Awareness and Treatment of Talar Osteochondral Lesions after Ankle Injuries

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PART I
INTRODUCTION

1 General introduction

PROBLEM STATEMENT – THE OSTEOCHONDRAL LESION

An osteochondral lesion can be present in any joint but in practice the knee, the ankle and the elbow are most frequently involved[312]. An osteochondral lesion is defined by damage to the articular cartilage in combination with the underlying subchondral bone. These lesions can occur at every age but are often seen in the young and active population. In this thesis there will be a focus on osteochondral lesions of the talus (OCLT)[125, 289]. It is frequently described as an uncommon diagnosis, however, exact incidence rates are unclear. A retrospective study however among military personnel estimated an incidence of 27 OCLTs per 100.000 persons[199]. These lesions can have a great impact on the quality of life of active patients since complaints especially intensify during sports and weight bearing activities[64, 81, 116, 125]. They cause impairment because of deep joint pain with major limitations for the patient[125, 289].

Some patients present with an OCLT without any known history of ankle trauma and it is thought that ischemia, subsequent necrosis and genetics are etiological factors in the origin of these lesions[232]. However, it is widely accepted that an ankle trauma is the most important etiological factor of an OCLT[83, 125, 289, 299]. Trauma can cause an acute lesion by a single event or the lesion can originate over the course of time. It can arise after a series of less intense traumas causing micro damage resulting in macroscopic failure of the cartilage with subsequent damage of the subchondral bone[289]. A lesion can heal spontaneously and remain asymptomatic or it can progress and form subchondral cysts. This subsequently can give typical remaining deep ankle pain during weight bearing[79, 104, 236, 289]. These different origins and presentations of lesions should be considered when choosing the optimal treatment type. Numerous types of surgical treatment strategies exist but there is no clear consensus as to which surgical intervention is considered preferable for which type of lesion.

The **general aim of this thesis** is to evaluate the incidence of traumatic OCLTs and to review respective treatment options for OCLTs.

THE OSTEOCHONDRAL LESION - WHAT TYPES ARE THERE?

There are several descriptive terms being used for this kind of pathology. Next to osteochondral lesion other used terms are osteochondritis dissecans, osteochondral defect (OCD), osteochondral fracture, transchondral fracture or flake fracture. In some terms it says itself if the lesion is more acute or chronic by nature but this sometimes can be unclear. Some use the term lesion for the acute acquired osteochondral damage whereas the term defect might be used to describe the more chronic types. Nowadays there is a trend towards using the term osteochondral lesion as an overarching term in the recent literature[125, 286]. The use of different terms can be somewhat confusing but in essence these acute or chronic type lesions share a lot of similarities. For the acute lesions it is clear that the origin is of traumatic nature. But for the chronic late presenting osteochondral defects it is nowadays widely accepted that the most important etiological factor also is a prior ankle trauma[289]. Both type of lesions can be classified according to the most used system of Berndt and Harty[24]. This classification system later got the addition of Loomer who added the presence of cysts with it, which is per definition a chronic type since these cysts are characteristic for longer existing damage to the subchondral plate (Figure 1.)[104, 157].

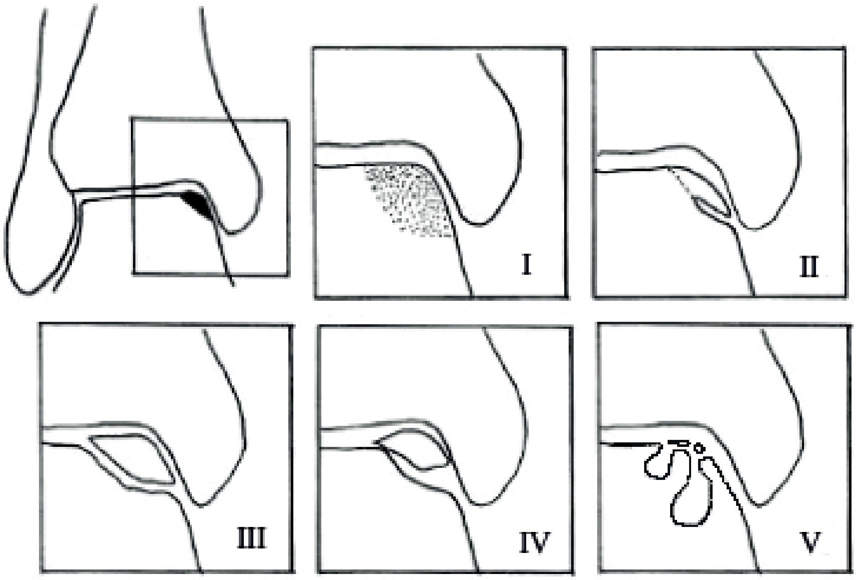

Figure 1. Classification of Berndt and Harty with the addition of Loomer et al.

Berndt and Harty described the causal trauma mechanism in multiple cadaver ankles creating different types of osteochondral lesions after a cascade of different directional forces passing through the ankle complex[24]. A differentiation can be made if a lesion is incomplete or complete and in case of the latter with or without displacement[24, 157]. Another differentiation can be made between patients who present themselves directly after a single trauma with an acute lesion (with or without concomitant ankle fracture) and between those who present themselves after gradual progression of the lesion with an increase of pain and the possible development of cysts. Finally, the lesion can be primary as a new presentation or non-primary after a previous surgical treatment.

In the acute setting and origin of an osteochondral lesion symptoms might be unrecognized. This because the swelling and pain from ligament or other osseous injury can prevail[327]. In up to 50% of the OCLTs they are not visualized on the standard radiographs alone[286]. Therefore, patient history, repeated physical examination and additionally more advanced imaging are of uppermost importance in achieving an accurate and thorough diagnosis[280, 286, 292]. Symptoms of persistent swelling, pain during weight bearing and a limited range of motion may continue after healing of a ligamentous injury and an OCLT should be suspected if complaints do not resolve within 4-6 weeks. Patients present with recognizable tenderness when the talus is palpated in maximal plantarflexion of the ankle. Symptoms like locking and catching can be signs of a displaced fragment[289].

Aims of Part I: Introduction

With trauma being the major epidemiologic factor in the origin of osteochondral lesions, an important **first question** that is addressed in this Thesis is: what is the incidence of patients with ankle injuries presenting to the emergency department? This question is assessed in chapter 2 as part of Part I, the introduction of this thesis.

Aims of Part II: Early Detection of Intra-Articular Osteochondral Lesions in Ankle Fractures

Up to 50% of surgically treated ankle fractures show suboptimal functional results with residual complaints at long-term follow-up[59, 114, 167, 240, 256]. As the vast majority (70-78%) of ankle osteoarthritis can be assigned to be of posttraumatic origin it raises the question which factors might be of underlying cause[229, 278, 320].

Important well described factors associated with poor outcome are ligamentous injury, luxation, dislocation and/or malunion[122, 208, 249, 277, 311]. For example, it is known that syndesmotic instability is a prognostic factor of worsened results in the outcome of ankle fractures[302]. Egol and colleagues showed in their landmark article about the follow up on patients with ankle fractures that patients who required syndesmotic stabilization had poorer outcomes[73]. This might be attributed to the fact that these fractures tend to be more unstable and more prone to malalignment but might also be because of other reasons. For example, other factors possibly influencing the outcome are acute intra-articular (osteo) chondral lesions that can occur in ankle fractures[111, 154, 158, 198, 268, 291, 324].

There is growing evidence that the OCLTs are associated with posttraumatic osteoarthritis and thus an unfavorable long term outcome[172, 193, 217, 255]. One study in 1980 already noted that 48% of patients with deep OCLs after ankle injuries showed radiologic signs of existing osteoarthritis[39]. And while further reviewing the literature, OCLTs after ankle injuries (specifically ankle fractures) seem to play a certain role in the development of posttraumatic osteoarthritis[84, 256]. Injuries to the cartilage and subchondral layer might originate without notice but eventually disturb the joint homeostasis where the cartilage is suddenly incapable of a sufficient repair response and the ankle further degrades as the osteoarthritis progresses. With this in mind, the initial OCLT might be amendable to direct treatment such as fixation or debridement and bone marrow stimulation which then theoretically would improve outcome.

With the as previous described reported poorer results in patients that require syndesmotic stabilization, a subsequent **second question** arises that is addressed in this Thesis: what is the incidence of associated osteochondral lesions in patients with rotational type ankle fractures. Especially those which may benefit from arthroscopic treatment? Could the poorer outcome in these specific ankle fractures be because of the presence of significant OCLTs? The incidence of OCLTs in this type of fracture and the specific types of OCLTs in these fractures are assessed in chapter 3.

Besides these rotational ankle fractures, for all fractures at primary presentation, OCLTs might not be visible or be overshadowed by the more eye catching ankle fracture and thus easily missed. Awareness that these possible concomitant injuries can occur is highly important and when studying the relationship between ankle fractures and the presence of osteochondral lesions there is a lack of knowledge. The exact incidence of these acute lesions after ankle fractures is unclear, with highly various incidence rates[111, 190]. Furthermore, there are conflicting conclusions reported when looking at the association between ankle fracture type and the incidence of osteochondral lesions of the ankle[167]. For example, where Hintermann et al. described that the severity of the lesions significantly increased from type B to type C fractures (according to the Danis-Weber classification), other studies failed to demonstrate this correlation[111, 190, 270]. We therefore formulated the following **third question**: what is the osteochondral lesion incidence and location after ankle fractures and is there an association between fracture type and the presence of these osteochondral lesions? Chapter 4 further investigates this incidence and anatomic location as well as the association between fracture type and presence of these OCLTs.

Aims of Part III: Treatment Options for Osteochondral Lesions of the Talus. Salvage or Intrinsic Healing?

The development of a chronic osteochondral lesions is dependable on numerous factors which include damage and insufficient repair to the subchondral bone plate[214]. It is primarily linked to previous ankle trauma but this correlation sometimes may not be totally clear since the development of symptomatic osteochondral defects can happen over a long period of time. At the moment of becoming symptomatic the original trauma can be already long forgotten but pain is gradually increasing inside the ankle. It is believed that the pain is most probably caused by intermittent local rises in intra-osseous fluid pressure which occur during every weight bearing action[12, 97, 289]. The changes in local pressure are thought to interfere with the normal perfusion of the bone and subsequently can lead to osteonecrosis, bone resorption and eventually to the formation of cysts[12, 72, 120, 233]. Therefore, it is thought that an originally small cartilage defect up to the subchondral plate sustained after an ankle sprain can cause major disability over time.

Initial treatment is most often conservative and aimed at immobilization, restriction of activities and administration of non-steroidal anti-inflammatory drugs (NSAID's)[327].

Results are varying and a following surgical option is not uncommon. The surgical options are widespread, have substantially increased over the last decade and still more treatment types are being developed.

The general consensus is that bone marrow stimulation (BMS) is the treatment of choice for smaller defects. Other options include internal fixation, retrograde drilling, osteochondral autograft transfer systems (OATS), chondrocyte implantation, metal resurfacing, offloading osteotomy, distraction arthroplasty, total ankle prosthesis or arthrodesis[125, 299, 326, 56].

The effectiveness of the different surgical options vary greatly in the available literature and while multiple systematic reviews have been performed, a definite treatment option that would be accepted as the golden standard has yet to be established.

Previous literature either investigates sole treatment options or does not distinguish between the different groups of primary and non-primary OCLTs[56]. This can be regarded as a possible introduction of misinterpretation of the reported success rates. In chapter 5 therefore, we further discuss these treatment options specifically for the primary OCLTs and aim to address the **fourth** clinically relevant **question** in this Thesis: Is it possible to extract the preferred type of treatment of OCLTs and is there any difference between therapies?

Whilst BMS is the most frequently described treatment and proves to have reproducible good clinical results at short-term and mid-term, this technique potentially might not have superior results at long term[107, 143]. BMS focusses on the intrinsic capacity of the ankle to heal due to the formation of new fibrocartilage[143]. This fibrocartilage however has been said to be of inferior quality compared to the original hyaline cartilage and might deteriorate over time[81, 160]. Therefore, cartilage sparing techniques might have an advantage over the BMS technique since they have the theoretical advantage of preserving hyaline cartilage. With this in mind a new arthroscopic internal fixation technique was developed called the lift, drill, fill and fix (LDFF) procedure[126]. This specific technique can be used for the arthroscopic fixation of primary, large enough (>10mm) and fixable OCLs of the talus[143]. This technique should restore the original congruency of the ankle mortise and the subchondral bone quality.

The usage of this fixation technique is dependable on the type of OCLT. Only the fragmented OCLTs are amendable for fixation and only if they have an osseous part great enough to be fixated[220]. If the OCLT is more cystic of nature it obviously can't be fixated and thus should be debrided. But if it is possible to retain the original cartilage by fixation this should be highly considered, for example with the LDFF technique. But whilst this technique showed promising short-term results, previous research was conducted with a limited number of patients and further research has to be performed to show consistency and persistency over time and to show any difference with the classic bone marrow stimulation technique. The following **fifth** research **question** logically follows: what are the clinical and radiological results of this arthroscopic fixation technique (LDFF) for primary OCLTs?

Therefore, a second follow up study was performed to report about the sequent mid-term clinical and radiological results of this LDFF technique which are described in Chapter 6.

Since this technique has the theoretical advantages of cartilage salvage over BMS one could therefore ask themselves a **sixth question**: what is the difference between this arthroscopic fixation technique (LDFF) and an arthroscopic bone marrow stimulation procedure in primary fixable OCLTs? Therefore, a comparison study at one year follow up was also performed and is described in chapter 7.

And in continuation of the theory that the newly intrinsic formed hyaline cartilage after BMS might show deterioration over time, chapter 8 reports on a prospective long term follow up study that was performed to compare outcomes between the short one year follow up and the final long term follow up of BMS. This is order to try to answer our subsequent **seventh** research **question**: Is the clinical and sports outcome after arthroscopic bone marrow stimulation durable over time? Since OCLTs are, as previously described, mainly seen in the young and sportive patients, this follow up study specifically focusses on sports outcome. Whichever technique is chosen, literature states that the vast majority of lesions will improve after surgical treatment[142, 159]. However, a small part of treated patients will fail the first-line surgical treatment and will need revision surgery[49, 159, 188, 322, 326]. As said before, a difference therefore can be made between primary and non-primary lesions although in the literature it is not always clear which type of lesion is described[159, 299, 326]. An **eight question** that therefore remains, if primary treatment of an OCLT fails: would it be possible to point out a preferred subsequent type of treatment for non-primary OCLTs? Chapter 9 describes the different used subsequent procedures and tries to report different success rates of these non-primary treatment types.

OUTLINE OF THIS THESIS

To try to answer the above stated research questions this thesis is constructed in 3 parts.

As a section of **Part I**, the introduction to this thesis, a registry study was performed in order to get insight in the incidence of general lower extremity injuries presenting at the emergency department. For this, a national injury surveillance system (NEISS) was used to obtain a probability sample of all these injuries of which the results are presented in **chapter 2**. The incidence rates and age groups could be derived for ankle injuries separately.

Part II Early Detection of Intra-Articular Osteochondral Lesions in Ankle Fractures

Part II focusses on the acute sustained osteochondral lesions in ankle fractures. **Chapter 3** tries to get insight in the incidence of (osteo)chondral lesions after rotational ankle fractures, the original injuries used in the cadaveric experiments of Berndt and Harty. This thereafter raises the question how often osteochondral lesions arise after ankle fractures in general and if there is a relation with the type of fracture. We want to answer this in **chapter 4**, a general incidence study where we get insight in how often and at which location in the ankle acute (osteo)chondral lesions are sustained after ankle fractures. It also tries to find a correlation between different type of ankle fractures and the existence of these (osteo)chondral lesions.

Part III Treatment Options for Osteochondral Lesions of the Talus. Salvage or Intrinsic Healing?
Part III focusses on the treatment options for talar osteochondral lesions. **Chapter 5** gives a complete overview of all the different described techniques in primary treatment and their success percentages. Next to that the outcome after an arthroscopic fixation technique is described in **chapter 6**. This same technique is compared to the microfracture technique in a comparative study in **chapter 7**. The outcome after microfracture with a focus on sport activities is discussed in **chapter 8**. This is followed by **chapter 9** which gives an overview of all different described techniques in non-primary (i.e. revision) surgery.

Part IV General discussion and summary
Chapter 10 provides the general discussion and **chapter 11** gives a summary of this thesis in English and Dutch.

CONCLUDING: AIMS OF THIS THESIS

When the previous described research questions are collected, the following research goals can be formulated for this thesis:

1. What is the incidence of patients with lower extremity injuries presenting to emergency departments?
2. What is the incidence of associated osteochondral lesions in patients with rotational type ankle fractures with syndesmotic injury which may benefit from arthroscopic treatment
3. What is the osteochondral lesion incidence and location after ankle fractures as well as the association between fracture type and the presence of these osteochondral lesions?
4. What is the preferred type of treatment for primary OCLTs?
5. What are the clinical and radiological results of a novel arthroscopic fixation technique (LDFF) for primary OCLTs?
6. What is the difference between this arthroscopic fixation technique (LDFF) and an arthroscopic bone marrow stimulation procedure in primary fixable OCLTs?
7. Is the clinical and sports outcome after arthroscopic bone marrow stimulation durable over time?
8. If primary treatment of OCLTs fails, is there a preferred subsequent type of treatment?

2

Incidence of patients with lower extremity injuries presenting to US emergency departments by anatomic region, disease category, and age

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ABSTRACT

Background The incidence of patients with lower extremity injuries presenting to emergency departments in the United States with respect to specific anatomic regions and disease categories is unknown. Such information might be used for injury prevention, resource allocation, and training priorities.
Questions/purpose We determined the anatomic regions, disease categories, and circumstances that account for the highest incidence of leg problems among patients presenting to emergency departments in the United States.
Methods We used the National Electronic Injury Surveillance System (NEISS) to obtain a probability sample of all lower extremity injuries treated at emergency departments during 2009. A total of 119,815 patients who presented to emergency departments with lower extremity injuries in 2009 were entered in the NEISS database. Patient and injury characteristics were analyzed. Incidence rates for various regions, disease categories, injuries, and age groups were calculated using US census data.
Results We identified 112 unique combinations of disease categories and anatomic regions. Strains and sprains accounted for 36% of all lower extremity injuries. The injury with the greatest incidence was an ankle sprain (206 per 100,000; 95% confidence interval, 181–230). Younger patients were more likely to have ankle sprains, foot contusions/abrasions, and foot strains/sprains. Older patients were more likely to have lower trunk fractures and lower trunk contusions/abrasions. The most common incidence for injury was at home (45%).
Conclusions Given relatively low-acuity leg problems such as strains and sprains account for a substantial number of emergency department visits pertaining to leg problems, use of telephone triage, scheduled same or next-day urgent care appointments, and other alternatives to the traditional emergency room might result in better use of emergency healthcare resources.

INTRODUCTION

According to the National Hospital Ambulatory Medical Care Survey of the approximately 117 million visits to emergency departments in the United States in 2007, 14.6% were for lower extremity injuries, but this report provided no additional details regarding the injuries[7]. More detailed characterization of leg problems that bring patients to emergency departments would inform public health measures such as injury prevention, resource allocation, and training priorities.

The US Consumer Product Safety Commission's (CPSC) NEISS database is a probability sample of emergency departments with data keyed directly into personal computers by staff at the participating hospitals. The 100 participating hospitals have varied geographic locations and are grouped in five strata, four representing hospital emergency departments of different sizes (small, medium, large, very large) and a fifth representing emergency departments from children's hospitals. The CPSC creates a new sampling frame each year. This frame lists all hospitals with emergency departments in the United States and its territories and includes the annual number of emergency department visits. By assuring the hospitals are appropriately adjusted to required specifications, the sampling frame is used to ratio-adjust the statistical weights for the current NEISS hospital sample to the total number of emergency department visits. Data are accessible to all through the CPSC Web site, which also provides a description of utilization and an explanation of background[234, 265, 273]. The NEISS provides data on anatomic site, disease category, age, and circumstance of injury[264].

We analyzed the NEISS data to determine: (1) the regions and disease categories that accounted for the greatest incidence of leg problems that sent patients to emergency departments in the United States in 2009; (2) the age groups of patients that accounted for the largest portion of the 10 injuries with the highest incidence; (3) the incidence of injuries by location or circumstances where the injury occurred; and (4) the consistency of annual incidence rates year-to-year from 2000 to 2009 for the four most common injuries, and all fractures by anatomic region.

MATERIALS AND METHODS

We analyzed all presentations of patients with lower extremity injuries to an emergency department between January 1, 2009, and December 31, 2009. There were 119,815 reports of lower extremity injuries in the NEISS for 2009, including 62,368 injuries in males (52%) and 57,428 in females (48%). Gender was not recorded for patients with 19 injuries. Incidence rates were calculated using the combination of estimates of total numbers of lower extremity injuries by region and disease category in the United States calculated according to the

NEISS methodology and population data from the corresponding year of the US census[273]. The 95% confidence interval was calculated for the 10 highest incidence rates.

The NEISS uses a body part diagram in which the lower extremity is schematically divided into toe, foot, ankle, lower leg, knee, upper leg, and lower trunk[264]. The toe includes the phalanges whereas the foot includes the metatarsal and tarsal bones. The lower leg is described as the tibia and fibula excluding the ankle and knee. For example, a tibia fracture is considered a lower leg fracture but when it goes through the tibial plateau, according to the NEISS coding manual it is considered a knee fracture. The patella also is considered the knee. The upper leg is the femur excluding from the part that goes into the knee or the femoral neck. This femoral neck is included in the lower trunk together with the hip, pelvis, and lumbar vertebrae.

The NEISS disease categories are amputation, contusion/abrasion, crushing, dislocation, presence of a foreign body, fracture, hematoma, laceration, nerve damage, puncture, strain or sprain, hemorrhage, avulsion (meaning a skin tear or avulsion including avulsion of a toenail), dermatitis, burns, and other/not stated. Burns can be divided into electrical, scald, chemical, radiation, thermal, and burns not specified. As the incidences of specific burn types were low, we combined the burn categories into one group. Although these categorizations do not neatly correspond with the anatomic and disease categories most commonly used by orthopaedic surgeons, they do provide a level of detail that may help provide public health considerations. The different anatomic regions and disease categories result in a total of 112 different injury combinations.

The circumstances of injury are classified by NEISS as home, farm/ranch, street or highway, other public property, manufactured/mobile home, industrial place, school, place of recreation or sports, and not recorded.

To calculate the age groups that accounted for the largest proportion of the 10 highest incidence injuries in 2009, we calculated age-specific incidences by 5-year age groups to age 105 years. To calculate incidences, we used data from 2009 US Census data[274]. The Spearman correlation test was used to see whether age correlated with incidence. We also calculated the incidence according to the location/circumstances of the injury. Finally, we chose to analyze a small sample of the highest incidence injuries (sprains of the ankle, knee, and lower trunk and contusions/abrasions of the lower trunk) and fractures by anatomic region for year-to-year consistency of incidence rates between 2000 and 2009. The choice to analyze these specific injuries is arbitrary and just an example of trends. Linear regression was performed and analyzed to see if there was an increase or decrease in incidence with time. No correction was made to limit type-I (false positive) error for the number of statistical tests applied.

RESULTS

The most common area of injury was the lower trunk (28%), followed by the ankle (20%), knee (16%), foot (15%), lower leg (11%), toe (7%), and upper leg (4%) (Table 1). Strains and sprains accounted for 36% of all lower extremity injuries followed by contusions/abrasions (19%), fractures (18%), and lacerations (8%) (Table 2). Fractures are the most common injuries of the toe, lower leg, and upper leg (38%, 29%, and 31%, respectively). Strains or sprains are the most common injuries in the ankle (72%), the knee (43%), and lower trunk (37%) (Table 3). The majority of the amputations involved the toe (88%). Burns occurred mostly in the lower trunk, lower leg, foot, and upper leg (28%, 25%, 21%, and 19%, respectively). Most crushing injuries were in the toe and foot; together they accounted for 80% of all crushing injuries. The most foreign body injuries were in the foot (60%). Most dislocations were diagnosed in the knee (66%), presumably patellar dislocations because knee dislocations are rare severe injuries. Fractures were distributed over the lower trunk (25%), ankle (19%), lower leg (18%), foot (15%), and toe (14%). Punctures happened mostly in the foot (81%). Most strain or sprain injuries were in the ankle, followed by the lower trunk and knee (39%, 29%, and 19%, respectively). Hemorrhage was seen mostly in the lower leg (39%) and the lower trunk (34%). As for avulsion, the toe was the most affected body part (69%) (Table 4). We found the greatest incidence of lower extremity injuries to be ankle strains or sprains with a calculated incidence of 206 per 100,000 per year (95% CI, 181–230). Lower trunk strains or sprains were second with an incidence of 155 per 100,000 per year (95% CI, 128–183). The third greatest incidence rate was also of strains or sprains but for the knee, with an incidence of 102 per 100,000 per year (95% CI, 88–116). We found incidence rates of 98 per 100,000 per year (95% CI, 82–113) for lower trunk contusions/abrasions, 62 (95% CI, 54–71) for knee contusions/abrasions, and 50 (95% CI, 43–57) for foot contusions/abrasions. For fractures we found incidence rates of 70 per 100,000 per year (95% CI, 59–81) for the lower trunk and 49 (95% CI, 42–57) for ankle fractures (Table 5).

Table 1. Distribution of lower extremity injuries

Diagnosis	Percentage
Toe	6.6
Foot	14.8
Ankle	19.8
Lower leg	10.6
Knee	16.4
Upper leg	3.5
Lower trunk	28.3

Table 2. Distribution of lower extremity injuries

Diagnosis	Percentage
Amputation	< 0.0
Burns, total	1.2
Contusion/abrasion	18.6
Crushing	0.1
Dislocation	1.4
Foreign body	0.8
Fracture	17.6
Hematoma	0.6
Laceration	8.0
Nerve damage	0.4
Puncture	2.2
Strain/sprain	36.2
Hemorrhage	< 0.0
Avulsion	0.5
Dermatitis	0.2
Other/not stated	12.2

Table 3. Distribution of lower extremity diagnoses*

Diagnosis	Toe	Foot	Ankle	Lower leg	Knee	Upper leg	Lower trunk
Amputation	< 0.0	< 0.0	0	< 0.0	0	0	0
Burns	0.2	2.0	0.2	2.9	0.2	7.1	0.8
Contusion/abrasion	21.0	23.5	4.0	20.6	25.7	15.6	21.4
Crushing	0.9	0.4	< 0.0	0.2	< 0.0	0	0
Dislocation	1.6	0.1	0.3	< 0.0	5.9	0	1.1
Foreign body	1.1	3.2	< 0.0	0.6	0.2	1.3	0.4
Fracture	38.1	17.2	17.0	29.2	3.6	31.0	15.4
Hematoma	2.2	0.3	0.1	1.5	0.2	2.0	0.4
Laceration	15.6	12.8	1.8	23.4	7.8	18.3	1.1
Nerve damage	0	< 0.0	0	0.1	< 0.0	0.2	1.3
Puncture	1.1	11.8	0.1	1.2	0.3	2.3	0.2
Strain/sprain	5.1	18.8	71.7	8.7	42.9	14.9	36.7
Hemorrhage	0.1	< 0.0	< 0.0	0.1	< 0.0	0.1	< 0.0
Avulsion	5.4	0.2	0.1	0.9	0.1	0.1	< 0.0
Dermatitis	< 0.0	0.1	0.1	0.4	< 0.0	0.7	0.4
Other/not stated	7.4	9.7	4.8	10.2	13.0	6.5	20.7
Total	100	100	100	100	100	100	100

* Presented in percentages.

Table 4. Anatomic distribution of lower extremity injuries*

Diagnosis	Toe	Foot	Ankle	Lower leg	Knee	Upper leg	Lower trunk	Total
Amputation	87.5	6.3	0	6.3	0	0	0	100
Burns	1	20.9	3.3	25	2.6	18.9	28.3	100
Contusion/abrasion	7.4	18.6	4.2	11.8	22.6	2.9	32.5	100
Crushing	40.7	39.5	4.1	12.2	2.9	0	0.6	100
Dislocation	7.2	0.7	3.4	0.1	66.3	0	22.3	100
Foreign body	9	59.4	0.6	8.5	3.4	5.5	13.6	100
Fracture	14.3	14.5	19.2	17.7	3.3	6.2	24.8	100
Hematoma	25.3	6.5	2.7	28.6	6.8	12.2	17.9	100
Laceration	12.8	23.6	4.4	31.1	16	8	4	100
Nerve damage	0	1.3	0	3.5	0.2	1.5	93.5	100
Puncture	3.2	80.8	0.9	5.9	2.5	3.8	3	100
Strain/sprain	0.9	7.7	39.3	2.5	19.4	1.5	28.7	100
Hemorrhage	9.1	4.6	4.6	38.6	4.6	4.6	34.1	100
Avulsion	69	4.7	1.8	19.2	3.6	0.8	1	100
Dermatitis	0.4	7.8	4.7	21.5	3.1	11.7	50.8	100
Other/not stated	4	11.8	7.8	8.9	17.5	1.9	48.2	100

* Presented in percentages.

Table 5. Estimated incidence rates of lower extremity injuries*

Diagnosis	Toe	Foot	Ankle	Lower leg	Knee	Upper leg	Lower trunk
Burns	N/A	3	N/A	4	N/A	3	3
Contusion/abrasion	19	50	11	30	62	9	98
Crushing	1	1	N/A	N/A	N/A	N/A	N/A
Dislocation	2	N/A	1	N/A	15	N/A	5
Foreign body	1	6	N/A	1	N/A	1	2
Fracture	37	37	49	38	9	13	70
Hematoma	2	1	N/A	3	1	1	2
Laceration	15	27	5	36	20	10	4
Nerve damage	N/A	N/A	N/A	N/A	N/A	N/A	7
Puncture	1	28	N/A	2	1	1	1
Strain/sprain	5	41	206	12	102	8	155
Avulsion	6	N/A	N/A	2	30	N/A	N/A
Dermatitis	N/A	N/A	N/A	1	N/A	N/A	1
Other/not stated	6	21	N/A	14	30	3	88

* Presented in percentages; N/A = sample count is too low to calculate historical estimate.

We observed a correlation between increasing age and lower trunk fractures ($r = 0.96$; $p < 0.000$) (Fig. 1) and increasing age and lower trunk contusions/abrasions ($r = 0.60$; $p = 0.005$) (Fig. 2). Age inversely correlated with ankle strain/sprains ($r = 0.65$; $p = 0.003$) (Fig. 3), foot contusions/abrasions ($r = 0.89$; $p < 0.001$) (Fig. 4), and foot strains/sprains ($r = 0.75$; $p < 0.001$) (Fig. 5), with younger patients more likely to have these injuries.

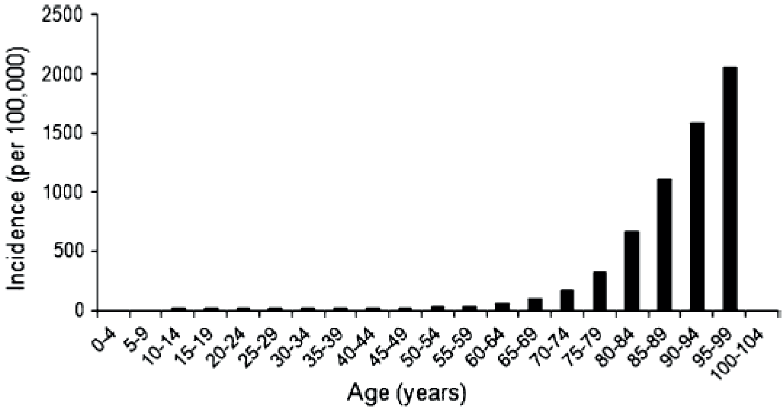

Figure 1 The incidence per age for lower trunk fractures during 2009 is shown.

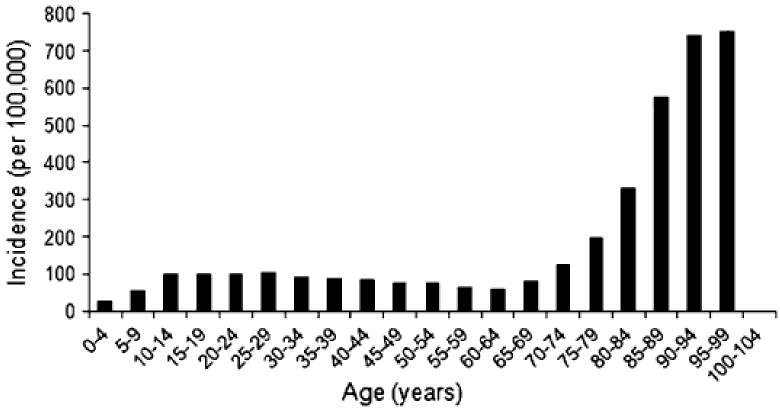

Figure 2 The incidence per age for lower trunk contusions during 2009 is shown.

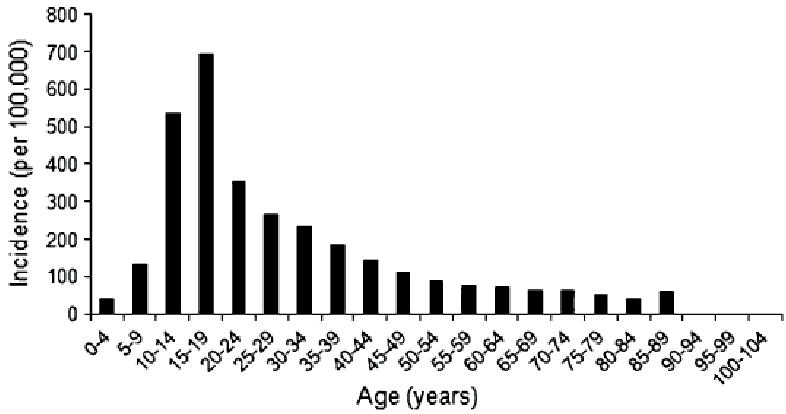

Figure 3 The incidence per age for ankle strains/sprains during 2009 is shown

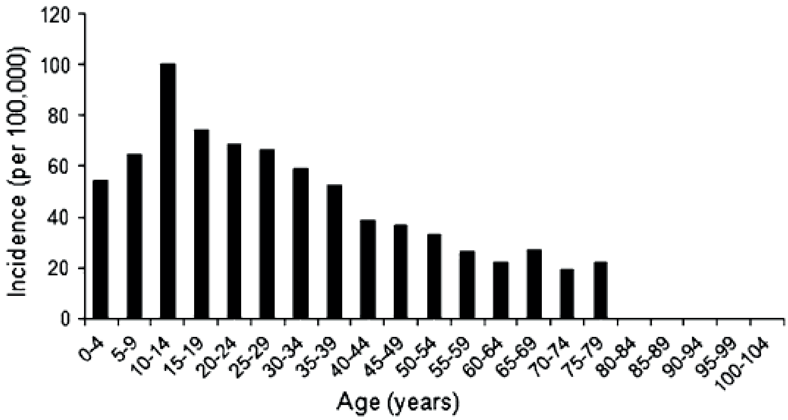

Figure 4 The incidence per age for foot contusions during 2009 is shown.

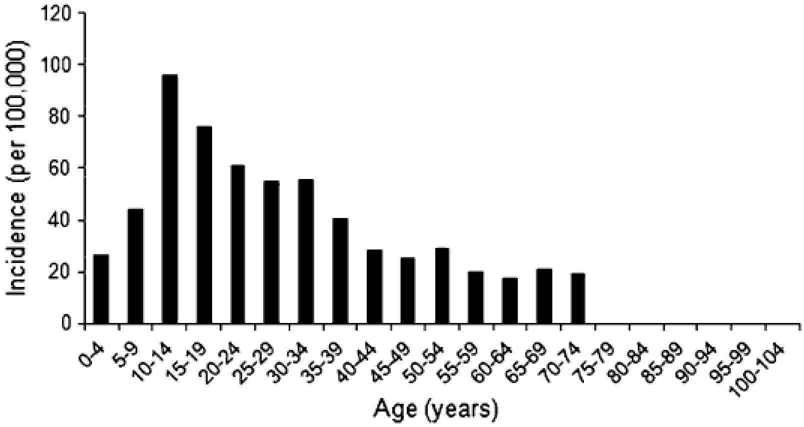

Figure 5 The incidence per age for foot strains/sprains during 2009 is shown.

The most common circumstance of injury was at home (45%) followed by place of recreation or sports (15%); however, location frequently was not recorded (26%) (Table 6).

The incidence rates for strains and sprains of the ankle decreased (B = - 5.2; p = 0.001; R^2 = 0.8) between 2000 and 2009, whereas the incidence of lower trunk contusions/abrasions increased (B = 1.7; p = 0.000; R^2 = 0.9). The incidence of strains and sprains of the knee and lower trunk were consistent between 2000 and 2009. There was an increase in the incidence of ankle fractures (B = 0.4; p = 0.014; R^2 = 0.55) and lower trunk fractures (B = 1.2; p = 0.001; R^2 = 0.75) and a decrease in toe fractures (B = - 0.5; p = 0.02; R^2 = 0.5). The incidence rates for the other fractures were stable.

Table 6. Percentage of injuries in each circumstance

Location	Percentage
Home	45
Farm/ranch	0.1
Street or highway	2.5
Other public property	6.4
Manufactured (mobile) home	< 0.0
Industrial place	< 0.0
School	4.9
Place of recreation or sports	15.1
Not recorded	25.9

DISCUSSION

Knowledge of the relative incidence of injuries according to these categories can provide public health initiatives that address injury prevention, resource allocation, and training priorities. Comparison of seven different data sources available for conducting analyses of emergency department visits (the American Hospital Association Annual Survey DatabaseTM, Hospital Market Profiling Solution, National Emergency Department Inventory, Nationwide Emergency Department Sample, National Hospital Ambulatory Medical Care Survey, National Electronic Injury Surveillance System, and the National Health Interview Survey) showed the NEISS contains the most comprehensive surveillance of injuries treated in the emergency department[203]. The database has been used for various studies[7, 61, 296, 307, 325]. Some of these studies use the NEISS to give an in-depth analysis of a specific injury type such as a shoulder dislocation, scaphoid fracture, or an ankle sprain. Others use the NEISS to map injuries sustained during certain activities (such as ice hockey) or with certain products (such as trampolines).

We analyzed the NEISS data to determine leg injury incidence according to (1) region and disease category; (2) age; and (3) location, and we assessed the consistency of these incidence rates over the years in a subsample of injury types.

We acknowledge the limitations of our study. As we used the NEISS database to collect our data, the main limitations are related to this database. Although being the most usable database for our data collection, several issues should be kept in mind when interpreting the data. First, the NEISS data reflect only a sampling and therefore create estimates rather than precise counts; the error rate in the entered data is unknown, but the likelihood of major errors is low. The population data provided by the US Census Bureau are also estimates based on every 10-year sampling. Second, the classification of the different anatomic regions and different injury types is debatable. For example, it is likely that the diagnosis of sprains and strains in this database is not a very specific category but is commonly used for emergency department patients with complaints of lower extremity pain without a fracture or other specific diagnosis. The percentage of these patients with an identifiable torn ligament or tendon is unknown but certainly less than 100%. Furthermore, using the NEISS anatomic classification of the lower trunk, it is not possible to be more specific than we were in this investigation. For instance, when referring to a fracture of the lower trunk it is not clear if the fracture involves the femoral neck, the intertrochanteric region, or even the lumbar vertebrae. Third, data may change with time. We found some variance in consistency with annual incidence rates during the last 10 years. The incidence of ankle strains decreased during the study period. However, most of the observed injuries showed consistency and where variation was present the difference was small. Fourth, these data show incidence rates of emergency department presentations only. The actual incidence of some injury types presumably is greater than those treated by emergency departments. For example, it is likely everyone with a crushing injury of the foot will visit an emergency department, but many people with a hematoma of the foot may not go to the emergency department.

The most common injury was an ankle sprain, with an incidence of 206 per 100,000 per year, and this is an injury of young adults and teenagers. This is also the only lower extremity injury that was evaluated using the NEISS by another study[307]. In that study, the epidemiology of ankle sprains between 2002 and 2006 was investigated in greater detail and factors associated with ankle sprains were age, race, gender, and involvement in athletics. Other previously described incidence rates for ankle sprains vary widely. In settings such as sports, the reported incidence is greater, and in the military, the incidence was as high as 5840 per 100,000 persons per year[82, 85, 306]. Other studies that report incidences at emergency departments also report higher incidences of 530 to 700 per 100,000 persons per year[32, 113]. Waterman et al. concluded that the lower incidence of ankle sprains found with the NEISS database could be explained by the fact that only one-third of the individuals with ankle sprains or strains seek treatment in an emergency department[307]. One of these studies also included strains/sprains of the foot, which might explain the higher incidence reported in that study, but if we were to combine incidence rates of ankle and foot strain/sprains in our study, it still would be far less than their reported incidence (247 versus 700)[113].

The high correlation between advancing age and lower trunk fractures is well recognized[124, 135, 178, 209, 248]. We found injuries in the knee or below the knee were associated with younger age whereas injuries above the knee were associated with increasing age. Our analysis also showed the ability to track incidence rates, although we think it is important to have many more years of data given that our study from 2000 to 2009 showed an increasing incidence of ankle sprains, but a prior study between 2000 and 2006 did not, suggesting a strong influence of sampling[307]. The finding that most lower extremity injuries occur at home indicates preventative measures are needed.

Relatively low-acuity lower extremity problems such as strains and sprains account for a substantial prevalence of emergency department visits. Different approaches to triage and evaluation of lower extremity injury might result in better utilization of emergency healthcare resources. For instance, patients with ankle injuries might call an emergency phone number to be triaged for an urgent visit or a scheduled visit during regular business hours based on factors such as the Ottawa ankle rules[252, 253].

PART II

EARLY DETECTION OF INTRA-ARTICULAR OSTEOCHONDRAL LESIONS IN ANKLE FRACTURES

3

Prevalence of osteochondral lesions in rotational type ankle fractures with syndesmotic injury

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ABSTRACT

Background The aim of this study was to report the incidence of associated osteochondral lesions (OCLs) on postop CTs, which may benefit from arthroscopic treatment, in patients with rotational type ankle fractures with syndesmotic injury. The diagnosis and treatment of associated OCLs may be an additional benefit of the use of arthroscopy in the management of rotational type ankle fractures with syndesmotic injury.
Methods We retrospectively reviewed data of a prospective cohort study of patients who underwent open reduction and surgical fixation of an ankle fracture with syndesmotic injury. These patients underwent routine bilateral postoperative CT assessment. Two independent observers classified ankle fractures according to Weber and OCLs according to the classification system by Berndt and Harty. Fifty-nine patients were included. There were 19 (32%) Weber B type ankle fractures and 39 (66%) Weber C type fractures. One patient (2%) had fixation for a medial malleolus fracture and syndesmotic rupture without fibula fracture.
Results Talar OCLs were present in 8 patients (14%). In one patient, 2 OCLs were found, which resulted in a total of 9 lesions. Two lesions were found on the medial side, both anterior. The other 7 were located laterally, of which 1 was anterior, 3 central, and 3 posterior on the talus. According to the Berndt and Harty classification, 1 was classified as stage I, 4 as stage III, and 4 as stage IV.
Conclusion The prevalence of OCLs in ankle fractures with syndesmotic instability was 14%. We believe that lesions were arthroscopically accessible in 6 patients (10%). Moreover, most lesions were located on the lateral dome, and thus also potentially approachable through an anterolateral arthrotomy during open reduction and internal fixation. The majority of OCLs found in this series were Berndt and Harty type III or IV, and so likely would preferably have been addressed during the index procedure.
Level of Evidence: Level III, diagnostic cohort study.

INTRODUCTION

Rotational type ankle fractures with associated syndesmotic injuries are generally considered the most severe and have a high risk of dislocation and joint surface injury[258, 311]. Egol and colleagues showed that patients who require syndesmotic stabilization (in addition to malleolar fracture fixation) have poorer outcomes[73]. This is possibly due to the fact that these fractures tend to be more unstable or comminuted, and thus more prone to malalignment, even after open reduction and internal fixation (ORIF). It can also be attributed to the fact that there is an association between the incidence of joint surface lesions and the severity of ankle fractures[111, 154, 217]. However, in their landmark article on outcomes of ankle fracture with syndesmotic injury, the authors did not record whether there were osteochondral injuries to the talus[73]

There is growing evidence that initial deep chondral and osteochondral lesions (OCLs) of the talus and distal tibia are associated with posttraumatic osteoarthritis and therefore a less favorable long-term outcome[190, 217, 255]. Also, ankle arthroscopy-assisted open reduction and internal fixation (ARIF) of rotational type ankle fractures is currently performed by a small proportion of surgeons, but it is becoming increasingly popular as a diagnostic as well as treatment adjunct facilitating reduction[2, 30, 99]. Some authors claim that arthroscopic diagnosis of suspected syndesmotic injury associated with rotational type ankle fractures may be the gold standard[302]. In addition to arthroscopic diagnosis and management of the syndesmosis, multiple studies report on the arthroscopic assessment of these chondral or OCLs in patients with ankle fractures, reporting a high incidence of up to 0%[4, 42, 111, 154, 158, 302].

However, to date it is unclear how often these OCLs were amenable to arthroscopic treatment (Berndt and Harty types III and IV), either arthroscopy-assisted fixation or debridement and bone marrow stimulation. Data based on radiographic incidence (MRI and CT) of (osteo-)chondral lesions after a sustained ankle fracture report a much lower incidence (5% to 40%) but are scarce[27, 190, 217].

Therefore, the purpose of this study was to evaluate a prospective cohort of patients with bilateral postoperative low-dose CT scans after ORIF of rotational type ankle fractures that required syndesmotic fixation, in order to diagnose OCLs that in retrospect may have been amenable to arthroscopic treatment (Berndt and Harty types III and IV) during the index procedure. Our hypothesis was that the incidence of OCLs that would be amenable to operative fixation would be higher in ankle fractures with associated syndesmotic injuries than in the complete spectrum of rotational type ankle fractures that have been the subject of previous reports.

METHODS

Subjects

We retrospectively reviewed our medical records from January 2013 to December 2016 for patients that underwent ORIF for rotational type ankle fracture with associated syndesmotic injury that required screw or suture button fixation and additionally had a low-dose post-operative bilateral CT scan of both ankles, with axial cuts limited to the distal tibiofibular joint as per hospital protocol. In 2013, standard postoperative screening for malreduction with low-dose bilateral CT was initiated in our institution: first, as part of our prospective randomized trial of static (positioning screws) versus dynamic fixation (Tightrope, Arthrex, Device Technologies, Melrose, NSW, Australia) for randomized patients only; subsequently, up to the surgeon's discretion of nonrandomized patients; and recently, per our hospital postoperative protocol. After review of all operatively treated rotational type ankle fractures, 59 patients fit the inclusion criteria (ie, syndesmotic screw or TightRope fixation and postop bilateral axial CT images of sufficient quality) and were included as a convenience sample in this diagnostic imaging study. Patient demographics were recorded. We found 59 patients who fit our inclusion criteria.

The median patient age was 37 (range, 13-81) years. There were 32 males (54%) and 27 females (46%). In 32 patients (54%), the fracture occurred in the left ankle. The average time from injury to surgery was 4 days (range, 0-17), and the average time from surgery to postoperative CT was also 4 days (range, 0-28). None of the CT evaluations were affected by the hardware. Our institutional review board (IRB) approved this study, in accordance to the Declaration of Helsinki.

The existence of a posterior malleolus fracture or medial malleolus fracture was recorded. Fractures were categorized according to the Danis-Weber and Lauge-Hansen classifications by 2 authors not involved in patient care (K.L., H.T.)[270]. Deltoid ligament injury in Lauge-Hansen stage IV supination-external rotation (SER) was defined if the medial clear space measured more than 5 mm[288]. There was no protocol in place for gravity stress radiographic assessment of deltoid injury at the time of the present study. All SER fracture types were considered to be at least type III since complete instability of the syndesmoses complex was noted intraoperatively and treated accordingly. The same applied to pronationexternal rotation (PER) type injuries since with instability of the syndesmosis complex and true diastasis, a complete rupture of all ligaments is expected. This would include the posterior talofibular ligament, which automatically resulted in a type IV classification. The existence of intra-articular loose bodies was also recorded. Finally, the method of syndesmotic fixation was recorded, as was any medial or posterior malleolus type of fixation. Operative treatment was according to the principles of the Arbeitgemeinschaft für Osteosynthesefragen (AO), and specifics were up to the treating surgeon's discretion. All patients were tested intraoperatively for syndesmotic injury using standardized hook and external rotation stress tests under fluoroscopy, and all patients received fixation of the syndesmosis accordingly with the technique of fixation depending on the treating surgeon's preference. Postoperatively, in all patients, a high-resolution multidetector helical scanner was used (Aquilion ONE, Toshiba Medical Systems or iCT 256, Philips Healthcare).

Protocol Low-Dose Bilateral CT Assessment of Syndesmotic Reduction

Postoperative CT scans were analyzed by a radiology fellow in musculoskeletal imaging (H.T.) and a senior orthopedic resident (K.L.), neither of whom were involved in patient care, to classify OCLs. Disagreement was resolved by discussion with a senior author (R.J.) as a third independent observer. For each OCL, the location in the talus was determined according to the 9-grid scheme previously described by Elias et al[76]. Concomitant tibial lesions were determined and described through a similar grid scheme, if present[75]. OCLs were classified according to the Berndt and Harty classification system (type I: subchondral depression, type II: partially fractured, type III: completely fractured but not displaced, type IV: displaced fracture)[24]. This classification system was adjusted by Loomer et al to also include cystic lesions defined as a type V lesion[157]. However, these types of lesions were excluded, since they are considered to be chronic in nature and this study focused on traumatic lesions.

Statistical Analysis

To investigate whether a correlation could be found between associated injuries, such as a posterior or medial malleolar fracture, and the existence of OCLs, a chi-square test was performed. Statistical data analysis was performed with IBM SPSS Statistics version 24 (IBM Corp., Armonk, NY). $P < .05$ was considered significant.

RESULTS

Ankle Fracture Characteristics

There were 19 (32%) Weber B type and 39 (66%) Weber C type ankle fractures. This corresponds to the Lauge-Hansen classification where 19 and 39 fractures were classified as SER and PER injuries, respectively. One patient (2%) had a syndesmotic rupture without a fibula fracture and therefore could not be classified according to the Weber or Lauge-Hansen classification. This patient, however, had a medial malleolar fracture and since the trauma mechanism was of a rotational type, with radiographically demonstrated syndesmotic instability requiring fixation, we decided to keep this patient in our study group. Of the SER type injuries, 3 were considered type III and 16 were considered type IV. All 39 PER injuries were considered to be type IV based on operative fluoroscopic testing, with 17 ankles having a clear posterior malleolar fracture. Of the Weber C and PER injuries, 8 (21%)

were Maisonneuve type fractures. In total, there were 27 (46%) associated posterior malleolus fractures and 26 (44%) medial malleolar fractures. Four posterior malleolar fractures needed fixation with 1 or more screws (3 in the anterior-posterior direction and 1 in the posterior-anterior direction). The medial malleolus fracture was fixed in all 26 cases, in 1 patient with 1 screw, in 17 patients with 2 screws, in 2 patients with a plate, and in 1 patient with a screw and K-wire. In 15 ankles, the syndesmotic injury was fixed with 1 positioning screw, and in 38 ankles 2 positioning screws were used for fixation. One TightRope was used in 2 ankles and 2 TightRopes were used in 3 ankles. In one patient, a TightRope was used in combination with a screw. The choice to use an additional screw in the latter was because this patient showed previous noncompliance, and a supplemental rigid way of fixation by use of this additional screw was deemed necessary by the treating surgeon. Patient and fracture characteristics are displayed in Table 1.

Table 1. Patient and Injury Characteristics (*n* = 59).

Gender	Value
Male	32 (54%)
Female	27 (46%)
Median age	37 (range, 13-81)
Side injured	
Left	32 (54%)
Right	27 (46%)
Danis-Weber classification	
Weber B	19 (32%)
Weber C	39 (66%)
Not classifiable	1 (2%)
Lauge-Hansen classification	
SER III	3 (5%)
SER IV	16 (27%)
PER IV	39 (66%)
Not classifiable	1 (2%)
Medial malleolar fracture	26 (44%)
Posterior malleolar fracture	27 (46%)

Abbreviations: PER, pronation-external rotation; SER, supination-external rotation.
Values are reported as number (%) unless otherwise indicated.

Osteochondral Lesions

We observed talar OCLs in 8 patients (14%). In one patient, 2 OCLs were found, which resulted in a total of 9 talar lesions. Additionally, in 2 patients a cystic lesion (type V) was found, but they were excluded for review, as stated previously. As for the 9 OCLs, 1 was classified as stage I, 4 as stage III, and 4 as stage IV (Figure 1).

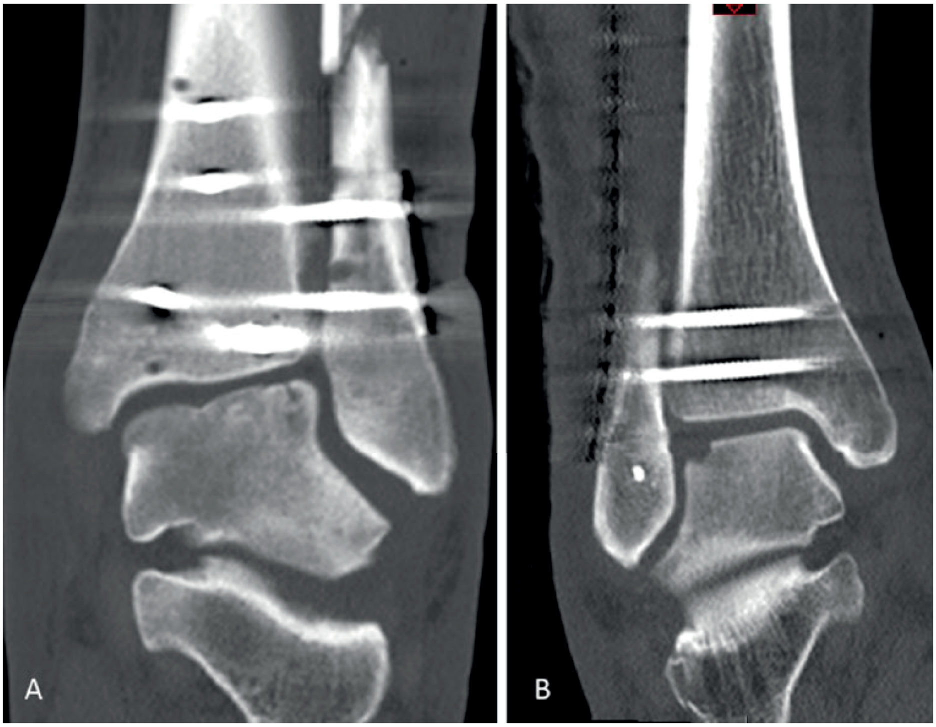

Figure 1. Examples of a Berndt and Harty (A) type III and (B) type IV osteochondral lesion seen on postoperative CT.

The median OCL size (largest diameter) was 6.5 mm (range, 4.6-14.4). Two lesions were found on the medial side, both anterior. The other 7 were located laterally, of which 1 was anterior, 3 central, and 3 posterior in the talus. In only one patient a tibial OCL was found, which was situated in the posterolateral corner, measuring 9 x 5 x 5 mm. In an additional 6 patients (10%) without an identifiable OCL, loose intra-articular bodies were visible. One patient was already preoperatively diagnosed with a Berndt and Harty type III OCL on standard radiographs. This was fixed with 2 smart screws, after which an acceptable surface reduction was achieved (Figure 2). With the numbers available, chi-square test showed no association between a talar OCL or the existence of a medial malleolar fracture ($P = .697$), a posterior malleolar fracture ($P = .614$), or a trimalleolar fracture ($P = .560$), and the type of injury ($P = .615$).

Figure 2. Postoperative CT scan of an operatively treated pronation-external rotation type ankle fracture with additional fixation of a Bernd and Harty type III osteochondral lesion with 2 smart screws.

DISCUSSION

In this study, we aimed to investigate the incidence of OCLs in patients with ankle fractures and syndesmotic instability. Syndesmotic instability is a prognostic factor for poorer results in the outcome of ankle fractures[302]. In addition, there is growing evidence that acute OCLs are correlated with less favorable outcome. For example, in 1991 Lantz and colleagues reported that they found a significantly poorer result in patients with these chondral lesions, which was followed by several studies reporting on the arthroscopic assessment of these lesions in patients with ankle fractures[4, 42, 111, 146, 154, 158]. We therefore aimed to evaluate the incidence of OCLs in patients with rotational type ankle fractures and syndesmotic injury, and the number of OCLs amenable to arthroscopic treatment during the index procedure. After analyzing available data, we found a 14% incidence of talar OCLs in ankle fractures with syndesmotic rupture. In retrospect, one may argue that these OCLs would have been amenable to arthroscopy-assisted or mini-open fixation according to the grading system by Berndt and Harty, or could have received an arthroscopic debridement with additional bone marrow stimulation treatment. Most OCLs, however, were located directly on the lateral side of the talus, and one could argue that these lesions would also have been amendable for fixation or debridement by opening the anterolateral ankle joint at the time of ORIF. Additionally, 3 of them were situated on the posterior aspect of the talus and therefore also would have been difficult to reach by scope. These results contribute to our understanding and the current discussion to consider ARIF in patients with ankle fractures with syndesmotic rupture. With OCLs being present in only 1 out of 7 patients and with not all OCLs reachable by scope and actually treatable through an arthrotomy during the initial ORIF, we would not advocate using standard ARIF for diagnosing or treatment of these OCLs. Although ARIF might be beneficial to assess syndesmotic injury and articular reduction in ankle fractures with syndesmotic instability, we did not find convincing support for it to be the preferred choice for diagnosing or treating talar OCLs in this patient group.

This study should be interpreted in the light of strengths and weaknesses. Evaluation of CT images does not account for isolated pure chondral injuries, as reported in the series of Hintermann et al[111]. In order to do so radiographically, MRI and evaluation according to the classification of Hepple et al (adapted from the Berndt and Harty classification) or Dipaola et al would account for chondral damage[63, 110]. However, we believe it is of greater clinical importance to detect the larger OCLs since they are the ones that would possibly benefit from fixation. Smaller, solely chondral lesions, just up to the level of the subchondral plate, however, may also benefit from treatment, such as bone marrow stimulation. As the incidence of these chondral lesions is without a doubt even higher than the OCL incidence identified in our study, the possible advantages of the additional arthroscopy would be even more substantial in these injuries. Another limitation is the relatively small sample size. Previous studies with larger numbers, however, mostly describe all types of ankle fractures or the less severe types. We did not identify any other studies describing the OCL incidence in ankle fractures that received syndesmotic fixation, and therefore we believe that this study provides valuable additional information when dealing with this kind of injury in a clinical environment.

In the literature, numerous studies present data in regards to associated OCLs in patients with ligamentous injuries and chronic instable ankles[4, 62, 131, 176, 196, 261]. Furthermore, there is literature available concerning (osteo-)chondral lesions in association with different operatively treated ankle fractures, with the most recent studies summarized in Table 2[4, 27, 42, 111, 154, 158, 190, 217, 250].

Table 2. Incidences of (Osteo-)Chondral Lesions Associated With Operatively Treated Ankle Fractures.

Year	Assessment	Author	Type of Fracture	No. of Patients	Incidence	Talus/Tibia/Malleoli
2016	CT	Nosewicz et al	Weber A	1	0%	Talus
			Weber B	71	13%	
			Weber C	22	5%	
2016	Arthroscopy	Chan & Lui	Weber A	6	0%	
			Weber B	177	26%	Talus + tibia
			Weber C	51	24%	
			Isolated medial malleolar	20	20%	
2016	MRI	Regier et al	Weber B/C	100	40.4%	Talus + tibia
2009	MRI	Boraiah et al	All types	153	17%	Talus
2009	Arthroscopy	Leontaritis et al	Weber B/C	84	73%	Talus + tibia + malleoli
2008	Arthroscopy	Aktas et al	Weber B/C	86	28%	Talus
2002	Arthroscopy	Hintermann et al	All types	288	79.2%	Talus + tibia + mall.
2002	Arthroscopy	Loren & Ferkel	All types	48	19%	Talus + tibia
2000	Operative report	Sorrento & Mlodzienski	Weber B (SER IV)	50	38%	Talus

Abbreviations: SER, supination-external rotation.

Apart from one other CT-based study, most studies describe OCLs and the chondral lesions, which, as discussed above, explains the high incidences in some of these studies. They included all patients in their incidence count if any form of cartilage damage was present. In our study, we only looked at OCLs visible on CT and potential loose bodies.

Although we did not account for the smaller cartilage-only injuries, we did get good images of the bigger lesions, which are the ones suitable for potential fixation or debridement. For example, Figure 3 shows an OCL that was potentially amenable for fixation, but this was not performed. In a recent study by Nosewicz et al, 10% of 100 prospectively included ankle fractures treated with ORIF showed associated talar OCLs on CT[190]. They did not find a significant association between fracture type and OCLs, and although they did not mention the number of syndesmotic injuries, the study showed that lesions were only found in Lauge-Hansen stage III/IV ankle fractures[190]. Compared with our study, the severity of the lesions they presented was slightly less, since they mainly found type II lesions, whereas we mainly identified type III and IV lesions.

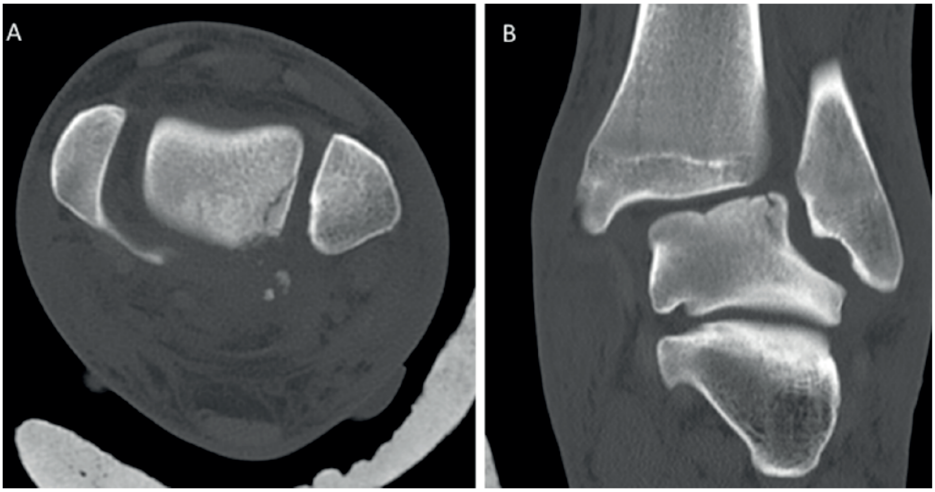

Figure 3. Preoperative (A) axial and (B) coronal CT images from a patient with a pronation-external rotation injury type IV with a large osteochondral lesion type III.

The association between the severity of the ankle fracture and the existence of OCLs has been previously described in other studies. Leontaritis et al found that the number of intra-articular chondral lesions associated with the more severe ankle fracture patterns (PER and SER type IV fractures) was greater than that with the less severe ankle fractures[154]. Regier et al also found a significant correlation between the severity of fracture and the number of OCLs[217]. Furthermore, they found a significant correlation between the incidence of OCLs and the clinical outcome as measured by the American Orthopaedic Foot & Ankle Society (AOFAS) score. Some statements concerning syndesmosis injuries and OCLs can also be found. Loren and Ferkel, for example, showed that 9 out of 12 fractures with syndesmosis disruption sustained full-thickness damage to the talar chondral surface[158]. Another study, by Sorrento and Mlodzienski, presented patients with SER IV injuries, where one would assume they all had syndesmotic instability, but it is unclear how many really received syndesmotic stabilization[250]. They found an incidence of 38%. This incidence was calculated by retrospectively screening the operative reports of the ORIF. Only intraoperative reports with specific reference to the absence or presence of lesions were omitted, which could potentially bias the results.

The outcome of our study further expands on the subject of the possible advantages of ankle arthroscopy in the management of ankle fractures. However, an important finding was that 3 OCLs in our study were found posterolateral, which means they were not reachable via anterior arthroscopy. This should be an important part of the discussion and has to be taken into account when analyzing the data and subsequent assessment if ARIF is to be of any additional value. An additional arthroscopy can possibly improve the outcome, but of course only if intra-articular pathologies are reachable and treatable. Although there are some data available, until now there have been no conclusive data about the effectiveness of arthroscopically assisted fracture treatment[26, 87, 158, 271]. A recently published protocol describes the plans for a randomize controlled trial that will hopefully give more insight into this matter[30]. With regard to the syndesmosis itself, previous cadaveric research showed that arthroscopy has the potential to also evaluate even partial disruption of the syndesmotic ligament complex and significantly predicted isolated disruption of the anteroinferior tibiofibular ligament (AITFL), as well as the deltoid ligaments. This can possibly further help surgeons during operation to understand the extent of potential syndesmotic injury[80, 308]. Finally, ARIF should only be performed in the hands of a skilled surgeon. The fact that it could cause complications, such as neurological problems, and will lengthen the required total operating time should be taken into account when considering ARIF[87, 328].

CONCLUSION

The prevalence of OCLs in ankle fractures with syndesmotic instability was 14%. Lesions would likely have been arthroscopically reachable in 6 patients (10%). Most lesions were situated laterally and thus also reachable through an anterolateral arthrotomy during ORIF. Although ARIF might be beneficial to assess syndesmotic injury and articular reduction in ankle fractures with syndesmotic instability, we did not find convincing support for it to also be the preference when diagnosing and treating OCLs in these injuries. The OCLs we found were mostly Berndt and Harty type III or IV lesions and thus potentially amenable to treatment by either fixation or debridement with a type of bone marrow stimulation. This study therefore mainly points out that these sometimes forgotten associated OCLs, although small, might correlate with a more unfavorable outcome if left untreated.

4 High incidence of (osteo)chondral lesions in ankle fractures

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ABSTRACT

Purpose To determine the incidence and location of osteochondral lesions (OCLs) following ankle fractures as well as to determine the association between fracture type and the presence of OCLs. Up to 50% of patients with ankle fractures that receive surgical treatment show suboptimal functional results with residual complaints at a long-term follow-up. This might be due to the presence of intra-articular osteochondral lesions (OCL).
Methods A literature search was carried out in PubMed (MEDLINE), EMBASE, CDSR, DARE and CENTRAL to identify relevant studies. Two authors separately and independently screened the search results and conducted the quality assessment using the MINORS criteria. Available full-text clinical articles on ankle fractures published in English, Dutch and German were eligible for inclusion. Per fracture classification, the OCL incidence and location were extracted from the included articles. Where possible, OCL incidence per fracture classification (Danis–Weber and/or Lauge–Hansen classification) was calculated and pooled. Two-sided p values of less than 0.05 were considered statistically significant.
Results Twenty articles were included with a total of 1707 ankle fractures in 1707 patients. When focusing on ankle fractures that were assessed directly after the trauma, the OCL incidence was 45% ($n = 1404$). Furthermore, the most common location of an OCL following an ankle fractures was the talus (43% of all OCLs). A significant difference in OCL incidence was observed among Lauge–Hansen categories ($p = 0.049$). Post hoc pairwise comparisons between Lauge–Hansen categories (with adjusted significance level of 0.01) revealed no significant difference (n.s.).
Conclusion OCLs are frequently seen in patients with ankle fractures when assessed both directly after and at least 12 months after initial trauma (45–47%, respectively). Moreover, the vast majority of post-traumatic OCLs were located in the talus (42.7% of all OCLs). A higher incidence of OCLs was observed with rotational type fractures. The clinical relevance of the present systematic review is that it provides an overview of the incidence and location of OCLs in ankle fractures, hereby raising awareness to surgeons of these treatable concomitant injuries. As a result, this may improve the clinical outcomes when directly addressed during index surgery.
Level of evidence: IV.

INTRODUCTION

Ankle fractures are common injuries, with a global annual incidence of 0.1–0.2%[250, 260, 261]. Operative treatment focuses on achieving stability, anatomic reduction and congruity of the ankle joint by means of open reduction and internal fixation. Up to 50% of the surgically treated patients show suboptimal functional results with residual complaints at long-term follow-up[59, 189, 240, 256]. A frequent residual complaint is a persistent pain, which can have a large impact on the daily-functioning of patients[173]. One of the potential explanations for this residual pain could be the presence of (osteo)chondral lesions (OCLs) thereby impeding the clinical recovery of the individual patients[146, 250, 260, 261].

When studying the relationship between ankle fractures and the presence of OCLs in the ankle, it becomes clear that there is a substantial lack of knowledge on (1) the exact incidence of these lesions in ankle fractures, (2) the location of these OCLs and (3) the association between OCLs and ankle fracture type. Although no exact incidence of OCLs after ankle fracture is known, incidences in the literature range from 10% to almost 90%[111, 190]. A post-traumatic talar OCL is thought to occur when the talus is rotated or translated in the loaded ankle mortise until the fracture occurs[111]. As demonstrated by Bruns et al. in cadaveric ankle joints, the maximum pressure on the lateral talar border was observed in valgus and pronation position, whereas trauma in supination stresses the medial half of the ankle joint[36, 111]. Raikin et al. confirmed this in a large study in which medial talar OCL incidence was 63%[215]. The high incidence could be explained because many OCLs are related to inversion injuries and could, therefore, result in an impaction of the medial talar dome. Verhagen et al. reported an incidence of 61% of medial dome OCL after ankle trauma[299].

Furthermore, conflicting findings have been reported concerning the association between ankle fracture type and the incidence of OCLs in the ankle. For instance, Hintermann et al. described that the frequency and severity of the lesions significantly increased from type-B to type-C fractures (classification according to AO-Danis-Weber), whereas Nosewicz et al. found no significant association between these fracture types[57, 111, 190, 309]. Regier et al. illustrated that patients with trimalleolar fractures or dislocated ankle fractures had a significantly higher risk of developing an OCL compared to patients with unimalleolar type B fractures[217]. The discrepancies between the scarce amount of evidence make it clear that the exact incidence of OCLs in ankle fractures is not yet known. This also holds for the exact location of post-fracture OCLs, as well as the association between OCLs and the severity of ankle fracture types. Therefore, we hypothesized that the incidence of OCLs is higher in rotational type ankle fractures. To the best of our knowledge, no previous systematic review has been published studying the before-mentioned. Therefore, the aim of the present study is to systematically review the current literature to determine the OCL incidence after ankle fractures, to determine the most common location, and, finally, to determine the association between OCLs and fracture type. If concomitant OCLs in acute ankle fractures are correctly diagnosed and treated accordingly, this may improve the clinical and functional outcome after surgery.

MATERIALS AND METHODS

The PRISMA statement (Preferred Reporting Items for Systematic reviews and Meta-Analyses) was used as a guideline for the present study. The protocol for our systematic review and meta-analysis was prospectively registered in the PROSPERO register with registration number [CRD42018086653][46].

Search strategy

PubMed (MEDLINE), EMBASE, CDSR, DARE and CENTRAL were used for a systematic search performed in May 2019 to identify potentially suitable studies. Backward citation chaining strategy was used to identify additional eligible studies. The full search strategy can be found in (Appendix I).

Eligibility criteria and study selection

Clinical studies that investigated the treatment of any type of ankle fracture and also reported findings of OCLs of the ankle were included. Available full-text studies published in English, Dutch and German were eligible for inclusion. No restrictions were set on the publication date nor the age of patients. The exclusion criteria can be found in (Table 1). When necessary, authors were contacted for questions or uncertainties regarding published data. This was also done when additional data was required to be able to execute more detailed data analyses of the included patients. In the case of no response, two reminder e-mails were sent. If there was still no response after three emails, the specific data, and in some cases the whole article, was excluded for (sub)analysis. Independent screening of the title/abstract and full-text of included articles was carried out by two reviewers (H.M. and K.L.). In the case of a conflict, the two reviewers first tried to solve it through a discussion. If this conflict persisted, the judgement of a third investigator (J.D.) was decisive. Studies were not blinded for author, affiliation or source, and no limitation was put on publication status. The literature selection algorithm according to the preferred reporting items for systematic reviews and meta-analyses (PRISMA) is presented in (Figure 1).

Quality assessment of included studies

To assess the methodological quality of studies the methodological index for non-randomized studies (MINORS) criteria was used[247]. Quality assessment was performed independently by two reviewers (H.M. and K.L.). In the case of a conflict, the judgement of a third, independent investigator (J.D.) was decisive.

Table 1 Study exclusion criteria

Exclusion criteria
Case report studies
< 5 patients included
Data not interpretable
Medical history of ankle surgery
Chronic ligamentous ankle instability
Patient overlap in different studies and no response from corresponding authors after requesting additional information on patient data
Treatment option inappropriately described
Follow-up > 4 years
Level V evidence studies
Animal studies
Cadaveric ankles

Data extraction

Data were extracted from each included study by one reviewer (H.M.) and cross-checked by one other author (K.L.). Standardised data extraction was performed using a data collection form. Data on study design and study characteristics were extracted and included: year of conduct; number of patients and fractures; patient characteristics (age, sex); type of fracture (according to Danis-Weber classification, Lauge-Hansen classification or other classification/type of fracture); method of OCL diagnosis; OCL incidence; and, lastly, the type of treatment of the OCL[57, 148, 309]. Location and distribution of OCLs were described and classified according to the anatomical osseous location [i.e., talus, tibial plafond, medial malleolus (tibia) or lateral malleolus (fibula)]. If possible and reported, location was specified to an exact location; e.g., anterior, medial, posterior or lateral, and if possible subdivided into anterolateral, anteromedial, posterolateral or posteromedial. If included studies reported on chondral lesions and/or OCL incidence, both incidences were extracted and reported. If included studies reported assessment of OCLs more than 12 months after the initial trauma, we defined the reporting in these studies as 'late assessment' and pooled these studies to investigate persistent OCLs after trauma. The before-mentioned studies were excluded from the analysis of the direct assessment of OCL incidence. The intention of this study was to focus mainly on providing a summary of the evidence of incidence rates of OCLs and there was, therefore, less focus on their treatment.

Terminology

Many derivatives and combinations of chondral, cartilage, defect, lesions and injury were used. Therefore, all reported lesions were considered OCLs and were referred to as OCLs in the results. If studies further classified the lesions as chondral or osteochondral, or if studies used an OCL classification system, stage one of Cheng classification[45, 81], Loomer classification[157], Dipaola classification[63], Outerbridge classification[202] and Berndt and Hardy classification[24] were considered as chondral damage. Subdivision of chondral and osteochondral lesions were reported separately where possible.

Statistical and data analysis

Reported OCL incidence after ankle fractures was extracted from the original article. If no OCL incidence percentage was reported, we calculated the OCL incidence by dividing the total number of OCLs by the total number of ipsilateral fractures reported in the article. Some studies only reported a specific location (i.e., the talus, tibial plafond, medial malleolus or fibula) but did not specify its sublocation (i.e., anterior, posterior, etc.). If no location of the OCL was reported, only the total number of OCLs was included in the OCL incidence and the OCL incidence was not included in the subanalysis of location. The incidence of OCL per sublocation is based on the number of OCLs per sublocation divided by the total OCL incidence per location. Therefore, it is possible that the number of OCLs in the sublocations will not add up to the total since not all studies reported on the sublocations. The sum of reported OCLs on the sublocations may be greater than the reported OCL incidence after ankle fractures due to the presence of multiple OCLs in a single ankle fracture. If possible and reported, OCL incidence per fracture classification (Danis-Weber and/or Lauge-Hansen classification) was made. Data management and analysis were executed utilizing SPSS. For each variable, frequency distribution, means and standard deviations were calculated. Association between the OCL and fracture type was evaluated by means of an overall χ^2 test. In the case of a statistical significance, post-hoc pairwise comparisons were performed with adjusted significance levels (Bonferroni). Two-sided p values of less than 0.05 were considered statistically significant.

RESULTS

Search results

The systematic search in PubMed (MEDLINE), EMBASE, CDSR, DARE and CENTRAL yielded 1950 records. After removing the duplicates, 1349 records remained of which title and abstract were screened for relevance. After screening the title and abstract, 1284 records were excluded because the inclusion criteria were not met. The full-text articles of 65 records were screened and assessed for eligibility, resulting in twenty studies eligible for inclusion in the systematic review (Figure 1). A total of seven authors were contacted to request data according to the inclusion criteria. Additional data from three studies were received, two of which were studies by our co-author. Three of the remaining four studies were excluded for subanalysis of OCL location and subanalysis of association between OCL location and fracture type[27, 41, 136]. After screening and discussion between the first two authors there was overall consensus in all cases of the selection procedure and grading of methodological quality.

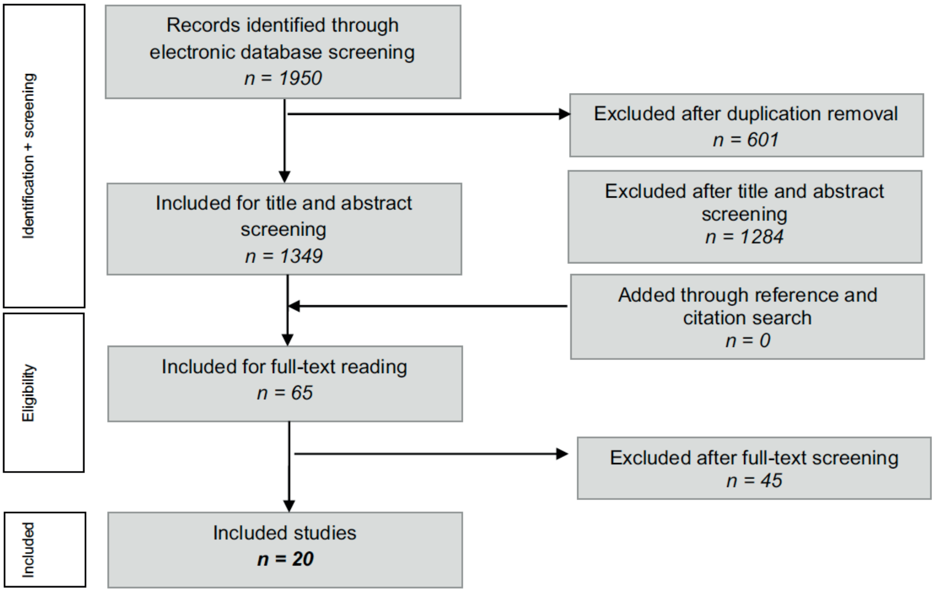

Figure 1.
Literature selection algorithms – Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA)

Study and patient characteristics

The study and patient characteristics are summarized in (Table 2). A total of 1707 ankle fractures were included in 1707 patients, and eleven studies (55%) reported on the incidence of the fracture side[42, 111, 136, 145, 158, 190, 198, 217, 255, 321, 329]. Of these studies, 50.5% of the patients had a right ankle fracture and 49.5% a left ankle fracture. No cases of bilateral ankle fractures were reported. Furthermore, the mean MINOR score was 10.5 ± 2.1 (Table 2).

Osteochondral lesion incidence directly after trauma

The pooled incidence of OCLs in ankle fractures assessed directly after trauma was 45.1%, as seen by 633 of the 1404 ankle fractures having concomitant OCLs[4, 27, 42, 55, 87, 111, 145, 158, 190, 198, 250, 255, 260, 329]. Thirty nine of these 633 lesions (6.2%) were described as solely chondral lesions according to grade 1 of their corresponding classification[27, 145, 190, 261].

Location of osteochondral lesions

Twelve studies reported on the location of the OCLs of which three studies described lesions on the talus, tibial plafond, medial malleolus and fibula[111, 198, 255]. A different four of the twelve studies described lesions on the talus and tibial plafond[42, 87, 145, 158], and the remaining five studies described lesions solely on the talus[27, 55, 190, 250, 329]. Figure 2 displays the location of OCL per osseous ankle structure. The incidence of OCLs after ankle fractures is 45.1%.

Table 2. Study and patient characteristics

Investigator	Year	Study design	Patient (n)	Fractures (n)	Male (n)	Female (n)	Mean age (yr)	Age range (±SD) (yr)	Method of diagnosis	Minors
Aktas et al.	2008	Retrospective	86	86	48	38	41.4	14-85 (±16.65)	Arthroscopical	8
Boraiah et al.	2009	Retrospective	153	153	64	89	51.8	NR	MRI	11
Cha et al.	2015	Retrospective	53	53	33	20	40.98	NR	Arthroscopical	8
Chan et al.	2016	Retrospective	254	254	106	148	45.1	NR	Arthroscopical	12
da Cunha et al.	2017	Retrospective	116	116	66	50	42.7	NR	Arthroscopical	10
Dawe et al.	2014	Retrospective	66	66	41	25	40	NR	Arthroscopical	10
Fuchs et al.	2015	Retrospective	42	42	NR	NR	NR	NR	Arthroscopical	10
Hintermann et al.	2000	Prospective	177	177	86	93	47.2	14-88 (±18.7)	Arthroscopical	11
Kortekangas et al.	2015	Prospective	48	48	30	18	NR	NR	MRI	11
Kraniotis et al.	2011	Prospective	21	21	13	8	35	NR	CT	13
Lambers et al.	2018	Retrospective	59	59	32	27	37	NR	CT	11
Loren et al.	2002	Prospective	48	48	29	19	35	NR	Arthroscopical	10
Nosewicz et al.	2016	Prospective	100	100	46	54	44	20-77 (±14)	CT	13
Ono et al.	2004	Prospective	105	105	59	46	45.9	NR	Arthroscopical	10
Regier et al.	2015	Retrospective	99	99	53	46	41.3	NR	MRI	12
Sorrento et al.	2000	Retrospective	50	50	NR	NR	44	NR	Intra-operative	5
Stufkens et al.	2010	Prospective	109	109	61	48	37.4	NR	Arthroscopical	14
Takao et al	2003	Prospective	92	92	61	31	31.4	18-47 (±8.7)	MRI + Arthroscopical	11
Ye et al.	2011	Prospective	16	16	13	3	37	NR	Intra-operative	8

Abbreviations: SD, standard deviation; MINOR, methodological index for nonrandomized studies; NR, not reported

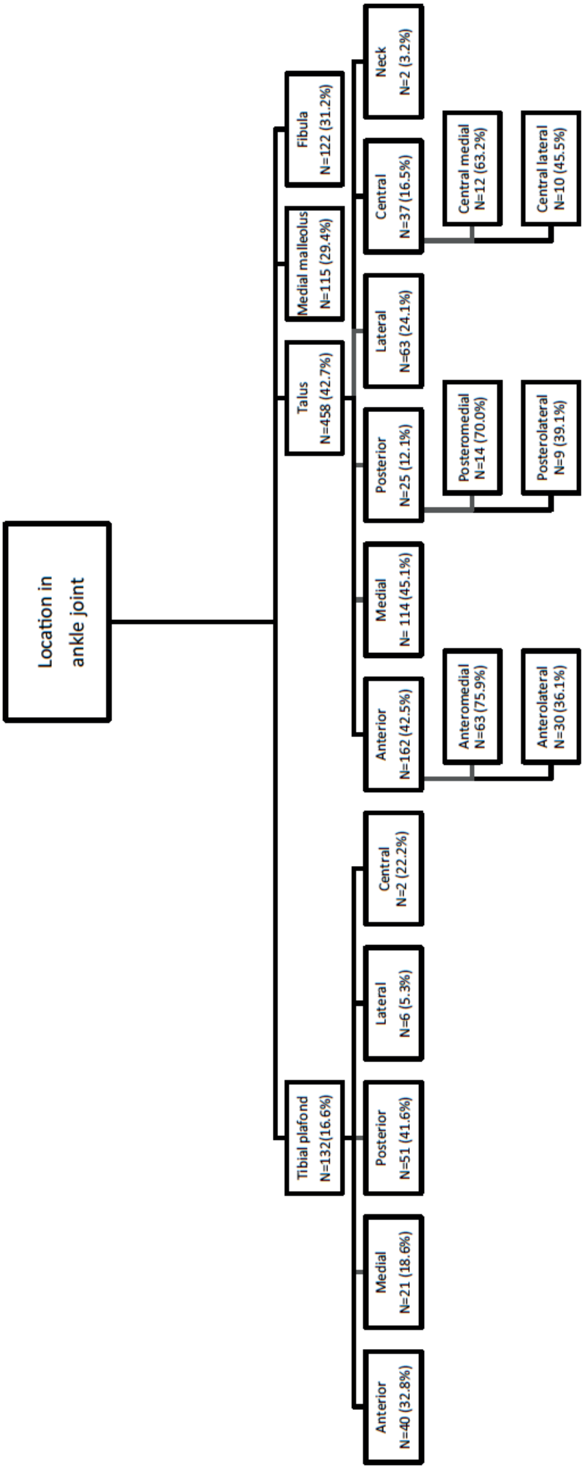

Figure 2. Location of OCL after ankle fractures

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Among all of the OCLs, the talus is the location with the highest incidence (42.7%), followed by the fibula (31.2%), medial malleolus (29.4%), and the tibial plafond (16.6%).

Fracture characteristics

All of the included studies used a type of fracture classification. The Lauge–Hansen was the most utilized fracture classification method and was described in eight of the twenty studies (40%)[27, 41, 55, 132, 198, 250, 329], followed by the Weber classification in three studies (20%)[87, 111, 255]. Three studies used both the Lauge-Hansen and Weber classifications (15%)[56, 158, 190]. Moreover, a combination of the Weber classification with the addition of classification according to isolated medial malleolar fracture, bi- or trimalleolar fracture was used in three studies (10%)[42, 58, 217]. Two studies (10%)[4, 136] classified fractures according to bimalleolar, trimalleolar and distal fibula fracture and one study (5%)[321] described fracture according to the Gustillo open fracture classification.

Fracture type and OCL incidence and location

Table 3 shows the OCL incidence and location per fracture classification (Danis–Weber[42, 87, 111, 158, 190, 255] and Lauge–Hansen[55, 158, 190, 198, 250, 329]). Furthermore, Figure 3 shows the OCL incidence per fracture classification. OCL incidence for Weber classification ankle type fractures was 50.0%, 49.6% and 52.1% for Weber A, B and C, respectively. In Lauge–Hansen ankle type fractures the OCL incidence was 43.4%, 41.6%, 25.0% and 19.0% for Lauge–Hansen supination external rotation (LH-SER), supination adduction (LH-SAD), pronation external rotation (LH-PER), pronation abduction (LH-PAB), respectively. Overall comparison showed no significant difference in OCL prevalence among Weber categories (n.s.), whereas a significant difference was observed among Lauge Hansen categories ($p = 0.049$). Post hoc pairwise comparisons between LH categories (with an adjusted significance level of 0.01) revealed no significant difference (n.s).

Direct evaluation versus late evaluation of OCLs after ankle fracture

The time-window between trauma and OCL assessment varied between direct evaluation and late evaluation. Whilst fourteen studies[4, 27, 42, 55, 87, 111, 145, 158, 190, 198, 250, 255, 261, 329] evaluated OCL directly after trauma or during primary surgery, six studies[41, 58, 132, 136, 217, 321] assessed OCLs postoperatively, with a mean duration between trauma and assessment varying between 12.3 months and 34.5 months.

Table 3 OCL incidence and location per fracture classification

	Total OCL incidence	Talar OCL	Location talar OCL	Tibial plafond OCL	Location distal tibia OCL	Medial malleolus OCL	Distal fibula OCL
Weber A	50.0% (17/34)	48.0% ($N=12$)	Anterior: 25.0% ($N=3$) Medial: 33.3% ($N=4$) Lateral: 41.7% ($N=5$)	24.0% ($N=6$)	Anterior: 50.0% ($N=3$) Medial: 16.7% ($N=1$) Posterior 16.7% ($N=1$) Lateral: 33.3% ($N=2$)	48.0% ($N=12$)	20.0% ($N=5$)
Weber B	49.6% (243/490)	40.7% ($N=189$)	Anterior: 16.4% ($N=76$) [ant-med 8.1% ($N=15$), ant-lat 5.4% ($N=10$)] Medial: 13.8% ($N=64$) Posterior: 4.1% ($N=19$) [post-med 6.5% ($N=12$), post-lat 2.7% ($N=5$)] Lateral: 6.7% ($N=31$) Central: 4.5% ($N=8$) Neck: 1.1% ($N=2$)	19.8% ($N=78$)	Anterior: 10.2% ($N=22$) Medial: 6.0% ($N=13$) Posterior: 15.3% ($N=33$) Lateral: 1.4% ($N=3$)	36.5% ($N=70$)	47.9% ($N=92$)
Weber C	52.1% (87/167)	49.0% ($N=74$)	Anterior: 22.9% ($N=33$) [ant-med 11.0% ($N=8$), ant-lat 1.4% ($N=1$)] Medial: 19.9% ($N=30$) Posterior: 1.3% ($N=2$) [post-med 1.4% ($N=1$), post-lat 1.4% ($N=1$)] Lateral: 6.6% ($N=10$) Central: 3.9% ($N=2$)	43.6% ($N=34$)	Anterior: 17.9% ($N=14$) Medial: 6.4% ($N=5$) Posterior: 20.5% ($N=16$) Lateral: 1.3% ($N=1$)	43.3% ($N=29$)	26.9% ($N=18$)
LH SER	41.6% (126/303)	28.2% ($N=61$)	Anterior: 1.3% ($N=2$) [Ant-med 1.4% ($N=1$); ant-lat 1.4% ($N=1$)] Medial: 8.9% ($N=14$) Posterior: 4.4% ($N=7$) [post-lat 4.2% ($N=7$), med-lat 5.6% ($N=3$)] Lateral: 17.7% ($N=28$)	5.2% ($N=3$)	N.A	1.7% ($N=1$)	10.3% ($N=6$)
LH PER	43.4% (33/76)	18.4% ($N=9$)	Medial: 15.6% ($N=5$) Posterior: 3.1% ($N=1$) [post-med 100% ($N=1$)] Lateral: 6.3% ($N=2$)	5.9% ($N=1$)	N.A	5.9% ($N=1$)	0% ($N=0$)
LH SAD	19.0% (4/21)	5.3% ($N=1$)	Medial: 100% ($N=1$)	5.3% ($N=1$)	N.A	5.3% ($N=1$)	5.3% ($N=1$)
LH PAB	25.0% (4/20)	15.8% ($N=3$)	Lateral: 25.0% ($N=1$)	0% ($N=0$)	N.A	0% ($N=0$)	0% ($N=0$)

N.A Not applicable

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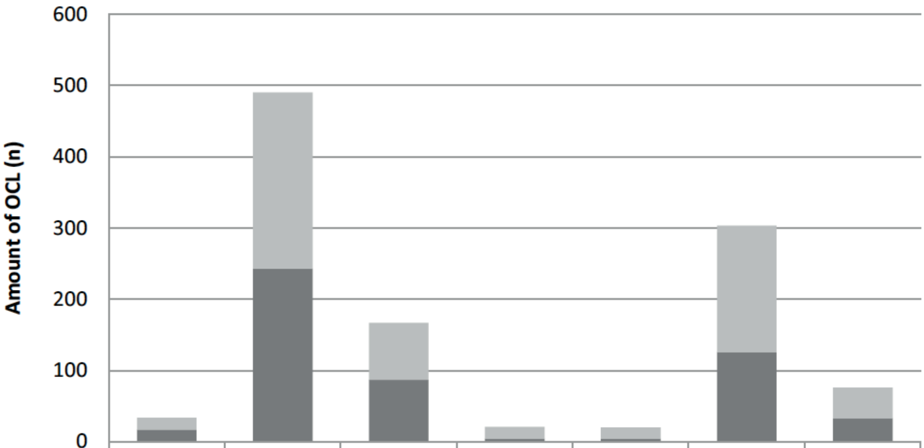

	Weber A	Weber B	Weber C	LH SAD	LH PAB	LH SER	LH PER
No OCL	17	247	80	17	16	177	43
OCL	17	243	87	4	4	126	33

Figure 3. OCL incidence shown per Danis-Weber and Lauge-Hansen classification

In total, 633 OCLs were found in 1404 ankle fractures which were assessed directly after trauma and during primary surgery, thus resulting in an OCL incidence of 45.1%. The OCL incidence of studies which evaluated OCLs more than 12 months after trauma (considered as late evaluation) was 47.5% (144 OCLs in 303 ankle fractures). Direct evaluation and late evaluation in OCL incidence were compared and evaluated by the same assessment mode as shown in (Table 4).

Table 4. Mode of assessment of OCL and OCL incidence

Mode of assessment	OCL incidence in direct evaluation	OCL incidence in late evaluation
Ankle arthroscopy	49.5% (406/821)	49.6% (59/119)
MRI	17.0% (26/153)	44.2% (65/147)
CT	12% (19/159)	86% (18/21)
MRI + ankle arthroscopy	70.7% (65/92)	N.A.

N.A. Not Applicable

DISCUSSION

The most important findings of the present review are, firstly, that the OCL incidence directly after ankle fractures is 45.1%. Secondly, it was seen that the most common location of OCLs after an ankle fracture was the talus; it being affected in 42.7% of the reported OCLs.

The OCL incidence ranged from 10 to 88% in the included studies. This broad range could indicate that different definitions, assessment methods and/or staging classifications were used to assess the OCL. Although the term OCL indicates that both the cartilage and the underlying subchondral bone are affected, it is possible that studies included chondral lesions or subchondral cysts under the heading of the definition of an Osteochondral Lesion. This would give rise to an overestimation of OCL incidence as eight studies did not discriminate between chondral and osteochondral lesions nor did they use a classification system. Staging classification systems are based on the assessment modality; i.e., intra-operative, MRI and CT based assessment. In our study, thirty-nine of the 633 lesions (6.2%) that were assessed directly after trauma were lesions according to grade one of their corresponding classification. On the other hand, an underrepresentation of OCL incidence may also be possible since our search contained ankle fractures and OCL, as well as surgical treatment of all ankle fractures. In addition, no studies were included reporting on the incidence of OCLs after conservative treatment of ankle fractures. It might, however, be important to assess both OCL and solely chondral lesions as a study by Stufkens et al. showed that ankle fractures with OCLs and deep chondral lesions of the talus and distal tibia negatively influence long-term results and is are independent predictors of posttraumatic ankle osteoarthritis[255].

Methods of diagnosing and assessing OCLs are by radiographs, CT and MRI. Arthroscopic assessment does not discriminate between purely chondral versus osteochondral lesions. This might explain the higher amount OCLs detected through arthroscopy compared to CT and MRI in our study, as both diagnostic methods clearly detect the osseous component[298]. The surrounding soft tissue and cartilage are best visualized by MRI, although that might give an overestimation of osteochondral extent due to bone-marrow oedema[289]. Another possibility of diagnosing an OCL is intra-operatively when utilising an arthroscopically-assisted ankle fracture fixation[44, 152]. Braunstein et al. was, to the best of our knowledge, the first researcher to conduct a RCT in which patients with ankle fractures were randomized into an intervention group (AORIF) or comparison group (ORIF), after which the subjective and functional outcome measurements were evaluated[30]. The 1-year follow-up showed that AORIF lead to good to excellent results in complex ankle fractures[31]. This is in line with previous articles published by Braunstein et al., Liu et al. and Lee et al.[29, 152, 156]. However, Fuchs et al. showed no significant functional outcome improvement in patients who underwent AORIF[87]. Another point of discussion is what the surgeon should do when detecting a (osteo)chondral lesion pre- or intra-operatively. Different treatment strategies are possible;

ranging from conservative treatment to debridement of the defect, and to bone marrow stimulation and fixation[71]. A recent study by Duramaz et al. found that microfracturing results in significantly more successful clinical results than debridement[71]. Future studies need to focus on identifying the golden surgical treatment option.

Location

Overall, the most common location of OCLs after ankle fractures was the talus with 42.7% of the OCLs being located here. The medial side was the most common sublocation of the talus, accounting for 45.1% of the talar OCLs, whilst the posterior aspect was the most common sublocation of the tibial plafond OCLs with 41.6% being located here. Only 25 lesions (12.1%) were found on the posterior aspect of the talus. This number could be the result of reporting bias since the OCLs assessed via an arthroscopy were solely performed anteriorly, thus leading to underestimation of posterior-sided talar OCLs. Multiple studies indicate that the occurrence of an OCL on the lateral or medial side of the talus depends on the trauma mechanism, of which medial OCLs usually indicate a mechanism of axial loading and torsional impaction[36, 39, 254]. The systematic review of Verhagen et al. studied the incidence of trauma-associated OCLs and their location, in which they found an incidence of 93% for lateral talar lesions and 61% for medial talar lesions[299]. Comparable findings on the incidence of OCLs in these specific locations were not observed in this review. This could be due to selection bias as not all of the included studies specified the location of talar dome lesions.

Fracture type and OCL incidence/location

Eight of the included studies used the Lauge–Hansen classification to classify ankle fractures. The rotational impaction factor in ankle fractures is embodied by the Lauge–Hansen classification[148]. Many studies have shown that Lauge–Hansen's fracture classification has a poor level of agreement among physicians as well as a poor interobserver correlation[8, 37, 270]. This could imply that classifying fractures according to Lauge–Hansen could lead to misinterpretation of the trauma mechanism and its consequences with regards to the analysis of fracture classification and location of the OCL.

Conflicting data have been reported regarding whether there is a significant difference in OCL incidence per fracture type in the Danis-Weber classification. Hintermann et al. reported a significantly higher OCL incidence in patients with a Weber C fracture compared to patients with a Weber B fracture[111]. On the other hand, both Fuchs et al. and Loren et al. found that there was no significant difference in OCL incidence between ankle fractures in the Danis-Weber classification[87, 158]. This is in line with the results of the present systematic review.

A number of previous studies have shown an association between the increase in OCL incidence and the severity of an ankle fracture[111, 217]. Leontaritis et al. found that the number of chondral lesions was significantly associated with more severe ankle fractures, such as Lauge-Hansen PER and SER[154]. In this study, a significant difference in Lauge-Hansen categories ($p = 0.049$) was found. However, post-hoc pairwise comparisons between Lauge-Hansen categories revealed no significant differences. The incidence of OCLs in SER and SAD ankle fractures was 42% and 19%, respectively. This demonstrates that rotational type ankle fractures show a higher incidence of OCLs, and encourages clinicians to be aware of possible OCLs when assessing these types of fractures fractures.

Direct vs. late assessment

The natural history of OCL and its treatment is described in many studies[17, 39, 83, 158, 172]. However, to the best of our knowledge, no study has been published regarding the healing process of OCLs after ankle fractures. This can be done by assessing the OCL during primary trauma surgery or preoperative radiographs and at the end of follow-up by the same modality. Our study suggests that the natural healing of OCLs is not common as the OCL incidence assessed more than 1 year (range 12.3–34.5 months) after surgery is 47.5% whilst the OCL incidence assessed directly after trauma or during primary surgery is 45.1%. However, it is unclear whether patients had symptomatic OCLs at follow-up and if the assessed OCL was the result of the initial ankle fracture. Interestingly, when studying the OCL incidence in CT-assessed OCLs, Kraniotis et al. found an incidence of 86% as measured by a CT arthrography scan at late evaluation[136]. This high OCL incidence was most likely due to the mode of assessment, as a CT-arthrography scan evaluates all lesions including cartilage erosions in the form of exposed subchondral bone.

There were a number of limitations in the present review. First, the heterogeneity in the diagnostic assessment methods, the classification systems of OCLs, the terminology, and the locational description of the OCLs. Second, there might have been an underestimation of the OCL incidence because the search excluded studies in which no mentioning was made of OCLs or their incidence after ankle fractures. In addition, there might have been an underestimation of solely chondral lesions since not all assessment methods are capable of detecting these lesions. Another limitation is that the MINORS scores ranged from 5 to 14 out of a total of 16. This was mainly due the retrospective nature of the included studies and the lack of blinding. The strengths of the present systematic review include the thorough search strategy, the comprehensive quality assessment of the included studies, the data checking by a second reviewer and the extensive contact with authors to retrieve more data as well as asking questions regarding published data and methodology.

The clinical relevance of the present systematic review is that it provides an overview of the incidence of OCLs and their location after ankle fractures. This means that the treating clinical team should pay close attention to the detection of concomitant OCLs in patients with ankle fractures by carrying out adequate pre-operative or intra-operative radiological assessment, or ankle arthroscopy. Hereafter, the team may choose to treat the concomitant intra-articular defect with adequate treatment. The outcomes of the present study will raise awareness to the trauma and orthopedic field of concomitant OCLs in acute ankle fractures and will facilitate the shared-decision making process by enhancing the knowledge on the prognosis and long-term outcomes of acute ankle fractures.

CONCLUSION

OCLs in association with acute ankle fractures are frequently seen, as demonstrated by the fact that 45.1% of patients also had an OCL at follow-up until 3 years after the initial trauma. The talus was found to be the specific location with the highest incidence of OCLs (42.7%) and the incidence of OCLs was significantly associated with rotational type ankle fractures.

PART III

TREATMENT OPTIONS FOR OSTEOCHONDRAL LESIONS OF THE TALUS. SALVAGE OR INTRINSIC HEALING?

5

No superior treatment for primary osteochondral lesions of the talus

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ABSTRACT

Purpose The purpose of this systematic literature review is to detect the most effective treatment option for primary talar osteochondral defects in adults.
Methods A literature search was performed to identify studies published from January 1996 to February 2017 using PubMed (MEDLINE), EMBASE, CDSR, DARE, and CENTRAL. Two authors separately and independently screened the search results and conducted the quality assessment using the Newcastle–Ottawa Scale. Subsequently, success rates per separate study were calculated. Studies methodologically eligible for a simplified pooling method were combined.
Results Fifty-two studies with 1236 primary talar osteochondral defects were included of which forty-one studies were retrospective and eleven prospective. Two randomized controlled trials (RCTs) were identified. Heterogeneity concerning methodological nature was observed, and there was variety in reported success rates. A simplified pooling method performed for eleven retrospective case series including 317 ankles in the bone marrow stimulation group yielded a success rate of 82% [CI 78–86%]. For seven retrospective case series investigating an osteochondral autograft transfer system or an osteoperiosteal cylinder graft insertion with in total 78 included ankles the pooled success rate was calculated to be 77% [CI 66–85%].
Conclusions For primary talar osteochondral defects, none of the treatment options showed any superiority over others.
Level of evidence IV

INTRODUCTION

A talar osteochondral defect (OCD) is a combined lesion of the subchondral bone and its overlying cartilage and often has a severe impact on the quality of life of active patients[327]. The general consensus is that bone marrow stimulation (BMS) is administered for primary smaller defects. Other surgical options are internal fixation, osteochondral autograft transfer systems (OATS), chondrocyte implantation, retrograde drilling, metal resurfacing, total ankle prostheses or arthrodesis[93, 126, 285].

The effectiveness of the interventions varies greatly in the literature, and although a number of previous systematic reviews have been conducted, a definite treatment option regarded as the golden standard has yet to be identified[67, 159, 188, 272, 326]. Additionally, prior systematic reviews either investigated sole treatment options or did not distinguish between primary and non-primary talar defects[67, 159, 188, 326]. Therefore, this could introduce a mis-presentation of the reported success rates. Furthermore, the most comprehensive review by Zengerink et al. included articles published up to 2006[326]. Since then, a high number of articles investigating novel interventions for talar OCDs have been published[153, 206, 207, 276]. The aim of the present review is therefore to examine and compare the clinical effectiveness of all treatment strategies for exclusively primary talar OCDs in adults. The hypothesis is that no significant differences considering clinical outcome of these different treatment strategies are to be found. This study presents novel findings and gives novel insight into the clinical effectiveness of treatment strategies for primary talar osteochondral defects exclusively.

MATERIALS AND METHODS

The systematic review was prospectively registered at the PROSPERO register[46].

Search strategy

Electronic databases PubMed (MEDLINE), EMBASE, CDSR, DARE and CENTRAL were screened from January 1996 to February 2017 for potential suitable articles (Appendix II). This time frame was chosen as by 1996 the arthroscopic techniques for treating talar OCDs were fully developed and established in the orthopaedic field[290]. The full search strategy for all electronic databases is outlined in Appendix II. Backward citation chaining strategy was applied as an additional search technique.

Eligibility criteria and study selection (Figure 1)

Suitable randomised controlled trials (RCT) and observational studies assessing the effectiveness of all treatment strategies for primary talar OCDs in the adult patient population were included in the present study. The rationale for including non-randomised clinical studies is based on the substantial presence of the low-quality evidence research into talar osteochondral defects that has been conducted over the past two decades. The exclusion criteria for our review are presented in Table 1. When necessary, authors were contacted to provide separate data for patients with primary lesions only and/or for patients ≥18 years old. When no reply was reported, contact was sought by two reminder e-mails. If no response was recorded, the specific article was excluded. Independent evaluation of the articles and a subsequent discussion were performed by two reviewers (J.D. and K.L.) after title, abstract screening and full-text reading. In case of any disagreement after discussion, the opinion from an independent third investigator (G.K.) was decisive. Studies were not blinded for author, affiliation or source, and no limitations were put on language and publication status. The literature selection algorithm according to the preferred reporting items for systematic reviews and meta-analyses (PRISMA) is presented in Figure 1[155].

Table 1. Exclusion criteria

Exclusion criteria	No. of studies
Non-primary OCDs	91
<5 patients	20
Age: <18 years old	17
Patient overlap	14
Treatment inappropriately described	13
Combination of diagnoses (bipolar, fracture etc.)	13
Combination of treatment groups and/or no separate data per group	8
Follow-up <6 months	2
Interpretable data not available	2
Asymptomatic lesion	1
Total no. of excluded studies	**181**

Some publications were excluded due to a combination of reasons

Critical appraisal

A for-talar-OCD-modified Newcastle-Ottawa Scale (NOS) was utilised to assess the methodological quality (Appendix III). Each included study was graded on methodological quality by two independent reviewers (J.D. and K.L.). When there was no agreement on the number of stars graded, assessment by an independent third investigator (G.K.) was decisive.

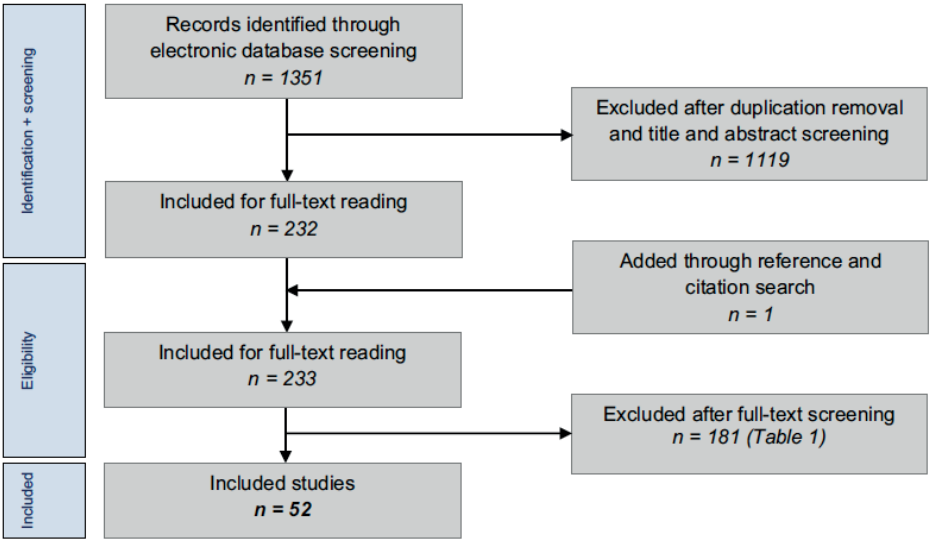


Figure 1. Literature selection algorithm—preferred reporting items for systematic reviews and meta-analyses (PRISMA)

Data extraction

By means of a standardised extraction form, data from the articles were extracted on study characteristics. Data on patient characteristics were retrieved and included age, gender, number of patients and ankles, symptom duration, location, side, size and stage of the defect according to a specifically reported OCD classification system, clinical scoring system utilised, history of ankle trauma and follow-up duration. Pre-operative and post-operative clinical outcome scores were extracted on mean scores, subjective satisfaction and number of patients treated successfully. The treatment strategy in question was defined to be successful when a good or excellent result at follow-up was reported, in combination with an accepted scoring system. The results were incorporated into the scoring system of Thompson and Loomer (Appendix IV) when separate patient data were available though no success rates of specific treatment strategies were included[269]. An ankle was considered to be successfully treated when at latest follow-up a post-operative AOFAS score at or above 80 was reached[130]. In case of the FAAM (Foot and Ankle Ability Measure) score, a percentage of 80 or higher was regarded to be a successful treatment[168].

Statistical and data analysis

In case of identifying studies with highly differing methodological natures, a formal meta-analysis will not be performed. It will be decided upon visualising the results per study by means of a forest plot. If possible, a simplified pooling method will be used to combine data from different studies describing the results of similar treatment groups research by means of analogous methodologies. 95% binomial proportion confidence intervals for the success percentages of each study and the pooled studies will be calculated with the Wilson score interval and included in the forest plots *(CIA, Confidence Interval Analysis for Windows, version 2.2.0)*[35].

RESULTS

Search results

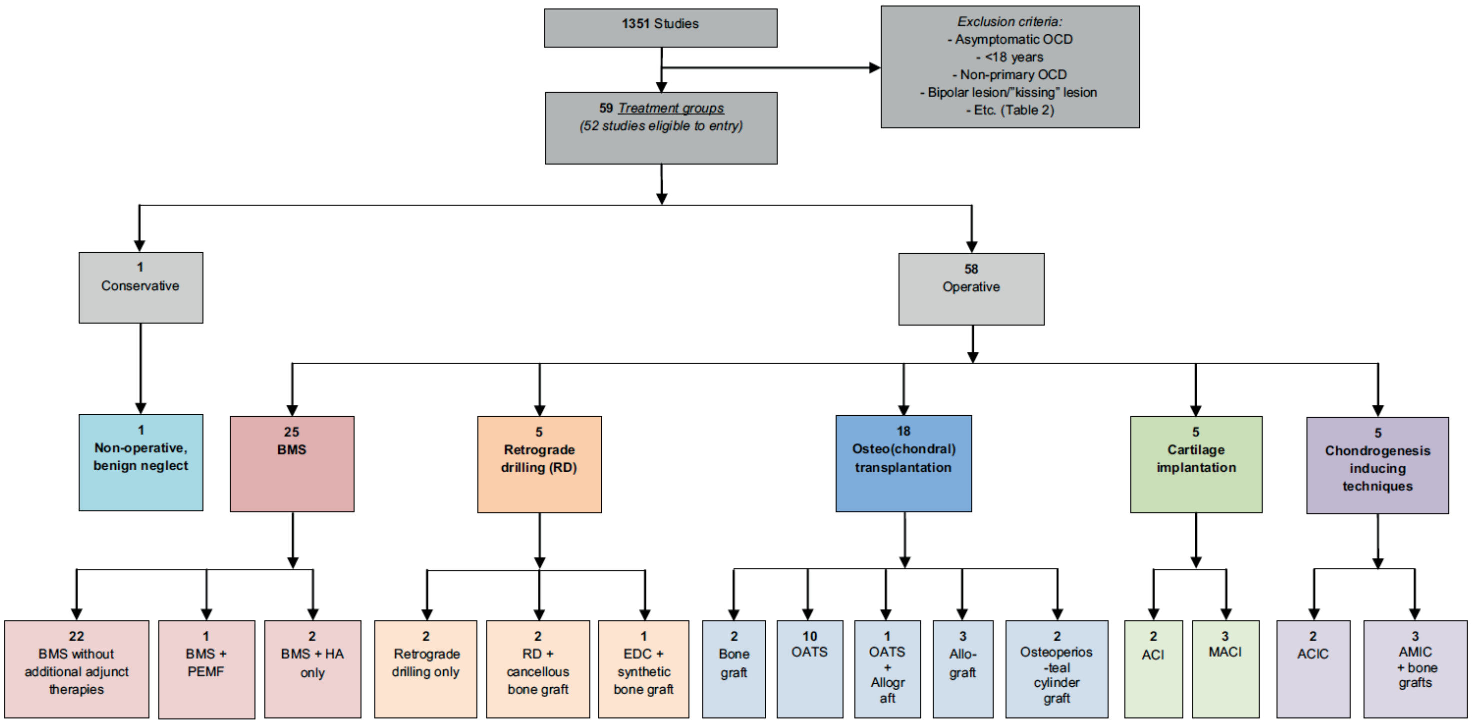
The literature search yielded 1351 articles, and after title and abstract screening, 232 potentially suitable articles were included for full-text reading (Figure 2). One study was added through reference and citation search. In total, 127 authors were contacted to request data according to our inclusion criteria. Subsequently, 33 studies could be included and 31 had to be excluded attributable to the extensive author contact process. In total, 181 publications had to be excluded due to a variety and combination of reasons (Table 1). This left 52 studies in total.

After screening and discussion between the first two authors there was overall consensus in all cases except for four where disagreement persisted. These were resolved by discussion with the senior author (G.K.). Full consensus was reached between the reviewers regarding grading of methodological quality.

Evaluation of the characteristics of included studies

A total of 1236 primary talar OCDs were included in the 52 studies. The average age was 36 [range 18–77], and the percentage of females and males was 34 and 66%, respectively. The right ankle was involved in 54% of the cases and the left ankle in 46%. The percentages of medial, lateral, central and combined medial and lateral location involvement were 77, 21, 2 and 0.4%, respectively. In 71% of the patients, a history of ankle trauma was reported. The most frequently used clinical scoring system and osteochondral damage classification system were the AOFAS and the Berndt and Harty Classification system, respectively[24, 130]. In total 25 different types of clinical scoring systems (Table 2)[14, 15, 24, 40, 70, 88, 103, 109, 130, 141, 161, 164, 168, 172, 183, 184, 191, 195, 222, 231, 242, 263, 266, 305] and 18 different utilised osteochondral damage classification systems were found (Table 3)[11, 24, 34, 63, 69, 81, 92, 100, 110, 165, 176, 191, 213, 236, 237, 291].

Data were extracted on the combined Berndt and Harty[24] and Loomer[157] stages for 257 ankles: there were 56 (22%), 68 (27%), 70 (27%), 37 (14%) and 26 (10%) Berndt and Harty stage I, II, III, IV and V cases, respectively. Lastly, the mean of the follow-up time ranged from 6 to 143 months.



>**Figure 2.** Flow chart of study inclusion and treatment of talar OCDs between 1996 and 2017. ACI autologous chondrocyte implantation, ACIC autologous collagen-induced chondrogenesis, AMIC autologous matrix-induced chondrogenesis, RD retrograde drilling, BMS bone marrow stimulation, MACI matrix-associated chondrocyte implantation, OATS osteochondral autograft transfer system, HA hyaluronic acid, PEMF pulsed electromagnetic fields, ECD endoscopic core decompression

Table 2. Clinical scoring systems utilized for treatment of talar OCDs and associated knee scores in case of implantation techniques

Clinical Scoring system	No. of studies
AOFAS Ankle/Hindfoot scale	43
VAS (Visual Analog Scale)	27
Patient Satisfaction Score	17
Tegner score	3
Short Form-36	4
Hannover score	3
Freiburg Ankle Score	3
Criteria Proposed by Berndt and Harty	3
Ogilvie Harris Score	3
Ankle Activity Score	2
Modified Cinicinnati Knee Rating System	2
Hospital of Special Surgery Patella Score	2
Clinical Evaluation proposed by Shearer and Loomer	1
RTA (Return to Activity)	1
NRS (Numeric Rating Scale for pain and satisfaction)	1
Saxena Criteria	1
FAAM (Foot and Ankle Ability Measure)	1
McCullough Score	1
Foot Functioning Index	1
MODEMS AAOS Foot and Ankle Follow-up Questionnaire	1
IKDC Subjective and Objective Knee Evaluation Form	2
Modified Cincinnati Knee Documentation Rating	1
Bandi Knee Global Assessment Score	1
Lysholm	1
Foot and Ankle Disability Index (FADI)	1

Some studies utilized >1 scoring system

Methodological quality

The fifty-two publications altogether scored 182 stars out of maximum 260 stars (Table 4). Forty-one studies were assessed to be retrospectively conducted, and all studies except for two were conducted according to the study protocol. Therefore, all studies together scored a total number of 65 stars (max. = 104) on study design. Regarding the selection procedure, 43 out of 52 stars were scored in total, indicating that most studies reported a representative talar OCD patient population. Seventy-four out of 104 stars were scored on the outcome part of the adjusted Newcastle–Ottawa Scale. Independent blind assessment was performed in none of the studies, and in all except for one study outcome was assessed through record linkage. Numerical star outcomes on adequacy of follow-up of series were not uniform across the included studies.

Treatment strategies

The different treatment strategies were divided into six corresponding treatment groups. It was deemed methodologically appropriate to perform a simplified pooling method for the largest groups of those publications with corresponding methodological nature (i.e.

Table 3. Classification systems utilized for osteochondral damage staging assessment

Classification Systems	No. of studies
Berndt and Harty Classification System	16
MOCART	8
International Cartilage Repair Society (ICRS)	8
Hepple et al.	5
Ferkel and Cheng	3
Anderson et al.	3
Dipaola et al.	3
Outerbridge Classification System	2
Bristol Classification System	2
Osteoarthritis Classification system	1
Sefton Articular Stability Scale	1
Pritsch Classification System	1
FOC (Fracture, Osteonecrosis, Cyst)	1
Takakura Radiologic Arthrosis Clssification System	1
Giannini Classification System	1
Scranton and McDermott Classification System	1
Mintz et al.	1
Guhl	1

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

retrospective case series together) in the groups of BMS and osteo(chondral) transplantation—more specifically OATS and an osteoperiosteal cylinder graft insertion. No studies describing a mosaicplasty procedure were included in this pooling group as mosaicplasty uses multiple graft insertion procedures applied for the treatment of larger talar defects which is in contrast to the classic OATS procedure. Consequently, pooling the mosaicplasty studies was not appropriate. The forest plot describing the clinical results in percentages per separate study in their corresponding treatment group is presented in Figure 3, and the forest plot describing the results of the simplified pooling method is presented in Figure 4.

Table 4. Table presenting the separate results of the adjusted Newcastle-Ottawa Scale

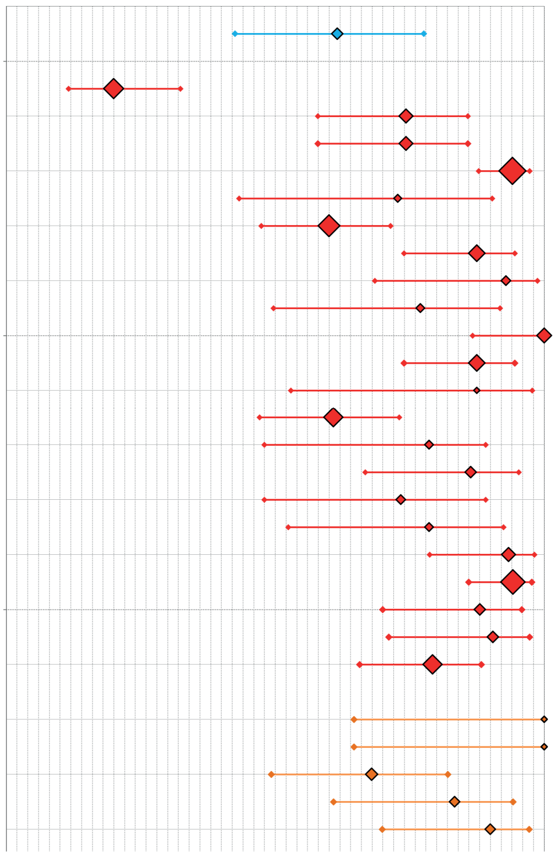
Category in question	Number of stars	Maximum number of stars	Proportion
Study design	65	104	65/104 = 63%
Selection	43	52	43/52 = 83%
Outcome	74	104	74/104 = 71%
Total	182	260	182/260 = 70%

Non-operative

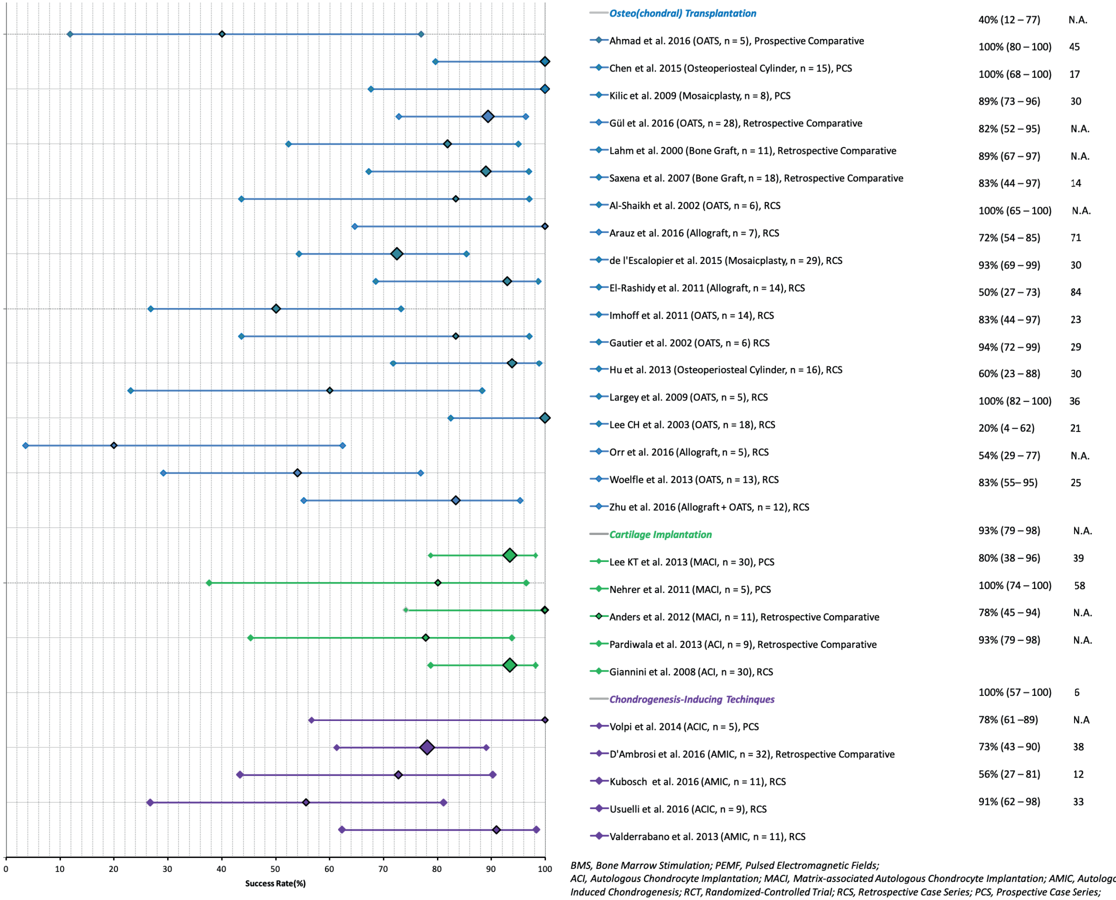
The objective of non-operative treatment is to unload the damaged cartilage potentially resolving accumulated oedema within the joint.

One retrospective case series study investigated solely chronic-type V cystic lesions as classified by Loomer et al.[157, 242]. Non-operative treatment consisted of continuation of activities "as tolerated"[242]. Mean symptom duration, mean follow-up, patient satisfaction scores and preoperative OCD size could not be recorded. Eventually, in 16 out of 26 patients conservative treatment yielded successful results, which corresponded to a success rate of 62% [CI 43–78%] (Figure 3)[242].

Forest Plot of the Success Rates of the Included Studies



Studies	Success Rate (95% CI)	Follow-up (months)
Conservative		
Shearer et al. 2002 (n = 26), RCS	62% (43 – 78)	N.A.
BMS		
Doral et al. 2012 (BMS +/- HA, n = 55) RCT	20% (12 – 32)	N.A.
Reilingh et al. 2016 (BMS +/- PEMF, n = 35), RCT	74% (58 – 86)	13
Shang et al. 2015 (BMS +/- HA, n = 35), Prospective Cohort	74% (58 – 86)	11
Lee KB et al. 2015 (BMS, n = 102), Prospective Cohort	94% (88 – 97)	48
Takao et al. 2010 (BMS, n = 11), Retrospective Cohort	73% (43 – 91)	N.A.
Goh et al. 2015 (BMS, n = 60), PCS	60% (47 – 71)	N.A.
Yoshimura et al. 2013 (BMS, n = 40), PCS	88% (74 – 95)	N.A.
Becher et al. 2005 (BMS, n = 14), PCS	93% (69 – 99)	N.A.
Pardiwala et al. 2013 (BMS, n = 13), Retrospective Comparative	77% (50 – 92)	N.A.
Saxena et al. 2007 (BMS, n = 25), Retrospective Comparative	100% (87 – 100)	N.A.
Choi et al. 2015 (BMS, n = 40), Retrospective Comparative	88% (74 – 95)	38
Baker et al. 1999 (BMS, n = 8), RCS	88% (53 – 98)	125
Cuttica et al. 2011 (BMS, n = 51), RCS	61% (47 – 73)	N.A.
Domayer et al. 2011 (BMS, n = 14), RCS	79% (48 – 89)	55
Jung et al. 2011 (BMS, n = 22), RCS	86% (67 – 95)	32
Kuni et al. 2012 (BMS, n = 15), RCS	73% (48 – 89)	N.A.
Mendicino et al. 1998 (BMS, n = 14), RCS	79% (52 – 92)	34
Ming et al. 2004 (BMS, n = 30), RCS	93% (79 – 98)	63
Polat et al. 2016 (BMS, n = 69), RCS	94% (86 – 98)	106
Sallakh et al. 2012 (BMS, n = 25), RCS	88% (70 – 96)	32
Tao et al. 2014 (BMS, n = 21), RCS	91% (71 – 97)	19
van Bergen et al. 2013 (BMS, n = 48), RCS	79% (66 – 88)	130
Retrograde Drilling		
Beck et al. 2016 (Endoscopic Core Decompression, n = 7), PCS	100% (65 – 100)	24
Takao et al. 2010 (RD + Bone Graft, n = 7), Retrospective Cohort	100% (65 – 100)	N.A
Anders et al. 2012 (RD Only, n = 28), Retrospective Comparative	68% (49 – 82)	28
Lahm et al. 2000 (RD + Bone Graft, n = 18), Retrospective Comparative	83% (61 – 94)	N.A.
Geerling et al. 2009 (RD Only, n = 20), RCS	90% (70 – 97)	25



BMS, Bone Marrow Stimulation; PEMF, Pulsed Electromagnetic Fields;
ACI, Autologous Chondrocyte Implantation; MACI, Matrix-associated Autologous Chondrocyte Implantation; AMIC, Autologous-Matrix Induced Chondrogenesis; RCT, Randomized-Controlled Trial; RCS, Retrospective Case Series; PCS, Prospective Case Series;

Figure 3. Forest plot of all included studies with the success rates and the corresponding 95% confidence interval per separate study *(sorted on treatment strategy group, methodological quality and alphabetical order accompanied by number of ankles and mean follow-up duration; the size of the diamond representing the success rate is adjusted for the number of ankles included in the publications)*

Bone marrow stimulation (debridement and/or drilling)

BMS consists of debriding the OCD after which additional microfracturing or antegrade drilling can be performed establishing openings into the subchondral bone. This disrupts intraosseous vessels introducing blood and bone marrow cells into the OCD allowing a clot of scar tissue to form resulting in fibrocartilaginous tissue. Supplementary, one can administer hyaluronic acid (HA) injections acting as a synovial lubricator targeting pain levels and inflammatory cytokine concentrations[180, 257]. Another possibility is the use of pulsed electromagnetic fields (PEMF)[1, 28, 51, 197, 227, 300].

Twenty-two studies describing the results of BMS for 747 ankles were identified[13, 19, 47, 53, 65, 68, 98, 123, 140, 151, 174, 175, 204, 211, 222, 228, 231, 241, 259, 262, 281, 323]. There were two RCTs, two prospective cohort studies and one retrospective cohort study, three prospective case series, three retrospective comparative studies and eleven retrospective case series. This shows the great heterogeneity in methodological nature of the studies within this group. The means of the symptom duration of these studies ranged from 4 to 49 months, and the range of the means of the follow-up duration in months was as follows: 10–143 months (Figure 3). For 194 ankles data on Berndt and Harty staging could be extracted: 23, 31, 33 and 13% were affected by stage I, II, III and IV lesions, respectively[13, 47, 151, 175]. The means of the pre-operative size of the talar OCD ranged from 1.0 to 1.7 cm2[47, 151, 211, 231, 241, 262]. The success percentages of the separate studies corresponding to the BMS group ranged from 20 to 100% [CI 12–100%] (Figure 3)[13, 19, 47, 53, 65, 68, 98, 123, 140, 151, 174, 175, 204, 211, 222, 228, 231, 241, 259, 262, 281, 323]. There were eleven studies within the BMS group that all investigated the patients in a retrospective case series setting, making it methodologically appropriate to perform a simplified pooling method for this subgroup[13, 53, 65, 123, 140, 174, 175, 211, 228, 262, 281]. It contained 317 talar OCDs yielding a pooled success rate of 82% [CI 78–86%] (Figure 4).

Retrograde drilling

Retrograde drilling (RD) is a non-transarticular procedure preventing injury to the articular cartilage. Consequently, the technique is primarily used when defects contain a relatively small amount of articular cartilage damage or when it is challenging to reach the OCD via the common arthroscopic portals. The aim is to revascularise the subchondral bone and induce novel bone formation. Additional procedures one can administer are cancellous bone grafts.

Five studies with a total of 80 ankles having undergone retrograde drilling were identified[10, 20, 90, 141, 259]. One prospective case series, one retrospective cohort study, one retrospective case series and two retrospective comparative studies were identified. Therefore, due to the heterogeneity this did not allow for pooling. Furthermore, concerning symptom duration, Berndt and Harty staging and sizes of the talar OCDs, there was insufficient information to provide data on ranges of means reported in the cited literature. The range of the means of follow-up duration was 24–28 months (Figure 3). The success percentages in this treatment group ranged from 68 to 100% [CI 49–100%] (Figure 3)[10, 20, 90, 141, 259]. Included in this range were two studies that implemented cancellous bone grafting additional to retrograde drilling with mean success rates ranging from 83 to 100% [CI 61–100%] and two studies that performed retrograde drilling (range 68–90%, CI 49–97%, Figure 3)[10, 90, 141, 259]. One study by Beck et al. investigated a transtalar endoscopic core decompression combined with the injection of synthetic osteoconductive bone graft substitute[20]. It included 7 patients and yielded a success rate of 100% (Figure 3) [CI 65–100%].

Osteo(chondral) transplantation

A number of osteo(chondral) transplantation techniques exist to treat talar OCDs: osteochondral autograft transfer systems (OATS), mosaicplasty, (autogenous) bone grafting, autologous osteoperiosteal cylinder grafting and an osteochondral allograft transfer. The procedures consist of debriding the degenerated cartilage, the fibrous tissue and the necrotic subchondral bone, after which the osteo(chondral) grafts are harvested and subsequently implemented into the remaining OCD. The aim is to achieve a higher-quality restoration of the functional unit of the subchondral bone plate including the articular cartilage.

Eighteen studies were identified, which included a total of 230 primary OCDs[3, 5, 43, 60, 74, 89, 101, 115, 118, 127, 141, 147, 149, 200, 231, 316, 319, 330]. There were two prospective case series, one prospective comparative study, three retrospective comparative studies and twelve retrospective case series. This did not allow for subsequent overall osteo(chondral) transplantation group pooling. It was not possible to extract sufficient information on the symptom duration, patient subjective satisfaction scores and staging of the defect. The range of the means of the follow-up duration was 14–84 months, and the range of the means of the sizes per particular study 1.0 to 2.4 cm2 [5, 43, 74, 89, 101, 127, 149, 200]. The range of the success percentages per study for the treatment strategy group of osteo(chondral) transplantation was 20 to 100% [CI 4–100%] (Figure 3) [3, 5, 43, 60, 74, 89, 101, 115, 118, 127, 141, 147, 149, 200, 231, 316, 319, 330]. The range of the means of the success percentage per separate publication for the OATS group was 40–100% [CI 12–100%] (Figure 3), for the mosaicplasty group 72–100% [CI 54–100%] and for one study that combined an OATS and an allograft procedure it was 83% [CI 55–95%] (Figure 3)[3, 5, 60, 89, 101, 118, 127, 147, 149, 316, 330]. After extracting data on donor-site morbidity of 93 primary and secondarily treated talar OCDs by OATS, it became clear that 32% of the participants showed some form of donor-site knee joint morbidity[3, 5, 60, 89, 147, 149]. Two studies including 31 ankles researched an osteoperiosteal cylinder graft and reported mean success percentages of 94–100% [CI 72–100%] (Figure 3)[43, 115]. Three studies—with in total 19 ankles—investigated the clinical effectiveness of a fresh allograft transplantation, and the success rates ranged from 20 to 100% [CI 4–100%][74, 200, 319]. Additionally, there were two studies performing implementation of cancellous bone grafting into 29 debrided talar OCDs[141, 231]. In this group the success rate ranged from 82 to 89% [CI 52–97%] (Figure 3). It was possible to perform a simplified pooling method for those studies with a retrospective case series setting investigating an OATS procedure and an osteoperiosteal cylinder graft procedure, and this group of 78 treated talar OCDs yielded a pooled success rate of 77% [CI 66–85%] (Figure 4)[5, 89, 115, 118, 147, 149, 316].

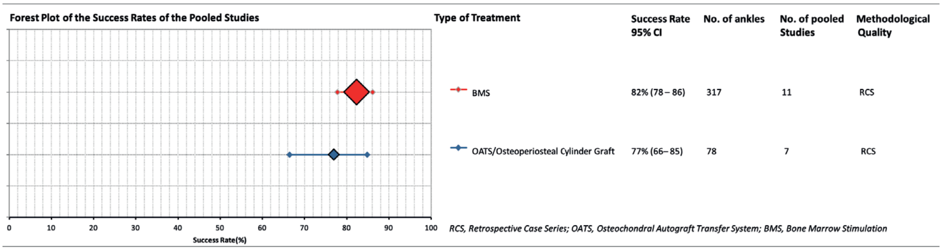


Figure 4. Forest plot of the pooled success rates of different treatment strategies with the corresponding 95% confidence intervals *(accompanied by the total number of ankles and total number of studies included in the pooled group, and the corresponding methodological quality; the size of the diamond representing the pooled success rate is adjusted for the number of ankles included)*

Cartilage implantation

Cartilage implantation techniques aim at regenerating tissue with hyaline-like type II cartilage. Generally, in two-step procedures viable chondrocytes are isolated from a donor site, after which the chondrocytes are cultivated and expanded in a laboratory medium. The cultured chondrocytes are then implanted into the excised lesion. When applying the ACI procedure, a periosteal tissue cover is used after expansion of isolated chondrocytes, whereas MACI replaces the periosteal cover by a collagen type 1–3 or Hyalograft C membrane[92]. The latter has the advantage that there is no need for an additional donor site and potentially delivers more viable cells to the OCD[177].

Five studies including 85 ankles investigating cartilage implantation were identified[9, 94, 153, 187, 204]. Two prospective case series, two retrospective comparative studies and one retrospective case series were included in this group. The authors decided not to perform a simplified pooling method. There was insufficient homogeneity and substantial missing data to report mean symptom duration, patient subjective satisfaction scores and staging of the defect. Concerning follow-up duration, it was possible to extract data from two studies, yielding a range of the means of follow-up of 39–58 months (Figure 3)[9, 187]. From four studies information on talar OCD size could be extracted, which yielded a range of 1.6–1.9 cm2 [9, 94, 153, 187, 204]. The success rate ranged from 78 to 100% [CI 45–100%] (Figure 3). From these five studies, there were two investigating ACIs[94, 204]. The range of the success rate was 78–93% [CI 45–98%] (Figure 3). The other three publications performed a MACI procedure with a total of 46 ankles, and the success percentages ranged from 80 to 100% [CI 38–100%] as illustrated in Figure 3[10, 153, 187].

Chondrogenesis-inducing techniques (CITs)

CITs aim at the repair of a bone-cartilage lesion by means of a combined single-step procedure and can be applied for larger, cystic OCDs[21, 22]. The goal is to induce chondrogenesis, and in case of an adjusted autologous matrix-induced chondrogenesis (AMIC) procedure, spongiosa bone—rich in mesenchymal stem cells—is implanted into the defect[38]. Thereafter, an acellular collagen I/III matrix is glued onto the defect. In case of an autologous collagen-induced chondrogenesis (ACIC) procedure, the debrided defect is filled with a mixture of synthetic fibrin glue and collagen gel-based matrix.

Five publications describing the results of 68 ankles treated by CIT were identified[54, 138, 275, 276, 301]. One study was a prospective case series, one was a retrospective comparative study, and the other three were retrospective case series, which discouraged pooling. There was no sufficient data to allow a presentation of the symptom duration, patient subjective satisfaction scores, staging and sizes

of the defect. The range of the means of follow-up duration was 6–38 months (Figure 3). The range of the success rate was 56–100% [CI 27–100%] (Figure 3)[54, 138, 275, 279, 301]. For the AMIC procedures, the range of success percentages was 73 to 91% [CI 43–98%] (Figure 3)[54, 138, 279]. Volpi et al. and Usuelli et al. described the results of ACIC, and the means of the success rate ranged from 56 to 100% [CI 27–100%] (Figure 3)[275, 301].

DISCUSSION

To the best of our knowledge, this is the first systematic review investigating the effectiveness of all treatment options for solely primary talar OCDs in adults. The most important finding of the present study is that although aiming at the application of the most appropriate and complete methodology, none of the interventions showed any definite clinical superiority over the others. This was caused by the observed heterogeneity in methodological nature of the studies and the variety in success rates, both intra-treatment strategy group-wise and inter-treatment strategy groupwise. Additionally, performing a simplified pooling method for retrospective case series studies in the BMS group and in the osteo(chondral) transplantation group yielded comparable pooled success rates.

The main finding is partially in contrast to the one derived from the research by Zengerink et al. which concluded that BMS is the most effective treatment strategy for talar OCDs[326]. This systematic review from 2010, however, included both primary and non-primary talar OCDs, which potentially affected the results and the conclusions based on them. It should be acknowledged that the most important finding of the present study was not a consequence of the methodology, as it aspired to include as many suitable articles as possible by not excluding particular treatment strategies —in contrast to previous reviews[67, 188]— and by adhering to a strict author contact protocol.

BMS was the most studied intervention for primary talar OCDs indicating that it is the most frequently practised treatment option for primary talar OCDs worldwide. This is due to the fact that BMS is a relatively inexpensive intervention compared to implantation techniques, has low morbidity, a quick recovery and a fast return to sports. This was shown by studies conducted by Saxena et al. and Reilingh et al. presenting return to sports times ranging from 15 to 17 weeks[222, 231]. The two most recent systematic reviews on BMS reported success rates of 80 and 86%[67, 326]. When pooling eleven BMS studies, a pooled success rate of 82% was calculated [CI 78–86%] (Figure 4). As this success rate is comparable to the success rate of the pooled retrospective case series design studies in the osteo(chondral) transplantation group describing the results of OATS and an osteoperiosteal cylinder graft insertion (77% [CI 66–85%]), it is difficult to assess which surgical treatment strategy is clinically superior, thereby supporting the most important finding of the present study. Important factors play a vital role in the success of the clinical outcome after BMS. BMS does not aim at preserving a hyaline cartilage layer but rather promotes the formation of a fibrin clot subsequently becoming fibrocartilage or cartilage/collagen type I, which may then decrease in quality over time, resulting in osteoarthritic changes[160, 192, 194]. Moreover, research indicates that deterioration of the natural congruency of the ankle joint occurs as cartilage type I demonstrates inferior wear characteristics in comparison with hyaline cartilage (cartilage/collagen type II) being associated with the degradation of a repaired articular surface[166, 214, 255]. However, long-term studies have not yet confirmed this[81, 281]. A clear correlation between inferior clinical outcomes and follow-up duration concerning the included studies in this review was not observed either, possibly due to the fact that it was not possible to gather data on mean follow-up durations from all included studies. Concerning pre-operative size and clinical outcome after BMS, a study from Choi et al. including 120 primary ankles indicated that there is a definite cut-off point, that is, 1.5 cm2, as a prognostic influence on the risk of clinical failure[49]. A more recent study by Ramponi et al. shows that the cutoff point might be lower, around the size of 107 mm2[216]. In our review, the range of the means of the reported pre-operative size for the BMS studies was 1.0 to 1.7 cm2 suggesting that BMS is indeed administered for smaller primary defects. The reported success rates of BMS therefore suggest that BMS could be regarded as a fair treatment strategy for the smaller primary defects.

As an alternative to BMS, a number of treatment options have focused on preserving hyaline cartilage and treating larger defects. The consensus that most of these interventions are considered as suitable treatment options when primary surgery to the OCDs has failed explains why there was a relatively lower number of patients included in these particular treatment groups. Furthermore, a number of publications on the osteochondral autograft system had to be excluded. Studies by Hangody et al. and Fraser et al. have yielded promising results, but were excluded as legal cases needed to be reopened for data provision[86, 106].

Interestingly, only one study described the results of non-operative treatment implying that since 1996 studies have focused on developing novel surgical treatment options[242]. Likely, this is due to the poor success rates of non-operative treatments reported before 1996[25, 225]. Although only twenty-six conservatively treated ankles were included in our review—with a success percentage of 62% [CI 43–78%]—it is still recommended that initial treatment of symptomatic OCDs should consistently commence with a conservative protocol.

The AOFAS score was the most frequently used clinical score among the included studies. Sierevelt et al. indicated that there are some concerns regarding this outcome score[245]. A significant part of the 100 points depends on patient subjective outcomes introducing bias to the interpretation of the calculated success rates, as a high-level athlete would subjectively rate his or her surgery more critically than the average patient included in our systematic review. Moreover, the AOFAS score is not officially validated for the clinical evaluation of the treatment of talar OCDs. Therefore, future research should focus on developing a for talar-OCD-validated outcome scale, in order to increase the homogeneity and uniformity in outcome assessment.

As the review shows that in 71% of the cases a history of ankle trauma was reported, it is as important to focus on prevention strategies as focusing on effective surgical treatment measures. Progression has been made regarding the development of cost-effective prevention programs for lateral and medial ankle sprains, for example by Verhagen through the development of a mobile application system[297].

Furthermore, the analysis concerning methodological quality showed that a high number of studies included were of low methodological quality, except for two included RCTs[68, 222]. This underlines that the necessity for more sufficiently powered randomised studies is of paramount importance. Future research should therefore focus on conducting more randomised comparative clinical trials with uniform methodology and extended follow-up times. BMS should be compared to newly developed promising treatment options that focus on preserving hyaline cartilage and preventing the development of additional clinical complaints, such as donor-site morbidities observed in patients undergoing an OATS procedure. A possible future direction for such a promising treatment strategy is the internal fixation surgeries. In small patient series, these have been shown to induce a significant clinical improvement, possibly because these aim at preserving hyaline cartilage[126, 128].

There were a number of limitations concerning the present review. Firstly, the low quality of the included studies and the substantial heterogeneity regarding methodology account as major limitations. Additionally, separate success rates were calculated based on different scoring systems, as the AOFAS score was not always available for statistical analysis. Due to this, it was not possible to perform the conventional measure of summarising estimates of effectiveness. Concerning patient characteristics there was heterogeneity observed in the patient population. It was not possible to collect data concerning mean follow-up duration on all studies included, as these were not provided in all cases. Another limitation of the study is that it was not possible to perform a formal meta-analysis utilizing mixed-effects logistics regression in order to compare between treatment groups. Regarding the BMS group and the studies within the osteo(chondral) transplantation group, those publications that had utilised a retrospective case series setting were pooled. This implies that the evidence retrieved from this simplified pooling method is based on lower level of evidence and may therefore contain methodological bias indicating that the pooled calculated success rates should not be used for decision of a particular treatment technique for talar OCDs, but merely be applied to inform patients in the process of explaining the expected success percentages of a particular treatment strategy. Moreover, the pooled success rate of the osteo(chondral) transplantation group combined studies reporting the effects of OATS procedures and an osteoperiosteal cylinder procedure possibly introducing some form of heterogeneity in this group as the type of grafts inserted in the OATS group was slightly different from the ones in the osteoperiosteal cylinder group[89, 115, 118, 147, 149, 316]. The strengths of the present review are the inclusion of solely primary lesions, the thorough reference selection and the quality assessment of the included studies. Another major strength is the extensive corresponding author contact protocol regarding additional data retrieval and further clarification on methodology of included studies.

The clinical relevance of the present systematic review is that the separate and pooled success rates for the different surgical and non-surgical management options can be utilised to inform patients about the expected success percentages when undergoing treatment for primary talar osteochondral defects, which will facilitate the shared decision-making process between patients and physicians.

CONCLUSIONS

In conclusion, the present systematic review shows that none of the interventions for the treatment of primary osteochondral defects to the talus showed clinical superiority over another or others. A simplified pooling method for eleven retrospective case series in the BMS group yielded a success rate of 82% [CI 78–86%], and for the seven combined OATS and osteoperiosteal cylinder graft studies the pooled success rate was calculated to be 77% [CI 66–85%]. A high number of studies with low methodological quality were included, and heterogeneity in methodological nature of the studies and variety in reported success rates was observed. As a consequence, future research should focus on conducting sufficiently powered prospective investigations in a randomised comparative clinical trial setting using outcome scores validated for the treatment of talar OCDs.

6 Arthroscopic lift, drill, fill and fix (LDFF) is an effective treatment option for primary talar osteochondral lesions

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ABSTRACT

Purpose The purpose of this study was to describe the mid-term clinical and radiological results of a novel arthroscopic fixation technique for primary osteochondral defects (OCD) of the talus, named the lift, drill, fill and fix (LDFF) technique.

Methods Twenty-seven ankles (25 patients) underwent an arthroscopic LDFF procedure for primary fixable talar OCDs. The mean follow-up was 27 months (SD 5). Pre- and post-operative clinical assessments were prospectively performed by measuring the Numeric Rating Scale (NRS) of pain in/at rest, walking and when running. Additionally, the Foot and Ankle Outcome Score (FAOS) and the Short Form-36 (SF-36) were used to assess clinical outcome. The patients were radiologically assessed by means of computed tomography (CT) scans pre-operatively and 1 year post-operatively.

Results The mean NRS during running significantly improved from 7.8 pre-operatively to 2.9 post-operatively ($p = 0.006$), the NRS during walking from 5.7 to 2.0 ($p < 0.001$) and the NRS in rest from 2.3 to 1.2 ($p = 0.015$). The median FAOS at final follow-up was 86 for pain, 63 for other symptoms, 95 for activities of daily living, 70 for sport and 53 for quality of life. A pre- and post-operative score comparison was available for 16 patients, and improved significantly in most subscores. The SF-36 physical component scale significantly improved from 42.9 to 50.1. Of the CT scans at 1 year after surgery, 81% showed a flush subchondral bone plate and 92% of OCDs showed union.

Conclusion Arthroscopic LDFF of a fixable primary talar OCD results in excellent improvement of clinical outcomes. The radiological follow-up confirms that fusion of the fragment is feasible in 92%. This technique could be regarded as the new gold standard for the orthopedic surgeon comfortable with arthroscopic procedures.

Level of evidence Prospective case series, therapeutic level IV.

INTRODUCTION

Management of talar osteochondral defects (OCD) is still a challenge. Multiple factors are to be taken into account when determining the best available treatment. There are numerous surgical treatment strategies available, with a substantial increase in the number of procedures over the past decades. For primary talar OCDs, bone marrow stimulation is the most frequently performed treatment[56]. This technique has shown good clinical results at short-term and mid-term follow-up[56, 107, 142]. It aims at focusing on the intrinsic capacity of the ankle to heal the cartilage due to the formation of fibrocartilage[192]. However, previous studies have shown that the quality of fibrocartilage decreases over time, that it shows inferior wear characteristics, and it has been proven that the subchondral bone plate shows irregularities and depressions at follow-up; all of these factors potentially being the explanation why one-third of the patients show progression of ankle osteoarthritis at long-term follow-up[81, 160, 166, 214, 221, 255, 281].

Subsequently, a novel technique has been developed, the arthroscopic internal fixation technique of talar OCDs, having the theoretical advantage of preserving hyaline cartilage, restoring the original congruency of the ankle mortise, facilitating healing of the cartilage and the subchondral bone, and thus restoring subchondral bone plate quality, thereby potentially leading to reduced percentages of ankle osteoarthritis at follow-up[126, 219, 220]. Recently, the authors of the present study reported on a promising minimally invasive arthroscopic internal fixation technique, the lift, drill, fill and fix (LDFF) procedure. This is a novel technique used for arthroscopic fixation of primary and large (>10 mm) OCDs of the talar dome. Although the technique showed highly promising clinical and radiological short-term results, the study contained a limited number of patients[126].

Consequently, the aim of the present study is, therefore, to present the mid-term follow-up clinical and radiological results of the arthroscopic LDFF technique for large primary talar OCDs. The hypothesis is that the results of the short-term follow-up are similar in this extended patient cohort, are durable over time and show a high rate of fusion.

MATERIALS AND METHODS

This study was approved by the local Medical Ethics Committee at the University of Amsterdam with reference number MEC 08/326, and it was performed in accordance with the current ethical standards (Declaration of Helsinki).

The indication for an LDFF technique was a large primary OCD of the talar dome with a diameter of more than 10 mm (anterior–posterior or medial–lateral) and a bony fragment of at least 3 mm in depth on computed tomography (CT). The patients had to have persistent deep ankle pain for more than 1 year. The contraindications were ankle osteoarthritis grade II or grade III[290], type IV (displaced) OCDs according to the modified Berndt and Harty classification scale[24, 157], rheumatoid arthritis, chondral lesions, a concomitant defect in the tibia, an ankle fracture <6 months old, tendinopathy, advanced osteoporosis, concomitant painful or disabling disease of the lower limb and infectious pathology or any kind of malignancy.

Pre-operative planning

Patients were assessed at the outpatient clinic pre-operatively. A pre-operative computed tomography (CT) scan was made to assure the diagnosis as well as to determine size, location, shape, morphology of the talar osteochondral defect and to determine arthroscopic (anterior/posterior) access of the defect.

Operative technique

All of the patients were operated by the senior author (GK) (Figure 1). Procedures were carried out under spinal or general anaesthesia. Patients were placed in a supine position. Standard anteromedial and anterolateral portals were used. A standard 4-mm, 30° arthroscope was used, and arthroscopic portals were interchangeably used to achieve optimal vision of the defect. The location of the OCD was identified and then a beaver knife was used to make a sharp osteochondral flap. The posterior side of the flap was left intact and used as a lever. Consequently, this flap was lifted from anterior with use of a chisel (lift). Then the attached bone of the osteochondral flap and the osteosclerotic area of the bed were both debrided and drilled to stimulate revascularisation (drill). Any subchondral cysts were also curetted and drilled. With the use of a chisel, cancellous bone was harvested from the distal tibial metaphysis, and the defect was filled with these cancellous chips, transported

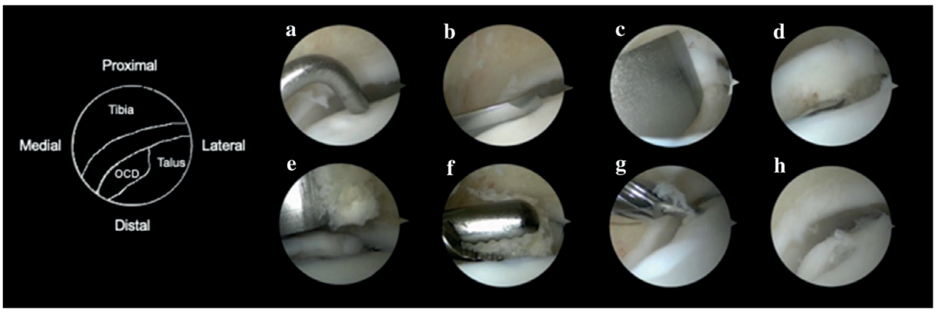

Figure 1. Arthroscopic LDFF technique. **a** A medial OCD is identified. **b** An osteochondral flap is created with use of a beaver knife. **c** With a chisel the osteochondral flap is lifted. **d** The bone flake is drilled with a K-wire to promote revascularization. **e** Cancellous bone is harvest from the distal tibia using a 4-mm chisel. **f** With an arthroscopic grasper the cancellous bone is transported into the defect. **g** A cannulated system allows predrilling and tapping of a compression screw (Arthrex Inc, Naples, USA). **h** an absorbable Bio-Compression screw is placed recessed relative to the surrounding surface of hyaline cartilage

into the defect with a grasper (fill). The last step consisted of fixating the fragment (fix) with either a Bio-Compression screw (Arthrex Inc., Naples, USA), with multiple chondral darts (Arthrex Inc., Naples, USA), or a combination of those two. Skin incisions were sutured with 3.0 Ethilon single stitches.

Postoperative management

After surgery, all patients were placed in a short-leg cast and were kept non-weight bearing for 6 weeks post-operatively. Then the cast was exchanged for a short-leg walking cast. This cast was set in neutral flexion and neutral hindfoot position. At that time, full weight bearing was allowed. Flexion and extension exercises in between all cast changes were encouraged. After a total of 12 weeks of immobilisation, the cast was removed. Physical therapy was then prescribed to assist functional recovery.

Patient cohort

The study group consisted of 25 patients, of whom 2 received an operation on both ankles, which resulted in a total of 27 operated ankles. The patients who received an operation on both ankles filled in a questionnaire for each ankle. The operation on the contralateral ankle was performed 1.5 year after the first surgery in one patient and after 1 year in the other patient. There were 14 males and 11 females. The median age at surgery was 17 years (range 11–63 years). The mean body mass index was 22. Eight patients were operated on their left ankle, 17 on their right ankle and 2 patients bilaterally. No previous surgery on any of the treated ankles was reported. One patient reported a bipolar chevron operation on the ipsilateral hallux due to a hallux valgus. Another patient reported a previous bone marrow stimulation treatment of an earlier osteochondral defect but on the contralateral ankle. The median follow-up was 27 months (range 18 to 43 months).

Clinical analysis

Patients were assessed pre-operatively, and at 1 and 2 years post-operatively. At all moments, patients were requested to fill out a Numeric Rating Scale (NRS) for pain in rest, during walking and during running if possible. The NRS is an 11-point scale that represents the spectrum of no pain to the worst pain imaginable (0–10)[88]. Additionally, a numeral rating scale for satisfaction was used to capture personal satisfaction of the whole management procedure.

At the beginning of the inclusion period, the authors used a native language validated American Orthopedic Foot and Ankle Society (AOFAS) Score as a clinical outcome scale[130]. However, during the proceeding of this study, a systematic review on different reported outcome measures showed that a native language validated Foot and Ankle Outcome Score (FAOS) was the best available Dutch Patient Reported Outcome Measure (PROM) for assessing the clinical status of various foot and ankle injuries [40]. Therefore, we initiated the use of pre-operative and post-operative clinical evaluation by means of the Foot and Ankle Outcome Score (FAOS)[287]. Since this questionnaire also is a completely patient-based questionnaire and therefore can be taken without the interference of a clinician thereby giving it a highly logistic advantage, it was decided to use this as our ankle outcome scale for any further future documentation. Finally, the 36-item Short Form Health Survey (SF-36) was used to assess general quality of life. For all questionnaires, a version validated in the native language was used[244, 246, 287].

Radiological analysis

Pre-operatively as well as at 1 year post-operatively, the patients were evaluated by means of a computed tomography scan (CT scan). Defects were classified according to the modified Berndt and Harty classification system[24, 157]. A nine-grid scheme as previously described by Elias et al. was used to assess the location in the talus for each osteochondral lesion[76]. Defect size was measured in three planes, including surface area and depth of the lesion. Postoperatively, the CT scans were scored on level of subchondral bone plate (flush/depressed)[81, 160, 166, 214, 221, 255, 281], and were scored on union rate of the fixated defect[126, 219, 220]. The scanning protocol involved 'ultra high-resolution' axial slices with an increment of 0.3 mm and a thickness of 0.6 mm. Multiplanar coronal and sagittal reconstructions were 1.0 mm.

Statistical analysis

All statistics were performed with SPSS version 24 (IBM corp, Armonk, NY, USA). Categorical data are presented as frequency and continuous data as mean with SD or median with range, all depended on its distribution. The paired Student's t test was used for comparison of the normal distribution of pre- and post-operative means. A Wilcoxon signed-rank test was used if data were skewed. The comparisons with $p < 0.05$ were considered to be statistically significant.

RESULTS

Clinical outcome

In all patients, LDFF led to a significant improvement of the NRS of pain and the majority of the FAOS and SF-36 subscales. Of the 25 patients, 23 played sports before their injury. Of these, 20 were able to return to sports of which 7 played at a competitive level and 13 at a recreational level. The NRS significantly improved on each subscale (Table 1). Median satisfaction of the procedure was reported to be 8 (SD 3.3, range 0–10).

Table 1 NRS scores pre- and post-operative

	Pre-operative	Final follow-up	*p* value
NRS pain in rest	2.3 (SD1.8)	1.2 (SD1.8)	0.015
NRS pain during walking	5.7 (SD 2.6)	2.0 (SD2.5)	< 0.001
NRS pain during running	7.8 (SD1.8)	2.9 (SD2.6)	0.006

Results are expressed as mean ± standard deviation

Although we were able to obtain all post-operative FAOS on all patients, the pre-operative FAOS was not available in 11 patients for reasons as stated above in the "Materials and methods" section, meaning that a pre-operative to postoperative comparison could only be performed in 16 cases. Pre- and post-operative scores for pain were 67 (SD 20) and 86 (SD 22), respectively (p = 0.026). For other symptoms, 66 (SD 18) and 63 (SD 19) (n.s.), for activities of living 87 (SD 22) and 95 (SD 18) (p = 0.029), for sport 40 (SD 20) and 70 (SD 22) (p = 0.002) and for quality of live, 22 (SD 17) and 53 (SD 27) (p = 0.006) all pre- and post-operative, respectively. FAOS are displayed in Figure 2.

The Physical Component Scale of the SF-36 improved from a pre-operative score of 42.9 (SD 9.2) to 50.1 (SD 7.7) at final follow-up (p = 0.007). The Mental Component Scale decreased from 55.7 (SD 6.0) to 49.8 (SD 12.0), though not statistically significant.

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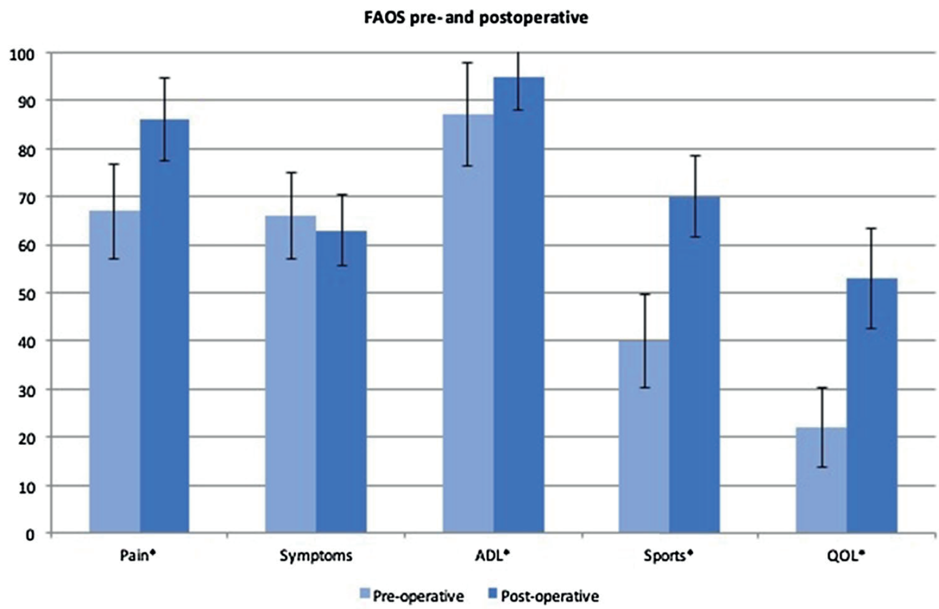

Figure 2. Pre- and post-operative FAOS Scores. *FAOS* Foot and Ankle Outcome Score, *ADL* activities of daily living, *QOL* quality of life; *significant p value

Radiological outcomes

All patients but one received a CT scan at their 1-year follow-up appointment. One patient did not show up at his post-operative CT scan appointment. The mean pre-operative OCD size was 14 mm (SD 2.8 mm) in the anterior–posterior direction, 8 mm (SD 2.2) in the medial–lateral direction and 7 mm (SD 3.1 mm) in depth. Twenty-three defects were located on the medial talar dome (13 at the center and 10 anterior) and 4 on the lateral talar dome (1 at the center and 3 anterior). Six defects were classified as partially fractured and thus stage II lesions. Twenty-one defects were classified as non-displaced fragments without attachment and, therefore, classified as stage III lesions.

Of the 26 post-operative CT scans, 81% of the patients (21/26) showed a flush subchondral bone plate, and 92% (24/26) of OCDs showed union of the osteochondral fragment (Figure 3).

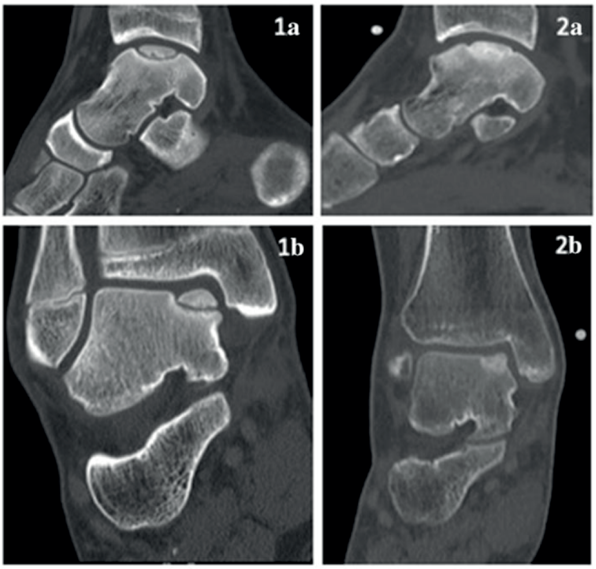

Figure 3. Example of a pre-operative sagittal **(1A)** and coronal **(1B)** CT scan of the OCD of a 15-year-old patient and sagittal **(2A)** and coronal **(2B)** CT scan from the same patient 1 year after the LDFF procedure

Complications

No serious adverse events occurred after the arthroscopic LDFF procedure, and there were no complications reported. One patient received a re-operation due to unsatisfactory results. This patient received a bone marrow stimulation operation 2 years after the initial LDFF surgery.

DISCUSSION

The most important finding of the present study was that we found satisfactorily outcome scores with a high fusion rate. Treatment of large OCDs by fixation has been shown to be a successful method both for acute and chronic lesions but the literature on this topic is scarce, and there are very few studies describing its clinical and radiological results[126, 139, 186, 218, 235]. This present prospective study describes the clinical and radiological outcomes of a previously published arthroscopic method of fixation, named the lift, drill, fill and fix (LDFF) technique[126]. It can be stated that, at a 2-year follow-up period, this technique shows a high rate of satisfaction, a significant decrease of experienced pain during weight-bearing activities such as walking and running, and it shows that a high rate of return to sports could be achieved. Furthermore, the present study showed that a significant improvement in the quality of life and physical well-being was observed.

Clinically, perceived pain decreased after surgery, especially during normal weight-bearing activities like walking. Although perceived pain during running also showed a significant drop post-operatively, with an average postoperative value of 2.9 there is still room for improvement, especially since most OCD patients are young and still very active, and thus there is high demand to return to their previous level of sport.

Numerous surgical options can be used to treat primary talar osteochondral defects. For the small defects, there is general consensus that a type of bone marrow stimulation (BMS) can be a successful treatment option yielding success rates around 82%, and high return-to-sports at short-term follow-up[56, 116]. In the literature, this is also the most described treatment option for primary osteochondral defects[56].

Arthroscopic BMS has been used for a long time and thanks its popularity to the relative simplicity, low costs and minimal invasiveness[6, 17, 50, 67, 95, 108, 182]. It aims at focusing on the intrinsic capacity of the ankle to heal the cartilage due to the formation of fibrocartilage[192]. Results are good in up to 80% of patients but the technique also gives concerns since this fibrocartilage shows decrease in quality over time with a possible increase in osteoarthritic changes[56, 67, 160]. In up to one-third (33–34%) of patients, a progression of ankle osteoarthritis can be seen at mid-term and long-term follow-up, and the subchondral bone plate seems depressed on CT analysis in about three-fourth (74%) after 1 year[81, 219, 281]. Also, second look arthroscopy showed an incomplete healing of the defect 1 year post-operatively in 40% of the treated patients[150].

From an evidence-based standpoint, it can therefore be concluded that BMS can be a successful treatment option in case of disappearance of the chondral layer of the talar dome, or in cases of severely damaged or ulcerated cartilage. However, in case of a fragmented defect of bone with intact overlying cartilage, a fixation technique to treat these defects can be highly suitable. The theoretical advantages of a fixation technique are the restoration of the subchondral bone and preservation of the hyaline cartilage. A recent publication by

Reilingh et al. showed that the subchondral bone healing in patients operated by means of a fixation was significantly higher in comparison with patients being operated by means of a bone marrow stimulation procedure. The authors, therefore, share the opinion that a method of fixation is the preferred treatment of an osteochondral fragment with an intact overlying cartilage layer. For theoretical superior healing, it is necessary for the loose fragment to have an osseous part. Next to the biological advantages, the risk of an attempt of fixation is low since, if fixation would fail, it is still possible to perform a subsequent bone marrow stimulation procedure.

As surgical techniques develop and improve, the optimal way of fixation stays debatable. There is a growing number of fixation possibilities which consist of biocompression or steel screws and additional bioabsorbable darts or pins. Other described methods are K wires and bony pegs[126, 139, 186, 205, 220, 235]. Since numbers of patients are low in the included case series, it is difficult to make methodologically correct comparisons and, therefore, the optimal method of fixation should be evaluated for each individual case, taking into account all potential prognostic factors, the radiological pre-operative morphological characteristics of the defect and the individual wishes of the patient. An International Consensus Meeting on Cartilage Repair of the Ankle held in Pittsburgh in November 2017 showed that there was a strong consensus that if possible the fragment should be fixed with two devices with at least one being used for compression and the other to prevent rotation[220]. Fragments, however, may be very small and fragile, and double fixation will not always be possible without compromising the stability of the fragment.

The LDFF procedure as described above is an arthroscopic method and can be technically demanding. In our institution, with the gained experience over the past years performing this type of surgery, we also perform an open procedure—by means of a medial malleolar osteotomy—when the full potential of this procedure cannot be reached with an arthroscopic procedure alone. Location of the OCD and its arthroscopic accessibility has to be taken into account during pre-operative planning[283, 284]. We found that during arthroscopic treatment, it can often be difficult to find the optimal angle to fixate the fragment and create optimal stability. A recent study investigating the influence of the angle of pin insertion on the clinical outcomes concerning clinical efficacy of a fixation procedure for osteochondral defects of the talus showed that shallow pin insertion was significantly associated with osteolytic changes around the pins and persistence of bone marrow edema on MRI[186]. The patients with these radiological inferior outcomes, however, still had good to excellent results at 1 year of follow-up after the surgery. It is, therefore, highly important to weigh the pros and cons of the arthroscopic versus the open procedure in combination with a proper shared decision making with the patients, so that the proper surgical choice can be made.

This study should be interpreted in the light of its strengths and weaknesses. The study group is small but relatively large when compared to the previous study groups describing the results of fixation. Another disadvantage is some missing pre-operative FAOS. Since this questionnaire was validated after inclusion of the first patients, we started using this outcome measure during the study, resulting in the absence of 11 pre-operative FAOS. We changed to the FAOS whilst, at that moment, a systematic review about different reported outcome measures showed the FAOS as the best available Dutch PROM[310]. Further evaluation of the FAOS showed good responsiveness in patients 1 year after hindfoot and ankle surgery[246]. Since we were able to obtain all outcome measures at the 2-year follow-up, we believe this study shows representative results. The clinical relevance behind the work of the present study is that it raises awareness amongst orthopedic surgeons that fixating a fragment of an osteochondral defect in the ankle is an effective, safe surgical treatment option, and should be considered when treating these patients.

CONCLUSION

Arthroscopic fixation by means of the Lift–Drill–Fill–Fix method for primary osteochondral defects of the talus results in excellent clinical improvement at 2-year follow-up and confirms radiological (CT) union in 92%. This novel technique could be regarded as the new gold standard for the orthopedic surgeon comfortable with arthroscopic procedures.

7

The subchondral bone healing after fixation of an osteochondral talar lesion is superior in comparison with microfracture

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ABSTRACT

Purpose Arthroscopic bone marrow stimulation (BMS) has been considered the primary surgical treatment for osteochondral defects (OCDs) of the talus. However, fixation has been considered as a good alternative. Recently, a new arthroscopic fixation technique was described: the lift, drill, fill and fix procedure (LDFF). The purpose of this study was to evaluate the clinical and radiological results between arthroscopic LDFF and arthroscopic BMS in primary fixable talar OCDs at 1-year follow-up.

Methods In a prospective comparative study, 14 patients were treated with arthroscopic BMS and 14 patients with arthroscopic LDFF. Pre- and postoperative clinical assessment included the American Orthopaedic Foot and Ankle Society (AOFAS) score and the numeric rating scales (NRSs) of pain at rest and running. Additionally, the level of the subchondral plate (flush or depressed) was analysed on the 1 year postoperative computed tomography scans.

Results No significant differences in the AOFAS and NRS pain at rest and running were found between both groups at 1-year follow-up. After LDFF the level of the subchondral bone plate was flush in 10 patients and after BMS in three patients ($p = 0.02$).

Conclusion No clinical differences were found between arthroscopic LDFF and arthroscopic BMS in the treatment of talar OCDs at 1-year follow-up. However, the subchondral bone plate restores significantly superior after arthroscopic LDFF compared to arthroscopic BMS. It may therefore give less progression of ankle osteoarthritis in the future with a thus potential better long-term outcome.

Level of evidence III

INTRODUCTION

Osteochondral defects (OCDs) of the talus often have a severe impact on the quality of life of patients[289]. Currently, arthroscopic bone marrow stimulation (BMS) has been considered the primary surgical treatment for chronic OCDs up to 15 mm. This preference is based on the ease of execution of the technique, the low complication rate and high success rates reported in the literature[326, 328]. However, BMS does not aim at the preservation of a hyaline cartilage layer, but rather promotes the formation of fibrocartilage which decreases in quality over time and shows inferior wear characteristics[160, 166, 255]. Furthermore, after debridement and bone marrow stimulation the subchondral bone plate is often irregular and depressed[221]. These factors might be the reason why progression of ankle osteoarthritis is seen in 33–34% of the patients at long-term follow-up[81, 214, 281].

Recently, a new arthroscopic fixation technique for chronic primary talar OCDs was described: the lift, drill, fill and fix procedure (LDFF)[126]. The assumed theoretical advantages of this technique are the restoration of the subchondral bone plate and the preservation of hyaline cartilage. Promising clinical and radiological results were found in the first seven patients at 1-year follow-up. However, at present, no comparative study has been conducted between LDFF and BMS in primary fixable talar OCDs. Consequently, the aim of this study was to evaluate the clinical and radiological results between arthroscopic LDFF and arthroscopic BMS in primary fixable talar OCDs at 1-year follow-up.

MATERIALS AND METHODS

This study was approved by the local medical ethics committee at the University of Amsterdam with reference number MEC 08/326 and performed in accordance with the current ethical standards (Declaration of Helsinki).

The study included patients with a symptomatic fixable primary talar OCD with a diameter >10 mm (in three dimensions) as measured on computed tomography (CT) scans. Fixable defects were defined as type II–IV, based on the Berndt and Harty classification[24]. Exclusion criteria were open physis of the distal tibia, ankle osteoarthritis grade II or III[291], concomitant OCD of the tibia, ankle fracture within 6 months before treatment of the OCD, surgical treatment of the index ankle performed within 1 year before treatment of the OCD, concomitant painful or disabling disease of the lower limb and rheumatoid arthritis.

Population

As of 2013, we have prospectively recorded all patients undergoing an arthroscopic LDFF procedure[126]. For the control group (arthroscopic BMS), we used data from a randomized controlled trial (RCT) investigating pulsed electromagnetic fields (PEMF) after arthroscopic debridement and BMS[222]. Both the PEMF treatment and the placebo group were included in the arthroscopic BMS control group of the present study, as neither functional nor radiological differences between the groups were found in the previous trial. Patients were retrospectively selected to the BMS control group if their lesion could be defined as a fixable defect.

Operative technique

Arthroscopic LDFF

All arthroscopic LDFF procedures were performed using a standardized technique by the senior author (GK)[126]. Anteromedial and anterolateral portals were created with the ankle in full dorsiflexion. The OCD was identified with a probe by moving the ankle in full plantar flexion. Subsequent to this, an osteochondral flap was created with use of a beaver knife and lifted with a chisel. The bone flake of the osteochondral fragment as well as the osteosclerotic area of the bed was drilled with the use of a K-wire and a shaver blade. Cancellous bone was harvested from the distal tibia and transported into the defect until there was sufficient substantial filling. Finally, the osteochondral flap was fixed with an absorbable bio-compression screw(s) (Arthrex Inc, Naples, USA) or/and a chondral dart(s) (Arthrex Inc, Naples, USA). Postoperatively, a short-leg non-weight-bearing cast was applied for 4 weeks. After these 4 weeks, the foot was placed in a short-leg walking cast in neutral flexion position and neutral hindfoot position, with full weight bearing allowed. At 8 weeks postoperatively, the cast was removed. Physical therapy was prescribed to assist in functional recovery and extend to full weight bearing in approximately 2 weeks[126].

Arthroscopic BMS

All arthroscopic BMS procedures were performed using a standardized technique by the senior author (GK)[222]. Like in the LDFF technique, an anteromedial and an anterolateral portal was created. After identification of the OCD, all unstable bone and cartilage were removed with a curette and bone cutter shaver. This was followed by perforation with a microfracture awl, with intervals of approximately 3 mm. At the end of the procedure, a pressure bandage was applied. Postoperative management consisted of a protocol-based rehabilitation programme, guided by a physiotherapist. Partial (eggshell) weight bearing on crutches was allowed as tolerated and progressed to full weight bearing over a period of 6 weeks. During this 6-week period, active nonweight- bearing and partial weight-bearing sagittal range of motion exercises were encouraged[293].

Outcome assessment

Clinical outcome was assessed by means of numeric rating scales (NRSs) for pain (at rest and running) and the American Orthopaedic Foot and Ankle Society (AOFAS) ankle-hindfoot score[88, 117, 130]. These questionnaires were evaluated preoperatively and at 1 year postoperatively. The NRS is an 11-point scale, representing the spectrum of no pain (0 points) to the worst pain imaginable (10 points)[88, 117, 130]. The AOFAS is a 100-point score, with a subjective and an objective component, which devotes 40 points to pain, 50 to function and 10 to alignment[88, 117, 130].

Imaging

Computed tomography (CT) scans of the affected ankle were obtained preoperatively and at 1 year postoperatively. The scanning protocol involved "ultra-high-resolution" axial slices with an increment of 0.3 mm and a thickness of 0.6 mm, and multi-planar coronal and sagittal reconstructions of 1.0 mm[222]. CT scanning has been proven to be accurate in the detection and follow-up of OCDs of the talus, regarding location and extent as well as healing of the defect[185, 222, 298, 331].

On the preoperative CT scans, we graded the talar OCDs according to the modified Berndt and Harty classification and evaluated the OCD size by measuring the largest diameter (mm) in the anterior–posterior direction, medial–lateral direction and depth[24, 236].

The level of the subchondral plate (flush or depressed) was analysed on the 1 year postoperative CT scans. Reilingh et al. reported a good reliability in the measurements of the subchondral bone plate on CT scans[222]. Furthermore, the union rate was evaluated on the postoperative CT scans after the LDFF procedure.

Statistical analysis

Statistical analyses were conducted with Statistical Packages for Social Sciences (SPSS 23.0 Inc, Chicago, IL, USA) software. Continues data are presented as means with standard deviations or as medians with interquartile ranges (IQRs), depending on their distribution (normal or skewed). Comparison of the clinical outcome between groups was performed by the Student's t test on normal distribution and the Mann–Whitney U test on skewed distribution. Additionally, the scale score differences between baseline and 1-year outcome assessment within each treatment group were analysed by using the paired t test on normal distribution and Wilcoxon signed-rank test on skewed distribution. The CT findings were analysed using the Chisquare test.

RESULTS

Out of our previous cohort, 14 patients were included who were treated with arthroscopic BMS in case of the presence of a fixable talar OCD[222]. To create a similar and comparable cohort, we therefore only included the first 14 patients who were treated with arthroscopic LDDF. Both groups completed all questionnaires and the CT follow-up at 1 year postoperatively. The baseline characteristics are presented in Table 1. Patients in the LDFF group were significantly younger ($p < 0.01$) and had a lower body mass index (BMI) ($p < 0.01$). There was no significant difference in OCD classification or size of the lesion. Fixation was performed in nine cases with bio-compression screw(s), in three cases with chondral dart(s) and in two cases with a combination of both.

Table 1 Baseline characteristics of the patients

	LDFF, *n* = 14	BMS, *n* = 14	*p* value
Age (years), median (IQR)	17 (16–18)	23 (20–30)	<0.01
Gender, *n* (% male)	5 (36)	5 (36)	n.s.
BMI, mean (SD)	22 (3)	27 (4)	<0.01
Included side, *n* (% right)	10 (71)	12 (86)	n.s.
OCD size, mean (SD)			
Anteroposterior (mm)	13 (2)	12 (3)	n.s.
Medial–lateral (mm)	9 (2)	9 (2)	n.s.
Superior–inferior (mm)	6 (3)	5 (2)	n.s.
OCD classification, *n* (%)			
Partially fractured	2 (14)	2 (14)	n.s.
Completely undisplaced fracture	12 (86)	10 (72)	n.s.
Displaced fracture	0 (0)	2 (14)	n.s.

IQR interquartile range, *SD* standard deviation, *n.s.* not significant

Clinical results

Both preoperatively and 1 year postoperatively, no significant differences in the AOFAS and NRS pain at rest and running were found between arthroscopic LDFF and arthroscopic BMS (Figures 1+2).

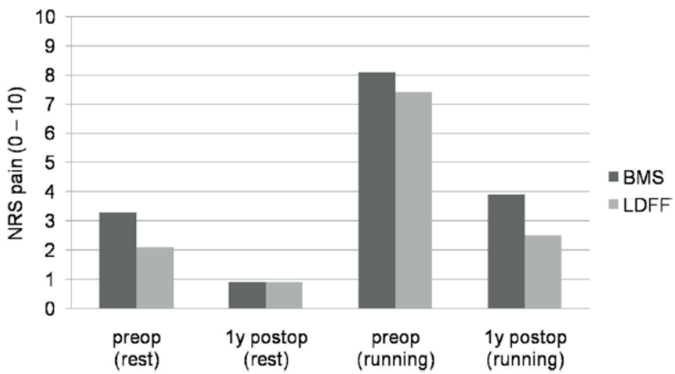

Figure 1. Graph showing the mean numeric rating scales (NRSs) for pain (at rest and when running) pre- and postoperatively. No significant differences were found between arthroscopic LDFF and arthroscopic BMS

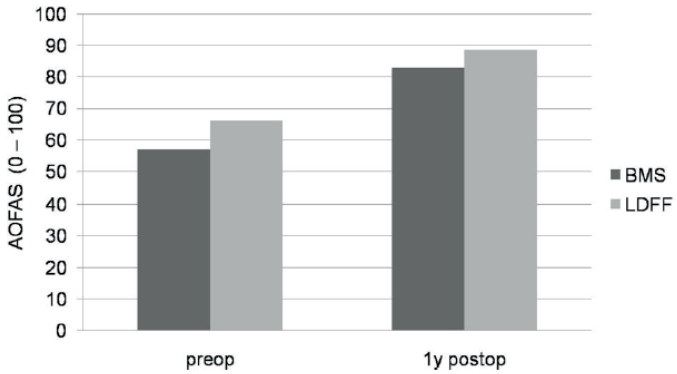

Figure 2. Graph showing the mean American Orthopaedic Foot and Ankle Society (AOFAS) ankle–hindfoot score pre- and postoperatively. No significant differences were found between arthroscopic LDFF and arthroscopic BMS

Within both treatment groups, the NRS pain and AOFAS improved significantly from preoperatively to 1 year postoperatively. After arthroscopic LDFF, the AOFAS significantly improved from 66 (SD 10.1) to 89 (SD 17.0) ($p = 0.004$). The NRS pain at rest significantly improved from 2.1 (SD 1.8) to 0.9 (SD 1.3) ($p = 0.043$), and NRS pain when running improved from 7.4 (SD 1.9) to 2.5 (SD 3.1) ($p = 0.004$) (Figures 1+2). After arthroscopic BMS, the AOFAS significantly improved from 57.1 (SD 13.6) to 83 (SD 15.9) ($p < 0.001$). The NRS pain at rest significantly improved from 3.3 (SD 1.5) to 0.9 (SD 1.7) ($p = 0.001$), and NRS pain when running improved from 8.1 (SD 1.7) to 3.9 (SD 2.8) ($p < 0.001$) (Figures 1+2).

Radiological results

A significant difference ($p = 0.02$) was found in the healing of the subchondral bone plate between both groups. After arthroscopic BMS, a depressed subchondral bone plate was observed in 11 patients and three patients had a flush subchondral bone plate (Figure 3), while after arthroscopic LDFF, a depressed subchondral bone plate was found in four patients and a flush subchondral bone plate in 10 patients (Figure 4). Union of the osteochondral fragment was found in nine patients after arthroscopic LDFF.

Complications

No serious adverse event occurred in either groups. One patient had prolonged wound leakage during the first week after arthroscopic BMS. No complications were reported after arthroscopic LDFF.

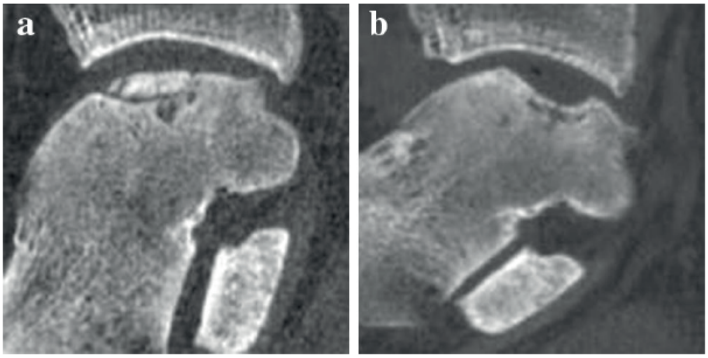

Figure 3. a Preoperative sagittal CT of a medial osteochondral talar defect of a right ankle. b Postoperative sagittal CT of the same ankle after arthroscopic debridement and bone marrow stimulation (BMS) at 1-year follow-up

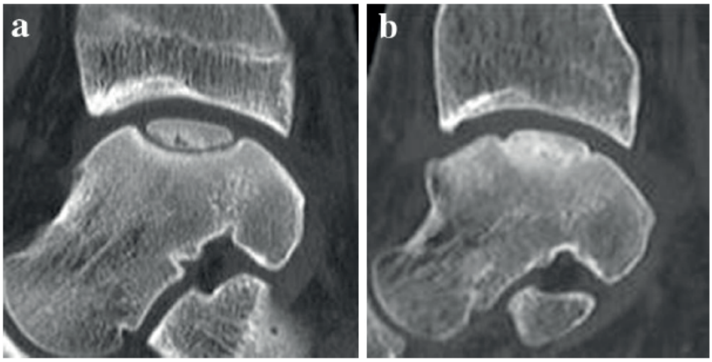

Figure 4. a Preoperative sagittal CT of a medial osteochondral talar defect of a right ankle. b Postoperative sagittal CT of the same ankle after arthroscopic lift, drill, fill, and fix (LDFF) at 1-year follow-up

DISCUSSION

The most important findings of the present comparative study were that no clinical differences were found between arthroscopic LDFF and arthroscopic BMS at 1-year follow-up. However, the subchondral bone plate restores significantly better after LDFF in comparison with BMS. Union of the fragment was found in nine out of 14 patients, but was not associated with a better outcome. This could be explained because a non-united fragment was stabilized by scar tissue and was no longer an intra-articular loose body.

The healing of the subchondral bone plate is important in the surgical treatment of OCDs. Research has indicated that an irregular subchondral bone plate has a negative effect on cartilage repair and thus plays an important role in the development of osteoarthritis[133, 134, 160, 201, 214]. Progression of ankle osteoarthritis is seen in 33–34% of the patients following arthroscopic debridement and BMS at long-term follow-up[81, 214, 281]. Although the long-term clinical and radiological outcomes of the arthroscopic LDFF procedure have not been researched yet, it is postulated that progression of ankle osteoarthritis is less than in patients treated with BMS because the subchondral bone plate restores more in accordance with the normal congruency of the ankle. 78–100% of the patients were regarded clinically successful in case series describing open fixation of talar OCDs at mid-term follow-up[139, 218, 235]. Furthermore, in an earlier study we found no progression of osteoarthritis after open fixation of talar OCDs in children at mid-term follow-up[218].

To the best of our knowledge, this is the first prospective comparative study investigating the clinical and radiological changes between arthroscopic LDFF and arthroscopic BMS. Strengths of this study include the prospective methodology and the complete radiological and clinical follow-up. Furthermore, the defect size was equally distributed between both groups. This is important because larger defects are associated with poorer outcomes[49, 50, 216]. Limitations include the lack of longterm follow-up and power analysis. Furthermore, BMI was significantly lower and patients were significantly younger in the LDFF group. These factors are associated with superior outcomes[218, 222]. However, it must be noted that none of the patients were classified as obese according to the WHO standards[317]. Furthermore, only skeletally mature patients were included in this study.

Based on the radiological results, fixation of a talar OCD with a bony fragment should be considered as the primary surgical treatment.

CONCLUSION

No clinical differences were found between arthroscopic debridement and BMS and arthroscopic LDFF in the treatment of osteochondral talar defects at 1-year follow-up. However, the subchondral bone plate restores significantly superior after arthroscopic LDFF compared to arthroscopic BMS.

8 Bone marrow stimulation for talar osteochondral lesions at long-term follow-up shows a high sports participation though a decrease in clinical outcomes over time

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ABSTRACT

Purpose Although bone marrow stimulation (BMS) as a treatment for osteochondral lesions of the talus (OCLT) shows high rates of sport resumption at short-term follow-up, it is unclear whether the sports activity is still possible at longer follow-up. The purpose of this study was, therefore, to evaluate sports activity after arthroscopic BMS at long-term follow-up.

Methods Sixty patients included in a previously published randomized-controlled trial were analyzed in the present study. All patients had undergone arthroscopic debridement and BMS for OCLT. Return to sports, level, and type were assessed in the first year post-operative and at final follow-up. Secondary outcome measures were assessed by standardized questionnaires with use of numeric rating scales for pain and satisfaction and the Foot and Ankle Outcome Score (FAOS).

Results The mean follow-up was 6.4 years (SD±1.1 years). The mean level of activity measured with the AAS was 6.2 pre-injury and 3.4 post-injury. It increased to 5.2 at 1 year after surgery and was 5.8 at final follow-up. At final follow-up, 54 patients (90%) participated in 16 different sports. Thirty-three patients (53%) indicated they returned to play sport at their pre-injury level. Twenty patients (33%) were not able to obtain their pre-injury level of sport because of ankle problems and eight other patients (13%) because of other reasons. Mean NRS for pain during rest was 2.7 pre-operative, 1.1 at 1 year, and 1.0 at final follow-up. Mean NRS during activity changed from 7.9 to 3.7 to 4.4, respectively. The FAOS scores improved at 1 year follow-up, but all subscores significantly decreased at final follow-up.

Conclusion At long-term follow-up (mean 6.4 years) after BMS for OCLT, 90% of patients still participate in sports activities, of whom 53% at pre-injury level. The AAS of the patients participating in sports remains similar pre-injury and postoperatively at final follow-up. A decrease over time in clinical outcomes was, however, seen when the follow-up scores at 1 year post-operatively were compared with the final follow-up.

Level of evidence Level II

INTRODUCTION

Osteochondral lesions of the talus (OCLT) are lesions to the subchondral bone and the overlying cartilage layer. These injuries have a high association with inversion injuries and ankle fractures[125, 231, 327]. Small (<15mm in diameter) lesions are initially treated with conservative treatment; however, in case of persistence of complaints, bone marrow stimulation (BMS) can provide good clinical outcomes with a success rate of 82%[48, 56]. Large primary defects that are amenable to fixation should be fixed whenever possible[126, 143]. In case of failure of primary surgical treatment, surgical treatment through an (osteo)chondral replacement strategy is indicated[125, 142]. As OCLTs are highly frequently seen in the athletic population, it is necessary to put specific emphasis on outcomes of treatment in athletes[243]. A recent systematic review by Steman et al. showed that return to sport (RTS) rates decreased when solely considering return to pre-injury level of sports[251]. Specifically considering BMS, in their review, the rate of return to any level of sports was 88%, and return to pre-injury level of sports 79%. Another recent review of the literature by Hurley et al. showed a rate of return to play as high as 86.8% after BMS with a mean time to return to play of 4.5 months[116]. In other research being conducted by Ramponi et al., an RTS rate of 77% was found[216]. None of these reviews, however, could provide adequate information on sports-related outcomes over time, as there is little literature on these outcomes on the long term. One retrospective study by van Eekeren found a return to sport rate of 76% after a median of 118 months[294]. Interestingly, the authors showed that the activity level seemed to decrease at long-term follow-up[294].

In most studies, it is often unclear whether authors reported on return to pre-injury level or return to any associated level of sports. Furthermore, there is a significant deficiency reported in rehabilitation protocols[116, 293]. Especially, the effect of BMS on return to sport after a longer period of time is scarcely reported in the literature. Bone marrow stimulation leads to the formation of fibrocartilage with an inferior subchondral bone plate as compared to original hyaline cartilage[192]. To date, it remains unclear whether this tissue enables high-level sports participation over time at the long term. The purpose of this study was, therefore, to prospectively evaluate return to sport and level of sport activity in patients treated with arthroscopic debridement and bone marrow stimulation and its persistence over time. It was hypothesized that return to sport rate and functional outcome would decrease over time.

MATERIALS AND METHODS

The study has been approved by the local medical ethics committee at the University of Amsterdam and was performed in accordance with the current medical ethical standards

(Declaration of Helsinki, MEC 08/326). Written informed consent for participation was obtained from every patient. We included the patient cohort of Reilingh et al. and adhered to the inclusion and exclusion criteria of this previously published study (Figure 1).

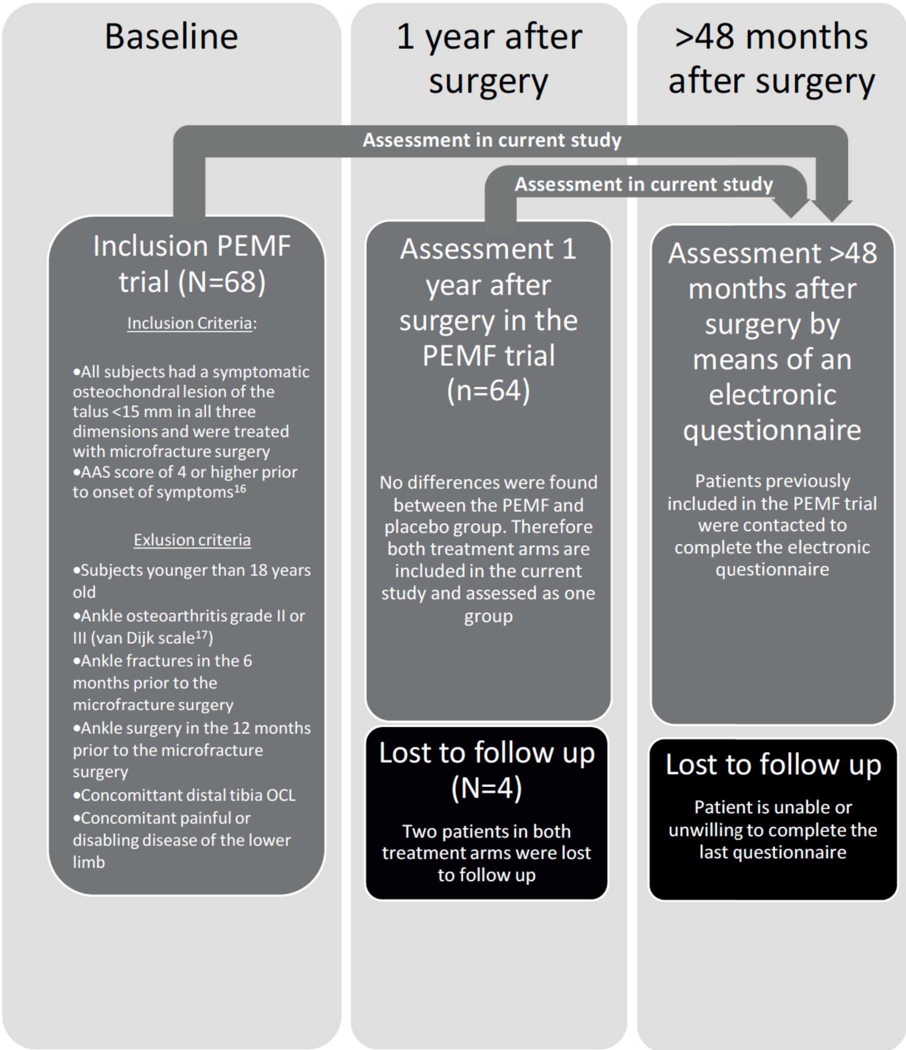

Figure 1. Study design

Population

Patients included in a previously trial, the Pulsed Electro Magnetic Fields (PEMF) trial, were analyzed in the present study[222]. In that study, patients had undergone arthroscopic debridement and bone marrow stimulation alone in the control group, and patients included in the experimental group had undergone the same surgical treatment, but were treated post-operatively with pulsed electromagnetic fields (PEMF). Detailed information on the surgical procedure and post-operative rehabilitation in the PEMF trial have been previously described by Reilingh et al.[222]. Since the onset of the index trial, all patients have been followed up in a prospective manner by the institution. As the RCT by Reilingh et al. concluded that PEMF did not lead to significant functional, sports nor radiological differences, we included both treatment arms as one treatment group in the present study.

Postoperative rehabilitation

Patients followed a protocol-based rehabilitation program post-operatively and were guided by a physiotherapist. The patient was allowed to progress to full weight-bearing in 6 weeks. During this 6-week period, active nonweightbearing and partial weight-bearing sagittal range of motion exercises were encouraged. After this period, resumption of sports was permitted as tolerated[293].

Outcome measures

Clinical outcome assessment of the patients was performed by reaching out to the patients, requesting them to fill out an online questionnaire via the CASTOR © portal. To reach all patients from the previous PEMF trial, consisting of a cohort of 68 patients, a personalized email was sent out to the potential subjects of the study[222]. In case of no response from the study subjects, two personalized reminder emails were sent. If the questionnaire still was incomplete, the authors of the present study sought contact by means of reaching out to the patients via telephone. Through the online post-operative questionnaire, return to sports was assessed, including type and level of sports. Concerning sports activities, the Ankle Activity Scale (AAS) was used[103]. The AAS is a survey containing a high number of sports (n = 53), 3 working activities, and 4 general activities. Scoring zero points on the scale indicates the lowest activity and ten points indicate the highest activity. The AAS was developed by Halasi et al. with the purpose to develop a widely usable, ankle specific activity scoring system that includes most internationally known sports[103]. The score was based on a previously developed activity score for knee injuries, named the Tegner score[33]. Furthermore, secondary outcome measured was assessed by means of the numeric rating scale 0–10 (NRS) for pain (at rest and during activity)[88], the Foot and Ankle Outcome Score (FAOS)[226, 244], work activities, and the subjective satisfaction concerning the surgery. Patients were requested to fill out whether they suffered from any other musculoskeletal injuries from the time of surgery till the moment of filling out the online questionnaire. The NRS is an 11-point scale, representing the spectrum of no pain (0 points) to the worst pain imaginable (10 points)[88]. The sport outcomes, the AAS, the NRS scales (at rest and when running), the FAOS, and return to work had also been assessed in the previous study by

Reilingh et al. both pre-operatively and 1 year post-operatively which, therefore, facilitated a formal comparison in changes over time[222].

Statistical analysis

All analyses were done using Statistical Packages for Social Sciences (SPSS 24.0 Inc, Chicago, IL, USA). To minimize the risk of attrition bias, we included all patients with a completed electronic questionnaire at final follow-up in the statistical analyses. This includes the patients who underwent a reoperation. No additional sample size calculation was performed as this study was a follow-up study of a previously published study. Detailed information on the sample size calculation is described in this previous study[222]. Descriptive statistics of categorical variables were presented as frequencies with percentages per category. Differences in FAOS scores, NRS of pain, and AAS at final follow-up were assessed between patients in the two different original treatment groups (PEMF and Placebo) by means of an independent samples t-test. Descriptive statistics of continuous variables were calculated as means ± standard deviations or median and ranges in case of a skewed distribution. Categorical variables were presented as frequencies with percentages. Differences of the continuous outcome variables were assessed between baseline and final follow-up and between 1 year follow-up and final follow-up. In case of normally distributed data, a paired t-test was used; in case of skewed data, a Wilcoxon signed-rank test was used. The comparisons with $p < 0.05$ were considered to be statistically significant.

RESULTS

Four patients of the 64 (6%) were lost to follow up and could not be reached. The other 60 patients were available for follow-up. No patients declined to participate. The mean post-operative follow-up was at 6.4 years after surgery (SD ± 1.1 years). Mean age of the patients at follow-up was 39 years (SD ± 8.5 years).

Sub-analysis original group

A sub-analysis of the original groups (the PEMF group and the placebo group) showed no significant difference at any of the outcome measures (AAS, NRS pain rest, NRS pain activity, FAOS other symptoms, FAOS pain, FAOS ADL, FAOS sport, and FAOS QOL). Data could thus be interpreted as one group.

Outcome

Sports outcomes

Of all included patients, all participated in sports before injury of which 6 on a professional level, 29 on a competitive level, and 25 on a recreational level. The median preinjury ankle activity score of the 60 included patients was 6.2 (range 4–8). After onset of complaints pre-operatively, only 27 patients were still participating in sports of which 2 on a professional level, 6 competitive, and 19 recreational. The other 33 were not able to participate in sports anymore. The AAS decreased to 3.4 post-injury. After surgery, the median time to return to sports of the 60 included patients was 18 weeks. At 1 year after surgery, 85% of patients returned to playing sport and the AAS increased to 5.2. At final follow-up, 90% of patients participated in sports. These 54 patients participated in 16 different sports, some participating in more than one sport. Most played sport was soccer (16 patients) followed by running (14 patients), fitness (12 patients), cycling/mountainbiking (9 patients), and tennis (7 patients). Of all patients playing sports at follow-up, 35 patients played at a recreational level and 18 patients played at a competitive level. One patient played table tennis on a professional level for years after surgery. At final followup, the median current level of activity of all the patients measured with the AAS was 5.8 (range 1–9) (Figure 2). If median AAS of the 54 patients still playing sports was 6.0 (range 3–9). At time of final follow-up, 32 patients (53%) indicated that they returned to play sport at their pre-injury level. Twenty patients (33%) were not able to obtain their preinjury level of sport because of ankle problems despite the operation. Another eight patients (13%) indicated that they were not able to play sport at their pre-injury level because of different reasons than their ankle.

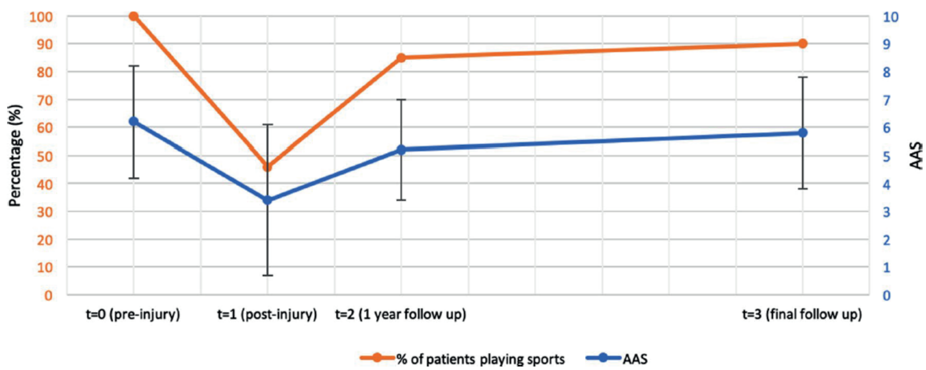

Figure 2. Percentage of patients playing sports and Ankle Activity Score (AAS) over time

Reoperations

Three patients underwent 4 reoperations in total. One patient received an ankle arthrodesis at 6 years after the original surgery because of progressive osteoarthritis and experienced pain. One patient received a reoperation due to posterior impingement 15 months after the original surgery. This and another patient also underwent an adjacent procedure in another hospital.

Additional injuries

Twenty-six patients experienced one or more additional injuries, e.g., back pain or spine injuries (5 patients), anterior cruciate ligament tears (4 patients), other knee problems (5 patients), and achilles tendon problems (3 patients).

Work-related outcomes

Fifty-eight patients resumed to their pre-injury work. One patient indicated that he worked less due to persisting ankle problems. Seven worked less due to other reasons. Four patients reported to be working more because of a decrease in ankle problems.

Clinical outcomes

The clinical outcomes (NRS and FAOS scores) are presented in Figures 3 and 4. Between the pre-operative scores and final follow-up, the NRS pain during rest decreased from 2.7 to 1.0 ($p < 0.01$) and the NRS pain during activity from 7.9 to 4.3 ($p < 0.01$). The FAOS other symptoms decreased from 64 to 52 ($p < 0.01$), the FAOS pain increased from 61 to 67 ($p = 0.01$), the FAOS ADL from 66 to 79 ($p < 0.01$), the FAOS sport from 41 to 48 (n.s.), and the FAOS QOL from 29 to 44 ($p < 0.01$). Between 1 year and final follow-up, the NRS did not change significantly with the NRS during rest from 1.1 to 1.0 (n.s.) and the NRS activity from 3.7 to 4.3 (n.s.). All the FAOS scores, however, significantly decreased. The FAOS other

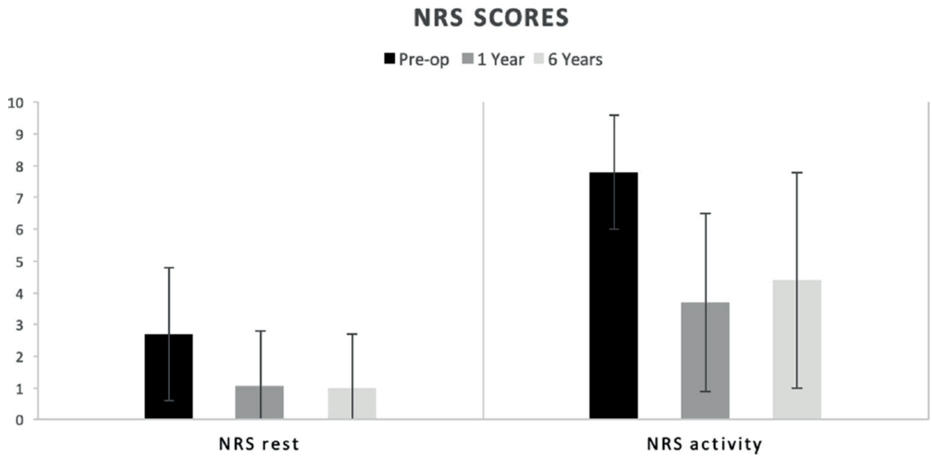

Figure 3. NRS subscores (mean scores and SD) at different follow-up moments (pre-operatively, at 1 year follow-up and at final follow-up at 6.4 years)

symptoms decreased from 70.6 to 52 ($p < 0.01$), the FAOS pain from 82 to 67 ($p < 0.01$), the FAOS ADL from 86 to 78 ($p = 0.02$), the FAOS sport from 67 to 48 ($p < 0.01$), and the FAOS QOL from 54 to 44 ($p < 0.01$).

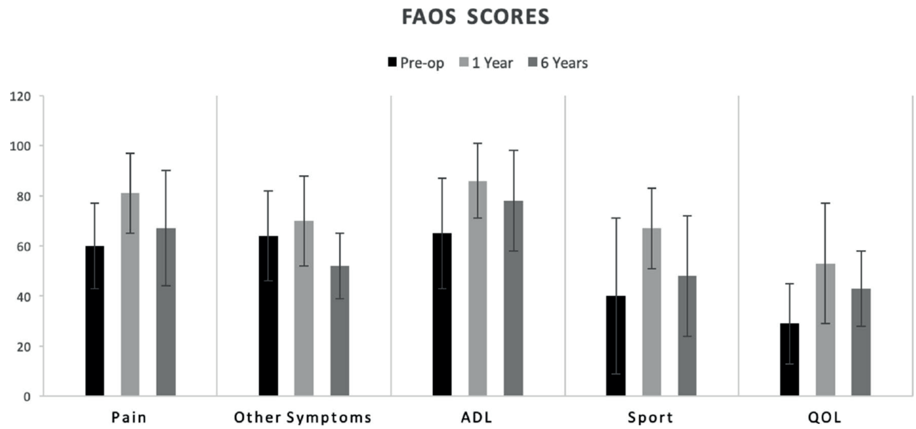

Figure 4. FAOS subscores (mean scores and SD) at different follow-up moments (pre-operatively, at 1 year follow-up and at final follow-up at 6.4 years). ADL activities of daily living, QOL quality of life

Patient satisfaction

In total, 26% of patients were very satisfied with the procedure, 43% of patients said they were satisfied, 17% were neutral, and 15% were unsatisfied. No patients reported to be very unsatisfied. 65% indicated that they would undergo the same procedure if they had to choose again, 15% would not, and 20% were neutral on this subject. Patients rated the end result with a mean of seven in a score ranging from 0–10 (SD = 2).

DISCUSSION

The most important finding of the present study was that arthroscopic BMS in OCLT results in 90% of return to sports/physical activity with 53% being able to return to their pre-injury level of sport at a mean follow-up of 6.4 years. This percentage of sports participation is comparable with follow-up at 1 year post-operatively. The AAS of the patients participating in sports remains similar pre-injury and postoperatively at final follow-up. However, a decrease over time in clinical outcomes were seen when we compare the FAOS follow-up scores at 1 year post-operatively with the final follow-up. Return to sports is important in most young and active patients and of course of uttermost importance in professional athletes. The sustainability of the repaired cartilage is essential in this group to remain active at the highest level. High reported RTS rates at pre-injury level have been reported after BMS in the ankle of up to 94% in elite athletes after a mean follow-up of 3.6 years[238]. Similar percentages are found when looked at autologous bone grafting techniques with a slightly longer RTS time (19.6 ± 5.9 vs 15.1 ± 4 weeks, respectively)[86, 231, 238]. These numbers are much higher than the RTS to pre-injury level which we found being 53% at final follow-up. Multiple explanations can be imagined. Of course, general aging can be of a factor when a lessened level of sport is found. Furthermore, the follow-up time has a negative influence in sport participation, because the quality of fibrocartilage may decrease in time and progression of osteoarthritis may increase in time. Other reasons for decrease of level of activity can also be found in problems other than the ankle, but we tried to overcome this by asking why patients were not able to play sports at their pre-injury level anymore. This still left 33% of them not being able to perform on pre-injury level because of problems with their ankle. Another possibility why the found percentage at the high active patients is higher might be because of the competitive nature of elite athletes and their high drive to perform on the highest possible level. With multiple techniques being available, bone marrow stimulation still is worldwide the most performed intervention for both primary and secondary osteochondral lesions of the talus[56, 142]. It is a relative easy and low-demanding technique with low costs compared to the costlier transplantation or implantation techniques. It is also still the most studied technique showing good-to-excellent results in general [56, 129, 142]. The outcome regarding RTS time and rates after bone marrow stimulation is less described. A few studies focusing specifically on high demanding athletes previously reported good results and a review by Hurley et al. showed a high reported return to play in general after BMS [116, 231, 238]. However, only 14% of the included studies in this review adequately reported the rate of return to sports and they conclude that there is little literature on long-term outcome of BMS for OCLTs in the athletic population[116]. With the larger studies that do describe sports outcome at long-term follow-up being retrospective in nature, we can conclude that there is still a lack of prospective studies collecting data about the long-term outcome[116, 231, 238, 243, 281, 294]. This while more causes for concern are shown in the long term. These concerns are regarding the sustainability of this technique with second-look arthroscopies showing lack of infill at the lesion or the inability to return to the same level of sport[181, 243]. Deterioration of the repaired cartilage was noted in 35% of patients at 5 years second-look arthroscopy and a progress of osteoarthritis by one grade on standard radiographs was reported in 33% of patients with a mean follow-up of 141 months[81, 281]. Long-term (prospective) research is scarce especially concerning sport activities. The aim of this study was, therefore, to report on these outcomes after BMS.

The present study has to be interpreted in light of its strengths and weaknesses. Since four patients were lost to follow up from a group of 64 patients, the lost to follow-up percentage is calculated to be 6%. An acceptable lost to follow up, however, according to the Center for Evidence Based Medicine. Furthermore, since the lost to follow up presumable is missing at random after a mean follow-up period of more than 6 years, we think that it is an adequate follow-up and representative study group[137]. Another limitation is that not all outcome measures were used at final follow-up compared to baseline and 1 year after surgery. In contrast to the pre-operative and short-term follow-up moments, the AOFAS hindfoot score was not conducted at final follow-up. The AOFAS clinical rating systems have insufficient reliability and validity, and would, therefore, provide limited additional information, while patient burden would have been significantly increased as this is a clinician based score[210]. Finally, at final follow-up, no radiological examination by means of a CT scan has been performed which could have been interesting from a research point of view. The results of this study can be used to inform patients, specifically active patients, about expectations around long-term sports outcome after bone marrow stimulation. It also shows that although there is a high return to sport participation, there is still room left for improvement, since outcome scores decreased over time. Possible further research could focus on sport outcome after treatment types that are more based around the preservation of hyaline cartilage such as transplantation or fixation techniques.

CONCLUSION

Arthroscopic BMS in OCLT results in 90% of return to sports/physical activity with 53% being able to return to their pre-injury level of sport at a mean follow-up of 6.4 years. The percentage of sports participation is comparable with follow-up at 1 year post-operatively. The AAS of the patients participating in sports remains similar pre-injury and postoperatively at final follow-up. A decrease over time in clinical outcomes was seen at final follow-up.

9 No superior surgical treatment for secondary osteochondral lesions 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 Twenty-one studies with 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. Calculated success percentages varied widely and ranged from 17 to 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 with 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, neither a clear nor a significant difference between treatment options could be demonstrated. 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.

INTRODUCTION

For the treatment of talar osteochondral defects (OCDs), 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[159, 188, 326]. This was exemplified by studies conducted by Yoon et al. and Choi et al., in which 11% of 399 patients and 6.7% out of 120 ankles, respectively, required revision surgery[49, 322]. These numbers indicate that secondary and tertiary surgical treatment for talar OCDs is not uncommon[282]. 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[322]. 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[159, 188, 326]. 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

The systematic review was prospectively registered at the PROSPERO register[46]. Electronic databases PubMed (MEDLINE), EMBASE, CDSR, DARE and CENTRAL were screened from January 1996 till July 2016 for potential articles of interest (Appendix V). Since not all titles or abstracts in these databases clearly describe whether 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 were primary OCDs, a study cohort of <5 patients, aged <16 (the age around which epiphyseal fusing takes place), concomitant distal tibial lesions and a follow-up of less than 6 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, or when necessary a fourth email was sent. Ultimately, if no response was recorded from the corresponding author, then their specific article was excluded. Independent evaluation of the articles was conducted and then discussed by two reviewers (K.L. and J.D.). In cases of disagreement between the reviewers, the opinion from an independent third investigator (G.K.) 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, a Newcastle–Ottawa scale (NOS) modified for talar OCD was used[313]. This scale assesses the methodological quality of non-randomized studies (Appendix III). Each included study was graded on methodological quality by two independent reviewers (K.L. and J.D.).

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 postoperative AOFAS score of 80 or above[130]. When the FAOS (Foot and Ankle Outcome Score) was used, a score of also 80 or above was regarded to be a successful treatment[226]. When the original ankle score by Mazur et al. was used, a score of 70 or higher was considered to be a successful treatment[171]. 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[121].

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), it was decided to present the 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. 95% binomial proportion confidence intervals were calculated for the success percentages of each study with the Wilson score interval and included in the forest plot (CIA, Confidence Interval Analysis for Windows, version 2.2.0)[35]. To compare between groups with categorical variables, a Fisher's 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 1273 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 were 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 1).

Characteristics of included studies (Tables 1, 2, 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[24, 130]. In total, 17 different scoring systems were found[16, 40, 66, 78, 103, 119, 130, 169, 184, 195, 226, 304, 305, 318] and ten different osteochondral damage classification systems[11, 24, 34, 81, 110, 163, 165, 176, 202, 223] were used (Tables 2, 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 stage I, II, III, IV and V cases, respectively. In 87 of the 299 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 to 76.3%. The mean follow-up was 40 months [range 12–66].

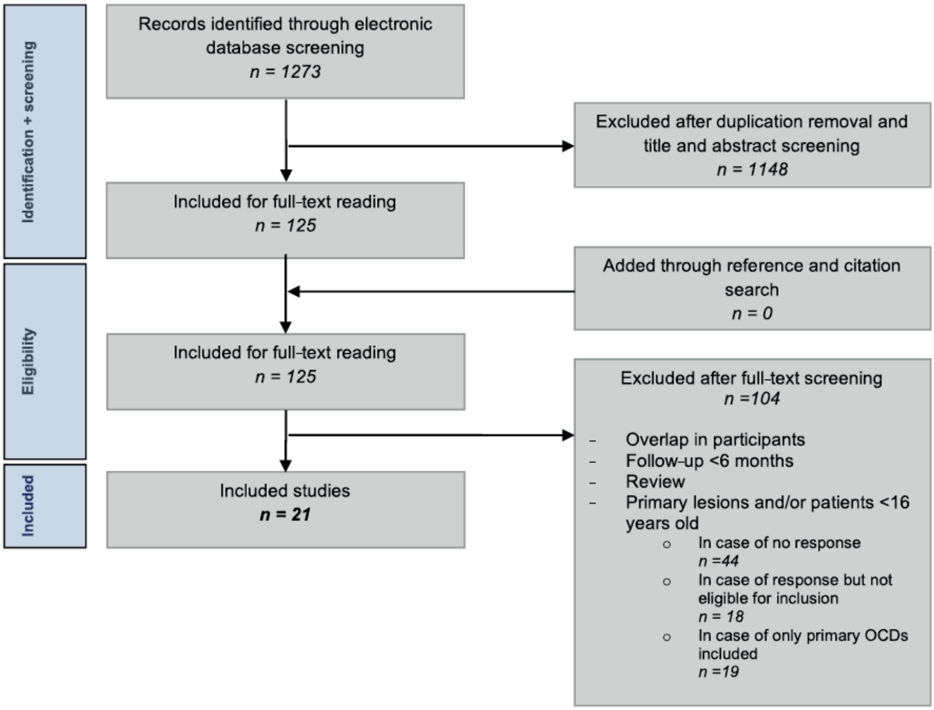

Figure 1. Literature selection algorithms—Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA)

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 orthopaedic 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, either the percentage loss to follow-up was more than 5% or the follow-up rate was not stated.

Treatment strategies

The treatment strategies were divided 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

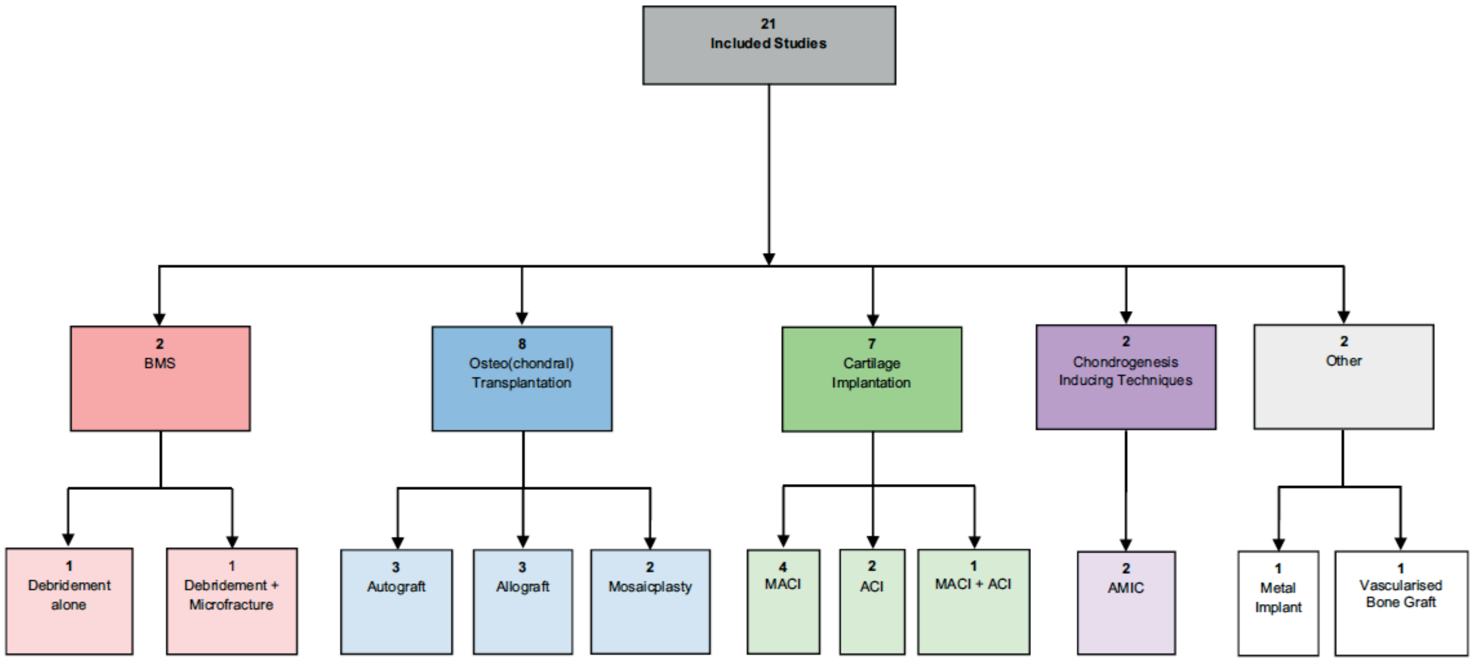

Figure 2. Flow chart of study inclusion and different treatment groups (ACI autologous chondrocyte implantation, AMIC autologous-matrixinduced chondrogenesis, BMS bone marrow stimulation, MACI matrix-associated chondrocyte implantation)

ACI) and chondrogenesis-inducing techniques (AMIC). Two studies did not correspond to any of these groups and are presented separately (Figure 2). All calculated success percentages with their respective confidence intervals are also visually presented in a forest plot (Figure 3). The calculated success percentages of the pooled groups are shown in an additional forest plot (Figure 4).

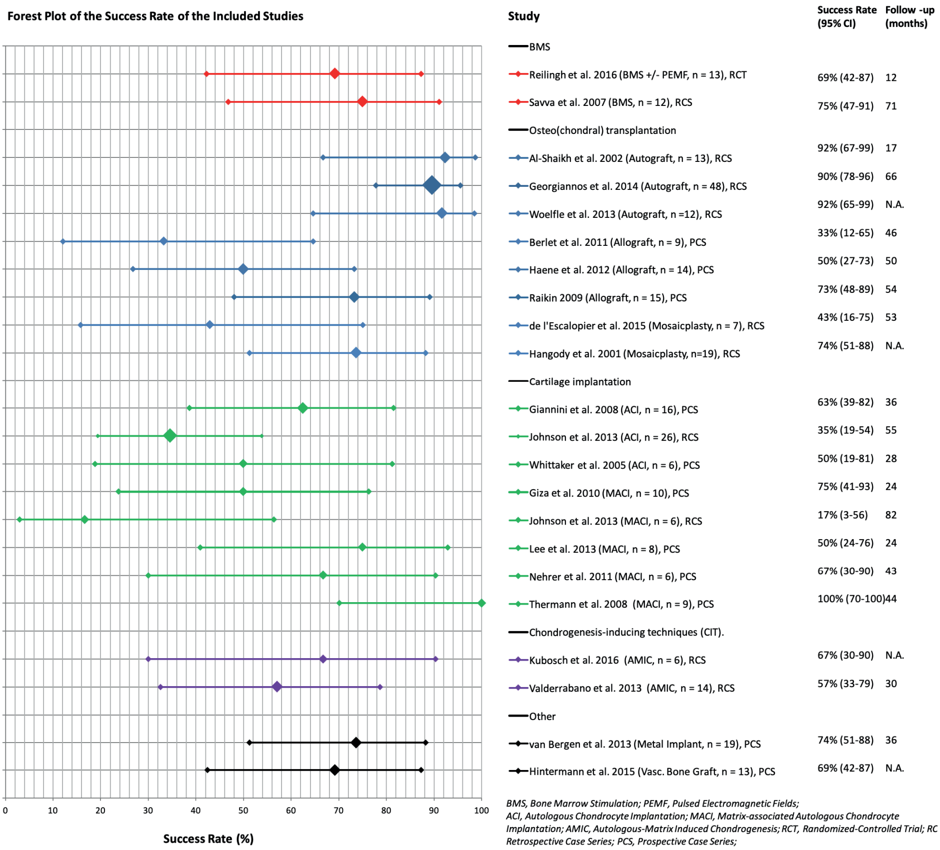

Figure 3. Forest plot of all included studies with the success rates per separate study sorted on treatment strategy and alphabetical order accompanied by number of ankles and follow-up duration (the size of the diamond representing the success rate is categorically adjusted for number of ankles included in the publications)

Bone marrow stimulation (BMS)

Two studies described the outcome of BMS as a secondary treatment for a total of 25 treated ankles[222, 230]. One of these studies (Savva et al.) solely reported the results of repeat arthroscopic treatment[230]. 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 in these type of lesions[224]. The second study by Reilingh et al.

is an RCT investigating the effects of pulsed electromagnetic fields (PEMF) on debridement and microfracture[222]. Due to the fact that the authors indicated that there was no significant difference between the randomized treatment groups, patients from both groups were included. 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.

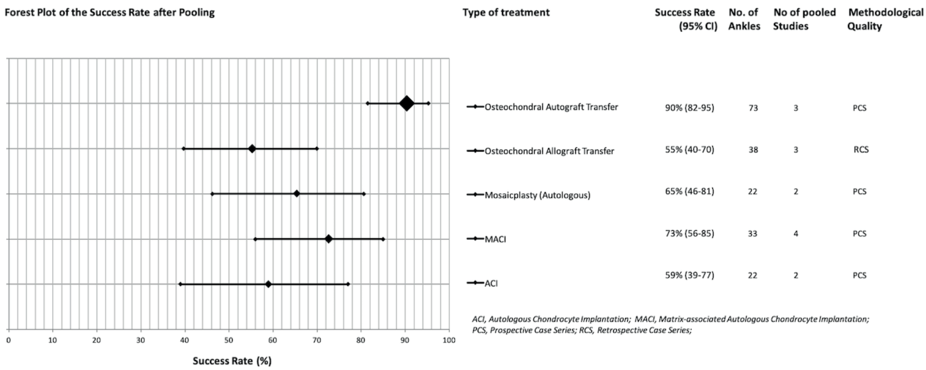

Figure 4. Forest plot of the success rates after pooling sorted on treatment strategy accompanied by the number of included studies, the success rate with confidence interval and the total number of ankles per group (the size of the diamond representing the success rate is categorically adjusted for the number of ankles included)

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[5, 23, 60, 91, 102, 105, 215, 315]. 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 4 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)[5, 91, 315]. Two studies described a (autogenous) mosaicplasty procedure, which is similar to an OATS technique but uses multiple grafts creating a mosaic pattern[60, 105]. Three other studies described an allograft procedure[23, 102, 215]. 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). It was therefore possible to use a simplified pooling method to combine data from these groups (Fig. 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 autogenous in nature for both studies was 65% [CI 46.2–80.6%]. A Fisher's exact test showed no difference between mosaicplasty and the allograft transfer procedure (p = 0.449). A comparison between these two groups and the aforementioned autograft group was not performed since a mosaicplasty or an allograft procedure is 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[94, 96, 121, 153, 187, 267, 314]. 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[96, 153, 187, 267] and two described an ACI procedure[94, 314]. One study described both an ACI and a MACI procedure[121]. 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 groups. 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 combining data on the ankles from the studies methodologically suitable for pooling, thirty-three ankles in the MACI group and twenty-two in the ACI group were found. 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.

Chondrogenesis-inducing techniques (CIT)

Two studies that investigated the effects of a chondrogenesis-inducing technique were identified[138, 279]. 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[138, 279]. The study by Valderrabano et al. describes the iliac crest as a site to obtain the cancellous bone[138, 279]. 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 post-operative 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[285]. Almost all lesions (18 out of 20) were classified as type V (cystic) lesions. The defect was debrided after which the metal implant was introduced into the defect, and this occurred 2 years (mean) after the last failed surgical treatment. The median AOFAS score improved from 62 points pre-operatively to 87 points postoperatively. 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[112]. 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. Data solely on the non-primary lesions were obtained, which included thirteen patients. The mean VAS for pain decreased from 5.8 to 1.7. The mean AOFAS hindfoot 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%].

Table 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 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 Analoge 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
Olgilvie-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 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

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[159, 188, 326]. 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, it was the goal to give 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[192]. 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, 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[95]. 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[216]. It should also be noted that a study by Yoon et al.—which was not included in the present review—described a clinically inferior outcome which corresponded to a calculated success rate of 32%[322]. 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 multiple requests, it was not possible to obtain the separate data, and therefore, this article had to be excluded. Another remark that has to be made in the light of the study by Yoon et al. 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. subchondral cysts were deliberately excluded[230, 322]. As stated above, an underlying cyst is associated with 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 were 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[18, 170, 171, 212]. 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. When comparing the allograft procedure with mosaicplasty, no significant difference was found, and therefore, it is not possible to indicate 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 initially being desired to collect in the 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 included in the studies was substantially lower than required to obtain stable parameters estimates for this type of analysis[179]. 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 is 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.[121]. 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 with 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, neither a clear nor a significant difference between treatment options could be demonstrated. The need for sufficiently powered prospective investigations in a randomized comparative clinical setting remains substantially high.

10 Key findings, general discussion and conclusion

KEY FINDINGS

Chapter 2 Relatively low-acuity lower extremity problems such as strains and sprains of the ankle account for a substantial prevalence of emergency department visits.

Chapter 3 Ankle fractures with syndesmotic instability show arthroscopically accessible OCLTs in 10% of the patients, mostly Berndt and Harty type III or IV and might preferably also be fixated during ORIF.

Chapter 4 Overall, (osteo)chondral lesions of the ankle are found in up to 45% in association with all ankle fractures at follow up until 3 years after initial trauma with the talus as most common location.

Chapter 5 For primary talar osteochondral lesions, none of the treatment options available show any superiority over others when comparing the available literature.

Chapter 6 Arthroscopic LDFF of a fixable primary talar OCLs results in excellent improvement of clinical outcomes. Arthroscopic fixation could be regarded as the new gold standard for the orthopedic surgeon comfortable with arthroscopic procedures.

Chapter 7 The subchondral bone plate restores significantly superiorly after arthroscopic LDFF compared to arthroscopic BMS, however, at 1-year follow-up, clinical differences were not yet found.

Chapter 8 At long term follow up after BMS for OCLT, 90% of patients still participate in sports activities, of whom 53% at pre-injury level. A decrease over time in clinical outcomes was seen when we compared the follow up scores at one year post-operatively with the final follow up.

Chapter 9 More invasive methods are administered in comparison with primary treatment. A clear and significant difference between treatment options could not be demonstrated.

GENERAL DISCUSSION

Part I

It is widely accepted that ankle trauma is the most important etiological factor of an OCLT[83]. As our data also shows, up to 71% of the patients with an OCLT report a history of previous ankle trauma such as strains and sprains[56]. Next to that, the OCL is a not uncommon accompanying injury in ankle fractures. The OCL can originate as an acute lesion at a single traumatic event or the lesion can originate over the course of time but the starting point was most often a force inflicting moment on the articular cartilage and/or subchondral layer. Our research presented in chapter 2 about patients with lower extremity injuries presenting to the emergency department shows that the most common injury was an ankle sprain with an incidence of 206 per 100,000 per year[144]. It also showed that this injury is predominantly contracted by young adults and teenagers. The reported incidence in settings such as sport or active professions is of course even higher[52, 82, 85, 306]. The numbers retracted from emergency databases such as the NEISS (National Health Interview Survey) most likely underestimate all ankle sprains since a large number of individuals would probably not seek emergency treatment. This only strengthens the already highly addressed impact on society. Next to the high incidence for ankle sprains the ankle fracture also attributed a substantial amount to emergency visits with an estimated incidence rate of 49 per 100,000[144]. These numbers might touch on the importance to focus on prevention looking at these high incidences for ankle fractures and ankle sprains. Especially in ankle strains prevention research has gradually increased over the last decade where next to the obvious benefit preventing ligamentous ankle injuries the positive effect on the prevention of cartilage damage are likewise beneficial[77, 162, 239, 295, 303].

Part II: Early Detection of Intra-Articular Osteochondral Lesions in Ankle Fractures

Next to prevention, discussed in the above section, it might also be beneficial to recognize and diagnose OCLTs in the case of ankle fractures. Growing evidence supports the idea that initial deep chondral and osteochondral lesions of both the talus and tibia have an association with posttraumatic osteoarthritis and a therefore less favorable long term outcome[190, 217, 255]. For treatment of ankle fractures this might stipulate the possible advantages of ankle arthroscopy during the index surgery. This arthroscopically assisted open reduction and internal fixation (ARIF) has a growing interest in recent literature with possible beneficial factors accomplishing a visible intra-articular reduction and treating concomitant intra-articular injuries[26, 154, 158]. Since syndesmotic instability in ankle fractures is a prognostic factor of worsened results this might also have a correlation with OCLs. In chapter 3 we aimed to report the incidence of associated OCLs, possible beneficial from arthroscopic treatment in patients with rotational type ankle fractures with syndesmotic injury[145]. We found a 14% incidence of talar OCLs of which most were graded type III or IV according to the Berndt and Harty classification. Although not all, most were situated anteriorly and one could argue that these would have been amendable to arthroscopically assisted or mini open fixation or bone marrow stimulation. One could also argue these lesions would have been amendable for anterolateral ankle joint opening to initiate the fixation or debridement and bone marrow stimulation. Therefore, with OCLs being present in only 1 out of 7 patients and with not all OCLs reachable by scope we would not advice using standard ARIF for diagnosing or treating these OCLs. Although it might be beneficial to assess syndesmotic instability and articular reduction we did not find convincing support for ARIF to be the preferred choice for diagnosing or treating OCLs in this patient group. However, when pre-operative CT scans are made in these rotational ankle fractures, clinicians should be aware of the possible presence of concomitant treatable OCLs.

Elaborating on that subject we executed a systematic review in Chapter 4 where we tried to determine the incidence of OCLs in surgically treated ankle fractures in general as well as the association between type of fracture and the location of the sustained lesions[167]. This might be of importance since previous research by Stufkens et al. showed that ankle fractures with OCLs negatively influenced long term results and were found as a predictor of posttraumatic ankle osteoarthritis[255].

After reviewing the literature, the pooled reported incidence was high with a percentage of 45% with the talus as most reported location of the OCL. Looking at all studies the incidence number per study ranged widely from 10% till 88%. Although the term OCL indicates damage to both the cartilage layer as well as the underlying subchondral layer, this high incidence number suggest that studies included solely chondral lesions or subchondral cysts under the definition of an OCL. This as well as the differences in assessment modality and the fact that multiple studies did not use a differentiating classification system or division between chondral and osteochondral lesions could explain the high incidence[24, 63, 157].

Initially a significant difference was found when comparing different Lauge-Hansen classification types with a higher incidence of OCLs in rotational ankle fractures. A post hoc analysis however could not confirm this difference. When looking at the literature, conflicting data is also reported, some separate case series found a correlation between the number of intra-articular chondral lesions and more severe fracture patterns but multiple other studies were not able to show the same results[154, 217]. That the presence of OCLs is important is further underlined by Regier et al. who found a significant correlation between the incidence of OCLTs and the clinical outcome[217].

The review described in chapter 4 should raise attention to the possible concomitant OCLs in ankle fractures, especially on the talus. Next to treating the ankle fracture, optimal treatment might include the concomitant treatment of these OCLs at initial surgery. Different treatment options for these OCLs exist, ranging from debridement, bone marrow stimulation, fixation or more extensive treatment methods (like osteochondral autograft transfer systems, chondrocyte implantation or metal resurfacing) which are being discussed in Part III of this thesis.

Part III: Treatment Options for Osteochondral Lesions of the Talus. Salvage or Intrinsic Healing?

To create an overview of all possible treatments and their outcome a systematic review was performed that is presented in this thesis as chapter 5. Prior systematic reviews investigated single treatment options or did not differentiate between primary and non-primary lesions[56]. By separating those we were able to exclude an expected misinterpretation of reported success rates. The review focuses on articles from 1996 and after, as since this year, the arthroscopic techniques for the treatment of OCLTs were fully developed and integrated in the orthopaedic workfield[56, 290]. Interestingly, only one study in the review describes the outcome of non-operative treatment[242]. This shows that, as for recent years, most studies focus on (*novel*) surgical treatment options. This is possible linked to the poor and disappointing success rates described in articles published before 1996[25, 56, 225]. The objective of commenced non-operative treatment is to unload the OCL to facilitate healing of the damaged cartilage and the underlying damaged subchondral layer[56]. With a described success rate of only 62%, conservative treatment is still recommended as initial treatment of OCLTs. Treatment is low invasive, inexpensive and has a very low complication rate. Conservative treatment is therefore perfectly suited as a first step in OCL management. When comparing the surgical results we were not able to show any clinical superiority for any of the interventions. The most studied intervention we found was bone marrow stimulation (BMS), this was in concordance with previous reviews. The fact that BMS still is the most described intervention probably indicates that it is still the most practiced surgical intervention for primary OCLTs worldwide[56]. Its popularity owes it to the fact that it is a relative cheap intervention when its compared to the implantation techniques. It furthermore has a low morbidity and allows for a relative quick recovery and fast return to sports[6, 17, 50, 56, 67, 222, 231]. When pooling the results of the BMS studies we found a success rate of 82%. BMS aims at the intrinsic healing properties of the ankle to form fibrin cloths which subsequently becomes fibrocartilage or cartilage/collagen type I. Fibrocartilage has similar properties as the original hyaline cartilage (collagen type II) but is however associated with inferior wear characteristics. Furthermore, not much is known on the restoring properties of the subchondral bone after BMS and this might be of great importance in the long term results of this type of treatment. An irregular shaped subchondral bone plate might for example affect cartilage restoration and may be of importance in the development of osteoarthritis[134, 166, 255]. This might influence the final outcome but is not yet confirmed by long-term clinical studies. Some studies however show that a progression of osteoarthritis can be seen in up to one third of the patient[81, 281]. Theoretically, the conclusion can be made that BMS is a successful treatment option when there is disappearance of the overlying chondral layer of the talus but the subsequent new cartilage is inferior to the original cartilage[143]. Therefore, in cases with a fragmented bony lesion with intact overlying cartilage a fixation technique might be more suitable. This gives a theoretical advantage of the preservation of the hyaline cartilage and the restoration of the subchondral bone. Furthermore, next to these biological advantages, if the fixation of the lesion would fail it would subsequently still be possible to perform a following bone marrow stimulation procedure[143]. Some studies about fixation of large OCLTs have shown promising results for both the acute and chronic lesions but overall the literature describing the clinical results on this topic is scarce[126, 139, 186, 218, 235]. In Chapter 6 we describe a prospective study which describes the clinical and radiological follow up of a previously published arthroscopic method of fixation named the lift, drill, fill and fix (LDFF) technique[126, 143]. At a two year follow up period the technique showed a significant decrease in experienced ankle pain during weight bearing, a high return to sports and a high rate of satisfaction[143]. Although a significant decrease was seen, pain during running was still valued 2.9 at a numeral rating scale from 0 to 10 letting room for improvement[143].

Especially because most of the patients are young and active and have a high wish of playing sports on a competitive level[143]. Not all patients would be suitable for a fixation technique and it is thought necessary for the fragment to have a large enough osseous part to be eligible for fixation[220]. During pre-operative planning, the Location of the OCL and the arthroscopic accessibility has to be taken into account[283, 284]. The arthroscopic method is technically demanding and if it is not possible to acquire the optimal angle to fixate the fragment during arthroscopy an open procedure has to be considered. Because if the optimal angle is not reachable, creating optimal stability is also not possible and this would negatively influence the preferred outcome.

Chapter 7 further describes the difference of BMS and fixation by the LDFF technique by reporting on a comparative study between the two. The most important finding was that although no clinical difference was found between the two treatment types, the subchondral bone plate restores significantly better after fixation compared to BMS[219]. As described before, healing of this subchondral bone plate is important since irregularity of the bone plate has a negative effect on the cartilage restoration.

Therefore, theoretically, progression of osteoarthritis of the ankle should be less in the patients who are treated with the arthroscopic LDFF procedure[219]. Based on the results of described in chapter 6 and 7, when treating an OCLT with intact overlying cartilage and a large enough osseous part, fixation should be considered as the primary treatment. That BMS still has a large part in the treatment of specific OCLTs however is discussed in chapter 8. This chapter describes the results of this treatment type at a mean follow up of 6.4 years. A high return to sport of 90% is demonstrated with 53% being able to return to their pre-injury level. This is in concordance with a previous review which showed a high return to play after BMS[116]. It has to be said however that only 14% of the included studies in this review adequately reported the rate of return to sports and most studies were retrospective and short term. Our study shows that despite a high return to sport, a much smaller group was able to return to their pre-injruy level. This furthermore underlines the causes for concern when evaluating this type of treatment especially regarding the sustainability with second look arthroscopies showing lack of infill at the lesion or similar reports about the inability to return to the same level of sport[181, 243]. BMS should therefore be used in cases were fixation of the OCL is not possible, for instance in small defects or defects without a proper osseous layer.

If primary treatment of an OCLT fails, another consideration about the type of treatment has to be made. In chapter 9 we try to give insight in the different surgical treatment options if primary treatment fails and try to demonstrate any superior treatment type. As expected, more invasive treatment types are described compared to the treatment types used in primary OCLTs. However, the most described treatment type for primary OLCTs, namely BMS, is still used as revision surgery showing acceptable success rates between 69% and 75%. This is lower than the overall described success rate of BMS in primary OCLT surgery of 82% but because BMS is relative non-invasive and treatment is relative inexpensive it should still be considered for the smaller secondary lesions[56, 142]. Most of the included articles reported about a more invasive osteochondral or cartilage transplantation method as a following treatment method after failed primary surgery. Most of the included studies were of low quality when the methodological quality was evaluated. As long as no randomized comparative clinical trials are conducted data will not be sufficient to draw any firm conclusions[142]. The results found thus also should not be used in decision making about the technique necessary but should give patients and clinicians an indication about the expected success percentages of different treatment methods after failed primary surgery[142].

Conclusions and Implications of this Work

Concluding: How to treat a patient with an osteochondral lesions of the talus?

Due to the extensiveness in diversity of osteochondral lesions this is not a question that has a straightforward answer. For the healing of articular cartilage, treatment options of lesions can be sorted according to four principles: it can be restored, replaced, relieved and resected[192].

When choosing the right treatment option, it is important to have an understanding of the origin of the OCL, its type, its location, and of course the needs of the patient.

The work in this thesis will aid and direct surgeons in their clinical decision making when diagnosing and treating patients with ankle injuries and subsequent osteochondral lesions of the talus.

Incidence of ankle injuries such as strains and sprains and ankle fractures are substantial when looking at lower extremity injuries[144]. As our research show a high amount of OCLTs are preceded by ankle injuries with up to 71% of patients reporting a history of ankle trauma (fractures excluded)[56]. Furthermore, in up to 47% of all ankle fractures a concomitant type of chondral or osteochondral damage is described[167]. A non-operative treatment type as immobilization and/or non-weight bearing should always be the first line in treatment as treatment is simple, inexpensive and low invasive. More invasive treatment types should be considered when non-operative treatment fails. With most patients being young and active it is of great importance to get optimal outcome rates with high sustainability as these patients are high demanding and are expected to use their ankles for many years after surgery. Based on this fact and our research we would advise that, if possible, fixation of a OCLT should be the primary surgical treatment of choice. This in order to preserve the more superior hyaline cartilage which would give better outcomes at longer term.

When the lesion is not fixable, bone marrow stimulation is still a viable option if the lesion in not too large. If the primary surgery fails, there are numerous secondary treatment types available including more invasive osteochondral or cartilage transplantation methods.

Future research should focus on the execution of sufficiently powered prospective investigations, preferably in a randomised and comparative clinical trial setting using outcome scores that are validated for the treatment of talar OCLs.

11 Summary in English and Dutch

SUMMARY

PART I Introduction

Problem statement – The Osteochondral Lesion

An osteochondral lesion is defined by damage to the articular cartilage and the underlying subchondral bone. These lesions can occur at every age but are often seen in the young and active population. They cause impairment because of deep joint pain with major limitations for the patient. This thesis specifically focusses on osteochondral lesions of the talus (OCLT). It is frequently described as an uncommon diagnosis, however, exact incidence rates are unclear. Numerous types of surgical treatment strategies exist but there is no clear consensus as to which surgical intervention is considered preferable for which type of lesion. The general aim of this thesis was therefore to evaluate the incidence of traumatic OCLTs and to review respective treatment options for OCLTs.

Chapter 2

Incidence of patients with lower extremity injuries presenting to US emergency departments by anatomic region, disease category, and age.

In this chapter we tried to determine the disease categories, anatomic regions, and circumstances that are accountable for the highest incidence of lower extremity problems among patients presenting to emergency departments. To obtain a probability sample of all the lower extremity injuries we used an emergency department database, the National Electronic Injury Surveillance System (NEISS). In total, a number of 119,815 patients with lower extremity injuries who presented to emergency departments in the U.S. were found in this database. We analyzed their injury and patient characteristics. With help of US census data we were able to calculate disease categories, injuries, age groups and incidence rates for various anatomical regions. We found that 36% of all lower extremity injuries were strains and sprains and the specific injury that had the highest incidence was a sprain of the ankle (206 per 100,000; 95% confidence interval, 181–230). It can be concluded that relative low-acuity leg problems account for a substantial number of emergency department visits.

Part II: Early Detection of Intra-Articular Osteochondral Lesions in Ankle Fractures

Chapter 3

Prevalence of osteochondral lesions in rotational type ankle fractures with syndesmotic injury.

The aim of this chapter was to determine the incidence of associated OCLs in patients with rotational type ankle fractures and an accessory syndesmotic injury. Specifically the OCLs that may benefit from arthroscopic treatment. For this study we reviewed data of patients who were surgically treated by fixation of an ankle fracture with a concomitant syndesmotic rupture. All patients received a low dose bilateral postoperative CT. In total 59 patients were included in this study. We found associated OCTLs in eight patients (14%). When classified according to the Berndt and Harty classification system, one was defined as a stage I, four a stage III, and another four as a stage IV. Of these lesions, six were arthroscopically accessible (10%). As the majority of OCTLs found in this series were fixable (Berndt and Harty type III or IV) they might preferably also be addressed during index surgery.

Chapter 4

High incidence of (osteo)chondral lesions in ankle fractures

Suboptimal functional results and residual complaints at follow up are found in up to 50% of patients with ankle fractures that receive surgical treatment. This might be caused by the presence of concomitant intra-articular OCLs. Therefore, the aim of chapter 4 was to determine the incidence of OCLs following an ankle fracture as well as their location. We also tried to determine if there was an association between type of fracture and the presence of the lesions. A literature search was performed to identify relevant studies. We extracted OCL incidence and location, per fracture classification, from the included articles. We included 20 articles with a total of 1707 patients. OCL incidence directly after the trauma was high as we found a percentage of 45% ($n = 1404$). Described incidence of OCLs at least 12 months after the initial trauma was 47%. Most common location of a lesion after an ankle fracture was the talus (43% of all lesions). There was a significant difference among Lauge–Hansen categories and lesion incidence ($p = 0.049$) which showed that rotational type fractures showed a higher incidence of OCLs.

Part III: Treatment Options for Osteochondral Lesions of the Talus. Salvage or Intrinsic Healing?

Chapter 5

No superior treatment for primary osteochondral lesions of the talus.

The aim of this chapter was to detect the most effective treatment option for primary OCLs. Therefore a

literature search was executed to identify studies describing different treatment options for these lesions.

If possible and methodologically eligible, the different studies were pooled. We included 1236 primary talar osteochondral lesions that were described in 52 different studies. Of these selection, 41 studies were retrospective and 11 were prospective. There were only two randomised controlled trials (RCTs). In the bone marrow stimulation group we were able to perform a simplified pooling method for 11 retrospective case series which included

317 ankles. The pooled success rate we found for bone marrow stimulation was 82% [CI 78–86%]. As for an osteochondral autograft transfer system or an osteoperiosteal cylinder graft insertion we pooled 7 case series with in total 78 ankles with a calculated pooled success rate of 77% [CI 66–85%]. None of the different analyzed treatment options showed superiority over others.

Chapter 6

Arthroscopic Lift, Drill, Fill and Fix (LDFF) is an effective treatment option for primary talar osteochondral lesions.

In this chapter we wanted to report about the radiological and clinical results of an arthroscopic fixation technique for primary osteochondral lesions of the talus named the lift, drill, fill and fix (LDFF) method. In 27 ankles an arthroscopic LDFF procedure was performed for primary and fixable OCLTs. Mean follow-up was 27 months. We found a significant improvement in mean Numeral Rating Scale (NRS) during running from 7.8 pre-operatively to 2.9 post-operatively ($p = 0.006$). This was also found for the NRS during walking which improved from 5.7 to 2.0 ($p < 0.001$) and the NRS in rest which improved from 2.3 to 1.2 ($p = 0.015$). As for the Foot and ankle Outcome Score (the FAOS) a score of 86 for pain, 63 for other symptoms, 95 for activities of daily living, 70 for sport and 53 for quality of life was found at final follow up. A score comparison pre-operative and postoperative was possible for 16 patients and showed significant improved subscores. Also, 81% of the CT scans after one year following surgery showed a flush subchondral bone plate. In 92% of OCLs union was present. We concluded that arthroscopic LDFF of a fixable primary OCLT resulted in an excellent improvement of clinical outcomes and radiological follow-up showed a high fusion rate. For the orthopedic surgeon that is comfortable with arthroscopic procedures this technique could be regarded as the new gold standard.

Chapter 7

The subchondral bone healing after fixation of an osteochondral talar lesion is superior in comparison with microfracture.

A generally accepted primary surgical treatment for osteochondral lesions of the talus is arthroscopic bone marrow stimulation (BMS). A good considered alternative however is fixation. The aim of this chapter was to evaluate and compare radiological and clinical results between arthroscopic bone marrow stimulation and arthroscopic fixation in primary fixable OCLTs. In a comparative and prospective study, fourteen patients were treated with arthroscopic BMS and fourteen with the arthroscopic lift-drill-fill-fix (LDFF) method. Clinical assessment was performed with the American Orthopaedic Foot and Ankle Society (AOFAS) score and the numeric rating scale (NRS) for pain. We analyzed the level of the subchondral plate (flush or depressed) on the postoperative CT scans at one year follow up. No significant difference in clinical assessment was found between the two groups at one year follow-up. After BMS a flush subchondral bone plate was observed in three patients and in ten patients after LDFF (p = 0.02). We therefore concluded that the subchondral bone plate seems to restore significantly superior after an arthroscopic LDFF procedure compared to arthroscopic BMS. This might result in less progression of subsequent ankle osteoarthritis in the future and thus has a potential better outcome on the long term.

Chapter 8

Bone marrow stimulation for talar osteochondral lesions at long-term follow-up shows a high sports participation though a decrease in clinical outcomes over time.

A high rate of sport resumption is seen at short-term follow-up after bone marrow stimulation (BMS). However, it is unclear if this sports activity is also possible at longer follow up. Therefore, the aim of this chapter was to perform a long term follow up evaluation of sport participation after arthroscopic BMS. We included 60 patients from a previous randomized controlled trial which all received arthroscopic BMS for an OCLT. We assessed the return to sports, type and level as well as some secondary outcome measures, namely the numeric rating scales and the Foot and Ankle Outcome Score (FAOS). Final follow up was after a mean of 6.4 years. The level of activity which was measured with the ankle activity scale (AAS) was 6.2 pre-injury and decreased to 3.4 post-injury. We subsequently found an increase to 5.2 at 1 year after surgery and to 5.8 at moment of final follow-up. We found that at time of final follow-up, up to 54 patients (90%) still participated in sport activities of whom 33 patients (53%) at pre-injury level. We observed an improvement in the FAOS scores at one year follow-up but however saw a significantly decrease in all subscores when scores were compared with the final follow-up.

Chapter 9

No superior surgical treatment **for secondary** osteochondral lesions **of the talus.**_

To identify the most effective surgical treatment for OCLTs after previously failed primary surgery we performed a systematic review described in this chapter. If studies were eligible for pooling they were combined. We found 21 studies describing a total of 299 patients with 301 OCLTs that failed primary surgery. Of these studies, 8 were retrospective case series, 12 were prospective case series and only one was a randomized controlled trial. The success percentages we calculated had a wide variety and ranged from 17 to 100%. Since level of evidence was low in most studies and we found a scarce number of patients it was not possible to perform a methodologically proper meta-analysis. With a simplified pooling method we were able to calculate a mean success rate for the osteochondral autograft transfer procedure (90% [CI 82–95%]), for a mosaicplasty procedure (65% [CI 46–81%]) and an osteochondral allograft transfer procedure (55% [CI 40–70%]). We could not find a significant difference between the classic autologous chondrocyte implantation and matrix-associated chondrocyte implantation (success rates of 59% [CI 39–77%] and

73% [CI 56–85%] respectively). Overall, there were many surgical treatments described for OCLs after primary surgical failure. Compared with primary treatment more invasive methods were administered. Since it was not possible to perform a proper meta-analysis it is not appropriate to draw firm conclusions when evaluating the data. No clear or significant difference between various treatment options could be demonstrated besides an expected difference between the extensive allograft and mosaicplasty procedures compared to the single autograft transfer procedure. We therefore conclude that more sufficiently powered and prospective investigations in a randomized comparative clinical setting are needed. This review however can be used to inform patients about expected success rates after different treatment methods following failed primary surgery.

Chapter 10
General discussion
When choosing the right treatment option for OCLTs, it is important to have an understanding of the origin of the OCL, its type, its location, and of course the needs of the patient.

This thesis shows that a high amount of OCLTs are preceded by ankle injuries with up to 71% of patients reporting a history of ankle trauma (fractures excluded). Furthermore, in up to 47% of all ankle fractures a concomitant type of chondral or osteochondral damage is described. A non-operative treatment type as immobilization and/or non-weight bearing should always be the first line in treatment as this treatment is simple, inexpensive and low invasive. More invasive treatment types should be considered when non-operative treatment fails. With most patients being young and active it is of great importance to get optimal outcome rates with high sustainability. Based on this fact and our research we would advise that, if possible, fixation of a OCLT should be the primary surgical treatment of choice. This in order to preserve the more superior hyaline cartilage which would give better outcomes at longer term.

When the lesion is not fixable, bone marrow stimulation is still a viable option if the lesion is not too large. If the primary surgery fails, there are numerous secondary treatment types available including more invasive osteochondral or cartilage transplantation methods. The work in this thesis will aid and direct surgeons in their clinical decision making when diagnosing and treating patients with ankle injuries and subsequent osteochondral lesions of the talus.

NEDERLANDSE SAMENVATTING

Deel I Introductie

Hoofdstuk 1
Het osteochondrale defect

Een osteochondraal defect wordt gedefinieerd door schade aan het gewrichtskraakbeen en het onderliggende subchondrale bot. Deze defecten kunnen op elke leeftijd voorkomen, maar worden vaak gezien bij de jonge en actieve populatie. Ze veroorzaken een beperking door diepe gewrichtspijn met grote gevolgen voor de patiënt. Dit proefschrift richt zich specifiek op osteochondrale defecten van de talus. Het wordt vaak beschreven als een ongebruikelijke diagnose, maar de exacte incidentiecijfers zijn onduidelijk. Er bestaan talloze soorten chirurgische behandelingsstrategieën, maar er is geen duidelijke consensus welke chirurgische ingreep de voorkeur verdient voor welk type defect. Het algemene doel van dit proefschrift is daarom om de incidentie van traumatische osteochondrale defecten van de talus te evalueren evenals de respectievelijke behandelopties.

Hoofdstuk 2
Incidentie van patiënten met onderste extremiteit letsel presenterend op spoedeisende hulp afdelingen naar anatomische regio, ziekte categorie en leeftijd.

In dit hoofdstuk hebben we geprobeerd het soort letsel, de anatomische regio en de omstandigheden vast te stellen die verantwoordelijk zijn voor de presentatie op de spoedeisende hulp van patiënten met een letsel van de onderste extremiteit. Voor het verkrijgen van een waarschijnlijkheids steekproef van alle letsels aan de onderste extremiteit hebben we gebruik gemaakt van een database op de spoedeisende hulp, het National Electronic Injury Surveillance System (NEISS). In totaal werden in deze database een aantal van 119.815 patiënten met verwondingen aan de onderste ledematen gevonden die zich hadden gemeld op de spoedeisende hulp in de VS. We analyseerden hun letsel- en patiëntkenmerken. Met behulp van Amerikaanse inwonersgegevens konden we ziektecategorieën, verwondingen, leeftijdsgroepen en incidentiecijfers voor verschillende anatomische regio's berekenen. We ontdekten dat 36% van alle verwondingen aan de onderste extremiteit verrekkingen en verstuikingen waren en dat de specifieke verwonding met de hoogste incidentie een verstuiking van de enkel was (206 per 100.000; 95% betrouwbaarheidsinterval: 181-230). Geconcludeerd kan worden dat letsels met een relatief lage ernst verantwoordelijk zijn voor een aanzienlijk aantal bezoeken aan de spoedeisende hulp.

Deel II: vroege detectie van intra-articulaire osteochondrale defecten bij fracturen van de enkel

Hoofdstuk 3

Prevalentie van osteochondrale defecten bij rotatiefracturen van de enkel met syndesmose letsel.

Het doel van dit hoofdstuk was om de incidentie van geassocieerde osteochondrale defecten te bepalen bij patiënten met rotatie enkelfracturen en accessoir syndesmose letsel. Met name de defecten die baat kunnen hebben bij arthroscopische behandeling. Voor deze studie hebben we gegevens beoordeeld van patiënten die operatief werden behandeld door fixatie van een enkelfractuur met een gelijktijdige syndesmose ruptuur. Alle patiënten kregen een lage dosis en bilaterale postoperatieve CT. In totaal werden 59 patiënten geïncludeerd in deze studie. We vonden geassocieerde osteochondrale defecten bij acht patiënten (14%). Wanneer geclassificeerd volgens het classificatiesysteem van Berndt en Harty, werd één gedefinieerd als stadium I, vier als stadium III en nog eens vier als stadium IV. Van deze laesies waren er zes arthroscopisch toegankelijk (10%). Aangezien de meeste defecten die in deze serie werden gevonden te fixeren waren (Berndt en Harty type III of IV), zouden ze bij voorkeur ook kunnen worden aangepakt tijdens de indexprocedure.

Hoofdstuk 4

Hoge incidentie van (osteo)chondrale defecten bij fracturen van de enkel

Suboptimale functionele resultaten en restklachten bij follow-up worden gevonden bij tot 50% van de patiënten met enkelfracturen na een chirurgische behandeling. Dit kan mogelijk worden veroorzaakt door de aanwezigheid van gelijktijdige intra-articulaire osteochondrale defecten. Daarom was het doel van hoofdstuk 4 om de incidentie van deze defecten na een enkelfractuur alsmede hun locatie te bepalen. We hebben ook geprobeerd vast te stellen of er een verband was tussen het type fractuur en de aanwezigheid van de defecten. Er is een literatuuronderzoek gedaan om relevante studies te identificeren. We hebben de incidentie en locatie van de defecten per fractuurclassificatie geëxtraheerd uit de geïncludeerde artikelen. We includeerden 20 artikelen met in totaal 1707 patiënten. Incidentie van (osteo) chondrale defecten direct na het trauma was hoog, aangezien we een percentage van 45% vonden ($n = 1404$). De beschreven incidentie ten minste 12 maanden na het eerste trauma was 47%. De meest voorkomende plaats van een defect na een enkelfractuur was de talus (43% van alle laesies). Er was een significant verschil tussen de Lauge-Hansen-categorieën en de incidentie van defecten ($p = 0.049$) wat aantoonde dat een fractuur van het rotatoire type een hogere incidentie van defecten vertoonde.

Deel III: Behandelingsopties voor osteochondrale defecten van de talus. Herstellen of intrinsieke genezing?

Hoofdstuk 5

Geen superieure behandeling voor primaire osteochondrale defecten van de talus.

Het doel van dit hoofdstuk was om de meest effectieve behandelingsoptie voor primaire osteochondrale defecten te detecteren. Er werd daarom een literatuuronderzoek uitgevoerd om studies te identificeren die verschillende behandelingsopties voor deze defecten beschrijven. Indien methodologisch verantwoord en als ze in aanmerking kwamen om te poolen werden de verschillende onderzoeken gecombineerd. We includeerden 1236 primaire talaire osteochondrale laesies die werden beschreven in 52 verschillende onderzoeken. Van de artikelen waren 41 onderzoeken retrospectief en 11 prospectief. Er waren slechts twee gerandomiseerde gecontroleerde onderzoeken (RCT's). In de beenmergstimulatiegroep waren we in staat om een vereenvoudigde poolingmethode uit te voeren voor 11 retrospectieve artikelen met 317 enkels. Het gepoolde succespercentage dat we vonden voor beenmergstimulatie was 82% [CI 78-86%]. Wat betreft een osteochondraal autograft transfer systeem of een osteoperiostale cilinder graft insertie hebben we 7 retrospectieve case series gepoold met in totaal 78 enkels met een succes percentage van 77% [CI 66-85%]. Geen van de verschillende geanalyseerde behandelingsopties vertoonde superioriteit ten opzichte van de rest.

Hoofdstuk 6

Arthroscopische Lift, Drill, Fill and Fix (LDFF) is een effectieve behandelingsoptie voor primaire osteochondrale defecten van de talus.

In dit hoofdstuk rapporteren we over de radiologische en klinische resultaten van een arthroscopische fixatietechniek voor primaire osteochondrale defecten van de talus, de zogenaamde lift, drill, fill and fix (LDFF) methode. In 27 enkels werd een arthroscopische LDFF-procedure uitgevoerd voor een primair en fixeerbaar defect. De gemiddelde follow-up was 27 maanden. We vonden een significante verbetering in de Numeral Rating Scale (NRS) tijdens hardlopen van 7,8 preoperatief tot 2,9 postoperatief ($p = 0{,}006$). Dit werd ook gevonden voor de NRS tijdens lopen die verbeterde van 5,7 naar 2,0 ($p < 0{,}001$) en de NRS in rust die verbeterde van 2,3 naar 1,2 ($p = 0{,}015$). Wat betreft de Foot and Ankle Outcome Score (de FAOS) werd bij de laatste follow-up een score gevonden van 86 voor pijn, 63 voor overige symptomen, 95 voor activiteiten van het dagelijks leven, 70 voor sport en 53 voor kwaliteit van leven. Een vergelijking van scores preoperatief en postoperatief was mogelijk voor 16 patiënten en toonde significant verbeterde subscores. Ook toonde 81% van de CT-scans een jaar na de operatie een egale subchondrale botplaat. In 92% van de defecten was consolidatie aanwezig. We concludeerden dat arthroscopische LDFF van een fixeerbaar primair defect resulteerde in een uitstekende verbetering van klinische uitkomsten en radiologische follow-up toonde een hoge consolidatie. Voor de orthopedisch chirurg die vertrouwd is met arthroscopische procedures zou deze techniek als de nieuwe gouden standaard kunnen worden beschouwd.

Hoofdstuk 7

De subchondrale botgenezing na fixatie van een osteochondrale defecten van de talus is superieur in vergelijking met beenmergstimulatie.

Een algemeen aanvaarde primaire chirurgische behandeling voor osteochondrale defecten van de talus is arthroscopische beenmergstimulatie (BMS). Een goed overwogen alternatief is echter fixatie. Het doel van dit hoofdstuk was het evalueren en vergelijken van radiologische en klinische resultaten tussen artroscopische beenmergstimulatie en artroscopische fixatie in primair fixeerbare defecten. In een vergelijkende en prospectieve studie werden veertien patiënten behandeld met arthroscopische BMS en veertien met de arthroscopische lift-drill-fill-fix (LDFF) methode. Klinische beoordeling werd uitgevoerd met de American Orthopaedic Foot and Ankle Society (AOFAS) score en de Numeric Rating Scale (NRS) voor pijn. We analyseerden het niveau van de subchondrale plaat (egaal of inzakking) op de postoperatieve CT-scans na een follow-up van een jaar. Er werd geen significant verschil in klinisch resultaat gevonden tussen de twee groepen. Na BMS werd een egale subchondrale botplaat waargenomen bij drie patiënten en bij tien patiënten na LDFF ($p = 0{,}02$). We concludeerden daarom dat de subchondrale botplaat significant superieur lijkt te herstellen na een arthroscopische LDFF-procedure in vergelijking met arthroscopische BMS. Dit kan in de toekomst resulteren in minder progressie van latere artrose van de enkel en heeft dus een potentieel beter resultaat op de lange termijn.

Hoofdstuk 8

Beenmergstimulatie voor osteochondrale defecten van de talus bij langdurige follow-up laat een hoge sportdeelname zien, de klinische resultaten nemen in de loop van de tijd echter af.

Een hoge mate van terugkeer naar sport wordt gezien op de korte termijn follow-up na beenmergstimulatie (BMS). Het is echter onduidelijk of deze sportactiviteit ook aanwezig is ten tijde van lange termijn follow-up. Daarom was het doel van dit hoofdstuk om een lange termijn follow-up evaluatie uit te voeren van sportdeelname na artroscopische BMS. We includeerden 60 patiënten uit een eerdere gerandomiseerde gecontroleerde studie die allemaal een arthroscopische BMS procedure kregen voor een osteochondraal defect van de talus. We hebben de terugkeer naar sport, type en niveau beoordeeld, evenals enkele secundaire uitkomstmaten, namelijk numerieke beoordelingsschalen en de Foot and Ankle Outcome Score (FAOS). De laatste follow-up was na gemiddeld 6,4 jaar. Het activiteitsniveau dat werd gemeten met de Ankle Activity Scale (AAS) was 6,2 vóór de blessure en nam af tot 3,4 na de blessure. Vervolgens vonden we een stijging tot 5,2 op 1 jaar na de operatie en tot 5,8 op het moment van de laatste follow-up. We ontdekten dat op het moment van de laatste follow-up tot 54 patiënten (90%) nog aan sport deden, van wie 33 patiënten (53%) op het niveau van vóór de blessure. We zagen een verbetering in de FAOS-scores na een jaar follow-up, maar zagen echter een significante afname in alle subscores wanneer de scores werden vergeleken met de laatste follow-up.

Hoofdstuk 9

Geen superieure chirurgische behandeling voor secundaire osteochondrale defecten van de talus.

Om de meest effectieve chirurgische behandeling voor osteochondrale defecten van de talus te identificeren na een eerder gefaalde primaire operatie, hebben we een systematische review uitgevoerd die in dit hoofdstuk wordt beschreven. Als studies in aanmerking kwamen voor pooling, werden ze gecombineerd. We hebben 21 onderzoeken gevonden met een totaal van 299 patiënten met 301 osteochondrale defecten van de talus die een gefaalde primaire operatie hadden ondergaan. Van deze onderzoeken waren er 8 retrospectieve casusseries, 12 prospectieve casusseries en slechts één was een gerandomiseerde gecontroleerde studie. De door ons berekende succespercentages waren zeer divers en varieerden van 17 tot 100%. Omdat het niveau van bewijs in de meeste onderzoeken laag was en we een schaars aantal patiënten vonden, was het niet mogelijk om een methodologisch goede meta-analyse uit te voeren. Met een vereenvoudigde poolingmethode konden we een gemiddeld succespercentage berekenen voor de osteochondrale autograft-transplantatie procedure (90% [CI 82-95%]), voor een mozaïekplastiek (65% [CI 46-81%]) en een osteochondrale allograft transplantatie procedure (55% [BI 40-70%). We konden geen significant verschil vinden tussen de klassieke autologe chondrocyten implantatie en matrix-geassocieerde chondrocyten implantatie (succespercentages van respectievelijk 59% [CI 39-77%] en 73% [CI 56-85%]). Over het algemeen zijn er veel chirurgische behandelingen beschreven voor osteochondrale defecten na primair operatief falen. In vergelijking met de primaire behandeling werden meer invasieve methoden toegepast. Aangezien het niet mogelijk was om een goede meta-analyse uit te voeren, is het niet gepast om harde conclusies te trekken bij het evalueren van de gegevens. Er kon geen duidelijk of significant verschil tussen de verschillende behandelingsopties worden aangetoond, behalve een verwacht verschil tussen de uitgebreide allograft- en mozaïekplastiek procedures in vergelijking met de enkele autograft-transplantatie procedure. We concluderen daarom dat meer voldoende krachtige en prospectieve onderzoeken in een gerandomiseerde vergelijkende klinische setting nodig zijn. Deze huidige systematische review kan echter worden gebruikt om patiënten te informeren over verwachte succespercentages na verschillende behandelmethoden na een gefaalde primaire operatie.

Hoofdstuk 10

Algemene discussie

Bij het kiezen van de juiste behandelingsoptie voor osteochondrale defecten van de talus is het belangrijk om inzicht te hebben in de oorsprong van het defect, het type, de locatie en natuurlijk de behoeften van de patiënt. Dit proefschrift laat zien dat een groot aantal van de osteochondrale defecten wordt voorafgegaan door enkelletsel, waarbij tot 71% van de patiënten een voorgeschiedenis van enkeltrauma rapporteert (exclusief fracturen). Bovendien wordt bij tot 47% van alle enkelfracturen een gelijktijdige chondrale of osteochondrale schade beschreven. Een niet-operatieve behandeling zoals immobilisatie moet altijd de eerste lijn van de behandeling zijn, aangezien de behandeling eenvoudig, goedkoop en weinig invasief is. Meer invasieve behandelingstypen moeten worden overwogen wanneer niet-operatieve behandeling mislukt. Aangezien de meeste patiënten jong en actief zijn, is het van groot belang om optimale uitkomstpercentages te krijgen met een hoge duurzaamheid. Op basis van dit feit en ons onderzoek zouden we adviseren dat, indien mogelijk, fixatie van een osteochondraal defect van de talus de primaire chirurgische behandeling van keuze zou moeten zijn. Dit om het meer superieure hyaliene kraakbeen te behouden, wat op langere termijn betere resultaten zou geven. Wanneer het defect niet kan worden hersteld, is beenmergstimulatie nog steeds een haalbare optie als het defect niet te groot is. Als de primaire operatie mislukt, zijn er tal van secundaire behandelingstypen beschikbaar, waaronder meer invasieve osteochondrale of kraakbeentransplantatiemethoden. Het werk in dit proefschrift zal chirurgen helpen en sturen bij hun klinische besluitvorming bij het diagnosticeren en behandelen van patiënten met enkelblessures en de daaropvolgende osteochondrale defecten van de talus.

A

References
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APPENDICIS

Appendix I

Search terms and results 18-01-2018

Databases		
PubMed, embase (Ovid) cochrane library	Before deduplication	After deduplication
Total	1844	1271

PubMed

830 results
((((“Osteochondritis Dissecans[Mesh] OR Osteochondritis dissecans[tiab] OR osteochondrosisdissecans[tiab] OR osteochondrolysis[tiab] OR OCD[tiab] OR OLT[tiab] OR ((osteochondral[tiab] OR chondral[tiab] OR transchondral[tiab] OR cartilage*[tiab]) AND (defect*[tiab] OR lesion*[tiab])))))) AND (((“Ankle Fractures”[Mesh] OR “Ankle Injuries” [Mesh] OR “Ankle Joint”[Mesh] OR “Ankle”[Mesh])) OR (ankle*[tiab] AND (fracture*[tiab] OR injur*[tiab])))

EMBASE (Ovid)

# Searches		Results
1	osteochondritis dissecans/ or (osteochondritis dissecans or osteochondrosisdissecans 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	31,561
2	exp ankle fracture/ or exp ankle injury/ or exp ankle/ or (ankle* and (fracture* or injur*)).ti,ab,kw	47,510
3	1 and 2	986

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Cochrane library

CDSR, DARE, CENTRAL: 28 results.
IDSearchHits. #1MeSH descriptor: (Osteochondritis Dissecans) explode all trees8. #2osteochondritis dissecans or osteochondrosisdissecans or osteochondrolysis or OCD or OLT:ti,ab,kw (Word variations have been searched)1315. #3(osteochondral or chondral or transchondral or cartilage*) and (defect* or lesion*):ti,ab,kw (Word variations have been searched)445. #4#1 or #2 or #3 1738. #5MeSH descriptor: (Ankle Fractures) explode all trees41. #6MeSH descriptor: (Ankle Injuries] explode all trees604. #7MeSH descriptor: [Ankle Joint) explode all trees639. #8MeSH descriptor: (Ankle) explode all trees465. #9ankle* and (fracture* or injur*):ti,ab,kw (Word variations have been searched)1576. #10#5 or #6 or #7 or #8 or #9 2371. #11#4 and #10 in Cochrane Reviews (Reviews and Protocols), Other Reviews and Trials28.

Appendix II

1. PUBMED

#	Searches	Results
1	"Osteochondritis Dissecans"[Mesh]	Total number of results 1996 – 2017: 1053 hits
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	

2. EMBASE (OVID)

#	Searches	Results
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.)	1475
2	limit 1 to yr="1996 -2017"	1220

3. COCHRANE LIBRARY

#	Searches	Results
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)	1188
3	(osteochondral or chondral or transchondral or cartilage*) and (defect* or lesion*):ti,ab,kw (Word variations have been searched)	343
4	#1 or #2 or #3	1516
5	MeSH descriptor: [Talus] explode all trees	33
6	talus or talar* or ankle:ti,ab,kw (Word variations have been searched)	5266
7	#5 or #6	5266
8	#4 and #7, Publication Year from 1996 to 2017, in Cochrane Reviews (Reviews and Protocols), Other Reviews and Trials	33

Appendix III

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 in the community*
   b. Somewhat representative of the average talar osteochondral defect patient 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. Independent blind assessment*
   b. Record linkage*
   c. Self-report
   d. No description
5. 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).

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Appendix IV

Grading scale as proposed by Thompson and Loomer

Rating	Pain	Function	Exam	X-ray
Good	None	No restriction on activities	Normal	Normal
Fair	Occasionally with activity	Some limitation of activities	Mild swelling; slight decrease in motion	Minimal change
Poor	As before or worse	Moderate restriction of activities	Arthrosis, i.e., increased swelling and crepitus	Degenerative change

Appendix V

Pubmed

#	Searches	Results
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

EMBASE (OVID)

#	Searches	Results
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.)	1351
2	limit 1 to yr="1996 -Current"	1097

Cochrane Library

#	Searches	Results
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)	1117
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	1410
5	MeSH descriptor: [Talus] explode all trees	27
6	talus or talar* or ankle:ti,ab,kw (Word variations have been searched)	4866
7	#5 or #6	4866
8	#4 and #7, Publication Year from 1996 to 2016, in Cochrane Reviews (Reviews and Protocols), Other Reviews and Trials	23

LIST OF PUBLICATIONS

Articles

- Lambers K, Ring D. **Elbow fracture-dislocation with triceps avulsion: report of 2 cases.**
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- Dahmen J, Lambers KTA, Reilingh M, van den Bergen CJ, Stufkens SA, Kerkhoffs GMMJ. **Reply to the letter to the editor: comment on "No superior treatment for primary osteochondral defects of the talus"**
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CURRICULUM VITAE

Kaj Timo Adriaan Lambers was born in the city of Haarlem, the Netherlands on June 30th, 1987. He spent part of his kindergarten time in Amsterdam but was subsequently raised in Haarlem. He graduated from high school (Stedelijk Gymnasium Haarlem) in 2005. This was where his interest in medicine originated and he decided to study Medicine at the University of Amsterdam (UvA). At the end of his bachelor's degree he commenced a scientific internship at the Department of Orthopaedics at the Academic Medical Centre (University of Amsterdam) under supervision of dr. Job Doornberg, his current co-promotor of this thesis. This was followed by a research internship in Boston, at the Massachusetts General Hospital (Harvard University) under the supervision of prof. dr. David Ring. Following this research fellowship and after a few months travelling he came back to Amsterdam to start his clinical rotations. He finished his medical degree in 2013. After a short period as an orthopaedic resident not in training at the Sint Lucas Andreas hospital he started his orthopaedic residency in 2014, with his surgical pre-training at the department of general surgery at the same hospital (supervised by dr. B.C. Vrouenraets). In 2016 he started his orthopaedic residency at the Academic Medical Center (supervised by prof dr. G.M.M.J. Kerkhoffs). This resident period was intermitted to expand his scientific knowledge by a new research fellowship in 2017 at Flinders Medical Center (Flinders University) in Adelaide, Australia, under supervision of prof. dr. Jaarsma and again dr. Job Doornberg who was a fellow there at the time. Afterwards he headed back to the Netherlands, again after some traveling, to continue his orthopaedic surgery training, first at the Academic Medical Center, Amsterdam (supervised by prof dr. G.M.M.J. Kerkhoffs), followed by the Amphia Hospital, Breda (supervised by prof. dr. D. Eygendaal) and Tergooi Hospital, Hilversum (supervised by dr. A.M.J.S. Vervest). He will conclude his orthopaedic training back at the Amphia Hospital where he aims to further develop his knowledge about the foot and ankle and prosthesiology of the lower extremity.

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