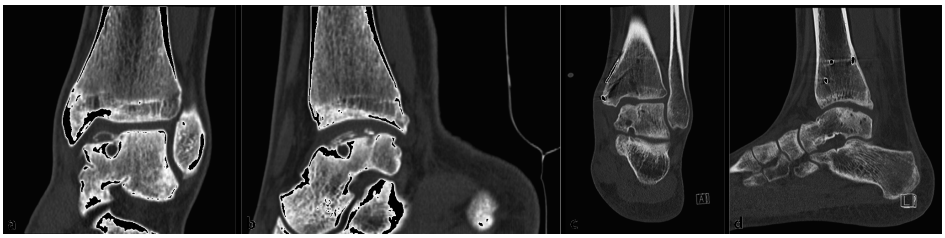


Figure 7.8: Preoperative and postoperative (1 year follow-up) computed tomography (CT) scans of the same patient. (a) Coronal preoperative CT scan. **(b)** Sagittal preoperative CT scan. **(c)** Coronal postoperative CT scan. **(d)** Sagittal postoperative CT scan.

We present a novel press-fit autograft transfer technique for large talar osteochondral defects. Talar OsteoPeriostic grafting from the Iliac Crest (TOPIC) proved to be a reproducible and safe technique, with good short-term functional results and

early radiographic consolidation of the graft on CT scan. We consider an improvement of on average of 30 points on the AOFAS scale and 2.3 (during activity) and 4.5 points (during running) on the NRS very promising. This, as a mean improvement of −2.0 on the NRS scale of 0 to 10 is significantly associated with the concept of a "much better improvement".[49]

Further advantages of the technique are its relative ease to perform, limited operation time, and the costs being relatively low in comparison to other extensive techniques such as for example an allograft implantation technique or chondrogenesis-inducing techniques. In addition, the iliac crest as a harvesting site not only matches the talar surface geometry, but it also has a chondrogenic potential to regenerate articular cartilage utilizing periosteum.[27,40] If a TOPIC does fail, various salvage procedures are available: a redo, an ankle fusion or a total ankle prosthesis.

Disadvantages are the use of an autograft of the ipsilateral iliac crest that has potential complications such as persistent pain, neuralgia, or contour loss of the crest; however, with the technique used for harvesting the graft, this is minimized.[3,14] Another disadvantage might be the use of a fairly large medial distal tibial osteotomy that has to extend into the tibial plafond in order to be able to excise the entire defect. All medial malleolar osteotomies showed complete union at 3 months postoperatively. Another complication of the present technique may be the complaints of the medial malleolar screws that were inserted.[6,17] We encountered this in 3 patients, and hardware removal was necessary in 2 patients. A further disadvantage of the TOPIC technique might be the requirement of a high level of surgical skill for exact graft shaping. It needs to be 0.5 mm oversized in the sagittal plane while the width and depth in the coronal and axial plane should exactly fit the depth of the created defect in order to allow the graft to be placed 1–2 mm subchondral after impaction.

In a recent review, we described that there are several options that appear to be safe and provide good results in prospective case series, with up to 90% success of OATS techniques for larger talar osteochondral defects after failed prior surgical treatment.[30] In these OATS results, there were several harvesting sites described for the plugs. The iliac crest as a graft site has been previously described with good results; however, all techniques have the potential disadvantage of a nonfully anatomical fit and the possibility of new cyst formation in medium and long-term follow-up along the plugs used.[26]

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Ethics declarations
The study was performed in accordance with the current ethical standards.

Conflict of interest
G.M.M.J. Kerkhoffs, J.N. Altink, S.A.S. Stufkens and J. Dahmen declare that they have no competing interests.

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Chapter 8

Talar OsteoPeriostic grafting from the Iliac Crest (TOPIC) for lateral osteochondral lesions of the talus: operative technique

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Abstract

Objective
To provide a natural scaffold, good quality cells and growth factors, facilitating a replacement of the complete osteochondral unit with matching talar curvature for large osteochondral lesions of the lateral talar dome.

Indications
- Symptomatic primary and non-primary lateral osteochondral lesions of the talus not responding to conservative treatment
- Anterior-posterior or medial-lateral diameter should exceed 10mm on computed tomography (CT) for primary lesions – for secondary lesions there are no size limitations

Contraindications
- Tibiotalar osteoarthritis grade III
- Malignancy
- Active infectious ankle joint pathology
- Hemophilic or other diffuse arthropathy

Surgical technique
An anterolateral arthrotomy is performed after which the ATFL is disinserted from the fibula. Additional exposure is achieved by placing a Hintermann distractor subluxating the talus ventrally. Thereafter, the osteochondral lesion is excised in toto from the talar dome. The recipient site is micro-drilled in order to disrupt subchondral bone vessels. Then, the autograft is harvested from the ipsilateral iliac crest with an oscillating saw, after which the graft is adjusted to an exact fitting shape to match the extracted lateral osteochondral defect and the talar morphology as well as curvature. The graft is implanted with a press-fit technique after which the ATFL is re-inserted again followed by a potential augmentation with an Internal Brace™.

Postoperative management
Non-weight bearing cast for 6 weeks, followed by another 6 weeks with a walking boot. After 12 weeks, a computed tomography (CT) scan is performed to assess consolidation of the inserted autograft. The patient is referred to a physiotherapist.

Keywords: Ankle · Cartilage regeneration · Osteochondral autograft · Iliac crest · Transplantation technique · Talar osteochondral defect

Osteoperiostale Beckenkammtransplantation (TOPIC) bei lateralen Osteochondralläsionen des Talus: Operationstechnik

Zusammenfassung

Operationsziel
Ziel der Therapie bei lateralen osteochondralen Defekten am Talus ist die Verschaffung eines natürlichen Gerüsts, qualitativ hochwertige Zellen und Wachstumsfaktoren bereitzustellen, Erleichtern des Austausches der gesamten Osteochondralen Einheit mit entsprechender Talus Krümmung für größeren primäre und sekundäre lateralen osteochondralen Defekten am Talus.

Indikationen
- Symptomatische primäre und sekundäre lateralen Osteochondrale Defekten am Talus nach fehlgeschlagener Physiotherapie
- Größere Läsionen (anteroposteriore oder mediolateralen Durchmesser großer als 10mm auf Computertomographie für primäre läsionen – fur sekundären Läsionen gibt es keine Einschränkungen

Kontraindikationen
- Generalisierte Osteoarthrose im gesamten Sprunggelenk
- Aktive Infektion
- Malignität
- Hämophilie oder andere diffuse Arthropathie

Operationstechnik
Eine anterolaterale Arthrotomie wird durchgeführt, wonach die ATFL aus der Fibula entfernt wird. Zusätzliche Chirurgische Exposition kann durch das Aufsetzen eines Hintermann Distractor erreicht werden, danach wird der Talus nach ventral subluxiert. Zunächst wird den osteochondralen Defekt vollständig aus der Talus Kuppel herausgeschnitten. Die Empfängerstelle wird mit einer Mikrobohrung versehen, um die subchondralen Knochengefäße zu öffnen. Anschließend wird das Autotransplantat mit einer oszillierenden Säge vom ipsilateralen Beckenkamm extrahiert, wonach das Transplantat auf eine genau passende Form gebracht wird, die dem extrahierten osteochondralen Defekt und der Talar Morphologie sowie der Krümmung entspricht. Das Implantat wird mit einer Press-Fit-Technik implantiert, wonach die ATFL wird erneut eingesetzt, gefolgt von einer möglichen Augmentation mit einer Internal Brace™.

Nachbehandlung
Unbelastete Mobilisation im Unterschenkelgips für 6 Wochen, vollbelastende Mobilisation in einer Unterschenkelorhtese (Walker) für weitere 6 Wochen. Nach 12 Wochen: Computertomographie für Analyse der Konsolidierung des Transplantats. Verweisung für Physiotherapie.

Schlüsselwörter: Talus · Osteochondrale Defekte · Osteochondrosis Dissecans · Knorpeltherapie · Knorpelregeneration · Autogener Beckenkammspan

Introductory remarks

An osteochondral lesion of the talus (OLT) is characterized as damage to the talar articular cartilage and the underlying subchondral bone. These lesions are predominantly caused by ankle fractures or ankle sprains, but can also have an idiopathic or genetic origin.[11,33] This is evidenced by recent literature from which we know that 45% of the acute ankle fractures are associated with concomitant damage to the (osteo)chondral unit of the ankle, with the talar bone being the most frequently reported location.[22]

Currently, there is no superior treatment for primary nor secondary OLTs.[9,18] However, it is recommended to initiate treatment of patients with painful OLTs with an appropriate conservative treatment protocol in the context of individualized care. This treatment protocol can consist of supervised neglect, a period of immobilization, (multiple) injections of hyaluronic acid, supervised physiotherapy as well as specific prescription of insoles.[9,34,42] However, the majority of the patients will remain symptomatic and will progress to a surgical strategy. The choice for the specific surgical intervention in question largely depends on specific lesion factors, such as the primary or non-primary nature of the lesion, lesion dimensions, and lesion morphology.[31]

For small primary defects, first-line surgical management may consist of (arthroscopic) bone marrow stimulation or retrograde drilling.[7,9,18] For lesions that are amenable to fixation (fragmentous lesions), arthroscopic and open internal fixation procedures have proven to be effective.[15,16,19,29,30] In the case of relatively large (cystic) lesions to the talar dome or in the case of lesions that have failed prior surgical intervention(s), it is probable that more invasive surgical interventions are necessary in order to adequately address the patients' complaints.[18] These surgical interventions may consist of transplantation techniques such as (osteo) chondral transplantation, including the classical osteochondral autograft transfer system (OATS) and the chondrocyte implantation techniques.[38] Alternatively, one can consider the application of bulk allografting – a surgical technique being used whenever the lesion can be considered 'massive' and a surgeon expects insufficient autografting material can be obtained. The aforementioned techniques show adequate clinical efficacy in terms of clinical success rates, as previously assessed by Dahmen et al.[9] and Lambers et al.[18] However, it can be stated that each of the surgical techniques for larger and/or cystic OLTs are associated with specific downsides. For example, it has been proven that the OATS procedure can cause a

donor-site morbidity incidence rate ranging from 11% to 35% when the graft was harvested from the ipsilateral femoral condyle.[9,12] A different example of a specific downside can be non-union whereas for the cartilage implantation techniques the financial investment for this procedure can be regarded a downside.[1]

A potential alternative to the aforementioned techniques can be the harvesting of autologous osteoperiosteal grafts. The cylindrical usage of osteoperiosteal grafts has been previously documented by Hu et al.[12] and Chen et al.[6] and yielded clinically effective outcomes. It is however a common downside of the usage of cylindrical grafts that the size of the cylinder autograft is static and determined pre-operatively.[39]

In order to overcome the aforementioned downsides, a novel technique for the treatment of large talar osteochondral lesions had recently been developed and was previously described in the present journal for medially located lesions.[14] The *Talar Osteo-Periostic grafting from the Iliac Crest (TOPIC)* procedure utilizes the ipsilateral iliac crest with the overlying periosteal layer as harvesting location for the autograft. The periosteal layer has the potential to induce articular cartilage-like tissue regeneration as the cambium layer of the periosteum contains chondrocyte precursor cells.[13,23,26] The TOPIC bone-periosteal transplant meets the three requirements for tissue engineering for bone-cartilage repair: a source of cells, a scaffold, and local growth factors.[3,21,32,36] In addition, the curvature of the iliac crest is highly similar to the curvature of the talar bone, and the harvested graft can be exactly fitted to the excised OLT, leading to a press-fit graft.[25]

However, the previously published description of the TOPIC technique was solely limited to medially located osteochondral lesions of the talus. We know from a recent publication by van Diepen et al.[40] that 24% of the lesions that are located on the talar bone are specifically located on the lateral talar dome. The previous description focusing on medially located lesions can be considered substantially different in comparison to lateral lesions as for the medially located lesions a distal tibial osteotomy is considered a necessary first step in the procedure through which an appropriate visualization is created. Laterally located lesions can be approached without the usage of distal tibial osteotomies though require different steps for approaching the lesion. This substantiates the necessity for a detailed presentation of the surgical technique of the lateral TOPIC procedure consisting of a specific step-wise approach.

In the study, it is therefore the purpose to describe the surgical technique of the newly developed lateral TOPIC procedure, to evaluate potential pearls and pitfalls, and to present the first clinical outcomes of patients who have undergone the lateral TOPIC procedure.

Surgical principle and objective

Large symptomatic osteochondral lesions to the talus that are of primary or non-primary nature are challenging in its kind. Currently, there are many surgical techniques available for this indication with their individual advantages and disadvantages. Over the past decades, surgical and scientific attention has been focused on medially located lesions on the talar dome. However, as we are aware of the fact that 24% of the OLTs are located the lateral talar dome and that the laterally located OLTs are associated with chronic lateral ankle instability, there is a clinical necessity for presenting surgical techniques that are amenable and effective for laterally located OLTs.[2,37,40,41,43] Moreover, it is stated that concomitant lateral ankle instability is considered a negative prognostic factor regarding the clinical outcomes of surgical treatment of OLTs.[17,20,27] Consequently, this highlights the clinical relevance and importance to address laterally located lesions appropriately in the case of lesions of large (cystic) nature and in case of concomitant (chronic) lateral ankle instability. A novel innovative surgical technique for the surgical treatment of large OLTs had recently been developed and was previously described in the present journal – however, this technique exclusively focused on medially located OLTs, not on laterally located OLTs with possible concomitant (chronic) lateral ankle instability.[14] The present surgical technique paper therefore describes the surgical technique for the treatment of large (cystic) primary and secondary lateral osteochondral lesions of the talus. The technique comprises a(n) (antero)lateral arthrotomy, a press-fit talar autograft transplantation from the ipsilateral iliac crest, and a lateral ankle ligament reconstruction potentially augmented with an InternalBrace™. The technique provides a natural scaffold, good quality cells and growth factors, facilitating a replacement of the complete osteochondral unit – a triad being considered of vital importance in the treatment of these defects. Moreover, the technique can directly and simultaneously address (chronic) lateral ankle instability which is a common concomitant diagnosis for painful osteochondral lesions of the talus.[2,37,40,41,43]

Advantages

- Concomitant lateral ankle ligament reconstruction (with potential augmentation of InternalBrace™) in the case of (chronic) lateral ankle instability
- Surface geometry talus and curvature crest[25]
- Iliac crest graft provides scaffold, cells and growth factors.[3,21,32,36]
- No need for an osteotomy due to localization of the defect (whenever the lesion is located on the anterior 80% of the lateral talar dome). If the lesion is located on the posterior 20% of the lateral talar dome, a fibular osteotomy can be considered).
- Cost-effective
- Single-stage technique
- Limited operation time

Disadvantages

- Complications specifically for the harvest site, the iliac crest, and hyp(er) aesthesia skin[10]
- Potential complications to nervus peroneus superficialis due to surgical approach
- Secondary osteoarthritis

Indications

- Symptomatic large (cystic) laterally located osteochondral lesion with deep ankle pain not responding to conservative treatment with or without the presence of (chronic) lateral ankle instability
  - Anterior-posterior or medial-lateral lesion diameter should exceed 10 mm on computed tomography (CT)
  - The depth of the defect is no limitation for this procedure
- Both primary and secondary surgical lesions are eligible for treatment with a TOPIC
- In case of malalignment, a corrective osteotomy can be considered.

Contraindications

- Tibiotalar osteoarthritis grade III (Kellgren and Lawrence)
- Malignancy
- Active infectious ankle joint pathology
- Hemophilic or other diffuse arthropathy

Patient information

- Surgical risks include infection, hematoma, thromboembolic event, wound healing problems
- Transient or permanent nerve damage leading to hyper/o aesthesia of the nervus peroneus superficialis
- Non-weight bearing cast for 6 weeks, followed by a walking boot for another 6 weeks

Preoperative work-up

At the Department of Orthopedic Surgery and Sports Medicine of the Amsterdam University Medical Centers (AUMC), we have a standardized work-up for all patients as these are carefully screened for patient history (including recurring ankle sprains and/or a feeling of giving way of the ankle), undergo a thorough physical examination of both lower extremities and ankles, during which there is a specific attention for recognizable pain on palpation over the site of the osteochondral lesions the foot in plantar flexion.[31] Special emphasis is also put on the range of motion of the ankle joint, especially plantar flexion.[8] Moreover, a highly important part of the physical examination is to carefully assess whether there is presence of (chronic) lateral ankle instability that is of symptomatic nature as well.

For the confirmation of the diagnosis and the assessment as a pre-operative sizing and planning-tool, an additional dual-energy computed tomography scan (CT) is made. In our center, experienced fellowship-trained musculoskeletal radiologists and the orthopaedic surgeons assess all OLTs for lesion size, morphology, shaping as well as curvature. Lesion size is assessed three-dimensionally taking into account the morphology of the lesions in a simultaneous fashion in order to yield a 3-dimensional visualization and representation of the lesion allowing for a personalized approach.[31] The three-dimensional analysis concerns measuring

the sclerotic borders of the lesion. This is performed by measuring the lesion from the most anterior point to the most posterior point (AP-direction), as well as from the most medial point to the most lateral point (ML-direction), and finally, the depth is measured by measuring the distance from the joint line to the most distal part of a cyst most often including the caudal sclerotic zone of the cyst as this will be removed accordingly. After a careful shared-decision making process together with the patient and his/her family, the patient and the treating team will decide for the lateral TOPIC procedure together.

Instruments and implants

- Coagulation knife
- Hohmann retractors
- Oscillating saw and/or chisel with thin blades
- Beaver knife
- Hemostatic gelatin sponge (Spongostan®)
- Impactor
- Standard orthopedic set
- Chisel set
- Hintermann Distractor
- Ligament bracing equipment (Internal Brace™)

Anesthesia and positioning

- General or spinal anesthesia
- Antibiotic prophylaxis (Cefazolin 2 grams intravenous injection) is administered to each patient
- Supine position with a tourniquet applied around the thigh

Surgical technique

Step 1: Anterolateral approach

After prepping and draping, a curvilinear incision of approximately 10 centimeters is made just anteriorly from the distal fibula extending inferiorly towards the sinus tarsi joint (Figure 8.1a). The anterolateral joint capsule is exposed as well as the

inferior extensor retinaculum without damaging the superficial peroneal nerve. Hohmann retractors are placed in order to protect the neurovascular structures and the tendons. The anterior talofibular ligament (ATFL) and the anterior syndesmosis are exposed and identified. Potential anterolateral and/or anterocentral osteophytes are removed to increase exposure to the osteochondral lesion on the lateral dome. The ATFL is released from the footprint at the fibula after which the Hintermann Distractor is placed on the talar bone and the distal fibula in order to translate and subluxate the talar dome anteriorly (Figure 8.1b, 8.1c). An alternative evidence-based approach is a fibular osteotomy, through which an adequate exposure to the joint is also possible and could be performed based on surgeon's experience and preference or when the lesion is located on the far posterior part of the lateral dome (posterior 20%).[24]

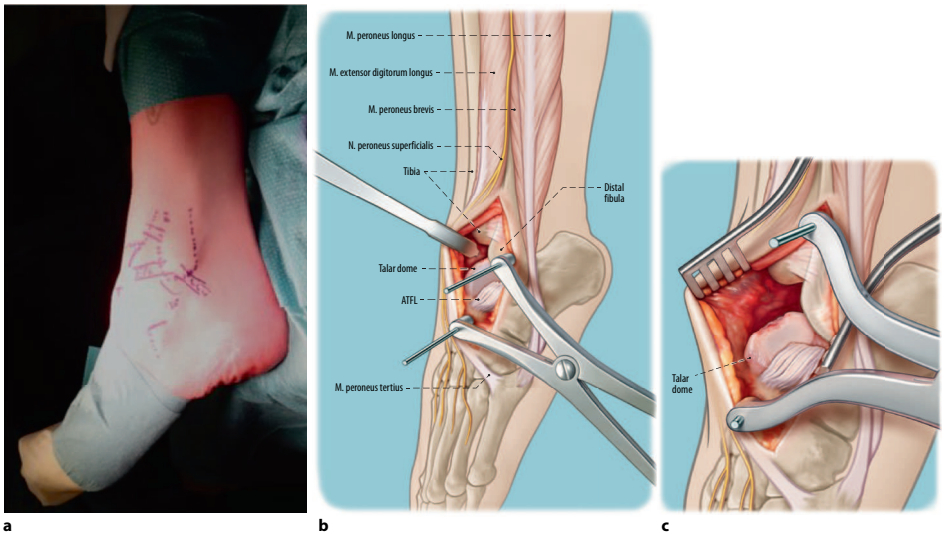
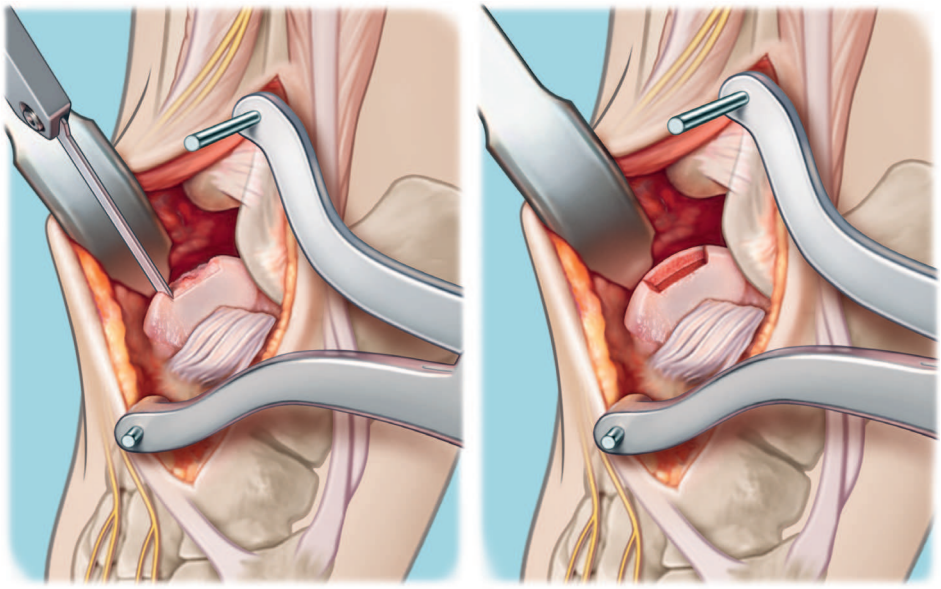


Figure 8.1: Anterolateral approach. After prepping and draping, a curvilinear incision of approximately 10 cm is made just anteriorly of the distal fibula, extending inferiorly towards the sinus tarsi joint **(a)**. The anterolateral joint capsule is exposed as well as the inferior extensor retinaculum without damaging the superficial peroneal nerve. Hohmann retractors are placed in order to protect the neurovascular structures and the tendons. The anterior talofibular ligament (ATFL) and the anterior syndesmosis are exposed and identified. Potential anterolateral and/or anterocentral osteophytes are removed to increase exposure to the osteochondral lesion on the lateral dome. The ATFL is released from the footprint at the fibula, after which the Hintermann distractor is placed on the talar bone and the distal fibula **(b)**. The talar osteochondral lesion is fully exposed due to anterior translation and subluxation of the talar dome **(c)**. An alternative evidence-based approach is a fibular osteotomy, through which adequate exposure of the joint is also possible and could be performed based on the surgeon's experience and preference or when the lesion is located on the far posterior part of the lateral dome (posterior 20%[24]).

Step 2: Excision of the diseased osteochondral defect

After adequate exposure and identification of the lesion, the cartilage is incised in a rectangular fashion to preserve as much healthy cartilage as possible and to prevent the cartilage from rupturing in the following steps of the procedure (Figure 8.2a, 8.2b). Potentially available cysts and/or present necrotic bone is resected en-bloc through the usage of a chisel with thin blades and/or an oscillating saw.



a b

Figure 8.2: Excision of the diseased osteochondral defect. (a) After adequate exposure and identification of the lesion, the cartilage is incised in a rectangular fashion to preserve as much healthy cartilage as possible and to prevent the cartilage from rupturing in the following steps of the procedure. Potentially available cysts and/or present necrotic bone is resected en bloc using a chisel with thin blades and/or an oscillating saw. **(b)** End result: total removal of the premeasured osteochondral lesion of the talus, deep enough so that healthy bone can be observed.

Step 3: (Micro)drilling of the recipient's bone base

The base of the autograft recipient is (micro)drilled so that bone marrow stimulation by means of a 2.0 mm drill takes place (Figure 8.3a). This step results in a totally debrided and pre-measured (three dimensional; anteroposterior, mediolateral, and depth) prepared recipient site with healthy bone present lesion's base (Figure 8.3b). In the case of presence of cysts extending beyond the en-bloc resection of the talar OCL, additional debridement with curettage is performed, and these cysts will be filled with spongious bone coming from the iliac crest (step 4 and 5).

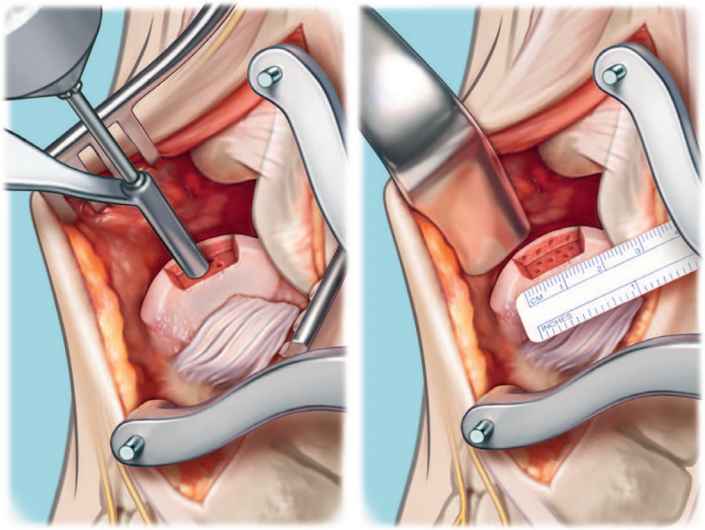


Figure 8.3: Drilling of the recipient's bone base. The base of the autograft recipient is (micro-)drilled so that bone marrow stimulation by means of a 2.0-mm drill takes place **(a)**. This step results in a totally debrided and premeasured (three dimensionally; anteroposterior, mediolateral, and depth) prepared recipient site with healthy bone present at the lesion's base **(b)**. In the case of the presence of cysts extending beyond the en bloc resection of the talar osteochondral lesion (OCL), additional debridement with curettage is performed, and these cysts will be filled with spongious bone coming from the iliac crest (Figures 8.4 and 8.5).

Step 4: Measuring and harvesting the donor autograft from the Iliac Crest

Harvesting of the graft is initiated keeping in mind the measurements of the excised OLT (as illustrated in step 3) and combining these measurements with the pre-defined CT measurements. This is performed in order to correctly approximate the donor autograft. The goal is to oversize in all directions (antero-posterior and medio-lateral diameter as well as depth) for 1 mm. The ipsilateral iliac crest is approached through a horizontal incision of 3.5 cm (Figure 8.4a). The pre-defined measurements are applied three-dimensionally when harvesting the graft. The coagulation knife should not be used in order to keep the periosteum attached to the bone. Subsequently, a monocortical, bicortical or tricortical osteoperiosteal autograft from the ipsilateral iliac crest is harvested with the use of an oscillating saw and chisel (Figure 8.4b). The combination of the width of the iliac crest and the graft's size needed dictates the selection of a monocortical, bicortical or tricortical graft. A hemostatic gelatin sponge (Spongostan®) is left in the iliac crest after harvesting.

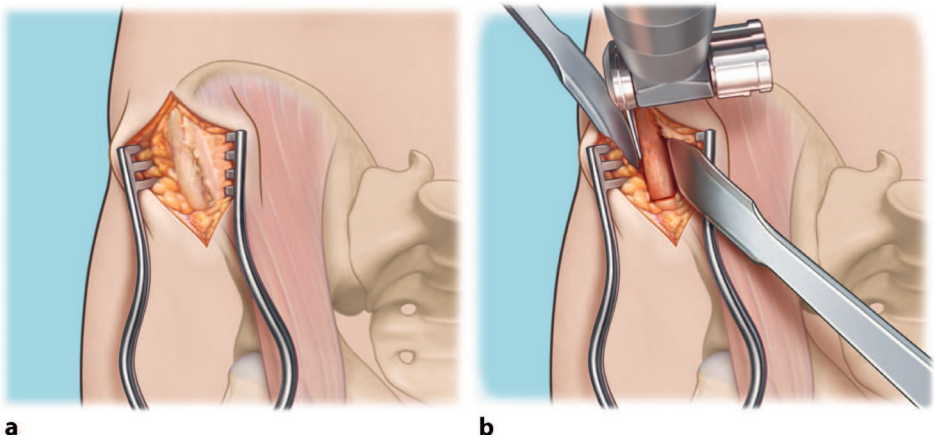


Figure 8.4: Measuring and harvesting the donor autograft from the iliac crest. Harvesting of the graft is initiated, keeping in mind the measurements of the excised osteochondral lesion of the talus (as illustrated in step 3) and combining these measurements with the predefined CT measurements. This is performed in order to correctly approximate the donor autograft. The goal is to oversize in all directions (anteroposterior and mediolateral diameter as well as depth) by 1 mm. The ipsilateral iliac crest is approached through a horizontal incision of 3.5 cm **(a)**. The predefined measurements are applied three-dimensionally when harvesting the graft. The coagulation knife should not be used, in order to keep the periosteum attached to the bone. Subsequently, a monocortical, bicortical, or tricortical osteoperiosteal autograft from the ipsilateral iliac crest is harvested with the use of an oscillating saw and chisel **(b)**. The combination of the width of the iliac crest and the graft size needed dictates the selection of a monocortical, bicortical, or tricortical graft. A hemostatic gelatin sponge (Spongostan®; Ethicon, Somerville, NJ, USA) is left in the iliac crest after harvesting.

Step 5: Adjusting the fitting shape of the autograft

The autograft is adjusted and fine-tuned to fit size, curvature, depth and morphology of the excised OLT, as described in our earlier publication[14] (Figure 8.5a). The graft should not be positioned too proud; it is best to place the graft 1 to 2 millimeters under the cartilage level of the talar dome in order to prevent a proud position of the graft. The graft will be placed press-fit; 1 mm should be added to all the dimensions of the excised OLT. An additional trick is to compare the graft to the excised OLT (in toto) in order to enhance similarity of the autograft to the excised OLT (Figure 8.5b).

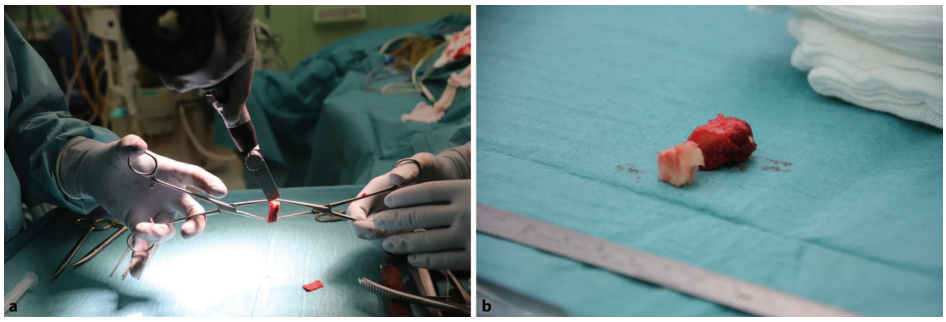


Figure 8.5: Adjusting the fitting shape of the autograft. The autograft is adjusted and fine-tuned with an oscillating saw to fit size, curvature, depth, and morphology of the excised osteochondral lesion of the talus (OLT), as described in our earlier publication **(a)**.[14] The graft should not be positioned too proud; it is best to place the graft 1 to 2 mm under the cartilage level of the talar dome in order to prevent a proud position of the graft. The graft will be placed press fit; 1 mm should be added to all the dimensions of the excised OLT. An additional trick is to compare the graft (right side of this image) to the excised OLT (in toto) in order to enhance similarity of the autograft to the excised OLT **(b)**.

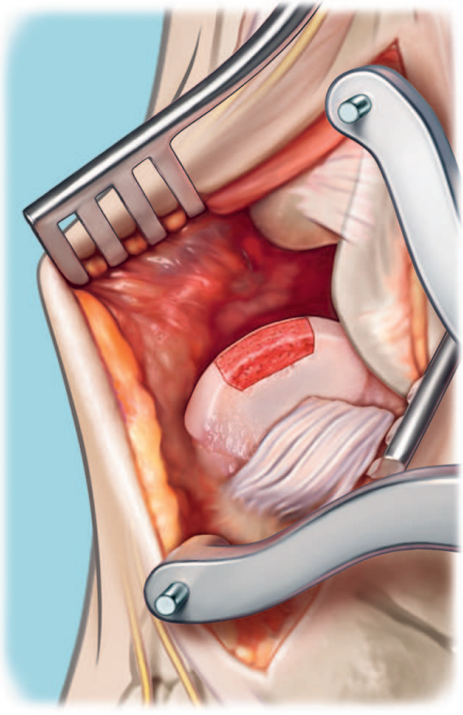


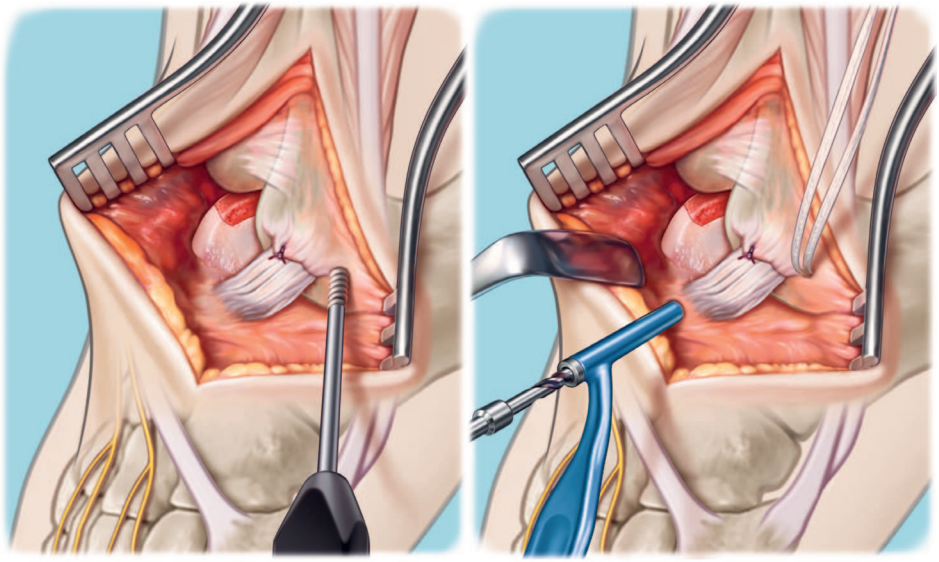
Figure 8.6: Implanting the graft through a press-fit technique. After trying and fitting the graft, the optimal fitting shape may be reached, after which the autograft is placed into the recipient site. Using a rounded impactor, the adjusted iliac crest autograft will be placed 1–2 mm underneath the level of the cartilage of the remaining talar dome. No screws are necessary to fixate the inserted autograft due to the press-fit nature of the present surgical technique. If there is instability of the graft, a potential alternative is to use one or two bioscrews to fixate the graft.

Step 6: Implanting the graft through a press-fit technique

After trying and fitting the graft, the optimal fitting shape may be reached, after which the autograft is placed into the recipient site. By making use of a rounded impactor, the adjusted iliac crest autograft will be placed 1–2 mm underneath the level of the cartilage of the remaining talar dome. No screws are necessary to fixate the inserted autograft due to the press-fit nature of the present surgical technique (Figure 8.6a). If there is instability of the graft, it is a potential alternative to utilize one or two bioscrews to fixate the graft.

Step 7: Broström and Potential Augmentation with InternalBrace™

After inserting the autograft in a press-fit manner, the range of motion (ROM) of the ankle is properly analyzed. The footprint of the ATFL is cleared and cleaned followed by the reinsertion of the ATFL with use of a bone anchor 2.4–3.5 mm as well as the overlying periosteum. In the case of a fragile ATFL, an augmentation of the ATFL re-insertion with an InternalBrace™ technique is performed (Figure 8.7a, 8.7b).



a b

Figure 8.7: Augmentation with InternalBrace™. After inserting the autograft in a press-fit manner, the range of motion (ROM) of the ankle is properly analyzed. The footprint of the anterior talofibular ligament (ATFL) is cleared and cleaned, followed by reinsertion of the ATFL with use of a bone anchor 2.4–3.5 mm and the overlying periosteum. In the case of a fragile ATFL, augmentation of the ATFL re-insertion with an InternalBrace™ technique is performed with positioning of anchors on the distal fibula and the nonarticulating surface of the lateral border of the talar dome **(a, b)**. Both the final ROM and the lateral ankle stability are tested, after which the incision layers are closed and additional rinsing takes place.

Both the final ROM and the lateral ankle stability is tested for after which the incision layers are closed and additional rinsing takes place.

Special surgical considerations

- A pre-operative dual-energy CT scan allows for an optimal radiological assessment of lesion morphology and lesion size. This method yields a 3-dimensional visualization and representation of the lesion allowing for a personalized approach both pre-operatively as well as intraoperatively.[31]
- A concomitant lateral ankle ligament reconstruction with the potential augmentation of an InternalBrace™ is clinically relevant and surgically located in an optimal position due to the (antero)lateral approach, allowing for prognostically positive outcomes.[17,20,27]
- The iliac crest autograft transplantation is adjusted for and customized for each individual patient
- Press-fit autograft transplantation allows for a one stage procedure and quick rehabilitation without the clinical necessity for intra-articular screw removal.
- An optimal (osteoperiosteal) graft to replace an osteochondral unit has the following characteristics: natural scaffold, good quality cells and growth factors.[28,35]

Postoperative management

Postoperatively a lower leg splint is provided for the first 24 hours after which a fresh circular non-weight bearing lower leg cast is applied for 2 weeks. 2 weeks post-operatively, the stitches are removed and the patient is motivated and allowed to perform dorsoplantar motion of the ankle so that postoperative deficits in range of motion in the dorsoplantar direction can be addressed. Moreover, these movements may simulate the progenitor cells from the periosteum to produce an optimal chondral layer following stimulation through ankle joint motion.[4,5]

The non-weight bearing period is 6 weeks and at the 6-week follow-up, a walking boot is applied for another 6 weeks, allowing the patient (gradual) weightbearing as tolerated. At 12 weeks post-operatively, a dual-energy computed tomography (CT) scan is performed in order to assess consolidation of the inserted iliac crest autograft. At this particular outpatient visit, a personalised physiotherapeutic plan is provided to the patient and the physiotherapist in question in order to allow for

an evidence-based individualized build-up of activities, gradual and protocol-based return to sport and work. In order to monitor the progress, the patient is clinically assessed at 6 months and 1- and 2-years postoperatively. The patient is advised to not perform any axial-loading peak forces for at least 6 months post-operatively.

Errors, hazards and complications

At every follow-up, patients are checked for potential complications, such as crest pain, hyp(er)aesthesia in the crest and ankle joint region, infections, ankle joint synovitis, and post-operative pain. A CT scan will be made respectively at 3, 12 months and 24 months after surgery to assess consolidation, talar remodeling and ingrowth of the transplant (Figure 8.8). Potential pitfalls:

- In case of inadequate restoration of lateral ankle biomechanics by means of lateral ligament reconstruction, persistent (symptomatic) lateral ankle instability may occur
- Avulsion or fracture of the Iliac Crest when harvesting the graft too close to the anterior superior iliac spine
- Proudness of the autograft might result in chondral wear or a kissing lesion to the opposing distal anterolateral corner of the ankle joint (fibula/distal tibia)
- Graft failure (rare)
- Ankle joint stiffness in dorsoplantar direction
- Persistent ankle pain because of progressive osteo-arthritis (OA) complaints
- Potential osseous impingement of the lateral gutter in the case that the graft has slight overhang or in case of presence of a lateral osteophyte or multiple osteophytes on the lateral side of the ankle joint

Figure 8.8: Pre-operative and post-operative (1 year follow-up) CT-scans of the same patient. (a) Sagittal preoperative CT scan. **(b)** Sagittal postoperative CT scan. **(c)** Coronal preoperative CT scan. **(d)** Coronal postoperative CT scan.

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Chapter 9

Talar OsteoPeriostic grafting from the Iliac Crest (TOPIC): two-year prospective results of a novel press-fit surgical technique for large, complex osteochondral lesions of the medial talus

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Abstract

Background: Press-fit Talar OsteoPeriostic grafting from the Iliac Crest (TOPIC) is a novel technique for the treatment of large osteochondral lesions of the talus. The purpose of the present study was to prospectively evaluate the 2-year clinical outcomes for patients with medial osteochondral lesions of the talus that were treated with the TOPIC procedure.

Methods: Forty-three patients were prospectively assessed before and 24 months after the TOPIC procedure. All procedures were performed through a medial distal tibial osteotomy. Clinical assessment preoperatively and at 24 months of follow-up included determination of the Numeric Rating Scale (NRS) scores for pain during walking (primary outcome), at rest, during running, and during stair-climbing. The Foot and Ankle Outcome Score (FAOS) and the Mental Component Summary (MCS) score and Physical Component Summary (PCS) score of the Short Form-36 (SF-36) were also assessed. A computed tomography (CT) scan was performed 12 weeks postoperatively to assess union of the distal tibial osteotomy site and at 1 and 2 years postoperatively to assess consolidation of the graft as well as cyst development in the graft.

Results: All enrolled patients were available for follow-up. The median NRS score for pain during walking improved from 7 points preoperatively to 2 points at 2 years postoperatively ($p < 0.001$). All other NRS scores for pain improved significantly. All FAOS subscale scores improved significantly, including those for pain (from 53 to 75), symptoms (from 50 to 61), activities of daily living (from 68 to 88), sports (from 30 to 55), and quality of life (from 19 to 38). The SF-36 PCS score improved from 43 to 48 ($p < 0.001$), and the MCS score changed from 28 to 26 ($p > 0.05$). There was a 100% rate of union of the osteotomy site at the distal tibia and 100% of the grafts showed consolidation at 1 and 2 years postoperatively.

Conclusions: The TOPIC procedure for large osteochondral lesions of the medial talar dome is an effective technique that resulted in significant improvement exceeding the minimal clinically important difference in pain scores (primary outcome) as well as in other outcomes, with 100% consolidation of the grafts.

Introduction

Currently, there is no consensus regarding the best treatment for primary or non-primary osteochondral lesions of the talus.[7,19,30,35,50] Large osteochondral lesions of the talus may require strategies that involve autograft or allograft transplantation.[44,47] However, it is known that autologous osteochondral transplantation causes donor-site morbidity in up to 35% of cases when the graft is harvested from the ipsilateral femoral condyle.[7,15] A specific disadvantage of allografts is nonunion and failure of the graft.[13,38,47] An alternative can be the implantation of autologous osteoperiosteal grafts from the iliac crest. The use of cylindrical osteoperiosteal grafts was described by Hu et al.[15] and Chen et al.,[4] who reported clinically effective outcomes. A disadvantage of cylindrical autografts is that their sizes are static and may not allow for a perfect fit on the talar side.[22,45]

To overcome these disadvantages, a novel joint-sparing technique for the treatment of large osteochondral lesions of the talus was developed.[17] This technique, known as Talar OsteoPeriostic grafting from the Iliac Crest (TOPIC), involves using the iliac crest with the overlying periosteal layer as an autograft.[16,24,25]

The primary aim of the present study was to investigate the 2-year clinical and radiographic outcomes following the use of the TOPIC procedure for the treatment of large medial osteochondral lesions of the talus. The secondary aim was to assess the outcomes of this procedure in terms of safety, reoperations, and donor-site morbidity. We hypothesized that the use of the TOPIC procedure for the treatment of large, complex, medial osteochondral lesions of the talus would be clinically effective with good radiographic and safety outcomes and low donor-site morbidity at 2 years of follow-up.

Materials and methods

The present study is a prospective, single-center, nonrandomized, clinical cohort study with a 2-year follow-up. The study was approved by the local Medical Ethics Committee at the University of Amsterdam (reference number MEC 08/326) and was performed in accordance with the current ethical standards (Declaration of Helsinki). Our center is a tertiary referral academic hospital accredited as national and international expertise center for the diagnosis and treatment of cartilage and osteochondral lesions of the foot and ankle.

Patient selection

All patients with a medial osteochondral lesion of the talus who were managed with the TOPIC procedure (Figure 9.1) and followed for a minimum of 24 months were included in this study. The indication for the TOPIC procedure was a large (> 10 mm in anteroposterior and/or mediolateral diameter and/or depth) symptomatic osteochondral lesion of the talar dome that was treated in either a primary or non-primary (i.e., underwent prior surgical treatment that failed) fashion and was determined to be not fixable[20,29] (i.e., underwent a standardized prior nonoperative treatment protocol for at least 6 months without success) in a patient with a closed epiphyseal growth plate.[17] (Relative) contraindications included rheumatoid arthritis, advanced osteoporosis, advanced osteoarthritis, concomitant painful or disabling disease of the lower limb, infectious pathology, or any kind of malignancy. Lateral and central osteochondral lesions of the talus were excluded from the analysis in order to keep the study group homogeneous.

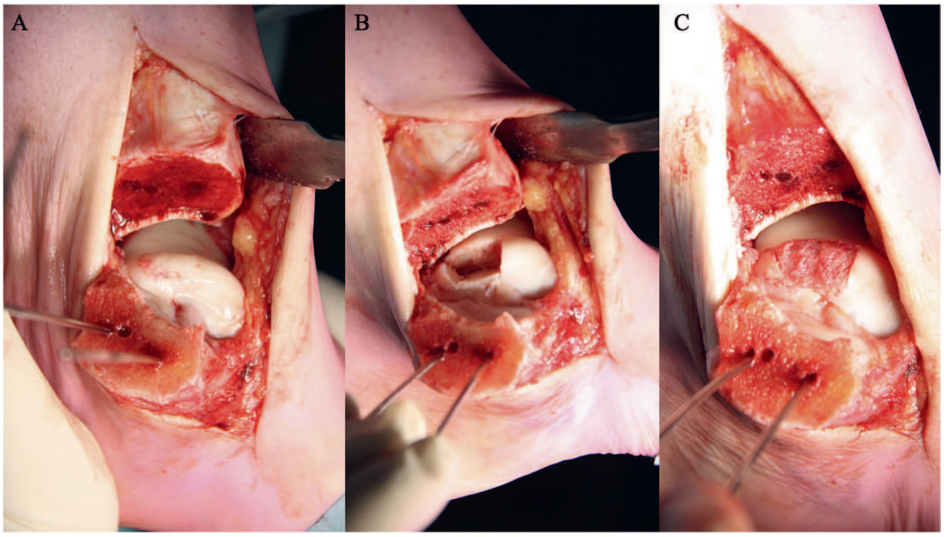

Figure 9.1: Intraoperative visualization of an osteochondral lesion (A), en bloc trapezoidal resection of the lesion (B), and press-fit insertion of the osteoperiosteal graft matching the curvature of the medial talar dome (C).

Preoperative planning

As part of our clinical workup for patients with a suspected osteochondral lesion of the talus, all patients were evaluated with a dual-energy computed tomography (CT) scan to confirm the diagnosis and to determine the location, morphology, and

size of the lesion.[30] After the diagnosis had been confirmed, patients participated in a comprehensive individualized shared decision-making process during which the different treatment options were discussed.

Surgical technique and postoperative management

All procedures were performed by 2 experienced fellowship-trained foot and ankle academic orthopaedic surgeons (G.M.M.J.K. and S.A.S.S.). The surgical technique and postoperative management have been previously described.[17] An intraoperative example is shown in Figure 9.1. When there was lateral ankle instability, a Broström/Duquennoy procedure was added in selected cases, and when there was varus or valgus hindfoot malalignment, a supramalleolar osteotomy was added.

Clinical evaluation

Standard preoperative patient demographics were extracted. Preoperative and postoperative assessment consisted of an electronic questionnaire consisting of the following patient-reported outcome measures (PROMs): the Numeric Rating Scale[12] (NRS) for pain during walking, at rest, during running, and during stair-climbing, the Foot and Ankle Outcome Score (FAOS)[46] including its subscales, and the Short Form-36 (SF-36) Mental Component Summary (MCS) score and Physical Component Summary (PCS) score.[1] Preoperatively and postoperatively, the American Orthopaedic Foot and Ankle Society (AOFAS)[8] ankle-hindfoot score was measured. To minimize the risk of bias, the treating orthopaedic surgeons were not involved in any outcome assessment. Validated Dutch versions of all questionnaires were used.[1,41,42,46]

Other, prospectively assessed clinical outcomes consisted of additional surgical procedures, complications, and donor-site morbidity. At the 2-year follow-up, patients were specifically asked to report on the presence of donor-site morbidity, which was defined as pain, disability, or hindrance related to the donor site or surrounding area affecting activities in daily living.

Radiographic evaluation

Baseline radiographic assessments included the maximum anteroposterior and mediolateral diameters and depth, surface area (ellipsoid formula: area = abπ = coronal length × sagittal length × 0.79), and volume (formula: volume = abc = coronal length × sagittal length × depth).[5] Morphological description consisted of 3

categories (fragmentary, cystic, or crater).[31] The lesion location was reported using a 9-grid scheme.[10] The preoperative stage of osteoarthritis (OA) was determined by a modified Ankle Osteoarthritis Score based on the preoperative CT scan was assessed including the presence and number of osteophytes.[6] A CT scan was performed 12 weeks postoperatively to assess union of the distal tibial osteotomy site and consolidation of the graft, and at 1 and 2 years postoperatively to assess consolidation of the graft as well as cyst development in the graft.

Statistical analysis

The primary outcome was the comparison between the NRS score for pain during walking preoperatively versus postoperatively (2 years). All statistical analyses were performed with SPSS version 28.0 (IBM). Dichotomous and categorical outcome variables were reported as absolute numbers and percentages. Continuous outcome variables were reported as means and standard deviations (SDs) in cases of a normal distribution of the data and as medians and interquartile ranges (IQRs) in cases of non-normally distributed data. Preoperative and postoperative data were compared using a paired t test in cases of normally distributed data and with a Wilcoxon signed rank test in cases of non-normally distributed data.

Interrater and intrarater reliability for the lesion size measurements and interrater reliability for the lesion morphology and location assessments were determined with a subset of 20 osteochondral lesions of the talus assessed by 2 independent raters (J.D. and Q.R.). Intrarater reliability was assessed by repeating the measurements at a 2-week interval. Lesion size measurements were assessed with use of intraclass correlation coefficient (ICC) analysis.[28] The Cohen kappa value was used to test interrater reliability for lesion location and morphological classification.[21] A consensus meeting between the 2 independent raters (J.D. and Q.R.) was organized to agree upon lesion localization and morphological category. In cases of disagreement, the senior author (G.M.M.J.K.) made the final decision.

For correlation analyses and subgroup comparisons, the principal dependent variable was the primary outcome. Data were compared between 2 subgroups using a Mann-Whitney U test for non-normally distributed data and a 2-sample unpaired t test for normally distributed data. One-way nonparametric analysis of variance (ANOVA) using a Kruskal-Wallis test was used to compare the dependent variable among the different morphological groups and the OA subgroups. Significance values were adjusted by the Bonferroni correction for multiple tests in case of

significance. A Spearman rho test was used for the assessment of correlation of continuous non-normally distributed data with the principal dependent variable, and a Pearson rho test was used for the assessment of correlation of continuous normally distributed data. The level of significance was set at $p < 0.05$.

A prospective sample size calculation was performed to detect a minimal clinically important difference (MCID) of 1.0 point on the NRS for pain during walking between baseline and follow-up.[34] The calculation indicated that 34 ankles were needed. To correct for a potential loss to follow-up of 15%, the required sample size for the present study was 39 ankles.

Source of funding

No external funding was received for this study. The authors did not receive grants or outside funding in support of their research or for preparation of this manuscript.

Results

A total of 44 patients were eligible for inclusion. One patient underwent an arthroscopic ankle arthrodesis before the 2-year follow-up and was excluded in order to not assess the outcomes of the arthrodesis (Figure 9.2). Thus, 43 patients were assessed. No patients were lost to follow-up. Patient demographics are summarized in Table 9.1, and preoperative radiographic characteristics are shown in Table 9.2. An example of a preoperative 3D visualization of a typical lesion is shown in Figure 9.3.

Clinical outcomes

NRS for pain

The primary outcome, the NRS for pain during walking, decreased from a median of 7 (IQR: 5 to 8) preoperatively to a median of 2 (IQR: 1 to 5) postoperatively ($p < 0.001$) (Figure 9.4). The change in the NRS score for pain during walking for each patient is shown in Figure 9.5.

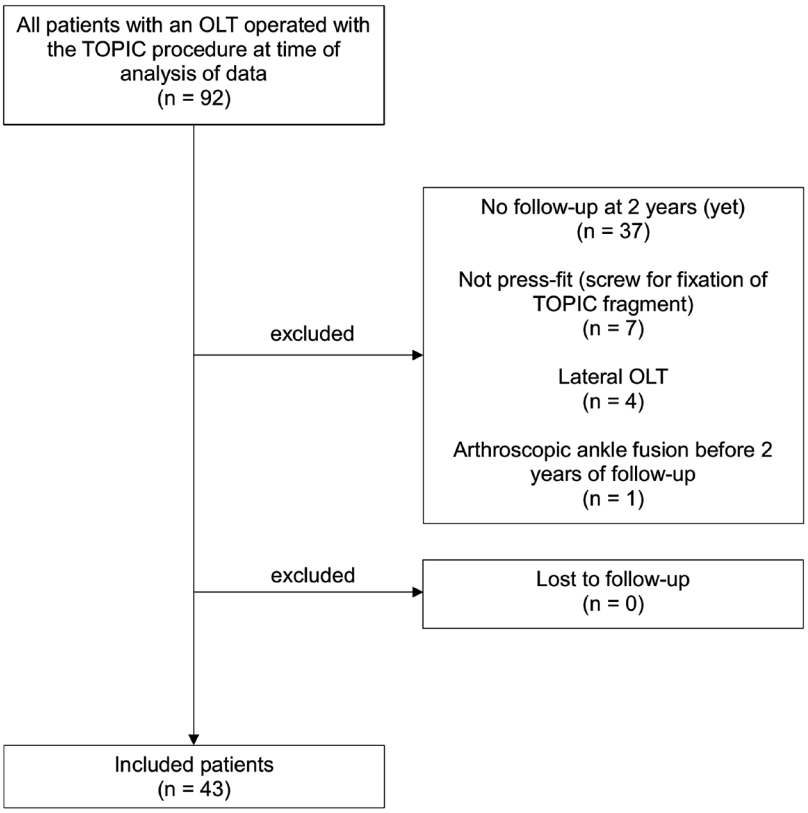

Figure 9.2: Flowchart of patient selection. OLT, osteochondral lesion of the talus.

Table 9.1: Preoperative patient demographics

Factor	Value
Patient age* (yr)	29 [21–37]
Body mass index* (kg/m^2)	26 [22–29]
Follow-up* (mo)	26 [24–30]
Right/left	23 (53%)/20 (47%)
Male/female	13 (30%)/30 (70%)
Smoking, yes/no	7 (16%)/36 (84%)
Concomitant lateral ankle instability, yes/no	8 (19%)/35 (81%)
Concomitant procedures performed during TOPIC	4 (9%) (3 Duquennoy procedures, 1 supramalleolar osteotomy)
Patients with primary/non-primary lesion	14 (33%)/29† (67%)
Total no. of previous operations for osteochondral lesion	39
Mean no. of previous operations for osteochondral lesion per patient	0.9

* Median [IQR]. † Nineteen patients had 1 previous operation and 10 had > 1.

Table 9.2: Preoperative radiographic characteristics

Factor	Value
Lesion size*	
Anteroposterior diameter (mm)	18 [17–21]
Mediolateral diameter (mm)	13 [10–15]
Depth (mm)	10 [8–14]
Surface area (mm^2)	177 [148–243]
Volume (cm^3)	2.4 [1.6–3.7]
Lesion location on 9-grid scale[28]	
Location 4	29 (67%)
Location 7	14 (33%)
Lesion morphology	
Crater	22 (51%)
Cystic	19 (44%)
Fragmentary	2 (5%)
Preoperative ankle osteoarthritis stage[29]	
Median [IQR]	1 [1–2]
No. (%) of patients with:	
Stage 0	1 (2%)
Stage 1	31 (72%)
Stage 2	11 (26%)
Stage 3	0 (0%)
Preoperative osteophytes	
No. of patients	39 (91%)
Total no. osteophytes	77
Mean no. of osteophytes per patient	1.8

* Median [IQR].

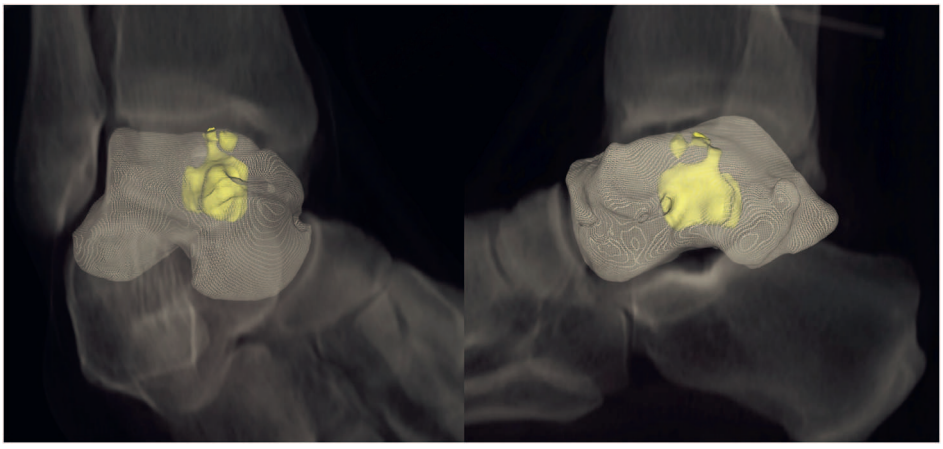

Figure 9.3: Preoperative 3D visualization of a cystic osteochondral lesion (same lesion as in Figure 9.8) that has a 3D volume measurement of 2,249 mm^3.

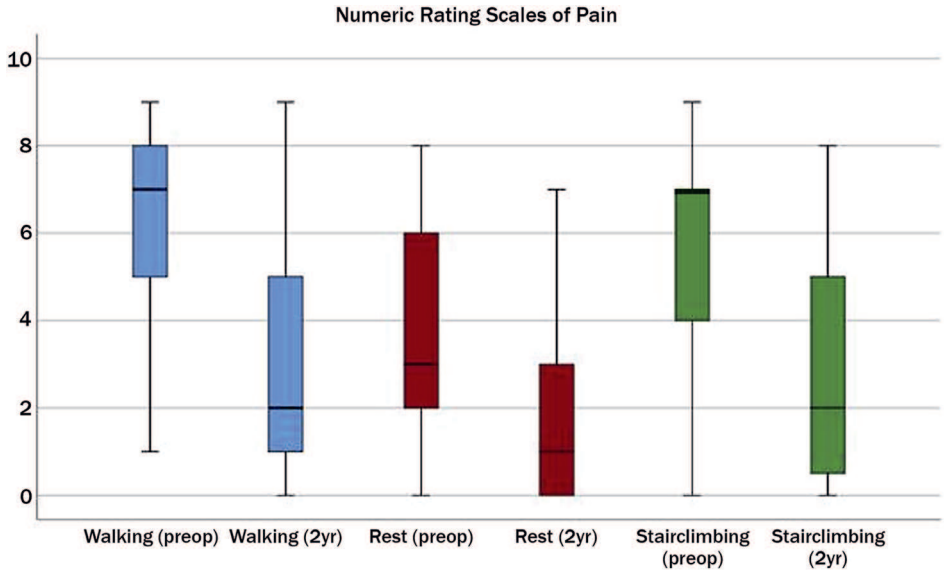

Figure 9.4: Preoperative and postoperative (2-year) Numeric Rating Scale scores for pain during walking, at rest, and during stair-climbing. The IQR is indicated by a box, the median is indicated by a line within the box, and the whiskers indicate the highest and lowest values.

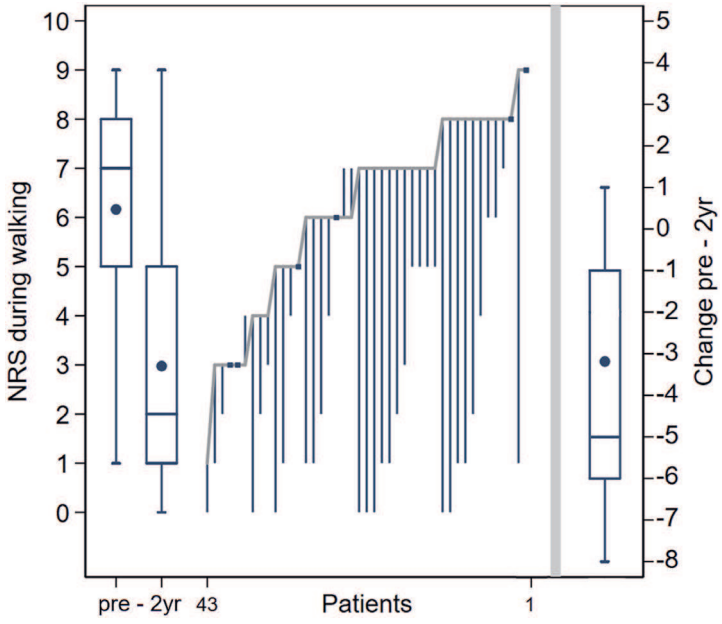

Figure 9.5: Preoperative to postoperative (2-year) changes in Numeric Rating Scale scores for pain during walking for each patient. The bars on the left side indicate the preoperative and 2-year scores for the series as whole, and the bar on the right side indicates the change between the preoperative and postoperative scores for the series as a whole; the IQR is indicated by a box, the median is indicated by a line within the box, the dot in the box plot represents the mean, and the whiskers indicate the highest and lowest values.

The NRS score for pain at rest decreased from a median of 3 (IQR: 2 to 6) preoperatively to a median of 1 (IQR: 0 to 3) postoperatively ($p < 0.001$). The NRS score for pain during stair-climbing decreased from a median of 7 (IQR: 4 to 7) preoperatively to a median of 2 (IQR: 0.5 to 5) postoperatively ($p < 0.001$) (Figure 9.4). The NRS for pain during running decreased from a median of 9 (IQR: 8 to 9) preoperatively to a median of 4 (IQR: 1 to 6) postoperatively ($p < 0.001$); this variable was analyzed for the 29 patients in the series who were able to run preoperatively and postoperatively (Figure 9.6).

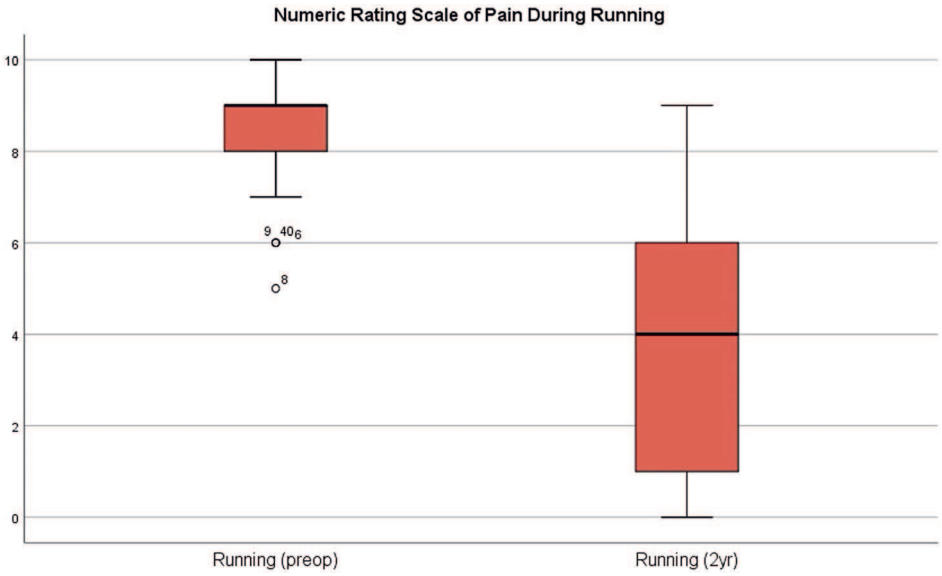

Figure 9.6: Preoperative and postoperative (2-year) Numeric Rating Scale scores for pain during running. The IQR is indicated by a box, the median is indicated by a line within the box, and the whiskers indicate the highest and lowest values. Observed data points (small circles) outside the boundaries of the whiskers are plotted as outliers.

AOFAS

The AOFAS scores are presented in Figure 9.7.

FAOS and SF-36

The preoperative and postoperative FAOS and SF-36 subscale scores are shown in Table 9.3.

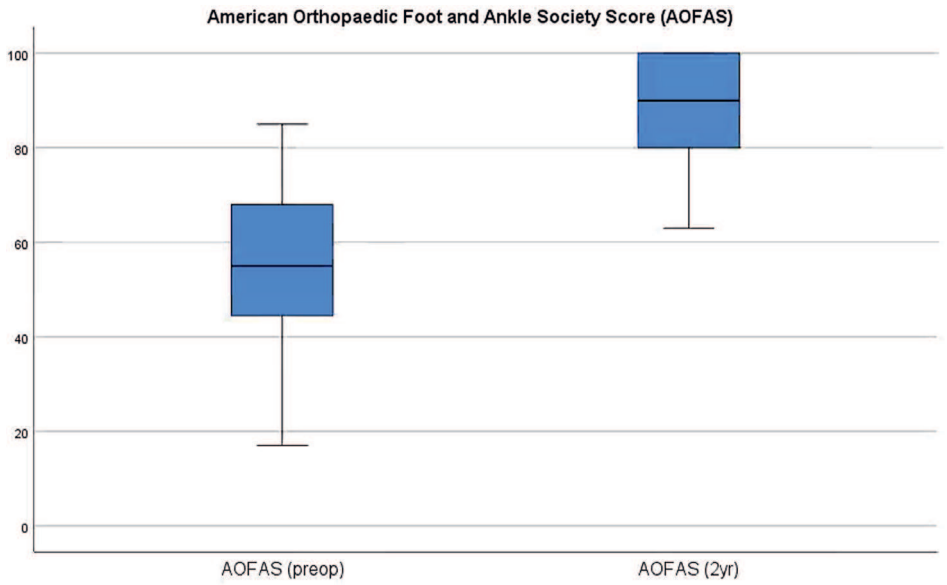

Figure 9.7: Preoperative and postoperative (2-year) AOFAS scores. The IQR is indicated by a box, the median is indicated by a line within the box, and the whiskers indicate the highest and lowest values.

Table 9.3: Preoperative and postoperative FAOS and SF-36 subscale scores

	Preoperative median [IQR]	Postoperative median [IQR]	p-value*
FAOS			
Pain	53 [44–64]	75 [53–89]	< 0.001
Symptoms	50 [39–64]	61 [43–71]	< 0.05
Activities of daily living	68 [51–81]	88 [71–97]	< 0.001
Sports	30 [20–45]	55 [30–75]	< 0.001
Quality of life	19 [6–31]	38 [25–56]	< 0.001
SF-36			
PCS	43 [36–48]	48 [44–56]	< 0.001
MCS	28 [24–32]	26 [23–31]	Not significant

* Wilcoxon signed rank test.

Radiographic outcomes

One hundred percent of the CT scans were performed at 12 weeks postoperatively and at 2 years postoperatively, although 1 patient did not have a CT scan at 1 year postoperatively due to a pregnancy.

There was a 100% rate of union of the distal tibial osteotomy site at 3 months postoperatively. One hundred percent of the grafts showed consolidation at 3 months

and at 1 and 2 years postoperatively. The 1-year postoperative CT scans showed cyst formation in the graft in 48% of the patients, and the 2-year postoperative CT scans showed cyst formation in the graft in 67% of the patients. Interobserver reliability and intraobserver reliability related to radiographic characteristics are shown in Appendix 9.1. Examples of preoperative and postoperative CT scans are shown in Figures 9.8, 9.9, and 9.10.

Additional surgical procedures, donor-site morbidity, and complications

Additional surgical procedures are described in Table 9.4. There were 4 complications (9%). Two of these were hypoesthesia: 1 case of temporary hypoesthesia around the iliac crest wound and 1 case of ongoing hypoesthesia of the first web space. One patient developed complex regional pain syndrome (CRPS) postoperatively, and 1 had a fracture within the osteoperiosteal graft 23 months postoperatively. The fracture was treated nonoperatively and clinical symptoms improved. No patients reported symptoms related to donor-site morbidity at the 2-year follow-up.

Table 9.4: Additional surgical procedures

	No. (% of total no. of included patients)
Total no. of patients requiring additional surgery*	16 (37%)
Total no. of additional operations	19
Total no. of additional sub-procedures performed during the additional operations	35
	No. (% of total no. of additional procedures)
Total no. of procedures related to graft†	5 (14%)
Arthroscopic shaping/reduction of the graft	2 (6%)
Arthroscopic shaping of the graft and debridement/bone marrow stimulation of the graft	2 (6%)
Open shaping/reduction of graft	1 (3%)
Procedures unrelated to graft†	30 (86%)
Implant removal for discomfort at osteotomy site	15 (43%)
Arthroscopic debridement for ankle impingement	8 (23%)
Open debridement for ankle impingement	2 (6%)
Open and arthroscopic debridement for ankle impingement	2 (6%)
Other, minor procedures	3 (9%)

* No. (% of total no. of included patients). † No. (% of total no. of additional procedures).

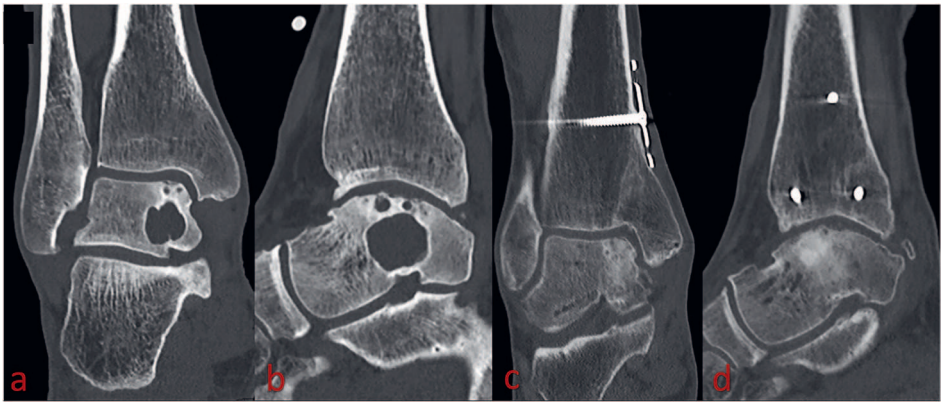

Figure 9.8: Preoperative and 2-year postoperative CT scans of patient example 1. (A) Preoperative coronal CT scan. **(B)** Preoperative sagittal CT scan. **(C)** Postoperative coronal CT scan. **(D)** Postoperative sagittal CT scan.

Figure 9.9: Preoperative and 2-year postoperative CT scans of patient example 2. (A) Preoperative coronal CT scan. **(B)** Preoperative sagittal CT scan. **(C)** Postoperative coronal CT scan. **(D)** Postoperative sagittal CT scan.

Figure 9.10: Preoperative and 2-year postoperative CT scans of patient example 3. (A) Preoperative coronal CT scan. **(B)** preoperative sagittal CT scan. **(C)** Postoperative coronal CT scan. **(D)** Postoperative sagittal CT scan.

Subgroup and correlation analyses

Subgroup analyses with the primary outcome as dependent variable are shown in Table 9.5 and factors correlated with the primary outcome, in Table 9.6.

Table 9.5: Subgroup analyses*

Factor	Median NRS [IQR]	p-value
2 subgroups		
Primary/non-primary lesion treatment		0.326
Primary (n = 14)	1.5 [0–4]	
Non-primary (n = 29)	3.0 [1–5]	
Sex		0.056
Male (n = 13)	2.0 [0–3]	
Female (n = 30)	3.5 [1–6]	
Smoking		0.790
Yes (n = 7)	2.0 [1–5]	
No (n = 36)	2.5 [0–7]	
Graft cyst(s) at 2-year follow-up		0.704
Yes (n = 29)	2.0 [1–5]	
No (n = 14)	2.5 [1–4]	
> 2 subgroups		
Osteoarthritis		Pairwise comparisons: 0 vs. 1: 0.177, 0 vs. 2: 0.177, 1 vs. 2: 0.456
Stage 0 (n = 1)	0 [NA]	
Stage 1 (n = 31)	2.0 [1–5]	
Stage 2 (n = 11)	3.0 [2–4]	
Stage 3 (n = 0)	—	
Morphology		Pairwise comparisons: cystic vs. crater: 0.698, cystic vs. fragmentary: 0.731, crater vs. fragmentary: 0.857
Cystic (n = 19)	2.0 [1–5]	
Crater (n = 22)	2.5 [1–5]	
Fragmentary (n = 2)	3.0 [NA]	

* NA = not applicable due to < 3 values.

Table 9.6: Correlation of continuous data with primary outcome

Factor	Correlation coefficient	p-value
Age	0.142	0.364
Body mass index	0.376	0.013
Lesion size		
Anteroposterior	-0.133	0.395
Mediolateral	0.072	0.648
Depth	-0.156	0.318
Surface	0.014	0.927
Volume	-0.065	0.677

Discussion

In our prospective study, the TOPIC procedure proved to be a clinically effective and safe technique for large medial osteochondral lesions of the talus, with good mid-term functional results and consolidation of all grafts and medial distal tibial osteotomy sites on the postoperative CT scans. The median improvements of 5 points on the NRS for pain during walking and of 35 points on the AOFAS scale are considered highly effective, as a mean improvement of 2 on the NRS of 0 to 10 is significantly associated with “much better” and is (far) beyond the MCID.[33]

An advantage of the TOPIC procedure is that it is a single-stage technique that requires limited surgical time.[17] Additionally, the geometry of the iliac crest matches the talar geometry and it has a chondrogenic potential due to the periosteal layer.[16,35] As such, the iliac crest autograft provides a scaffold, an appropriate bone block, and growth factors.[3,23,32,43] All transplantation techniques have the potential disadvantage of a less than fully anatomical fit and thus new cyst formation. Cyst formation was observed in our study, but it has not been found to have any correlation with clinical symptoms at 2-year follow-up.[15] Another advantage of the TOPIC procedure is that the defect depth is not a limiting factor when determining whether the procedure is indicated. Lastly, if the TOPIC procedure fails, a repeat TOPIC procedure, an allograft procedure, an ankle arthrodesis, or a total ankle replacement are among the salvage procedures to be considered.[17]

The access route to the talar dome through a fairly large osteotomy of the medial distal tibia may be considered a relative disadvantage of the procedure. In our cohort, all osteotomy sites showed complete union on CT scans performed 3 months postoperatively. The screw was removed in 15 patients (43%) because of concern that it would cause discomfort.

With regard to the indications for the TOPIC procedure as compared with the autologous osteochondral transplantation procedure, autologous osteochondral transplantation is indicated for 100 and 150-mm^2 lesions,[40] reflected by preoperative defect sizes ranging from 78 to 113 mm^2 in the literature,[14,37,40] whereas the median surface area of the defects in our analyzed cohort was 177 mm^2 and in some cases the surface area was twice as large as the area suitable for autologous osteochondral transplantation. Another important comparison in the context of indications is the percentage of prior surgical procedures. In a large study on autologous osteochondral transplantation by Shimozono et al.,[40] the percentage of primarily treated osteochondral lesions of the talus ranged from 75% to 81%, while in our study the percentage was 33%. However, the 2 procedures are similar with regard to reoperation rates and the clinical outcomes.[14,36,37,40] With regard to donor-site morbidity, Shimozono et al.[39] found that the estimated proportion of this complication ranged from 7% to 11% after autologous osteochondral transplantation and a retrospective study[26] showed that donor-site morbidity of the knee after autologous osteochondral transplantation led to functional impairments in patients with previously asymptomatic knees. In our prospective study, the patients were specifically asked to report donor-site morbidity of the iliac crest; none reported functional impairments due to iliac crest donor-site morbidity, which is in line with studies by Wang et al.[49] and Shi et al.,[36] who also used an autograft harvested from the iliac crest.

With regard to indications and demographic factors, the application of bulk allograft is comparable with the TOPIC procedure.[2,9,11,27,38,49] In a recent publication by Fletcher et al.,[11] the preoperative size (volume as based on CT scans) was 1879 mm^3, which is 22% smaller than that in our cohort (2400 mm^3). Concerning the reoperation rate, fresh osteochondral allograft transplantation was associated with an additional surgery rate of 48%,[11] which is substantially different from the rate of 37% in our study. It must also be noted that the majority of the additional procedures in our study were implant removal unrelated to the graft, which is considered a minor procedure not requiring access to the joint. A comparative analysis of survival of the TOPIC graft versus the allograft procedure may not be applicable as we did not include long-term follow-up with an appropriate survival analysis. However, the survival rate at 2 years of follow-up in our cohort was 98%, which is higher than the 87% extracted from the literature on osteochondral allograft transplantation.[27]

Our study has limitations. It was limited to a single treatment arm, and only medial osteochondral lesions of the talus were included even though central and lateral TOPIC procedures are also performed at our institution.[8] Another limitation is the low statistical power concerning the subgroup analyses and potentially correlated factors. Strengths of the present study are the prospective nature, the 100% follow-up rate, and the usage of a high number and diverse set of clinical outcome scores. Moreover, 2 independent raters scored the CT scans for both preoperative measurements and postoperative outcomes with high interrater reliability as well as intrarater reliability. Lastly, due to the prospective power calculation, the study was sufficiently powered for the primary outcome.

Conclusions

The novel press-fit TOPIC procedure for large primary and secondary osteochondral lesions of the medial talar dome is an effective and safe surgical technique with good short-term clinical results (significant decrease in pain, the primary outcome) and with 100% radiographic incorporation of the grafts. As such, the procedure may serve as a clinically effective joint-sparing alternative to an autologous osteochondral transplantation procedure, a bulk allograft, an (arthroscopic) ankle arthrodesis, and a total ankle replacement. Future research is necessary to assess long-term results of the TOPIC procedure, effectiveness in other centers, as well as the efficacy for central and lateral talar lesions.

Acknowledgements

The authors thank Dr. J.G.G. Dobbe for his contribution concerning the 3D visualization of a preoperative osteochondral lesion of the talus.

Appendix 9.1

Supporting material provided by the authors is posted with the online version of this article as a data supplement at jbjs.org (https://links.lww.com/JBJS/H595).

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Chapter 10

Sex-specific analysis in patients undergoing Talar OsteoPeriostic grafting from the Iliac Crest (TOPIC) for large osteochondral lesions of the talus

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Abstract

Purpose: Talar OsteoPeriostic grafting from the Iliac Crest (TOPIC) is a novel technique for the treatment of large osteochondral lesions of the talus. It is the purpose of the present study to assess the gender-specific differences in the presentation and outcomes following TOPIC between male and female patients.

Methods: A prospective comparative analysis was performed comparing consecutive female and male patients having been treated by the press-fit TOPIC procedure. Clinical comparative assessment pre-operatively and at 12 months of follow-up included determination of the Numeric Rating Scale (NRS) scores for pain during walking (primary outcome), at rest, and during stair-climbing. The Foot and Ankle Outcome Score (FAOS) was also assessed. A computed tomography (CT) scan was performed 10–12 weeks postoperatively to assess union of the distal tibial osteotomy site and at 1 years postoperatively to assess consolidation of the graft as well as cyst development in the graft.

Results: A total of 48 patients (30 women, 18 men) were eligible for inclusion. Men presented with OLTs significantly larger in diameter (155 mm, 134–195 mm versus 208 mm, 184–249 mm, $p < 0.0090$) when compared with women. Both men and women demonstrated significant functional improvements post-operatively, although there was no significant difference between men and women (n.s.). There was a greater improvement in postoperative FAOS pain scores in women. At 1-year post-operatively, all patients with a CT scan (n = 47) showed graft consolidation. Cyst formation was present in 11 females (37% of the group) and 10 males (59% of the group), respectively ($p = 0.24$). There were no statistical differences in complication rates following the TOPIC procedure, although a higher proportion of women did require hardware removal.

Conclusion: Both male and female patients showed clinically relevant improvements in the clinical outcomes after undergoing the TOPIC procedure, with significant differences in pre-operative size. There were no statistical differences in complication rates following the TOPIC procedure, although a higher proportion of women did require hardware removal. TOPIC procedure is a good treatment strategy for large OLTs in both men and women.

Level: Prospective comparative cohort, level 3.

Keywords: OCD · Ankle · TOPIC · Return-to-sports

Introduction

At present, the optimal approach to treating primary and non-primary osteochondral lesions of the talus remains a matter of debate within the medical community.[5,19,22,29] Managing large osteochondral lesions in the talus often necessitates techniques such as autograft or allograft transplantation.[26,28] However, it is worth noting that autologous osteochondral transplantation from the ipsilateral femoral condyle has been associated with donor-site morbidity in a substantial proportion of cases, reaching up to 35%.[5,16] Conversely, allografts come with their own set of challenges, including the risk of nonunion and graft failure.[12,23,28] In an effort to address these limitations, the Talar OsteoPeriostic grafting from the Iliac Crest (TOPIC) technique was developed as a novel approach for treating substantial osteochondral lesions of the talus while preserving the joint.[6,8,17] Preliminary results from a recently published series with a two year prospective follow-up, have shown encouraging clinical outcomes.[6]

Specifically, the study focused on assessing pain during weight-bearing using the Numeric Rating Scale (NRS) as the primary outcome, and the authors made an attempt to compare the differences in this primary outcome between male and female patients: no significant differences were observed between male and female patients in this regard. However, it is essential to emphasize that this subgroup analysis was limited to the primary outcome of the study and did not entail any other parameters, such as radiological outcomes, demographics analytics, or any other clinically relevant parameters. Interestingly, recent investigations by Gianakos et al.[14,15] concerning bone marrow stimulation and autologous osteochondral transplantation for talus osteochondral lesions have hinted at potential gender-related disparities in presentation and treatment outcomes. It is of utmost clinical relevance and importance to study potential sex-related differences in the presentation and outcomes after treatment of osteochondral lesions of the talus as novel knowledge on this field can enhance our understanding of the condition and may enable a more tailored and personalized approach for the individual patient.[13]

Consequently, it is our primary objective of the present study to delve deeper into sex-specific distinctions in clinical outcomes at the 1- and 2-year marks after employing the TOPIC procedure for large osteochondral lesions of the talus. Our secondary aim encompasses evaluating sex-specific variations related to demographic and radiological presentation, as well as other outcomes such as safety, radiological findings, reoperations, and more, following the TOPIC procedure for

talus osteochondral lesions. In light of these considerations, we hypothesize that no significant discrepancies may exist between male and female patients undergoing the TOPIC procedure in terms of presentation and overall outcomes.

Methods

The present study is a prospective, single-center, nonrandomized, comparative clinical cohort study with a 1-year follow-up. The study performed in accordance with the current ethical standards (Declaration of Helsinki) and approved by the local Medical Ethics Committee at the University of Amsterdam (W14_237#14.17.0288). The Amsterdam UMC is a tertiary referral academic hospital and is accredited as (inter)nationally recognized expertise center for the diagnosis and treatment of cartilage and osteochondral lesions of the foot and ankle.

Patient selection

All patients with a medialosteochondral lesion of the talus who were operated with the press-fit TOPIC procedure and had a minimal follow-up of 12 months were candidates to be included in this study. All procedures were performed by two experienced fellowship-trained foot and ankle academic orthopaedic surgeons (S.A.S.S. & G.M.M.J.K). The indications and contra-indications, as well as the preoperative planning, surgical technique and postoperative rehabilitation process have been described in our previous studies.[8,17,20] It was chosen to exclude lateral and central osteochondral lesions of the talus from the analysis in order solely focus on the potential sex-related differences and exclude possible confounding factors, as location has been shown to be a confounding factor.[15]

Clinical evaluation and outcome assessment

Preoperative patient demographics were extracted conform the previously published report.[6] The evaluation of patients both before and after surgery involved the utilization of an electronic questionnaire encompassing a set of Patient-Reported Outcome Measures (PROMs). These measures included Numeric Rating Scales (NRS)[11] to assess pain levels during various activities such as walking, resting, and stairclimbing. Additionally, the Foot and Ankle Outcome Score (FAOS)[27] along with its respective subscales[1] were employed. Additionally, preoperatively and postoperatively, the American Orthopaedic Foot and Ankle Society (AOFAS)[18] ankle-hindfoot score was taken. To minimize the risk of bias,

the treating orthopaedic surgeons were not involved in any outcome assessment. For all questionnaires, a version validated in the native language was used.[1,24,25,27] Additional clinical outcomes included a prospective evaluation of the occurrence of additional surgical procedures, complications, and the presence of donor-site morbidity. Patients were actively encouraged to report any donor-site morbidity at the two-year follow-up, with such morbidity defined as any pain, disability, or hindrance in or around the operated area that affected daily activities.

Radiological evaluation

As previously described, baseline radiological assessments included the following parameters: maximum anteroposterior, mediolateral and depth diameters, surface assessment (ellipsoid formula: area = abπ = coronal length x sagittal length x 0.79) and volume assessment (formula: volume = abc = coronal length x sagittal length x depth).[4,10] Morphological description was described in three categories (fragmentous, cystic, crater).[6,21] Lesion location was assessed with the 9-grid scheme. A 10-12-week postoperative CT scan was performed to assess distal tibia osteotomy union and consolidation of the graft. At one year postoperatively, a new CT scans was taken to assess consolidation of the inserted graft and cyst development within the graft.

Statistical analyses

The primary outcome was the comparison of the numeric rating scale (NRS) of pain during walking at 1 year postoperatively between the female and male population included in the study cohort. All other (comparative) outcomes were noted as secondary outcomes of the present study and were also compared on the basis of gender – similar to the primary outcome of the study. Statistical analyses were carried out Python version 3.11.4 with SciPy package (version 1.11.2). For dichotomous and categorical outcome variables, we presented the results as absolute numbers and corresponding percentages. In cases where the data followed a normal distribution, continuous outcome variables were expressed as means with accompanying standard deviations. Conversely, for non-normally distributed data, we utilized medians and interquartile ranges (IQR) for representation. To assess the differences between preoperative and postoperative data, we employed paired t-tests for normally distributed data and the Wilcoxon signed rank test for non-normally distributed data. Data of both groups (female versus male) were compared using the unpaired t-test, the Mann-Whitney U test, the Chi-Squared or the Fisher's exact test depending on the normality of distribution and depending on the type of data (continuous or non-continuous).

Inter-rater and intra-rater reliability for lesion size was assessed in a previous study which analyses a subset (n = 20) of the currently included study population and showed good to excellent outcomes.[6] Hence, these measurements were not performed again for the sake of the present study. A consensus meeting consisting of 2 independent raters (J.D. and Q.G.H.R) was organised to agree upon lesion localization and morphology. The decision of the senior author (G.M.M.J.K) was considered decisive in case of disagreement.

Results

Clinical and radiological characteristics

A total of 48 patients were eligible for inclusion. As such, 48 patients were assessed. No patients were lost to follow-up. Patient demographics are summarized in Table 10.1, radiological demographic characteristics in Table 10.2.

Table 10.1: Patient demographics

	Female (n = 30)	Male (n = 18)	p-value
Patient age* (yr)	28.0 [20.0–45.2]	33.0 [25.0–35.5]	0.390
BMI* (kg/m^2)	24.6 [22.2–26.8]	26.9 [23.3–29.2]	0.405
Right/left ankle	16 (53%) / 14 (47%)	9 (50%) / 9 (50%)	1.0
Smoking (yes/no)	4 (13%) / 26 (87%)	5 (28%) / 13 (72%)	0.317

* Median [IQR].

Table 10.2: Baseline radiological lesion characteristics

Variable	Female	Male	p-value
Lesion size			
Anteroposterior (AP) diameter (mm)*	17.5	21	N/A
Mediolateral (ML) diameter (mm)*	11.5	14	N/A
Depth (mm)*	9	11	N/A
Surface area (mm^2)	155 [134–195]	208 [184–249]	0.0090
Volume (cm^3)	1.8 [1.5–2.4]	3.0 [1.9–4.5]	0.0135
Lesion location on 9-grid zone			0.07
Zone 4	16	15	
Zone 7	14	3	
Lesion morphology			0.07
Crater	10	5	
Cystic	18	12	
Fragmentous	2	1	

* Median [IQR].

Clinical outcomes

Numeric rating scale of pain

The primary outcome, the NRS of pain during walking, decreased from a median of 6 [IQR: 5–7] preoperatively to a median of 2.5 [IQR: 1–4] postoperatively at 1 year for the female group. For the males, the NRS during walking decreased from 6.0 [IQR: 3–8] to 3 [IQR: 2–5]. This is visualized in Figure 10.1. No between-group significant differences could be found at any timepoint in the follow-up.

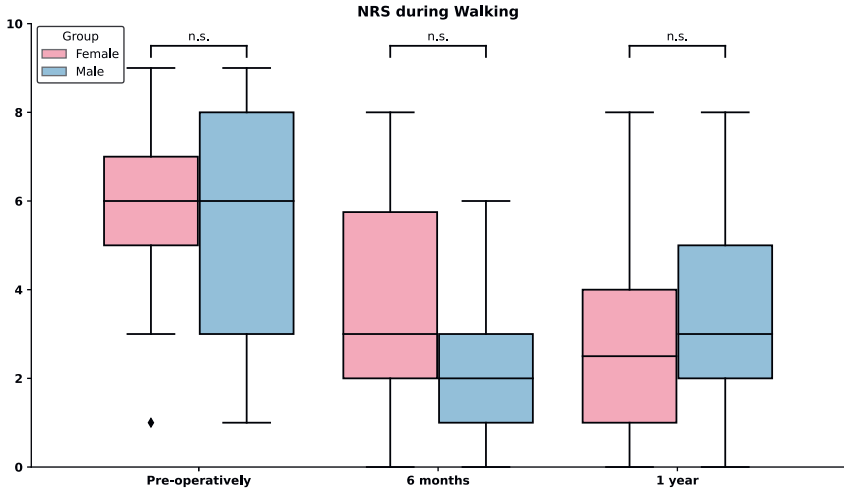

Figure 10.1: NRS during walking for females and males.

The NRS of pain in rest, decreased from a median of 3 [IQR: 2–5.5] preoperatively for females and 2 [IQR: 0.5–5] for males to a median of 1 [IQR: 0–3] and 1 [IQR: 0.2–2.8] postoperatively, respectively (subgroup difference at 1-year: p = 0.939). The NRS of pain during stairclimbing, decreased from a median of 6.5 [IQR: 4.2–7] preoperatively for females and 5 [IQR: 3–7] for males to a median of 1.5 [IQR: 1–5] and 2.5 [IQR: 1–4] postoperatively, respectively (subgroup difference at 1-year: p = 0.589). These secondary outcomes are visualized in Figure 10.2.

American Orthopaedic Foot and Ankle Society Score (AOFAS)

The outcomes of the AOFAS scores are presented in Figure 10.3.

Foot and Ankle Outcome Score (FAOS)

The preoperative and postoperative changes concerning the FAOS and SF-36 subscales can be appreciated in Table 10.3.

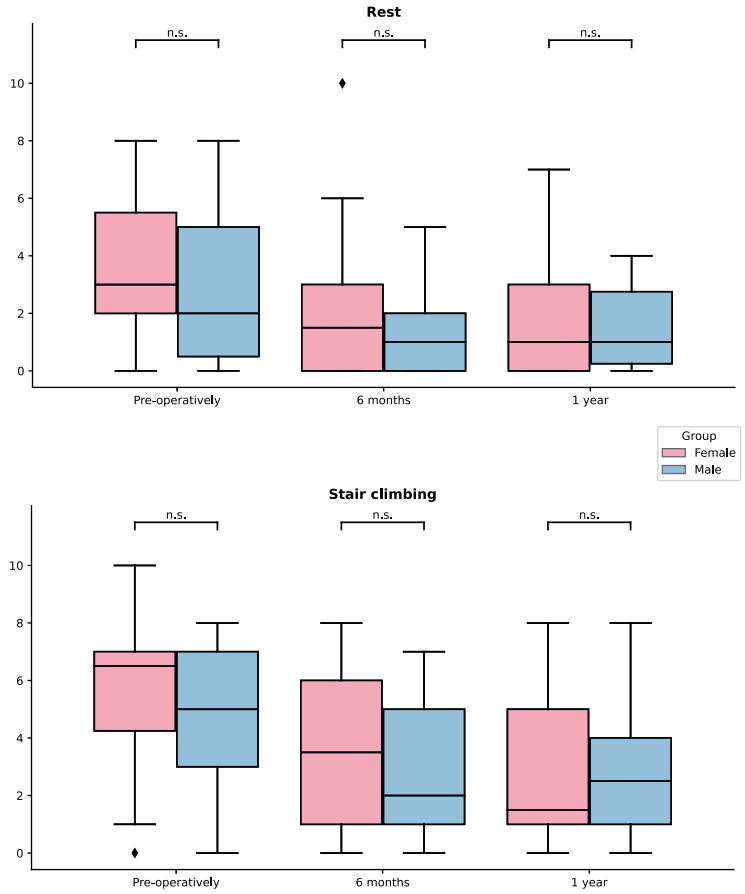

Figure 10.2: NRS during rest and stairclimbing for females and males.

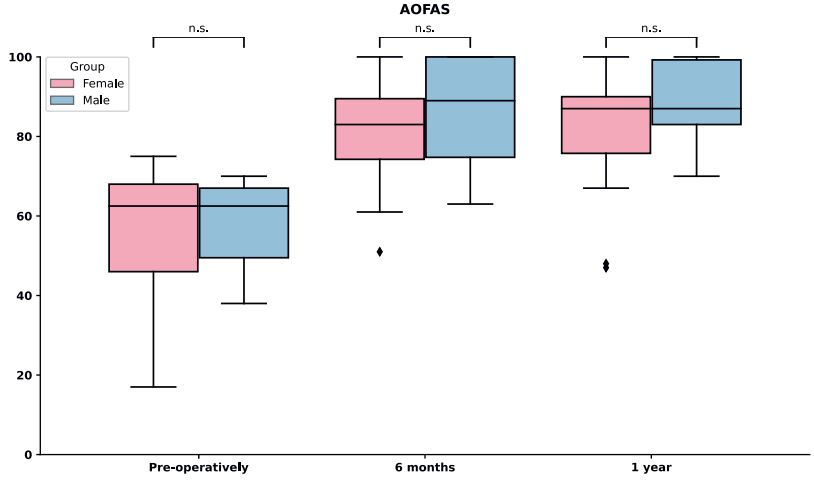

Figure 10.3: AOFAS for females and males.

Table 10.3: FAOS subdomains

Time	Baseline			6m			1yr		
Group	Male	Female	p-value	Male	Female	p-value	Male	Female	p-value
Pain	53.0 [39.8–67.8]	53.0 [44.5–56.0]	0.594	55.0 [39.8–67.0]	59.5 [50.0–81.0]	0.228	57.0 [36.8–81.0]	71.5 [56.2–86.0]	0.056
Symptoms	53.5 [35.5–67.8]	48.5 [42.2–64.0]	0.543	70.0 [58.0–78.8]	57.0 [43.2–74.2]	0.136	62.5 [47.0–86.0]	66.0 [47.0–78.8]	0.957
ADL	59.5 [44.0–74.0]	68.0 [51.5–77.5]	0.296	79.5 [63.0–90.0]	77.0 [66.5–91.0]	0.949	82.5 [63.0–85.0]	92.0 [72.2–96.0]	0.107
Sports	22.5 [6.2–47.5]	25.0 [15.0–35.0]	0.822	45.0 [26.2–62.5]	45.0 [21.2–72.5]	0.789	40.0 [35.0–57.5]	55.0 [32.5–73.8]	0.272
QoL	19.0 [0.0–25.0]	16.0 [6.0–31.0]	0.328	38.0 [20.5–56.0]	38.0 [25.0–56.0]	0.805	34.5 [14.5–50.0]	38.5 [31.0–54.5]	0.227

Radiological outcomes

100% of the CT scans were performed at 10 or 12 weeks postoperatively. All but one patient received a CT scan one year postoperatively, as that patient received his CT at 6 months postoperatively already due to logistical planning.

At 10 or 12 weeks postoperatively, all patients (100%) showed union of their medial malleolar osteotomy and graft consolidation. At 1-year post-operatively, all patients with a CT scan (n = 47) showed graft consolidation. There were cysts present in the osteochondral graft in 21 patients. There were 11 females (37% of the group) and 10 males (59% of the group), respectively (p = 0.24).

Donor-site morbidity, complications and hardware removal

Only 1 female had donor site morbidity. In total, 2 other complications occurred (between-group: p = 1.0). There was 1 case of complex regional pain syndrome (CRPS) in a female and one male had complaints of temporary hypoesthesia of the saphenous nerve.

5 (28%) of the males and 12 (40%) of the females had hardware removal (between-group: p = 0.59) at a median of 18.9 and 12.5 months post-operatively. Additionally, numerous additional surgeries to the graft and unrelated to the graft were performed, this is presented in Table 10.4.

Discussion

This prospective study demonstrated that the TOPIC procedure is an effective technique for larger OLTs in both male and female patient populations. This study found that men typically present with OLTs of larger sizes when compared with women. While the TOPIC procedure proved to result in good overall clinical outcomes with successful consolidation of grafts based on postoperative CT scans of all patients, there was a higher percentage of postoperative cyst formation in the male population although not statistically significant. Of note, there was a greater improvement in postoperative FAOS pain scores in women. Lastly, our study demonstrated no statistical differences in complication rates following the TOPIC procedure, although a higher proportion of women did require hardware removal.

Table 10.4: Additional procedures and hardware removal

Variable	Female	Male	p-value
No. of patients requiring additional surgery*	12 (40%)	6 (33%)	0.88
No. of additional operations	14	6	0.53
No. of procedures performed during the additional operations	23	12	0.83
No. of procedures related to the graft†	3 (13%) - Arthroscopic shaping/reduction of graft (n = 1) - Open shaping/reduction of graft (n = 1)‡ - Arthroscopic shaping of the graft and debridement/bone marrow stimulation of the graft (n = 1)‡	1 (8%) - Arthroscopic shaping of the graft and debridement/ bone marrow stimulation of the graft (n = 1)	0.69
No. of procedures unrelated to the graft†	20 (87%) - Hardware removal (n = 12) - Arthroscopic debridement ankle impingement (n = 5) - Open debridement ankle impingement (n = 1) - Open and arthroscopic debridement ankle impingement (n = 1) - Other minor procedures (n = 1)	11 (92%) - Hardware removal (n = 5) - Arthroscopic debridement ankle impingement (n = 5) - Other minor procedures (n = 1)	0.69

* No. (% of total no. of patient in the group).
† No. (% of total additional procedures in the group).
‡ Performed in the same patient.

The TOPIC procedure has been utilized as an alternative treatment strategy in the management of large osteochondral lesions of the talus. This technique is a single-stage procedure whereby a donor iliac crest graft is harvested, prepared to press-fit shape, and implanted into the ipsilateral talar defect, allowing for minimal chondral damage during the procedure. The iliac crest periosteal layer has been shown to have chondrogenic potential, thereby serving as a source of cells and scaffold with growth factors.[18,22,23,28] Previous studies have demonstrated that this bone-periosteal transplant for bone-cartilage repair has been an efficient and safe treatment strategy yielding good clinical and radiologic outcomes in the short to medium term follow-up.[6,7,17] In addition, the TOPIC procedure does not preclude future salvage procedures including a revision TOPIC procedure, allograft transplantation procedure, ankle fusion, or total ankle replacement.

While previous studies have demonstrated that the TOPIC procedure is a safe and effective treatment strategy in the management of larger OLTs, there has been a paucity of data evaluating whether there are any sex-specific differences in either the presentation of the injury or outcomes following intervention with TOPIC. Our study demonstrates that men oftentimes present with lesions that are larger in size, particularly in both surface area and volume, when compared with women. Men often have higher BMI and are taller in height which can result in greater forces, particularly shearing forces, with injury. There may also be an increase in axial load placed through the ankle joint at the time of injury, resulting in larger talar defect sizes.[15,30] Previous literature has demonstrated anatomic differences in the foot between men and women. Women typically have shorter feet, with wider forefeet and shorter arch lengths, as well as shorter metatarsal lengths when compared with men.[3,31] In addition, the trochlear breadth of the talus is greater in men than women. These differences may account for the disparities in lesion characteristics between men and women.

Our study did report a significant improvement in outcomes following the TOPIC procedure for both men and women. There was a greater improvement found in women when comparing FAOS pain sub-scores. All patients, both men and women, demonstrated good incorporation and consolidation of the graft as evaluated on CT scan. Notably, there was a higher percentage of men who developed post-operative cyst formation. This factor may contribute to our findings of a lower reported pain scores in the female population, although a previous study by Dahmen et al.[6] demonstrated that postoperative cyst formation did not correlate with clinical symptoms. In addition, our study demonstrates that men typically present with lesions of larger sizes, which may also be a factor in postoperative clinical scores.

Our study demonstrates no statistical differences in complication rates following the TOPIC procedure between men and women. In our prospective study, only one female patient reported donor-site morbidity of the iliac crest. Donor-site morbidity is often a concern when harvesting graft from the iliac crest leading to pain and an incisional scar. Previous studies have demonstrated iliac crest donor rates site from 2.4 to 6.2% which may result in a revision surgery or long-term postoperative pain.[2,9] The majority of the patients in our cohort did not report functional or mental/emotional impairments as a result of the iliac crest harvest. This was substantiated by our recent study of Dahmen et al.[6] in which it was concluded that 0% of the patients reported functional impairment due to iliac

crest donor-site morbidity. Lastly, it is important to mention that there were no statistically significant differences in the rate of revision surgery following the TOPIC procedure between men and women. Notably, there was a higher proportion of women who required hardware removal (40% women versus 28% men), although this was unrelated to the graft and did not require accessing the joint.

There are several limitations to this study. The statistical power is low regarding sub-group analysis. In addition, all OLTs were evaluated and therefore further analysis based on lesion location had not been performed which may have demonstrated variability based on sex. Additionally, lateral lesions were excluded for the present study. Strengths of this present paper include the prospective nature of the paper and sufficient power analysis. There was also a 100% follow up rate. Lastly, outcomes were independently scored, resulting in high inter- and intra-relater reliability.

Conclusion

Men and women showed clinically relevant improvements in the clinical outcomes after undergoing the TOPIC procedure, with significant differences in pre-operative size. There were no statistical differences in complication rates following the TOPIC procedure, although a higher proportion of women did require hardware removal. TOPIC procedure is a good treatment strategy with good functional outcomes for large OLTs in both men and women.

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Chapter 11

No difference between 5 and 6 weeks of non-weight bearing after osteochondral grafts for medial osteochondral defects of the talus with medial malleolar osteotomy

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Abstract

Purpose: The aim of the present study to compare the clinical outcomes and safety at 1-year follow-up after 5 or 6 weeks of non-weightbearing after a Talar OsteoPeriostic grafting from the Iliac Crest for a medial Osteochondral Lesion of the Talus (OLT).

Methods: A retrospective comparative case-control analysis of prospectively followed patients who underwent a TOPIC procedure with medial malleolus osteotomy was performed. Patients were matched in two groups with either 5 or 6 weeks non-weightbearing. Clinical outcomes were evaluated using the NRS during walking, rest, running and stairclimbing. Additionally, the Foot and Ankle Outcome Score (FAOS) and AOFAS ankle-hindfoot score were assessed. Moreover, radiology and complications were assessed.

Results: 11 patients were included in the 5 weeks immobilization group and 22 in the 6 weeks immobilization group. No significant differences were found in all baseline variables. The NRS during walking in the 5 weeks group improved with 3.5 points and 4 points for the 6 weeks group ($p = 0.576$ at 1-year post-operatively). In addition, all other NRS scores, FAOS subscales and the AOFAS scores improved (all n.s. at 1 year follow-up). No significant differences in radiological (osteotomy union and cyst presence in the graft) were found. Moreover, no significant differences were found in terms of complications and reoperations.

Conclusion: No significant differences were in terms of clinical, radiological and safety outcomes were found between 5 weeks or 6 weeks of immobilization following a TOPIC for a medial OLT. Therefore, we advise that clinicians can decrease the immobilization period from 6 to 5 weeks.

Level of evidence: Level 3.

Keywords: Osteochondral · Talus · Ankle · Immobilization · Rehabilitation

Introduction

An osteochondral lesion of the talus is a lesion of the subchondral bone and the overlying articular cartilage, and may develop after trauma, such as a lateral ankle sprain or an ankle fracture.[6,30,50] Patients often complain of deep ankle pain during weightbearing activities. Therefore, patients may seek treatment and different options are available and range from non-operative to operative modalities.[37] For large lesions that do not respond well to non-operative treatment, osteo(chondral) auto- and allograft transplantation therapies may be indicated.[37] Different techniques exist, such as the Talar OsteoPeriostic grafting from the Iliac Crest (TOPIC) procedure.[7,17,21-23,37] When treating medially located osteochondral lesion of the talus (OLT), which are most frequently seen, a medial malleolar osteotomy may be needed to gain adequate access.[46] This as, the posteromedial talus may be difficult to reach using arthroscopic or minimally-invasive techniques.[28,51]

After such a procedure in which a medial malleolus osteotomy is performed when transplanting an osteochondral graft, patients will be immobilized for adequate osteotomy healing, with sufficient loading for graft incorporation and cartilage restoration.[3] There is an increasing attention for post-operative rehabilitation protocols, as early weightbearing may improve clinical outcomes in ankle surgery, including the treatment of osteochondral lesions of the talus.[9,10,25,29,40,45,49] However, weightbearing too early might result in inadequate healing process of the osteotomy, and, for example, leading to malunion of the osteotomy or degenerative changes to the graft.[24,26]

Treatment protocols typically have a period of weightbearing and followed by partially weightbearing.[8,21] Most treatment algorithms use an immobilization period of 6 to 12 weeks.[1,31,41] Currently, our tertiary academic expert referral centre immobilizes patients for either 5 or 6 weeks. Subsequently, patients are placed in a walking cast for another 5 or 6 weeks. However, no studies have compared different post-operative immobilization protocols for osteo(chondral) grafts yet. It is, thus, unknown whether the period of 6 weeks may be shortened.

Therefore, it is the goal of the present study to compare the clinical outcomes and safety at 1-year follow-up after 5 or 6 weeks of non-weightbearing after a TOPIC procedure.

Materials and methods

The present study is a single-center, non-randomized, case-control comparative cohort study. The study was approved by the Medical Ethical Committee of the Amsterdam UMC, location AMC, University of Amsterdam (reference number: W14_237#14.17.0288). The study was performed in accordance with the principles of the Declaration of Helsinki and with the Dutch Medical Research Involving Human Subjects Act (WMO).

Patient selection

All patients that underwent a press-fit TOPIC procedure for a primary or non-primary medially located OLT in the Amsterdam UMC were eligible for inclusion. All in- and exclusion criteria are listed in Table 11.1. The surgical technique has been described in a previous publication,[22] and all patients have been treated by two experienced fellowship-trained foot and ankle academic orthopaedic surgeons (G.K. and S.A.S.).

Table 11.1: In- and exclusion criteria

Inclusion	Exclusion
- Medially located Osteochondral lesion of the Talus - Treated with a press-fit TOPIC graft - 5 weeks or 6 weeks of immobilization	- < 1 year follow-up - Concomitant osteochondral lesion of the tibial plafond (OLTP) - Concomitant injuries (e.g., rheumatoid arthritis, advanced osteoporosis, advanced OA, bacterial arthritis or malignancies)

The '5 week' and '6 week' groups were drafted. The 5 week-group were the patients with 5 weeks of non-weightbearing in a cast and subsequently 5 weeks of weightbearing in a walking cast. The 6 week-group had a period of non-weightbearing in a cast of 6 weeks followed with 6 weeks in a walking cast. These two groups existed due to a historical change and due to surgeon (G.K. and S.A.S.) preference.

Patients of the 5 week-group were matched in a 1:2 ratio with patients from the 6 week-group. Patients were matched based on variables that are recognized as being of prognostic value in osteochondral (autograft) transplantation therapies.[16,20,37] The variables that were used in the present study are sex, age at time of surgery, body mass index (BMI) and smoking. This was performed in a custom-made script using the NearestNeighbors-function from the Scikit-learn

package (version 1.3.0) in Python (version 3.11.4).[33,47] This used a sequential matching approach, in which the two matches (from the 6 week-group) were determined by calculating the shortest distance (from the patient of the 5 week-group), using the Euclidean method. After identifying the matches, all patients were removed from the subsequent matching process, and the next patient was matched.

Outcome measures

All data were prospectively collected, both pre- and post-operatively.

Clinical outcomes

All clinical outcomes were gathered and assessed pre-operatively, and at 6 months and 1-year post-operatively.

The primary outcome is the difference in Numeric Rating Scale (NRS) of pain during walking at 1-year follow-up between the 5 week-group and the 6 week-group.[15] This is a scale from 0–10, and 10 means that the patient has the highest pain possible.[15] It was chosen to analyse this at 1-year follow-up as the expectation is that most of the improvement occurs in the first year after treatment and that the two-week difference in immobilization would have the effect early in the rehabilitation period.[8]

The secondary clinical outcomes include the NRS of pain during rest, running and stair-climbing. Additionally, all five subscales (i.e., symptoms, pain, activities of daily living, sports/recreation and quality of life) from the Foot and Ankle Outcome Score (FAOS) were assessed.[38,42] This is the only patient-reported outcome measure (PROM) that has been validated for this specific patient population.[34] Furthermore, the American Orthopaedic Foot & Ankle Society (AOFAS) ankle-hindfoot score was assessed.[43]

All complications were recorded according to a definition that was used in a previous study,[18] which was: 'any undesirable, unintended, and direct result of an operation affecting the patient'.[44] Removal of hardware was counted separately from the complication rate. Additionally, all reoperations (both graft-related and not graft-related) were documented.

Radiological outcomes

All radiological outcomes were assessed on computed tomography (CT) scan. Patients received a CT preoperatively, 10 weeks (5 weeks group) or 12 weeks (6 weeks group) postoperatively and at 1-year follow-up. This was performed in accordance with a previous publication.[8]

Baseline lesion surface area (coronal length x sagittal length x 0.79),[4] volume (coronal length x sagittal length x depth),[4] morphology (fragmentous, cystic and crater-like)[35] and location (9-grid scheme)[13] were assessed by two independent authors (J.J.H. and J.D.). For the lesion dimensions (i.e., AP, ML and depth), both the interrater reliability was determined by calculating the intraclass correlation coefficient (ICC).[34] Regarding the location, and morphology, a discussion was held after primary assessment. If both raters (J.H. and J.D.) did not reach consensus after a discussion, a third senior author was decisive (G.K.)

The union of the medial osteotomy was assessed at 10- or 12-weeks follow-up. Graft consolidation and the presence of cysts were determined at 10 or 12 weeks and 1 year post-operatively. These outcomes were rated by two raters (J.J.H. and J.D.) and in case of no consensus after a discussion, the senior author (G.K.) was decisive.

Power analysis

A power analysis was prospectively performed using the Wilcoxon Rank-Sum Test for the primary outcome in nQuery version 8.5.1.0 (Statistical Solutions Ltd., Boston, MA). The minimal sample size was calculated with a power of 80% with $\alpha = 0.05$. A minimally clinical important difference (MCID) of 2.0 (± 1.3) was used, as this correlates with 2 out of 11 points of less pain and is in line with previous studies.[14,32,36,39] Based on the analysis, minimal 10 patients were needed per treatment group.

Statistical analysis

Variables were assessed for normality using visual inspection of box plots and the Shapiro-Wilk test. Baseline characteristics from all patients were presented in absolute numbers with percentages in case of categorical variables, and for continuous outcomes as means with standard deviations (SD) or medians with interquartile ranges (IQR).

Numerical variables will be compared using the unpaired t-test (normally distributed), Mann-Whitney-U test (skewed distributed). For categorical variables the Chi-square test was used. The significance level (α) was set at 0.05.

All statistical analyses were performed in Python (version 3.11.4) with SciPy package (version 1.11.2).[47,48]

Results

Patient selection and baseline characteristics

In total, 77 patients press-fit medial TOPIC patients were identified, of which 57 were eligible for inclusion. There was no loss to follow-up. After matching, a total of 33 patients were included in the present study, with 11 and 22 patients, respectively (Figure 11.1). The demographic characteristics can be found in Table 11.2 and the pre-operative radiographic lesion characteristics are shown in Table 11.3.

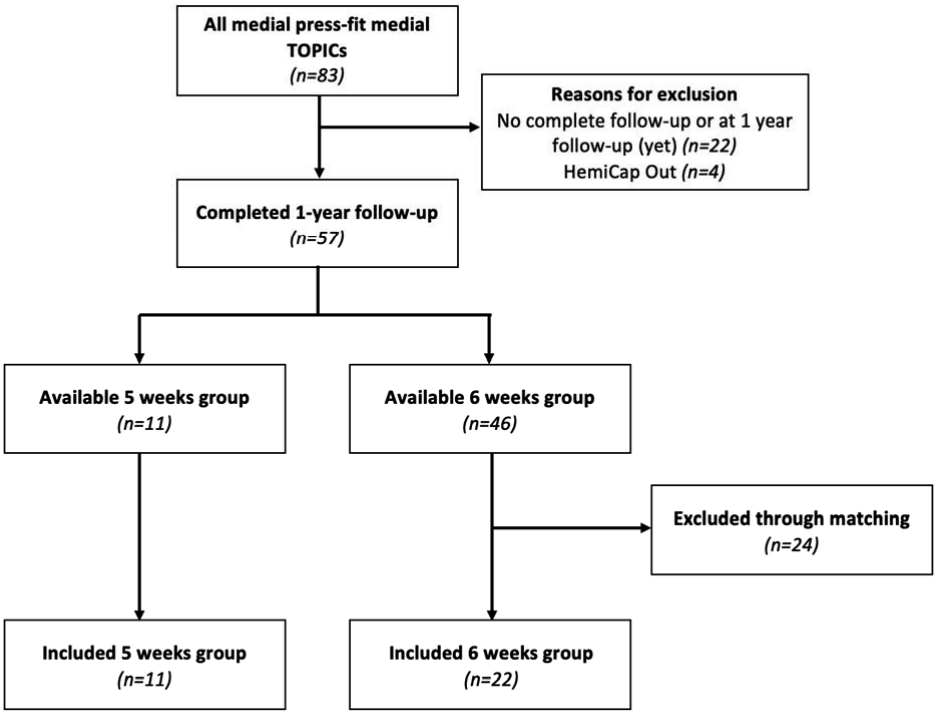

Figure 11.1: Flowchart of patient selection.

Table 11.2: Demographic characteristics of included patients

Variable	5 weeks	6 weeks	p-value
Sample size (n)	11	22	N/A
Age (yr)	24.0 [19.5–34.0]	24.5 [20.0–35.2]	1.0
BMI (kg/m^2)*	22.1 [19.9–24.5]	23.3 [21.8–26.7]	0.73
Male/female	3 (27%) / 8 (73%)	9 (41%) / 13 (59%)	0.70
Right/left	4 (36%) / 7 (64%)	15 (68%) / 7 (32%)	0.17
Smoker, yes/no	2 (18%) / 9 (82%)	3 (14%) / 19 (86%)	0.18

* Median [IQR].

Table 11.3: Pre-operative radiological lesion characteristics

Variable	5 weeks	6 weeks	p-value
Lesion size			
Anteroposterior (AP) diameter (mm)*†	20	18	N/A
Mediolateral (ML) diameter (mm)*†	12	13	N/A
Depth (mm)*†	8	10.5	N/A
Surface area (mm^2)*	195 [128–213]	199 [142–213]	0.82
Volume (cm^3)*	2.0 [1.5–2.7]	2.3 [1.7–3.2]	0.43
Lesion location on 9-grid zone[40]			0.25
Zone 4	6 (55%)	16 (73%)	
Zone 7	5 (45%)	6 (27%)	
Lesion morphology			0.57
Crater	6 (55%)	10 (45%)	
Cystic	5 (45%)	10 (45%)	
Fragmentous	0 (0%)	2 (10%)	

* Median [IQR].
† Inter- and intra-rater reliability outcomes are available in Appendix 11.1.

Primary outcome

The median NRS during walking improved for the 5 weeks group with 3.5 points and 4 points for the 6 weeks group (Figure 11.2). There were no significant between-group differences at any timepoint (baseline: p = 0.802, 6 months: p = 0.685, 1-year: p = 0.576).

Secondary outcomes

Clinical outcomes

The NRS during rest, running and stair climbing improved for both groups. Additionally, all FAOS subscales improved. No significant differences were found in any of these outcomes between both groups. The AOFAS was significantly different as

6 months follow-up and is visualized in Figure 11.3. All secondary clinical outcomes can be appreciated in Table 11.4, all boxplots are available in Appendix 11.2.

Radiological outcomes

All patients (100%) received a CT scan at 10 (5 weeks group) or 12 weeks (6 weeks group) postoperatively and at 1 year postoperatively.

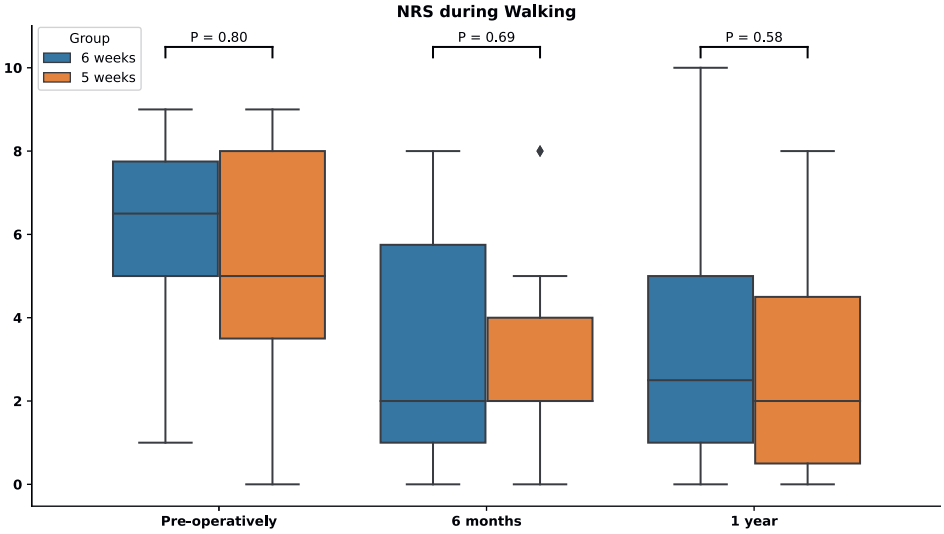

Figure 11.2: Boxplot of the NRS during walking at baseline, 6 months and 1 year follow-up for both treatment groups.

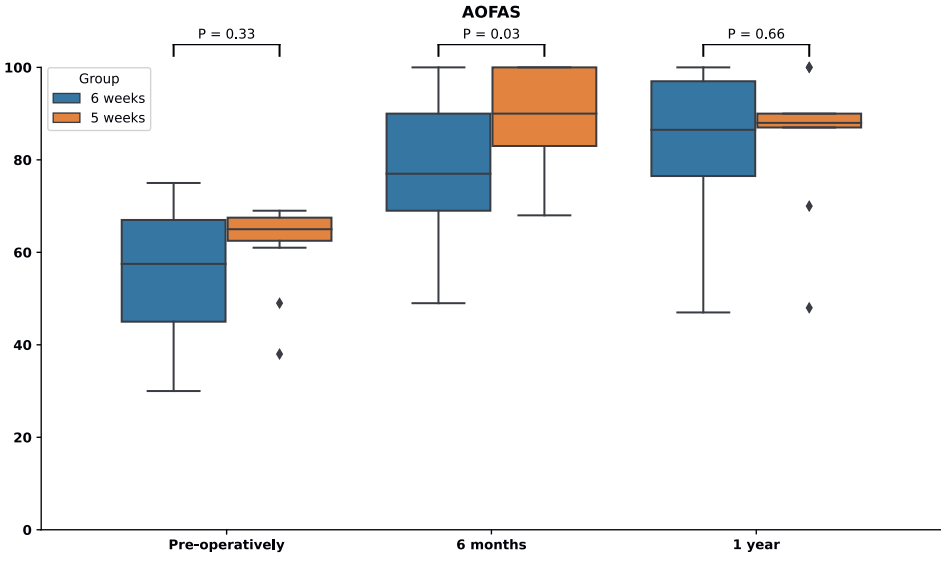

Figure 11.3: Boxplot of the AOFAS at baseline, 6 months and 1 year follow-up for both treatment groups.

Table 11.4: NRS during rest, running and stairclimbing and FAOS subscales

	Baseline			6 months			1 year		
Variable	5 week-group	6 week-group	p-value	5 week-group	6 week-group	p-value	5 week-group	6 week-group	p-value
NRS*									
Rest	3.0 [1.5–5.5]	3.5 [1.2–5.8]	1.000	2.0 [0.5–3.0]	1.0 [0.0–3.0]	0.635	1.0 [0.0–2.0]	1.0 [0.0–3.0]	0.647
Running†	8.5 [6.2–9.8] (n = 10)	8.5 [8.0–9.0] (n = 18)	1.000	5.5 [4.0–6.2] (n = 8)	5.0 [1.5–8.5] (n = 15)	0.922	4.0 [1.0–7.0] (n = 9)	4.0 [2.0–7.0] (n = 17)	0.892
Stairclimbing	5.0 [2.5–7.0]	5.5 [3.2–7.0]	0.847	2.0 [1.5–4.5]	2.0 [1.0–6.0]	0.877	1.0 [0.0–3.0]	2.5 [1.0–5.8]	0.244
FAOS*									
Pain	53.0 [43.5–55.0]	53.0 [43.2–63.2]	0.848	69.0 [54.0–78.0]	57.0 [39.0–87.0]	0.565	75.0 [59.0–87.5]	58.0 [54.5–92.0]	0.645
Symptoms	61.0 [35.5–64.0]	55.0 [42.2–68.0]	0.774	68.0 [56.5–71.0]	55.5 [39.0–77.2]	0.302	71.0 [59.0–80.0]	59.0 [47.0–82.0]	0.528
Activities of Daily Living	66.0 [42.0–81.5]	65.5 [54.0–81.8]	0.619	81.0 [68.5–90.5]	82.5 [63.0–90.8]	0.969	93.0 [80.0–95.0]	84.5 [71.0–94.0]	0.553
Sport/Recreation	35.0 [20.0–42.5]	17.5 [6.2–48.8]	0.591	55.0 [45.0–62.5]	42.5 [25.0–63.8]	0.347	55.0 [47.5–67.5]	50.0 [35.0–82.5]	0.618
Quality of Life	13.0 [3.0–25.0]	9.0 [1.5–25.0]	0.938	44.0 [34.5–59.0]	38.0 [12.2–54.5]	0.337	44.0 [38.0–53.0]	34.5 [20.5–50.0]	0.367
AOFAS*	65 [63–68]	58 [45–67]	0.329	90 [83–100]	77 [69–90]	**0.034**	88 [87–90]	87 [77–97]	0.658

* Median [IQR].

† This was not possible for all patients, as they were not able to run. The number of patients included in the analysis, are presented underneath the result.

All patients (100%) showed union of the distal tibial osteotomy at 10 weeks (5 week-group) or 12 weeks (6 week-group), respectively. In addition, all patients (100%) showed graft consolidation at both 10 or 12 weeks and at 1 year postoperatively. Furthermore, 4 patients (36%) from the 5 week-group and 12 patients (55%) from the 6 week-group showed cyst formation at their 1-year CT scan (p = 0.54).

Complications, donor-site morbidity, hardware removal and reoperations

No patients complained of donor-site morbidity. A total of two complications occurred in 2 patients, all in the 6 weeks group (between-group difference: p = 0.80). These were nerve injuries that were both a temporary hypoesthesia of the saphenous nerve.

A total of 4 (36% of all patients in the 5 weeks group) and 10 (45% of all patients in the 6 weeks group) underwent medial malleolar hardware removal (p = 0.81). The hardware removals took place at a median of 20.7 months and 18.1 months after the initial TOPIC procedure, for the 5 week-group and 6 week-group, respectively (p = 1.0). Additionally, several additional procedures both related and unrelated to the graft were performed (Table 11.5).

Table 11.5: Additional procedures and hardware removal

Variable	5 weeks-group	6 weeks-group	p-value
No. of patients requiring additional surgery*	4 (36%)	10 (45%)	0.63
No. of additional operations	5	12	0.73
No. of procedures performed during the additional operations	8	26	0.53
No. of procedures related to the graft†	0 (0%)	3 (12%) - Arthroscopic shaping of the graft and debridement/bone marrow stimulation of the graft (n = 3)	0.22
No. of procedures unrelated to the graft†	8 (100%) - Hardware removal (n = 4) - Arthroscopic debridement ankle impingement (n = 3) - Other minor procedures (n = 1)	23 (88%) - Hardware removal (n = 10) - Arthroscopic debridement ankle impingement (n = 8) - Open debridement ankle impingement (n = 1) - Other minor procedures (n = 4)	0.65

* No. (% of total no. of patient in the group).

† No. (% of total additional procedures in the group).

Discussion

The main finding of the present prospective study is that no significant difference was found for the primary outcome NRS during walking at 1-year follow-up (p = 0.576) for patients with either 5 weeks or 6 weeks of non-weightbearing following an osteochondral transplantation therapy with medial malleolar osteotomy for a medial OLT. Additionally, no significant differences were found in terms of radiological and safety outcomes.

To the best of the authors' knowledge, no previous studies have assessed and compared the immobilization period after a surgical treatment for an osteochondral defect of the talus with an osteochondral graft and medial malleolar osteotomy. Therefore, from a clinical perspective a study on this subject is highly needed. Several factors are of importance, being 1) clinical outcomes, 2) radiological healing of the osteotomy, 3) incorporation of the graft and 4) safety by means of complications. On all these four points, no significant differences were found between the 5 weeks and 6 weeks group. As 5 weeks immobilization has multiple advantages such as earlier ROM and thus less stiffness, earlier physical therapy and an increased patients' convenience, the present study suggests using 5 weeks of immobilization followed by 5 weeks of weightbearing in a walking cast.

All secondary outcomes were non-significant at all time-points, except the AOFAS at 6 months post-operatively (p = 0.034). This finding, however, needs to be interpreted with caution as it may be an incidental finding due to multiple testing and the AOFAS has not been validated for OLTs yet.

When comparing the results to the literature, a comparison with bone marrow stimulation may be made. However, these studies do not concern an osteotomy that needs to heal and are often performed arthroscopically. Multiple studies have investigated early weightbearing after arthroscopic microfracture (bone marrow stimulation) and showed similar or improved results compared to delayed weightbearing.[9,10,25,29,45,49] Early weightbearing is therefore advised, according to the International Consensus Meeting on Cartilage Repair of the Ankle statement.[5] It is, however, more appropriate to compare the results of the present study to other procedures that also involve an osteotomy. In studies that assessed ankle fusions or the HemiCAP implant, or studies reporting novel osteotomy techniques in the treatment of OLTs, all studies used a period of 6 weeks of non-weightbearing.[12,19,27] All studies showed uncomplicated union of all medial malleolar osteotomies, but none performed a comparison between early and delayed weightbearing

in these patient populations. This is in line with the present study, as all of the patients in both groups showed union at 10 weeks (5 week-group) or 12 weeks (6 week-group) follow-up.

The present study has some limitations, one of which being that a low number (n = 57) patients were eligible for the patient study. However, the minimum amount needed according to the power analysis was met, and matching allowed that a prospective case-control comparative design was made possible. Additionally, there was no non-inferiority methodology used so based on the results (i.e., non-significant) it cannot be concluded that one is better than the other nor can it be concluded that the results are similar/non-inferior to each other. This was unfortunately not performed as this was a retrospective study based on our prospective database, and thus a change to a non-inferiority design was not possible. Moreover, unfortunately it was not possible to assess the return to activity and work outcomes and to assess the patients' perspective in the present study. This is one of the things where future research should be focused on. Strengths of the present study are that the cohort from our tertiary academic referral centre was prospectively followed and matched. Additionally, all outcomes were assessed by two authors independently.

The clinical relevance of the present study is that it shows that patients can start weightbearing earlier after their surgery. No significant differences were found in terms of clinical outcomes, but also no complications occurred regarding the medial osteotomy in both patient groups. Therefore, a shorter period of non- and partial weightbearing may be safe and effective. Additionally, this improves the patient convenience and may shorten the time to return to work.[5,11,45] The present study, however, is based on a low number of patients and therefore further research should be performed on this. This should then focus on randomly and blinded assignment of patients to both rehabilitation regimens, to make sure that no confounding factors are present.

Conclusion

No significant differences were in terms of clinical, radiological and safety outcomes were found between 5 weeks or 6 weeks of immobilization following an Talar OsteoPeriostic grafting from the Iliac Crest for a medial osteochondral lesion of the talus. Therefore, based on the present study, we advise that clinicians can decrease the immobilization period from 6 to 5 weeks.

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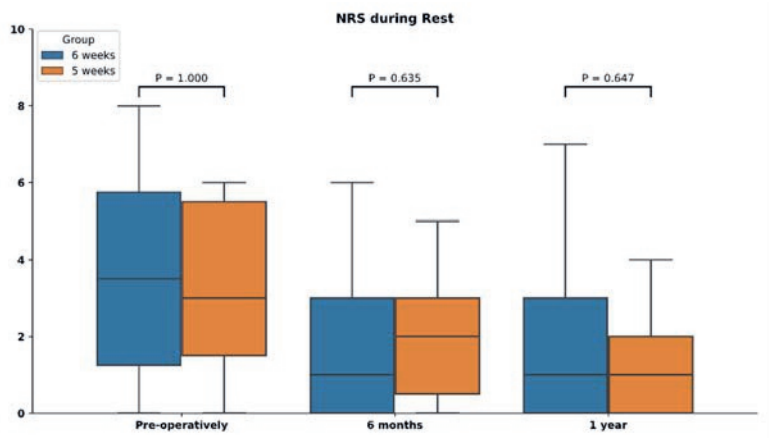
Appendices

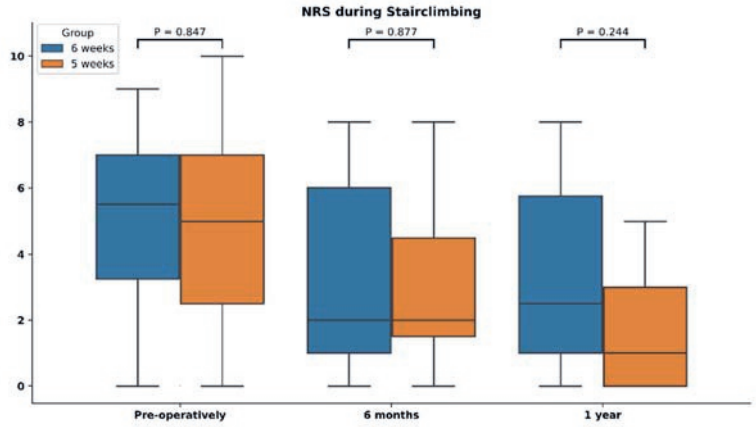
Appendix 11.1: Inter- and intrarater reliability

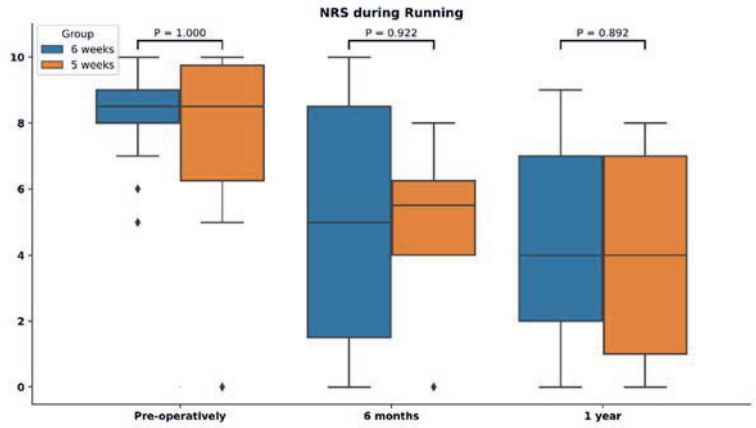
AP: 0.8 (excellent).
ML: 0.9 (excellent).
Depth: 0.8 (excellent).

Appendix 11.2: Boxplots of secondary clinical outcomes

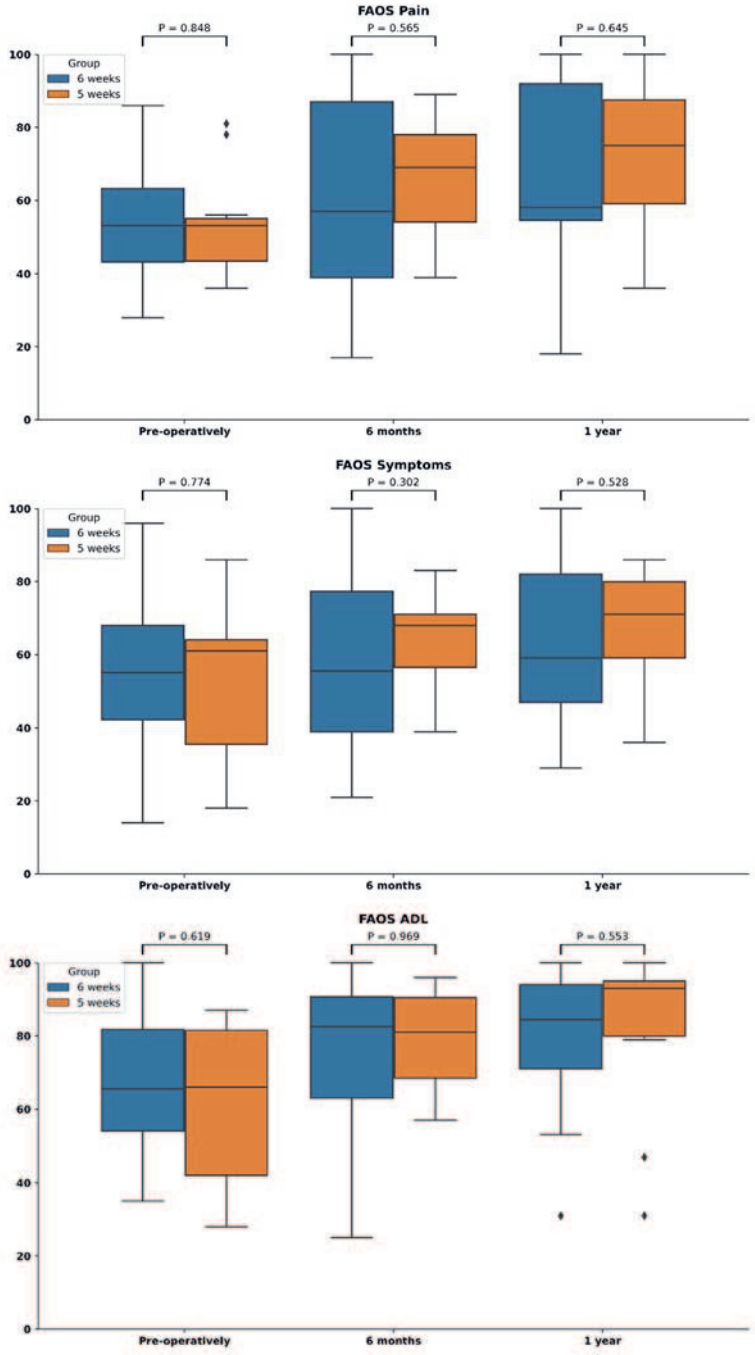
NRS during Rest, Running and Stairclimbing

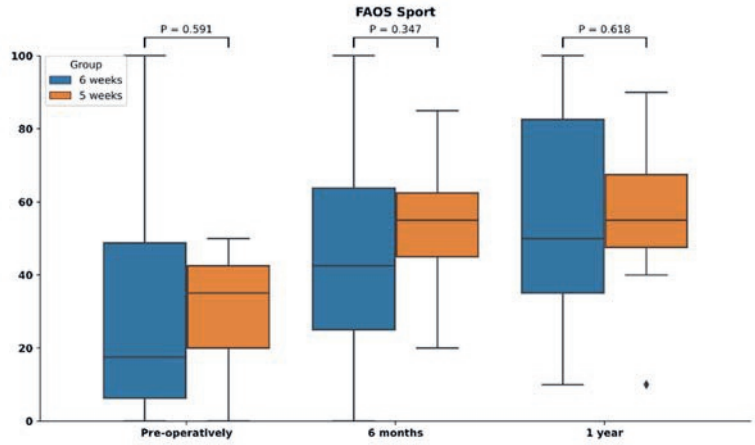


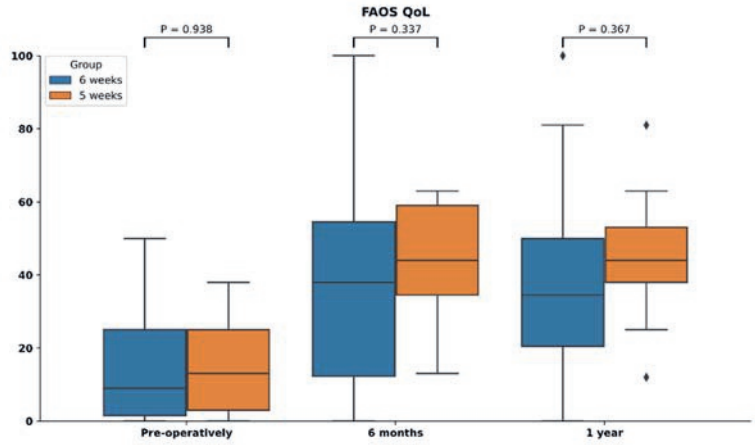




FAOS Subscales




FAOS Sport
P = 0.591
P = 0.347
P = 0.618
Group
6 weeks
5 weeks
100
80
60
40
20
0
Pre-operatively
6 months
1 year


FAOS QoL
P = 0.938
P = 0.337
P = 0.367
Group
6 weeks
5 weeks
100
80
60
40
20
0
Pre-operatively
6 months
1 year

Chapter 12

Eight out of ten patients participate at their desired level of sports after Talar OsteoPeriostic grafting from the Iliac Crest for large, complex osteochondral lesions of the talus

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Abstract

Background: The Talar OsteoPeriostic grafting from the Iliac Crest (TOPIC) procedure shows successful clinical outcomes up to 2-years follow-up for large osteochondral lesions of the talus (OLT). It is unknown what the sports outcomes are in this group of patients.

Purpose/hypothesis: The purpose of the present study was to prospectively evaluate sport outcomes for patients with large osteochondral lesions of the talus treated with the TOPIC procedure. Our hypotheses were that the TOPIC procedure would result in adequate (return to/participation in) sports outcomes and an improvement of pain scores during running 1- and 2-years after the surgery.

Study design: Prospective case series; Level 3.

Methods: Sixty-one patients having undergone the TOPIC procedure for a symptomatic OLT were prospectively included up to 24 months follow-up. Using digital questionnaires, an in-depth qualitative telephone interview, and electronic patient files, the return to any level of sports rate 1- and 2-years (primary outcome) after TOPIC procedure for OLT was assessed. Additionally, the secondary aims were to assess different levels of return to- and participation in sports rates, as well as the Ankle Activity Score (AAS) 1- and 2-years postoperatively.

Results: Of the sixty-one included patients, 59% and 82% of patients participated at their desired level of sport, 1-year and 2-years after TOPIC, respectively. Furthermore, 2 years postoperatively, the return to any level of sports was 96%, the return to preoperative level of sports 93%, and the return to pre-injury level of sports 59%. The AAS increased significantly from 2 points to 5 points comparing the preoperative situation to the 2 years postoperative situation ($p < 0.05$). The NRS for pain during running improved significantly from 9 points preoperatively to 5 points at the 2 years of follow-up ($p < 0.05$).

Conclusion: The TOPIC procedure for large osteochondral lesions of the talus results in 8 out of 10 patients participating at their desired level of sports 2 years postoperatively, while 10 out of 10 patients to return to any level of sports and 6 out of 10 patients return to their pre-injury level of sports 2 years postoperatively. As such, this joint sparing procedure for large osteochondral lesions of the talus yields successful sports outcomes. The findings of the present study may support patients and physicians in a more in-depth, shared decision-making process.

Keywords: OCD · OLT · Cartilage · Ankle · TOPIC · Return-to-sports

What is known about the subject: The TOPIC procedure for large osteochondral lesions of the talus results in 8 out of 10 patients participating at their desired level of sports 2 years postoperatively, while 10 out of 10 patients to return to any level of sports and 6 out of 10 patients return to their pre-injury level of sports 2 years postoperatively. As such, this joint sparing procedure for large osteochondral lesions of the talus yields successful sports outcomes. The findings of the present study may support patients and physicians in a more in-depth, joint shared decision-making process.

What this study adds to existing knowledge: This study shows that 2-years after the TOPIC procedure eight out of ten patients return to their desired level of sports while 10 out of 10 patients return to any level of sports and 9 out of 10 patients return to their preoperative level of sports 2 years postoperatively. As such, this study showed that the TOPIC procedure ensures successful sports outcomes for this relatively new surgical technique. Moreover, in this study, a self-reported desired level to sports outcome was developed which enhances decision making and expectation management.

Introduction

Ankle injuries, such as ankle sprains and fractures, are among the most common site of injury during sports.[4, 10] Such injuries may lead to cartilage damage in the ankle in the form of an osteochondral lesion of the talus (OLT).[5] Patients with OLT experience deep ankle pain during or after weight-bearing activities, which can substantially limit their level of physical activity and participation in sports.[9]

Currently, no consensus concerning the best treatment for OLT has been reached.[6,16,23,28] OLT vary greatly in presentation and depending on prior treatment, size, morphology and location, a treatment choice is made.[21] Large primary and non-primary osteochondral lesions (> 15 mm diameter) of the talus are often treated with an autograft or allograft transplantation in which the damaged bone-chondral unit is replaced.[25,27] Osteochondral autograft procedures allow for adequate clinical outcomes and return to sport rates.[6,16,24] However, a disadvantage of autologous osteochondral transplantation (AOT) is the harvesting of the graft from the ipsilateral femoral condyle, which can lead to donor-site morbidity in up to 32% of patients, which may impact the active patient from returning or participating in sport.[6,14] To avoid donor site morbidity, a new joint-sparing technique for large, primary and non-primary OLTs was created; the Talar OsteoPeriostic grafting from the Iliac Crest (TOPIC) procedure.[15] Although the TOPIC procedure showed satisfactory clinical outcomes up to 2-years follow-up, it is currently unknown what the (return to/participation in) sports outcomes are in this group of patients having received this relatively new surgical treatment option.[8]

As such, it is the primary aim of this study is to assess the participation at the desired level of sport rate 1- and 2-years after TOPIC procedure for OLT. The secondary aims were to assess the different levels of return to sports, level of participation in sports, and pain outcomes 1- and 2-years after TOPIC procedure. Our hypotheses were that the TOPIC procedure for large OLTs would result in adequate (return to) sport outcomes and an improvement of pain scores during running 1- and 2-years after the surgery.

Materials and methods

The present study is a prospective, nonrandomized, single-center, clinical comparative cohort study. The local Medical Ethics Committee (reference number MEC W14_237#14.17.0288) approved the study, and the study was performed in accord-

ance with the current ethical standards (Declaration of Helsinki). The department of Orthopedic Surgery and Sports Medicine of the Amsterdam UMC is a tertiary referral academic hospital and is an (inter)nationally accredited expertise center for the diagnosis and treatment of cartilage and osteochondral lesions of the foot and ankle.

Patient selection

The study included all patients with a symptomatic, osteochondral lesion of the talus who were treated with the TOPIC procedure and had a minimum follow-up of 24 months. The TOPIC procedure is indicated for primary large (> 10 mm in anteroposterior and/or mediolateral diameter and/ or depth) osteochondral lesions of the talus not amenable to fixation, and non-primary OLTs. The patients need to have failed a minimum 6 months of non-operative management. Inclusion and exclusion criteria can be found in Table 12.1 below.

Table 12.1: Inclusion and exclusion criteria

Inclusion criteria	Exclusion criteria
- Patients with a symptomatic OLT (independent of location) who underwent the TOPIC procedure with prospective follow-up - Follow-up > 24 months postoperatively - Patients participating in any form of sport pre-injury (pre-injury AAS > 3)	- Pathology other than OLT - Follow-up < 24 months - Arthrodesis after TOPIC - Non-sport-related injuries that prevented return to sport

Surgical technique and postoperative management

All procedures were performed by 2 experienced fellowship-trained foot and ankle academic orthopaedic surgeons. The TOPIC procedure completely replaces the osteochondral unit with an autograft including its overlying periosteal layer from the ipsilateral iliac crest. Depending on the location of the OLT, either a medial distal tibial osteotomy or an anterolateral arthrotomy is performed. Hereafter the OLT is inspected and excised in total; the underlying subchondral bone base is micro-drilled. The graft is harvested from the ipsilateral iliac crest (donor site) and thereafter personally customized based on the preoperative CT scan – after which the graft is inserted in a press-fit manner. The elaborate operative technique and postoperative management were previously described for both medial and lateral lesions.[7,15] In case of lateral ankle instability, a lateral stabilization procedure was added.

Clinical and sports evaluation

Preoperative patient demographics were extracted from the electronic patient files. At three points in time; preoperatively and 1- and 2-years postoperatively, an electronic questionnaire including type, level, hours of sport and Numeric Rating Scale[26] (NRS) of pain during running was filled in by all participants. To verify and elaborate on sport information, a standardized in-depth telephone qualitative and quantitative interview was performed after 2-years follow-up. The standardized qualitative interview format can be found in the Appendix. A graphic fictitious timeline of surgical interventions as well as the data extraction moments illustrating this process can be found in Figure 12.1. None of the treating surgeons involved in patient care collected or assessed data to avoid bias.

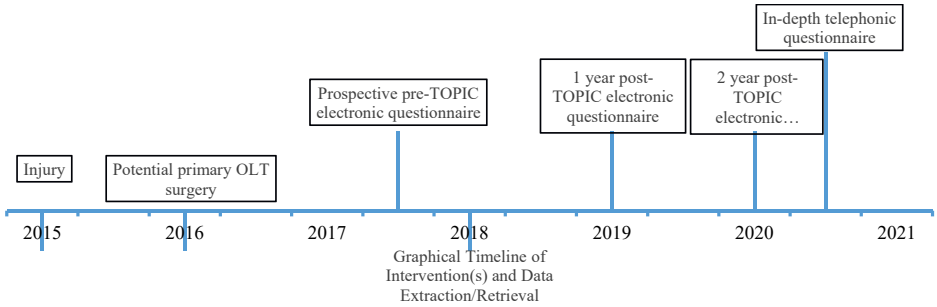

Figure 12.1: Example of a graphic timeline of interventions and moments of data extraction for one specific patient.

Information gathered from the electronic questionnaire and interview was used to determine the return to sport rates and Ankle Activity Scale (AAS).[11] In case of conflict between electronic questionnaire and the interview information, the interview information was determinative. In this study, a modified version of the Ardern return to sport criteria was used.[1] The definitions of the modified (return to/participation in) sports outcomes that were used in the present study can be found in Table 12.2. The primary outcome of this study was defined as the 2-year postoperative return to any level of sports rate. The AAS is an ankle specific standardized activity scoring system that includes 4 general activities including 3 working activities and 53 sports. A score of 0 points indicates the lowest possible ankle activity, and a score of 10 indicates the highest possible ankle activity. Sports can be categorized in low impact (AAS 3 & 4), medium impact (AAS 5, 6, and 7), and high impact (AAS 8, 9, and 10). Lastly, prospectively collected information on complications and additional surgeries were extracted from electronic patient files.

Table 12.2: Definitions of return to sports / sports participation outcomes

Return to sport category	Definition
Primary outcome: Postoperative participation rate (%) at the patient's desired level of sports	The postoperatively, self-defined level of sport the patient wishes to achieve following the rehabilitation from the TOPIC procedure, the attainment of this outcome was collectively determined by the participant and researcher during the postoperative interview.
Return to any level of sports rate (%)	The return to any level of sport (and/or participation in rehabilitation or modified training) of any type and intensity
Return to preoperative level of sport rate (%)	The return to the *same* level of sport as the *preoperative* situation
Return to pre-injury level of sport rate (%)	The return to the *same* level of sport as the *pre-injury* situation
Return to performance rate (%)	The return to a *higher* level of sport compared to the *pre-injury* situation
Participation rate (%) at improved preoperative level of sports	The participation in a *higher* level of sport compared to the *preoperative* situation

Radiological evaluation

Baseline radiological assessments, as per computed tomography (CT) scan, of the OLT included the maximum anteroposterior and mediolateral diameters and depth, surface area (ellipsoid formula: area = abπ = coronal length × sagittal length × 0.79), and volume (formula: volume = abc = coronal length × sagittal length × depth).[2] The morphological description of the OLT consisted of 3 categories (fragmentary, cystic, or crater).[22] The preoperative osteoarthritis (OA) stage was determined using an OA grading atlas for CT.[3]

Statistical analysis

All statistical analyses were performed with SPSS version 28.0 (IBM). In cases of a normal distribution of continuous variables, outcomes were reported as means and standard deviations (SD), in cases of non-normal distribution of continuous variables, outcomes were reported as medians and interquartile ranges (IQR). Categorical and dichotomous outcome variables were described as absolute numbers and percentages. To compare preoperative and postoperative data, a paired t-test in cases of normally distributed data, and a Wilcoxon signed rank test in cases of non-normally distributed data was used.

Inter-rater and intra-rater reliability for the lesion size and lesion morphology were determined with a subset of 20 OLT assessed by 2 independent raters (JD and EG). Intra-rater reliability was performed by repeating the evaluations 2 weeks later. With the use of intraclass correlation coefficient (ICC), lesion size measurements were evaluated.[20] To test interrater reliability for lesion morphology, the Cohen kappa value was used.[17] A consensus meeting between the 2 independent raters was organized to agree upon lesion localization and morphological category. A Mann-Whitney U test was used to compare the lesion sizes between the primary and non-primary subgroup in case of non-normally distributed data. A chi square test was used to compare the morphology, OA stage and RTS rates between the primary and non-primary subgroup. A Wilcoxon ranked test was used to compare the preoperative to the 1- and 2-year postoperative AAS and NRS. The level of significance was set at $p < 0.05$. A formal sample size calculation was not conducted prior to the study. Instead, we employed a convenience sampling approach by including all available and eligible patients within the defined timeframe.

Source of funding
The authors did not receive grants or outside funding in support of their research or for preparation of this manuscript.

Results

Patient selection and demographics

Sixty-one patients were assessed in the current study (Figure 12.2). No patients were lost to follow-up. Patient demographics can be found in Table 12.3 and preoperative lesion characteristics are summarized in Table 12.4. A subgroup comparison of the patient and preoperative lesion characteristics of the primary and non-primary group can be found in Table 12.5. The ICC values can be found in Table 12.6.

Return to sport outcomes

1-year and 2-years after TOPIC, 93% and 98% of patients returned to any level of sport respectively (primary outcome). All of the modified RTS outcomes can be found in Table 12.7. No significant difference in any of the (return to/participation in) sports outcomes was found between the primary and non-primary subgroup at both 1- and 2-years follow-up ($p = 0.6$ and $p = 0.2$ respectively).

Table 12.3: Preoperative patient demographics

Factor	Value
Patient age* (yr)	31 [25–44]
Body mass index* (kg/m^2)	25 [22–28]
Follow-up (mo)	59 [45–67]
Right/left ankle	31 (51%) / 30 (49%)
Smoking, yes/no	8 (13%) / 53 (87%)
Concomitant lateral ankle instability, yes/no	11 (18%) / 50 (82%)
Male/female	24 (39%) / 37 (61%)
Concomitant procedures performed during TOPIC	5 (9%) (4 Duquennoy procedures, 1 supramalleolar osteotomy)
Primary/non-primary lesion	23 (38%) / 38† (62%)
Total no. of previous operations for the OLT	44
Mean no. of previous operations for osteochondral lesion per patient	0.9

* Median [IQR].
† 22 patients with 1 previous surgery for the OLT and 16 patients with > 1 previous surgeries for the OLT.

Table 12.4: Preoperative lesion characteristics

Factor	Value
Lesion size*	
Anteroposterior diameter (mm)	17 [14–19]
Mediolateral diameter (mm)	10 [8–11]
Depth (mm)	8 [6–8]
Surface area (mm^2)	159 [127–223]
Volume (cm^3)	1.6 [0.8–2.2]
Lesion location	
Medial	54 (89%)
Lateral	7 (11%)
Lesion morphology	
Crater	12 (20%)
Cystic	38 (62%)
Fragmentary	9 (15%)
Hemicap	2 (3%)
Preoperative ankle osteoarthritis stage	
Median [IQR]	1 [1–1]
No. (%) of patients with:	
Stage 0	7 (10%)
Stage 1	40 (60%)
Stage 2	14 (21%)
Stage 3	0 (0%)
Preoperative osteophytes	
No. of patients	53 (87%)
Total no. osteophytes	99
Osteophytes per patient*	2 [1–2]

* Median [IQR].

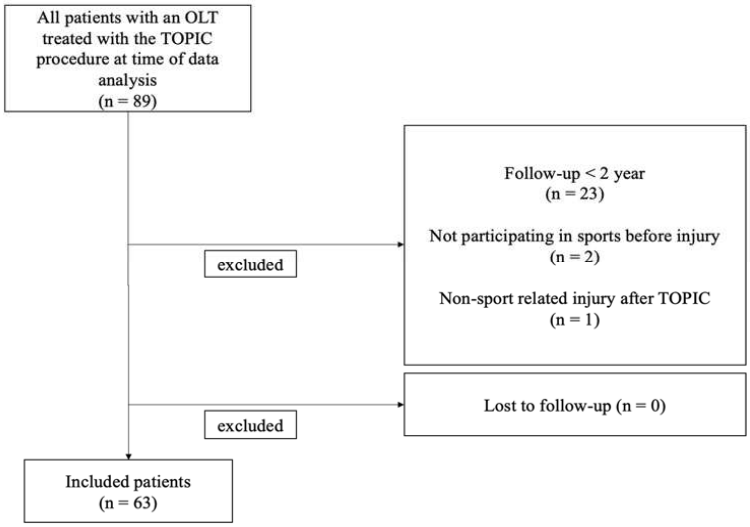

Figure 12.2: Flowchart of the inclusion process.

Table 12.5: Preoperative patient and lesion characteristics subgroup comparison

	Primary	Non-primary	p-value
Patient age* (yr)	31 [25–40]	33 [24-50]	0.51
Body Mass Index (kg/m²)	25.9 [22–29.6]	24.9 [22.4–27.3]	0.80
Smoking (yes/no)	4 (17%) / 19 (83%)	4 (11%) / 34 (89%)	0.99
Ankle instability (yes/no)	4 (17%) / 19 (83%)	7 (23%) / 31 (77%)	0.92
Size			
Depth (mm)	9 [6–14.5]	7 [6–10]	0.26
AP diameter (mm)	18 [13–21]	16 [14–18]	0.14
Lesion surface (mm²)	175 [109–269]	157 [128–200]	0.37
ML diameter (mm)	10 [8–13]	10 [8–12]	0.52
Lesion volume (cm³) *	1.2 [0.9–3.5]	1.1 [0.8–1.8]	0.25
Morphology			
Crater lesions	2 (9%)	10 (26%)	0.31
Cystic lesions	16 (69%)	22 (58%)	0.36
Fragmentary lesions	5 (22%)	4 (11%)	0.09
Hemicap	0 (0%)	2 (5%)	0.28
Press-fit/non-press-fit TOPIC procedure			
Press-fit	21 (91%)	31 (82%)	0.30

* Median [IQR].

Table 12.6: Interrater and intrarater reliability for the lesion size and lesion morphology

	Interrater reliability	Intrarater reliability
Lesion size	0.86	0.89
Lesion morphology	0.71	0.82
OA grading	0.80	0.83

Table 12.7: Return to sport rates and subgroup comparison

	1-year				2-years			
	Total	Primary	Non-primary	p-value*	Total	Primary	Non-primary	p-value*
Postoperative participation rate at desired level of sport (primary outcome)	59% (36/61)	61% (14/23)	58% (22/38)	0.82	82% (50/61)	78% (18/23)	84% (32/38)	0.56
Return to any level of sports rate	93% (57/61)	91% (21/23)	95% (36/38)	0.60	98% (60/61)	96% (22/23)	100% (38/38)	0.20
Return to preoperative level of sport rate	83% (25/30)	80% (8/10)	85% (17/20)	0.44	93% (28/30)	90% (9/10)	95% (19/20)	0.41
Return to pre-injury level of sport rate	44% (27/61)	43% (10/23)	45% (17/38)	0.92	59% (36/61)	61% (14/23)	58% (22/38)	0.82
Return to performance rate	2% (1/61)	4% (1/23)	0% (0/38)	0.20	3% (2/61)	9% (2/23)	0% (0/38)	0.09
Participation rate at improved preoperative level of sports	75% (46/61)	74% (17/23)	76% (29/38)	0.83	90% (55/61)	78% (18/23)	97% (37/38)	0.02

* Comparison primary vs non-primary.

Clinical sport outcomes

The number of patients participating in sports and their level of sport before injury, before TOPIC, 1 year after TOPIC, and 2 years after TOPIC can be found in Table 12.8. The AAS increased significantly from 2 preoperatively to 5 points both 1- and 2-years post-TOPIC ($p < 0.05$). The NRS during running improved significantly from 9 to 5 points both 1- and 2-years post-TOPIC ($p < 0.05$). The pre-injury, preoperative, 1-year post-TOPIC and 2-years post- TOPIC AAS and NRS scores are shown in Table 12.9. A graphic distribution of patients participating in high, medium and low impact sports pre-injury, preoperatively, 1-year post-TOPIC and 2 years post-TOPIC can be found in Figure 12.3, two of the 63 participants were not included in these analyses due to getting an ankle fusion after TOPIC.

Table 12.8: Type and level of sport pre-injury, preoperatively and 1- and 2-years after Talar OsteoPeriostic Grafting from the Iliac Crest

	Pre-injury	Preoperatively	1-year postoperatively	2-years postoperatively
Total sports participation	61 (100%)	29 (49%)	57 (93%)	60 (98%)
Recreational level	31 (51%)	27 (44%)	52 (85%)	55 (90%)
Competitive level	30 (49%)	2 (3%)	3 (5%)	4 (7%)
Professional level	0 (0%)	0 (0%)	1 (2%)	1 (2%)
No sports	0 (0%)	32 (52%)	5 (8%)	1 (2%)

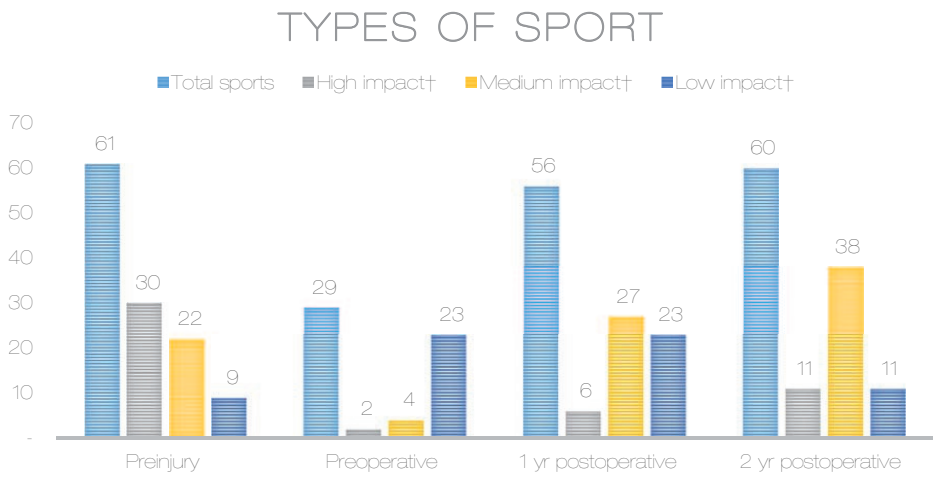

Figure 12.3: Distribution of high, medium and low impact sports at various times. High impact: AAS of 8, 9, and 10; Medium impact: AAS of 5, 6 and 7; Low impact: AAS of 3 and 4.

Table 12.9: Ankle Activity Scale and Numeric Rating Scale for pain pre- and postoperatively

	Pre-injury	Preoperative	1 year	p-value†	2 years	p-value†
AAS*	7 [5–8]	2 [2–3]	5 [3–5]	< 0.01	5 [5–6.5]	< 0.01
NRS Running*	inapplicable	9 [8–10]	5 [1–8]	< 0.01	5 [1–8]	< 0.01

* Median [IQR]. † Comparison pre-operative to 1- or 2-years postoperatively.

Complications and additional surgeries

In this cohort, 2 complications (3%) were encountered; 1 case of temporary hypoesthesia surrounding the iliac crest wound and 1 case of ongoing hypoesthesia of the first web space. Both complications resolved conservatively and did not limit the rehabilitation process or the ability to participate in sports 1- and 2-years after TOPIC. No patients suffered from donor-site morbidity 2 years postoperatively. A total of 22 additional surgeries on 19 patients were performed with a mean interval of 14.2 months between TOPIC and the additional surgical procedure. All information on the additionally performed surgical procedures after TOPIC can be found in Table 12.10.

Table 12.10: Additional surgical procedures after Talar OsteoPeriostic Grafting from the Iliac Crest

	No. (% of total no. of included patients)
Total no. of patients requiring additional surgery*	19 (31%)
Total no. of additional surgeries	22
Total no. of additional sub-procedures performed during the additional operations	39
Total no. of procedures related to graft†	5 (13%)
Arthroscopic shaping/reduction of the graft	2 (5%)
Arthroscopic shaping of the graft and debridement/BMS of the graft	2 (5%)
Open shaping/reduction of graft	1 (3%)
Procedures unrelated to graft†	34 (87%)
Implant removal for discomfort at osteotomy site	18 (46%)
Arthroscopic debridement for ankle impingement	9 (23%)
Open debridement for ankle impingement	2 (5%)
Open and arthroscopic debridement for ankle impingement	2 (5%)
Other procedures	3 (8%)

* No. (% of total no. of included patients). † No. (% of total no. of additional procedures).

Discussion

The primary finding of the present study is that the TOPIC procedure for large, complex osteochondral lesions of the talus results in 8 out of 10 patients participating at their desired level of sports 2 years after the surgery. The other primary findings are that 10 out of 10 patients return to any level of sports and 6 out of 10 patients return to their pre-injury level of sports 2 years postoperatively. These findings show that the vast majority of the patients return to some (type of) sports following the TOPIC procedure, with a high rate of self-defined goal attainment. These results show the clinical efficacy of the TOPIC procedure and may benefit the joint patient-physician shared-decision making process through a more informative expectation management.

When evaluating the return to sports rates following autograft procedures for large OLTs, a systematic review found that 90% of patients returned to any level of sports after at least 24 months follow-up.[24] These results can be considered comparable to those found in the present study. With respect to the return to pre-injury level of sports, the previously mentioned systematic review found that osteochondral autograft procedures show a slightly higher return to pre-injury level of sport rate of 72% compared to the 59% observed in the present study. The authors hypothesize that this difference may be due to the difference in the type of included patients, wherein the TOPIC procedure can be regarded as a 'salvage-procedure' due to the challenging nature of the treated OLTs (large, mostly non-primary, challenging morphology and relatively high OA scores).[21] This hypothesis can be underscored by referencing to the recently published two-year prospective clinical results of the TOPIC procedure in which it was also stated that the included patients undergoing the TOPIC procedure present with larger sized lesions as well as a higher percentage of non-primary lesions, as compared to osteochondral autograft procedures.[8] As such, it may be of more relevance – in relation to the indication of the TOPIC procedure – to compare the postoperative sports outcomes after the TOPIC procedure to for example ankle arthrodesis studies and allograft transplantation studies.

When considering the change in the level of sports, participation level, and AAS it can be observed that patients returned to a lower impact and level of sports. In line with the observations of the present study, Paul et al.[19] observed that the level of sporting activities changed in nature and the number of patients participating in high-impact and contact sports decreased, Moreover, the aforementioned

authors found that the AAS in 130 OLT cases treated with osteochondral transplantation decreased from 5.9 pre-injury to 5.0 postoperatively and the activity rating scale[18] decreased from 8.9 preoperatively to 6.8 postoperatively. It can be hypothesized that both physical restrictions (i.e., residual pain, postoperative restrictions in range of motion or function) and mental restrictions (i.e., fear of re-injury, pain catastrophizing, unwillingness to return to previous sport) may play a role in the return to sports and level of participation, as has previously been suggested in other orthopedic literature such as anterior cruciate ligament reconstruction patients.[29] Moreover, when considering the rate of participation at the desired level of sport one can conclude that such factors may have already played a role before the surgery had been performed, and thus could influence post-operative results. It is therefore important to optimally counsel patients and monitor the physical and mental wellbeing of patients in both the pre-operative setting as well as the rehabilitation phase in order to obtain optimal outcomes. The abovementioned results should however be interpreted in the light of the high level of return to sports rates in the patient group with 98% of the patients returned to any level of sports 2 years after the TOPIC surgery.

Even though a high percentage of reoperation was found in this study, high patient reported outcome measures were found in a clinical study following TOPIC for large OLTs with a pre- to postoperative numeric rating scale of pain (NRS) improvement of 7 points during walking and a significant improvement of all Foot and Ankle Outcome Score subscales scores 2 years after TOPIC.[8] Additionally, all of the RTS outcomes found in this study were higher 2 years after the TOPIC procedure as compared to the 1-year postoperative timepoint thereby indicating that the reoperations may have a limited impact on the midterm to long-term (sporting) results after TOPIC. A longer follow-up study is necessary to confirm this hypothesis.

The strengths of this study are the 100% follow-up rate, the prospective nature of the study, and the use of independent assessors for the radiological data collection from CT-scans with high intra and interrater reliability. An additional strength is the use of a mixed design wherein both quantitative and qualitative data was collected from the telephonic interviews and in which the prospectively collected data was verified and double-checked. These interviews included a full reconstruction of the patients' course of disease with regards to their OLT and therefore provides a clinically representative view of the (return to/participation in) sports outcomes. Another strong point of the study is that we were able to use a newly developed outcome, namely, the desired level of postoperative return to sports.

This method of scoring return to sports involves a self-defined, personalized goal set by the patient, functioning as goal-attainment scaling (GAS). GAS is a tool that ensures a holistic, patient-centered evaluation, and it is a valuable component in patient care, facilitating a more individualized, engaging, and effective treatment process.[12,13] On the other hand, the desired level of sport outcome is more subjective compared to the other sports-outcomes and potential biases could occur.

The present study is not without limitations. First, this is a comparative study focusing on the differences between primary and non-primary lesions rather than focusing on inter-treatment differences. Future studies may also focus on analyzing the differences in postoperative sports outcomes after different surgical interventions in order to test for clinical superiority. Secondly, no return to sport times were assessed, and no prognostic factors for returning to sports following TOPIC were explored. However, a previous study found that high BMI was associated with patient-reported pain outcomes[8] but another study found no BMI was not significantly correlated with the reported activity levels of patients treated with osteochondral transplantation of the talus – as such, this needs to be further explored in future studies.[19] Another limitation that should be mentioned is that the desired level of sports was determined by the patient and assessed and recorded post-operatively by the study team to verify the pre-operative expectations (also known as goal attainment scaling). A different limitation of the study is that no formal power calculation was performed – we rather aimed at including the highest number of patients in a prospective manner through the employment of a convenience sampling approach. As such, the power of the comparative analyses may be considered low. Also, no correlation was found between preoperative factors and RTS outcomes, which may be related to the study size. We must also mention the heterogeneity in the study's population, postoperative rehabilitation, age, (pre-injury and pre-operative) level of sport, lesion size and morphology and osteoarthritic grading of patients varied greatly.

The TOPIC procedure is a new procedure, therefore research on this topic is scarce and only covers short-term follow-up results. Mid- and long-term follow-up studies including more participants are required in the future to get a better understanding of the long-term (RTS) outcomes of the TOPIC procedure. More research on specific study groups such as (high performing) athletes and primary versus secondary OLT, OA grading, specific lesion sizes and morphologies is needed to get a more patient-specific prognosis which will benefit both the surgeon and the patient.

The present study is of clinical relevance in the sense that through the present study patients opting for autologous osteoperiostic grafting for large OLTs can be adequately and informatively counseled with regards to the expectations concerning postoperative sports outcomes. As such, the study broadens the framework for expectation management to patients and as such can improve the quality of the shared decision-making process. From a research perspective, the novel methodological framework with the use of an in-depth qualitative telephone interview and modified definitions of return to sport and participation in sport may help with better understanding (return to/participation in) sports outcomes following cartilage surgery of the ankle. This is important as return to sports is a complex outcome measures influenced by multiple variables, but highly clinically important for patients.

Conclusions

The TOPIC procedure for large osteochondral lesions of the talus results in 8 out of 10 patients participating at their self-reported desired level of sports 2 years postoperatively. Ten out of ten patients return to any level of sports and 6 out of 10 patients return to their pre-injury level of sports 2 years postoperatively. As such, this joint-sparing procedure for large osteochondral lesions of the talus ensures successful and durable sports (participation) outcomes after the TOPIC procedure. The findings of the present study may support patients and physicians in a more in-depth, joint shared decision-making process.

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Appendix 12.1: Standardized qualitative interview format

Pre-operative characteristics

- According to the online questionnaire, you played … right before your surgery, is that right/ Did you play sports right before your surgery?
- At what level did you practice this sport? (Top level, competitive, recreational) Can you specify this?
  - Top level/Professional (Olympic games, World Championships, European Championships, Worldcups, National team, National championships at the highest level, payed sport)
  - Competitive (soccer/ hockey/ rugby competition on the 3rd league or lower, national championships on any level lower than elite sports)
  - Recreative (50+ hours of sport annually)
- How many hours did you train a week right before surgery?
- Did you do another sport/ activity right before your surgery?

Post-operative characteristics

- According to the online questionnaire, one year after your surgery you played … is that correct? Did you play sports one year after surgery?
- At what level did you practice this sport? (Top level, competitive, recreational) Can you specify this?
  - Top level/Professional (Olympic games, World Championships, European Championships, Worldcups, National team, National championships at the highest level, payed sport)
  - Competitive (soccer/ hockey/ rugby competition on the 3rd league or lower, national championships on any level lower than elite sports)
  - Recreative (50+ hours of sport annually)
- How many hours did you train one year after the surgery?
- Did you play another sport or do another physical activity one year after surgery?
- If yes: how many hours per week did you do this activity?
- Before getting the surgery, what were your expectations regarding returning to sports after recovery?
- Did you meet these expectations?
- How did your sport/physical activity ability develop from one year after surgery until now?

Chapter 13

Towards automated curvature matching for iliac crest autograft harvesting

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Abstract

Background: Talar OsteoPeriostic grafting from the Iliac Crest (TOPIC) uses an autograft of the ipsilateral iliac crest to restore the talar dome after the resection of the osteochondral lesion of the talus (OLT). Curvature matching of the medial talar dome surface and the corresponding graft is clinically relevant in order to restore the biomechanical properties, but is currently performed by eye. As such, quantitative data is lacking regarding the statistical and visual comparison of this match for possible further technical and clinical improvement of the surgical technique.

Purpose: The primary purpose was to calculate the surface similarity between the medial talar dome and ipsilateral iliac crest in healthy individuals. The secondary purpose was to determine the optimal location of the grafts with respect to the spina iliaca anterior superior (SIAS).

Methods: Patients were selected from an electronic patient file system, based on presence of a computed tomography (CT) scan of both the talus and ipsilateral iliac crest. No power calculation was performed. DICOM files were used for segmentation of the talus and ipsilateral iliac crest. The medial talar dome was virtually resected through a 3D model based on average pre-defined OLT measures and thereafter cut-out. This medial talar dome surface was placed on the ipsilateral iliac crest within a region of interest, manually and also followed by Iterative Closest Point (ICP) registration. Surface similarity was quantified by calculating the average nearest neighbor distance (NND) across all mesh points on the medial talar dome surface to the mesh points of the iliac crest. The graft location was determined by measuring the distance from the SIAS (proximally onwards) to the centroid of the resected medial talar dome.

Results: A total of 20 patients (10 men, 10 women) were included. Surface similarity showed a maximum and median NND of 1.9 mm and 0.52 mm respectively after ICP, and 2.3 mm and 0.61 mm respectively after manual placement, and no significant differences between men and women ($p > 0.92$). Surface similarity values after ICP were significantly lower than after manual placement ($p < 0.001$). The graft location after ICP was 49 ± 11 mm proximally from the SIAS.

Conclusion: Our study showed high surface similarity between the medial talar dome and the iliac crest with iterative closest point registration reducing surface variability with approximately 0.5 mm and with no gender differences regarding this primary outcome. The optimal mean location of ipsilateral iliac crest graft harvesting regarding surface similarity lies at 49 ± 11 mm proximally from the SIAS, with no found gender differences.

Keywords: Curvature · Iterative closest point · Nearest neighbor distance · Talar osteochondral lesion · Segmentation · TOPIC

Introduction

Osteochondral lesions of the talus (OLTs) are predominantly caused by a traumatic event, such as a sprain or a fracture of the ankle.[17,18,29] The majority of the lesions are located on the postero- or centromedial zone of the talar dome.[18,19,29,32] Initial treatment of an OLT usually involves conservative management.[2,3,15,18,19] When conservative treatment fails, surgical options remain, such as retrograde drilling, arthroscopic bone marrow stimulation, and autologous chondrocyte implantation.[18,19,27] However, these techniques may not suffice in cases where the OLT is relatively large, of secondary nature, or are of cystic morphological presentation. In such cases, remaining solutions involve transplantation of an osteo(chondral) auto- or allograft.[2,15,25] Talar OsteoPeriostic grafting from the Iliac Crest (TOPIC) is such a surgical procedure and is developed and performed at the Amsterdam UMC.

TOPIC uses an autologous graft of the ipsilateral iliac crest to fill up the talar defect.[5,7,15] The iliac crest is a preferred location for graft harvesting for two reasons: it is a non-weight bearing location and it is covered with a periosteal layer which consists of cambium of which the included cell can function as precursor cells for the formation of hyaline cartilage post transplantation.[15] Additionally, harvesting must take place at least 1 cm proximal to the SIAS to prevent avulsion.[7,25] Lastly, the curved iliac crest is matched by the surgeon to the talar surface to determine the best match and thus the location of the graft. After harvesting the graft, its shape is adjusted until it matches the talar defect in a press-fit manner.[15] The restoration of the talar surface is required for an adequate contact area and pressure distribution in the ankle, both of which are important biomechanical properties.[2] TOPIC is a clinically effective technique since it shows consolidation in 100% of these grafts and significant improvement regarding different pain scores.[5]

As stated above, surface matching of the talus and iliac crest is a crucial step in the procedure. Currently, this assessment is performed intra-operatively by eye, relying on surgical experience comprising a long learning period and time-consuming due to the need for high precision. However, quantitative data is desired to objectively support the presumed surface match between the talar dome and the iliac crest and in order to pre-operatively determine the optimal position and dimensions of the autograft harvesting on the iliac crest. This all with the final goal to further enhance the precision and improve the clinical efficacy of the TOPIC procedure.[5,7,15]

To contribute towards the further improvement of the TOPIC surgical technique, the current study therefore aimed to calculate the surface similarity between the talar

surface and ipsilateral iliac crest. In this study, surface similarity can in this sense be regarded as a surrogate measure for (also) the similarity in curvature between the iliac crest and the medial talar dome. The primary objective was to identify the surface similarity between the medial talar dome and ipsilateral iliac crest, after a manual match and with the additional use of iterative closest point (ICP) registration. The secondary objective involved determining the optimal location of the grafts on the iliac crest regarding surface similarity. The tertiary purpose was to determine inter- and intra-observer variability in manual placement of the medial talar dome cut on the ipsilateral iliac crest.

Methods

The present study is a retrospective, single-centre, nonrandomized cohort study using computed tomography (CT)-images of an existing database.

Study population and patient selection

A local electronic patient file system (EPIC/AFGA) was searched from 2016 to November 2023 for patients who had undergone both a CT-scan of the pelvis and a CT-scan of the ankle. CT-scans were made with a GE Medical Systems Discovery CT750 or a Siemens SOMATOM Drive following the then applicable protocol for either the ankle or pelvis. Resulting patients were discussed during a consensus meeting involving a musculoskeletal radiologist (FS) and a researcher (JD). Subjects that were included in the study were limited to adults without any medical condition affecting the bone contour of the talus and iliac crest. Inclusion and exclusion criteria are stated in Table 13.1. Eligibility criteria for ankle CT-scans were both weight-bearing and non-weight-bearing scans with a maximum slice thickness of 1.5 millimetres.

Table 13.1: Inclusion and exclusion criteria

Inclusion criteria	Exclusion criteria
- Adult (minimum age is 18 years) - CT-pelvis and CT-ankle (both weight and non-weight bearing) - Intact bone curvature of ipsilateral iliac crest and talus (assessed by musculoskeletal radiologist (FS) and researcher (JD))	- (Non-)traumatic pathology or previous surgical procedure to ankle and/or iliac crest (e.g. fractures, ankle dislocation) - Deformities to the bone that affect the contour (fracture, pathology) - CT-scan of pelvis and/or ankle that did not contain the entire talus or iliac crest - Low quality (e.g. movement, high slice thickness) or artefacts

The maximum thickness for the pelvis scan was set at 2 millimetres. For equal gender distribution, 10 males and 10 females were included with an equal distribution of left and right ankles in each group.

Segmentation

Digital Imaging and Communications in Medicine (DICOM) files of included patients were imported in in-house software of the Amsterdam UMC.[8] It provides segmentation of DICOM files and further processing of these models. Prior to segmentation, each scan was resampled through interpolation to obtain an isotropic voxel dimension of 0.5 mm. If the original dimensions were smaller, this value was applied. Segmentation then involved threshold-connected region growing, filling to close residual holes on the inside and outline of the bone, and to initialize a Laplacian level-set segmentation growth algorithm ($\sigma = 1$ mm). The marching cubes algorithm was used to extract a polygon mesh at the zero level of the level-set image. These polygon meshes were then imported into 3D Slicer (by Slicer community, www.slicer.org, version 5.6.1).[10]

In 3D slicer, the nine-grid scheme for localization of talar defects was drawn with curves onto the surface (Figure 13.1B).[22] Osteochondral lesions of the talus occur most frequently in the centromedial zone in 31% of the cases[32] (zone 4, Figure 13.1B) with mean dimensions of 18 millimeter anteroposteriorly and 13 millimeter mediolaterally.[5] It was chosen not to take CT scans of patients with osteochondral lesions of the centromedial talar dome, but to analyze intact tali so that the surface similarity (as a surrogate marker for curvature matching) between the native talus and the iliac crest would reflect the anatomical congruency in an unaffected state, thereby avoiding potential distortion caused by pathological morphology or subchondral collapse. These properties comprise the medial talar dome which are measured with linear measurements on the talar surface (Figure 13.1C). Through each of these lines, a plane was positioned to use for cutting. An additional fourth plane was placed at the medial side (Figure 13.1D) so only the medial talar dome surface remains after cutting, required for surface matching. Lastly, to ensure comparable starting positions for each talus and minimize observer bias, each talus was translated with its posterior side against the ipsilateral spina iliaca anterior superior (SIAS). This approach avoided the time-consuming process of first translating each talus towards the SIAS.

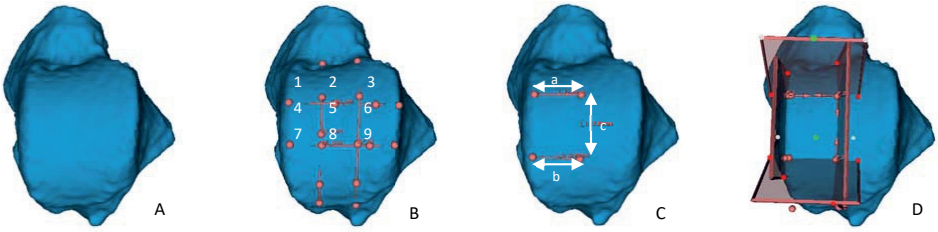

Figure 13.1: Superior view of segmented 3D models of a right talus during the process of determining the medial talar dome section. (A) A 3D model of the talus after segmentation. **(B)** The nine-grid scheme drawn onto the talar surface using curves.[1] Area 4 is the location where most lesions are located.[32] **(C)** Around area 4, the lesion is determined using average sizes from Dahmen et al.,[5] (a) mediolateral anterior, (b) mediolateral posterior, (c) anteroposterior. **(D)** Planes are placed through the lines of the determined medial talar dome section. An additional plane is set at the medial side of the talus to only obtain the surface of the talus.

Regarding the pelvis, the orthopedic surgeon determined the Region of Interest (ROI) on the ipsilateral iliac crest for graft harvesting. This side is chosen as it provides more direct surgical access and minimizes the need for additional repositioning or incisions compared to the contralateral side. This region had to start at least 1 cm proximally from the SIAS to prevent an avulsion fracture.[14] Considering additional surgical experience, a geodesic distance of minimal 2.5 cm proximally from the SIAS was chosen, measured with manually placed consecutive fiducials (Figure 13.2A) extending to the midpoint on the iliac crest (Figure 13.2A)

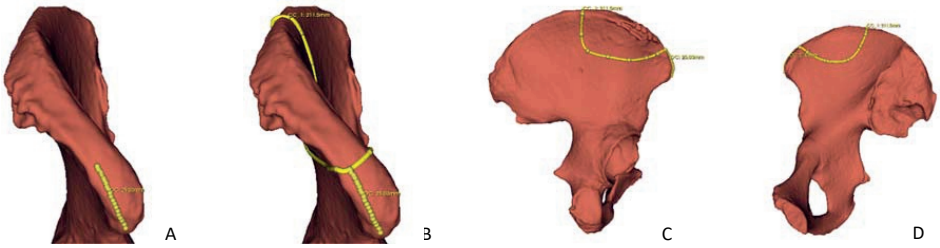

Figure 13.2: 3D models of a right iliac crest. (A) Anterior view. Yellow consecutive fiducials indicate the distance from the SIAS measured 2.5 cm proximally. **(B)** Anterior view. From 2.5 cm proximal of the SIAS a curve is drawn onto the pelvis, crossing the midpoint of the iliac crest. **(C)** Lateral and **(D)** medial view of the right pelvis with the determined ROI (yellow).

Manual matching

The medial talar dome section was manually positioned onto the ipsilateral side of the iliac crest within the ROI, by translation along, and rotation about the x-, y-, and z-axes with the aim to find an optimal match between the medial talar

dome section and iliac crest surface – as previously mentioned, the ipsilateral iliac crest is chosen for the harvesting of the graft during the TOPIC procedure.[4,6,14] This approach was similarly conducted by two observers (JD, SvB) within a region of interest that extended halfway of the iliac crest to 1 cm proximally from the SIAS.

Semi-automatic matching

Following manual positioning of the medial talar dome section, Iterative Closest Point (ICP) registration was applied to improve the level of agreement between the medial talar dome section and iliac crest surface.[1] In this procedure mesh points of the medial talar dome section mesh are repositioned iteratively with the aim to minimize the distances mesh point of the iliac crest surface.[20,21] Rigid ICP registration was executed using a randomly selected 25% of the existing medial talar dome section points until convergence was achieved (2000 iterations, tolerance 0,001 mm). Tolerance is defined as the maximum distance between the medial talar dome section and iliac crest that must be maintained during ICP.

Graft localization

For localization of the medial talar dome section on the iliac crest only models after ICP were exported to 3D Slicer together with the iliac crest since ICP was assumed to improve surface matching. 3D Slicer determined the centroid of the medial talar dome section that served as the starting location for the fiducials that were placed on the surface of the iliac crest to the SIAS. This length of the curve from the centroid of the medial talar dome section to the SIAS can also be performed intraoperatively.

Data collection

To quantify the surface similarity between the resected medial talar dome and the iliac crest, the maximum and average of the absolute nearest neighbor distance (NND) was used. This was evaluated for the resected medial talar dome after manual placement and after additional ICP registration, and for each individual patient. A value of 0 mm indicates a perfect match of both surfaces, hence a lower value represents a higher surface similarity.[30] Additionally, these NNDs were visualized using a heatmap on the iliac crest, using colors on a scale from 0.01 to 3.0 mm distance.

Statistical analysis

Statistical analyses were performed using IBM SPSS Statistics for Windows (version 28.0, IBM Corp, Armonk, NY, USA).[13] Descriptive statistics were used for patient characteristics. All data was checked on normality using the Shapiro-Wilk test. Normally distributed continuous data is shown as mean with standard deviation, otherwise as median with interquartile range. Statistical significance between group demographics was tested using the Mann-Whitney U test or an independent T-test, based on normality. For manual and resected medial talar dome placement by ICP registration, differences were assessed with a Wilcoxon signed rank test or a paired t-test, based on normality.[23] Graphs were designed with MATLAB (version R2024a).[31]

Intra- and interobserver reliability coefficients (ICCs) were estimated using the surface similarity after manual placement of the medial talar dome section on the iliac crest along with 95% confidence interval. No ICC measurements were performed for the ICP measurements as this was not a manual 'humanly' placed outcome. Intra-observer reliability was based on three measurements performed at least one day apart. Inter-observer reliability was based on one measurement across 2 raters. Interpretation of the ICC was based on the scale described by Koo, Li:[16] < 0.5 indicating poor reliability, 0.5 to 0.75 moderate, 0.75 to 0.9 good and > 0.9 excellent. Statistical significance was set at $p < 0.05$. The primary outcome measure of the present study is the NND in millimeter of each mesh point in the medial talar dome section to the iliac crest, the secondary outcome is the mean distance of the centroid of the medial talar dome section on the iliac crest, measured from the SIAS (proximally onwards). In this study, surface similarity is regarded as a surrogate indicator of curvature compatibility between the iliac crest and the medial talar dome.

Results

The database resulting from EPIC/AFGA consisted of 63 patients that had undergone a CT-scan of the ankle and ipsilateral pelvis. Resulting from the in- and exclusion criteria, 36 patients (26 males, 10 females) remained for inclusion Figure 13.3 shows the flowchart of the patient selection procedure. Patient characteristics of the included patients are shown in Table 13.2. An independent paired t-test showed no statistical difference between the mean cut out talar lesion surface of males and females (95% CI [-10.40, 60.80], $p = 0.147$).

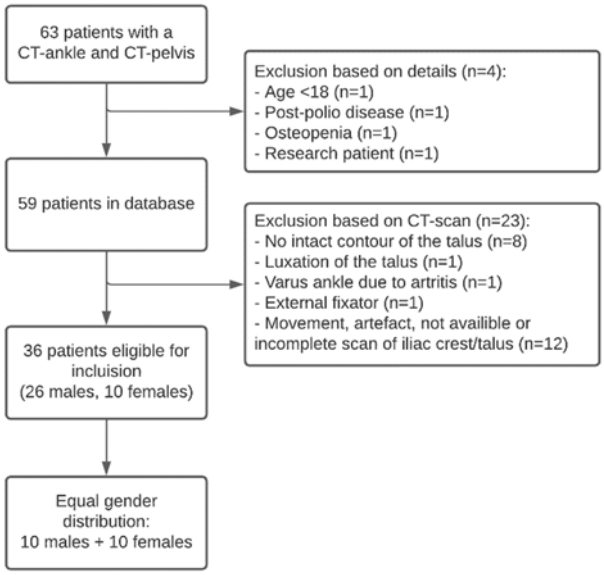

Figure 13.3: Flowchart of the patient selection procedure. CT, Computed Tomography.

Table 13.2: Patient demographics

Characteristic	Males (N = 10)	Females (N = 10)	All (N = 20)	p-value
Age at scan (y)	44.2 ± 17.9	53.3 ± 27.2	48.8 ± 22.9	0.19 (n.s.)
Lesion anteroposterior (mm)	17.95 [17.89, 17.96]	17.65 [17.11, 17.96]	17.91 [17.42, 17.96]	0.094 (n.s)
Lesion ML anterior (mm)	13.05 [12.95, 13.08]	12.98 [12.91, 13.06]	13.02 [12.91, 13.07]	0.31 (n.s.)
Lesion ML posterior (mm)	12.63 ± 0.72	12.65 [11.87, 12.94]	12.68 [12.11, 12.94]	0.45 (n.s.)
Lesion size talar surface (mm^2)	270 ± 15.02	257.59 [242.80, 273.10]	262.22 [250.30, 280.08]	0.070 (n.s.)

[a] Data are presented as mean ± SD if normally distributed, otherwise as median [25% percentile, 75% percentile]. ML, mediolateral.

Surface matching

The median of all maximum NNDs of the entire population was 2.3 mm [1.9, 3.2] for manual placement and decreased to 1.9 mm [1.3, 2.2] after ICP (Figure 13.4). The combined median of all median NNDs for each patient after manual placement was 0.61 mm [0.47, 0.72] and 0.52 mm [0.33, 0.61] after the use of ICP. A Wilcoxon signed rank test showed statistically significant differences between manual placement and additional ICP for both the maximum ($Z = -3.58$, $p < 0.001$), median ($Z = -3.55$,

p < 0.001) and range (Z = -3.58, p < 0.001). The median value after ICP was lower in 17 of the patients (85%) than after manual placement. An independent paired t-test did not show differences between males and females for the maximum (95% CI [-1.29, 1.42], p = 0.92) and median NND (95% CI [-0.33, 0.20], p = 6.2).

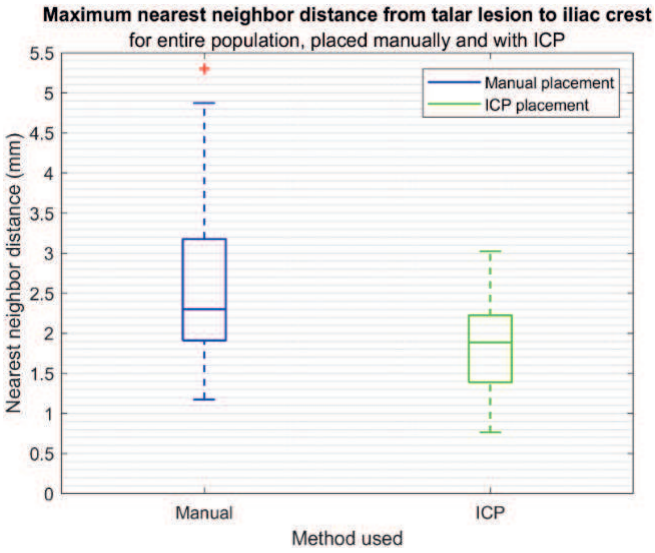

Figure 13.4: Maximum nearest neighbor distances of all patients after manual placement (blue) and additional ICP (green).

The boxplots in Figures 13.5 and 13.6 show the NNDs from the medial talar dome section OLT to the iliac crest for male and female patients, with the widest range after manual placement in patients M5 and F1. Figures 13.7B-C reveal increased medial talar dome section OLT overhang due to their narrower iliac crests, which corresponds to a broader outlier range in Figures 13.8B-C.

Both the maximum and median value showed in patient F4 the greatest decrease after using ICP. Also, the heatmap (Figure 13.8D) shows lower NND values. The surface is manually placed superior of the iliac crest, but after ICP it is located on the medial side of the iliac crest, as in Figure 13.7D.

In contrast, only in patient M3 does the maximum NND increase after ICP but the mean does decrease. Figure 13.7A and Figure 13.8A show that ICP has rotated the medial talar dome section OLT in the transversal plane counterclockwise, resulting in a greater part overhanging the iliac crest adding more high values but a lower median distance. Both surfaces mainly overlap so the heatmap does not show distinguishable differences.

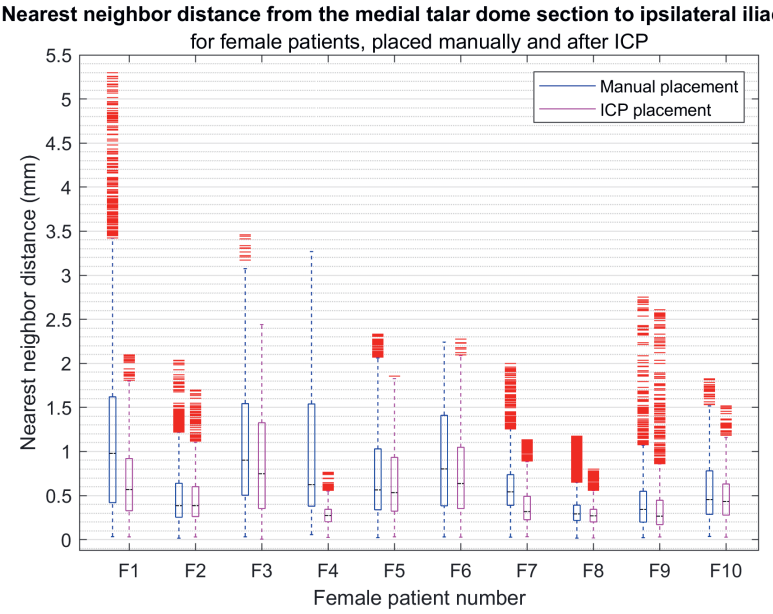

Figure 13.5: Boxplot for all female patients of the nearest neighbor distance (mm) of each mesh point measured from the medial talar dome section to the talus. The manual measurement (blue) and added ICP technique (green) are visualized with the outliers (red stripes).

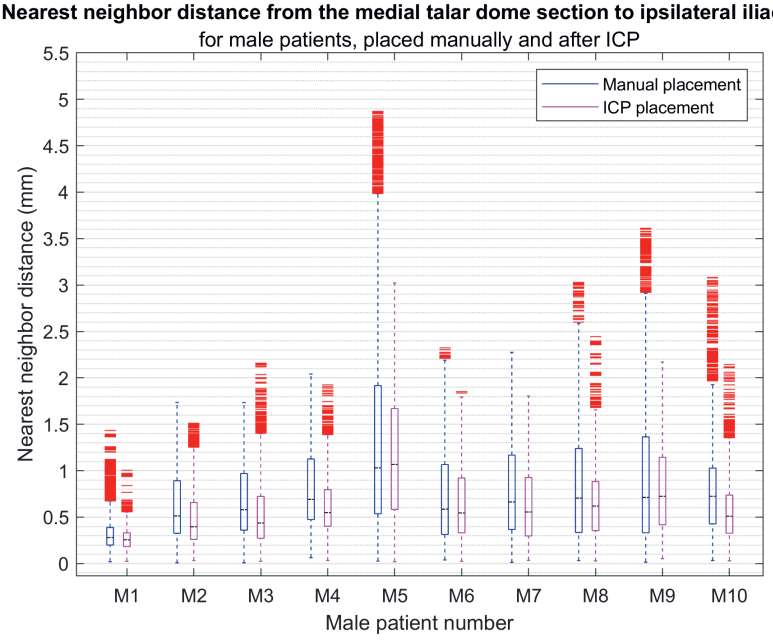

Figure 13.6: Boxplot for all male patients of the nearest neighbor distance (mm) of each mesh point measured from the medial talar dome section to the talus. The manual measurement (blue) and added ICP technique (green) are visualized with the outliers (red stripes).

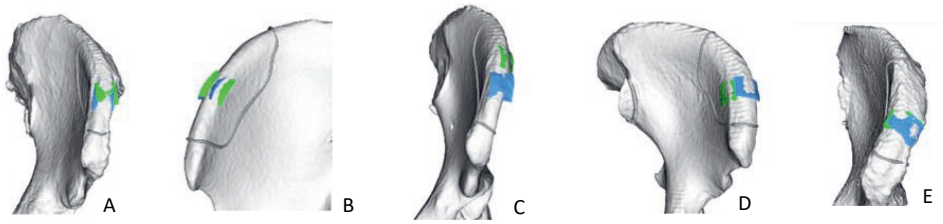

Figure 13.7: Medial-anterior view of the iliac crest with manually placed (blue) medial talar dome section and after the addition of ICP (green) of five patients. From A to E: M3, M5, F1, F4, F9.

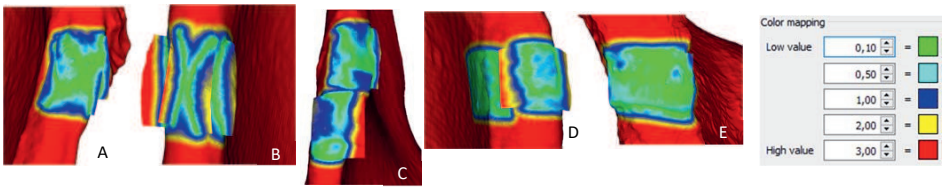

Figure 13.8: Nearest neighbor distances from the medial talar dome section to the iliac crest after manual placement and added ICP visualized as heatmaps. Figure 13.7 shows the location of both placements to distinguish in this figure. From A to E: M3, M5, F1, F4, F9. The scale (right) is in millimeter.

Adding ICP in patient F9 still shows a great number of outliers compared to other patients. Figure 13.7E shows that the surface location after ICP has barely changed, but NND values are still relatively low and below the combined median (Figure 13.8E).

In contrast, only in patient M3 does the maximum NND increase after ICP but the mean does decrease. Figure 13.7A and Figure 13.8A show that ICP has rotated the medial talar dome section in the transversal plane counterclockwise, resulting in a greater part overhanging the iliac crest adding more high values but a lower median distance. Both surfaces mainly overlap so the heatmap does not show distinguishable differences.

Adding ICP in patient F9 still shows a great number of outliers compared to other patients. Figure 13.7E shows that the surface location after ICP has barely changed, but NND values are still relatively low and below the combined median (Figure 13.8E).

Graft localization

The distance from the centroid of the medial talar dome section after ICP registration to the SIAS was normally distributed across the entire population and

no statistically significant differences were present between male and females. The mean distance measured proximally from the SIAS was 49.1 ± 11.4 mm with a maximum distance of 69.6 mm and minimum of 32.4 mm.

Intra- and inter-rater reliability

The ICCs on the manual placement methods (not the ICP methods) were estimated using a two-way mixed effects model based on the agreement between the median of the manual measurements. Results are shown in Table 13.3. The intra-rater reliability was 0.72 for the single measure representing moderate to good agreement. Inter-rater between two observers was 0.047, suggesting almost no agreement.[16] Additionally, locations of the medial talar dome section also vary between observers (Supplemental Figures S13.1 and S13.2).

Table 13.3: Intra- and interobserver reliability of surface similarity between the medial talar dome section and the iliac crest of manual measurements, evaluated by means of the ICC

	Intra-observer			Inter-observer		
	ICC*	95% CI	p-value	ICC*	95% CI	p-value
Median NND	0.722	0.517–0.867	< 0.001	0.047	0.275–0.418	0.399

ICC, intra-class coefficient; CI, confidence interval; NND, nearest neighbor distance.

Discussion

The Talar OsteoPeriostic grafting from the Iliac Crest (TOPIC) procedure has previously shown promising results for large, complex OLTs.[4] However, quantitative data evaluating the curvature congruence between the talar dome and harvesting site on the iliac crest had been absent. This study employed 3D visualizations to assess these aspects, quantifying distances and determining optimal graft locations. The maximum and median NND between the surface of the medial talar dome section to the iliac crest were 1.9 mm and 0.52 mm respectively. In this study, the observed low nearest neighbour distances (NNDs) indicated a high degree of surface similarity, which is consequently regarded as a surrogate indicator of curvature compatibility between the iliac crest and the medial talar dome The locations of these medial talar dome sections were on average 49 ± 11 mm proximally from the SIAS. The average location of the best-matching curvature on the iliac crest, identified in this study, provides a valuable reference point for surgical planning.

Strengths

The iterative closest point (ICP) algorithm is a robust and stable technique widely used in medical applications.[20,21,24] This study found that the NND was significantly lower following ICP placement compared to manual placement only, confirming its application and effectiveness in making minor adjustments based on location. Overall, this dual approach to curvature matching established the improved match after ICP proving essential for evaluating and enhancing the TOPIC procedure.

Additionally, our study found a higher occurrence of outliers when the iliac crest is relatively narrow compared to the medial talar dome section (patients M5 and F1, Figures 12.7 and 12.8). This occurs because surface similarity, the shortest distance between the iliac crest and medial talar dome section, increases as the medial talar dome section extends. As a result, these outliers can distort the interpretation, falsely suggesting a surface 'mismatch' when the discrepancy is primarily due to differences in width rations. Therefore, it is essential to complement numerical data with visual analysis.

Limitations

Patients were selected from an existing database with different scanning protocols, resulting in a potential heterogeneity regarding voxel dimensions, which may have affected our results. However, a study by Gryska and coworkers, has shown that for slice thickness up to ~1.5 mm the surface error is rather low (approx. 0.2 mm), which is not likely to have a big impact on our findings.[12]

Because the current study was a pilot study, it solely included patients with medially sided OLTs since medially sided OLTs have a relatively higher incidence than lateral lesions.[32] The workflow showed clinical promise and can be expanded to lateral lesions as well. The ICP algorithm has limited freedom, constrained by initial manual placement, which affects both surface matching and location selection. As a result, it may not fully utilize the surgeon-defined ROI, potentially missing better matches. Future research should incorporate this entire ROI for greater clinical relevance. In this study, the medial talar dome section location was manually measured from the centroid to the ASIS, with observer-dependent variation. Virtual measurements could assist intraoperative localization by comparing imaging and real-time assessment. Improved clinical applications may include anatomical landmarks, navigation or 3D-printed templates for precise donor site identification. Another limitation of the present study is that the

inter-rater reliability of the was low – this can be attributed to the complexity of aligning the medial talar dome in six degrees of freedom onto the ipsilateral iliac crest, introducing substantial variability in both translation and rotation across the x-, y-, and z-axes. Further research should include surgeons as observers and a detailed protocol for manual medial talar dome section placement.

Clinical relevance

This study's evaluation of the TOPIC surgical technique, with a focus on curvature matching between the talus and iliac crest, provides valuable preoperative and intraoperative insights. Preoperative matching of the medial talar dome section to the iliac crest helps assess the degree of curvature congruence and determines the size of the graft. This approach enables personalized care by allowing preoperative planning of the optimal graft location and the use of a custom cutting guide to excise a graft that best fits the defect. This may enhance biomechanical properties, increase durability, and reduce cyst formation at the recipient site. Intraoperatively, orthopedic surgeons can identify the potential graft site approximately 49 mm proximal to the anterior superior iliac spine, as suggested by this study, potentially improving clinical outcomes.

Future perspectives

This study used mean OLT surface dimensions described by Dahmen et al.[5] for the entire population. However, Gianakos et al.[11] reported that OLTs are smaller females than in males. Given that the reliability of manual medial talar dome section measurements in this study is unknown, this may lead to variations in OLT location, which could affect curvature and, consequently, graft harvesting site on the iliac crest. Since females have a smaller volume of the iliac crest than males,[9] a representative OLT size and location is required for adequate graft harvesting. To conclude, including patients with an existing OLT in further research can personalize curvature matching and may help in pre-operatively predicting the optimal location of the graft.[1,26,28]

Seki et al.[28] showed that both tali within a healthy patient are almost symmetrical. Hence, registration of the unaffected talus onto the post-TOPIC talus is expected to be symmetrical. Therefore, further research may also consider the agreement between the post-TOPIC talus and the contralateral talus which may work prospectively as an indicator for the clinical outcome.

Conclusion

Our study showed high surface similarity between the medial talar dome and the iliac crest with iterative closest point registration reducing surface variability with approximately 0.5 mm and with no gender differences regarding this primary outcome. The optimal mean location of ipsilateral iliac crest graft harvesting regarding surface similarity lies at 49 ± 11 mm proximally from the SIAS, with no found gender differences.

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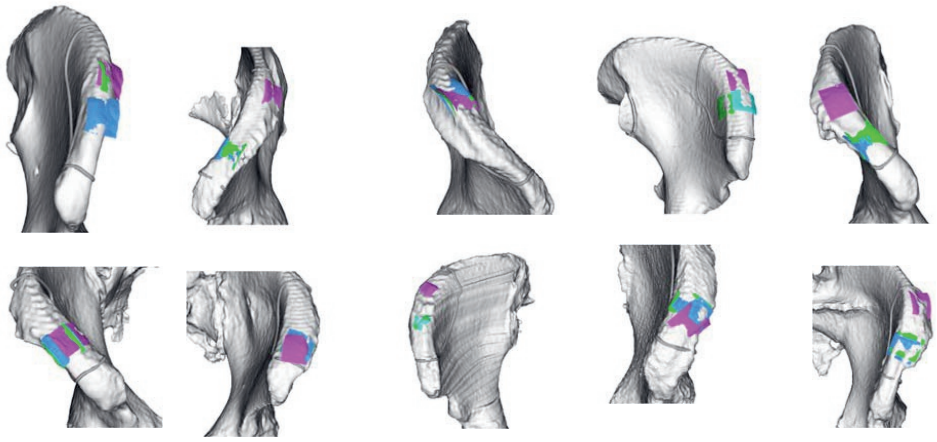
Appendix

Supplemental Table S13.1: The median and maximum values of the nearest neighbor distance (mm) for each male patient after manual placement and additional ICP

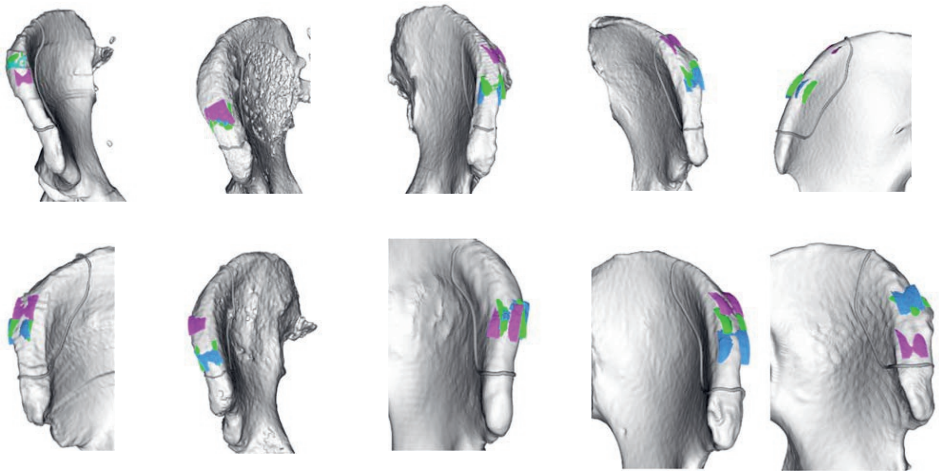
	Manual (mm)		ICP (mm)	
Males	Median	Maximum	Median	Maximum
Patient 1	0.28	1.43	0.26	1.0
Patient 2	0.51	1.36	0.40	1.25
Patient 3	0.58	1.73	0.44	2.16
Patient 4	0.69	2.04	0.55	1.92
Patient 5	1.03	4.87	1.07	3.02
Patient 6	0.59	2.33	0.55	1.85
Patient 7	0.66	2.28	0.56	1.81
Patient 8	0.71	3.03	0.62	2.45
Patient 9	0.71	3.61	0.72	2.17
Patient 10	0.73	3.08	0.51	2.15

Supplemental Table S13.2: The median and maximum values of the nearest neighbor distance (mm) for each female patient after manual placement and additional ICP

	Manual		ICP	
Female	Median	Maximum	Median	Maximum
Patient 1	0.978	5.2982	0.567	2.096
Patient 2	0.385	2.0335	0.385	1.696
Patient 3	0.902	3.4708	0.747	2.441
Patient 4	0.623	3.2684	0.274	0.764
Patient 5	0.564	2.3320	0.533	1.856
Patient 6	0.802	2.2414	0.637	2.276
Patient 7	0.542	1.9998	0.318	1.131
Patient 8	0.291	1.1730	0.270	0.799
Patient 9	0.343	2.7525	0.266	2.606
Patient 10	0.454	1.8237	0.433	1.518



Supplemental Figure S13.1: Visualizations of all female patients after manual placement of the medial talar dome section (blue), after additional ICP (green) and the placement of observer 2 (pink). Upper row, left to right: patient 1–5. Lower row, left to right: patient 6–10.



Supplemental Figure S13.2: Visualizations of all male patients after manual placement of the medial talar dome section (blue), after additional ICP (green) and the placement of observer 2 (pink). Upper row, left to right: patient 1–5. Lower row, left to right: patient 6–10.

Chapter 14

What are these cysts doing in my graft?! A meta-analysis on cystic occurrence after autografting and allografting for osteochondral lesions of the talus

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Abstract

Background: The exact incidence of cyst formation after graft transplantation for osteochondral lesions is unknown. The primary purpose was to assess and compare cystic occurrence after autografting, allografting and osteoperiosteal grafting for osteochondral lesions of the talus. Our secondary aim was to assess correlation of clinical outcomes with the presence of postoperative cysts.

Methods: A literature search was performed up to October 2023 through PubMed, Embase (Ovid), and Cochrane Library. The primary outcome was the postoperative cystic occurrence rate. A random effects model with moderator analysis was used to calculate differences in occurrence rates between treatment groups. The relationship between the presence of cysts and clinical outcomes was described.

Results: Thirteen studies were included with 382 ankles. The average radiological follow-up at which the presence of cystic occurrence was assessed ranged from 12 to 84 months. The rates of cystic occurrence for the osteochondral autograft transplantation group, the allograft transplantation group, and the osteoperiosteal transplantation group were 42% (95% CI 24–61), 58% (95% CI 40–74), and 34% (95% CI 12–67), respectively, without any significant differences noted. No relationship between the presence of cysts and clinical outcomes was found.

Conclusion: Postoperative cystic occurrence is common after osteochondral autograft transplantation (42%), allograft transplantation (58%), and osteoperiosteal transplantation (34%) in osteochondral lesions of the talus – without significant intertreatment differences. The postoperative presence of cysts was not correlated with clinical outcomes. Future research should assess whether the postoperative presence of cysts correlates with (clinical) outcomes at longer follow-up.

Introduction

An osteochondral lesion of the talus (OLT) is defined as damage to the talar cartilage and its underlying subchondral bone,[2] often caused by ankle trauma.[3,8] These lesions typically manifest with non-specific symptoms thus are often not identified due to a low index of suspicion, leading to debilitating pain and impaired joint function. Surgical interventions have shown to be clinically effective treatment options,[9,22] with autograft procedures, allograft procedures, and osteo-periosteal autograft procedures typically recommend for larger lesions.[18,40] Grafting procedures ensure high quality bone and/or cartilage restoration, and satisfactory clinical outcomes have been reported at mid-term follow-up.[9,13,14,22,27,35,37] However, development of cysts within the transplanted graft has been frequently seen as a complication or adverse event after the surgery.[15,17,27,37] It is unclear whether certain transplantation techniques produce a significantly higher or lower rate of cystic development at short-term, mid-term, and long-term follow-up, nor is it certain if the presence of post-operative cyst affects clinical outcomes. Several factors may play a role in the development of these cysts including but not limited to subchondral bone alterations, immune reactions (in case of allografts, quality of graft integration, post-operative rehabilitation, and/or potential (over)loading of the joint specifically where the graft is implanted.[20,21,28,33]

The primary research aim of the present meta-analysis is, therefore, to provide a comprehensive assessment of the rate of development of postoperative cysts within transplanted grafts following treatment of OLTs. We aim to quantify the prevalence of cyst formation after autograft procedures and allograft procedures for the treatment of OLTs and investigate potential variations in cyst development rates between these surgical techniques. The secondary research aim is to assess the potential correlation between the presence of cysts and patient-reported outcome measures (PROMs) to determine whether cyst formation is linked to inferior clinical outcomes.

The findings of the study will be of clinical relevance as the outcomes will form a strong basis towards further exploring the aetiology behind postoperative cyst formation, study the correlation between complaints (pain and/or other PROMs) and the presence of cysts, and will guide physicians to further improve the treatment outcomes for patients with large osteochondral lesions of the ankle.

Methods

A systematic review of the literature was performed and was reported according to the 2020 methodology of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA).[32]

Search strategy

The PubMed, EMBASE (Ovid) and Cochrane Library databases were searched from inception up to October 24, 2023 for potentially eligible articles. The full search strategy is outlined in Appendix 14.1.

Study selection and eligibility criteria

Two independent reviewers (JD and JH) screened titles and abstracts using predefined criteria in Rayyan.[31] Subsequently, articles were screened for full text and included when they met the inclusion criteria (Table 14.1). Discordant judgment in study inclusion was resolved by consensus discussion together with a third reviewer (GK).

Table 14.1: Inclusion and exclusion criteria

Inclusion	Exclusion
- Clinical studies assessing and describing the presence of occurrence of postoperative cysts after osteochondral autograft transplantation, osteochondral allograft transplantation, and en-bloc osteoperiosteal transplantation for osteochondral lesions of the talus with a mean minimum radiological (MRI/CT only) follow-up of 6 months after the transplantation procedure - A cohort of 5 or more patients needed to have had a follow-up MRI/CT during which the presence of cysts was specifically scored - Written in English - Full-text available	- Studies that did not present original data (e.g. reviews, technique papers, letters to the editor, editorial) - Conference abstracts - Animal or cadaveric studies - Double publication including overlap of patients

Methodological quality assessment

Methodological quality of the studies was evaluated using the validated Methodological Index for Non-Randomized Studies (MINORS) criteria[39] by two independent reviewers.

Data extraction

The following study characteristics were retrieved: authors, year of publication, and study design. Also, the following patient characteristics were retrieved: sex, age, number of lesions, number of ankles, lesion size and/or area, lesion location, type of index surgical intervention, timing of postoperative radiological (MRI/CT) assessment, and methods for clinical- and radiological assessment and their corresponding outcomes. Presence of postoperative cyst occurrence (including the description of localization of the cysts, i.e. within the transplant, elsewhere, or not described) was extracted as well as any correlation analyses between presence of postoperative occurrence of cysts and clinical outcomes. Subanalyses present in the publications on intra-treatment comparative analyses were also extracted (e.g. studying the comparative effect of the intraoperative addition of biologicals).

Statistical and data analysis

It should be noted that in the case of presence of both a postoperative CT-scan as well as an MRI-scan assessing the presence of postoperative occurrence of cysts, the CT scan was chosen as main radiological parameter to base the analyses on.[11,29,30] In the case of multiple radiological follow-up moments in time, the latest moment of follow-up was chosen. Furthermore, whenever there were multiple publications with an overlap of patients studied in the publications, the strategy of the authors was to choose the publication(s) yielding the highest number of patients for analysis. Another important methodological aspect to mention is that whenever the authors of the included studies mentioned both a postoperative presence of intra-transplant and outside-transplant cysts as assessed with the follow-up MRI and/or CT-scan, we chose to solely extract the intra-graft cyst occurrence rate. All included patients were assigned to treatment groups using the grouping method as previously described by Steman et al.[41]

Primary outcome measure

The primary outcome was the postoperative occurrence rate of cyst formation. The different occurrence rates of cysts were pooled using a random-effects model. These analyses were performed in an analysis model using R version 4.1.0 (R Core team, Vienna, Austria; metaprop function from the meta package[4]). The Clopper-Pearson interval was used to assess 95% confidence intervals. Differences in cystic development rates were compared amongst the following treatment groups using a moderator test for subgroup analysis with an $\alpha < 0.05$ indicating statistical

significance: osteochondral autograft transplantation, osteochondral allograft transplantation, and osteoperiosteal autograft transplantation.[25]

Secondary outcome measures

One of the secondary outcome measures was the explorative description of present relationships between the presence of postoperative cysts and clinical outcomes. Another secondary outcome measure was the explorative description of present relationships between the presence of postoperative cysts and patient or treatment-related factors.

Results

Search results

1,103 articles were included for full-text screening. A total of 13 articles were included for analysis (Figure 14.1).[10,12,15-17,19,24,26,34,36,42,44,45]

Methodological quality

The overall methodological quality scores with the MINORS-criteria for comparative and non-comparative studies are shown in Appendix 14.2.

Study characteristics

The 13 studies reported a total of 438 ankles, of these, 382 patients (88%) underwent postoperative MRI and/or CT after the auto- or allograft transplantation. The patients received the following surgical treatments: Osteochondral autograft transplantation (n = 247), osteochondral allograft transplantation (n = 31), osteoperiosteal transplantation (n = 104). The mean or median radiological follow-up at which the presence of cystic occurrence was assessed ranged from 12 months to 84 months postoperatively (Table 14.3). Six[12,16,24,26,34,42] out of 13 studies did not specify whether the postoperative cystic occurrence was specifically localized within or outside of the transplant, while 7[10,15,17,19,36,44,45] out of the 13 studies specifically stated that the cyst occurrence was within the transplant with one[36] of these 7 studies reporting on the occurrence rate of both the presence of cysts within the transplant and outside of the transplant. Other study and demographic patient characteristics are included in Table 14.2 and 14.3. Table 14.3 also described whether the authors reported whether the found cysts were located in or outside of the implanted graft.

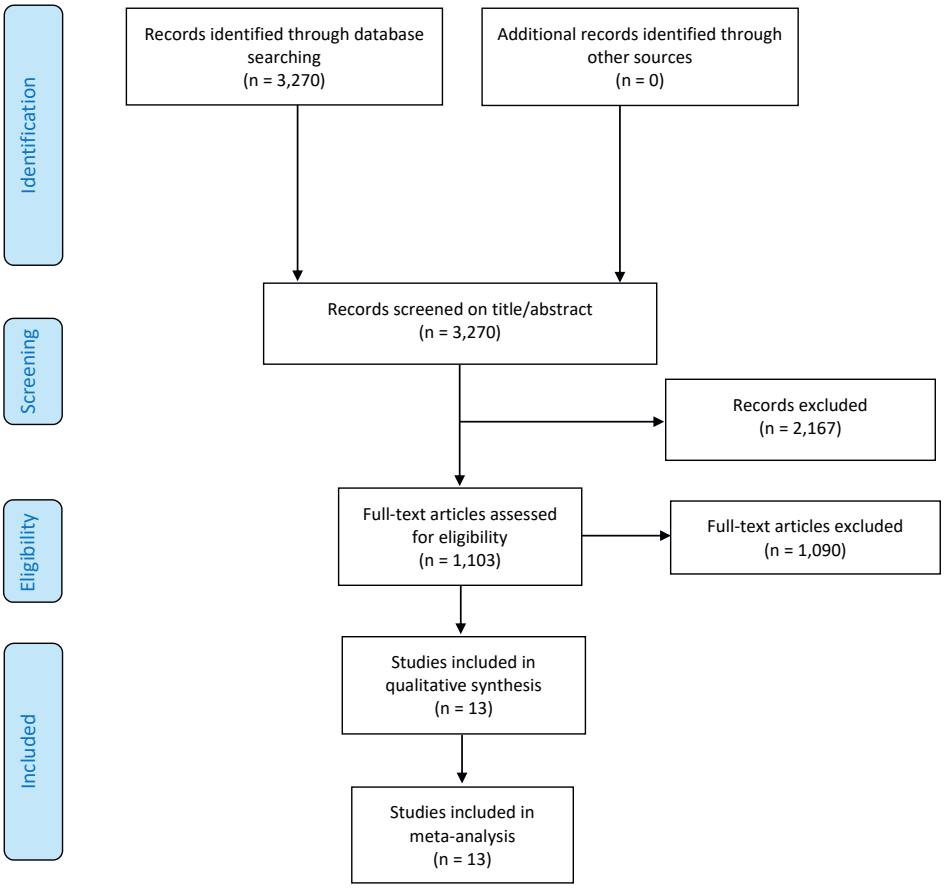

Figure 14.1: PRISMA flow diagram.

Postoperative cyst occurrence rate

The rates of postoperative cyst occurrence for the osteochondral autograft transplantation group, the allograft transplantation group, and the osteoperiosteal transplantation group were 42% (95% CI 24–61), 58% (95% CI 40–74), and 34% (95% CI 12–67), respectively, without any significant differences noted between these treatment groups (p = 0.31, Figure 14.2). The overall rate of postoperative cyst development was 42% (95% CI 28–57) (Figure 14.2).

Relationship between postoperative cysts and clinical outcomes

Six studies[10,12,34,42,44,45] described the relationship between the presence of postoperative cysts and clinical outcomes. No studies found a significant relationship between the presence of cysts and patient-reported clinical outcomes (Table 14.4).

Table 14.2: Study characteristics and patient demographic characteristics Part 1

Authors [ref] (year of publication)	Journal	Study design	Graft location	Additive treatment	Patients	Number of ankles	Males (%)	Median/mean age in years (range/SD)
Osteochondral autograft transplantation								
Fraser et al.[12] (2016)	KSSTA	Retrospective case series	Nonarticulating portion of ipsilateral femoral condyle	N.A.	36	36	24 (67%)	31 (7.6)
Hansen et al.[16] (2021)	Foot and Ankle International	Retrospective case series	Ipsilateral lateral trochlea	ECM + BMAC	25	25	N.A.	37.7 (14.8)
Imhoff et al.[19] (2011)	AJSM	Retrospective case series	Proximal lateral and medial femoral condyle	None	25	26	13 (52%)	33 (9)
Ross et al.[34] (2016)	Arthroscopy	Retrospective case series	Nonarticulating portion of ipsilateral femoral condyle	None	76	76	50 (66%)	35.8 (13.1)
Shimozono et al.[36] (2018)	JBJS	Retrospective comparative case series	Nonarticulating portion of ipsilateral femoral condyle	BMAC	25	25	9 (36%)	38.4 (13.0)
Valderrabano et al.[42] (2009)	AJSM	Cross-sectional follow-up	Lateral femoral condyle	None	12	12	8 (67%)	42 (23–58)
Wan et al.[44] (2022)	International Orthopaedics	Retrospective case series	Talar articular facet	None	24	24	16 (66.7%)	39.1 (17–64)
Woelfle et al.[45] (2013)	Foot and Ankle International	Retrospective case series	Ipsilateral lateral femoral condyle	None	32	32	17 (49%)	24.5 (15–49)

Authors [ref] (year of publication)	Journal	Study design	Graft location	Additive treatment	Patients	Number of ankles	Males (%)	Median/mean age in years (range/SD)
Osteochondral allograft transplantation								
Haene et al.[15] (2012)	JBJS	Prospective case series	Talar allograft	None	16	17	8 (50%)	35.8 (11.3)
Shimozono et al.[36] (2018)	JBJS	Retrospective comparative case series	Talar allograft	BMAC	16	16	10 (63%)	43.6 (13.5)
Osteoperiosteal autograft transplantation								
Dahmen et al.[10] (2023)	JBJS	Prospective case series	Crista Iliaca Autograft	None	43	43	13 (30%)	29 (IQR: 21–37)
Hu et al.[17] (2013)	Arthroscopy	Retrospective case series	Cylinder Crista Iliaca Autograft	None	17	17	16 (94%)	37.3 (24–53)
Leumann et al.[24] (2014)	KSSTA	Prospective case series	Crista Iliaca Autograft	None	14	14	11 (79%)	39.6 (14.4)
Li et al.[26] (2023)	Arthroscopy	Retrospective case series	Cylinder Medial Tibia Autograft	None	75	75	46 (61%)	41.23 (10.34)

BMAC, bone marrow aspirate concentrate; CT, computed tomography; ECM, extracellular matrix; MRI, magnetic resonance imaging; N.A., not available; SD, standard deviation.

Table 14.3: Study characteristics and patient demographic characteristics Part 2

Authors (year of publication)	Journal	Ankles which underwent post-operative MRI/CT (%)	Postoperative radiology used	Mean clinical follow-up in months(range/SD)	Mean radiological follow-up time after surgery in months (range/SD)	Description of localization of cystic occurrence - G: Within graft - N.A.: Overall postoperative cystic occurrence – described as not available - Both: Separate description of within graft and outside
Osteochondral autograft transplantation						
Fraser et al.[12] (2016)	KSSTA	36 (100%)	MRI	70.8 (12–144)	12.0 (N.A.)	N.A.
Hansen et al.[16] (2021)	Foot and Ankle International	22 (88%)	MRI	PROMIS: 24.4 (10.8) FAOS: 28.8 (11.6)	16.7 (4–47)	N.A.
Imhoff et al.[19] (2011)	AJSM	26 (100%)	MRI	84 (53–124)	84 (53–124)	G
Ross et al.[34] (2016)	Arthroscopy	76 (100%)	MRI	51 (12–97)	26 (24–36)	N.A.
Shimozono et al.[36] (2018)	JBJS	23 (92%)	MRI	26.3 (8.2)	21.8 (N.A.)	Both
Valderrabano et al.[42] (2009)	AJSM	12 (100%)	SPECT-CT and MRI	72 (43–91)	72 (43–91)	N.A.
Wan et al.[44] (2022)	International Orthopaedics	24 (100%)	CT	50.9 (25–117)	50.9 (25–117)	G
Woelfle et al.[45] (2013)	Foot and Ankle International	28 (88%)	MRI	29 (14–77)	N.A.	G

Authors (year of publication)	Journal	Ankles which underwent post-operative MRI/CT (%)	Postoperative radiology used	Mean clinical follow-up in months(range/SD)	Mean radiological follow-up time after surgery in months (range/SD)	Description of localization of cystic occurrence - G: Within graft - N.A.: Overall postoperative cystic occurrence – described as not available - Both: Separate description of within graft and outside
Osteochondral allograft transplantation						
Haene et al.[15] (2012)	JBJS	16 (94%)	CT	49.2 (24–168)	49.2 (24–72)	G
Shimozono et al.[36] (2018)	JBJS	15 (94%)	MRI	22.3 (6.5)	20.0 (N.A.)	Both
Osteoperiosteal autograft transplantation						
Dahmen et al.[10] (2023)	JBJS	43 (100%)	CT	26 (IQR: 24–30)	N.A.	G
Hu et al.[17] (2013)	Arthroscopy	16 (94%)	MRI	32.6 (24–48)	12 (N.A.)	G
Leumann et al.[24] (2014)	KSSTA	11 (79%)	SPECT-CT	25 (24–28)	25 (24–28)	N.A.
Li et al.[26] (2023)	Arthroscopy	34 (45%)	MRI	75.6 (60–112.8)	75.6 (60–112.8)	N.A.

CT, computed tomography; MRI, magnetic resonance imaging; N.A., not available; SPECT-CT, single photon emission computed tomography-computed tomography; SD, standard deviation.

Table 14.4: Study outcomes

Authors (year of publication)	Relationship cystic presence and clinical outcomes studied (yes/no)	Outcome of relationship	Relationship cystic presence and demographic factors/sub-treatment groups (yes/no)	Outcome of relationship
Osteochondral autograft transplantation				
Fraser et al.[12] (2016)	Yes	Sub-analysis: group of patients with postoperative cysts did not show a significant difference in postoperative AOFAS outcome score compared with patients without postoperative cysts.	No	N.A.
Hansen et al.[16] (2021)	No	N.A.	No	N.A.
Imhoff et al.[19] (2011)	No	N.A.	No	N.A.
Ross et al.[34] (2016)	Yes	Sub-analysis: group of patients with postoperative cysts did not show a significant difference in preoperative to postoperative changes in the FAOS score when compared with patients without postoperative cysts.	Yes	Primary osteochondral autograft therapy did not show a significantly different rate in postoperative cyst occurrence (59%) when compared to patients undergoing non-primary osteochondral autograft therapy (50%).
Shimozono et al.[36] (2018)	No	N.A.	No	N.A.
Valderrabano et al.[42] (2009)	Yes	Correlations analysis: (all/any) radiological findings did not have a significant correlation with clinical results (VAS pain score and AOFAS ankle score, $r = 0.42$ with $r^2 = 0.18$).	No	N.A.

Authors (year of publication)	Relationship cystic presence and clinical outcomes studied (yes/no)	Outcome of relationship	Relationship cystic presence and demographic factors/sub-treatment groups (yes/no)	Outcome of relationship
Wan et al.[44] (2022)	Yes	Sub-analysis: group of patients with postoperative cysts did not show a difference in postoperative AOFAS outcome score compared with patients without postoperative cysts.	No	N.A.
Woelfle et al.[45] (2013)	Yes	No significant differences of AOFAS scores, VAS ankle pain in patients with or without abnormal MRI findings in general (including but not limited to cystic degradation).	No	N.A.
Osteochondral allograft transplantation				
Haene et al.[15] (2012)	No	N.A.	No	N.A.
Shimozono et al.[36] (2018)	No	N.A.	No	N.A.
Osteoperiosteal autograft transplantation				
Dahmen et al.[10] (2023)	Yes	No significant differences in numeric rating scale (NRS) of pain during walking in patients with or without postoperative cysts.	No	N.A.
Hu et al.[17] (2013)	No	N.A.	No	N.A.
Leumann et al.[24] (2014)	No	N.A.	No	N.A.
Li et al.[26] (2023)	No	N.A.	No	N.A.

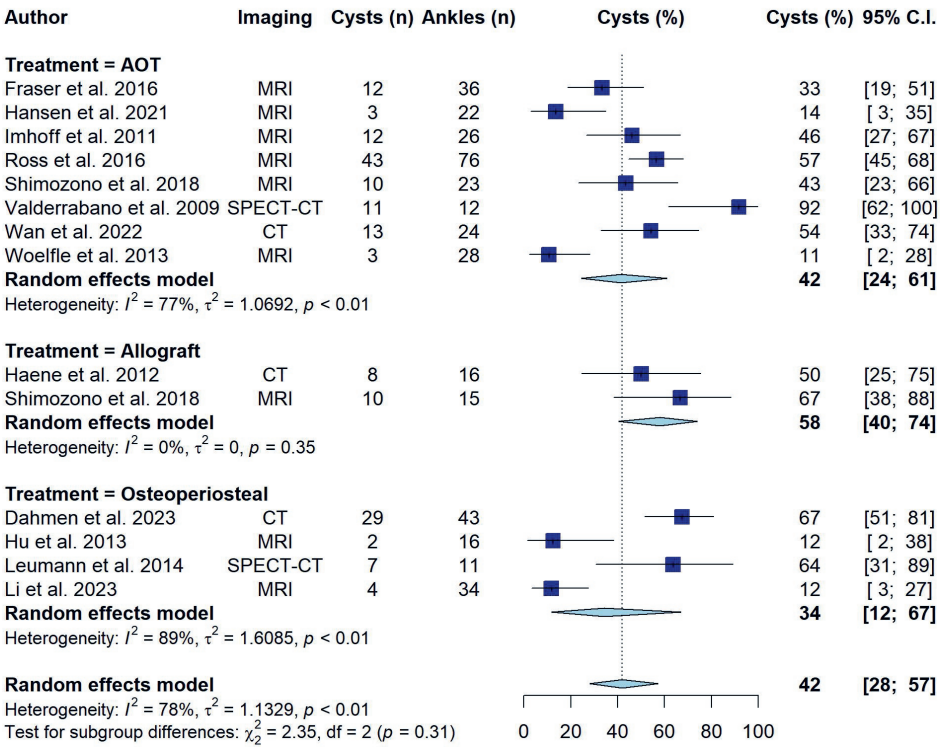

Figure 14.2: Forest plot of included studies. AOT, Osteochondral autograft transplantation; C.I., Confidence Interval; CT, computed tomography; MRI, Magnetic Resonance Imaging.

Relationship between postoperative cysts and treatment aspects or other non-clinical outcomes related factors

One study, Ross et al.,[34] out of the total of 13 studies (8%) evaluated the presence of a potential relationship between cyst presence and other non-clinical outcomes related variables (Table 14.4). Ross et al.[34] assessed whether primary osteochondral autograft therapy showed a different rate in postoperative cyst occurrence when compared to patients undergoing non-primary osteochondral autograft therapy: no significant differences were found.

Discussion

The most important finding of this current systematic review and meta-analysis is that postoperative cyst formation is a common finding following osteochondral autograft transplantation (42%), allograft transplantation (58%), and osteoperiosteal graft transplantation (34%) for the management of OLTs. There did

not appear to be a statistically significant difference in the prevalence of these cysts between different surgical treatment techniques (p = 0.31). More so, the postoperative presence of cysts was not correlated with inferior clinical outcomes in any of the included studies. These findings provide valuable insights into the prevalence of postoperative cysts and shed light on the clinical relevance of cyst development in patients undergoing osteochondral/periosteal autograft and allograft procedures for OLT.

The postoperative development of cysts following osteochondral grafting procedures in the treatment of osteochondral lesions of the talus has been a matter of clinical concern.[36] This concern arises from the hypothesis that cyst development could inherently lead to deterioration of the subchondral bone structure, vitality of the articular, transplanted or newly formed cartilage, and could subsequently lead to gradual deterioration of clinical outcomes. The findings of this study reveal that postoperative cysts are a commonly seen phenomenon after these procedures, but that the formation of cysts within the graft is not inherently linked to inferior clinical results. When comparing the literature of the ankle to that of the knee, The prevalence of postoperative cysts following surgical treatment of ankle OCLs are comparable in patients treated for knee OCLs, with rates ranging from 41% to 100% observed in the literature.[5,6,38,43] Ackermann et al.[1] described that the thickness of an osteochondral allograft is associated with subchondral cyst formation in the short-term, namely that thinner grafts potentially have a higher likelihood for the development of subchondral cysts. In a different study on OLTs which was excluded due to overlap in patients, no significant differences were found concerning the development of cysts between uncontained and contained lesions.[35] Additionally, Shimozono et al.[37] proposed that potential cyst formation is due to the inferior host-graft integration. An interesting outcome however in the study by Shimozono et al.[37] was that patients who received bone marrow aspirate concentrate (BMAC) after autologous osteochondral transplantation showed a significantly lower postoperative cyst occurrence rate than patients who did not receive BMAC (46% vs 77%, with a p-value of p = 0.022). In future research, it would therefore be of high interest to further explore the potential influence of biological adjuncts on the postoperative occurrence of cysts after osteochondral autograft, allograft and osteoperiosteal transplantation.

The observed differences in cyst formation rates between autograft, allograft, and osteoperiosteal graft procedures were not statistically significant. This lack of significance suggests that the type of graft material utilized does not appear to

be a major contributing factor to the development of postoperative cysts. Additionally, allografts are possibly less vascularized, and this may contribute to more cyst formation if they are not fully incorporated in the talus. Future research with larger sample sizes could help elucidate whether there are any subtle differences that may not have been apparent in the present study.

It must be noted that cysts itself are purely a radiological finding, and might not be of clinical relevance. Therefore, it was the secondary aim of the present study to explore the correlation between the presence of postoperative cysts and clinical outcomes. The lack of a significant correlation between postoperative cysts and clinical outcomes could be interpreted in several ways. It is possible that the cysts that develop following these grafting procedures are largely asymptomatic and do not have a substantial impact on the function or subjective well-being of the patients. This may be due to the facts that the grafting procedures may be effective in restoring the biomechanical properties of the talus, even in the presence of cysts, resulting in favourable clinical outcomes. Another potential reason could be that the new graft is not fully innervated and thus it could not transmit pain signals. The clinical effect of cyst formation in the long-term may, however, be more of importance.

At longer term follow-up, the biomechanical effects of the graft in the ankle may become more apparent. For example, it has been proposed that the subchondral bone is not communicating adequately with the articular joint space and that bone channels and thus cysts are formed.[7,23] This may only become symptomatic at longer follow-ups. Possible sealing of the grafts with a fibrin sealant may be options in that case. However, the clinical relevance is not known and should be investigated further before the routine recommendation of the use of adhesive sealant.

The management of postoperative cysts is another aspect to consider. The findings of this study suggest that the mere presence of these cysts may not warrant immediate intervention. However, it is essential to monitor patients for any potential symptoms or complications related to cysts, as some individuals may still experience discomfort or other issues. Identifying the characteristics of cysts that are more likely to become symptomatic and/or lead to failure of the graft together with developing guidelines for intervention based on these characteristics could be an important area for future research.

It is of importance to consider the potential limitations of the present study. First, the included studies were subject to variability in terms of sample size, follow-up duration, and the methods used to assess clinical outcomes. Furthermore, it should be noted that it is a limitation that it was not possible to perform a sub-analysis on cyst occurrence in- and outside of the graft, this due to the fact that solely Shimozono et al.[36] reported on this outcome specifically. Such heterogeneity in the study design and assessment criteria may introduce biases or confounding factors that could influence the results. Additionally, there is a possibility that the true clinical impact of postoperative cysts may be more subtle and require longer follow-up periods and larger sample sizes to become apparent. Moreover, studies using the MOCART score were excluded, as the question regarding cyst formation also includes oedema. An important limitation which also should be mentioned here is the fact that it was not possible to assess the impact of body mass index (BMI), pre-operative lesion size, size and number of grafts, potentially performed concomitant surgical procedures as well as variations in postoperative rehabilitation protocols on outcomes due to the underreporting and heterogeneity in reporting of these data in the included studies.

The clinical implication of the present study is that cysts occur frequently autograft, allograft, and osteoperiosteal graft procedures, but that these cysts alone are not of immediate concern. It must, however, be investigated further which persons develop cysts, and in which patients these cysts become symptomatic. This can help in the shared decision-making process by managing patients' expectations.

Future research in this field could benefit from a more standardized approach to assessing clinical outcomes, radiological protocols as well as radiological scoring systems at follow-up, which would allow for better comparisons between different studies. As part of this, future research can also focus on a more in-depth analysis of the localization, morphology and size of postoperative presence of cysts in order to shed more light on the aetiology behind the occurrence of these cysts. Awareness of the high frequency may encourage future studies to include standardized assessment of cyst presence, location, and development over time. Moreover, longer-term follow-up studies could provide more insight into whether the presence of postoperative cysts has any delayed or cumulative effects on clinical outcomes, which may not be immediately evident.

Conclusions

The occurrence of postoperative cysts is common following osteochondral autograft transplantation (42%), allograft transplantation (58%), and osteoperiosteal graft transplantation (34%) for osteochondral lesions of the talus – without significant inter-treatment differences. However, the presence of postoperative cysts was not correlated with clinical outcomes in any of the studies. These findings suggest that postoperative cysts are common but may have limited clinical implications for patients and surgeons. Future research should assess whether the postoperative presence of cysts correlates with (clinical) outcomes at longer follow-up.

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Appendices

Appendix 14.1: Search strategy until October 23, 2023

PUBMED	Search terms
#1	"Osteochondritis Dissecans"[Mesh]
#2	Osteochondritis dissecans[tiab] OR osteochondrosis dissecans[tiab] OR osteochondrolysis[tiab] OR OCD[tiab] OR OLT[tiab]
#3	(osteochondral[tiab] OR chondral[tiab] OR transchondral[tiab] OR cartilage*[tiab]) AND (defect*[tiab] OR lesion*[tiab])
#4	#1 OR #2 OR #3
#5	"Talus"[Mesh]
#6	talus[tiab] OR talar*[tiab] OR ankle[tiab]
#7	#5 OR #6
#8	#4 AND #7

EMBASE	Search terms
#1	(osteochondritis dissecans/or (osteochondritis dissecans or osteochondrosis dissecans or osteochondrolysis or OCD or OLT).ti,ab,kw. or ((osteochondral or chondral or osteochondral or transchondral or cartilage*) adj3 (defect* or lesion*)).ti,ab,kw.) and (talus/ or (talus or talar* or ankle).ti,ab,kw.)

COCHRANE	Search terms
#1	MeSH descriptor: [Osteochondritis Dissecans] explode all trees
#2	osteochondritis dissecans or osteochondrosis dissecans or osteochondrolysis or OCD or OLT:ti,ab,kw (Word variations have been searched)
#3	(osteochondral or chondral or transchondral or cartilage*) and (defect* or lesion*):ti,ab,kw (Word variations have been searched)
#4	#1 or #2 or #3
#5	MeSH descriptor: [Talus] explode all trees
#6	Talus or talar* or ankle*:ti,ab,kw (Word variations have been searched)
#7	#5 or #6

Appendix 14.2: Outcomes of MINORS assessment

	MINORS								Additional criteria for comparative studies				
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
Dahmen et al. (2023)[10]	2	2	2	2	1	2	2	2	-	-	-	-	15/16
Fraser et al. (2016)[12]	2	2	1	2	2	2	2	0	-	-	-	-	13/16
Haene et al. (2012)[15]	1	0	2	1	2	2	2	0	-	-	-	-	10/16
Hansen et al. (2021)[16]	2	2	1	2	1	2	2	0	2	2	2	2	20/24
Hu et al. (2013)[17]	2	2	0	2	0	2	0	0	-	-	-	-	8/16
Imhoff et al. (2011)[19]	2	2	2	2	1	1	1	0	-	-	-	-	11/16
Leumann et al. (2014)[24]	1	2	2	1	1	2	1	0	-	-	-	-	10/16
Li et al. (2023)[26]	1	2	2	2	1	2	1	0	-	-	-	-	11/16
Ross et al. (2016)[34]	2	0	1	2	2	1	2	0	-	-	-	-	9/16
Shimozono et al. (2018)[36]	2	2	2	2	1	2	2	0	2	2	2	2	21/24
Valderrabano et al. (2009)[42]	2	2	2	2	0	2	0	0	-	-	-	-	10/16
Wan et al. (2022)[44]	2	2	1	2	2	1	2	0	-	-	-	-	12/16
Woelfle et al. (2013)[45]	1	2	0	1	1	2	1	0	-	-	-	-	8/16

Addendum

Clinical efficacy of the Ankle Spacer for the treatment of multiple secondary osteochondral lesions of the talus

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Abstract

Background: The Ankle Spacer was developed as a joint-sparing alternative to invasive end-stage surgeries. Currently, there are no clinical studies on the Ankle Spacer.

Aim: To describe the operative technique and the clinical efficacy of the Ankle Spacer for the treatment of multiple, cystic osteochondral lesions of the talus in patients with failed prior operative treatment.

Methods: This is a prospective study during which patients were assessed preoperatively, at 2- and 6 wk, and at 3, 6, 12 and 24 mo postoperatively. Patients with multiple, cystic or large (≥ 15 mm) osteochondral lesions of the talus (OLT) after failed prior surgery were included. The primary outcome measure was the numeric rating scale (NRS) for pain during walking at 2 years postoperatively. Secondary outcome measures included the NRS in rest and during stair climbing, the American Orthopaedic Foot and Ankle Society (AOFAS) Hindfoot Score, the Foot and Ankle Outcome Score (FAOS), the Short- Form 36 (SF-36) physical and mental component scale, and the Range of Motion (ROM). Radiographic evaluations were conducted to evaluate prosthetic loosening and subsidence. Revision rates and complications were also assessed.

Results: Two patients underwent an Ankle Spacer implantation on the talus. The NRS during walking improved from 6 and 7 preoperatively to 2 and 2 points postoperatively at 2 years, in patient 1 and 2, respectively. The other patient-reported outcome measures also improved substantially. There were no re-operations nor complications. Radiological imaging showed no loosening of the implant and no change of implant position.

Conclusion: The Ankle Spacer showed clinically relevant pain reduction during walking, improvement in clinical outcomes as assessed with PROMs, and no complications or re-operations. This treatment option may evolve as a joint-sparing alternative to invasive end-stage surgeries.

Core tip: Our aim was to provide an overview of the clinical efficacy of a novel implant system that is a hemi-arthroplasty of the ankle. This device can be used for multiple, secondary osteochondral lesions of the talus and isolated osteo-arthritis of the talar dome. In this prospective case series, it was shown that this novel device showed promising clinical outcomes and can be considered safe.

Keywords: Hemi-arthroplasty · Ankle Spacer · Talar surface implant · Osteochondral lesions of the talus · End-stage

Introduction

Osteochondral lesions of the Talus (OLT) are pathologic lesions of the talar cartilage and the subchondral bone. These lesions can occur in up to 50% of acute ankle fractures and sprains.[20] For OLTs of larger size (i.e., above 10 or 15 mm in diameter) and of non-fragmentous morphology, the 'standard' operative treatment options such as autologous chondrocyte implantation (ACI), osteochondral autograft transfer systems (OATS), and a Talar OsteoPeriostic grafting from the Iliac Crest (TOPIC) procedure may result in satisfactory clinical outcomes.[7,17,25] However, in some patients, there are multiple secondary lesions present of large and cystic nature. For these lesions, it is not always possible to harvest an osteo(chondral) autograft that is large enough to replace all the diseased osteochondral tissue of the talus without damaging the donor site or compromising the congruency of the ankle joint. Allograft treatment could be considered for the treatment of these type of lesions. However, these contain the disadvantages of loss of viability and stability in one-third of the grafts, and possibly clinically fail due to immunological reactions.[10,21] However, when there are multiple secondary (i.e., failed prior surgery) lesions present on the talar articular surface in combination with a large and cystic nature, the above-described operative interventions are to be expected to result in relatively inferior outcomes.

To avoid inferior surgical outcomes in patients with persisting complaints after previous unsuccessful conservative management and operative therapy, other effective operative interventions are performed including an ankle arthrodesis or a total ankle prosthesis.[4,30,31] An (arthroscopic) ankle arthrodesis results in satisfactory clinical outcomes mostly concerning pain.[9,12,13] However, the operative intervention in question can result in functional limitations due to loss of the range of motion (ROM) of the ankle.[28] Furthermore, an ankle arthrodesis may potentially result in an increased long-term risk of arthritis in adjacent hindfoot joints, particularly the subtalar joint.[38] An alternative option is the placement of a total ankle prosthesis, for which a substantial amount of bone needs to be resected.[14] In order to address the problem of decreased joint motion (in the case of an ankle arthrodesis) and major bone resection (in the case of a prosthesis), a one-piece hemi-arthroplasty covering the talar surface, and leaving the tibia plafond untouched, can be a potential solution to the aforementioned challenges.

Although previous operative interventions similar to such a hemi-arthroplasty have been described in the literature, the studies applied operative techniques

with resection of a substantial part of the talar cortical bone and cartilage in order to verify fitting of the implant thereby taking away a potential successful ankle arthrodesis in case of clinical failure.[24,33,34] Consequently, a novel bone-sparing hemi-prosthesis has been developed (The Ankle Spacer) to enable resurfacing of the talar dome and simultaneously preserving the ROM and potentially optimize physical functioning. Potential advantages include preservation of ankle motion, decreased stress on the midfoot and subtalar joints, and the possibility to perform an ankle fusion after failed hemi-arthroplasty. Up to now, no operative technique description combined with the first clinical outcomes has been described in the literature. It is therefore the purpose of the present study to describe the operative technique and the clinical efficacy of the Ankle Spacer for the treatment of multiple, cystic OLTs in patients with failed prior operative treatment. Despite the fact that no clinical trials have been published on this specific implant, it is hypothesized that the 2-year postoperative follow-up will show a clinically relevant pain reduction and prosthesis survival.

Materials and methods

Study design

The study concerns a non-randomized, non-blinded, non-comparative prospective trial, with a 2-year follow-up period at the outpatient clinic aiming at assessing pain, function and implant survival, and thereby investigating the clinical efficacy of the Ankle Spacer. The study was approved by the local Medical Ethics Committee (Internal Review Board, IRB) of the Amsterdam University Medical Centre with reference number MEC 2017_175 and was performed in accordance with the principles of the Declaration of Helsinki and the medical Research Involving Human Subjects Act (WMO). The study was sponsored by Arthrex as a post market study with reference number EMEA-17037.

Patient selection

All patients eligible for operative implantation of the Ankle Spacer visiting the outpatient clinic between March 2017 and March 2019 for an OLT with a diameter of 15mm or more (anterior-posterior or medial-lateral), an OLT that failed prior operative intervention(s) or patients with multiple OLTs on the talar dome surface, were requested if they were willing to participate in the present clinical trial. If

they were interested, patients were informed about this study and were given two weeks to decide upon participation. In case patients provided their consent, they were screened for meeting the inclusion and exclusion criteria (Table A.1).

Table A.1: Inclusion and exclusion criteria

Inclusion criteria	Exclusion criteria
- Age ranging from 18 to 80 years - Failed previous conservative treatment - Complaints for at least 6 mo - Talar osteochondral lesions (multiple degenerative talar cysts present, and/or prior failed operative treatment and/or multiple defects and/or a diameter of 15 mm or more)	- Severe ankle malalignment (more than 5° varus or valgus). - Suspicion of grade two or higher (Kellgren-Lawrence-Score) ankle joint degeneration on the tibia side. - Ankle Fracture less than 6 mo ago - Tendinitis - Advanced osteoporosis - Adiposity grade I (BMI of 30 kg/m^2 or more) - Diabetes mellitus / rheumatoid arthritis / severe neuro-arthropathy - Blood supply limitations and active infections, which may retard healing - Foreign-body sensitivity - Currently participating in an investigational drug or another device study that clinically interferes with the current study endpoints.

Abbreviations: BMI, body mass index; F, female; M, male.

Timeframe and outcome assessment

Preoperatively, standing weight bearing conventional radiographs and a computed tomography scan (CT) were taken. Preoperative patient-reported outcome measures (PROMs) consisted of the Numeric Rating Scale (NRS) of pain (during walking, in rest and during stairclimbing), patient satisfaction regarding complaints, activity and treatment, the American Orthopaedic Foot and Ankle Society (AOFAS) Hindfoot Score, Foot and Ankle Outcome Score (FAOS) and the Short-Form 36 (SF-36 physical and mental component scale). The AOFAS score physician subscale and ROM were assessed by an independent researcher who was not involved in the operative procedure.[18,23] Follow-up assessment was performed at two and six weeks, three and six months, one-year and two years postoperatively. At these follow-up moments the patients were requested to fill out a questionnaire consisting of the above-mentioned PROMs and a physical examination was performed to test the ROM (expect for the postoperative visits at 2 wk and 6 wk after the surgery). Radiographs were taken one day, 6 wk, one year and two years postoperatively. At one-year of follow-up, a CT-scan was made

(Figure A.1 describes the flow-chart outlining the study procedures). In addition, postoperative complications were recorded. Demographic data were also collected. The primary outcome measure in question was the NRS of pain during walking at 2-years follow-up and implant survival. All other outcome measures described above were secondary outcomes.

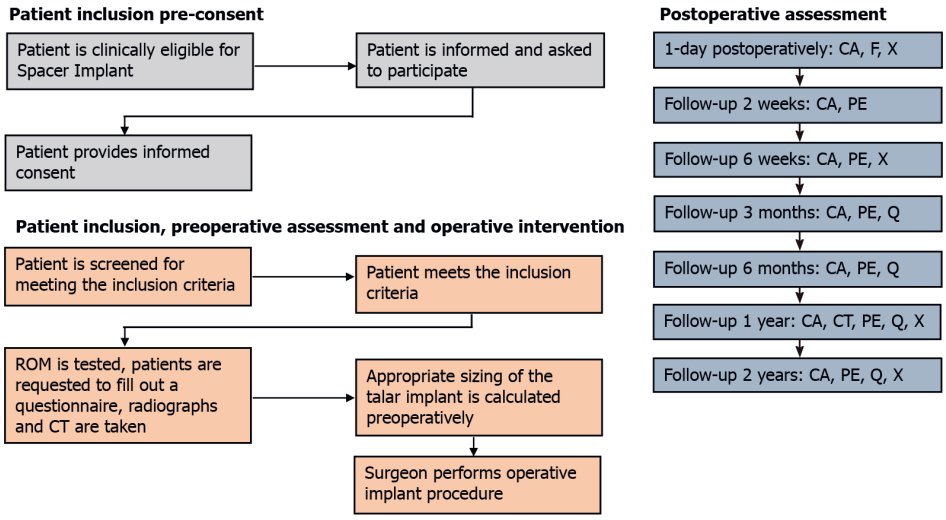

Figure A.1: Flow-chart of the study design and main procedures participants will undergo during this study. CA, Complication assessment; CT, Computed tomography; PE, Physical examination; Q, Questionnaires; ROM, Range of motion; X, Mortise and lateral radiographs.

Description of the device

The Arthrex Ankle Spacer is a one-piece implant system that replaces the talar side of the tibio-talar joint (Figure A.2). The Ankle Spacer replaces the articulating upper surface of the talus and offers several implant sizes in millimeters (18, 20, 22, 24, 26, 28) in order to fit to the different sizes of the talus. It is anatomically designed to the native talar dome to provide an optimal fit to the distal articular tibial surface. The implant is polished to a mirror effect on the articulating surface and has a rough titanium plasma spray (TPS) coated under surface with two posts and spikes for implant fixation (US10,350,079 B2). The rough surface enables secondary fixation due to bone ingrowth. Spikes at the posterior part of the prosthesis allow for further fixation to the bone. The weight of the ankle spacer varies from 11 to 22 g, depending on the size of the spacer.

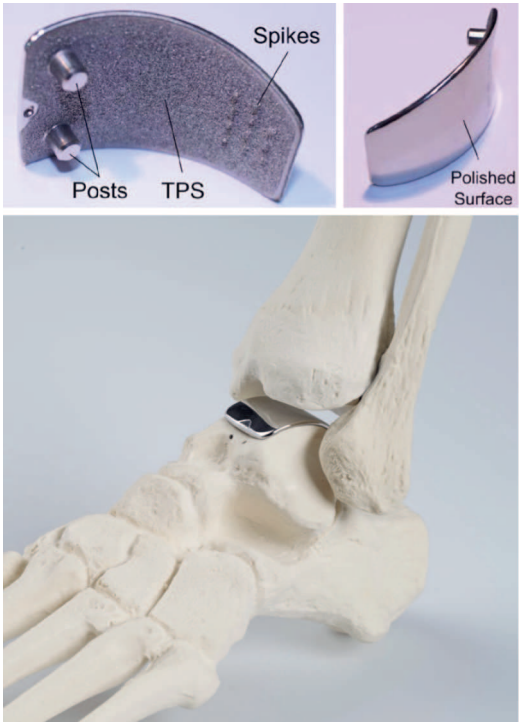

Figure A.2: The Ankle Spacer Implant.

Operative technique

Before receiving the Ankle Spacer, the patient received 2 g of cefazoline pre-operatively. The procedure was carried out under general anesthesia. The patient was placed in the supine position with a tourniquet applied around the thigh and a rolled-up apron underneath the lateral malleolus to facilitate eversion of the foot to improve exposure of the talus. A longitudinal incision between 10 and 15 cm was centered over the ankle immediately lateral to the tibialis anterior tendon. The incision was deepened to the ankle joint while retracting the extensor hallucis longus and the neurovascular bundle laterally. If present, the osteophytes on the anterior tibia edge were removed. Subsequently, the cartilage was removed (Figure A.3A) on the upper talar surface as well as part of the underlying subchondral bone (Figure A.3B).

Additionally, microfracturing was performed to support ingrowth for secondary ankle spacer fixation (Figure A.3C).

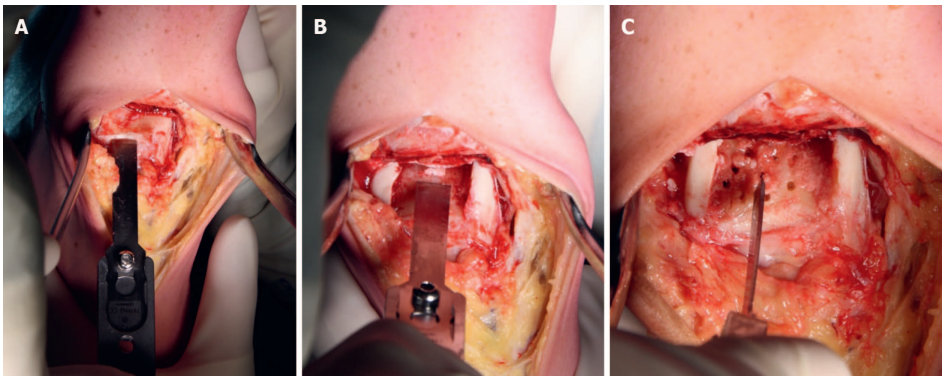

Figure A.3: Preparation of cartilage and bone prior to insertion. (A) Removal of the talar cartilage (Top-Left); **(B)** (Top-Right): Removal of the subchondral bone; **(C)** Bone marrow stimulation of the subchondral bone (Bottom).

The tibiotalar joint was manually distracted and the appropriate trial Ankle Spacer was inserted into the joint. The trial Ankle Spacer was placed in a central position in the medial-lateral direction. The trial was fixated in the slotted hole with a K-wire and the trial inserter was removed afterwards.

Then, dynamic dorsi- and plantarflexion of the ankle was performed as this allowed self-alignment of the temporarily fixed trial. Afterwards, the trial spacer was fixated with a K-wire in the second hole in order to prevent dislocation, after which both K-wires were advanced bi-cortically in order to achieve proper fixation. Fluoroscopy was used to confirm proper sizing and positioning of the trial Ankle Spacer.

The double drill sleeve was aligned to the two holes on the Ankle Spacer and were maintained in a perpendicular angle relative to the surface of the ankle spacer. Subsequently, drilling was started with the first drill until the moment it stopped on the drill sleeve. This first drill was left for fixation in the drill hole, and then the second drill was to drill the second hole, in exactly the same manner.

Then all instruments were removed. Prior to inserting the Ankle Spacer, the prepared bone bed was thoroughly cleaned and inspected. The Ankle Spacer was inserted on the talar dome using the ankle space inserter, while placing the two posts on the bottom of the Ankle Spacer into the prepared drill holes for fixation. The implant was impacted with an impactor until the posts were fully seated in the drill holes (Figure A.4A and Figure A.4B). The joint capsule was closed and the layers were closed subsequently.

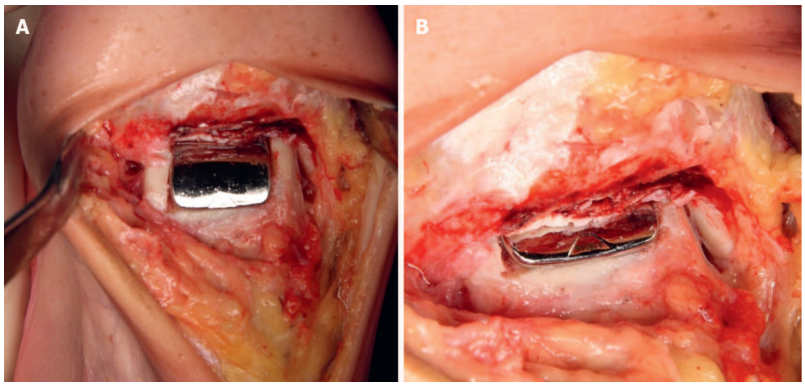

Figure A.4: After the insertion of the Ankle Spacer. (A) End-result after the insertion of the Ankle Spacer (Left Image); **(B)** End-result after the insertion of the Ankle Spacer (Right Image).

Post-operative protocol

Postoperatively, wound dressing with adequate padding was applied. At hospital discharge a removable lower leg splint was applied. Careful active and passive dorsi- and plantarflexion motion (flexion-extension exercises) without weight bearing monitored by a physiotherapist were started two days after surgery. After two weeks of non-weight bearing, depending on the degree of wound and soft tissue healing, mobilization was started with progressive weight bearing to tolerance in a Walker. Flexion-extension exercises were continued. Six weeks after surgery, intensive physiotherapy and rehabilitation was started for at least a period of 6 wk.

Power calculation and study population

A power analysis was conducted to estimate the needed sample size for this prospective non-comparative trial using the NRS for pain as primary outcome measure with a clinical relevant difference of 1 point and a standard deviation of 1.5 points. Additionally, in this calculation a standard p-value of 0.05 ($\alpha = 0.05$) and a power of 80% were used. This indicated that a total of 20 patients would need to be included in the trial in order to detect a clinically important difference in pain comparing pre- and postoperative NRS scores. Due to the relative rarity of patients presenting at our outpatient department with the exact above-described inclusion and exclusion criteria, two patients could be identified with fitting indications who were operated on with the implantation of the Ankle Spacer. The age of these patients was 36 and 56 years old (one male, one female). No patients were lost to follow-up. Prior procedures that were performed are listed in Table A.2 alongside demographic factors. The pre-operative CT scans of the patients as presented in Figures A.5 and A.6.

Table A.2: Patient characteristics

Patient	Gender	Age	BMI (kg/m^2)	Prior procedures
1	M	36	27	2013: Removal of anterior bony ankle impingement 2013: Arthroscopic screw fixation of talar osteochondral lesion 2014: Screw removal 2015: Hyaluronic acid injections (multiple) 2016: Arthroscopic Bone Marrow Stimulation for talar osteochondral lesion
2	F	56	23	2005: Spongiosaplasty for talar osteochondral lesion 2008: Arthroscopic bone marrow stimulation for talar osteochondral lesions 2014: Retrograde drilling for talar osteochondral lesion 2017: Hyaluronic acid injections (multiple)

Figure A.5: Pre-operative CT scan of patient number 1. Upper part shows coronal slides with the images from left to right going into the posterior to anterior direction. The lower part shows sagittal slides with the images from left to right going from lateral to medial.

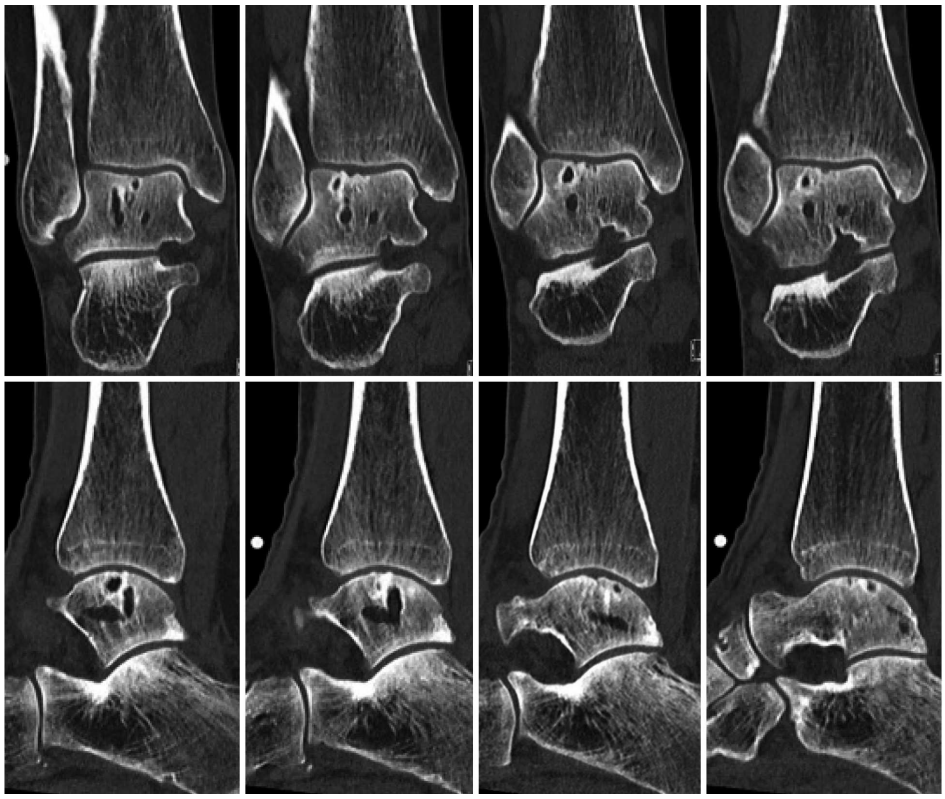

Figure A.6: Pre-operative CT scan of patient number 2. Upper part shows coronal slides with the images from left to right going into the posterior to anterior direction. The lower part shows sagittal slides with the images from left to right going from lateral to medial.

Statistical analysis

All statistical analyses were performed by means of SPSS version 20.0 (SPSS Inc., Chicago, IL, USA). Data will be presented as descriptive analyses through qualitative comparisons in the different patients. Consequently, data will be presented per patient, aiming at presenting changes in scores preoperatively vs postoperatively.

Results

Primary outcome

The primary outcome measure, the NRS of pain during walking improved from 6 preoperatively to 2 points at 2 years follow-up in patient 1, and from 7 preoperatively to 2 points postoperatively at 2 years follow-up in patient 2. This entails an improvement of 4 points and 5 points in patient 1 and 2, respectively (Figure A.7).

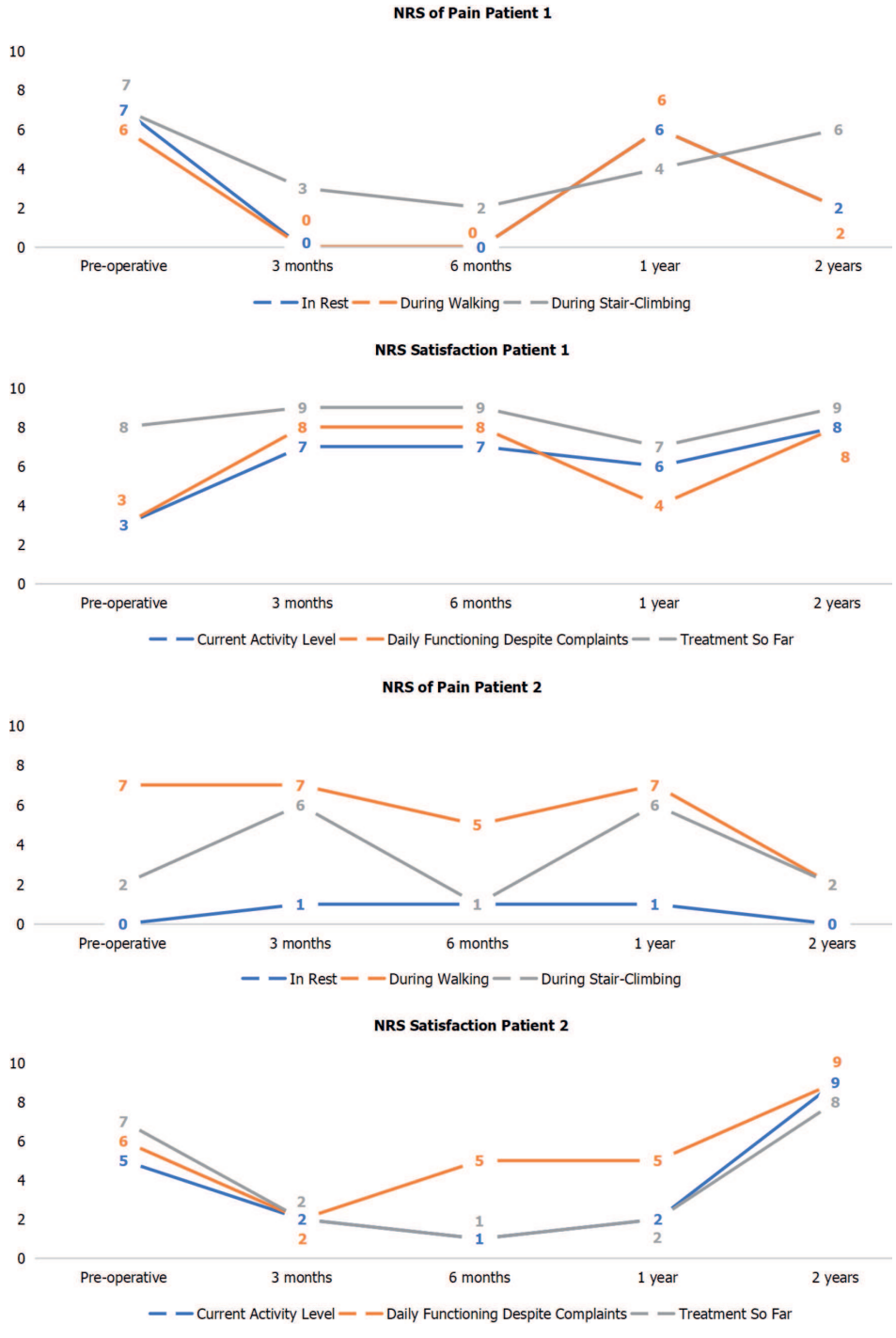

Figure A.7: Pre-and postoperative Numeric Rating Scale (NRS) scores of pain and satisfaction for patients 1 and 2.

Secondary outcomes

The other PROMs can be appreciated in Table A.3. There were no complications and no reoperations. Radiologically, for all postoperative radiographs and CT-scans

Table A.3: Preoperative and postoperative outcomes for patients 1 and 2

Time-point	FAOS	SF-36	AOFAS ankle hindfoot score	NRS satisfaction with current activity level	NRS satisfaction with daily functioning despite any complaints	NRS satisfaction with treatment so far
Patient 1						
Preoperatively	Pain: 56; Symptoms: 46; ADL: 68; Sports: 20; QoL: 25	PCS: 28; MCS: 61	61	3	3	8
3 mo postoperatively	Pain: 86; Symptoms: 82; ADL: 91; Sports: 40; QoL: 63	PCS: 44; MCS: 55	82	7	8	9
6 mo postoperatively	Pain: 79; Symptoms: 86 ; ADL: 93; Sports: 60; QoL: 63	PCS: 45; MCS: 53	75	7	8	9
1 year postoperatively	Pain: 46; Symptoms: 67; ADL: 79; Sports: 25; QoL: 44	PCS: 39; MCS: 56	77	6	4	7
2 years postoperatively	Pain: 62; Symptoms: 81; ADL: 90; Sports: 55; QoL: 69	PCS: 51; MCS: 52	100	8	8	9
Patient 2						
Preoperative	Pain: 81; Symptoms: 79; ADL: 91; Sports: N.A.; QoL: 25	PCS: 44; MCS: 56	72	5	6	7
3 mo postoperatively	Pain: 64; Symptoms: 68; ADL: 66; Sports: 30; QoL: 0	PCS: 33; MCS: 41	69	2	2	2
6 mo postoperatively	Pain: 68; Symptoms: 69; ADL: 72; Sports: 30; QoL: 13	PCS: 29; MCS: 54	71	1	5	1
1 year postoperatively	Pain: 72; Symptoms: 50; ADL: 72; Sports: 30; QoL: 19	PCS: 33; MCS: 51	68	2	5	2
2 years postoperatively	Pain: 81; Symptoms: 68; ADL: 78; Sports: 55; QoL: 50	PCS: 43; MCS: 53	88	9	9	8

Abbreviations: ADL, activities in daily living; AOFAS, American Orthopaedic Foot and Ankle Society; FAOS, foot and ankle outcome score; MCS, mental component scale; NRS, numeric rating scale; PCS, physical component scale; QoL, quality of life; SF-36, short-form 36.

it was concluded that there were no indications of loosening of the implant, no implant migration, and no subsidence was noted (Figure A.8). The ROM assessments were described in Table A.4.

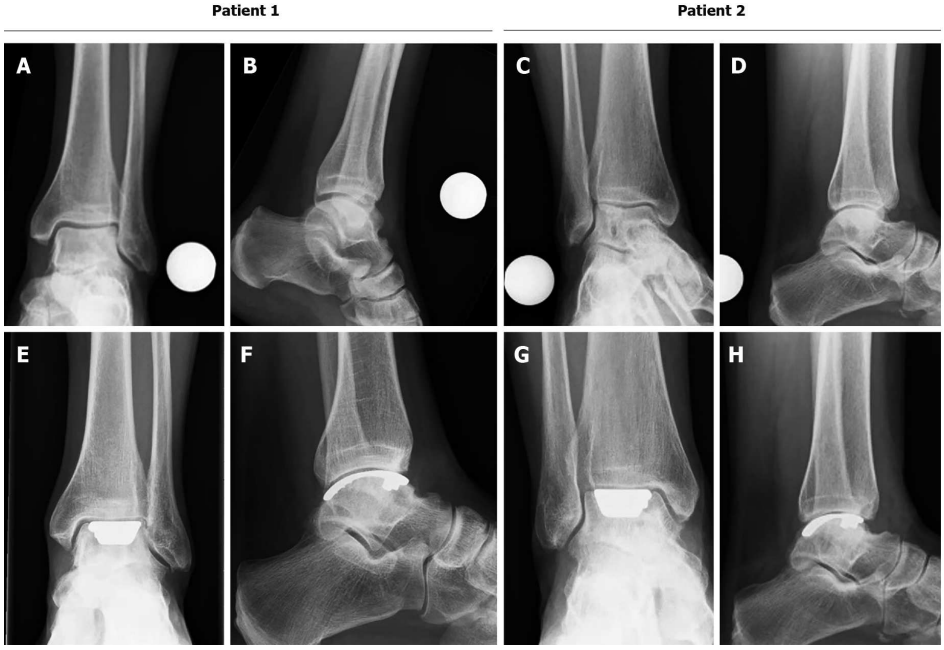

Figure A.8: Preoperative and postoperative radiographs. Patient 1: **(A)** preoperative mortise radiographs, **(B)** preoperative lateral radiograph, **(E)** 2-year postoperative mortise radiograph, **(F)** 2-year postoperative radiograph. Patient 2: **(C)** preoperative mortise radiographs, **(D)** preoperative lateral radiograph, **(G)** 2-year Postoperative mortise radiograph, **(H)** 2-year postoperative radiograph.

Table A.4: Preoperative and postoperative range of motion outcomes patient 1 & 2

	Patient 1		Patient 2	
	Dorsiflexion in degrees (affected/ unaffected side)	Plantarflexion in degrees (affected/ unaffected side)	Dorsiflexion in degrees (affected/ unaffected side)	Plantarflexion in degrees (affected/ unaffected side)
Preoperative	5 / 10	35 / 40	5 / 5	40 / 40
2 weeks postoperatively	5 / 15	20 / 40	2 / 15	25 / 40
6 weeks postoperatively	7 / 10	35 / 40	5 / 10	35 / 40
3 mo postoperatively	10 / 10	35 / 45	5 / 10	35 / 40
6 mo postoperatively	10 / 10	35 / 45	10 / 10	35 / 40
1 year postoperatively	10 / 10	35 / 45	10 / 10	35 / 40
2 years postoperatively	10 / 10	35 / 45	7 / 10	35 / 40

Discussion

This is the first study describing the results of the newly developed Ankle Spacer. The Ankle Spacer is a one-piece implant system that replaces the talar side of the tibiotalar joint, and can therefore be considered a hemi-arthroplasty procedure. The implant had been designed in order to overcome a number of downsides that are associated with the current treatment options for large, cystic, or multiple osteochondral lesions of the talus that have failed prior operative intervention(s). One of these treatment option being applied in the younger patient population is an arthroscopic ankle arthrodesis which results in highly satisfactory clinical outcomes mostly concerning pain outcomes.[9,12,13] The downside of this operative intervention is that it results in functional limitations due to loss of ROM of the ankle.[28] Furthermore, an ankle arthrodesis increases the long-term risk of (radiographic) osteoarthritis in adjacent hindfoot joints, particularly in the subtalar joint.[32,38] An alternative option is the placement of a total ankle prosthesis, for which a substantial amount of bone needs to be resected.[14,16] In order to tackle the downsides of these treatment options, develop a bone-sparing procedure and resurfacing the talar dome to preserve ROM and potentially optimize physical functioning, the Ankle Spacer, a novel bone-sparing hemi-prosthesis, has been developed. The outcomes of treatment with the Ankle Spacer were described in the present article. Potential advantages include preservation of ankle motion, decreased stress on the midfoot and subtalar joints, and the possibility to perform an ankle fusion after failed hemi-arthroplasty.

It is therefore clear that the Ankle Spacer is a new and innovative device. The current study is the first clinical trial performed investigating the efficacy of the Ankle Spacer, and therefore there is no clinical literature on this particular prosthetic device at this time to compare our clinical results to. Our current clinical results must therefore be compared to similar devices having been researched over the past decade. An articular and subchondral bone resurfacing implant procedure on one side of the joint (hemi-arthroplasty) can be considered a relatively novel operative intervention. Promising clinical results have been reported for similar treatment in the femoral and humeral head, as well as the first metatarsal and patellar surface.[2,8,11,24,29,35] Van Bergen et al.[33,34,36] showed that a focal resurfacing implant is a promising treatment for talar OLTs that have failed prior operative treatment.[36] They concluded that in a patient series including 38 patients the clinical results at a mean follow-up of three years were satisfactory. A different study by Holton et al.[15] demonstrated that the use of a different resurfacing

implant in the form of an articular resurfacing component maintained a good clinical improvement for patients at mid-term follow-up. A study by Brunner et al.[5] which is less clinically comparable as it replaces the whole entity of the ankle, as opposed to the resurfacing of the talar surface as done by the Ankle Spacer or as opposed to the resurfacing implant as used by van Bergen et al.,[24-26] showed that short- term to mid-term results for patients treated with the Scandinavian Total Ankle Replacement (STAR) prosthesis have been encouraging. The long-term results were clinically inferior compared to the short-term and mid-term results. Additionally, studies on the Total Ankle Replacement (TAR), which is, to a certain though limited extent, comparable to the Ankle Spacer, have shown that long-term results demonstrated improved pain scores as it was observed to be a viable and durable operative implantation option.[1,19] Another implantation technique in the form of a Tornier Salto Talaris Anatomic Ankle has been described in the literature. Mid- term results showed that the survivorship of this implant was calculated to be around 95%.[3,27] A study by Queen et al.[22] found that at a follow-up of 2 years investigating 51 patients after a fixed-bearing Total Ankle Replacement significant improvements in gait mechanics, pain reduction and functioning were observed.

As an objective conclusive remark on the evidence found on similar operative techniques, one can state that similar operative techniques yielded favorable clinical, radiological and safety outcomes. When comparing these three aspects to our results it can be concluded that in our treated patients, similar outcomes were found. Postoperative improvement was especially clear in the observed primary outcome measure which was the NRS pain during walking. This outcome measures typically describes the state and magnitude of pain in patients with OLTs of the talus as these patients experience pain especially when performing weight bearing activities, but often are unable to participate in sports due to complaints.[25] It was shown that this primary outcome measure improved from 6 and 7 preoperatively to 2 and 2 postoperatively at 2 years, in patient 1 and 2, respectively. As a result, we can conclude that for both patients a minimal clinically important difference was reached when comparing the preoperative state of pain to the postoperative state of pain at 2 years after the surgery. As an improvement of at least −1.0 on the NRS scale of 0 to 10 points is significantly associated with the concept of a “better improvement”, and an improvement of -2.0 on this scale is associated with a “much better improvement”.[26] The improvement was also reflected in the radiological outcomes and the subjective satisfaction scores that were taken both preoperatively and postoperatively at the different follow-up moments in which it was clear that

the patients stated that they were satisfied with their level of activity. Moreover, this was also reflected in the postoperative AOFAS Hindfoot Scale, which ranged from 88 to 100, scores that can be considered to represent a successful surgery.

Furthermore, it was observed that there were no complications, no reoperations nor revisions, which implicates that, when extrapolating these results for a larger population based on our experience, the insertion of the Ankle Spacer can be regarded a safe procedure. This outcome should be interpreted in the light of the high re-intervention rates that are associated with Total Talar Prostheses, as some studies report that up to 38% of the patients need revision surgery within the first year after total ankle arthroplasty.[6] With regards to ROM, it was shown that the ROM did not decrease in the patients, potentially due to the fact that patients received adequate postoperative physiotherapy and because of the fact that the Ankle Spacer was inserted just below the level of the subchondral bone plate not affecting joint congruency. This is clinically relevant to take into account when comparing ROM outcomes after placement of the Ankle Spacer to outcomes after an ankle arthrodesis procedure.[37]

This study should be interpreted in light of its strengths and weaknesses. Strengths of this study include its prospective and thorough methodology, completeness of follow-up, and the use of various validated outcome measures in the assessment of a not yet studied resurfacing implant. Limitations include the absence of a controlled group, lack of long-term follow-up outcomes ranging past the two years follow-up, and the small series of patients. However, we have found in our tertiary referral clinic that operates in an academic setting with the status of an official (inter)national expertise center for the treatment of OLTs in the ankle that the indication for an Ankle Spacer implantation is highly rare, even though we receive a high number of patients on a yearly basis. As a result, it was therefore noted that the Ankle Spacer has been removed from the market due to limited indications and strict regulatory requirements.

The clinical relevance of the present study can be interpreted in the light of the highly specific indication for the implantation of the Ankle Spacer. This device is particularly suited for patients with multiple OLTs of the talar dome having failed prior operative intervention(s) with an unaffected distal tibial part of the ankle joint. This study shows that the Ankle Spacer is effective for this particular and rare patient group, thereby functioning as a joint-sparing alternative to more invasive operative interventions, such as an ankle arthrodesis or total ankle arthroplasty.

Conclusion

The Ankle Spacer showed clinically relevant pain reduction during walking, improvement in clinical outcomes as assessed with PROMs, and no complications or re-operations. This treatment option may therefore evolve as a joint-sparing alternative to an ankle arthrodesis, a total talar implant or a total ankle arthroplasty/resurfacing.

Article highlights

Research background

Osteochondral lesions of the Talus (OLT) are pathologic lesions of the talar cartilage and the subchondral bone. These lesions can occur in up to 50% of acute ankle fractures and sprains. For OLTs of larger size (i.e., above 10 or 15 mm in diameter) and of non-fragmentous morphology, the 'standard' operative treatment options such as autologous chondrocyte implantation (ACI), osteochondral autograft transfer systems (OATS), and a Talar OsteoPeriostic grafting from the Iliac Crest (TOPIC) procedure may result in satisfactory clinical outcomes. However, in some patients, there are multiple secondary lesions present of large and cystic nature. For these lesions, it is not always possible to harvest an osteo(chondral) autograft that is large enough to replace all the diseased osteochondral tissue of the talus without damaging the donor site or compromising the congruency of the ankle joint. Allograft treatment could be considered for the treatment of these type of lesions. However, these contain the disadvantages of loss of viability and stability in one-third of the grafts, and possibly clinically fail due to immunological reactions. However, when there are multiple secondary (i.e., failed prior surgery) lesions present on the talar articular surface in combination with a large and cystic nature, the above-described operative interventions are to be expected to result in relatively inferior outcomes.

Research motivation

Currently, it is difficult to treat patients with osteochondral lesions of the ankle that are of multiple, cystic and secondary nature. This is because the lesions are considered relatively large and difficult to treat. For this indication, it was usually performed to fuse the ankle joint. However, in the past 2 to 5 years, novel innovative surgical options have been developed, such as the Ankle Spacer, in order to overcome an ankle fusion or ankle prosthesis.

Research objectives

It was the purpose of the present study to describe the operative technique and the clinical efficacy of the Ankle Spacer for the treatment of multiple, cystic OLTs in patients with failed prior operative treatment.

Research methods

In a prospective study including patients with multiple, cystic or large osteochondral lesions of the talus were included who failed previous surgical treatment. We looked at the numeric rating scale (NRS) for pain during walking at 2 years after implantation of the Ankle Spacer and we also assessed the NRS in rest and during stair-climbing, the American Orthopaedic Foot and Ankle Outcome Score (AOFAS), the Foot and Ankle Outcome Score (FAOS), the Short-Form 36 and the range of motion of the ankles both pre-operatively as well as post-operatively. Radiographic evaluations were conducted to evaluate prosthetic loosening and subsidence. Revision rates and complications were also assessed.

Research results

In this prospective study, two patients underwent the implantation of an Ankle Spacer for osteochondral damage on the talar dome. We found that there were clinically relevant pain reductions during walking as well as important improvements in clinical outcomes as assessed with the patient-reported outcome measures. Furthermore, it was found that there were no complications nor re-operations.

Research conclusions

The Ankle Spacer showed good clinical outcomes and clinically relevant pain reduction during walking, improvement in clinical outcomes as assessed with PROMs, and no complications or re-operations. This treatment option may therefore evolve as a joint-sparing alternative to an ankle arthrodesis, a total talar implant or a total ankle arthroplasty/resurfacing.

Research perspectives

Future research should be focused at the development of a prospective, self-learning algorithm taking into account the individual patient factors influencing outcomes after conservative and surgical treatment so that we can assess which patients would benefit most from which treatment options.

Footnotes

Institutional review board statement: The study was approved by the local Medical Ethics Committee (Internal Review Board, IRB) of the Amsterdam University Medical Centre with reference number MEC 2017_175 and was performed in accordance with the principles of the Declaration of Helsinki and the medical Research Involving Human Subjects Act (WMO).

Informed consent statement: All patients provided informed consent prior to the participation in the study.

Conflict-of-interest statement: The study was sponsored by Arthrex as a post market study with reference number EMEA-17037

Data sharing statement: No additional data available.

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PART III

General discussion
and appendices

Chapter 15

General discussion and future perspectives

The rationale behind this thesis has started a number of hundred years ago when Hunter already stated that "*From Hippocrates down to the present age, ulcerated cartilage is a troublesome disease; when destroyed, it is not recovered*".[49] The present thesis highlights the aetiology, incidence, phenotypes as well as management of (osteo)chondral injuries to the ankle throughout a wide and inter- and multidisciplinary scope with its overreaching goal of working towards an evidence-based personalized approach for the treatment of incremental cartilage damage of the ankle with a specific focus on the treatment of large, secondary osteochondral lesions of the talus, hence aiming to prevent the further progression in the above-mentioned cascade from osteochondral lesion to end-stage osteo-arthritis. The thesis was divided into three main parts. **Part I** focused on introducing the content, and assessing the aetiology, incidence, and phenotypic presentations of (osteo)chondral injuries of the ankle. **Part II** assessed the (after)treatment of osteochondral lesions of the talus that have failed prior surgical intervention(s). **Part III** is the current section and includes discussive scientific thoughts with an intertwined exploratory description of future perspectives.

Part I: Introduction, aetiology, incidence, and phenotypes of cartilage damage of the ankle

Part I was commenced by **Chapter 2** in which the progression of incremental cartilage damage in the ankle joint was described through the resemblance of a cascade.[25] This editorial highlighted the different stages of the cartilage damage starting with an ankle trauma consisting of either a sprain or a fracture. A number of stages were presented including the invisible cartilage crack, the osteochondral lesion and the osteo-arthritis stage. Limitations of the study were that it was a descriptive summary of the literature on pathophysiological pathways leading to cartilage damage and osteochondral damage, specifically focused on the ankle. The focus was put mainly on, firstly, asymptomatic superficial cartilage lesions which are most probably of inert nature and posttraumatic cartilage cracks with damage to the subchondral bone and posttraumatic chondrocyte apoptosis.[18,63,71,93,108] An important question that has still not been answered is why some of the posttraumatic cartilage cracks or lesion with damage to the subchondral bone do heal while others not, which could be a highly interesting scientific research endeavor for future research projects. The editorial also described that there can be alternative pathophysiological pathways potentially inducing cartilage damage such as large superficial lesions due to a posttraumatic or biomechanical problem, or the

development of chondrolysis after intrasynovial haemorrhage. Both alternative pathways can on their turn lead to the development of osteochondral lesions and osteoarthritis of the ankle joint.[60,61,95] Interpreting the different pathophysiological pathways, it should be emphasized that greater focus should be placed on the early detection of cartilage damage and the implementation of tailored primary preventive measures during the subclinical phase. By intervening at this stage, it may be possible to delay or even halt the progression of cartilage cracks that trigger the degenerative cascade, thereby preventing the onset of osteochondral lesions and end-stage osteoarthritis – two conditions that significantly impair a patient's quality of life.[5,68] From a societal viewpoint, this effort is of relevance and importance, as prior research indicates that end-stage osteoarthritis is associated with substantial direct and indirect costs.[38,67] To achieve these objectives, advanced imaging techniques and innovative methods to cushion the joint are required, enabling earlier diagnosis and treatment of cartilage damage during the subclinical phase.[90-92] Moreover, although one should acknowledge that this a simplified representation of incremental cartilage damage of the ankle, the presented cartilage cascade provides an easy to grasp overview of the development of posttraumatic cartilage damage finally resulting in osteo-arthritis, making the visualization a readily interpretable figure for scientists, doctors as well as (most importantly) patients. By introducing the concept of the Ankle Cartilage Cascade, we also aimed to inspire future research to prioritize the subclinical phase following ankle trauma, ultimately interrupting the cascade at this stage and working toward the prevention of end-stage ankle osteoarthritis.

Building upon chapter two in which osteochondral lesions of the ankle were described as a separate stage being part of the cartilage cascade analogy, one can note the variety of types of osteochondral lesions of the ankle in different ways: size of the lesion, location of the lesion and morphology of the lesion (i.e. the way the lesion looks on the baseline MRI or CT scan).[25] Van Diepen et al. concluded in an overview of the literature published in the journal Cartilage that currently there is substantial underreporting and no consensus on the reporting of morphology, lesion location nor size of the lesion [100]. Moreover, there are usually solely three groups which are referred to when (if described or categorized at all) the lesions are described from a morphological perspective: cystic, fragmentous and crater-type.[76] By limiting the categorization to three categories groups, relevant nuances and subtleties in morphology, such as the identification of new phenotypic types, can potentially be overlooked. As such, it was the aim of **Chapter 3** to evaluate,

describe and attempt to categorize these osteochondral lesions of the talus based on radiological phenotypic presentations from a geologist's perspective. From this cross-disciplinary approach integrating principles outside of orthopedic research, 5 groups were elucidated indicative of different deformation processes: brittle deformation, ductile deformation, dissolution, damage zone/cratering, and abrasion. Although a broad spectrum of different phenotypic morphologic presentation of osteochondral lesions of the talus was used, the sample of the CT scan samples may potentially have limited the generalizability of the findings due to the fact that other centers may use MRI. We found that analyzing lesion morphology and etiological mechanisms through a geological lens would be of relevance for understanding the interaction of biomechanical and chemical factors in lesion development. Regarding the undertaking of future studies, we think that through integrating geological models, new hypotheses concerning the etiological perspectives as well as prognosis of treatment outcomes for cartilage, osteochondral and similar bone injuries can potentially be formed, ultimately guiding the development of personalized primary, secondary and tertiary preventive options.[76, 79]

Posttraumatic cartilage cracks and osteochondral lesions are examples of stages part of the cartilage cascade as discussed above. Chapter 2 highlighted the nuances behind the pathophysiological mechanisms of the development of cartilage lesions of the ankle after a trauma. A specific example of such a trauma can be the so-called high-ankle sprain resulting in a syndesmotic ligament injury.[19,94] During these high-force external rotation hyperdorsiflexion injuries of the ankle, the talar dome can be impacted on the distal tibia or the fibula, as such, resulting in damage to the cartilage of the ankle. While studies by D'Hooghe et al.[18] and Rellensmann et al.[72] found cartilage damage of the talar dome in patients with isolated unstable syndesmotic injuries to be present in 23% to 48% of cases, respectively, specific incidence rates of the occurrence of (osteo)chondral lesions to the ankle in patients with acute and chronic isolated syndesmotic injuries were unknown. Hence, **Chapter 4** evaluated the incidence of (osteo)chondral lesions of the ankle in patients with acute and chronic isolated syndesmotic injuries. The study showed that (O)CLs of the ankle were present in at least 21% of the patients with isolated syndesmotic injuries.[24] The incidence rates of (O)CLs of the ankle were 22% in the acute group and 24% in the chronic isolated syndesmotic injuries group. Although the study showed that in almost 1 out of every 5 patients with an isolated syndesmotic injury, a form of (osteo)chondral damage to the ankle

was present, one could state that these rates may be an underrepresentation of the actual incidence rate as not all included publications in this meta-analysis used arthroscopy to assess the (osteo)chondral damage. The intra-operative arthroscopic assessment of (osteo)chondral damage may have a higher sensitivity and specificity rate in comparison to the sole usage of MRI.[7,102] Moreover, a high number of studies did not assess the incidence of (O)CLs as the primary outcome of the study, but rather reported the presence of (osteo)chondral injury as concomitant injuries. The 21% may therefore be an underestimation of the true incidence of (osteo)chondral injuries in patients with isolated acute and chronic syndesmotic injuries. For example, one included study, the one by Rellensmann et al.[72] thoroughly performed the inspection of the total ankle joint with a specific focus on identifying the presence of intra-articular pathologies thereby showing an incidence rate of 61%. This finding was further substantiated by a recent study by Walinga et al.[105] showing the presence of cartilage lesions in 15 out of 16 elite athletes having been treated for unstable syndesmotic injuries, as diagnosed by intra-operative needle arthroscopy.[106] These findings underscore the clinical relevance and importance of a comprehensive assessment for the presence of cartilage lesions in patients presenting with syndesmotic injuries, thereby raising awareness for the potential underdiagnosis of intra-articular lesions in acute ankle injuries.[63] Chapter 4 also paved the way for potential future research projects, as a number of new 'doors' were opened with scientific questions being raised, such as: are higher grades of syndesmotic injuries, leading to persistent instability, related to increased severity of cartilage damage in the ankle joint as well as higher incidence rates of cartilage damage? Additionally, which patients are high risk patients potentially being in the danger zone of sustaining a concomitant cartilage injury concomitantly to a syndesmotic injury? Which patients benefit from a concomitant minimally invasive (early) intra-articular assessment through a small arthroscope after a syndesmotic injury? As a last remark, one has to acknowledge the limitations of the methodology of Chapter 4, mainly consisting of the uncertainty of the symptomatology of the intra-articular (osteo)chondral lesions, the moderate methodological quality of the included studies the impossibilities to perform comparative analyses with regards to stable versus unstable syndesmotic injuries, and to purely chondral incidence rates and osteochondral incidence rates.

Part II: Surgical treatment for large, complex, and secondary osteochondral lesions of the ankle

The second part of the present thesis aimed to improve our understanding of the surgical outcomes of large, complex, and secondary osteochondral lesions of the talus (OLT). This focus was necessary as focus had so far been mostly on the diagnosis and treatment of primary, small osteochondral lesions of the talus, thereby underreporting the outcomes of treatment of OLTs that have failed prior surgical intervention(s).[26] This resulted in the uncertainty which surgical treatment option is superior regarding clinical success rates for failed primary OLTs. **Chapter 5** focused on answering this question.[55] There were a number of conclusions with the two most important ones being highlighted here: There was a wide range of surgical treatment options being used for talar OCDs in the case of primary surgical failure. Additionally, it was concluded that currently there is no superior surgical treatment for non-primary osteochondral lesions of the talus. The latter conclusion was due to a number of factors: the studies included were of large heterogeneity regarding number of patients included, study methodology, type of surgical treatment, as well as follow-up. Moreover, because of the low level of evidence and the scarce literature reporting on solely non-primary surgery, no methodologically proper meta-analysis could be performed. This study mainly opened a clear research gap for future studies focusing on a research methodology aiming to identify a superior (surgical) treatment option for the individual patient with a non-primary OLT, potentially through the usage of large prospective datasets including well-powered analyses. Due to the fact that (arthroscopic) bone marrow stimulation is still the most frequently used surgical treatment option for osteochondral lesions of the talus, a deeper meta-analysis in which the treatment bone marrow stimulation was assessed regarding its efficacy as a surgical treatment strategy for patients with osteochondral lesions of the talus who have failed a prior surgical intervention was undertaken in **Chapter 6**.[23] It was found that the overall clinical success rate of arthroscopic bone marrow stimulation for non-primary osteochondral lesions of the talus was 61% with a revision rate of 27%. Although the study included the highest number of patients possible in the literature, one could notice that solely 5 studies were included with 2 of these studies having a retrospective nature, and with a limited number of 70 included patients. This was one of the reasons to perform a prospective matched case-control study comparing the clinical, sports, work, and radiological outcomes between primary and secondary osteochondral lesions treated with

arthroscopic bone marrow stimulation, with the general outcomes that there were no differences found in the mentioned outcomes between the primary and secondary OLTs at 1 year of follow-up after arthroscopic bone marrow stimulation.[73] A clinically relevant and readily applicable conclusion of Chapter 5, 6 and the additionally mentioned study is that bone marrow stimulation can be regarded as a viable treatment option for relatively small non-primary osteochondral lesions of the talus, and, hence, should be included in the treatment algorithm as part of the shared-decision making process.[74] Lesion size is a demographic factor often considered a prognostic factor in the literature on treatment of osteochondral lesions of the talus and is measured (usually) as a non-relative assessment not correcting for body or talar size (absolute measurement.[40, 54, 62, 98-100] As briefly mentioned in the introduction of this thesis, the definition of a small lesion is relative and often referred to lesions with diameters less than 1.5 cm. However, a more refined assessment could involve evaluating the lesion size relative to the total talar diameter, surface, or volume, expressed as a percentage, thereby accounting for individual body size and proportions. This measurement method may be researched in future research projects.

As mentioned above, invasive surgical interventions may be necessary to address the patients' complaints in the case of symptomatic, large, non-primary OLTs.[55, 66] These interventions range from transplantation techniques such as (osteo) chondral transplantation, including the classical osteochondral autograft transfer system (OATS), the chondrocyte implantation techniques, and, alternatively, bulk talar allografting to restore large lesions is commonly used in the United States of America.[2,82,87] Although the different (more invasive) surgical treatment options for non-primary OLTs show clinical effectiveness and no superiority over one another, it can be stated that each of these surgical techniques are associated with specific downsides.[2,14,50,55,87,97,104] In order to overcome the aforementioned downsides, a novel technique for the treatment of large talar osteochondral lesions had recently been developed in Amsterdam; The *Talar Osteo-Periostic grafting from the Iliac Crest (TOPIC)*. In **Chapter 7**, the surgical technique of Talar OsteoPeriostic grafting from the Iliac Crest (TOPIC) procedure was described for osteochondral lesions residing on the medial talar dome, and in **Chapter 8**, the new procedure was described for lateral lesions.[28,53] Another novel surgical treatment strategy was introduced in this PhD thesis when the osteochondral damage has progressed to a stage between osteochondral lesions and osteo-arthritis: In the **Addendum**[21] section of the present PhD thesis, the technique and 2-year prospec-

tive outcomes of a novel bone- and joint sparing hemi-prosthesis surgery, the Ankle Spacer, for treating multiple secondary osteochondral lesions of the talus was described. Though this can be considered a promising technique with the outcomes being presented of solely two included patients, it was chosen not to further elucidate this Addendum in a discussive manner due to the fact that the Ankle Spacer has been taken off the market: discussing it is therefore not of high clinical nor scientific value.

After the presentation of the TOPIC technique in the mentioned chapters, the clinical effectiveness of the new technique for patients with large, complex, medial talar osteochondral lesions that have been operated on with the TOPIC procedure was analyzed in **Chapter 9**.[27] Forty-three patients were prospectively assessed before and 24 months after the TOPIC procedure with all patients being enrolled being available for follow-up at the 2-year follow-up mark. All outcomes, except for the Short-Form 36 mental component scale improved significantly with a 100% union rate of the osteotomy site at the distal tibia and 100% of the grafts showing incorporation at both 1- and two years of follow-up after the surgery. The lack of significant change in the mental component score may be due to a ceiling effect, insensitivity to specific mental health changes (for example solely a reduction in social functioning with no changes in the other domains) and/or already induced adaptation to the chronic condition.[13, 85] Conclusive remarks of this sufficiently powered study were therefore that the TOPIC procedure for large osteochondral lesions of the medial talar dome is an effective technique that resulted in significant improvement exceeding the minimal clinically important difference in pain scores (primary outcome) as well as in other outcomes, with 100% consolidation of the grafts. The findings of this study suggest that the novel surgical intervention may serve as a clinically effective, joint-sparing alternative to autologous osteochondral transplantation, bulk allografting, (arthroscopic) ankle arthrodesis, or total ankle replacement – each of which has its own advantages and disadvantages. Despite the study's strong methodological foundation, several limitations should be acknowledged. Firstly, this study involved a single treatment arm and did not compare the novel intervention to other surgical options that are used for a comparable patient group, such as the classical osteochondral autograft transfer system (OATS), metal inlay implants, bulk allografting, or arthroscopic ankle arthrodesis.[2,14,29,32,70,82,101,104] It is however of relevance and importance to compare the indications, advantages and disadvantages as well as the outcomes of the TOPIC procedure to firstly, the Autologous Osteochondral Transplantation (AOT).

In order to do so, it should first be explored to what extent the indications are similar to one another. As stated by Shimozono et al.,[84] the AOT procedure is typically indicated for patients who have failed conservative treatment and whose lesion size is > 100 mm^2 to 150 mm^2, or for those patients who have undergone failed bone marrow stimulation. This is reflected by the literature[36,81,84] on AOT with large studies showing a preoperative defect size ranging from 78 mm^2 to 113 mm^2. Aiming to place this into perspective, one could state that the surface area of our analyzed cohort – which was calculated with the same methodology as the previously cited studies on AOT – in some cases was twice as large (177 mm^2) as the mean surface areas in the publications on AOT. Another important comparison for the context on indication is the percentage of previous surgeries prior to the AOT procedure and prior to the TOPIC procedure. In two large studies by Shimozono et al. [84] studying the effect of containment type on clinical outcomes in osteochondral autograft transplantation, one can deduce that the percentage of primary OLTs ranged from 70 to 81%, while in our study the percentage of primary OLTs was 33%. These two factors (i.e., size and primary/non-primary nature) are of importance for the perspective and context on both clinical decision-making as well the expected outcomes, and, as such, it can be stated that the indication and demographic values are different comparing the AOT procedure to the TOPIC procedure. However, when considering a comparison of the two procedures on the reoperation rates as well as the clinical outcomes (FAOS and SF-36/SF-12), similar outcomes were found when placing our results into perspective with the literature on AOT.[36,80,81,84] The potential presence of donor-site morbidity after an AOT procedure is another important point of discussion. In a recent best-case and worst-case scenario, Shimozono et al.[83] showed that the estimated proportion of donor-site morbidity ranged from 7 to 11%. However, in a retrospective study by Paul et al.[69] which was specifically dedicated to the assessment of donor-site morbidity after osteochondral autologous transplantation for lesions of the talus, it was shown that donor-site morbidity of the knee led to functional impairments in patients with previously asymptomatic knees. In Chapter 9, the patients were specifically requested to report donor-site morbidity of the iliac crest, and it was noted that 0% of the patients complained of functional impairments due to donor-site morbidity of the iliac crest. This is in line with a study conducted by Wang et al.[109] having researched in a retrospective iliac bone autografting for Hepple stage V OLTs with the authors concluding that no patients complained of pain at the donor site. Shi et al. [80] concluded a similar result with solely 4% of the patients complaining of pain at the donor-site after autologous osteoperiosteal cylindrical transplantation for large, medial, cystic OLTs.

It is also of relevance to put the indications, advantages and disadvantages as well as the outcomes concerning the TOPIC procedure into perspective and compare these with bulk allografting and metal implantation. Concerning the indication setting as well as the demographic factors included amongst the different publications available, the application of bulk allografting is to some extent more comparable to the TOPIC procedure.[2,29,32,70,82,101] More specifically, in the most recent publication by Fletcher et al.[32] the preoperative size (volume as based on CT scan) was 1879 mm^3 which is 28% smaller in comparison to our included cohort (2400 mm^3). This finding was also (partially) confirmed when comparing the lesion volume of our cohort to the included studies on fresh osteochondral allograft transplantation for OLTs in the recent systematic review by Pereira et al.[70] Consequently, taking into account the lesion dimensions as well as the majority of the lesions being non-primary in nature, one could conclude that the indication for a TOPIC procedure – at least for the patients included in the present cohort – resembles a salvage joint-sparing procedure for large and complex OLTs when prior conservative and surgical intervention(s) may fail. Concerning the reoperation rate after fresh osteochondral allograft transplantation for OLTs, it is important to compare our prospective study to the most recent prospective study on fresh osteochondral allograft transplantation having found an additional surgery rate of 48%.[32] The additional surgeries that were performed consisted primarily of hardware removal from the allograft site. In comparison to the rate of 37% from our study, it can be noted that there is a substantial difference in additional surgery rates, and it must also be noted that the majority of the additional procedures having been performed in our analysis included hardware removal only from the distal tibial osteotomy being unrelated to the graft being considered a minor procedure not requiring any additional access to the joint. A comparative analysis on survival rate of the TOPIC graft versus the allograft procedure may not be entirely applicable to the complete extent as the currently presented study included a two-year prospective follow-up analysis without a specific survival analysis as outcome. As mentioned before, one patient had a failure of the TOPIC procedure and subsequently underwent an arthroscopic arthrodesis of the ankle. One could state that included this patient into the larger cohort, we could state that, to a certain extent, the survival rate of the procedure is 98%. As such, this rate accounts for a 98% survival of the included and analyzed cohort, and is relatively higher than the 87% being extracted from the literature in the study by Pereira et al.[70] Other factors to take into account for the fresh osteochondral allograft procedure that can be highlighted in the comparative course are donor disease

transmission, significant costs as well as donor (in)availability potentially leading to extended waiting times – these are not applicable to the TOPIC procedure.

A last comparison which can be performed is the comparison of the TOPIC procedure to metal inlay implants. One of the larger prospective studies on metal resurfacing for osteochondral lesions of the talus was published in 2018 by Vuurberg et al.[104] Although the study had a slightly longer follow-up, the indications for the metal implant can be regarded as the age at surgery, body mass index and percentage of included females were similar, as well as that all patients (100%) were operated for non-primary OLTs. one could argue that the baseline OLT size of the patients included by Vuurberg et al.[104] was slightly smaller than the included TOPIC group with the baseline size of the metal implant group being 16mm in the antero-posterior direction, 11 mm in the medio-lateral direction, and 9mm in the superior-inferior direction. Regarding outcomes at follow-up, it can be concluded that the numeric rating scale of pain during walking at 2 years of follow-up was around 3 in the metal implant group, while this outcome was 2 in the TOPIC group. Furthermore, nine patients (id est, 24% of the patients) recorded complications in the metal implant group while in the TOPIC group this percentage was 9. Although the follow-up times regarding 'survival' were different, one could note that at 2 years of prospective follow-up, there was one patient in the TOPIC group needing a fusion or ankle prosthesis, while 5% of the patients in the metal inlay implant group needed an ankle fusion. Future research aiming to prospectively compare the survival rate of the TOPIC group versus the metal implant group need to be performed in order to give definitive answers on the superiority regarding survival and clinical outcomes. Taking into account the above-mentioned comparisons between the different available surgical interventions for large, non-primary osteochondral lesions of the talus, future research may focus on the cost-effectiveness as well as the patient experience and burden aspect of the surgical interventions, in order to also shed novel light on the application of different surgical interventions for osteochondral lesions of the talus is low and middle-income countries.

Deferring back to the limitations of chapter 9, it can be stated that a different limitation of the study was that the study focused exclusively on medial lesions to ensure a homogeneous group, as medial lesions are the most common.[99] However, it is worth noting that central and lateral TOPIC procedures are currently being performed at our institution, with results from these cases expected to be published soon.[28] Another limitation is the relatively short follow-up period

of two years, which does not account for long-term outcomes. Therefore, future research should evaluate the durability of the TOPIC procedure over extended periods of time surpassing the two years of follow-up. Additionally, further studies are needed to assess its generalizability by examining outcomes in other centers and exploring its efficacy for central and lateral talar lesions. Another future study could research in a comparative sufficiently-powered manner the clinical differences comparing the TOPIC procedure to for example a metal implant, bulk allografting and an ankle arthrodesis.[3,4,50,65,82,104,113]

Chapter 10[22] aimed at closing part of the existing knowledge gender gap in the field of musculoskeletal science by analyzing whether there were sex-specific clinical and radiological outcomes after Talar OsteoPeriostic grafting (TOPIC) for large osteochondral lesions of the talus.[6,31,34,41,52,56,57] Both males and females showed clinically relevant improvements after undergoing the TOPIC procedure with significant differences in preoperative lesion size – males had larger preoperative lesions than females. It was concluded that the TOPIC procedure is a clinically effective treatment strategy for large OLTs in both men and women. Although the study was prospective of methodological nature, included a sufficiently powered analysis for the primary outcome, had a 100% follow-up rate at the follow-up moment, it should be noted that the study may have been underpowered for the secondary outcomes. Moreover, lateral lesions were not included in the analysis. Through the development of this study, at least part of the research gap on gender-related differences in orthopedic surgery was studied to a certain extent. Especially for cartilage lesions of the ankle, studying this relatively 'hot' topic can be of interest for future high-powered international cohort studies in which a number of factors can be of a research focus (two examples will be given here): one, the differences in demographic data of cartilage lesions can be an interesting field for academic curiosity, in which it can be studied whether there are differences in location distribution, morphological presentations, and average size measurements.[35,37] Two, differences in outcomes at different moments in follow-up can be assessed in future studies regarding a wide variety of treatment options, ranging from conservative management options for cartilage lesions to extensive surgical interventions. Consequently, these future studies can further contribute to the larger goal of the present thesis: creating stepping stones towards an evidence-based personalized approach for incremental cartilage damage of the ankle for each and every patient, as such also taking into account potential sex-related differences.

With regards to outcomes in aftertreatment and postoperative rehabilitation after surgery for osteochondral lesions of the talus, Buck et al. recently concluded that this topic has been understudied substantially.[11,20] **Chapter 11**[42] aimed at answering whether there were differences in outcomes between 5 and 6 weeks of non-weight bearing after osteochondral grafting with medial malleolar osteotomy for medial talar defects by analyzing patients having undergone the TOPIC procedure for medial osteochondral lesions of the talus with a concomitant medial malleolus osteotomy.[44,45] We used a power analysis prior to the onset of the study in order to have a proper prospective methodology in which it was noted that 10 patients per analyzed group were necessary for inclusion. Patients of the 5-week non-weightbearing group were matched in a 1:2 ratio with patients from the 6-week non-weightbearing group. Patients were matched based on variables that were recognized as being of prognostic value in osteochondral (autograft) transplantation therapies, which were sex, age at time of surgery, body mass index, and smoking.[35,51,75] We found no statistical differences in terms of clinical, radiological, and safety outcomes between five and six weeks of non-weight bearing following the TOPIC procedure. Regarding the direct clinical relevance of the study, we showed that that patients can safely start weightbearing relatively earlier after the TOPIC procedure having been performed through a medial malleolar osteotomy – this finding was also mirrored by a recent systematic review by Hong et al.[45] in which it was concluded that there were no differences in clinical outcomes between early or late weight-bearing after autologous osteochondral transplantation. Although one may state the one week less of non-weightbearing in our study can be considered a small effect, it may well improve the patient convenience and shorten the time to return to work and sports.[20,30,44,88] This also directly brings us to the limitations of the study, as we should acknowledge that we did not study the effect of a shorter non-weightbearing period work and sports-specific related outcomes, which are highly clinically relevant and understudied scientific subjects to be studied for future scientific endeavours.

Sports-outcomes after the TOPIC procedure were studied in **Chapter 12**, in which we aimed to answer the question what the (return to) sports outcomes at one and two years of follow-up were in patients having undergone Talar OsteoPeriostic grafting (TOPIC) for large, complex medial talar osteochondral lesions, as this was previously unknown.[27,89] Sixty-one patients were analyzed in this prospective study, assessing different levels of return to sports at both 1 and 2-years of follow-up. A mixed-methods approach was utilized, combining both quantitative and quali-

tative data collected through telephone interviews, during which the prospectively gathered data was validated and cross-checked. The interviews enabled a comprehensive reconstruction of each patient's disease trajectory related to their OLT, offering a clinically representative perspective on sports participation and return-to-sports outcomes. The primary findings of the study were that the TOPIC procedure resulted in 8 out of 10 patients participating at their desired level of sports, 10 out of 10 patients returned to any level of sports, and 6 out of 10 patients return to their pre-injury level of sports 2 years after the TOPIC procedure. Our findings demonstrated that most patients successfully resumed participation in some form of sports activity after undergoing the TOPIC procedure, with a high level of self-reported achievement of personal goals. Although these outcomes highlight the clinical effectiveness of the TOPIC procedure and could enhance the shared decision-making process between patients and physicians by providing more comprehensive information for managing expectations, the study should also be interpreted in the light of the potential limitations of the study (methodology). Firstly, no prognostic factors regarding return to sport outcomes nor return to sport times were studied in this study, marking a potential future research project in order to even further counsel patients with regards to the expectations concerning postoperative sports outcomes after the TOPIC procedure. Secondarily, another limitation that must also be described here is that the desired level of return to sports was assessed and recorded post-operatively by the study team to verify the pre-operative expectations (also known as goal attainment scaling).[46,47,110,111]

Not only for example bulk allografts and (cylindrical) osteochondral autograft transfer system (OATS) grafts need to be fitted perfectly into the excised osteochondral lesion of the talus so that size, morphology and curvature of the talar dome can be matched appropriately, so do the iliac crest osteoperiosteal autografts.[16,27,28,48,53] As introduced, the restoration of the talar surface after auto- or allografting is required for an adequate contact area and pressure distribution in the ankle.[10] Although it was mentioned in chapter 9 that the first clinical prospective results can be considered highly promising at two years of follow-up, it was unknown to what extent the surface curvature of the medial talar dome matches the surface curvature of the ipsilateral iliac crest. This research gap was studied in **Chapter 13**. The study made use of the so-called nearest neighbor distance (NND) analysis, which can be considered a surrogate marker for surface matching regarding curvature. Based on CT-scans of the talus and the ipsilateral pelvis, segmentations were performed and a theoretical osteochondral lesion of the talar

dome was determined based on a 3D-model. This OLT surface was placed on the ipsilateral iliac crest within a region of interest, manually and also followed by Iterative Closest Point (ICP). Twenty patients were included (10 men and 10 women), and the primary outcome showed a maximum and median NND of 1.9 mm and 0.52 mm respectively after ICP, and 2.3 mm and 0.61 respectively after manual placement only. The secondary outcome showed a mean location of the OLT after ICP at 49 ± 11 mm proximally from the SIAS. Interpreting these outcomes, one could remark that when taking the NND as a surrogate marker for the curvature matching of the medial talar dome and ipsilateral iliac crest, adequate surface matching was found between the surfaces of the iliac crest and the medial talar dome. Additionally, it was found that optimal mean location of the grafts on the iliac crest lies at 49 ± 11 mm proximally from the SIAS. Lastly, no differences in curvature matching were observed between men and women, meaning that the results of the study are readily clinically applicable to both female and male patients with osteochondral lesions of the medial talar dome undergoing a medial TOPIC procedure. The clinical relevance for the described study is two-fold: firstly, the study's findings can be directly applied in daily practice, as the average location of the best-matching curvature on the iliac crest, provides a valuable reference point for surgical planning so that surgeons can now harvest the ipsilateral iliac crest osteoperiosteal autograft approximately 49 millimeters proximally from the anterior superior iliac spine for optimal surface matching. Whether this actually improves clinical outcomes instead of harvesting the graft at least two centimeters proximal to the anterior superior iliac spine was not researched in this study, but may be a research gap for future research. In order to further work towards individualized pre-operative planning of the TOPIC procedure, another future research project may be to analyze patients with different sizes and morphologies of their baseline OLTs instead of manually creating a theoretical average sized OLT based on mean dimensions from patients included in Chapter 10.[27] These subtle changes in location and individual size of the OLT may affect the curvature and subsequently the preferred iliac crest harvesting location based on the manual placement and the semi-automatic matching through the software patient per patient.[9,58,59]

Chapter 14 circles us back to part I in which the etiological perspectives behind the development of cartilage and osteochondral lesions of the ankle.

OLTs and cartilage damage of the ankle was described, with the geological visualization and discussion of cystic lesions being important. Not only can these cystic

lesions be present at baseline when a patient presents with a primary osteochondral lesion of the ankle, these cystic lesions can also (re)occur after a surgical intervention, for example after an autograft or allograft procedure.[27,39,43,48,64,84] Chapter 14 aimed to assess and compare the cystic occurrence after autografting, allografting and osteoperiosteal grafting for osteochondral lesions of the talus, and explore the presence of correlations of clinical outcomes with the presence of postoperative cysts. In the systematic review and meta-analysis 13 studies were included reporting on a total of 438 ankles. The most important findings of the study were that postoperative cyst formation was a common finding following osteochondral autograft transplantation (42%), allograft transplantation (58%), and osteoperiosteal graft transplantation (34%), and there appeared to be no statistically significant differences in the prevalence of these cysts between the mentioned surgical treatment techniques ($p = 0.31$). Another impacting finding was that the postoperative presence of cysts was not correlated with inferior clinical outcomes in any of the included studies.[27,33,77,96,107,112] One could argue still however that the (re)occurrence of postoperative cysts after autografting, allografting or osteoperiosteal grafting can be considered a potential matter of concern. Although the meta-analysis did not answer the question why these cysts (re) develop after time, this is an interesting field to further dive into as it touches on both the postoperative radiological and clinical outcomes as well as on etiological considerations behind the potential pathophysiological mechanisms leading to the (re)occurrence of postoperative cysts. Potential factors related to the (re)occurrence of cysts may be defects in graft sealing, insufficient cartilage regeneration, subchondral necrosis, residual mechanical stress on the affected part of the talar dome, graft thickness, immunological responses, and/or incomplete integration of the graft.[1,8,12,15,17,78,84,86,103] Food for thought for future studies!

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Appendices

English summary
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Dankwoord

English summary

The present thesis highlights the aetiology, incidence, phenotypes as well as management of (osteo)chondral injuries to the ankle throughout a wide and inter- and multidisciplinary scope with its overreaching goal of working towards an evidence-based personalized approach for the treatment of incremental cartilage damage of the ankle with a specific focus on the treatment of large, secondary osteochondral lesions of the talus, hence aiming to prevent the further progression in the above-mentioned cascade from osteochondral lesion to end-stage osteo-arthritis.

Part I: Introduction, aetiology, incidence, and phenotypes of cartilage damage of the ankle

Chapter 2 described the progression of incremental cartilage damage in the ankle joint through the resemblance of a cascade, highlighting the different stages of the cartilage damage starting with an ankle trauma consisting of either a sprain or a fracture. A number of stages were presented including the invisible cartilage crack, the osteochondral lesion and the osteo-arthritis stage.

Chapter 3 categorized and described osteochondral lesions of the talus based on radiological phenotypic presentations from the geologist's perspective. From this cross-disciplinary approach integrating principles outside of orthopedic research, 5 groups were elucidated indicative of different deformation processes: brittle deformation, ductile deformation, dissolution, damage zone/cratering, and abrasion.

Chapter 4 investigated the incidence of (osteo)chondral lesions of the ankle in patients with acute and chronic isolated syndesmotic injuries. The study was a meta-analysis and included nine articles with 402 syndesmotic injuries. It was shown that (O)CLs of the ankle were present in 21% of the patients with isolated syndesmotic injuries. The incidence rates of (O)CLs of the ankle were 22% in the acute group and 24% in the chronic isolated syndesmotic injuries group. 95% of the lesions were located on the talar dome, while solely 5% of them were located on the distal tibia.

Part II: Surgical treatment for large, complex, and secondary osteochondral lesions of the ankle

Chapter 5 focused on answering the question which surgical treatment option is superior regarding clinical success rates for failed primary OLTs. The study's methodology was a systematic review of the literature included in total 21 studies with a total of 301 talar osteochondral lesions. There were a number of conclusions. Firstly, there was a wide range of surgical treatment options being used for talar OCDs in the case of primary surgical failure. Additionally, it was concluded that currently there is no superior surgical treatment for non-primary osteochondral lesions of the talus.

Chapter 6, another systematic review of the literature, researched the specific clinical efficacy of (arthroscopic) bone marrow stimulation for patients with osteochondral lesions of the talus who have failed a prior surgical intervention. The study included 70 patients from a total of 5 studies, and it was found that the overall clinical success rate of arthroscopic bone marrow stimulation for non-primary osteochondral lesions of the talus was 61% with a revision rate of 27%. Return to sports, work, and complication outcomes that were yielded were considered fair to good.

Chapter 7 and **Chapter 8** described a novel technique for the treatment of large talar osteochondral lesions; The *Talar Osteo-Periostic grafting from the Iliac Crest (TOPIC)* technique, for medial and lateral lesions, respectively. Another new surgical treatment strategy, the Ankle Spacer, which represents a novel bone- and joint sparing hemi-prosthesis surgery for treating multiple secondary osteochondral lesions of the talus was described in the **Addendum** section at the end of this PhD thesis and also included two-year prospective radiological, clinical, and safety outcomes.

Chapter 9 analyzed the clinical effectiveness of the new TOPIC technique for patients with large, complex, medial talar osteochondral lesions. Forty-three patients were prospectively evaluated before and 24 months after undergoing the TOPIC procedure, with all enrolled patients available for assessment at the 2-year follow-up. All outcomes, except for the Short-Form 36 mental component scale, showed significant improvement. Additionally, a 100% union rate was observed at the osteotomy site of the distal tibia, and all grafts demonstrated full incorporation at both 1- and 2-year follow-ups. This adequately powered study concluded that the TOPIC procedure for large osteochondral lesions of the medial talar dome

is an effective technique, yielding significant improvements that surpassed the minimal clinically important difference in pain scores (primary outcome) and other metrics, with complete graft consolidation.

Chapter 10 presents a comparison of potential sex-specific differences in clinical and radiological outcomes following Talar OsteoPeriostic Grafting (TOPIC) for large osteochondral lesions of the talus. Both male and female patients demonstrated clinically significant improvements after the procedure. Interestingly, males were found to have larger preoperative lesions compared to females. The study concluded that the TOPIC procedure is an effective treatment for large osteochondral lesions of the talus (OLTs) in both sexes.

Chapter 11 explored whether outcomes differed between five and six weeks of non-weight bearing following osteochondral grafting combined with medial malleolar osteotomy for medial talar defects. The study included patients who underwent the TOPIC procedure with a concomitant medial malleolus osteotomy. A power analysis conducted prior to the study determined that 10 patients per group were necessary for robust prospective analysis. Patients in the five-week non-weight-bearing group were matched in a 1:2 ratio with those in the six-week group, ensuring matching based on prognostic variables, including sex, age at surgery, BMI, and smoking status. The results showed no statistically significant differences in clinical, radiological, or safety outcomes between the two groups.

Chapter 12 addressed the question of return-to-sports outcomes one and two years after the TOPIC procedure in patients with large, complex talar osteochondral lesions. A total of 61 patients were analyzed prospectively, with varying levels of sports participation evaluated at both time points. Using a mixed-methods approach, the study combined quantitative and qualitative data collected through telephone interviews, which allowed for validation and cross-checking of prospectively gathered data. These interviews facilitated a detailed reconstruction of each patient's disease trajectory and provided a representative view of sports participation outcomes. The findings revealed that 80% of patients participated in sports at their desired level, 100% returned to some form of sports activity, and 60% resumed sports at their pre-injury level within two years of undergoing the TOPIC procedure.

Chapter 13 explored the extent to which the surface curvature of the medial talar dome corresponds to that of the ipsilateral iliac crest. Using a nearest neighbor distance (NND) analysis, a proxy for evaluating curvature alignment, we assessed

the degree of surface matching. CT scans of the talus and the corresponding pelvis were segmented, and a theoretical osteochondral lesion of the talar dome was simulated using a 3D model. This simulated OLT surface was then positioned on the ipsilateral iliac crest within a predefined region of interest, both manually and with Iterative Closest Point (ICP) optimization. The study included 20 participants (10 male, 10 female), and the primary findings demonstrated a maximum NND of 1.9 mm and a median NND of 0.52 mm following ICP, compared to 2.3 mm and 0.61 mm after manual placement alone. Secondary outcomes revealed that the average location of the graft following ICP was 49 ± 11 mm proximal to the SIAS. These results suggest that the iliac crest provides a sufficiently close curvature match to the medial talar dome, as indicated by the NND values. Furthermore, the study determined that the optimal graft location on the iliac crest lies approximately 49 ± 11 mm proximal to the SIAS. No differences were observed between male and female participants regarding curvature matching.

Chapter 14 examined and compared cyst formation rates following autografting, allografting, and osteoperiosteal grafting for talar osteochondral lesions, as well as correlations between clinical outcomes and postoperative cyst presence. A systematic review and meta-analysis included 13 studies reporting on 438 ankles. Key findings highlighted that postoperative cyst formation was a common occurrence, with rates of 42% for autografts, 58% for allografts, and 34% for osteoperiosteal grafts. No statistically significant differences in cyst prevalence were observed between these techniques ($p = 0.31$). Additionally, the presence of postoperative cysts did not correlate with worse clinical outcomes in any of the analyzed studies.

Nederlandse samenvatting

Het huidige proefschrift belicht de etiologie, incidentie, fenotypes en de behandeling van (osteo)chondraallaesies van de enkel vanuit met als overkoepelend doel het leggen van bouwstenen voor een geïndividualiseerde, wetenschappelijk bewezen aanpak van het brede spectrum van kraakbeenschade aan de enkel. De specifieke focus ligt daarbij op de behandeling van grote, secundaire osteochondraallaesies van de talus waarmee wordt beoogd de verdere progressie van focale kraakbeenschade naar eindstadium artrose te voorkomen.

Deel I: Introductie, etiologie, incidentie en fenotypes van kraakbeenschade aan de enkel

Hoofdstuk 2 beschreef de progressie van kraakbeenschade in het enkelgewricht, weergegeven als een cascade (waterval). Hierbij werden de verschillende stadia van kraakbeenschade belicht, beginnend met een enkeltrauma in de vorm van een verzwikking of breuk. Een aantal stadia werd gepresenteerd, waaronder de onzichtbare kraakbeenscheur, de osteochondraallaesie van de enkel en het eindstadium slijtage.

Hoofdstuk 3 categoriseerde en beschreef osteochondraallaesies van de talus op basis van radiologische fenotypische kenmerken vanuit het perspectief van een geoloog. Met deze interdisciplinaire benadering, die principes buiten het orthopedisch onderzoek integreerde, werden vijf geologische groepen geïdentificeerd die wijzen op verschillende vervormingsprocessen.

Hoofdstuk 4 onderzocht de incidentie van (osteo)chondraallaesies ((O)CL's) van de enkel bij patiënten met acute en chronische geïsoleerde syndesmoselaesies. De studie was een meta-analyse en omvatte negen artikelen met in totaal 402 syndesmoselaesies. Uit de analyse bleek dat (O)CL's van de enkel aanwezig waren bij 21% van de patiënten met geïsoleerde syndesmoselaesies. De incidentie van (O)CL's bedroeg 22% in de acute groep en 24% in de chronische groep. Van de laesies was 95% gelokaliseerd op de talusrol, terwijl 5% zich op de distale tibia bevond.

Deel II: Chirurgische behandeling van grote, complexe en secundaire osteochondraallaesies van de enkel

Hoofdstuk 5 richtte zich op de vraag welke chirurgische behandelmethode superieur is qua klinische effectiviteit bij patiënten met osteochondraallaesies

van de talus na eerdere gefaalde chirurgische interventie(s). De studie was een systematisch literatuuronderzoek en omvatte in totaal 21 studies met 301 osteochondraallaesies van de talus. Een aantal conclusies werd getrokken. Ten eerste was er een breed scala aan chirurgische behandelopties voor talaire osteochondraallaesies bij patiënten bij wie eerder chirurgisch ingrijpen gefaald had. Bovendien werd geconcludeerd dat er op dit moment geen superieure chirurgische behandeling bestaat voor niet-primaire osteochondraallaesies van de talus.

Hoofdstuk 6, een andere systematische literatuurreview, onderzocht de klinische effectiviteit van (artroscopische) beenmergstimulatie bij patiënten met osteochondraallaesies van de talus na het falen van een eerdere chirurgische interventie. De studie omvatte 70 patiënten uit vijf studies en toonde aan dat het algehele klinische succespercentage van artroscopische beenmergstimulatie voor niet-primaire osteochondraallaesies van de talus 61% bedroeg, met een revisiepercentage van 27%. De uitkomsten voor sporthervatting, werkhervatting en complicaties werden als redelijk tot goed beoordeeld.

Hoofdstuk 7 en 8 beschreven een nieuwe chirurgische techniek voor de behandeling van grote osteochondraallaesies van de talus: de *Talar Osteo-Periostic grafting from the Iliac Crest* (TOPIC) techniek, respectievelijk voor mediale en laterale laesies. Een andere nieuwe chirurgische interventie, de Enkel Spacer, een bot- en gewrichtsbesparende hemi-prothese voor de behandeling van meerdere secundaire osteochondraallaesies van de talus, werd beschreven in het addendum van dit proefschrift, inclusief prospectieve radiologische, klinische en veiligheidsuitkomsten.

Hoofdstuk 9 onderzocht in hoeverre de curvatuur van de mediale talusrol overeenkomt met die van de ipsilaterale bekkenkam. Met behulp van een "*nearest neighbor distance*" (NND)-analyse, een maat voor de evaluatie van overeenkomst in curvatuur van een oppervlakte, werd de mate van gelijkheid t.a.v. de curvatuur van de mediale talusrol en de ipsilaterale bekkenkam onderzocht. CT-scans van de talus en het bekken werden gesegmenteerd, en een osteochondraallaesie van de mediale talusrol werd gecreëerd met behulp van een 3D-model. De oppervlakte van de osteochondraallaesie werd vervolgens zowel handmatig als met een *Iterative Closest Point (ICP)-optimalisatie* geplaatst op de ipsilaterale bekkenkam binnen een vooraf gedefinieerde regio van interesse. De studie omvatte 20 deelnemers (10 mannen, 10 vrouwen), en de primaire resultaten toonden een maximale NND van 1,9 mm en een mediane NND van 0,52 mm na ICP, vergeleken met 2,3

mm en 0,61 mm na handmatige plaatsing. Secundaire uitkomsten toonden aan dat de gemiddelde locatie van de graft na ICP 49 ± 11 mm proximaal van de Spina Iliaca Anterior Superior (SIAS) lag. Deze resultaten suggereren dat de bekkenkam een voldoende nauwkeurige curvatuurovereenkomst biedt ten opzichte van de mediale talusrol. Bovendien werd vastgesteld dat de optimale graftlocatie op de bekkenkam ongeveer 49 ± 11 mm proximaal van de SIAS ligt. Er werden geen verschillen waargenomen tussen mannen en vrouwen wat betreft curvatuurovereenkomst.

Hoofdstuk 10 onderzocht geslachtsspecifieke verschillen in klinische en radiologische uitkomsten na Talar Osteo-Periostale grafting (TOPIC) voor grote osteochondraallaesies van de talus. Zowel mannelijke als vrouwelijke patiënten vertoonden klinisch significante verbeteringen na de procedure. Mannen hadden grotere preoperatieve laesies dan vrouwen. De studie concludeerde dat de TOPIC-procedure een effectieve behandeling is voor grote osteochondraallaesies van de talus bij zowel mannen alsook vrouwen.

Hoofdstuk 11 onderzocht of de klinische uitkomsten verschilden tussen vijf en zes weken niet belasten na de TOPIC-procedure na een mediale malleolusosteotomie voor mediale osteochondraallaesies van de talus. De studie omvatte prospectief geïncludeerde patiënten die de TOPIC-procedure ondergingen met een gelijktijdige mediale malleolusosteotomie. De resultaten toonden geen statistisch significante verschillen in klinische, radiologische of veiligheidsuitkomsten tussen de twee groepen. Vijf weken in plaats van 6 weken niet belasten na een TOPIC-procedure met een mediale malleolusosteotomie is derhalve veilig en effectief.

Hoofdstuk 12 onderzocht de sporthervattingsuitkomsten één en twee jaar na de TOPIC-procedure bij patiënten met grote, complexe osteochondraallaesies van de talus. In totaal werden er 61 patiënten prospectief geanalyseerd. Met behulp van een mixed methods-benadering werden kwantitatieve en kwalitatieve gegevens verzameld via telefonische interviews, waarmee prospectief verzamelde gegevens werden gevalideerd en gecontroleerd. De interviews verzamelden een gedetailleerde reconstructie van het ziekteverloop van elke patiënt en boden een representatief en betrouwbaar beeld van de sportparticipatie-uitkomsten. De bevindingen toonden aan dat 80% van de patiënten deelnam aan sport op hun gewenste niveau, 100% keerde terug naar enige vorm van sportactiviteit, en 60% hervatte sport op hun niveau van vóór het letsel binnen twee jaar na de TOPIC-procedure.

Hoofdstuk 13 analyseerde de klinische effectiviteit van de nieuwe TOPIC-techniek voor patiënten met grote, complexe, mediale osteochondraallaesies van de talus. Drieënveertig patiënten werden prospectief geëvalueerd vóór en 24 maanden na de TOPIC-procedure, waarbij alle patiënten beschikbaar waren voor beoordeling bij de follow-up op twee jaar. Alle uitkomsten, behalve de mentale componentenschaal van de Short-Form 36, toonden significante verbetering. Daarnaast werd een fusiegraad van 100% waargenomen op de osteotomieplaats van de distale tibia, en alle grafts vertoonden volledige integratie bij zowel de 1- als de 2-jaars follow-ups. Deze studie concludeerde dat de TOPIC-procedure voor grote osteochondraallaesies van de mediale talusrol een effectieve techniek is, met klinisch relevante verbeteringen in pijnscores (primaire uitkomst).

Hoofdstuk 14 onderzocht middels een systematisch literatuuronderzoek de incidentie van cystevorming in en rondom de graft na verschillende transplantatietechnieken voor osteochondraallaesies van de enkel. De cystevormingspercentages waren 42% voor autografts, 58% voor allografts en 34% voor osteoperiostale grafts, zonder significante verschillen tussen technieken ($p = 0,31$). Postoperatieve cysten correleerden niet met klinische uitkomsten na de operatie.

PhD portfolio

Name: J. Dahmen
PhD period: June 2020 – November 2023
PhD supervisors: Prof. Dr. G.M.M.J. Kerkhoffs
PhD co-supervisor: Dr. S.A.S. Stufkens

1. PhD training

General courses	Year	ECTS
ASTERIX End Symposium for Rare Diseases	2017	1.0
E-BROK ('Basiscursus Regelgeving Klinisch onderzoek')	2019	1.5

Oral presentations including teaching activities	Year	ECTS
Surgical Treatment of Necrotizing Fasciitis. Brandwondencentrum Rode Kruis Ziekenhuis (RKZ), Tri-Monthly Evening Meeting [invited talk], Beverwijk, the Netherlands.	2017	0.5
Osteochondral Defects of the Talus: Radiology and Surgical Treatment. Education 3rd year medical students, University of Amsterdam [invited lecture], Amsterdam, the Netherlands.	2018	0.5
Osteochondral Defects of the Talus: Radiology and Surgical Treatment. Education residents and surgeons, Haga Teaching Hospital [invited lecture], The Hague, the Netherlands.	2018	0.5
Osteochondral Defects of the Talus: Radiology and Surgical Treatment. Education 3rd year medical students, University of Amsterdam [invited lecture], Amsterdam, the Netherlands.	2019	0.5
Talar OsteoPeriostic Grafting from the Iliac Crest; Clinical Outcomes. AOFAS Annual Meeting, Chicago, United States of America.	2019	0.5
OUTBACK STUDY: Presenting the Protocol for a Novel Randomized Controlled Trial. Scientific Meeting, Academic Medical Center, Amsterdam, the Netherlands.	2019	0.5
Systematic Review on Sports Outcomes after Talar OCD Surgery. International Ankle Symposium, Amsterdam, the Netherlands.	2019	0.5
Systematic Review on Sports Outcomes after Talar OCD Surgery. International Consensus Meeting on Cartilage Repair of the Ankle (ICCRA), Dublin, Ireland.	2019	0.5
OUTBACK STUDY: Presenting the Protocol for a Novel Randomized Controlled Trial. Dutch Foot and Ankle Society Meeting [invited lecture], Online, Microsoft Teams.	2020	0.5

Oral presentations including teaching activities	Year	ECTS
Talar OsteoPeriostic Grafting from the Iliac Crest; First Results. Webinar organized by Dr. F.G. Usuelli [invited lecture], Online, Microsoft Teams.	2020	0.5
Osteochondral Defects of the Talus: Radiology and Surgical Treatment. Education 3rd year medical students, University of Amsterdam [invited lecture], Online, Microsoft Teams.	2020	0.5
Cartilage Damage in the Ankle. Webinar VCMS (Vereniging Chirurgie voor Medisch Studenten) Education Day [invited lecture], Online, Microsoft Teams.	2021	0.5
Cartilage Damage in the Ankle. Webinar International Foot & Club, Academic Foot and Ankle Society, AMFAS Thailand. Theme: Treatments of Sport Injury in Foot and Ankle [invited lecture], Online, Microsoft Teams.	2021	0.5
Cartilage Damage in the Ankle. Webinar Amsterdam Bone Center [invited lecture], Amsterdam, the Netherlands.	2021	0.5
Cartilage Damage in the Ankle in Isolated Syndesmotic Injury: A Meta-Analysis. Friday Lecture Series, Amsterdam, the Netherlands.	2021	0.5
Cartilage Damage in the Ankle in Isolated Syndesmotic Injury and in Chronic Ankle Instability: A Meta-Analysis. NOV Najaarscongres [invited lecture], Den Bosch, the Netherlands.	2021	0.5
Osteochondral Defects of the Talus: Radiology and Surgical Treatment. Education 3rd year medical students, University of Amsterdam [invited lecture], Amsterdam, the Netherlands.	2022	0.5
Traumatic Sports Injuries of the Knee. Education 3rd year medical students, Vrije Universiteit Amsterdam [invited lecture], Amsterdam, the Netherlands.	2022	0.5
Traumatic Sports Injuries of the Ankle. Education 3rd year medical students, Vrije Universiteit Amsterdam [invited lecture], Amsterdam, the Netherlands.	2022	0.5
Clinical Outcomes after TOPIC Surgery. Friday Lecture Series, Amsterdam, the Netherlands.	2022	0.5
Clinical Outcomes after a Biological Resurfacing Arthroplasty. Friday Lecture Series, Amsterdam, the Netherlands.	2022	0.5
Talar OsteoPeriostic Grafting from the Iliac Crest. ESSKA Congress, Paris, France.	2022	0.5
Social Media Web-Editors Presentation: JEO & KSSTA Perspective. ESSKA Congress [invited talk], Paris, France.	2022	0.5
The Evidence Around the Usage of Biologicals for Cartilage Damage of the Ankle. Dutch Arthroscopy Society, Yearly Scientific Congress [invited lecture], Apeldoorn, the Netherlands.	2022	0.5

Oral presentations including teaching activities	Year	ECTS
Return to Sports Outcomes after Treatment for Cartilage Damage of the Ankle. AGA Kongress [invited lecture], Vienna, Austria. Regeneration or Repairing for Cartilage Lesions of the Ankle? Foot and Ankle Academy [invited lecture], Milan, Italy.	2022	0.5
TOPIC Outcomes. SEOHS, Amsterdam, the Netherlands.	2022	0.5
What We Know About Cartilage. Prevention in Sports Symposium [invited lecture], Amsterdam, the Netherlands.	2022	0.5
Amsterdam Ankle Cartilage Treatment Algorithm. Dutch Foot and Ankle Society Symposium [invited speaker lecture], Utrecht, the Netherlands.	2022	0.5
Amsterdam Ankle Cartilage Cascade. AMS Conference, Amsterdam, the Netherlands.	2022	0.5
Return to Sports After the TOPIC Procedure. ISAKOS Conference, Boston, United States.	2023	0.5
2-Year Clinical Outcomes After the TOPIC Procedure. ISAKOS Conference, Boston, United States.	2023	0.5
Second-Look Arthroscopy After Surgical Treatment for Osteochondral Lesions of the Ankle. ISAKOS Conference, Boston, United States.	2023	0.5
Cartilage Injuries in Ankle Instability: What are the Facts? ISAKOS Conference [invited speaker lecture], Boston, United States.	2023	0.5
Individualized Treatment of Cartilage Injuries of the Ankle. ACHSS Annual Scientific Day [invited speaker lecture], Amsterdam, the Netherlands.	2023	0.5
Padel-Related Injuries: Where in the Court Do We Stand? Monthly Scientific Meeting, UMC Utrecht, Sports Medicine, Rehabilitation and Physiotherapy Department [invited speaker lecture], Utrecht, the Netherlands.	2023	0.5
TOPIC Procedure. Webinar International Foot & Club, Academic Foot and Ankle Society, AMFAS Thailand. Theme: Treatments of Sport Injury in Foot and Ankle [invited lecture], Online, Microsoft Teams.	2023	0.5
Unstable Cartilage Lesions. ESSKA Specialty Days, AFAS Delegates, Potpourri [invited lecture], Warsaw, Poland.	2023	0.5
Talar OsteoPeriostic Grafting from the Iliac Crest (TOPIC): 2-Year Results of a Novel Press-Fit Surgical Treatment for Large Talar Osteochondral Lesions. 21st ESSKA Congress, Foot & Ankle - Cartilage Session [accepted oral], Milan, Italy.	2024	0.5

Oral presentations including teaching activities	Year	ECTS
Talar OsteoPeriostic Grafting from the Iliac Crest (TOPIC): 2-Year Results of a Novel Press-Fit Surgical Treatment for Large Talar Osteochondral Lesions. NOF Congress Rotterdam, Abstract Session Ankle/Foot [accepted oral], Rotterdam, the Netherlands.	2024	0.5
10-Year Survival Rate of 82% Following 262 Cases of Arthroscopic Bone Marrow Stimulation for Osteochondral Lesions of the Talus. NOF Congress Rotterdam, Abstract Session Ankle/Foot [accepted oral], Rotterdam, the Netherlands.	2024	0.5
Cyst Occurrence After Osteochondral/Periosteal Autografting and Allografting for Osteochondral Lesions of the Talus: A Systematic Review & Meta-Analysis. NOF Congress Rotterdam, Abstract Session Ankle/Foot [accepted oral], Rotterdam, the Netherlands.	2024	0.5
Return to Sports after Talar OsteoPeriostic grafting from the Iliac Crest (TOPIC). ICCRA 2025, Abstract Session [accepted oral], 3 April 2025, New York, United States of America	2025	0.5
Return to Desired Level of Sports after Talar OsteoPeriostic grafting from the Iliac Crest (TOPIC). Madrid Isokinetic 2025, Abstract Session [accepted oral], 4th of May 2025, Madrid, Spain	2025	0.5
Prediction of Treatment Success for Ankle Osteochondral Lesions. The process of the Development of an AI-integrated Personalized Treatment Algorithm. IOC Research Meeting, OSTRC 2025, Abstract Session [accepted oral], 14th of May 2025, Svolvaer, Norway	2025	0.5
Faculty & Chair Scientific Ankle Paper Session ISAKOS Congress Munich. ISAKOS Conference, June 6 2025, Munich, Germany	2025	0.5
Cross-continental treatment of Ankle OCLs: Cost-Effective Treatment Algorithm. ISAKOS Conference, June 6 2025, Munich, Germany	2025	0.5

Poster presentations	Year	ECTS
Good Results After Subtalar Arthroscopies: A Retrospective Case Series. Nederlandse Vereniging voor Arthroscopie (NVA): Jaarcongres, Nieuwegein 2019.	2019	0.5
Good Results After Endoscopic Calcaneoplasty: A Retrospective Case Series. Nederlandse Vereniging voor Arthroscopie (NVA): Jaarcongres, Nieuwegein 2019.	2019	0.5

Book chapters & publications
Book chapters 1: **Dahmen J**, Altink JN, Relingh ML, Kerkhoffs GMMJ. Lift, Drill, Fill, and Fix (LDFF): A New Arthroscopic Treatment for Talar Osteochondral Defects. Book: Sports Injuries of the Foot and Ankle. Editors: Canata, D'Hooghe, Hunt, Kerkhoffs, Giuseppe Longo. Year: 2019.

Book chapters & publications

2: Altink JN, **Dahmen J**, Vuurberg G, Kerkhoffs GMMJ. Outcome.
Book: Sports Injuries of the Foot and Ankle. Editors: Canata, D'Hooghe, Hunt, Kerkhoffs, Giuseppe Longo. Year: 2019.

3: Altink JN, **Dahmen J**, Kerkhoffs GMMJ. Outcomes Assessment for the Athlete.
Book: Sports Injuries of the Foot and Ankle. Editors: Canata, D'Hooghe, Hunt, Kerkhoffs, Giuseppe Longo. Year: 2019.

4: **Dahmen J**, Lambers KTA, Reilingh ML, Kerkhoffs GMMJ. Minimally Invasive Management of Osteochondral Defects to the Talus
Book: Sports Injuries of the Foot and Ankle. Editors: Canata, D'Hooghe, Hunt, Kerkhoffs, Giuseppe Longo. Year: 2019.

5: **Dahmen J**, Rikken QGH, Stufkens SAS, Kerkhoffs GMMJ. Return to Performance After Surgical Repair of a Massive Osteochondral Lesion of the Talus in an Upcoming Elite Young Elite Football Player: Is It Possible?
Book: ICRS Newsletter Winter 2020. Editors: N.A. Year: 2020.

6: Baur OLG, **Dahmen J**, Kerkhoffs GMMJ, Maas M. Ankle and Foot: Osteochondral Injuries.
Book: Imaging of Orthopedic Sports Injuries. Editors: Vanhoenacker, Maas, Gielen. Year: 2021.

7: Rikken QGH, **Dahmen J**, Altink JN, Canata GL, D'Hooghe P, Kerkhoffs GMMJ. Osteochondral Lesions of the Ankle: An Evidence-Based Approach for Track and Field Athletes.
Book: Management of Track and Field Injuries. Editors: Canata, D'Hooghe, Hunt, Kerkhoffs, Longo. Year: 2021.

8: van Dijk PAD, Franca G, **Dahmen J**, Kerkhoffs GMMJ, D'Hooghe P, Karlsson J. Achilles Tendon, Calf, and Peroneal Tendon Injuries.
Book: Management of Track and Field Injuries. Editors: Canata, D'Hooghe, Hunt, Kerkhoffs, Longo. Year: 2021.

9: Altink JN, Paget LDA, Blom RP, **Dahmen J**, Dalmau-Pastor M, Kerkhoffs GMMJ. Ankle Sprains and Instability.
Book: Management of Track and Field Injuries. Editors: Canata, D'Hooghe, Hunt, Kerkhoffs, Longo. Year: 2021.

10: Caravelli S, Massimi S, Baltes TPA, **Dahmen J**, D'Hooghe P, Kerkhoffs GMMJ. Foot and Ankle Stress Fractures in Athletics.
Book: Management of Track and Field Injuries. Editors: Canata, D'Hooghe, Hunt, Kerkhoffs, Longo. Year: 2021.

11: **Dahmen J**. Padel: De Sportevolutie van de 21e Eeuw
https://www.sportzorg.nl/sport-bewegen/sport-overzicht/padel. Year 2023.

12: Hollander JJ, **Dahmen J**, Stufkens SAS, Kerkhoffs GMMJ. Foot Stress Fractures
Book: Sports Injuries. Editors: Nedim Doral, Karlsson. Year: 2024

13: Walinga AB, ter Laak Bolk S, Janssen SJ, **Dahmen J**. Proximal Tibiofibular Joint Injury
Book: Orthopaedic Sports Medicine. Editors: Espregueira-Mendes, Karlsson, Musahl, Ayeni. Year: 2024.

Book chapters & publications

Publications (PubMed-Indexed)

1: **Dahmen J**, Lambers KTA, Reilingh ML, van Bergen CJA, Stufkens SAS, Kerkhoffs GMMJ. No superior treatment for primary osteochondral defects of the talus. Knee Surg Sports Traumatol Arthrosc. 2018 Jul;26(7):2142-2157. doi: 10.1007/s00167-017-4616-5.

2: Lambers KTA, **Dahmen J**, Reilingh ML, van Bergen CJA, Stufkens SAS, Kerkhoffs GMMJ. No superior surgical treatment for secondary osteochondral defects of the talus. Knee Surg Sports Traumatol Arthrosc. 2018 Jul;26(7):2158-2170. doi:10.1007/s00167-017-4629-0.

3: Reilingh ML, Lambers KTA, **Dahmen J**, Opdam KTM, Kerkhoffs GMMJ. The subchondral bone healing after fixation of an osteochondral talar defect is superior in comparison with microfracture. Knee Surg Sports Traumatol Arthrosc. 2018 Jul;26(7):2177-2182. doi: 10.1007/s00167-017-4654-z.

4: **Dahmen J**, Lambers KTA, Reilingh ML, van Bergen CJA, Stufkens SAS, Kerkhoffs GMMJ. Reply to the letter to the editor: comment on "No superior treatment for primary osteochondral defects of the talus". Knee Surg Sports Traumatol Arthrosc. 2017 Dec;25(12):3984-3986. doi: 10.1007/s00167-017-4715-3.

5: van Bergen CJA, Baur OL, Murawski CD, Spennacchio P, Carreira DS, Kearns SR, Mitchell AW, Pereira H, Pearce CJ, Calder JDF; **International Consensus Group on Cartilage Repair of the Ankle**. Diagnosis: History, Physical Examination, Imaging, and Arthroscopy: Proceedings of the International Consensus Meeting on Cartilage Repair of the Ankle. Foot Ankle Int. 2018 Jul;39(1_suppl):3S-8S. doi: 10.1177/1071100718779393.

6: Hannon CP, Bayer S, Murawski CD, Canata GL, Clanton TO, Haverkamp D, Lee JW, O'Malley MJ, Yinghui H, Stone JW; **International Consensus Group on Cartilage Repair of the Ankle**. Debridement, Curettage, and Bone Marrow Stimulation: Proceedings of the International Consensus Meeting on Cartilage Repair of the Ankle. Foot Ankle Int. 2018 Jul;39(1_suppl):16S-22S. doi: 10.1177/1071100718779392.

7: Smyth NA, Murawski CD, Adams SB Jr, Berlet GC, Buda R, Labib SA, Nunley JA 2nd, Raikin SM; **International Consensus Group on Cartilage Repair of the Ankle**. Osteochondral Allograft: Proceedings of the International Consensus Meeting on Cartilage Repair of the Ankle. Foot Ankle Int. 2018 Jul;39(1_suppl):35S-40S. doi: 10.1177/1071100718781097.

8: Hurley ET, Murawski CD, Paul J, Marangon A, Prado MP, Xu X, Hangody L, Kennedy JG; **International Consensus Group on Cartilage Repair of the Ankle**. Osteochondral Autograft: Proceedings of the International Consensus Meeting on Cartilage Repair of the Ankle. Foot Ankle Int. 2018 Jul;39(1_suppl):28S-34S. doi: 10.1177/1071100718781098.

9: Reilingh ML, Murawski CD, DiGiovanni CW, **Dahmen J**, Ferrao PNF, Lambers KTA, Ling JS, Tanaka Y, Kerkhoffs GMMJ; International Consensus Group on Cartilage Repair of the Ankle. Fixation Techniques: Proceedings of the International Consensus Meeting on Cartilage Repair of the Ankle. Foot Ankle Int. 2018 Jul;39(1_suppl):23S-27S. doi: 10.1177/1071100718781096.

10: Shimozono Y, Brown AJ, Batista JP, Murawski CD, Gomaa M, Kong SW, Vaseenon T, Takao M, Glazebrook M; **International Consensus Group on Cartilage Repair of the Ankle**. Subchondral Pathology: Proceedings of the International Consensus Meeting on Cartilage Repair of the Ankle. Foot Ankle Int. 2018 Jul;39(1_suppl):48S-53S. doi: 10.1177/1071100718781866.

Book chapters & publications

11: Rothrauff BB, Murawski CD, Angthong C, Becher C, Nehrer S, Niemeyer P, Sullivan M, Valderrabano V, Walther M, Ferkel RD; **International Consensus Group on Cartilage Repair of the Ankle**. Scaffold-Based Therapies: Proceedings of the International Consensus Meeting on Cartilage Repair of the Ankle. Foot Ankle Int. 2018 Jul;39(1_suppl):41S-47S. doi: 10.1177/1071100718781864.

12: D'Hooghe P, Murawski CD, Boakye LAT, Osei-Hwedieh DO, Drakos MC, Hertel J, Lee KB, Popchak A, Wiewiorski M, van Dijk CN; **International Consensus Group on Cartilage Repair of the Ankle**. Rehabilitation and Return to Sports: Proceedings of the International Consensus Meeting on Cartilage Repair of the Ankle. Foot Ankle Int. 2018 Jul;39(1_suppl):61S-67S. doi: 10.1177/1071100718781862.

13: Dombrowski ME, Yasui Y, Murawski CD, Fortier LA, Giza E, Haleem AM, Hamid K, Tuan R, Zhang Z, Schon LC, Hogan MV; **International Consensus Group on Cartilage Repair of the Ankle**. Conservative Management and Biological Treatment Strategies: Proceedings of the International Consensus Meeting on Cartilage Repair of the Ankle. Foot Ankle Int. 2018 Jul;39(1_suppl):9S-15S. doi: 10.1177/1071100718779390.

14: Mittwede PN, Murawski CD, Ackermann J, Görtz S, Hintermann B, Kim HJ, Thordarson DB, Vannini F, Younger ASE; **International Consensus Group on Cartilage Repair of the Ankle**. Revision and Salvage Management: Proceedings of the International Consensus Meeting on Cartilage Repair of the Ankle. Foot Ankle Int. 2018 Jul;39(1_suppl):54S-60S. doi: 10.1177/1071100718781863.

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102: Emanuel KS, **Dahmen J**, Sierevelt IN, Brittberg M, Kerkhoffs GMMJ. Regression to the Mean: Statistical Bias Can Mislead Interpretation in Cartilage and Osteoarthritis Clinics and Research. Cartilage. 2024 Nov 11:19476035241293048. doi: 10.1177/19476035241293048.

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105: Rikken QGH, **Dahmen J**, Stufkens SAS, Nakasa T, Kerkhoffs GMMJ. Fix while you can: A systematic review on outcomes of fixation for osteochondral lesions of the talus. JISAKOS. 2024. doi: https://doi.org/10.1016/j.jisako.2025.100389. Online ahead of print.

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111: Buck TMF, Steman JAH, **Dahmen J**, Rikken QGH, Sierevelt IN, Stufkens SAS, Kerkhoffs GMMJ. Nonoperative Treatment for Osteochondral Lesions of the Talus Provides Clinical Improvement in the Minority of the Patients at Short-term Follow-up. Foot Ankle Int. 2025 Apr 22:10711007251330881. doi: 10.1177/10711007251330881. Online ahead of print.

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113: **Dahmen J**, Kok LM. A Conserve or Reverse? Fractured Decisions! J Shoulder Elbow Surg. 2025 Apr 28:S1058-2746(25)00341-6. doi: 10.1016/j.jse.2025.03.018. Online ahead of print.

114: Buck TMF, Smithuis FF, Steman JAH, van Bergen CJA, Hemke R, **Dahmen J**, Terra M, Maas M, Kerkhoffs GMMJ, Struijs PAA. Casting and supervised rehabilitation versus supervised neglect in skeletally immature patients with osteochondral lesions of the talus: A Protocol for A Cohort Study. BMC Musculoskelet Disord. 2025 May 15;26(1):481. doi: 10.1186/s12891-025-08646-4.

115: Milking the Benefits: Can Bovine Milk Accelerate Bone Healing?: Commentary on an article by Faezeh Gouhari, MSc, et al.: "Therapeutic Effects of Bovine Colostrum on Bone Healing, Rehabilitation, and Postoperative Complications. A Prospective, Randomized, Double-Blinded Comparative Trial". **Dahmen J**, Kerkhoffs GMMJ.J Bone Joint Surg Am. 2025 Jun 18;107(12):e64. doi: 10.2106/JBJS.25.00009.

116: **Dahmen J**, Geurts E, Rikken QGH, Stufkens SAS, Kerkhoffs GMMJ. Eight out of Ten Patients Participate at Their Desired Level of Sports After Talar OsteoPeriostic grafting from the Iliac Crest for Large, Complex Osteochondral Lesions of the Talus. American Journal of Sports Medicine. 2025. Submitted.

117: ter Laak Bolk CS, Hollander JJ, Ramsodit KR, Rikken QGH, **Dahmen J**, Stufkens SAS, Kerkhoffs GMMJ. 64% of elite athletes return to performance after treatment of symptomatic osteochondral lesions of the ankle. American Journal of Sports Medicine. 2025. Submitted.

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120: Rikken QGH, **Dahmen J**, Hollander JJ, Steman JAH, Stufkens SAS, Kerkhoffs GMMJ. Non-primary arthroscopic bone marrow stimulation for osteochondral lesions of the talus yields limited improvements in patient reported outcomes compared to primary cases: a prospective 2-year follow-up study. Cartilage. 2025. Submitted.

121: Kerkhoffs GMMJ, Kennedy JG, Brittberg M, **Dahmen J**. Cartilage Injuries of the Ankle: New Beginnings. OOTR. 2025. Submitted.

122: Rikken QGH, Hollander JJ, **Dahmen J**, Stufkens SAS, Kerkhoffs GMMJ. Osteotomy and bone grafting for osteochondral lesions of the tibial plafond: surgical technique. OJSM. 2025. Submitted.

123: Rikken QGH, **Dahmen J**, Lambers KTA, Emanuel KS, Stufkens SAS, Kerkhoffs GMMJ, on behalf of the Amsterdam Ankle Cartilage Team. Open Lift, Drill, Fill and Fix (LDFF) for chronic osteochondral lesions of the talus: excellent two-year prospective clinical outcomes. AJSM. 2024. Submitted.

124: Steman JAH, Buck TMF, **Dahmen J**, Struijs PAA, van Bergen CJA, Stufkens SAS, Kerkhoffs GMMJ. Outcomes after initial non-operative treatment of osteochondral lesions of the talus in skeletally immature patients. Cartilage. 2025. Submitted.

125: **Dahmen J**, Paget LDA, Smithuis FF, Kerkhoffs GMMJ, Stufkens SAS, Verhagen RAW. [The typical and not so typical ankle sprain]. Nederlands Tijdschrift voor Geneeskunde. 2025. Submitted.

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126: Hollander JJ, **Dahmen J**, Stufkens SAS, Kerkhoffs GMMJ. Talar OsteoPeriostic Grafting from the Iliac Crest (TOPIC): 5 year clinical and radiological outcome. Journal of Bone and Joint Surgery. 2025. Submitted.

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129: Smeitink N, Schroder FF, Dorrestijn O, Spekenbrink-Spooren A, **Dahmen J**, van Noort A, van den Bekerom MPJ, Veen EJD. Revision After Anatomical Shoulder Arthroplasty: Influence of Age and Prior Surgery: Results from A Nationwide Large Registry Study. Journal of Bone and Joint Surgery. 2025. Submitted.

Articles (Non-PubMed-Indexed peer-reviewed)
1: Buck TMF, Rikken QGH, Altink JN, **Dahmen J**, Stufkens SAS, Kerkhoffs GMMJ. An Individualized and Evidence-Based Approach to Osteochondral Lesions of the Talus: In-Depth Focus on the Talar OsteoPeriostic grafting from the Iliac Crest (TOPIC) Technique. Minerva Ortopedica e Traumatologica. 2021 Jul;72(6):552-63. doi: 10.23736/S2784-8469.21.04065-7.

2: Rikken QGH, **Dahmen J**, Kerkhoffs GMMJ, Stufkens SAS. Unorganized Fibrocartilage and Osseous Proliferation after Bone Marrow Stimulation for an Osteochondral Lesion of the Talus. Journal of Cartilage & Joint Preservation. 2021 Dec;1(4): online. doi: 10.1016/j.jcjp.2021.100031.

Other	Year	ECTS
Journal club	2020–2023	3.0

2. Teaching

Tutoring, mentoring, co-supervising	Year	ECTS
Carlijn Ter Laak Bolk. Lisfranc Injuries and Return to Sports (BSc Medicine)	2017	1.0
Jason Steman. Osteochondral Defects and Return to Sports (BSc Medicine)	2017	1.0
Mats Teeken. Osteochondral Defects in Children (BSc Medicine)	2017	1.0
Aureline Boot. Osteochondral Defects and Lateral Ankle Instability (BSc Medicine)	2017	1.0
Koen Plug. Return to Sports in Ankle Fractures (BSc Medicine)	2017	1.0
Pascal van Diepen. 9-Grid Scheme Talar OCDs (BSc Medicine)	2018	1.0
Lisanne Brandsma. RTS TOPIC (MSc Medicine)	2018	2.0
Hugo Martijn. Incidence of Osteochondral Defects in Ankle Fractures (residency)	2019	2.0
Julian Hollander. MTV Stress Fractures (miscellaneous)	2019	2.0
Julian Hollander. Talocalcaneal and Calcaneonavicular Coalitions (miscellaneous)	2019	2.0
Quinten Dusoswa. Talocalcaneal and Calcaneonavicular Coalitions (residency)	2019	2.0
Quinten Rikken. MTV Acute Fractures (BSc Medicine)	2019	1.0
Kenny Lauf. Sinus Tarsi Syndrome & Conservative OCD Treatment (miscellaneous)	2019	2.0
Bas Louis. Distraction Therapy in Ankle OA (BSc Medicine)	2019	1.0
Eva van der Loos. Fixation for Osteochondral Lesions of the Talus (BSc Medicine)	2020	1.0
Sohaib Jaddi. Incidence of Associated Injuries in Isolated Syndesmotic Injuries (BSc Medicine)	2020	1.0
Jelmer Vreeken. Second-Look Arthroscopies (BSc Medicine)	2020	1.0
Dave de Keijzer. Prognostic Factors Determining Clinical Outcomes after Bone Marrow Stimulation and Osteochondral Autograft Transfer Systems for Osteochondral Lesions of the Ankle (BSc Medicine)	2020	1.0
Omar Soussa. Prognostic Factors Determining Clinical Outcomes after Bone Marrow Stimulation and Osteochondral Autograft Transfer Systems for Osteochondral Lesions of the Ankle (BSc Medicine)	2020	1.0
Joris Hendriks. Quality of Life and Satisfaction after Treatment of Osteochondral Defects in the Ankle (BSc Medicine)	2020	1.0
Emma Wijnhoud. CLAI and Incidence of Cartilage Lesions in the Ankle (BSc Medicine)	2021	1.0
Tim Bolk. Prognostic Factors Determining Clinical Outcomes after Arthroscopic Bone Marrow Stimulation for Osteochondral Lesions of the Talus (BSc Medicine)	2021	1.0
Elmer Petersson. Metatarsal V Fractures: Return to Sports (BSc Medicine)	2021	1.0
Sukhraj Singh. Sinus Tarsi Syndrome; Systematic Review (BSc Medicine)	2021	1.0
Carlijn Ter Laak Bolk. Return to Performance in Elite Athletes with Osteochondral Injuries of the Talus (MSc Medicine)	2021	2.0
Elze Geurts. Return to Performance in Elite Athletes with Osteochondral Injuries of the Talus (MSc Medicine)	2021	2.0
Lisanne Wolsink. Bilateral Osteochondral Lesions of the Ankle (MSc Medicine)	2021	2.0
Julian Hollander. Distraction Therapy for End-Stage Ankle Osteoarthritis (BSc Medicine)	2021	1.0
Pascal van Diepen. Localization and Size Measurement in Osteochondral Lesions of the Talus (MSc Medicine)	2021	1.0
Jason Steman. Osteochondral Defects and Outcomes in Children (MSc Medicine)	2021	2.0
Margot Aalders. Long-Term Survival of Arthroscopic Bone Marrow Stimulation for Osteochondral Lesions of the Talus (MSc Medicine)	2022	2.0
Daniek Raben. Prognostic Factors in Return to Sports after Surgical Treatment for Cartilage Lesions of the Ankle (BSc Physiotherapy)	2022	1.5
Megan Ooms. Prognostic Factors in Return to Sports after Surgical Treatment for Cartilage Lesions of the Ankle (BSc Physiotherapy)	2022	1.5
Chiel Klein. The Added Value of Bone Marrow Aspirate Concentrate in Treatment of Local Cartilage Damage in the Ankle (BSc Medicine)	2022	1.0

Tutoring, mentoring, co-supervising	Year	ECTS
Alexander Soethout. The Outcomes of Fixation of Osteochondral Lesions of the Knee (MSc Medicine)	2022	2.0
Myriam le Cosquino de Bussy. Surface Congruency of Osteochondral Autografts and Allografts in Treating Cartilage Lesions of the Knee (BSc Medicine)	2022	1.0
Filipe Sa Malheiro. Return to Sport Criteria Following Surgical Management of Osteochondral Lesions of the Ankle (miscellaneous)	2022	2.0
Indy Bernardy. Osteo-Arthritis Development after the Treatment and Presence of Osteochondral Lesions of the Ankle (BSc Medicine)	2023	1.0
Sophia van Beelen: automated curvature matching crista iliaca – talar dome, Master thesis medicine (MSc Medicine)	2024	2.0
Jasper Tiemersma: Incidence of OA after conservative and surgical treatment of osteochondral lesions of the talus (BSc Medicine)	2025	1.0
Berend Verbrugge: Incidence of OA after conservative and surgical treatment of osteochondral lesions of the knee (BSc Medicine)	2025	1.0

Other PhD-related activities	Year	ECTS
Peer reviewer, editorial board member, (past) web-editor, (past) associate editor, current deputy Editor-in-Chief, guest-editor different orthopedic-related PubMed-indexed journals	2016 – now	N.A.
Podcaster ON Foundation	2023 – now	N.A.
Member of the Expert Team, Orthoregeneration Network Foundation	2022 – now	N.A.
Elite Reviewer Journal of Bone and Joint Surgery	2022 – now	N.A.
Independent External Referent, ZonMW	2022 – now	N.A.
Osteoarthritis Review of the Dutch Arthritis Society / ReumaNederland	2020 – now	N.A.
Member International consensus group on cartilage repair of the ankle (ICCRA)	2018 – now	N.A.
Board Member Amsterdam Bone Center	2021 – 2023	N.A.
Organization Committee Prevention in Sports Symposium	2022	N.A.
Lecture for department nurses at the Orthopedic Surgery Ward: In-house treatment of cartilage injuries of the ankle	2021 + 2022	N.A.
Co-organization live surgery bachelor medicine	2021 + 2022	N.A.
Visiting Research Fellow, Humanitas San Pio X	2020	N.A.
Editorial Work for the ISAKOS Leg and Foot Committee: Track and Field Book	2020	N.A.
Acquisition Committee Traumaplatform Team, Davos Challenge	2017 – 2018	N.A.

3. Parameters of esteem

Grants and awards/prizes	Year
Recipient for ISAKOS 2023 Congress Scholarship Awarded by the Young Professionals Task Force	2023
Team member for successfully applying for the Accredited International ESSKA Teaching Centre	2022
Team member for successfully applying for the International Centre of Excellence for Treatment of Cartilage Lesions of the Ankle (International Cartilage Regeneration & Joint Preservation Society, ICRS	2022
Team member for successfully applying for the ISAKOS Approved Teaching Center	2022
Amsterdam Movement Sciences International Collaboration Grant	2022
Amsterdam Movement Sciences Kick Starter Grant Supporting Submission Team	2022
ON Grant for Biological Additions to Ankle Cartilage Treatment	2022
Amsterdam Movement Sciences Supporting Submission Team	2021
ON/ESSKA Literature Grant Talus: Return to Sports	2020
ESSKA AFAS Prof. Pau Golano Travelling Fellowship	2020
AMC PhD Scholarship	2020
Reviewer of the Year Award Knee Surgery, Sports Traumatolgy, Arthroscopy Journal (KSSTA)	2018
European Orthopaedic Research Society (EORS) Travel Award Winner	2018
Top reviewer ESSKA Glasgow	2018
Van Walree Fonds Winner, Travelling Grant	2018
Team member for successfully applying to the Expertise Center for the Amsterdam UMC for the treatment of osteochondral defects in the ankle	2018

About the author

Jari Dahmen was born on the 23rd of June, 1995, in Amsterdam, the Netherlands, as the second son of Edith and Rutger. Jari enjoyed growing up in Amsterdam alongside his two brothers, Cas and Hanno. After graduating from high school at the St. Ignatiusgymnasium in Amsterdam, he studied Liberal Arts & Sciences at the Amsterdam University College (AUC). As part of his studies at AUC, he spent half a year on an exchange programme at the Simon Fraser University in Vancouver, Canada. During his time at AUC, Jari enjoyed a broad multidisciplinary education, during which he was able to do two internships at the Department of Orthopedic Surgery at the Amsterdam Medical Centre (AMC), under the guidance of Prof. Gino Kerkhoffs. These internships inspired him to become a medical doctor through the graduate entry medicine program at the University of Leiden. Alongside his studies, Jari began a PhD under the supervision of Prof. Gino Kerkhoffs and Dr. Sjoerd Stufkens. In 2020 Jari graduated as a medical doctor and worked as a PhD student in a combined clinician-researcher role at the Department of Orthopedic Surgery and Sports Medicine of the Amsterdam University Medical Centers. Following this, he worked as a resident not-in-training at the Department of Orthopedic Surgery of the Flevoziekenhuis under the supervision of Dr. Rover Krips, and hereafter at the Department of Orthopedic Surgery at Tergooi Medical Center under the supervision of Dr. Ronald Verhagen. As of 2026, he will start his training to become an orthopedic surgeon. Jari happily lives in the vibrant “Amsterdam-East” together with his fiancée Janneke van Oosterhout.

Dankwoord

Allereerst met alle discretie een diepgaande dank aan alle **patiënten** die hebben meegedaan en meegewerkt aan het onderzoek – jullie zijn dé inspiratiebron voor klinisch relevant en toepasbaar wetenschappelijk onderzoek.

Promotor prof. Gino Kerkhoffs, Gino. Waar te beginnen? Meer dan een decennium geleden mocht ik bij jou een klinische stage doen als deel van mijn opleiding aan het Amsterdam University College (AUC). Jouw oprechte interesse voor de mens achter de persoon voelde gelijk goed. Het is buitengewoon knap en bewonderenswaardig hoe jij jouw team als coach weet te motiveren en te inspireren. Alhoewel de onderzoeksmeetings vaak over andere dingen dan onderzoek gaan, komen mijn collega's en ik altijd met een nieuwe drive en frisse energie weer uit jouw kantoor. Als coach-speler heb jij een duidelijke visie voor de toekomst, die de strategie uitzet en wanneer nodig ook de nr. 10 positie kan bespelen om een bal diep te geven, of soms even een balletje terug. Ik voel me vereerd je als orthopaedische vader te mogen beschouwen. Bedankt voor alle kansen, de begeleiding, het altijd waardevolle advies, en bovenal voor jouw mentor- en leiderschap. Cheers & chinchincheerio op onze samenwerking en vriendschap. PS: zullen we de Early Morning Meetings om 5:00 AM doen?

Co-promotor dr. Sjoerd Stufkens, Sjoerd. Allereerst bedankt voor jouw onvoorwaardelijke steun voor mij als clinicus en als wetenschapper. De vriendschap en vertrouwensband die we hebben voelt natuurlijk en dat is iets wat ik koester. Over de jaren heen heb ik jou op vele OK- en poli-dagen mogen schaduwen, en ik ben zo blij en dankbaar dat ik hiertoe de kans heb gekregen. Jouw droge humor werkt aanstekelijk, en ik zal de dinsdagen op het dagcentrum niet snel vergeten. Ik heb enorm veel geleerd van jouw chirurgische skills en jouw analytische denkvermogen. Een hele OK-dag in het Fries praten met Pieter kan ook vandaag nog zomaar een slappe lach doen opwekken – waarschijnlijk klopte er geen snars van wat we zeiden...

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vanaf day 1. Je begon in Boston als gezamenlijke wetenschappelijk stagestudent van Noortje en mij, en nu een échte maat. Ik denk dat ik met jou meer de wereld heb bereisd dan met Janneke, met een bezoekje aan de Tiergarten in Berlijn en Upstate New York als hoogtepunten... Binnenkort weer een congrestour doen?

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