The Role of Bone in Osteochondral Talar Defects

Mikel Reilingh

THE ROLE OF BONE IN OSTEOCHONDRAL TALAR DEFECTS

Mikel-Wing Lun Reilingh

Colophon

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CHAPTER 1

General introduction

HISTORICAL PERSPECTIVE

An osteochondral defect (OCD) is a lesion in a joint involving the articular cartilage and its subchondral bone. In 1743, Hunter[102] stated "If we consult the standard chirurgical writers from Hippocrates down to the present age, we shall find that an ulcerated cartilage is universally allowed to be a very troublesome disease; that is admits of a cure with more difficulty than a carious bone; and that, when destroyed, it is never recovered". In 1856, Monro[153] was the first to describe the presence of cartilaginous bodies in the ankle joint, that were believed to be of traumatic origin. König[123] first used the term "osteochondritis dissecans" in 1888, in reference to loose bodies found in the knee joint that he believed to be fragments from an avascular bone lesion. In 1922, Kappis[113] noted comparable lesions in the ankle. Nowadays, several descriptive terms exist for this type of lesion, including osteochondral defect, osteochondritis dissecans, osteochondral lesion, osteochondral fracture, transchondral fracture, talar dome fracture, and flake fracture.

ETIOLOGY

An ankle trauma is widely accepted as the most important etiological factor of an OCD of the talus. The trauma causing the lesion may be a single event or may consist of a series of repeated, less intense traumas causing micro damage that can accumulate to cause macroscopic failure[250]. When a talus twists inside the ankle mortise, the cartilage lining of the talus can be damaged. Berndt and Harty[24] clearly described the trauma mechanism in cadaver ankles. They were able to reproduce lateral defects by strong inversion of a dorsiflexed ankle, leading to compression of the lateral border of the talar dome against the face of the fibula. A medial lesion was reproduced by plantarflexing the ankle in combination with slight anterior displacement of the talus on the tibia, inversion, and internal rotation of the talus on the tibia.

However, some patients have OCDs without a history of an ankle trauma. These defects are called osteochondritis dissecans[222]. Ischemia, subsequent necrosis and possibly genetics are etiological factors in these defects[204]. Osteochondritis dissecans of the talus has been reported in siblings[10] and in identical twins[62, 85, 271]. Furthermore, the defect is bilateral in 4 to 10% of the patients[24, 39, 97]. An osteochondritis dissecans can become symptomatic after a trauma. The stable lesion that was fibrously attached to the talus for many years has now become unstable and will act as an intra-articular non-union.

It is still unclear why some OCDs remain asymptomatic and inert, while others develop pain and progress to subchondral bone cysts. Understanding the etiology

and physiology of OCDs might make it possible to interfere and prevent progressive joint damage.

CLINICAL PRESENTATION

OCDs often cause deep ankle pain on weightbearing, prolonged joint swelling, recurrent synovitis, diminished range of motion, and formation of subchondral bone cysts. A differentiation has to be made between an acute and a chronic situation[274]. In an acute situation, symptoms of a talar OCD are often unrecognized since the swelling and pain from the ligament injury prevails. Locking and catching are symptoms of a displaced fragment.

Chronic lesions typically present as persistent ankle pain after a prior history of an ankle distortion. Pain is usually experienced as deep ankle pain, during or after activity. Reactive swelling or stiffness may be present, but absence of swelling, locking or catching does not rule out an OCD. Recognizable tenderness is often inducible when the OCD is palpated in maximal plantairflexion.

CARTILAGE

The primary function of cartilage is to provide a smooth, lubricated surface for articulation and distribution of loads. Cartilage consists of a small amount of chondrocytes embedded within an extracellular matrix made up of a macromolecular framework and water. Water is the most abundant component of articular cartilage, contributing up to 80% of its wet weight[220]. In the healthy cartilage the negatively charged glycosaminoglycan side chains of the proteoglycans play an important role in attracting water[111]. The cartilage matrix resembles a sponge with directional pores. The small diameter of these functional pores and their arrangement in circuitous tunnels, created by the hydrophilic collagen end proteoglycan matrix components, prevent large molecules from entering the cartilage and offer considerable resistance to interstitial fluid flow. These characteristics provide adequate containment for the fluid to support the load. At any instant, only a part of the joint is load-bearing or compressed. If one part is in compression, the adjacent area is unloaded and liquid flows to the unloaded area. In a healthy situation, the liquid is not able to enter the subchondral bone plate.

SUBCHONDRAL BONE

The articular cartilage is supported by the subchondral bone and the combination is considered a connected osteochondral unit[80].

The subchondral bone plate has several important roles in this functional unit. First the subchondral bone plate is essential for the load distribution of the joint and for the survival of chondrocytes by releasing bone soluble factors[8,70]. Bone soluble factors, such as osteoprotegerin, impact the cartilage response to catabolic factors[70]. When the cartilage is not supported by the subchondral bone it loses functioning proteoglycans and glycoproteins, which causes a decrease in water containment and lower quality of the cartilage[35, 111, 180]. In addition it has been suggested that an irregular subchondral bone plate may negatively affect articular cartilage repair in OCDs[121, 169, 177].

Secondly, the subchondral bone is involved in the pain sensation of patients with an OCD. Nerve endings in the subchondral bone have been first detected in the early nineteen nineties[142]. These nerve fibers extensively innervate bone such as periosteum, compact and trabecular bone, and bone marrow space. Bone disorders with increased osteoclastic bone resorption are frequently associated with bone pain[103, 157].

SUBCHONDRAL BONE CYSTS

An untreated talar OCD can progress to a subchondral bone cyst. Several hypotheses regarding the pathogenesis of subchondral bone cysts have been proposed. Pressurized fluid through the subchondral bone plate is one of the hypotheses[63, 86, 165, 210, 250, 270]. Every step or other load-bearing activity causes fluid to be pressed out of the cartilage and into the microfractured areas of the subchondral bone[250]. High hydrostatic pressures within the subchondral bone can lead to osteonecrosis, bone resorption, and formation of lytic areas, thus resulting in a cyst[13, 14, 247]. However, a fissure through the subchondral bone is rarely visible on CT. The existence of these fissures needs to be determined.

Another hypothesis suggests that the process of mucinous degeneration of intraosseous connective tissue, most likely as a result of local aseptic necrosis or trauma, causes the formation of subchondral bone cysts[16, 65, 95].

TREATMENT

Conservative treatment is the first step in the treatment of symptomatic OCDs and may consist of administration non-steroidal anti-inflammatory drugs (NSAID's), restriction of (sporting) activities and/or application of cast immobilization[274]. The aim of conservative

treatment strategies is to unload the damaged cartilage, allowing decrease of edema and prevention of necrosis. A (partially) detached OCD fragment can also heal to the underlying bone. The results of non-surgical treatment strategies vary between 20 to 69%[273].

The number of surgical strategies after failed conservative treatment have substantially increased over the last decade[59, 67, 76, 161, 273]. Arthroscopic debridement and bone marrow stimulation is still considered the primary treatment in symptomatic lesions up to 1.5 cm in diameter[44, 46, 86, 273]. With this technique, all loose unstable cartilage and the underlying necrotic bone are removed, and small holes are punctured in the subchondral bone to promote revascularization and induce bone and fibrous tissue formation[250]. As described earlier, an irregular subchondral bone after debridement of an OCD may negatively affect articular cartilage repair[121, 169, 177]. Little is known about the bone healing after arthroscopic debridement and microfracture of a talar OCD.

Many patients aim to achieve resumption of sport activities after arthroscopic debridement and microfracture of talar OCDs. Various biological and biophysical possibilities have been suggested in order to improve the local healing process. A potential solution to obtain this goal is the application of pulsed electromagnetic fields (PEMFs), which relieve pain, suppress inflammation, and stimulates the repair process of bone and cartilage[38, 154, 198]. However, the effectiveness of PEMFs for talar OCDs after arthroscopic debridement and microfracture is not yet evaluated nor reported.

Internal fixation of the loose osteochondral fragment is a good alternative technique in primary OCDs[128, 207]. The advantage of this treatment option is that it restores the natural congruency of the subchondral bone and preserves the hyaline cartilage. In adults, good to excellent functional outcomes of 89 to 100% have been reported[128, 207]. However, a medial or lateral arthrotomy often combined with a malleolar osteotomy has to be performed to allow proper visibility and working access. With the development of an arthroscopic fixation technique a lower complication rate and a faster rehabilitation can be expected[275].

In case of failure of the primary treatment, current secondary treatment options include osteochondral autograft transfer, autogenous bone graft, and autologous chondrocyte implantation[18, 74, 88]. Although successful results can be achieved, disadvantages of these secondary methods include donor site morbidity, poor graft integration, and the requirement of a two-stage surgery, as for example in autologous chondrocyte transplantation[12, 163, 171, 185]. As an alternative, a non-biological solution may be applied. An option is the metal resurfacing inlay implant that was developed for secondary OCDs of the medial talar dome. Van Bergen et al.[244] reported encouraging results of 20 patients with a mean follow-up of 3 years. A longer follow-up is clearly required to conclude on the clinical success of the procedure over time.

Although the number of publications on the treatment of talar OCDs increases, little is known about the treatment and clinical outcome of OCDs in children. Few studies have investigated OCDs of the talus exclusively in children[98, 135]; however, these series are small and also include skeletally mature children. A larger series with strict inclusion criteria is therefore important to compare the clinical results with those of adults. Children have a higher healing potential and therefore a better clinical and radiological outcome is expected.

AIM AND OUTLINE OF THE THESIS

This thesis aims to evaluate several aspects of etiology and treatment of talar OCDs that were mentioned in the general introduction. **Part I** of the thesis describes the natural history of OCDs and the development of subchondral bone cysts. **Part II** contains chapters on different surgical treatment options of talar OCDs, the postoperative treatment and rehabilitation after arthroscopic debridement and microfracture, and the role of the subchondral bone after surgical treatment. **Part III** finalizes the thesis with a general discussion and a summary.

Part I – Natural history and subchondral bone cysts

It is still unclear why some OCDs of the talus remain asymptomatic, while others develop pain on weight bearing. **Chapter 2** aims to provide a review of the natural history of talar OCDs.

Osteochondral talar defects often present in conjunction with subchondral bone cysts. Pressurized fluid through a subchondral bone fissure is assumed to play an important role in the etiology of these cysts. The aim of **chapter 3** is to evaluate and compare the cyst morphology of human cadaveric tali by using microCT with morphological simulation results previously reported. Furthermore, the presence of an opening through the subchondral bone plate is analyzed. Early restoration of a subchondral fissure might prevent cyst development.

Part II – Surgical treatment and subchondral bone healing

There are numerous surgical options in the treatment of a symptomatic OCD of the talus. **Chapter 4** aims to provide an overview of the current treatment options.

Currently, the primary surgical treatment consists of arthroscopic debridement and microfracture in defects smaller than 15 mm. Early sport resumption after treatment in young and active population remains a challenge. The purpose of **chapter 5** is to investigate if the postoperatively applied PEMFs after arthroscopic debridement

and microfracture of an OCD of the talus lead to earlier resumption of sports, and an increased number of patients that resume sports.

Healing of the subchondral bone after surgery seems important because it affects cartilage repair and the pathogenesis of osteoarthritis. Understanding the healing of OCDs after debridement and microfracture might give us insight why some defects remain symptomatic after treatment. **Chapter 6** investigates the dimensional changes and bone healing of talar OCDs on CT-scans after arthroscopic debridement and microfracture.

Arthroscopically performed internal fixation of a primary OCD is a good alternative technique to an open performed procedure. The advantage of fixation of the OCD is that it restores the natural congruency of the subchondral bone and preserves the hyaline cartilage. **Chapter 7** describes the short-term clinical outcome of a new arthroscopic fixation technique: lift, drill, fill and fix (LDFF) for primary talar OCDs.

Several treatment strategies for OCDs of the ankle have substantially increased over the last decade. However, little is known about the treatment and clinical outcome of OCDs in children. **Chapter 8** aims to investigate the clinical and radiographic outcomes of conservative and primary surgically treated talar OCDs in skeletally immature children.

For treatment of large lesions of the medial talar dome or after failed primary treatment, a contoured articular inlay implant (HemiCAP®, Arthrosurface Inc., Franklin, MA, USA) with a fixed diameter of 15 mm has been developed. The goal of the study described in **chapter 9** is to evaluate the clinical effectiveness of the metal implant for OCDs of the medial talar dome after failed previous surgery.

Part III – General discussion and summary

Chapter 10 provides the general discussion and **chapter 11** a summary of the thesis.

PART I

Natural history and subchondral bone cysts

CHAPTER 2

Osteochondral defects in the ankle: why painful?

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ABSTRACT

Osteochondral defects (OCDs) of the ankle can either heal and remain asymptomatic or progress to deep ankle pain on weight bearing and formation of subchondral bone cysts. The development of a symptomatic OCD depends on various factors, including the damage and insufficient repair of the subchondral bone plate. The ankle joint has a high congruency. During loading, compressed cartilage forces its water into the microfractured subchondral bone, leading to a localized high increased flow and pressure of fluid in the subchondral bone. This will result in local osteolysis and can explain the slow development of a subchondral cyst. The pain does not arise from the cartilage lesion, but is most probably caused by repetitive high fluid pressure during walking, which results in stimulation of the highly innervated subchondral bone underneath the cartilage defect. Understanding the natural history of OCDs could lead to the development of strategies for preventing progressive joint damage.

INTRODUCTION

An osteochondral defect (OCD) of the talus is a lesion involving the talar articular cartilage and its subchondral bone mostly caused by a single or multiple traumatic events, but idiopathic OCD of the ankle do occur[31, 184, 190, 204]. The defect initially may consist only of cartilage damage caused by shearing stresses, with the subchondral bone intact, but a bone contusion following high-impact force also can cause a defect[178, 231, 258]. Ankle trauma associated with an OCD often leads to subchondral bone cysts. These cysts are associated with persistent deep ankle pain thereby limiting the patients mobility.

Most OCDs of the talus are localized on the anterolateral or posteromedial talar dome[273]. Lateral lesions are usually shallow oval shaped and are caused by a shear mechanism. Medial lesions in contrast are usually deep, and cup-shaped, indicating a mechanism of torsional impaction and axial loading[24, 39, 41, 68, 223, 261].

Even though elaborate knowledge exists concerning OCDs of the talus, its etiology and pathogenesis are still not fully understood. Increasing attention is paid to invasive and sometimes expensive surgical treatments, while research for pathogenesis of the lesions has somewhat been neglected. In order to treat OCDs in all its dimensions, more should be known about their natural history. The development of an OCD may have a sudden onset, but the development of a subchondral cyst is most often a slow process.

Why do some OCDs remain asymptomatic and inert, while others develop pain on weight bearing, demonstrate persistent bone edema on magnetic resonance imaging and result in the progressive formation of a subchondral cyst? Understanding this process might make it possible to interfere and prevent progressive damage to the joint. In this manuscript, the most important factors related to the development of OCDs are analyzed.

ETIOLOGY

A traumatic insult is widely accepted as the most important etiologic factor of an OCD of the talus. For lateral talar defects, trauma has been described in 93–98% and for medial defects in 61–70%[68, 261]. As not all patients report a history of ankle injury[66], a subdivision can be made in the etiology of nontraumatic and traumatic defects.

Ischemia, subsequent necrosis and possibly genetics are etiologic factors in nontraumatic OCDs[204]. Furthermore, OCDs in identical twins and siblings have been described[10, 62, 271]. The defect is bilateral in 10% of patients[97].

Traumatic cartilage injuries generally comprise three categories: microdamage or blunt trauma, chondral fractures and osteochondral fractures[69]. Ankle sprains have a predominant role in traumatic OCDs. When a talus twists inside its boxlike housing

during an ankle sprain, the cartilage lining of the talus can be damaged. This may lead to a bruise and subsequent softening of the cartilage or even a crack in the cartilage with subsequent delamination.

Separation in the upper layer of the cartilage occurs as a result of shearing forces. Alternatively, separation may occur in the subchondral bone, giving rise to a subchondral bone lesion. Fragments may break off, and float loose in the ankle joint, or they remain partially attached and stay in position. The lesions can either heal and remain asymptomatic or progress to deep ankle pain on weight bearing and formation of subchondral bone cysts.

In cadaver ankles, Berndt and Harty[24] reproduced lateral defects by strongly inverting a dorsiflexed ankle. As the foot was inverted on the leg, the lateral border of the talar dome was compressed against the face of the fibula. When the lateral ligament ruptured, avulsion of the chip began. With the use of excessive inverting force, the talus within the mortise was rotated laterally in the frontal plane, impacting and compressing the lateral talar margin against the articular surface of the fibula. A portion of the talar margin was sheared off from the main body of the talus, which caused the lateral OCD. A medial lesion was reproduced by plantarflexing the ankle in combination with slight anterior displacement of the talus on the tibia, inversion and internal rotation of the talus on the tibia.

CLINICAL PRESENTATION

In the acute situation, an OCD of the talus often remains unrecognized since the swelling and pain from the lateral ligament lesion prevails. The weight-bearing anteroposterior (mortise) and lateral radiographs may not reveal any pathology, or only show an area of radiolucency. In case of a large OCD the initial radiographs may be positive. When the symptoms of the ligament injury have resolved after some weeks, symptoms of persistent swelling, limited range of motion and pain on weight bearing may continue. If symptoms have not resolved within 4–6 weeks, an (osteo)chondral defect should be suspected. Locking and catching are symptoms of a displaced fragment.

Chronic lesions typically present as persistent or intermittent deep ankle pain during or after activity[67]. Most patients demonstrate a normal range of motion with absence of recognizable tenderness on palpation and absence of swelling. However, reactive swelling or stiffness may be present.

The natural history of osteochondral lesions of the talus whether treated or not is benign. We reported the long-term results of OCDs and found only one case of radiographic progression after 10 years in 38 cases[208]. Reports of ankle arthrodesis following OCDs of the talus are rare[67, 208].

CARTILAGE AND BONE ANATOMY

Cartilage consists of chondrocytes that lie groupwise in lacunae of the extracellular matrix they produce. The cartilaginous matrix consists of collagen, hyaluronic acid, proteoglycans and a small amount of glycoprotein's (Fig. 1). Its elasticity is based on the electrostatic connections between collagen fibers and the glycosaminoglycan (GAG) side chains of the proteoglycans, the containment of water by the negatively loaded GAGs of the central protein of proteoglycans and the flexibility and the mutual sliding of the collagen fibers.

Cartilage is avascular and is nourished by the intraarticular fluid. The tissue fluid of the cartilage matrix, which comprises about 75% of the total weight of the cartilage, functions as a transport medium. In the healthy cartilage the GAG side chains of the proteoglycans play an important role for the elasticity and maintenance of the water content of 75%. As a matter of fact, we all walk on water. Cartilage does not contain lymph vessels or nerves and has a slow metabolism[111]. Mineralized bone consists of

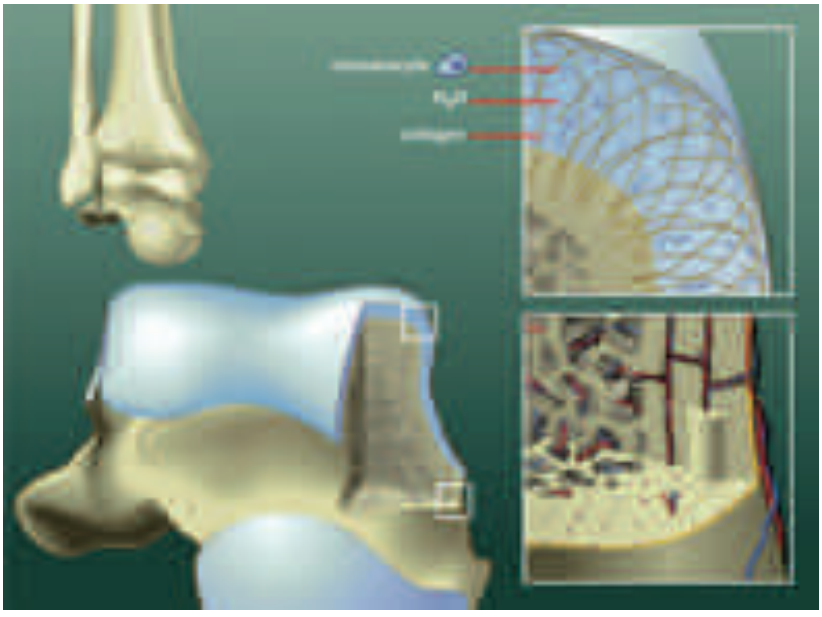

Figure 1: Schematic diagrams showing normal anatomy of ankle cartilage, subchondral plate and subchondral bone area. The cartilage consist of chondrocytes that lie groupwise in lacunae of the extracellular matrix, which contains collagen fibers in an arcwise configuration, hyaluronic acid, proteoglycans and 75% water (upper right). The hollow haversian canal that runs longitudinally down the center of the osteon in compact bone contains an arteriole, venule and lymphatic duct for vascular and lymphatic drainage. The Volkmann canals run perpendicular to and connect the Haversian canals (lower right).

both compact and trabecular bone. Compact bone is found beneath the periosteum and acts as the main weight-bearing pillar for the skeleton. It is not a solid tissue but rather an aggregation of osteons, the major multicellular unit of compact bone. Each osteon is composed of groups of concentric calcified cylinders, each of which is made up of bone matrix proteins that form long cylinders-shaped structures, oriented parallel to the long axis of the bone[142].

HISTOPATHOLOGY

Koch et al.[121] studied the cartilage and bone morphology in OCDs of the knee. They intra-operatively harvested cylinders of the osteochondral areas as part of a cartilage-bone transplantation in 30 patients. At the cartilage level there was a loss of acidic GAGs from the extracellular matrix and a decrease of the number of chondrocytes. Hyaline cartilage was often replaced by fibrocartilage. The subchondral bone plate was thinned compared to normal osteochondral samples and had fractured areas. Parallel with a general loss of proteoglycans from the superficial layers of the extracellular cartilage matrix, the amount of chondroitin sulfates and keratin sulfate was increased in deep cartilage layers and in the subchondral bone. Koch et al.[121] stated that all morphological features tend to indicate that the main area of action is around the subchondral bone plate.

In 2009 Uozumi et al.[233] studied the differences in the histological findings of OCDs in 12 knees. During the surgery, cylinder osteochondral plugs were taken from the center of the OCD and examined with light microscopy. They classified three types in the subchondral bone area: (1) necrotic subchondral trabeculae, (2) viable subchondral trabeculae, and (3) cartilage without bone trabeculae. Uozumi et al.[233] stated that the initial change in the subchondral area is bone necrosis or subchondral fracture; the necrotic bone is then absorbed and replaced either by viable subchondral trabeculae or cartilage without bone trabeculae.

An abnormal subchondral plate is likely to be one of the major factors in influencing the long-term outcome of articular cartilage repair. Qiu et al.[177] studied OCDs in femoral condyles of rabbits and found that the presence of an advanced and irregular subchondral plate was associated with degradation of repaired articular surface.

CAUSE OF PAIN IN OSTEOCHONDRAL ANKLE LESIONS

Several factors can play a role in the cause of pain in OCDs. A raise in intra-osseous pressure has been mentioned as a cause of pain and has been associated with joint

degeneration[13, 14, 247]. Restoration or decrease in the intra-osseous pressure can be accomplished by medullary decompression[116, 221].

A rise in intra-articular pressure can be a cause of pain in degenerative joint disease. Goddard and Gosling[78] have found a linear correlation between experience pain in osteoarthritis and resting intra-articular pressure of the synovial fluid. A connection of synovial hypertrophy and raised intra-articular pressure in arthritis has been demonstrated by Bünger et al.[37]. However, it is unlikely that in a localized osteochondral talar defect a raise in intra-articular pressure plays a role. These patients typically do not demonstrate relevant joint effusion.

Nerve endings can be found in the synovium and joint capsule. Joint capsule and the soft tissue around the joint are important triggers of nociception. The upregulation of substance P- and calcitonin gene-related peptide (CGRP)-positive neurons in response to arthritic changes suggests a mechanism involving neuropeptides in the maintenance of a painful degenerative joint disease[203]. Patients with an OCD of the ankle, however, generally do not show much synovitis. The synovium of the anterior ankle joint can be palpated since it lies directly under the skin. These patients usually can differentiate this secondary synovial pain from the deep ankle pain caused by the OCD. The disabling deep ankle pain on weight bearing cannot be reproduced during physical examination. The most probable cause of this pain is the nerve endings in the subchondral bone that have been firstly detected in the early nineties[142].

Within each osteon a hallow tube, known as a Haversian canal, runs longitudinally down the center of the osteon. It contains an arteriole, venule and lymphatic duct to provide the vascular and lymphatic drainage of compact bone. In addition to the longitudinally oriented Haversian canals, a series of canals known as Volkmann's canals run perpendicularly to and interconnect the Haversian canals (Fig. 1). Mach et al.[142] studied mouse femora and found that not all osteons are innervated. The likelihood of an osteon being innervated is greatest in the proximal head followed by the distal head and then the diaphysis of the femur. There are CGRP-immunoreactive and RT 97 (clone name of neurofilament) immunoreactive nerve fibers, which suggests that the mineralized bone, the bone marrow and the periosteum are innervated by both unmyelinized and myelinized fibers. These fibers contain A-β, A-δ and C-fibers that conduct sensory input from the periphery to the spinal cord. In general, the areas in mineralized bone that underwent the greatest mechanical stress and loading, that had the highest metabolic rate, and that were most vascularised, had the highest density of sensory and sympathetic fibers[142]. The fact that there is abundant innervations of bone marrow possibly explains the observation that patients with bone diseases already experience pain before there is any radiological evidence of bone destruction or involvement of the periosteum. Macrophages, the precursor cells of the osteoclasts, form important accessory cells in the regulation of bone metabolism and destruction.

Chronic macrophage activation and vascular derangements lead to low pH, local bone demineralization (acid attack), and H^+-mediated stimulation of the primary afferent nociceptive nerve fibers[131]. Pain probably develops as a rise in fluid pressure, and a decrease in pH excitates nerve fibers present in bone.

JOINT CONGRUENCY VERSUS CARTILAGE THICKNESS

The cartilage of the talar dome is thin in comparison with the cartilage of other articulating surfaces. The average cartilage thickness of the talar dome is 1.11 (±0.28 mm) in women and 1.35 (±0.22 mm) in men[224]. Shepherd and Seedhom[215] found almost similar values. In 1891, Braune and Fischer[28] proposed that articular cartilage is thicker in regions of low congruence. Simon et al.[219] related joint congruence to cartilage thickness. They calculated congruence ratios for canine joints by dividing the average length of the congruent surface by the average length of the total articular surface. The ankle with the thinnest articular cartilage had the highest ratio, and the knee with the thickest cartilage had the lowest ratio. Shepherd and Seedhom[215] conducted a similar study with human cadaver specimens. The average thickness of the cartilage in the ankle, hip, and knee joints were 1.2 mm (1.0–1.6), 1.6 mm (1.4–2.0) and 2.2 mm (1.7–2.6), respectively. The thickness of the cartilage appeared to be related to the congruence of a joint. Shepherd and Seedhom[215] hypothesized that congruent joint surfaces, such as those in the ankle and elbow, are covered only by thin articular cartilage because the compressive loads are spread over a wide area, decreasing local joint stresses and eliminating the necessity for large cartilaginous deformations. Incongruent joints are covered by thicker cartilage which more easily deforms, thereby increasing the load-bearing area and decreasing the stress per unit area.

CARTILAGE, SUBCHONDRAL BONE AND LOADING

Tissue changes the structure in response to the functional demands imposed on them. Connective tissue has the ability to alter structure in response to mechanical loading. Adaptation is affected by different cells. Cartilage has a much lower response to mechanical adaptation when compared to bone. Bone remodeling is regulated by osteocytes that respond to mechanical triggers by sending signals that promote osteoblastic bone formation. Osteoclasts resorb bone at the site of microcracks that frequently occur in the subarticular spongiosa during impact loading. Large number of osteoclasts digesting parts of the bone plate lie in close contact to osteoblasts that seem to be compensating for bony instability by constantly remodeling the bone stock.

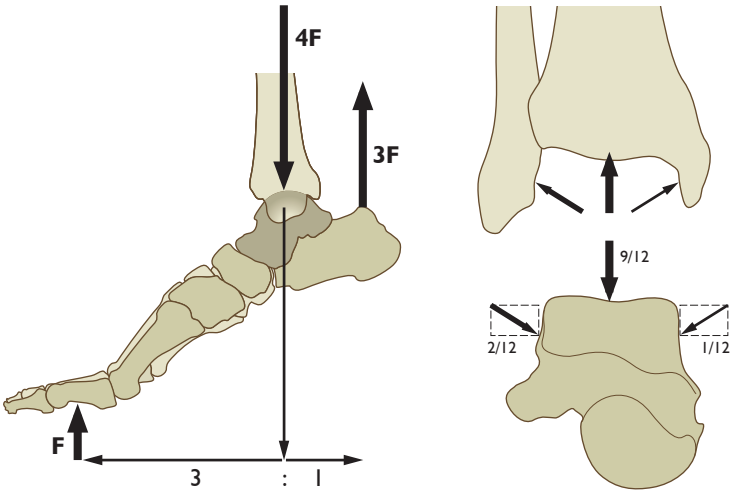

Figure 2: Schematic diagrams showing the calculation of load transmission through the ankle joint during walking. Approximately one-sixth of the load across the ankle is transmitted through the talofibular facet, and the remaining load is transmitted through the tibiotalar articulation. F = force.

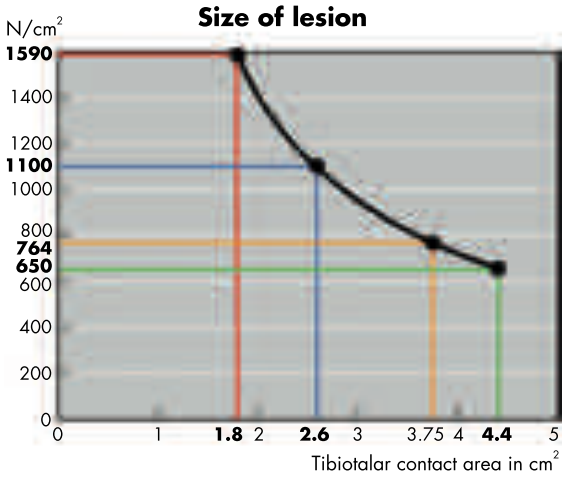

Figure 3: Graph showing load in relation to tibiotalar contact (black line). The green line represents the average tibiotalar contact area of 4.4 cm^2 for a 75 kg person during the stance phase of walking. The blue line represents the same person with a tibiotalar contact area diminished by 42% to 2.6 cm^2, as would occur after an ankle fracture with 1 mm of lateral displacement of the talus and fibula. The red line represents the same person with a tibiotalar contact area diminished by 58% to 1.8 cm^2, as would occur after an ankle fracture with 2 mm of lateral displacement of the talus and fibula. The yellow line represents a person weighing 75 kg with an OCD of the talus measuring 0.65 cm^2; the average load on the remaining cartilage is increased from 650 to 764 N/cm^2.

Loading tends to thicken the subchondral bone plate in cases of overlying cartilage damage. This results in sclerosis of the subchondral bone plate.

The load-bearing area of the ankle joint is relatively small compared to the forces it conducts. The load on the ankle joint during walking can be calculated. Procter and Paul[176] measured the load to be 3.9 times body weight at heel rise during the stance phase of walking (Fig. 2). Mow et al.[155] measured a load of 5.0 times body weight at heel rise during the stance phase of walking. Hence, according to the data of Procter and Paul[176], the force on the talus with every step taken by a person weighing 75 kg is 2867 N (3.9 × 75 kg × 9.8 m/s^2). The average tibiotalar contact area is estimated to be 4.4 cm^2 [182]. This means that the average load on the articular cartilage during the stance phase can be calculated to be 650 N/cm^2. During running, this load increases multiple times.

When the contact surface areas diminish in size, this will result in an increase in load on the remaining cartilage. This happens in malunion after an ankle fracture. Ramsey and Hamilton[182] have shown that 1 mm lateral talar shift reduces the contact area by 42%, while 2 mm lateral shift reduces the contact area by 56%. Lloyd et al.[137] found similar values. In the latter situation the average load per cm^2 in a person of 75 kg is increased from 650 to 1590 N (Fig. 3). A 2 mm shift is thus an indication for correction and operative reduction because of the high risk of developing degenerative changes[110]. An 1 mm shift is generally regarded to be acceptable. This would mean that talar cartilage can adept to an increase in load of up to 40%!

In the case of an OCD the following calculation can be made. The size of an average defect measures 0.85 cm^2 on magnetic resonance imaging (MRI)[60]. By means of computed tomography (CT) we measured the size of the talar OCD in 50 consecutive patients that were treated for a symptomatic OCD. We measured an average defect size of 0.65 cm^2 (0.5–0.8 cm^2). The size of an OCD can easily be overestimated on MRI because of bone edema, this can explain the difference. After debridement of a talar OCD with a diameter of 0.65 cm^2 it can be calculated that the load on the remaining talar cartilage is increased by 15% (Fig. 3). This increase in load is probably not enough to cause damage to the remaining cartilage since this figure lies far beyond the threshold of 40%. Any varus or valgus malalignment can increase the load[31] and hence increase the likelihood of progressive cartilage damage[35, 179, 227].

Radin and Paul[180] argued that articular cartilage by virtue of its thinness is not a good shock absorber considered in terms of reduction of peak impact force. Although the underlying bone is much stiffer, it is so much longer by comparison, that its total compliance exceeds that of cartilage. Peak stresses at the joint surface, however, are still greatly reduced through redistribution and deformation of cartilage. In contrast to the tibia, which is a long bone, the talus is compact, and peak impact force can only be distributed over a small volume of bone. The small talar volume combined with its

thin cartilage may explain why OCDs are more common on the talar dome than in the tibial plafond.

Thin cartilage is less elastic when compared to thick cartilage. Shepherd and Seedhom[215] suggested an inverse relation between the mean cartilage thickness and mean compressive modulus, i.e., thin cartilage has a high compressive modulus. After measuring cadaver cartilage of several species including humans, they found that two factors contribute to the deformability of the cartilage: the thickness of the cartilage and its intrinsic elasticity. There is a curvilinear relationship between the magnitude of the deformation and the thickness of the articular cartilage under a certain level of loading. In the congruent ankle joint, Wan et al.[264] measured a peak cartilage deformation of 34.5% ± 7.3% under full body weight in persons with a medial talar dome cartilage thickness of 1.42 ± 0.31 mm (Fig. 4).

Talar cartilage is thin and therefore less elastic. It makes the talus more susceptible to cartilage lesions and microfractures in the underlying bone when exposed to high-impact forces. However, OCDs occur in joints with thicker cartilage as well and whether or not an OCD occurs probably also depends on factors like impact force and shearing stress.

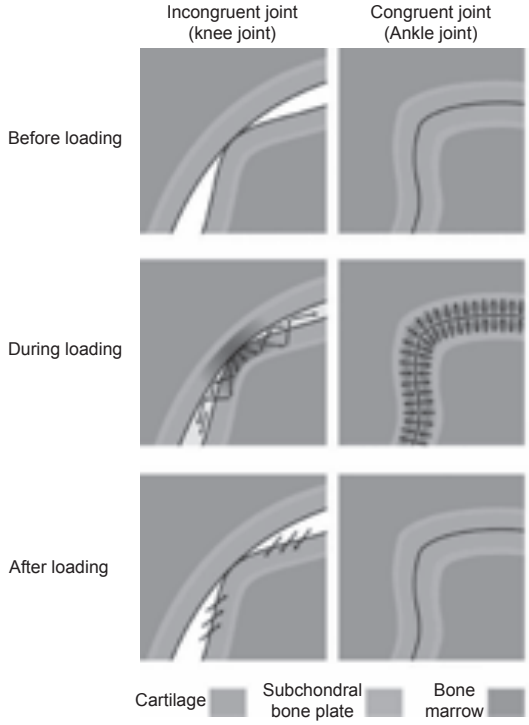

Figure 4: Schematic comparison of the deformation of the cartilage in a congruent (ankle) and incongruent (knee) joint before, during and after loading. Arrows = direction of water.

Cartilage has two components that enable the tissue to withstand compressive stress: a liquid and a multicomponent solid consisting of collagen and hydrophilic proteoglycan molecules. The liquid is a dialysate of synovial fluid that is incompressible, but able to flow. However, for this fluid to withstand the compressive loads that joints sustain, it must be contained. The cartilage matrix resembles a sponge with directional pores. The small diameter of these functional pores and their arrangement in circuitous tunnels, created by the hydrophilic collagen end proteoglycan matrix components, prevent large molecules from entering the cartilage and offer considerable resistance to interstitial fluid flow. These characteristics provide adequate containment for the fluid to support the load. At any instant, only a part of the joint is load-bearing or compressed. If one part is in compression, the adjacent area is being stretched and pulled apart and liquid flows to the unloaded area. In a healthy situation, the liquid is not able to enter the subchondral plate. It will only flow to adjacent cartilage. Fluid in cartilage is freely exchangeable, whether extra- or intra-fibrillar[145]. Herberhold et al.[96] studied patellar and femoral compression for 4 h under continuous static loading with 150% body weight. A maximal thickness reduction of 57 ± 15% was observed for patellar cartilage and a volume change of >30%, suggesting that more than 50% of the interstitial fluid were displaced from the matrix.

However, when trauma has caused microfractures in the subchondral plate and subchondral bone it creates a situation in which liquid not only flows within the cartilage, but it can enter into the subchondral bone through the microfractured area. Damaged subchondral bone is less able to support the overlying cartilage[35]. Inadequate subsurface support from an abnormal subchondral bone might be one of the main reasons for unsuccessful cartilage repair[148, 177, 212]. Cartilage that is not supported by the underlying bone plate loses proteoglycans and glycoprotein[111, 180]. The loss of negatively loaded GAG side chains and hydrophilic proteoglycans causes a decrease in containment of water; it flows more easily to other places. Each step or other load-bearing activity causes water to be pressed out of the cartilage and pressed into the microfractured areas of the subchondral bone (Fig. 5).

It has been demonstrated that continuous high fluid pressure causes osteolysis. An intermittent or continuous high local pressure can interfere with normal bone perfusion and lead to osteonecrosis, bone resorption and formation of lytical areas[13, 14, 58, 108, 206, 247] (Fig. 6). These changes in structure at the level of the subchondral bone are induced by mechanical forces, gravity, compression, fluid shear stress and hydrostatic pressure. In the undiseased situation we can say that ''form follows function''.

Irie et al.[105] studied CGRP-containing nerve fibers in bone tissue and their involvement in bone remodeling. The effect of CGRP on bone remodeling could be partly through its action on blood vessels, regulating local blood flow. Possibly high fluid pressures cause excitation of CGRP-containing nerve fibers, thereby diminishing blood flow

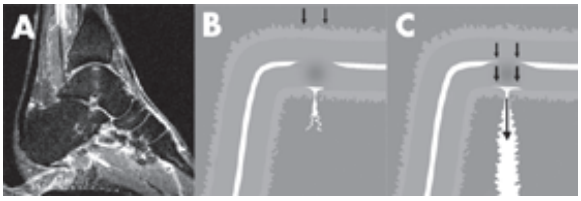

Figure 5A: Sagittal T2-weighted MRI study of an ankle with an OCD. The vertical configuration of the water column (seen in the center of the talus) suggests that the water is pumped directly caudal under high pressure, perpendicular to the talar joint surface. **B** and **C**: Schematic diagrams of fissures in the subchondral bone plate of an unloaded ankle (**B**) and a loaded ankle (**C**). When the ankle is loaded, the water is squeezed out of the cartilage into the subchondral bone. The diameter of the opening of the subchondral bone plate determines the pressure of the fluid flow (the smaller the diameter, the higher the pressure).

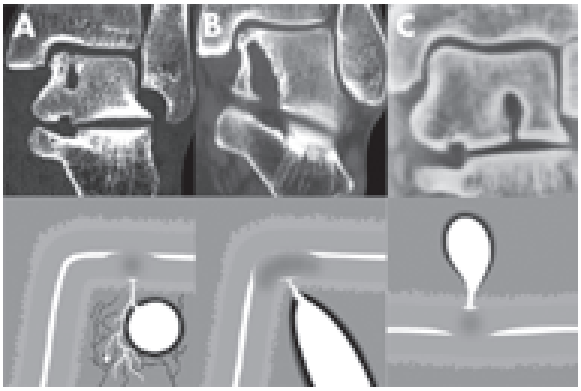

Figure 6A through **C**: Coronal CT scans (upper row) with corresponding schematic diagrams (lower row), showing the ankles of three young patients (26–37 years), who had deep ankle pain of 5–12 years duration. An opening in the subchondral bone plate can be seen in all three CT scans, with subchondral osteolysis that has developed into a subchondral cyst. **A**: Coronal CT, showing a cystic lesion in the talar body, with corresponding diagram schematically indicating the mechanism of cyst formation. Black lines = nerve endings in subchondral bone. **B**: In this patient, the cyst has extended to the subtalar joint. **C**: Sclerosis is visible around the subtalar cyst.

through bone, and causing osteolysis. Compression of incompressible fluid leads to local stress shielding. It is postulated that as long as the fluid pressure is preserved, the bone resorption will continue. When the fluid pressure drops, the resorption stops. Bone remodeling around the cystic bone defect will create a layer of dense bone adjacent to the cavity thus creating a sclerotic cystic wall.

When the subchondral bone lies exposed because overlying cartilage is sheared off or because the cartilagebone interface is damaged at microscopic level, it is subject to continuous high fluid pressures that cause osteolysis and subsequent large defects[58, 183, 272].

The subchondral bone becomes damaged because of damaged overlying cartilage and the cartilage damages further because the underlying bone is unable to provide support. This way, a vicious circle is started.

VARIOUS TYPES OF OSTEOCHONDRAL DEFECTS IN THE ANKLE

There are various factors that may play a role in the development of OCDs in the ankle. The ankle joint has a high congruency. A decrease in joint congruence will increase contact pressure per area. More displacement corresponds to increasing contact pressure[137, 182]. Thordarson et al.[229] confirm that substantial displacement of the fibula (≥2 mm shortening or lateral shift or ≥5° external rotation) increases the contact pressures in the ankle joint. Long-term follow-up studies have demonstrated that patients with persistent displacement of ankle fractures had poorer long-term results than those without persistent displacement[110]. Therefore, displacement of >2 mm of the fibula in injuries should not be accepted.

Varus or valgus malalignment of the ankle joint may also play an important role in the natural history by increasing the contact pressure in certain localizations of the ankle. Biomechanical experiments have demonstrated that in varus and supination the maximum pressure is located on the medial border of the talus, while in valgus and pronation the maximum pressure is located on het lateral talar border[33]. Increased pressure on an existing OCD may negatively influence the healing of the defect[35, 58, 124, 179]. Koshino et al.[124] observed the medial joint space in 146 knees during the removal of blade plate after a high tibial valgus osteotomy 2 years postoperatively. They found a clear relationship between the stage of cartilage regeneration and the postoperative limb alignment, with more mature regeneration seen in more valgus angulated knees. It is therefore important to detect and correct malalignment in patients with an OCD of the talus.

The consecutive stages of local OCDs may help us to understand the development of the defects. Superficial lesions consist of sheared off flakes with an intact subchondral bone plate (Fig. 7). In a more severe defect, the subchondral bone is damaged, as with, microfractures and bone bruises. Bone bruises are seen as a decreased signal intensity on T1-weighted MRI studies and an elevated intensity on T2-bone MRI. The reticular type bone bruise is not continuous with the adjacent articular surface[29, 158, 258] (Fig. 8). In general, this type heals normally and the healing occurs from the periphery to the center[51]. The geographic type bone bruise is continuous with the adjacent articular surface (Fig. 9). It is this type that is often associated with OCDs of the talus. Spontaneous healing is impaired or absent[158, 195, 258]. This impaired healing could possibly be caused by the cartilaginous water content being forced -on every step- into the persistent fissure

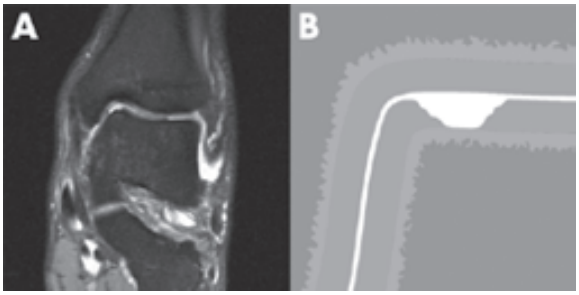

Figure 7A: MRI study showing a cartilage defect of the medial talar dome. The subchondral bone plate has remained intact, and there is no sign of bone bruise. **B**: Schematic diagram showing a fragment that probably was sheared from the underlying bone.

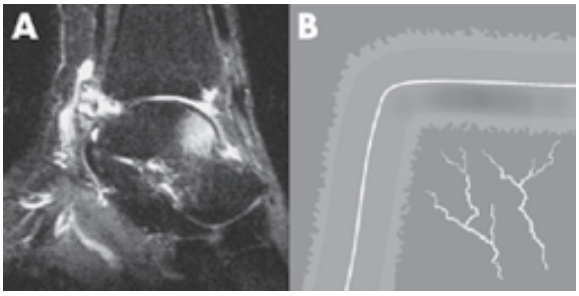

Figure 8A: Sagittal T2-weighted MRI study of an ankle with a reticular bone bruise. The white area in the anterior talus represents bone edema. **B**: Schematic diagram of a reticular bone bruise with intact subchondral bone plate. This type of bone bruise heals from the periphery to the center without complications.

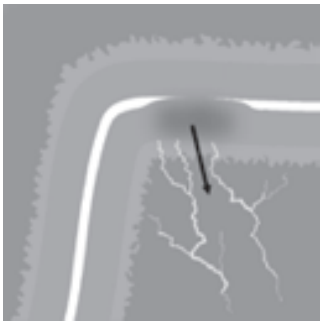

Figure 9: Schematic diagram showing the geographic type of bone bruise, which is continuous with the adjacent articular surface. Healing depends of the healing of the subchondral bone plate.

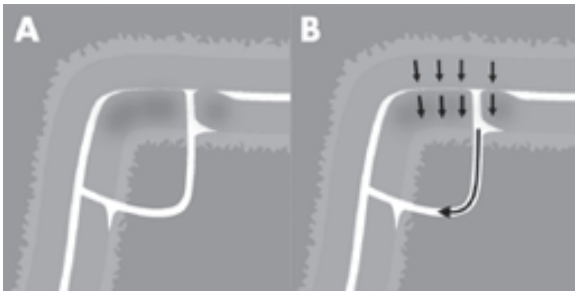

Figure 10: Schematic diagrams showing a loose osteochondral fragment when the ankle is unloaded (**A**) and loaded (**B**). Healing under loading may be precluded by intermittent fluid flow around the fragment.

in the bone plate underneath. In case of an osteochondral fragment, healing may be precluded by intermittent fluid flow on every step around the fragment (Fig. 10).

Subchondral cyst formation has been hypothesized to be caused by the damaged cartilage functioning as a valve[210]. This valve mechanism would allow intrusion of fluid from the joint space into the subchondral bone, but not in the opposite direction. On the weight-bearing phase of gait there is full contact between major parts of the talar and tibial cartilage, with most contact over the talar shoulders[151]. During this phase, pressures in opposing talar and tibial cartilage are theoretically identical, which may result in the forcing of fluid in the direction of the least resistance, i.e., the damaged subchondral bone. Backflow is prevented by the direct contact of opposing cartilage. During unloading of the joint, joint space fluid may re-enter the articular cartilage. On the next weight-bearing cycle, this fluid again is intruded in the subchondral bone. This repetitive mechanism represents a vicious circle, causing the intermittent shift of synovial fluid under high pressure into the damaged subchondral talar bone. Development of a subchondral cyst is then just a matter of time.

CONCLUSION

Most osteochondral talar defects are caused by trauma. They may heal and remain asymptomatic or progress to subchondral cysts with deep ankle pain on weight bearing. The pain in OCDs is most probably caused by an intermittent local rise in intraosseous fluid pressure with occurs on every step, and which thus sensitizes the highly innervated subchondral bone. The development of symptoms and subchondral cysts depends on the defect type, joint congruence, alignment, impact force and shearing stress. Symptoms and subchondral cyst formation will only occur in case of a local small diameter defect in the subchondral plate.

Cartilage has a liquid and a solid component (i.e., collagen and proteoglycans) that enables it to withstand compressive stress. A congruent joint surface, such as the ankle, is covered by thin articular cartilage. Incongruent joints, such as the knee, are covered by thicker cartilage. There is a curvilinear relation between the cartilage thickness and deformation. Thick cartilage easily deforms, thereby increasing the load-bearing area and decreasing the stress area.

Fluid from the damaged cartilage can be forced into the microfractured subchondral bone plate underneath during loading. The smaller the diameter of the defect in the subchondral plate, the higher the fluid pressure. This intermittent local rise in high fluid pressure will cause osteolysis and the eventual formation of a subchondral cyst. Malalignment of the ankle joint may aggravate this process by increasing the local pressure in specific locations of the ankle. The pain in OCDs is most probably caused by the repetitive high fluid pressure and decrease in pH, sensitizing the highly innervated subchondral bone.

CHAPTER 3

Morphological analysis of subchondral talar cysts on microCT

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ABSTRACT

Purpose: Osteochondral talar defects often present in conjunction with subchondral bone cysts. The exact etiology of these cysts is unknown. Recently was shown in a computational bone model that pressurized fluid and osteocytes death could lead to cyst growth, through mechanoregulated bone adaptation. However, a difference in cyst morphology was present between the mechanisms. The purpose of this study was to evaluate and compare the cyst morphology of human cadaveric tali by using microCT with the morphological simulation results previously reported.

Methods: Sixty-six fresh-frozen human cadaveric tali were screened in a regular CT for subchondral bone cysts, radiologically defined as unexpected rounded radiolucent area. Subsequently, the tali with a cyst were scanned in a microCT. The shape of the cysts, the presence of an opening through the subchondral bone plate, and the bone volume fraction around and next to the cyst were analyzed.

Results: In total, six tali were found to have a single cyst. Four cysts had an irregular shape, and two cysts were rounded. A clear opening from the cyst through the subchondral bone plate was found (diameter 0.5–1.7 mm) in four cysts. The bone volume fraction was higher ($p = 0.025$) around the cyst then next to the cyst.

Conclusions: The morphological findings that we found are only compatible with the previously reported simulation results of cyst growth in response to pressurized fluid, or pressurized fluid in combination with osteocyte death. It is therefore most likely that pressurized fluid plays a role in the pathoetiology of cyst growth. A better understanding of cyst growth may improve treatment and prevent further cyst formation.

INTRODUCTION

Subchondral bone cysts are often found in patients with an osteochondral talar defect (OCD) causing deep ankle pain on weight bearing. The etiology of these cysts remains unclear[24, 26, 249] and can occur in different joints, that is, hip, knee, and ankle[107, 117, 138, 140, 165, 250]. Development of these cysts is most often a slow process, and the cysts can be surrounded by a sclerotic rim[40, 49, 61, 205, 214] (Fig. 1). With the development of new diagnostic methods of magnetic resonance imaging (MRI) and computed tomography (CT), cystic lesions of the talus can be accurately determined and are found to be present in 29–46% of the chronic OCDs[63]. However, these cysts are usually diagnosed and surgically treated in a late stage, and the treatment results are poor[122, 194]. Understanding the pathomechanism of these cysts might result in more adequate treatment and better clinical outcome. Pressurized fluid has been proposed to play an important role in the development of a subchondral bone cyst[63, 86, 165, 210, 250, 270]. In this hypothesis, an opening through the subchondral bone plate is required for the development of pressurized fluid in the cyst. However, early and adequate treatment of the opening could prevent cyst development.

Cox et al.[48] concluded from computational model simulations that either pressurized fluid, osteocyte death, or a combination of both can be responsible for the growth of subchondral bone cysts, through a mechanoregulated bone adaptation process. Pressurized fluid as a mechanical stimulus decreased the load on the surrounding bone, thereby leading to net bone resorption and growth of the subchondral cyst. In this scenario, an irregularly shaped cyst developed which became rounded and

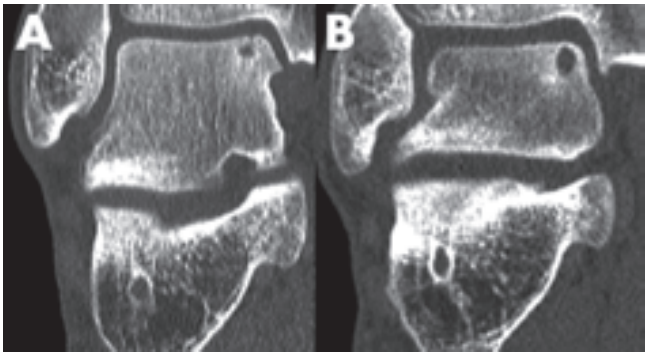

Figure 1A: Coronal CT of a patient with deep ankle pain. The CT shows an irregularly shaped subchondral bone cyst, with an opening in the subchondral bone plate. **B**: Coronal CT of the same patient after a conservative treatment of 2 years. The subchondral bone cyst has grown and developed a sclerotic rim, and the subchondral bone plate appears to be closed. Arthroscopic debridement and bone marrow stimulation was performed after 2 years of conservative treatment.

obtained a sclerotic bone rim after removal of the pressurized fluid (Fig. 2A). In the simulations of osteocyte death, subchondral cyst growth also occurred because of the reduced growth stimulus signal from the osteocytes. Contrary to the former mechanism, the cyst immediately obtained a rounded shape and a sclerotic rim (Fig. 2C). If both mechanisms were simultaneously present, the process of cyst growth was comparable to the response to pressurized fluid only, but the growth rate increased (Fig. 2B).

As there appears to be a morphological indicator for the specific mechanism of cyst growth, the purpose of this study was to evaluate and compare the subchondral

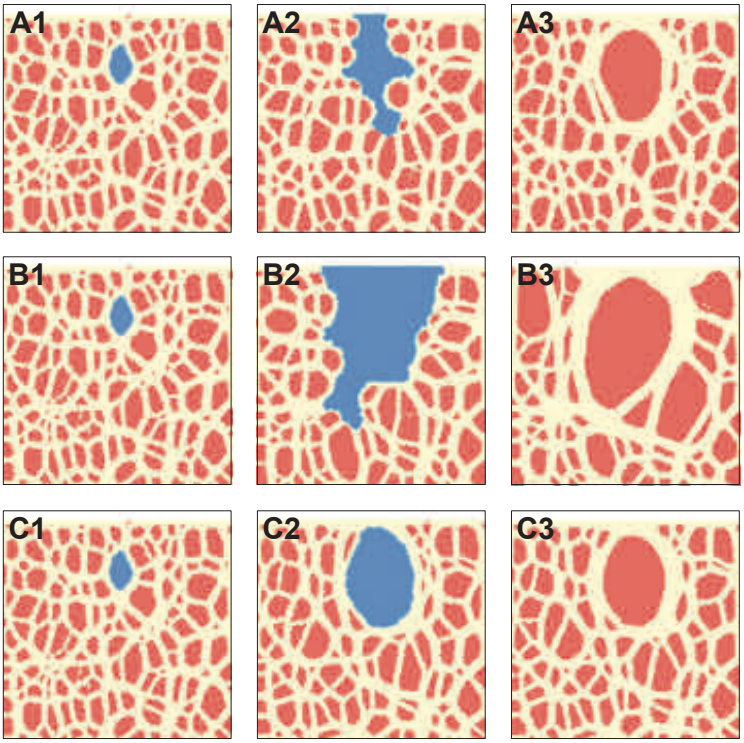

Figure 2A: Bone remodelling in response to cyst pressurized fluid. **A1**: A marrow cavity is filled with pressurized fluid. **A2**: Growth of an irregular cyst in response to pressurized fluid. **A3**: Development of a rounded cavity surrounded by a sclerotic rim after removal of the pressurized cyst fluid. **B**: Bone remodelling in response to cyst pressurized fluid in combination with osteocyte death. **B1**: A marrow cavity is filled with pressurized fluid and osteocytes in a close vicinity to the cavity are killed. **B2**: Growth of an irregular cyst in response to pressurized fluid and osteocyte death. **B3**: Development of a rounded cavity surrounded by a sclerotic rim after removal of the pressurized cyst fluid and when further osteocyte death was prohibited. **C**: Bone remodelling in response to osteocyte death. **C1**: Osteocytes in close vicinity to a marrow cavity are killed. **C2**: Growth of the cavity in response to dead osteocytes. **C3**: When further osteocyte death was prohibited, to mimic closing of the communication between the cyst and the joint space, a rounded cavity with a sclerotic rim remained.

bone cyst morphology of human cadaveric tali on microCT with the morphological results of the simulation study[48]. The shape of talar cysts was evaluated together with the bone volume fraction around the cysts and the presence of an opening through the subchondral bone plate.

MATERIALS AND METHODS

Imaging of subchondral talar cysts

Sixty-six fresh-frozen human cadaveric tali (40 female, 26 male) without macroscopic signs of osteoarthritis with an unknown medical history were collected after an anatomical practicum. The median age of the specimens was 75.0 years (range 58–88 years). First, the tali were screened in a regular CT system (Philips MX8000 spiral CT system, Philips Medical Systems, Eindhoven, the Netherlands) for subchondral bone cysts, radiologically defined as an unexpected radiolucent rounded area[40, 61, 214]. The slice thickness was 0.6 mm, and the increment was 0.3 mm, the radiation dose was ±0.1 mSv. Subchondral bone cysts on the talocrural joint and subtalar joint were both included because both joints are congruent and OCDs are also present on the subtalar joint[3, 43, 269]. Next, the tali with a subchondral bone cyst were scanned at high resolution (74 micron) in a microCT scanner (μCT80, Scanco Medical, Bassersdorf, Switzerland). The slice thickness was 60 μm, and the increment was 60 μm, the radiation dose was <5 mSv. Finally, 3D reconstructions were created with an isotropic spatial resolution of 60 μm, and grey-value images were segmented using a low-pass filter to remove noise ($\delta = 0.7$, support = 2 voxels). The images were segmented using a fixed global threshold (11.2% of the maximum grey value) to extract the mineralized bone phase[175].

MicroCT analysis of subchondral talar cysts

Cysts were classified as rounded or irregular in ten different cross sections on microCT by two different observers. The ten cross sections were selected to be perpendicular to the articular surface and equally spread over volume between the start- and end point of the cyst. A rounded cyst was defined as a cyst with a symmetric smoothen rim (Fig. 3A). An irregular cyst was defined as a cyst with an asymmetric irregular rim (Fig. 3B).

The appearance of an opening through the subchondral bone plate adjacent to the subchondral bone cyst was carefully evaluated in all cross sections. The maximum diameter of the opening was defined as the largest radiolucent distance on the y- or z-axis perpendicular to the opening. The maximum diameter of the subchondral bone cyst was defined as the largest radiolucent distance on the x-, y-, or z-axis. Both measurements were performed with ImageJ 1.43 software.

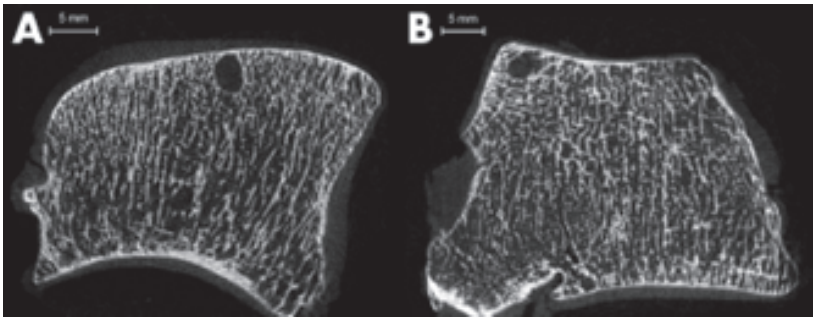

Figure 3A: Coronal microCT image of a rounded, symmetrical cyst located centrally on the talar dome. **B**: Coronal microCT image of an irregular, asymmetrical cyst located medially on the talar dome.

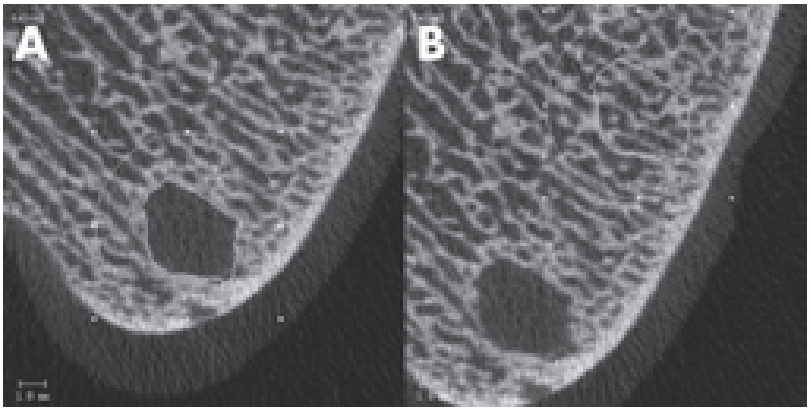

Figure 4A: The bone volume fraction around the cyst was evaluated on microCT by selecting an inner circle at the rim of the cyst and an outer circle of 1 mm around the cyst at ten different cross sections. The bone volume fraction next to the cyst (**B**) was evaluated by the same circles and threshold, but 1 mm next to the outer circle of the cyst. 3D reconstructions were mead on a fixed global threshold (11.2% of the maximum value).

A sclerotic rim (hyperdens area) as a result of increased bone formation around a subchondral bone cysts (radiolucent rounded area) are often seen on CT[107, 117, 138, 140, 165, 250]. To evaluate the existence of a sclerotic rim, we calculated in 3D the bone volume fraction of the rim around the cyst and compared this volume with an unaffected region next to the cyst. The bone volume fraction next to the cyst was assumed to be physiologic normal. Bone volume fraction was calculated by dividing the bone volume to the total volume of the area of interest. The bone volume fraction around the cyst was calculated by drawing an inner circle at the rim of the cyst and an outer circle of 1 mm larger radius around the cyst (Fig. 4A). The 1 mm larger radius was

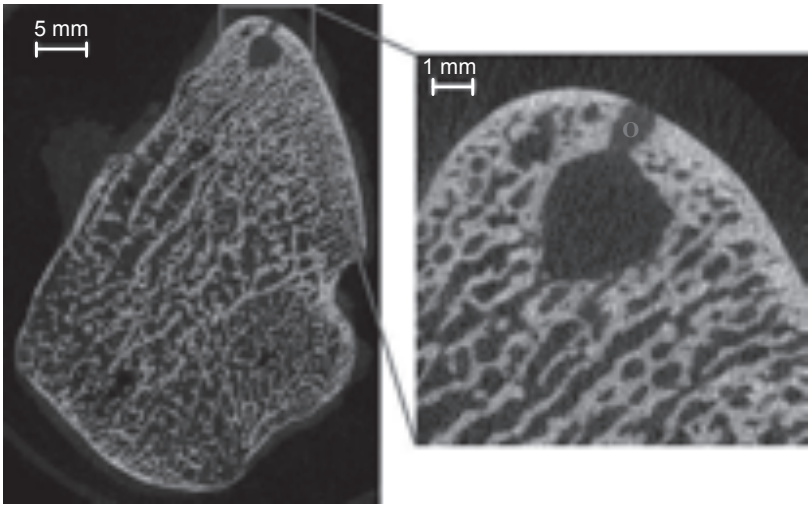

Figure 5: A microCT image showing an opening in the subchondral bone plate (circle) and openings in the cyst wall (asterisk).

chosen based on measurements of ten patients with a sclerotic subchondral bone cyst of the talus. In these ten patients, a median thickness of the sclerotic rim of 1.0 mm (range 0.6–1.3 mm) was measured on a coronal CT of the largest diameter of the subchondral bone cyst. In each cyst, a circle was drawn in ten different cross sections. The ten cross sections were selected to be equally spread over the start- and end point of the cyst (range of the total cross sections of the cysts 18–70). The bone volume fraction in an unaffected region location next to the cyst was calculated by the same circle and cross section, but 1 mm next to the outer circle of the cyst (Fig. 4B). Finally, 3D reconstructions were made using a fixed global threshold (11.2% of the maximum value) to extract the mineralized bone phase[175]. In addition, the trabecular thickness and trabecular separation (distance between the trabeculae) around and next to the cyst was calculated in mm.

Furthermore, we observed openings through the trabeculae bone surrounding the cysts (Fig. 5). Measurements of the diameter of each opening were performed over the same ten cross sections.

Statistical analysis

All statistics were performed with SPSS (version 16.0, SPSS Inc; Chicago, IL, USA). The bone volume fraction, trabecular thickness, and trabecular separation were presented as median and range.

To assess the differences in bone volume fraction, trabecular thickness, and trabecular separation around and next to the cyst, a nonparametric Wilcoxon test was used due to the small sample size. A p-value <0.05 was considered statistically significant.

RESULTS

In total, six tali of the 66 were found to have a single subchondral bone cyst. Two cysts were located medial on the talar dome, two were located central on the talar dome, one cyst was located central on the subtalar joint, and one cyst was located medial

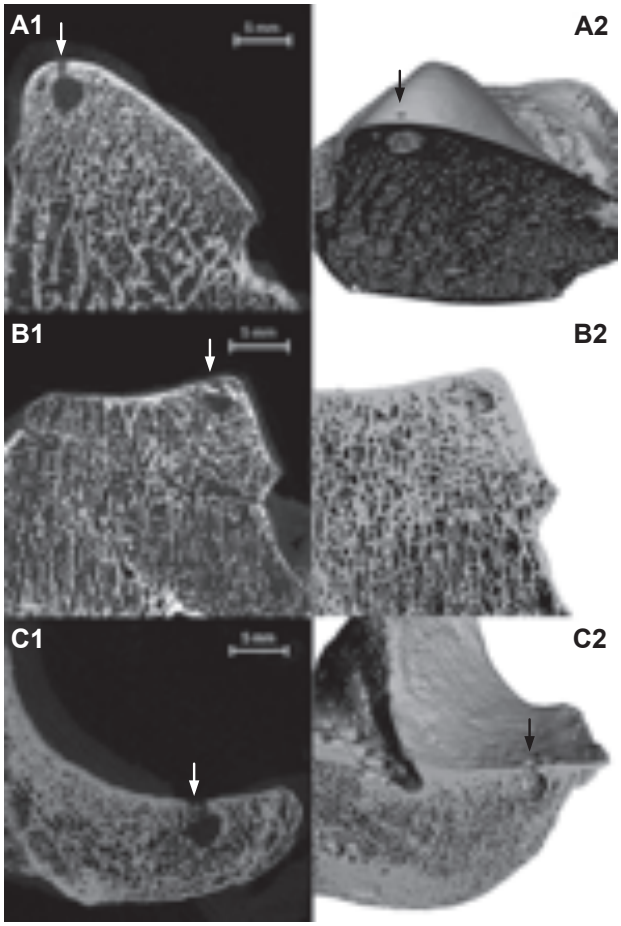

Figure 6: On the left coronal microCT images of three different tali with an opening through the subchondral bone plate (arrow). On the right 3D reconstructions of those tali.

Table I: Subchondral bone cyst morphology.

	Location cyst	**Diameter cyst**	**Shape cyst**	**Opening bone plate**	**BVF around the cyst**	**BVF next to the cyst**	**TT around the cyst**	**TT next to the cyst**	**TS around the cyst**	**TS next to the cyst**
Talus 1	Medial	4.9 mm	Irregular	Ø 1.7 mm	0.7	0.6	0.4 mm	0.3 mm	0.3 mm	0.5 mm
Talus 2	Medial	4.2 mm	Round	Ø 1.0 mm	0.9	0.8	0.6 mm	0.5 mm	0.2 mm	0.2 mm
Talus 3	Central	4.4 mm	Round	No	0.7	0.6	0.4 mm	0.3 mm	0.3 mm	0.2 mm
Talus 4	Central	3.3 mm	Irregular	No	0.7	0.6	0.3 mm	0.2 mm	0.2 mm	0.3 mm
Talus 5	Central subtalar	5.8 mm	Irregular	Ø 1.7 mm	0.6	0.6	0.4 mm	0.4 mm	0.4 mm	0.4 mm
Talus 6	Medial subtalar	1.6 mm	Irregular	Ø 0.5 mm	0.2	0.1	0.2 mm	0.2 mm	0.8 mm	0.7 mm
Median (range)		4.3 (1.6–5.8)		1.4 (0.5–1.7)	0.7 (0.2–0.9)	0.6 (0.1–0.8)	0.4 (0.2–0.6)	0.3 (0.2–0.5)	0.3 (0.2–0.8)	0.3 (0.2–0.7)
Wilcox-on test					$p=0.025$		$p=0.046$		n.s.	

BVF, bone volume fraction; TT, trabecular thickness; TS, trabecular separation.

on the subtalar joint. Both observers agreed and classified two cysts as a cyst with a rounded symmetric shape and four cysts with an irregular asymmetric shape (Table I). The median maximum diameter of the cysts was 4.3 mm (range 1.6–5.8 mm). In four cysts, a clear opening from the cyst through the subchondral bone plate was found (diameter 0.5–1.7 mm) (Fig. 6). Two of the four openings were also seen on the regular CT scans. In one cyst with a clear opening, a displaced chondral lesion was macroscopically observed above the cyst. The bone volume fraction around the cysts (median = 0.7 mm) was higher ($p = 0.025$) then next to the cysts (median = 0.6 mm). The trabecular thickness was also higher ($p = 0.046$) around the cyst (median = 0.4 mm) then next to the cysts (median = 0.3 mm). There were no significant differences between the trabeculae separation around the cyst (median = 0.3 mm) then next to the cyst (median = 0.3 mm). Furthermore, three dimensional microCT evaluation revealed in all cysts that the trabeculae surrounding the cyst did not completely enclose the subchondral bone cyst (Fig. 5). Openings with a mean diameter of 0.3 mm (SD 0.1) were visible at the edge of the lesions.

DISCUSSION

The most important finding of the study was the presence of a clear opening through the subchondral bone plate on microCT in talar cysts. Based on morphological analysis on microCT, it is most likely that pressurized fluid plays a role in the pathoetiology of cyst growth.

Recently, it was concluded from computational model simulation that either pressurized fluid, osteocyte death, or a combination of both can be responsible for the growth of subchondral bone cysts, through a mechanoregulated bone adaptation process[48]. However, an intriguing difference in the process of cyst growth was present between the conditions. In this study, the aim was to evaluate and compare the subchondral cyst morphology of human cadaveric tali on microCT with the previous morphologic simulation results[48].

In six out of 66 (9%) tali, a subchondral bone cyst was found during our screening. To our best knowledge, the incidence of talar cysts has never been described in patients with an unknown medical history. Bosien et al.[26] and later van Dijk et al.[249] reported an incidence of symptomatic osteochondral talar defects after a lateral ankle ligament rupture of 7 and 4%, respectively. It has been shown that in 29–46% of these defects, cystic lesions are also present[67, 94].

Four out of six cysts showed an irregular shape of the cyst on microCT. This shape fits with an active cyst growth in response to pressurized fluid (Fig. 2A) or pressurized fluid in combination with osteocyte death[48] (Fig. 2B). The rounded symmetrical shape fits on

the one hand with the above-mentioned mechanism after removal of pressurized fluid and on the other hand with an active cyst growth in response to osteocyte death only (Fig. 2C). However, the morphological finding of an irregular cyst shape cannot be clarified by cyst development in response to osteocytes death only[48]. In the literature, rounded and irregular shapes of cysts are both observed on MRI or CT[94, 107, 117, 138, 140, 165, 250, 268]. It is unclear which type is still in an active growth phase and which type is inactive.

Analysis of the microCT images showed a significantly higher bone volume fraction and trabecular thickness around the cyst then next to the cyst. Differences in the bone volume fraction around the cysts were only seen in the simulations of pressurized fluid or pressurized fluid in combination with osteocyte death[48] (Fig. 2A, B). A sclerotic rim was continuously present during the simulations of osteocyte death (Fig. 2C), while in simulations of pressurized fluid or pressurized fluid in combination with a sclerotic rim only developed after pressure release[48] (Fig. 2A, B). Pressure release could be a result of a healed subchondral bone plate[130, 147, 193]. A clear opening was observed through the subchondral bone plate in four tali. In the other two cysts, no clear opening was found. However, due to the slice thickness of 60 µm, the openings could have been missed. Although the numbers are small, there appears to be no indication that the opening in the subchondral plate is related to the bone volume fraction around the cysts. Welch et al.[267] found in a caprine study that pressure release after a period of intraosseous fluid pressurization led to increased bone formation. Furthermore, pressure release could be a result of fluid outflow through the small openings in the cyst wall (Fig. 5). The amount of possible fluid outflow depends on the time of loading, the pressure difference between the fluid cavity and the intratrabecular space, the size of the pores, the viscosity of the fluid, and the permeability of the tissue in the pores of the cyst.

An increased fluid outflow or closure of the subchondral bone plate will thus release the pressure in the cyst and may stop the growth[48]. However, natural healing of the subchondral bone plate in an OCD is difficult due to the osteolytic effect of pressurized fluid that results from loading of the joint[247, 250]. In the clinic, adequate detection of the condition of the subchondral bone plate could therefore be important to distinguish between conservative and operative treatment of OCDs. MicroCT could be used to determine if the subchondral bone plate is intact because, on regular CT, an opening is not always visible. The success rate of conservative treatment of OCDs is 45–53%[273]. However, if conservative treatment would only be applied in OCDs without an opening through the subchondral bone plate, the success rate could be improved because cyst development by pressurized fluid, osteocyte death, or a combination of both will probably not occur[48]. In an OCD with an opening through the subchondral bone plate, early restoration of the bone plate could prevent the development of a subchondral bone cyst. The restoration can be achieved by means of arthroscopic debridement and bone marrow stimulation[11, 68, 138]. The aim of this procedure is to induce subchondral bone

revascularization and subsequently to accomplish new bone formation[42]. In case of a large subchondral bone cyst, restoration of the subchondral bone plate or opening of the cyst wall may release the pressure inside the cyst[11, 68, 138]. Pressure release will stop the growth of the subchondral bone cyst, and bone marrow stimulation will stimulate new bone formation. A cancellous graft may be placed to fill the subchondral bone cyst[252].

Several limitations of this study must be mentioned. The medical history was unknown of the specimens, and therefore, it is unknown if the cysts were symptomatic. Furthermore, the number of specimens with a subchondral bone cyst of the talus was low and microCT was performed only once. More information for the validity of the model[48] could be found if different microCTs are made during an in vivo follow-up of cysts. In addition, limitations were also present in the model that was used for the simulations, that is, the choice for 2D simulations limited the structures that can be represented, and it is assumed that osteocytes can sense loading that is equivalent to strain energy density and that they can stimulate osteoblast cells in their vicinity[48]. Furthermore, more clinical studies are necessary to draw conclusions if microCT could be useful in the preoperative planning.

CONCLUSION

Morphological analysis of the subchondral bone cysts with microCT showed a clear opening through the subchondral bone plate in four out of six cysts and a higher bone volume fraction and trabecular thickness around the cysts. These findings and the presence of irregular cysts are seen in subchondral cyst growth as a result of pressurized fluid. It is therefore most likely that pressurized fluid plays a role in the pathoetiology of cyst growth. Better understanding of cyst growth may improve treatment and prevent further cyst formation.

PART II

Surgical treatment and subchondral bone healing

CHAPTER 4

Diagnosis and treatment of osteochondral defects in the ankle

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ABSTRACT

An osteochondral defect of the talus is a lesion involving talar articular cartilage and subchondral bone. It is frequently caused by a traumatic event. The lesions may either heal, stabilize or progress to subchondral bone cysts. The subchondral cysts may develop due to the forcing of cartilaginous or synovial fluid with every step. Malalignment of the hindfoot plays an important role in the development of further degeneration. Plain radiographs may disclose the lesion. Modern imaging technology has enhanced the ability to fully evaluate and accurately determine the size and extent of the lesion, which are fundamental for proper treatment. Asymptomatic or low-symptomatic lesions are treated nonoperatively. For surgical treatment the following types of surgery are in clinical use: debridement and bone marrow stimulation, retrograde drilling, internal fixation, cancellous bone grafting, osteochondral autograft transfer, autologous chondrocyte implantation, and allograft transplantation. Although these are often successful, malalignment may persist with these treatment options. Calcaneal correction osteotomy may be suitable for osteochondral defects in select cases.

INTRODUCTION

An osteochondral defect (OCD) is a lesion involving the articular cartilage and its subchondral bone. If only cartilage is involved in the pathology, the term chondral defect is used. Many synonyms are used, including osteochondritis dissecans[68], transchondral fracture[24], flake fracture[106], talar dome fracture[15], osteochondral fracture[11], osteochondral lesion[127] and osteochondral defect[208].

In the eighteenth century Monro[153] was the first to report the presence of cartilaginous bodies in the ankle joint. In 1888 König[123] used the term osteochondritis dissecans to describe loose bodies in the knee joint and suggested that these were the result of spontaneous necrosis. Since then, several etiologies for these lesions have been suggested. Trauma is known to be the most important etiologic factor, but ischaemia and idiopathic osteochondral ankle lesions do occur[204, 238]. The most common location of OCDs is in the knee, followed by the talar dome[274].

OCDs can either heal and remain asymptomatic or progress to deep ankle pain on weightbearing, prolonged joint swelling, recurrent synovitis, diminished range of motion and formation of subchondral bone cysts. The development of an OCD may have a sudden onset, but the development of a subchondral cyst is most often a slow process.

Early accurate diagnosis of OCDs of the talus is important because optimal ankle joint function requires talar integrity[201]. However, an OCD is often not recognized and therefore not adequately treated. The non-recognition is mainly due to the fact that the lesion produces symptoms that cannot be distinguished from the previous trauma, and it cannot always be identified on plain radiographs.

Even though elaborate knowledge exists concerning OCDs of the talus, its etiology and pathogenesis are still not fully understood. Increasing attention is paid to invasive and sometimes expensive surgical treatments, while research for pathogenesis of the lesions has been somewhat neglected. In order to treat OCDs in all its dimensions, more should be known about their natural history.

For the last decade great developments have been made in their surgical treatment. Despite advancements in options like osteochondral autograft transfer system (OATS) or autologous chondrocyte implantation (ACI), arthroscopic debridement and bone marrow stimulation remains the best treatment that is currently available for defects up to 15 mm in diameter[230, 261]. In larger (cystic) defects this treatment is less successful, hence there is more debate[46, 75].

In this review the natural history, diagnosis and treatment options for OCDs of the talus are summarized.

ETIOLOGY

A traumatic insult is widely accepted as the most important etiologic factor of an OCD of the talus. Trauma causing the lesion may be a single event or consist of a series of repeated, less intense (micro) traumas[31, 184, 204]. For lateral talar lesions trauma has been described in 93–98% and for medial lesions in 61–70%[68, 261]. Because not all patients report a history of ankle injury, a subdivision can be made in the etiology of non-traumatic and traumatic defects.

Non-traumatic OCDs are called osteochondritis or osteochondrosis dissecans[222]. Ischaemia, subsequent necrosis and possibly genetics are etiologic factors in non-traumatic OCDs[204]. Furthermore, OCDs in identical twins and in siblings have been described[10, 62, 271]. Less reported possible causes are metabolic, vascular, endocrine and degenerative factors, as well as morphologic abnormalities[24, 31, 274].

In the etiology of traumatic OCDs ankle sprains play the largest role. When a talus twists inside the ankle mortise, the cartilage lining of the talus can be damaged. This may lead to a bruise and subsequent softening of the cartilage or even a crack in the cartilage with subsequent delamination. Separation may occur in the upper layer, as a result of shearing forces, or may occur in the subchondral bone. Fragments may break off and float loose in the ankle joint, or remain partially attached and stay in position. The subchondral fracture has no soft-tissue attachments and is highly susceptible to subsequent avascular necrosis[274].

Berndt and Harty[24] clearly described the trauma mechanism in cadaver ankles. They were able to reproduce lateral defects by strong inversion of a dorsiflexed ankle, leading to compression of the lateral border of the talar dome against the face of the fibula. When the lateral ligament ruptured, avulsion of the chip began. With the use of excessive inverting force, the talus within the mortise was rotated laterally in the frontal plane, impacting and compressing the lateral talar margin against the articular surface of the fibula. A portion of the talar margin was sheared off from the main body of the talus, which caused the lateral OCD. A medial lesion was reproduced by plantarflexing the ankle in combination with slight anterior displacement of the talus on the tibia, inversion, and internal rotation of the talus on the tibia.

The most common location of OCDs in patients with ankle trauma is on the anterolateral or posteromedial side of the talar dome. The lateral lesions are usually shallow and wafer-shaped, indicating a shear mechanism of injury. Medial lesions in contrast are usually deep and cup-shaped, indicating a mechanism of torsional impaction and axial loading[24, 39, 41, 68, 223, 261]. Because of their shape, lateral lesions are more frequently displaced than medial lesions.

NATURAL HISTORY

Normal articular cartilage comprises chondrocytes and an extracellular matrix which consists primarily of collagen and proteoglycans[36]. Cartilage is avascular and is nourished by the intra-articular fluid. The tissue fluid of the cartilage matrix, which comprises about 75% of the total weight of cartilage, functions as a transport medium by its free exchangeability, whether extra- or intra-fibrillar[111, 145].

The progression of OCDs may be the result of repetitive fluid pressure from the damaged cartilage. During ankle trauma, microfractures often arise in the subchondral bone plate[217]. The damaged subchondral bone is less able to support the overlying cartilage[35]. When overlying cartilage is not supported by the underlying bone plate it loses quality due to loss of proteoglycans and glycoprotein's[111, 180]. In this situation liquid not only flows within the cartilage, but can also enter the subchondral bone through the microfractured area (Fig. 1). This fluid pressure causes osteolysis. An intermittent or continuous high local pressure can interfere with normal bone perfusion and lead to osteonecrosis, bone resorption and formation of lytical areas[13, 14, 58, 206, 247].

The damaged cartilage may also function as a valve, allowing intrusion of fluid from the joint space into the subchondral bone but not in the opposite direction[210]. On the weightbearing phase of gait there is full contact between the talar and tibial cartilage over the talar shoulders[151]. During this phase, pressures in opposing talar and tibial cartilage are theoretically identical, which may result in the forcing of fluid in the direction of least resistance, i.e. the damaged subchondral bone. During unloading of the joint, joint space fluid may re-enter the articular cartilage. On the next weightbearing cycle, this fluid is intruded in the subchondral bone. This repetitive mechanism would result in

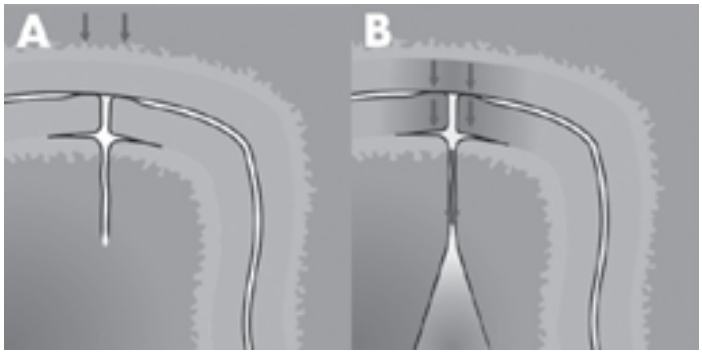

Figure 1A: Fissure in the cartilage and the subchondral bone plate. **B**: When loaded the water is forced out of the cartilage into the subchondral bone.

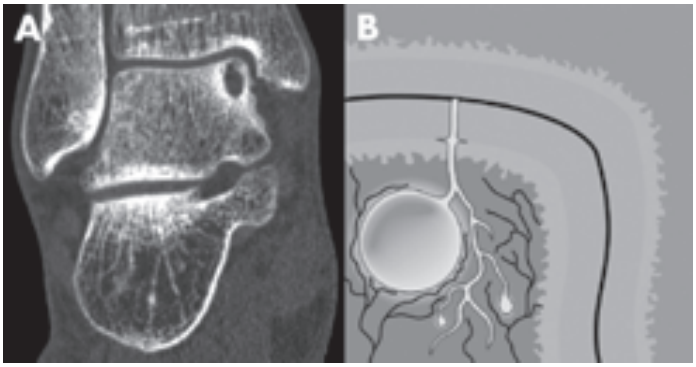

Figure 2A: Coronal CT of a young patient with a long history of deep ankle pain (6 years). The CT shows an opening in the subchondral bone plate. Subchondral osteolysis has caused a subchondral cyst. **B**: A schematic situation of the CT image and shows the mechanism of cyst formation. The black lines represent nerve endings in the subchondral bone.

a vicious cycle, causing the shift of synovial fluid into the damaged subchondral talar bone, thereby slowly developing a subchondral cyst (Fig. 2).

Varus or valgus malalignment of the ankle joint may also play an important role in the natural history by increasing the contact pressure. The ankle joint has a high congruency. A decrease in joint congruence will increase contact pressure per area[182]. More displacement corresponds to increasing contact pressure. Ramsey and Hamilton [182] have shown that a 1 mm lateral talar shift reduces the contact area by 42%, and a 2 mm lateral shift reduces the contact area by 58%. Long-term follow-up studies have demonstrated that patients with persistent displacement of ankle fractures had poorer long-term results than those without persistent displacement[110]. Bruns et al.[33] demonstrated that in varus and supination the maximum pressure is located on the medial border of the talus, while in valgus and pronation the maximum pressure is located on the lateral talar border. Increased pressure on an existing OCD may negatively influence the natural history of the lesion[35]. It is therefore important to detect and correct malalignment in patients with an OCD of the ankle.

CLINICAL PRESENTATION

OCDs often cause deep ankle pain on weightbearing, prolonged joint swelling, recurrent synovitis, diminished range of motion, and formation of subchondral bone cysts. A differentiation has to be made between the acute and the chronic situation[274]. In the acute situation, symptoms of an OCD of the talus are often unrecognized since the swelling and pain from the lateral ligament lesion prevails. In patients with an isolated

ligamentous ankle injury these symptoms usually resolve after functional treatment within two to three weeks. If symptoms have not resolved within 4–6 weeks, an OCD should be suspected. Locking and catching are symptoms of a displaced fragment.

Chronic lesions typically present as persistent ankle pain after a prior history of an inversion injury of the ankle. Pain is usually experienced as deep ankle pain, during or after activity. Reactive swelling or stiffness may be present, but absence of swelling, locking or catching does not rule out an OCD. Most patients demonstrate a normal range of motion with absence of recognizable tenderness on palpation and absence of swelling.

DIAGNOSIS AND CLASSIFICATION

The total incidence of symptomatic and asymptomatic localized traumatic articular cartilage damage and OCDs is unknown. With the increased awareness and newer diagnostic techniques, the incidence of OCD seems to have increased[138].

Plain radiographs should be the initial investigation of suspected OCDs of the talus, after careful history-taking and physical examination of the ankle. These consist of weight-bearing anteroposterior mortise and lateral views of both ankles. The sensitivity and specificity of the combination of medical history, physical examination and radiography are 59% and 91%, respectively[260]. The radiographs might not reveal any pathology, or show an area of detached bone, surrounded by radiolucency. Initially, the damage may be too small to be visualized on routine radiography. Only in cases of a large OCD, the initial X-ray may be positive. By repeating the imaging studies in a later stage, the abnormality sometimes becomes apparent. A heel rise view with the ankle in a plantarflexed position may reveal a posteromedial or posterolateral defect[260].

Computed tomography (CT) is useful in determining the size, location, shape and degree of displacement of osteochondral fragments[192]. CT is often invaluable in preoperative planning to define the exact size and location of the lesion[192, 223, 274]. The scanning protocol involves 'ultra high resolution' axial slices with an increment of 0.3 mm and a thickness of 0.6 mm. Multi-planar coronal and sagittal reconstructions should be 1 mm. However, CT is limited in its ability to visualize articular cartilage and bone bruises[204].

Magnetic resonance imaging (MRI) allows multiplanar evaluation and offers the advantage of visualising the articular cartilage and subchondral bone as well as edema and other features of the surrounding soft tissue. Nevertheless in diagnosing an OCD, CT has proven to be as valuable as MRI[260].

In 1959, Berndt and Harty[24] suggested a classification system for staging the lesions based on plain radiographs of the ankle (Table I). In grade I, there is local compression

Table I: Berndt and Harty (1959)

Grade I:	A small compression fracture
Grade II:	Incomplete avulsion of a fragment
Grade III:	Complete avulsion of a fragment without displacement
Grade IV:	A displaced fragment

of the cartilage and subchondral bone, and usually there are no radiographic findings. In grade II, there is avulsion or partial detachment of the osteochondral fragment, but the main part is still attached to the talus. In grade III, there is complete avulsion of an osteochondral fragment, without any displacement. In grade IV, the osteochondral fragment is completely detached and displaced inside the ankle joint. Later, classification systems based on MRI, CT and arthroscopic findings were made[11, 24, 95, 138, 225, 226]. The use of these classification systems is questionable since none of the systems are dually related to the current treatment options[261].

TREATMENT

There are widely published non-surgical and surgical techniques for treatment of symptomatic OCDs[237].

Non-surgical treatment

Many authors have suggested that the decision to operate should depend on the grade of the lesion. Berndt and Harty[24] grade I and II lesions should be managed non-surgically for up to 1 year to allow for resolution before resorting to surgery[7, 39, 174, 223, 246]. Nevertheless, a meta-analysis of 14 studies with a total of 201 patients showed only a 45% success rate of non-surgical treatment of grade I, grade II, and medial grade III talar OCD (not all injury types were specified)[261]. Non-surgical treatment of chronic lesions (>6 weeks) had a success rate of 56%[261].

Asymptomatic or low symptomatic OCDs should be treated with rest and/or restriction of (sporting) activities, non-steroidal anti-inflammatory drugs (NSAIDs), or cast immobilization for 3 weeks up to 4 months[261]. The aim is to either give the bruised talus rest so edema can resolve and necrosis is prevented, or stimulate reattachment of the (partly) detached fragment to the surrounding bone.

Surgical treatment

For years there has been an ongoing debate about the optimal surgical treatment regimen. Debridement of the lesion has been performed progressively since the 1950s.

This method was later combined with bone marrow stimulation, by means of drilling or microfracture, with favorable results[7].

Until the mid-1980s, surgical treatment of talar OCDs consisted of open procedures. In the case of posteromedially located OCDs, most surgeons performed an osteotomy of the medial malleolus to identify and treat the lesion[32, 39, 132, 160]. The introduction of arthroscopy has led to less invasive operative procedures and has gained much popularity[127, 208, 251, 252].

In general, failure of non-surgical management for symptomatic lesions necessitates surgical intervention. Various surgical techniques for symptomatic OCDs will now be discussed.

Bone marrow stimulation

This is the treatment of choice for most lesions. With this technique all unstable cartilage including the underlying necrotic bone is removed. Any cysts underlying the defect are opened and curetted. After debridement, multiple connections with the subchondral bone are created. They can be accomplished by drilling or microfracture. The objective is to partially destroy the calcified zone that is most often present and to create multiple openings into the subchondral bone. Intra-osseous blood vessels are disrupted and the release of growth factors leads to the formation of a fibrin-clot (Fig. 3). The formation of local new blood vessels is stimulated, marrow cells are introduced in the OCD and fibrocartilaginous tissue is formed[164]. In case of a large OCD a cancellous bone graft can be placed.

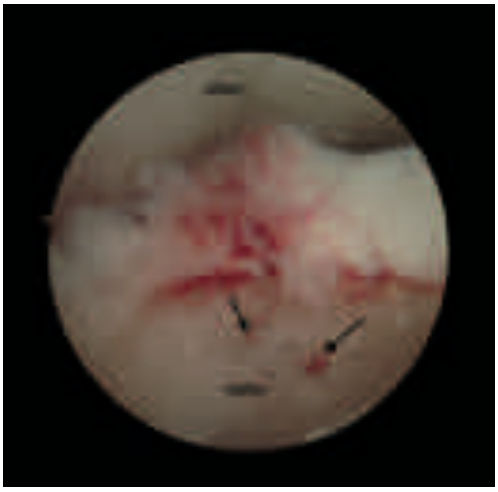

Figure 3: Arthroscopic view of the result of debridement and microfracture of an osteochondral defect of the talus. The arrows indicate microfracture holes; bleeding of the subchondral bone to create a fibrin clot is also visible.

Verhagen et al.[261] reported that debridement and bone morrow stimulation of the lesion by arthroscopy was successful in 87% and by open procedures in 84% of cases. These good results were confirmed more recently[89, 202].

Retrograde drilling

Retrograde drilling is done for primary OCDs when there is relatively intact cartilage with a large subchondral cyst. The aim is to induce subchondral bone revascularization and subsequently to accomplish new bone formation. A cancellous graft may be placed to fill the defect. Taranow et al.[226] reported successful outcome in 13 of 16 patients (81%).

Internal fixation

With this technique, the loose fragment is not removed but fixed to the underlying bone by a screw, Kirschner wires, absorbable fixation, or fibrin glue[143, 213]. DeLee[53] proposed that internal fixation is indicated when the injury occurs acutely and the fracture is larger than one-third the size of the respective dome. Stone et al.[223] suggested that the lesion should be at least 7.5 mm in diameter and that the patient should be young for surgical fixation. A meta-analysis of three studies with a total of 11 patients showed a 73% success rate of internal fixation with a variation from 40 to 100%[261].

Autologous chondrocyte implantation (ACI)

ACI is the implantation of in vitro cultured autologous chondrocytes using a periosteal tissue cover after expansion of isolated chondrocytes. ACI has been popularized by Brittberg[30] and Petersen[172] since 1994. Since that time, ACI has been performed in over 25000 patients: 95% in the knee, 3% in the ankle, and 2% in other joints[274]. Based on promising early results with ACI in the knee, surgeons have now started using ACI for OCDs of the talus. For patients with an OCD who remain symptomatic after primary surgical treatment, ACI is considered a valuable treatment option. The defect should be focal, contained, and preferably more than 1.5 cm in diameter. Large lesions with subchondral cysts may also be treated with ACI, using the 'sandwich technique', i.e. filling the base of the defect with autologous cancellous bone[19, 172].

Contraindications to ACI are bipolar lesions ('kissing lesions') and diffuse degenerative joint changes. Skeletal malalignment and ligamentous instability are also contraindications, unless they are concomitantly corrected at the time of surgery[19].

Osteochondral autograft transfer (OATS)

OATS consists of the harvesting of one or more osteochondral plugs in a lesser weight bearing area of the knee and transplanting them into the talar defect[87, 209]. The aim is to restore the articular surface with hyaline cartilage. One single graft or several smaller grafts (i.e. mosaicplasty) may be used. The use of several grafts provides a

better match to the curvature of the talar dome and surface area of the defect, and may reduce donor site morbidity[45, 88].

Although X-ray evaluation and CT may help to determine the extent of the lesion, indication of OATS is rather based on the size determined after excision of the defect. OATS can also be offered to patients in case of failed primary treatment. An essential aspect of the procedure is insertion of the osteochondral plugs perpendicular to the recipient site. Due to the constrained configuration of the talocrural joint with its highly contoured articular surfaces, the best approach is by means of open arthrotomy, most of the times using a malleolar osteotomy. The primary harvest site is the medial upper part of the medial femoral condyle. As a less frequent option the lateral supracondylar ridge can also be used through a mini-arthrotomy[274]. In case the knee is precluded as a donor site, the ipsilateral talar articular facet may also be used as a harvest site of small sized grafts (2.7 or 3.5 mm in diameter)[126].

Hangody et al.[88] reported on the outcomes of the talar mosaicplasty, with the medial or lateral femoral condyle as the donor site. In 36 patients, multiple grafts of 4.5 × 3.5 mm were harvested to reconstitute the talar defects, which averaged 1 cm in diameter. Good/excellent results were achieved in 34 patients (94%) at a follow-up of 2 to 7 years.

Calcaneal correction osteotomy (CCO)

Clinical and basic scientific investigations have shown that loading and motion of the joint can influence the healing of articular cartilage and joints[35]. The ankle joint has a high congruency. A decrease in joint congruence and malalignment will increase contact pressure per area, and may lead to osteolysis and large OCDs[58, 182, 183, 272].

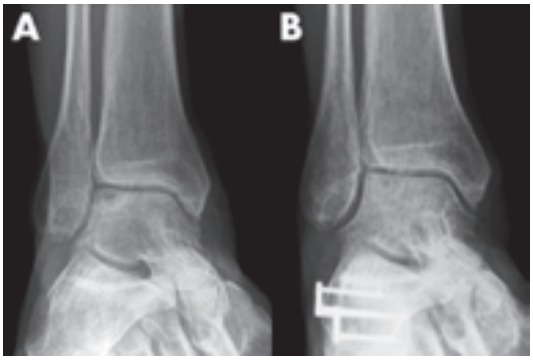

Figure 4: Weight-bearing anteroposterior radiographs of the right ankle of a 45-year-old male patient with valgus malalignment who had persisting complaints of deep ankle pain over four years. He had been treated by arthroscopy twice. **A**: The pre-operative radiograph shows a large osteochondral defect on the lateral talar dome. The lesion was treated by medial displacement of the hindfoot by calcaneal osteotomy with plate-fixation. **B**: The situation six months postoperatively, in which the lesion was almost healed.

In general the different treatment options as described above have good results. However, with these treatment options malalignment is not corrected. CCO may be necessary to restore the natural congruency of the ankle joint. CCO is an established procedure for acquired adult flatfoot[109], hindfoot valgus after recurrent pronation trauma and deltoid ligament insufficiency[99], and malaligned ankle with deformity[170]. We currently perform CCO to treat patients with malaligned hindfoot who have persistent complaints after initial arthroscopic treatment (Fig. 4).

CONCLUSION

Initial trauma causes an (osteo)chondral defect. During loading, compressed cartilage forces water into microfractured subchondral bone, which may cause osteolysis and the slow development of a subchondral cyst. To prevent further degeneration early diagnosis and accurate treatment are necessary. There are various treatment options for an OCD. Arthroscopic debridement and bone marrow stimulation, by nature of the minimally invasive approach, has great advantage in treating typical defects of up to 1.5 cm in diameter. For larger or secondary OCDs the optimal treatment may consist of osteochondral autograft transfer, cancellous bone graft and/or autologous chondrocyte implantation. However, with these treatment options malalignment may still exist, while malignment plays an important role in development of further degeneration in OCD. Therefore, calcaneal correction osteotomy may be suitable for OCDs in selected cases.

CHAPTER 5

Effects of pulsed electromagnetic fields on return to sports after arthroscopic debridement and microfracture of osteochondral talar defects: a randomized, double-blind, placebo-controlled, multicenter trial

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ABSTRACT

Background: Osteochondral defects (OCDs) of the talus usually affect athletic patients. The primary surgical treatment consists of arthroscopic debridement and microfracture. Various possibilities have been suggested to improve the recovery process after debridement and microfracture. A potential solution to obtain this goal is the application of pulsed electromagnetic fields (PEMFs), which stimulate the repair process of bone and cartilage.

Hypothesis: The use of PEMFs after arthroscopic debridement and microfracture of an OCD of the talus leads to earlier resumption of sports and an increased number of patients that resume sports. Study Design: Randomized controlled trial; Level of evidence, 1.

Methods: A total of 68 patients were randomized to receive either PEMFs (n = 36) or placebo (n = 32) after arthroscopic treatment of an OCD of the talus. The primary outcomes (i.e., the number of patients who resumed sports and time to resumption of sports) were analyzed with Kaplan-Meier curves as well as Mann-Whitney U, chi-square, and log-rank tests. Secondary functional outcomes were assessed with questionnaires (American Orthopaedic Foot and Ankle Society ankle-hindfoot score, Foot and Ankle Outcome Score, EuroQol, and numeric rating scales for pain and satisfaction) at multiple time points up to 1-year follow-up. To assess bone repair, computed tomography scans were obtained at 2 weeks and 1 year postoperatively.

Results: Almost all outcome measures improved significantly in both groups. The percentage of sport resumption (PEMF, 79%; placebo, 80%; $p = 0.95$) and median time to sport resumption (PEMF, 17 weeks; placebo, 16 weeks; $p = 0.69$) did not differ significantly between the treatment groups. Likewise, there were no significant between-group differences with regard to the secondary functional outcomes and the computed tomography results.

Conclusion: PEMF does not lead to a higher percentage of patients who resume sports or to earlier resumption of sports after arthroscopic debridement and microfracture of talar OCDs. Furthermore, no differences were found in bone repair between groups.

BACKGROUND

An osteochondral defect (OCD) of the talus often has a severe effect on the quality of life of young and athletic patients[274]. Currently, arthroscopic debridement and bone marrow stimulation are considered the primary treatment in osteochondral talar defects up to 1.5 cm in diameter[46, 191]. This treatment has an 85% overall success rate and a 76% satisfactory outcome at the long term[239, 273]. However, it can take up to 1 year to obtain improvement of clinical symptoms. Moreover, it is a great challenge to achieve early resumption of sports, which is the main goal of many of these young patients. Saxena and Eakin[202] reported a mean sport resumption of 15 weeks after debridement and microfracture of talar OCDs in ''high-demand'' athletic patients. Shortening this period would considerably improve the quality of life in these active patients. Various possibilities have been suggested to improve the recovery process after debridement and microfracture[149, 162, 254, 265]. A potential solution to obtain this goal is the application of pulsed electromagnetic fields (PEMFs). In vitro and in vivo studies have shown that PEMFs act as adenosine A2a agonists, leading to an increase of transforming growth factor β-1, thereby improving bone development, reducing cartilage damage, and increasing chondrocyte proliferation[1, 27, 47, 168, 198, 263]. This biophysical stimulation promotes tissue healing, suppresses inflammation, and relieves pain[38, 154]. Clinically, PEMF treatment improves the outcome of patients after arthroscopic treatment of chondral lesions in the ankle and knee[38, 277]. On the basis of these data, it can be postulated that PEMFs may act on OCDs by improving bone regeneration and suppressing inflammation evoked by surgery. To our knowledge, return to sports after OCD treatment with the use of PEMFs has not been investigated. We hypothesized that the use of PEMFs after arthroscopic debridement and microfracture of an OCD of the talus leads to earlier resumption of sports and an increased number of patients who resume sports.

METHODS

A randomized, double-blind, placebo-controlled trial was conducted in 4 centers in the Netherlands and Belgium from 2009 to 2014. The trial was registered in the Netherlands Trial Register (NTR1636). Details of the study protocol were published earlier[236]. Approval was obtained from the local medical ethics committees of each participating center. Written informed consent for participation was obtained from every patient. A clinical research associate from the primary center's Clinical Research Unit monitored the trial. Internet-based remote data capture (Oracle Clinical) was used for entering, managing, and validating data from the investigative sites.

The study included patients with a symptomatic OCD of the talus, with a diameter <15 mm (in 3 dimensions) as measured on computed tomography (CT) scans, who were scheduled for arthroscopic debridement and microfracture of the defect. Different studies have reported good clinical outcomes after arthroscopic debridement and bone marrow stimulation in osteochondral talar defects up to 1.5 cm in diameter[46, 191, 239, 273]. Furthermore, patients had to have an Ankle Activity Score (AAS) of at least 4 before symptoms[84]. Exclusion criteria were age <18 years, ankle osteoarthritis grade II or III[253], concomitant OCD of the tibia, ankle fracture <6 months before treatment of the OCD, surgical treatment of the index ankle performed <1 year before treatment of the OCD, concomitant painful or disabling disease of the lower limb, rheumatoid arthritis, pregnancy, and implanted pacemaker.

Electromagnetic stimulation was started within 3 days after surgery with a PEMF stimulator (I-ONE; IGEAmedical), which consisted of a portable generator that was connected to a coil attached to the ankle (Fig. 1). It was applied 4 hours daily for a period of 60 days[22, 52]. The coil of the PEMF stimulator generated a peak magnetic

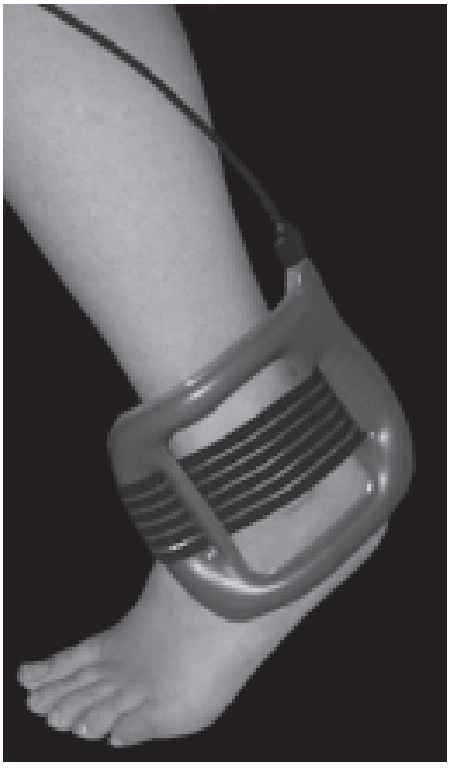

Figure 1: The application of pulsed electromagnetic fields on the ankle, generated in the green coil and attached with the elastic band (I-ONE; IGEAmedical).

field intensity of 1.5 mT, supplied by an electric pulse frequency of 75 Hz[52, 262]. The placebo device produced a negligible peak <0.05 mT, supplied by the minimal current necessary to power the device indicators. The placebo device did not differ from the PEMF active device in shape, color, weight, and acoustic or visual signaling. Patients and investigators were blinded to the allocation of treatment. A clock inside the device recorded the hours of stimulation to monitor the patient's compliance in both groups.

The participants were randomized to receive either an active or placebo device, stratified for participating center, body mass index (≤25 kg/m^2 vs >25 kg/m^2)[20, 46] and diameter of the defect (≤10 mm vs >10 mm)[274]. Randomization was performed in randomly allocated blocks of 2 or 4 patients via a validated web-based computer program (ALEA; NKIAVL)[6, 274]. Treatment allocation was managed by an independent, unblinded research assistant (I.N.S.) who was not involved in patient care or assessment. Any (serious) adverse event during the trial period was recorded and reported to the central medical ethics committee.

Operative Technique

All surgical procedures were performed with a standardized anterior ankle arthroscopy technique[252]. The OCD was identified with a probe and debrided with a curette and bone-cutter shaver. All unstable bone and cartilage were removed. Any cyst underlying the defect was opened, followed by curettage. After full debridement, the subchondral bone was perforated 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 program, guided by a physiotherapist. Partial (eggshell) weightbearing on crutches was allowed as tolerated and progressed to full weightbearing over a period of 6 weeks. During this 6-week period, active non-weightbearing and partial weightbearing sagittal range of motion exercises were encouraged. After this period, resumption of sports was permitted as tolerated[254].

Outcome Assessment

The primary outcome measures were the number of patients that resumed sports and the time to resumption of sports. Resumption of sports was defined as initiation of any sport with a minimum level of the presymptoms level minus 1 point on the AAS, maintained for at least 30 days. The AAS is a 10-point score based on the type and level of sport or work, with 0 points indicating the lowest activity and 10 points indicating the highest activity[84]. A diary was used to monitor resumption and maintenance of sports and activity levels.

The secondary clinical outcome measures included time to resumption of work, the American Orthopaedic Foot and Ankle Society (AOFAS) ankle-hindfoot score[104, 118],

Foot and Ankle Outcome Score (FAOS)[196, 216], EuroQol (EQ-5D)[129, 228], and numeric rating scales (NRSs) for pain (at rest and when running) and satisfaction. Resumption of work was defined as the ability to perform normal work activities without any deficits in work quality[218]. 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[118]. The FAOS is a validated subjective questionnaire consisting of 5 subscales: pain, other symptoms, activities of daily living (function), sports, and quality of life[196, 216]. Each subscale's highest possible score is 100. The EQ-5D is a validated and extensively used general health questionnaire to measure quality of life[57, 129, 218]. It comprises 5 dimensions: mobility, self-care, usual activities, pain/discomfort, and anxiety/depression. Patients' level of quality of life was assessed with the vertical visual analog scale of the EQ-5D, where the endpoints are labeled ''best imaginable health state (1.00)'' and ''worst imaginable health state (-0.33).'' The NRS is an 11-point scale, representing the spectrum of no pain (0 points) to the worst pain imaginable (10 points) and not satisfied (0 points) to maximal satisfaction (10 points)[72].

Patients were evaluated at the outpatient clinic preoperatively and at 2 weeks, 2 months, and 12 months postoperatively. Additionally, they completed questionnaires containing NRSs for pain and satisfaction, EQ-5D[129, 228] and resumption of sport and work at 1 month and 6 months postoperatively.

Radiology

CT scans were obtained preoperatively to measure the 3-dimensional size and to grade the defect according to the modified Berndt and Harty classification[24, 210]. To objectively assess bone repair, CT scans were also obtained 2 weeks postoperatively (only at the main research center) and 1 year after surgery. 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[159, 260, 276]. The level of the subchondral plates (i.e., flush, depressed, or proud) was analyzed on the 1-year postoperative CT scans. The bone volume filling of the OCDs at final follow-up was analyzed in comparison with the 2-week postoperative CT scans and graded as good (67%–100%), moderate (34%–66%), or poor (0%–33%)[77, 152]. To assess the intraobserver reliability, measurements were performed twice by a single physician with an interval of 1 week and in different order, and the assessor was blinded to both treatment allocation and clinical outcome.

Statistics

Sample size calculation was based on the combined primary endpoints. On the basis of our experience, it was expected that 50% of patients would resume and maintain sports within 1 year after the surgical intervention[236]. Offering additional PEMF treatment, we aimed to improve this outcome to 75%. Saxena and Eakin[202] reported a mean sport

resumption of 15 ± 4 weeks after debridement and microfracture. A 20% reduction in time to return to sports was considered clinically relevant (i.e., 3 weeks). A sample size of 30 patients in each group (60 patients in total) had an 80% power to detect a joint difference (control group proportion of 0.50 vs treatment proportion of 0.75; control group mean of 15 weeks vs treatment group mean of 12 weeks, assuming a common standard deviation of 4), based on a Fisher combination test with a 2-sided significance level of 0.05. In reported clinical trials with this device, 9% to 13% of included patients dropped out[22, 277]. Therefore, 34 patients were included in each treatment group (68 patients in total).

All data were analyzed according to the intention-to treat principle. Patient baseline characteristics were summarized in terms of simple descriptive statistics. Categorical data are presented as frequencies. Continuous data are presented as means with standard deviations or as medians with interquartile ranges (IQRs), depending on their distribution. The number of patients who resumed sports were analyzed with the chi-square test. The difference in time to sport resumption was analyzed by the Mann-Whitney U test. Kaplan-Meier survival curves and the log-rank test were also used for comparing time to resumption of sports. A p-value <0.05 was considered statistically significant for the primary outcomes.

Kaplan-Meier survival curves and the log-rank test were used for comparing time to resumption of work. With regard to the secondary clinical outcome scales, linear mixed models with a random intercept and -when model dimension permitted- random slope per patient were used to analyze the repeated data structure of the scales. The fixed part of the models consisted of a main linear time effect, a main group effect, and an interaction between time and group. For all outcomes, the interaction term was used to assess the difference in time trend between both groups. For NRS satisfaction, the main group effect was interpreted additionally, as this outcome was not measured preoperatively. To meet the normality assumption of the model, NRS pain at rest was analyzed on *log(x+1)* scale and EQ-5D, FAOS sports, FAOS symptoms, FAOS pain, FAOS function, FAOS quality of life, and AOFAS on *log(max(x)+1-x)* scale. We also analyzed within each treatment group the scale score differences between baseline and 12-month outcome assessment using the paired t test on normal distribution and the Wilcoxon signed-rank test on skewed distribution. To correct for multiple testing, the Holm method was used for the secondary outcomes[4, 100]. Because 8 secondary outcome measures were involved, the adjusted significance level of the p-value of the comparison with the smallest p-value was set at 0.00625 (0.05/8), and the significance level of comparison with the largest p-value was set at 0.05 (0.05/1). We analyzed the CT findings and number of adverse events using chi-square statistic. To assess the intraobserver reliability of the CT measurements, the intraclass correlation coefficient (ICC) was calculated; an ICC ≥0.85 indicates good reliability[54, 156]. All analyses were

performed in SPSS (v 20.0; IBM Corp) and R (v 3.2.1; The R Foundation) and were reviewed by an independent statistician.

RESULTS

After randomization, 36 patients were allocated to the PEMF group and 32 patients to the placebo group. As shown in Table I, the baseline characteristics and stratifica-

Table I: Baseline characteristics of the patients[a]

	PEMF group, *n*=36	**Placebo group, *n*=32**
Age (yrs), mean (SD)	32 (10)	34 (7)
Gender, *n* (% male)	20 (56)	21 (66)
BMI, mean (SD)[b]	25 (4)	26 (4)
Smoking, *n* (%)	3 (8)	9 (28)
Paid work, *n* (%)	32 (89)	30 (94)
Work hours per week, mean (SD)	33 (14)	35 (12)
Pre injured AAS, mean (SD)	6 (2)	7 (2)
Previous ankle trauma, *n* (%)	26 (72)	20 (63)
Previous ankle fracture, *n* (%)	4 (11)	1 (3)
Previous OCD operation, *n* (%)	5 (14)	8 (25)
Included side, *n* (% right)	20 (56)	17 (53)
Center, *n*[b]		
- A (two surgeons)	30	28
- B (one surgeon)	3	1
- C (one surgeon)	2	3
- D (one surgeon)	1	0
OCD size, mean (SD)[b]		
- Antero–posterior (mm)	9 (4.0)	9 (3.5)
- Medial–lateral (mm)	7 (3.0)	6 (2.3)
- Superior–inferior (mm)	5 (2.1)	5 (2.7)
OCD Location, *n* (%)		
- Medial	27 (75)	17 (53)
- Lateral	7 (19)	14 (44)
- Central	2 (6)	1 (3)
OCD classification, *n* (%)		
- Compression	10 (28)	10 (31)
- Partially fractured	1 (3)	0 (0)
- Completely undisplaced fracture	8 (22)	3 (9)
- Displaced fracture	0 (0)	2 (6)
- Cystic lesion	17 (47)	17 (53)

[a]AAS, Ankle Activity Score; BMI, body mass index; OCD, osteochondral defect; PEMF, pulsed electromagnetic field.
[b]Stratification factor.

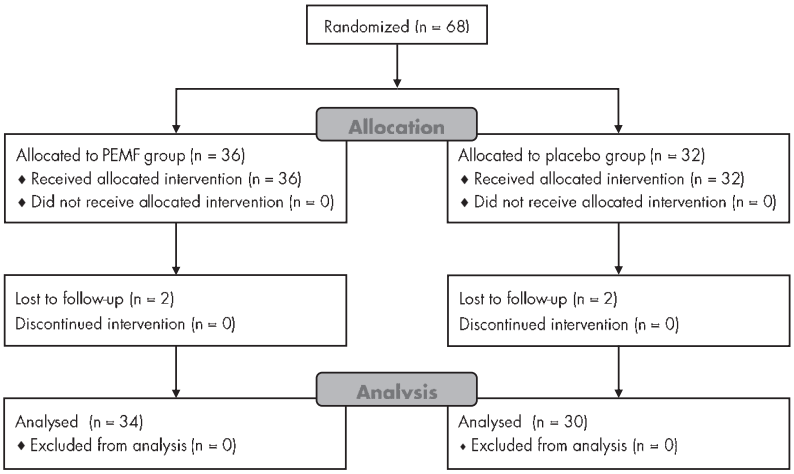

Figure 2: Flow diagram showing the randomization of included patients. Four patients were lost to follow-up after the surgical intervention and could not be included in the intention-to-treat analysis. PEMF, pulsed electromagnetic field.

tion factors are well balanced. Four patients were lost to follow-up after the surgical intervention (Fig. 2). The median compliance was 235 hours (IQR, 183–242) in the PEMF group and 217 hours (IQR, 187–240) in the placebo group, where the prescribed use was 240 hours.

Clinical Results

Resumption of sports was 79% in the PEMF group (27 of 34 patients) and 80% in the placebo group (24 of 30 patients) ($p = 0.95$). Of the patients who resumed sports, the median time to return was 17 weeks (IQR, 8–23) in the PEMF group and 16 weeks (IQR, 8–26) in the placebo group ($p = 0.69$) (Fig. 3). An equal mean AAS of 6 ± 2

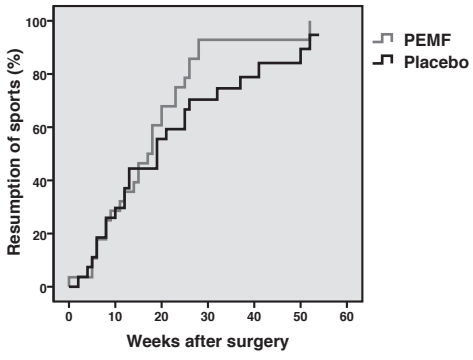

Figure 3: Kaplan-Meier curves of the patients who resumed sports after surgery (pulsed electromagnetic field (PEMF), n = 27; placebo, n = 24; $p = 0.69$).

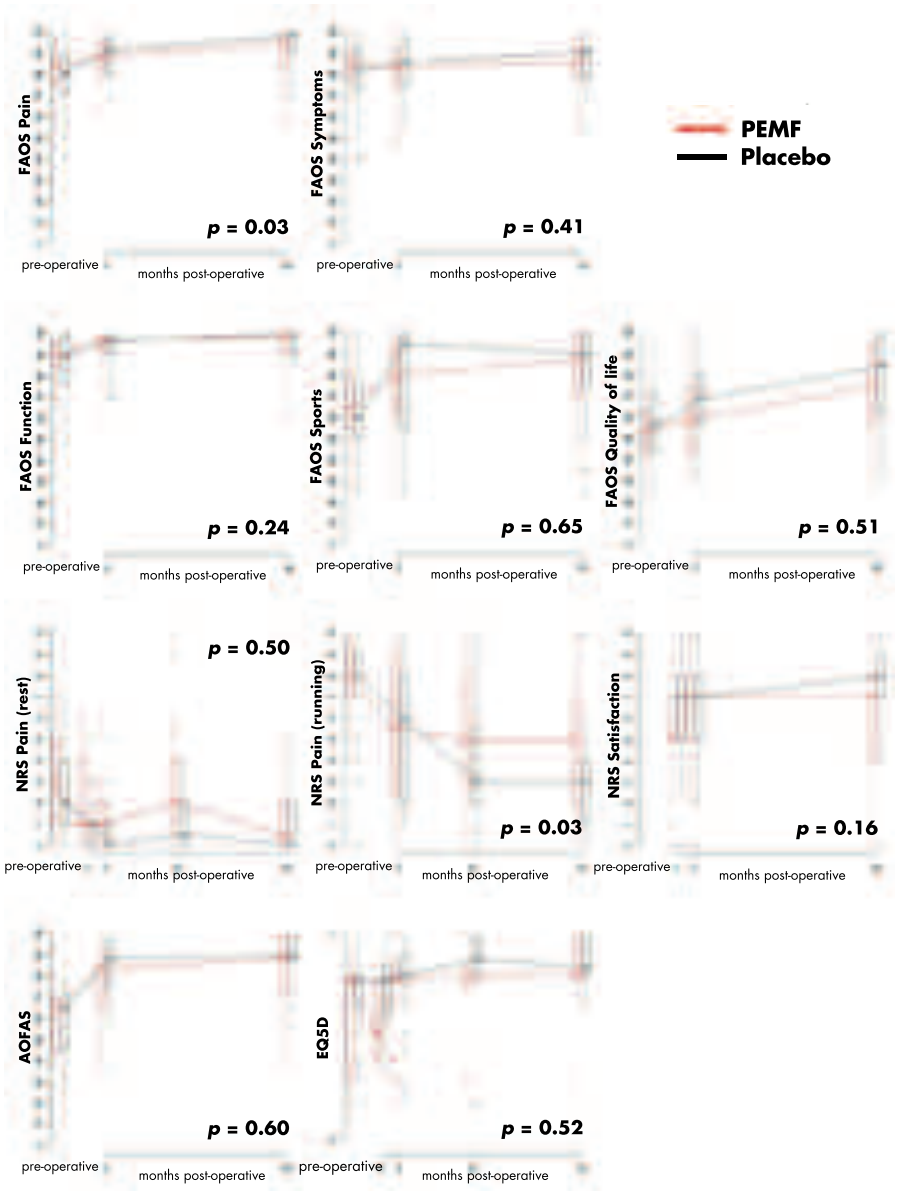

Figure 4: Linear mixed models showing secondary clinical outcome scores of the pulsed electromagnetic field (PEMF) and placebo groups. The boxes represent the interquartile range, and the lines denote the median. The error bars represent the minimum and maximum range. An adjusted significance level of the *p*-value of the comparison with the smallest *p*-value was set at 0.00625 (0.05/8), and the significance level of comparison with the largest *p*-value was set at 0.05 (0.05/1). AOFAS, American Orthopaedic Foot and Ankle Society ankle hindfoot score; EQ-5D, EuroQol; FAOS, Foot and Ankle Outcome Score; NRS, numeric rating scale.

Table II: Clinical outcome measures at baseline and at one year follow-up[a].

	PEMF group, *n* = 34			**Placebo group, *n* = 30**		
	Pre-op	**Post-op (1Y)**	***p*-value[b]**	**Pre-op**	**Post-op (1Y)**	***p*-value[b]**
AOFAS, mean (SD)	59.8 (13.3)	81.7 (19.6)	<0.001	60.7 (14.9)	89.2 (11.4)	<0.001
FAOS						
- Symptoms, median (IQR)	86 (79–89)	86 (78–96)	0.636	82 (71–92)	91 (78–94)	0.008
- Pain, median (IQR)	85 (76–91)	94 (83–98)	0.002	81 (69–89)	99 (90–100)	<0.001
- ADL, median (IQR)	90 (84–96)	99 (90–100)	0.003	90 (77–100)	100 (98–100)	<0.001
- Sports, mean (SD)	67.6 (18.5)	82.2 (20.0)	0.002	61.3 (18.3)	84.2 (20.3)	<0.001
- QOL, mean (SD)	54.3 (14.2)	71.1 (22.2)	<0.001	58.3 (19.6)	79.8 (20.3)	<0.001
EQ-5D, median (IQR)	0.78 (0.30–0.81)	0.81 (0.76–1.00)	0.003	0.78 (0.65–0.81)	0.84 (0.80–1.00)	<0.001
NRS pain (rest), mean (SD)	2.9 (2.3)	1.4 (2.2)	0.002	2.5 (2.0)	0.7 (1.2)	<0.001
NRS pain (running), mean (SD)	7.8 (1.7)	4.8 (3.3)	<0.001	7.8 (2.4)	2.9 (2.3)	<0.001
NRS satisfaction, mean (SD)		5.7 (3.5)			7.5 (2.5)	

[a]Values are presented as mean ± SD or median (interquartile range). ADL, activities of daily living; AOFAS, American Orthopaedic Foot and Ankle Society ankle-hindfoot score; EQ-5D, EuroQol; FAOS, Foot and Ankle Outcome Score; NRS, numeric rating scale; QOL, quality of life; PEMF, pulsed electromagnetic field; Preop, preoperative; Postop, postoperative.

[b]Wilcoxon signed-rank test/paired t test. Adjusted significance level of the *p*-value of the comparison with the smallest *p*-value was set at 0.00625 (0.05/8), and the significance level of comparison with the largest *p*-value was set at 0.05 (0.05/1).

at the time of sport resumption was found in both groups. In the PEMF group, 23 of 27 patients returned to the same sport and in the placebo group, 20 of 24 patients.

The median time to work resumption was 6.5 weeks (IQR, 2–9) in the PEMF group and 5 weeks (IQR, 2–8) in the placebo group ($p=0.26$). No statistically significant between-group differences over time were observed with regard to the AOFAS ($p=0.60$), FAOS (p range, 0.03–0.65), EQ-5D ($p=0.52$), and NRS pain (rest, $p=0.50$; running, $p=0.03$) and satisfaction ($p=0.16$) (Fig. 4).

As also can be observed from the graphs in Fig. 4, all secondary outcome measures within both treatment groups improved from baseline to 12 months, with the exception of the FAOS symptoms subscale in the PEMF group. This time effect is illustrated in Table II.

Radiologic Results

In the PEMF group, 33 of 36 patients completed the preoperative and 1-year postoperative CT scans. Two patients were lost to follow-up, and 1 patient did not undergo the final CT scan because of pregnancy. In the placebo group, 29 of 32 patients completed the preoperative and 1-year postoperative CT scans. Two patients were lost to follow-up, and 1 patient underwent a HemiCAP procedure during follow-up because of persisted deep ankle pain after a new ankle distortion[244]. Intraobserver reliability of CT scan measurements was good (level of the subchondral bone plate, ICC = 0.92; bone volume filling, ICC = 0.91). No significant differences were observed between the groups (level of the subchondral bone plate, $p=0.24$; bone volume filling, $p=0.33$) (Table III, Fig. 5).

Table III: CT findings after debridement and microfracture of osteochondral talar defects[a]

	PEMF group	Placebo group	*p*-value[b]
Level of subchondral bone plate	33	29	0.24
- Depressed	26 (79)	19 (66)	
- Flush	7 (21)	10 (34)	
- Proud	0 (0)	0 (0)	
Bone volume fill	30	27	0.33
- Good (67%–100%)	11 (37)	14 (52)	
- Moderate (34%–66%)	12 (40)	6 (22)	
- Poor (0%–33%)	7 (23)	7 (26)	

[a]Data are presented as No. of cases (%).

[b]Chi-square test. Adjusted significance level of the p-value of the comparison with the smallest p-value was set at 0.00625 (0.05/8), and the significance level of comparison with the largest p-value was set at 0.05 (0.05/1).

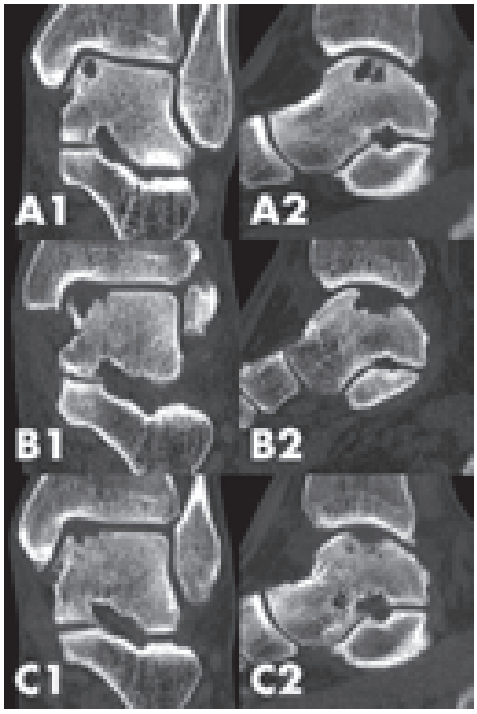

Figure 5: Preoperative (**A1**) coronal and (**A2**) sagittal computed tomography (CT) scans of a left ankle with a cystic osteochondral defect on the medial talar dome. Successful debridement and microfracture of the osteochondral defect are shown on the 2-week postoperative (**B1**) coronal and (**B2**) sagittal CT scans. (**C1**, **C2**) At 1-year follow-up, the subchondral bone plate is depressed; in comparison with the 2-week postoperative CT scans, a good bone volume fill (67%–100%) can be observed.

Complications

No serious adverse events occurred during the trial. Adverse events were seen in 7 patients. In the PEMF group, 2 patients reported temporary paraesthesia of the dorsum of the foot, and 2 had prolonged wound leakage during the first week after surgery. In the placebo group, 1 patient reported nausea, 1 had a delayed healing of the wound, and 1 reported postoperative paraesthesia of the dorsum of the foot and persistent deep ankle pain after a new distortion at 4-month follow-up. This patient was treated with a HemiCAP[244]. The number of adverse events did not differ significantly between groups ($p=0.81$).

DISCUSSION

This is the first double-blind, randomized, placebo-controlled trial to investigate the effect of PEMFs after debridement and microfracture of an OCD of the talus. In the present study, no differences were found in the percentage of sport resumption and time to sport resumption. Furthermore, there were no significant between-group differences with regard to the secondary functional outcomes or CT observations.

Our findings are in contrast with the scarce literature. Cadossi et al.[38] found, in a randomized controlled trial, a significant AOFAS score improvement >10 points in the PEMF group after bone marrow derived cell transplantation for OCDs of the talus at 1-year follow-up. However, the difference between the preoperative and 1-year postoperative AFOAS was 32 points in the control group and 40 points in the PEMF group. It is questionable if an 8 point difference on the AOFAS scale is clinically relevant. Furthermore, no placebo devices were used in the control group; therefore, a possible effect of the placebo intervention was not taken into account. In a randomized controlled pilot trial, Zorzi et al.[277] reported a reduction in the use of nonsteroidal anti-inflammatory drugs and clinical improvement with PEMF treatment after arthroscopic chondroabrasion and/or perforation and/or radiofrequency of the knee. Although the pilot study showed a clinical improvement, a cautious interpretation is needed because of the small groups (PEMF, n = 19; placebo, n = 12) and no power analysis.

Regarding the treatment of OCDs of the talus, we consider bone regeneration more important than cartilage regeneration. Cartilage is not innervated; the patient's pain probably arises from the bony lesion[250]. Furthermore, an advanced and irregular subchondral bone plate is associated with degradation of repaired articular surface[177]. Our study did not show any effect of PEMFs on the level of the subchondral bone plate repair. In both groups, more than two-thirds of the subchondral bone plates were depressed. This finding may explain why progression of ankle osteoarthritis is seen in 33% to 34% after arthroscopic debridement and bone marrow stimulation of an OCD of the talus at long-term follow-up[67, 239]. In the present study, no differences were found in the amount of bone volume filling between the PEMF and placebo groups on 2-dimensional CT analysis. Likewise, Hannemann et al.[91] studied the addition of PEMFs in the nonoperative treatment of acute scaphoid fractures and concluded that PEMFs do not accelerate bone healing on CT. Furthermore, a meta-analysis of randomized controlled trials showed no differences in time to radiologic union between PEMF and placebo after surgical treatment in acute fractures[90].

Strengths of this study include the randomized, double-blind, placebo-controlled design; the high compliance in wearing the device; and the use of a broad set of validated outcome measures. Limitations include the lack of long-term follow-up and the loss to follow-up of 4 patients; however, we anticipated a follow-up loss of 8 patients

in our sample size calculation. Another limitation is the 2-dimensional CT analysis of a 3-dimensional structure. Furthermore, the follow-up of the defects with CT scans may lead to higher radiation exposures, which is less accurate for cartilage evaluation in comparison with MRI; however, we were interested in the bone healing, which is better visible on CT.

In conclusion, applying PEMFs after arthroscopic debridement and microfracture of an OCD of the talus does not lead to earlier resumption of sports or to a higher percentage of patients who resume sports. Furthermore, PEMFs do not lead to functional and radiologic improvements up to 1-year follow-up.

CHAPTER 6

Computed tomography analysis of osteochondral defects of the talus after arthroscopic debridement and microfracture

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ABSTRACT

Purpose: The primary surgical treatment of osteochondral defects (OCDs) of the talus is arthroscopic debridement and microfracture. Healing of the subchondral bone is important because it affects cartilage repair and thus plays a role in pathogenesis of osteoarthritis. The purpose of this study was to evaluate the dimensional changes and bony healing of talar OCDs after arthroscopic debridement and microfracture.

Methods: Fifty-eight patients with a talar OCD were treated with arthroscopic debridement and microfracture. Computed tomography (CT) scans were obtained at baseline, 2 weeks postoperatively, and 1 year postoperatively. Three dimensional changes and bony healing were analyzed on CT scans. Additionally, clinical outcome was measured with the American Orthopaedic Foot and Ankle Society (AOFAS) ankle-hindfoot score and numeric rating scales (NRS) for pain.

Results: Average OCD size increased significantly ($p<0.001$) in all directions from 8.6 (SD 3.6) × 6.3 (SD 2.6) × 4.8 (SD 2.3) mm (anterior–posterior × medial–lateral × depth) preoperatively to 11.3 (SD 3.4) × 7.9 (SD 2.8) × 5.8 (SD 2.3) mm 2 weeks postoperatively. At 1-year follow-up, average defect size was 8.3 (SD 4.2) × 5.7 (SD 3.0) × 3.6 (SD 2.4) mm. Only average defect depth decreased significantly ($p<0.001$) from preoperative to 1 year postoperative. Fourteen of the 58 OCDs were well healed. No significant differences in the AOFAS and NRS-pain were found between the well and poorly healed OCDs.

Conclusion: Arthroscopic debridement and microfracture of a talar OCD leads to an increased defect size on the direct postoperative CT scan but restores at 1-year follow-up. Only fourteen of the 58 OCDs were filled up completely, but no differences were found between the clinical outcomes and defect healing at 1-year follow-up.

INTRODUCTION

An osteochondral defect (OCD) of the talus is a lesion of the cartilage and subchondral bone, mostly caused by a traumatic event. An OCD can either heal and become asymptomatic or progress to deep ankle pain[186, 248, 250].

Currently, arthroscopic debridement and microfracture is considered the primary treatment for symptomatic talar OCDs up to 15 mm in diameter[44, 46, 134, 248, 273]. With this technique, all unstable cartilage including the underlying necrotic bone is removed. Following this, small holes are punctured in the subchondral bone to promote revascularization and induce bone and fibrous tissue formation[250]. Any underlying cyst(s) are opened, followed by curettage and perforation to release the pressure, which is assumed to stop further progression of the cyst[48, 186, 250].

Recently, there has been an increasing awareness of the role that the subchondral bone plays in the pathogenic process and development of deep ankle pain in OCDs. It is a prognostic factor for the eventual clinical outcome[248]. It has been suggested that an irregular subchondral bone plate may negatively affect articular cartilage repair in OCDs[169, 177]. Furthermore, structural changes in subchondral bone play a role in the pathogenesis of osteoarthritis[79, 144]. At long-term follow-up, progression of ankle osteoarthritis is seen in 33–34% of patients following arthroscopic debridement and bone marrow stimulation of talar OCDs[67, 239]. Like in the knee, it was previously assumed that the bony defect would be filled primarily by bone, but this has never been investigated for the ankle[133, 159, 260, 276]. The question of this study therefore is: to what extent the defect is filled with bone after debridement and microfracture? The hypotheses are [1] the defect dimensions will reduce 1 year after debridement and microfracture and [2] the defect dimensions shortly after the surgery are increased by debridement and microfracture. The secondary purpose is to determine whether defect size and bony healing are determinants of clinical outcome.

MATERIALS AND METHODS

For this study, we used data from a randomized controlled trial investigating pulsed electromagnetic fields (PEMF) after arthroscopic debridement and microfracture of talar OCDs[189, 236].

Included were patients with a symptomatic talar OCD with a diameter smaller than 15 mm (in three dimensions), who were treated by arthroscopic debridement and microfracture at our centre. Both the PEMF treatment and placebo group were included, since no functional and radiological differences between the groups were found in the previous trial[189, 236]. Exclusion criteria were: age younger than 18 years, ankle

osteoarthritis grade II or III[253], concomitant OCD of the tibia, ankle fracture less than 6 months before treatment of the OCD, surgical treatment of the index ankle performed <1 year before treatment of the OCD, concomitant painful or disabling disease of the lower limb, rheumatoid arthritis, and pregnancy.

Operative technique

All arthroscopic procedures were performed using a standardized technique by one of the two experienced orthopedic surgeons (GMMJK and CNvD). Anteromedial and anterolateral portals were created with the ankle in full dorsiflexion after which a 4-mm arthroscope was introduced. The OCD was identified with a probe by moving the ankle in full plantar flexion. After identification, all unstable bone and cartilage were removed with a curette and bone-cutter shaver. Any underlying cyst(s) were opened, followed by curettage and perforation with a microfracture awl, with intervals of approximately 3 mm. At the end of the procedure, a pressure bandage was applied.

Radiology

Computed tomography (CT) scans of the affected ankle were obtained preoperatively (mean 29 ± 7 weeks before surgery), at 2 weeks (mean 2 ± 1 weeks), and 1 year postoperatively (mean 53 ± 7 weeks). 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[189, 236]. 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[159, 260, 276].

The OCDs were graded on the preoperative CT scans according to the modified Berndt and Harty[24] classification[210].

Three-dimensional changes in the OCDs were evaluated by measuring the largest diameter (mm) in the anterior–posterior direction, medial–lateral direction and depth on each scan. The anterior–posterior size was measured at the level of the subchondral bone plate on the sagittal CT reconstruction. The depth was determined by drawing a circle through the subchondral bone plate of the talus on the sagittal CT reconstruction. A perpendicular line form the circle to the deepest point of the defect was measured as the depth. The medial lateral size was measured on the coronal CT reconstruction from the most central point of the defect to the medial/lateral facet.

Different radiological aspects were assessed on the postoperative CT scans. The precision of addressing the entire OCD was evaluated on the two weeks postoperative CT scan. Cystic OCDs were specifically evaluated by assessing whether the cyst was opened and whether the cyst wall was perforated. The cyst was defined as opened when the wall of the cyst was disrupted on the two weeks postoperative CT scan in comparison with the preoperative CT scan. Formation of new cysts was evaluated on the one year

postoperative CT scans. The presence of a new cyst was defined as a new radiolucent rounded area at final follow-up that was not visible on the two weeks postoperative CT scan. Healing of the subchondral bone was evaluated at final follow-up. Good healing was defined as complete osseous union or ossification, fair as incomplete osseous union or ossification but improvement compared with the preoperative findings, and poor as no changes between preoperative and postoperative[127]. All scans were analyzed by a single physician who was blinded to the clinical outcomes. Measurements of the defect size were taken twice on the two weeks postoperative CT scans with an interval of 1 month and in different order to assess the intra-observer reliability.

Clinical outcomes

Clinical outcomes were assessed with use of the American Orthopaedic Foot and Ankle Society (AOFAS) ankle hindfoot score and numeric rating scales (NRS) for pain preoperatively and 1 year postoperatively[104, 118]. The AOFAS is a 100-point score, with a subjective and an objective component, which devotes 40 points to pain, 50 points to function, and 10 points to alignment[104, 118]. The NRS is comprised of an 11-point scale, which represents the spectrum of no pain (0 points) to the worst pain imaginable (10 points)[72].

The local Medical Ethics Committee at the University of Amsterdam approved the study with reference number MEC 08/326. The study is registered in the Netherlands Trial Register (NTR1636). Written informed consent was obtained from all participants.

Statistical analysis

All analyses were performed in SPSS version 20.0 (Statistical Packages for Social Sciences Inc, Chicago, IL, USA). Categorical data are presented as frequencies. Continuous data are presented as mean with standard deviation (SD) or as median with interquartile range (IQR) depending on their distribution. Paired *t* test analyses were performed to determine the dimensional changes in the OCDs and clinical changes between the preoperative and postoperative CT scans. Pearson correlation test was used to analyze the correlation between the one year postoperative defect size and clinical outcome (AOFAS and NRS-pain). Independent *t* test was performed to analyze the differences in clinical outcome (AOFAS and NRS-pain) between a good and poorly healed subchondral bone and between defects with or without a cyst at final follow-up. A p-value <0.05 was considered statistically significant. To assess the intra-observer reliability of the defect size measurements, the intra-class correlation coefficient (ICC) was calculated. An ICC of 0.85 or higher indicates good reliability[54, 156].

RESULTS

A total of 58 patients were included between 2009 and 2014 (Table I). One patient did not undergo the final CT scan as she underwent a HemiCAP procedure during follow-up because of persisted deep ankle pain after a new ankle distortion[244].

Table I: Baseline characteristics of the patients (n = 58)

Age (yrs), mean (SD)	32 (10)
Gender, *n* (% male)	35 (60)
BMI, mean (SD)	26 (4)
Smoking, *n* (%)	11 (19)
Ankle trauma, *n* (%)	41 (71)
Ankle fracture, *n* (%)	4 (7)
OCD operation of included side, *n* (%)	13 (22)
Side, *n* (% right)	32 (55)
Location, *n* (%)	
- Medial	38 (66)
- Lateral	17 (29)
- Central	3 (5)
OCD classification, n (%)	
- Compression	19 (33)
- Partially fractured	0 (0)
- Completely undisplaced fracture	10 (17)
- Displaced fracture	2 (3)
- Cystic lesion	27 (47)

Radiology

Table II shows the defect size at baseline and follow-up. Two weeks after arthroscopic debridement and microfracture, the defect size increased significantly ($p < 0.001$) in all three dimensions. At 1-year follow-up, the defect size decreased significantly ($p < 0.001$) in all directions when compared to the two weeks postoperative defect size. No statistically significant differences in the anterior–posterior and medial–lateral directions were observed between the preoperative and one year postoperative CT scans. The depth decreased significantly ($p < 0.001$) from preoperative to 1 year postoperative (Figs. 1, 2). Intra-observer reliability of defect size measurements was good (ICC = 0.98).

Analysis of the precision of addressing the OCD revealed that 45 of 58 OCDs were treated adequately, two defects were not debrided, three defects were debrided partially, three cystic lesions were only opened at the roof, while the wall was not debrided (Fig. 3), and five cysts were not opened. The follow-up of postoperative cyst formation are

Table II: Three-dimensional defect size (mm) at baseline and after debridement and microfracture

	Preoperative	Two-week postoperative	One-year postoperative
Anterior–posterior, mean (SD)	8.6 (3.6)	11.3 (3.4)	8.3 (4.2)
Medial–lateral, mean (SD)	6.3 (2.6)	7.9 (2.8)	5.7 (3.0)
Depth, mean (SD)	4.8 (2.3)	5.8 (2.3)	3.6 (2.4)

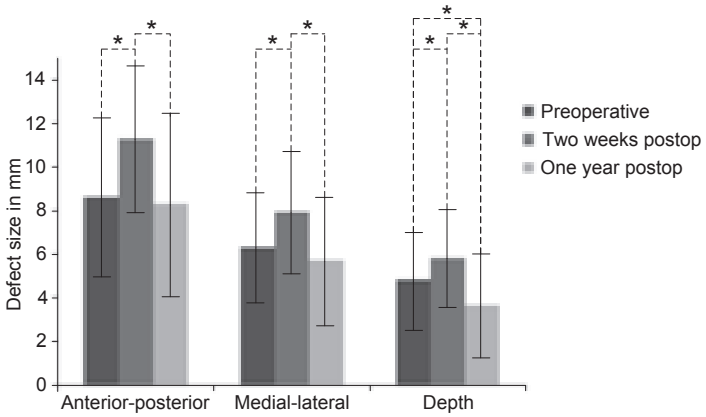

Figure 1: Mean defect size measured on the preoperative, two weeks postoperative, and one year postoperative CT scans. The *error bars* represent the standard deviation. Significant differences are indicated (*asterisk*).

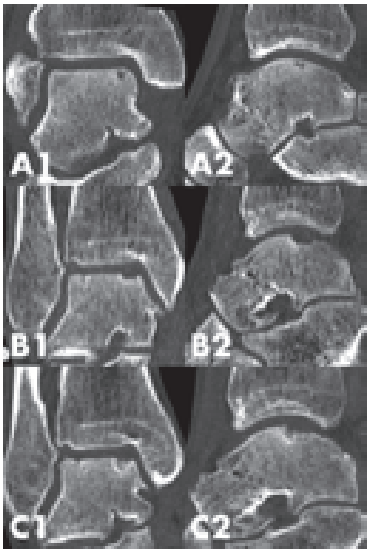

Figure 2A: Preoperative coronal (**A1**) and sagittal (**A2**) CT scans of right ankle show a cystic OCD of the medial talar dome. **B**: The two weeks postoperative coronal (**B1**) and sagittal (**B2**) CT scans show an increased defect size after technically successful debridement and microfracture. **C**: At 1-year follow-up, the defect size decreased and the level of subchondral bone plate was almost flush [coronal CT scan (**C1**); sagittal CT scan (**C2**)].

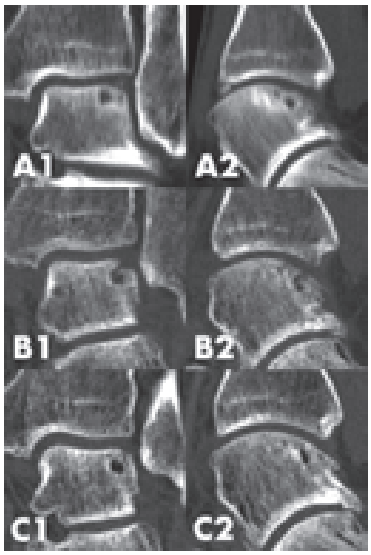

Figure 3A: Preoperative coronal (**A1**) and sagittal (**A2**) CT scans of a left ankle with a cystic OCD of the lateral talar dome. **B**: the two weeks postoperative coronal (**B1**) and sagittal (**B2**) CT scans show that the cystic OCD is opened but not debrided. **C**: At 1-year follow-up, the cyst is still visible [coronal CT scan (**C1**); sagittal CT scan (**C2**)].

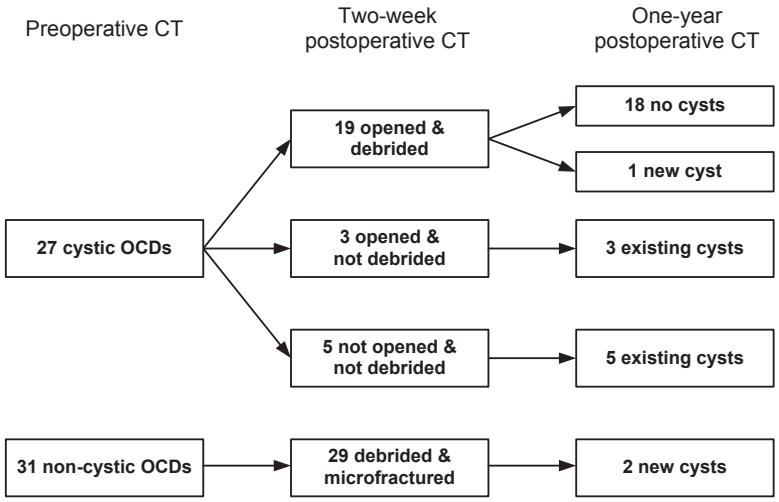

Figure 4: Follow-up of cyst formation after debridement and microfracture of OCDs of the talus. The two new cysts that developed from a non-cystic OCD were adequately treated during surgery.

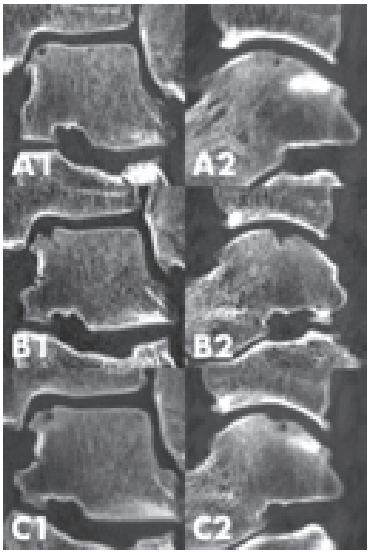

Figure 5A: Preoperative coronal (**A1**) and sagittal (**A2**) CT scans of a left ankle with a cystic OCD of the medial talar dome. **B**: The two weeks postoperative coronal (**B1**) and sagittal (**B2**) CT scans show that the cystic OCD is opened and a microfracture hole is visible. **C**: At 1-year follow-up, a new cyst has developed, possibly out of a microfracture hole [coronal CT scan (**C1**); sagittal CT scan (**C2**)].

presented in Fig. 4 and 5. The mean cyst size at final follow-up was 4.3 mm (SD 1.0) in the anterior–posterior direction, 4.1 mm (SD 0.7) in the medial–lateral direction, and 4.9 mm (SD 1.2) in depth.

Healing of the subchondral bone was good in 14 defects (25%), fair in 22 defects (38%), and poor in 21 defects (37%).

Clinical outcome

The preoperative mean AOFAS score improved from 58.8 (SD 14.2) to 84.5 (SD 17.3) at 1-year follow-up ($p<0.001$). The mean NRS-pain in rest improved from 2.8 (SD 2.2) preoperatively to 1.1 (SD 1.8) at 1-year follow up ($p<0.001$). The mean NRS-pain when running improved from 8.0 (SD 1.9) preoperatively to 3.9 (SD 2.9) at 1-year follow-up ($p<0.001$).

Association between CT and clinical outcomes

The one year postoperative defect size did not correlate with the AOFAS and NRS-pain.

OCDs with a good subchondral bone healing at final follow-up had a mean AOFAS score of 85.6 (SD 17), a mean NRS-rest of 1.4 (SD 2.6), and a mean NRS-running of 4.5 (SD 3.6). OCDs with a poor healing at final follow-up had a mean AOFAS score of 84.0 (SD 19.4), a mean NRS-rest of 1.3 (SD 1.7), and a mean NRS-running of 3.7 (SD 3.1). No statistically significant differences in the AOFAS and NRS-pain were found between a good and poorly healed subchondral bone.

Defects with the presence of a cyst at final follow-up had a mean AOFAS score of 90.5 (SD 7.0), a mean NRS-rest of 1.3 (SD 1.7), and a mean NRS-running of 2.9 (SD 2.2). Defects without the presence of a cyst at final follow-up had a mean AOFAS score of 83.9 (SD 18.3), a mean NRS-rest of 1.1 (SD 1.9), and a mean NRS-running of 4.1 (SD 3.0). No statistically significant differences in the AOFAS and NRS-pain were found between defects with or without a cyst at final follow-up.

DISCUSSION

The most important findings of the present study are that 2 weeks after arthroscopic debridement and microfracture, the defect size increased significantly in all three dimensions. At 1-year follow-up, the defect size decreased significantly in comparison with the two weeks postoperative CT scans. In comparison with the preoperative defect size, only the depth of the defect decreased significantly at 1-year follow-up. Fourteen of the 58 OCDs were well healed. However, no differences were found between the clinical outcomes and defect healing or defect size.

In 1988, Zinman et al.[276] found 17 of 20 OCDs healed on CT scans after debridement and bone marrow stimulation or fixation of the fragment. Unfortunately, the definition of a healed OCD was not described in that study. Using plain radiographs, Kumai et al.[127] found a decreased defect size in 15 of 18 patients after debridement and microfracture at a mean follow-up of 4.6 years. However, healing of an OCD on plain radiographs is difficult to interpret because of over-projection of bone. Magnetic resonance imaging (MRI) is often used to quantify cartilage repair after debridement and microfracture[21, 197, 211, 259], but is less accurate to visualize bone. In this study, we focused on bone repair of an OCD, because the subchondral bone has an essential role in cartilage repair and in the pathogenesis of osteoarthritis[79, 144, 169, 177].

In the present study, cystic OCDs were found in 27 out of 58 patients preoperatively. With the development of diagnostic methods MRI and CT, cystic lesions of the talus have been found to be present in 46–77% of the chronic OCDs[67,214]. When OCDs are treated nonoperatively, cyst development is seen in 12–14% during follow-up[61, 119]. These new cysts have been correlated with an increased pain sensation[119]. The possible association between pain and new cyst formation might be caused by repetitive high fluid pressure during walking, which results in stimulation of the highly innervated subchondral bone underneath the cartilage defect[119, 142, 248, 250]. In case the fissure through the subchondral bone plate is healed, it is assumed that no pressure builds up in the cyst, and the cyst will not grow[48, 186, 250]. In our study, 8 of the 11 cysts did not change in size between the two weeks and one year postoperative CT scans. This might explain

why in our study, no significant differences in pain were found between defects with or without a cyst at final follow-up.

This is the first study that investigated the radiological changes after arthroscopic debridement and microfracture of talar OCDs at different time points. Strengths of this study include the complete radiological and clinical follow-up. Limitations include the two-dimensional analysis of a three-dimensional structure and the lack of long-term follow-up. A longer follow-up might show us the correlation between the degree of defect healing and progression of ankle osteoarthritis. Furthermore, MRI scans may give additional information on the quality of cartilage repair in comparison with CT scans. Little is known about the bony healing of OCDs after arthroscopic debridement and microfracture. This study is useful as it suggests that no differences were found between the clinical outcomes and the degree of defect healing at 1-year follow-up.

CONCLUSION

Arthroscopic debridement and microfracture of a talar OCD leads to an increased defect size on the direct postoperative CT scan but restores at 1-year follow-up. Only fourteen of the 58 OCDs were well healed, but no differences were found between the clinical outcomes and defect healing at 1-year follow-up.

CHAPTER 7

Lift, drill, fill and fix (LDFF): a new arthroscopic treatment for talar osteochondral defects

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ABSTRACT

Purpose: The purpose of this study was to describe the short-term clinical outcome of a new arthroscopic fixation technique for primary osteochondral talar defects: lift, drill, fill and fix (LDFF).

Methods: Seven patients underwent an arthroscopic LDFF surgery for osteochondral talar defects; the mean follow-up was 12 months (SD 0.6). Pre- and postoperative clinical assessment included the American Orthopaedic Foot and Ankle Society (AOFAS) ankle-hindfoot score and the numeric rating scales (NRS) of pain at rest and during walking. Remodelling and bone ingrowth after LDFF were analyzed on weight-bearing radiographs during follow-up.

Results: In all patients, LDFF led to an improvement of the AOFAS and NRS of pain. The AOFAS significantly improved from 63 to 99 ($p < 0.001$). The NRS of pain at rest significantly improved from 2.9 to 0.1 ($p = 0.004$), and pain during walking significantly improved from 7.6 to 0.1 ($p < 0.001$). On the final radiographs, five of seven patients showed remodelling and bone ingrowth after LDFF.

Conclusions: The LDFF of an osteochondral talar defect appears to be a promising arthroscopic treatment option for primary talar osteochondral defects. Although the clinical and radiological results of 1-year follow-up are encouraging, more patients and longer follow-up are needed to draw any firm conclusions and determine whether the results stand the test of time.

INTRODUCTION

An osteochondral defect (OCD) of the talus is a lesion of the cartilage, and subchondral bone most often caused by a single or multiple traumatic events. An OCD can either heal, and therefore remain asymptomatic, or progress to present with deep ankle pain on weight-bearing and formation of subchondral bone cysts[186, 250].

Surgical treatment strategies for primary OCDs of the ankle have substantially increased over the last decade[59, 67, 76, 161, 273]. Arthroscopic debridement and bone marrow stimulation is still considered the primary treatment in symptomatic lesions up to 1.5 cm in diameter[44, 46, 86, 273]. With this technique, all unstable cartilage, including the underlying necrotic bone, is removed and small holes are drilled or punctured in the subchondral bone to promote revascularization. However, Qiu et al.[177] studied OCDs in femoral condyles of rabbits and found that the presence of an advanced and irregular subchondral bone plate was associated with degradation of repaired articular surface.

Internal fixation of an osteochondral talar defect is a good alternative technique[128, 187, 207]. The advantage of this treatment option is to restore the natural congruency of the subchondral bone and to preserve hyaline cartilage. However, until now, a medial or lateral arthrotomy often combined with a malleolar osteotomy had to be performed to allow proper visibility and working access. In this study, the short-term clinical outcome of a new arthroscopic fixation technique for primary osteochondral talar defects is described: lift, drill, fill and fix (LDFF).

MATERIALS AND METHODS

This study was approved by the local Medical Ethics Committee at the University of Amsterdam and performed in accordance with the current ethical standards (Declaration of Helsinki).

The indication for an arthroscopic LDFF technique was a primary, large OCD of the talar dome (anterior–posterior or medial–lateral diameter >10 mm on computed tomography) in patients with persistent complaints of recognizable deep ankle pain for more than 1 year. Contraindications were defined as loose chondral lesions, ankle osteoarthritis grade II or grade III[251], concomitant ankle pathology (tibial OCD, instability, fracture <6 months old, tendonitis), advanced osteoporosis, infectious pathology or malignancy.

Preoperative planning

The diagnosis was confirmed by weight-bearing plain radiographs (mortise and lateral) and/or computed tomography of the affected ankle. Computed tomography was made

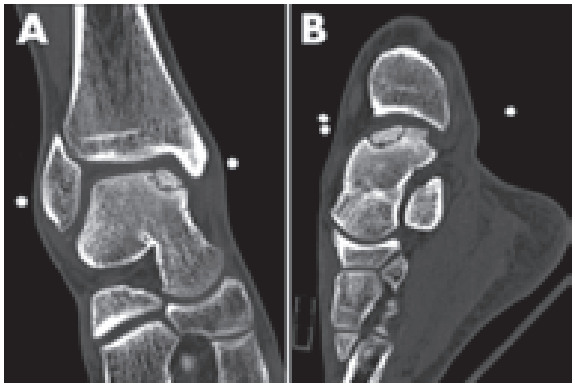

Figure 1: Preoperative coronal (**A**) and sagittal (**B**) computed tomography of a medial osteochondral talar defect of a right ankle in plantar flexion.

with the ankle in maximum plantar flexion in order to be able to both determine the size, location, shape, as well as the arthroscopic accessibility of the OCD[241] (Fig. 1). The preoperative shape was classified according to the modified Berndt and Harty's staging system[24]. On the original scale, defects are divided into four stages (I–IV) according to the amount of detachment and displacement of the OCD. The addition of a stage V by Scranton and McDermott[210] was used to classify cystic defects. The scanning protocol involved 'ultrahigh-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.

Surgical technique

All arthroscopic LDFF surgeries for osteochondral talar defects were carried out as an outpatient procedure under general or spinal anesthesia. All patients were operated by the senior author (GK). Patients were placed in a supine position with slight elevation of the ipsilateral buttock. A support was placed at the contralateral side of the pelvis to prevent the patient from moving when the table was turned sideways for straight ankle positioning. The heel of the affected foot rested on the very end of the operating table. This positioning enabled the surgeon to fully dorsiflex the ankle by leaning against the foot sole and to use the table as a lever when maximal plantar flexion was needed. A non-invasive soft-tissue distraction device was used on indication (Fig. 2).

The joint was assessed by an anteromedial and an anterolateral portal[252]. The anteromedial portal was made first with the ankle in slight dorsiflexion. A sharp incision through the skin only was made just medially to the anterior tibial tendon. Subsequently, the subcutaneous layer was bluntly dissected with a hemostat at the level of the ankle joint. A 4-mm 30°-angled arthroscope was introduced with the ankle in full dorsiflexion. In this ankle position, the talar cartilage is covered by the distal tibia and is therefore

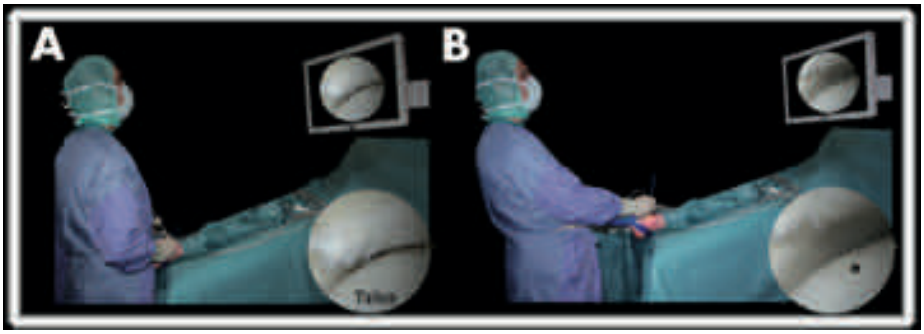

Figure 2A: Arthroscope is in the anteromedial portal, with the ankle in neutral position. In this position, the OCD is not visible. **B**: By brining the ankle in plantar flexion and with the use of a non-invasive soft-tissue distraction device, the OCD is visible.

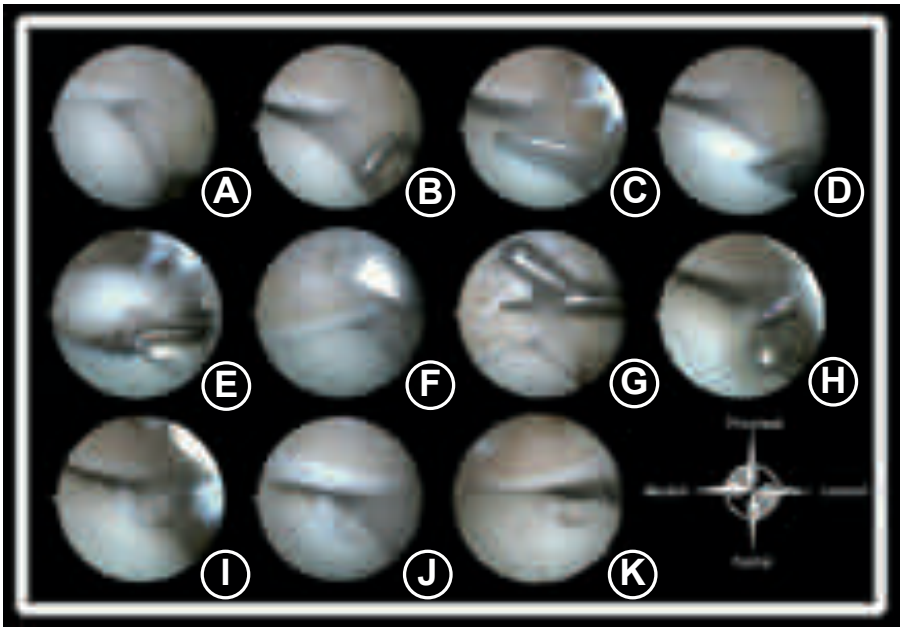

Figure 3: Arthroscopic images of a left talus with a medial osteochondral defect that is treated by LDFF. **A**: The arthroscope is in the anterolateral portal, with the ankle in neutral position. **B**: By brining the ankle in plantar flexion, the OCD can be seen. **C**: The exact location of the defect is identified by palpating the cartilage with a probe. **D**: An osteochondral flap is created by a beaver knife. **E**: With a chisel, the osteochondral flap is lifted up. **F**: Attached bone of the osteochondral flap is drilled to promote revascularization. **G**: The osteosclerotic area of the bed is debrided with a curette. **H**: Spongiosa is harvested from the distal tibia with a chisel. **I**: With a grasp, the spongiosa is transported to the defect. **J**: A drill hole is made over a guide wire. **K**: A solvable non-cannulated Bio-Compression screw is placed slightly recessed relative to the surrounding surface.

protected for iatrogenic damage on instrument insertion. Under direct arthroscopic vision, the location of the anterolateral portal was determined. A spinal needle was introduced just lateral to the peroneus tertius tendon. A vertical incision through the skin only was made with special attention to preserve the superficial peroneal nerve. The subcutaneous layers were bluntly dissected with a hemostat, and the desired instrument could be introduced.

The contour of the anterior tibia was identified, and the distal tibia rim removed with a shaver to facilitate better access to the ankle joint (Fig. 3A, B). The arthroscopic portals were interchangeably used to allow optimal vision. With a probe, the location of the OCD was identified and a beaver knife was used to allow the making of a sharp osteochondral flap (Fig. 3C, D). The posterior side of the flap was left intact and was used as a lever, allowing lifting from anteriorly with the use of a chisel (lift) (Fig. 3E). The attached bone of the osteochondral flap and the osteosclerotic area of the bed were debrided and drilled to promote revascularization (drill) (Fig. 3F, G). If there was a subchondral cyst, its contents were curetted and the circumference of its sclerotic wall punctured. After debridement and drilling, the defect was filled with cancellous bone of the distal tibial metaphysis. Cancellous bone was harvested with a chisel by creating longitudinal particles that were transported into the defect with a grasp (fill) (Fig. 3H, I). Finally, the osteochondral flap was correctly aligned and fixed with a Bio-Compression screw(s) (Arthrex Inc., Naples, USA) or with multiple chondral darts (Arthrex Inc., Naples, USA) (fix) (Fig. 3J, K). At the end of the procedure, the skin incisions were sutured with 3.0 Ethilon and a short-leg cast was applied at the operation theatre.

Postoperative management

A short-leg, non-weight-bearing cast was applied for 4 weeks postoperatively. 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.

The patients were assessed preoperatively and at 2, 8 weeks, 3, 6 months and 1 year postoperatively. The patient outcome was evaluated pre- and postoperatively with the American Orthopaedic Foot and Ankle Society (AOFAS) ankle-hindfoot score[118] and the numeric rating scales (NRS) of pain at rest and during walking[199]. The AOFAS is a 100-point scale, which devotes 40 points to pain, 50 points to function and 10 points to alignment. It is frequently used in the assessment of foot and ankle therapy, and the subjective component has been validated[104]. The NRS of pain consists of an 11-point scale, which represents the whole spectrum of no pain (0 points) up to the worst pain imaginable (10 points)[199]. Routine weight-bearing radiographs (anteroposterior mortise

and lateral views) were obtained at all follow-up visits from 8 weeks postoperatively. The radiographs were reviewed for the evaluation of remodelling and bone ingrowth of the fixated OCD.

Statistical analysis

All statistics were performed with SPSS version 20.0 (SPSS Inc., Chicago, IL, USA). The paired *t* test was used for comparison of the normal distribution of pre and postoperative means. The comparisons with $p < 0.05$ were considered to be statistically significant.

RESULTS

The study group consisted of 6 males and 1 female, with median age of 17 years (range, 14 to 58 years) at surgery. The mean operation time was 61 min (SD 12.7). The mean follow-up was 12 months (SD 0.6).

Clinical outcome

In all patients, LDFF led to an improvement of the AOFAS and NRS of pain. The AOFAS significantly improved from 63 ± 9.7 to 99 ± 1.6 ($p < 0.001$) at latest follow-up (Fig. 4A). The improvement in the AOFAS was mainly due to pain reduction. The NRS of pain at rest significantly improved from 2.9 ± 1.9 to 0.1 ± 0.4 ($p = 0.004$), and pain during walking significantly improved from 7.6 ± 0.5 to 0.1 ± 0.4 ($p < 0.001$) at latest follow-up (Fig. 4B). At the final follow-up, all seven patients were satisfied and indicated that they would undergo the procedure again.

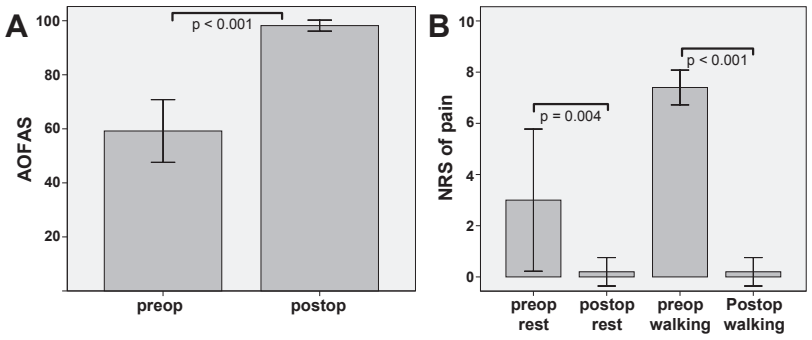

Figure 4A: Graph showing the mean American Orthopaedic Foot and Ankle Society (AOFAS) ankle-hindfoot score pre- and postoperatively. The *error bars* denote the 95% confidence intervals. **B**: Graph showing the mean numeric rating scale (NRS) of pain at rest and during walking pre- and postoperatively. The *error bars* denote the 95% confidence intervals.

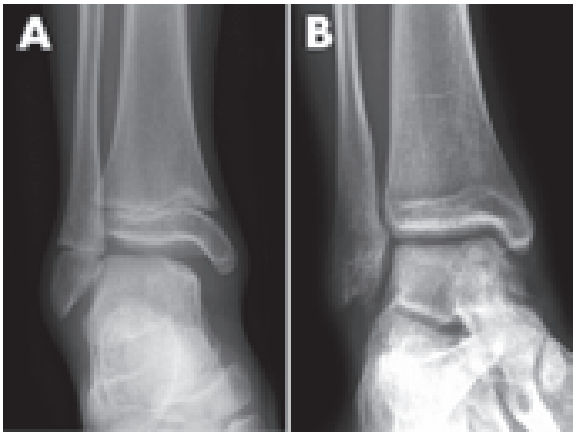

Figure 5A: Preoperative anteroposterior radiograph of a medial osteochondral talar defect of a right ankle. **B**: Postoperative anteroposterior radiograph of the same ankle after LDFF at 12-month follow-up.

Imaging

The mean preoperative size of the defects was 15.7 mm (SD 3.0) in the anteroposterior direction, 9.6 mm (SD 3.2) in the mediolateral direction and 6.7 mm (SD 1.4) in the craniocaudal direction. Six defects were located on the medial talar dome, and 1 defect was located on the lateral talar dome. Five defects were classified as stage III, and 2 as stage V lesions[210]. On the final radiographs, five of seven defects showed remodelling and bone ingrowth after LDFF (Fig. 5). Remodelling and bone ingrowth was seen in stage III lesions.

DISCUSSION

The most important finding of the present study was the excellent short-term clinical outcome of a new arthroscopic fixation treatment (LDFF) for primary talar OCDs. Internal fixation of an osteochondral talar defect shows good results in the literature[128, 187, 207]. Reilingh et al.[187] reported a good clinical outcome of 78% and a median AOFAS of 95 after screw fixation in children. Kumai et al.[128] reported a good clinical outcome of 89% after fixation using bone pegs. However, in both studies, arthrotomies with or without a malleolar osteotomy were performed to fixate the OCDs. In this manuscript, a new arthroscopic fixation technique of an osteochondral talar defect was described. The presented preliminary results of LDFF show that, at least in the short term, patients benefit from the procedure. This was evidenced by the statistically significant improvement in the AOFAS and the NRS of pain at rest and during walking.

Currently, arthroscopic debridement and bone marrow stimulation is considered the primary treatment in osteochondral talar defects up to 1.5 cm in diameter with a good clinical outcome of 85%[46, 273], lasting over the years to have a 76% satisfactory outcome at the long-term[239]. However, after debridement and bone marrow stimulation, the subchondral plate will be irregular, which is associated with degradation of repaired articular surface[177]. Furthermore, second-look arthroscopy after 12 months revealed that 40% of the defects were incompletely healed[133]. In contrast to native articular hyaline cartilage, bone marrow stimulation induces the formation of fibrocartilaginous tissue, which has inherently different biological and mechanical properties that are likely to degenerate over time[71]. Progression of ankle osteoarthritis is seen in 33–34% after arthroscopic debridement and bone marrow stimulation of an osteochondral talar defect at long-term follow-up[67, 239]. Other alternative treatment methods for primary OCDs are osteochondral autograft transfer system, autologous chondrocyte implantation and autogenous bone grafting[59, 161, 273]. These treatments can provide satisfactory clinical results but disadvantages include rates of donor site morbidity of up to 50%, talar surface mismatching, two-stage surgery and limited availability of graft material[17, 64, 202, 235].

If fixation of an osteochondral talar defect is possible, this should be performed. The theoretical advantages of fixation are restoration of the subchondral bone plate, and to preserve hyaline cartilage. Furthermore, after failed LDFF treatment, debridement and bone marrow stimulation is still a good option. Because of the new LDFF technique that is performed arthroscopically, a lower complication rate and a faster rehabilitation is expected as compared to open fixation of an OCD. The arthroscopic visualization of the OCD is an important part of the arthroscopic LDFF technique, since adequate fixation of the osteochondral flap depends on the accessibility and quality of vision. Computed tomography with the ankle in maximal plantar flexion can be advised to allow adequate preoperative planning[241]. Fixation of the osteochondral flap with Bio-Compression screw(s) (Arthrex Inc., Naples, USA) or chondral darts (Arthrex Inc., Naples, USA) should be performed perpendicular to the articular surface and slightly recessed relative to the surrounding surface to promote bone ingrowth. However, in this study, the cystic lesions (n = 2) did not show remodelling and bone ingrowth after LDFF. Less compression ability because of the thin bony fragment might be the cause of this observation. Furthermore, fluid pressure into a microfractured subchondral bone is the etiology of a cystic OCD[186, 250]. In both cystic lesions, the wall was opened and debrided to release the pressure. However, the microfractured subchondral bone was not restored and therefore new cyst formation is possible.

Strengths of this study include the prospective methodology and completeness of follow-up. Limitations are the small series, the absence of a control group, and the short-term follow-up. Furthermore, bone integration was assessed by plain radiographs during follow-up, while cartilage repair and cartilage integration was not evaluated. For

the near future, we will continue to follow-up our patients prospectively to see whether the results stand in a larger number of patients as well as over the long term. Little is reported about fixation of an OCD of the talus. This study is useful as it suggests, at least in the short-term, that arthroscopic fixation (LDFF) of a primary talar OCD is a good surgical option.

CONCLUSION

The LDFF of an osteochondral talar defect appears to be a promising arthroscopic treatment option for primary talar OCDs. Although the clinical and radiological results of 1-year follow-up are encouraging, more patients and longer follow-up are needed to draw any firm conclusions and determine whether the results stand the test of time.

CHAPTER 8

Treatment of osteochondral defects of the talus in children

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ABSTRACT

Purpose: Osteochondral talar defects are infrequent in children, and little is known about the treatment and clinical outcome of these defects. The purpose of this study was to evaluate the clinical and radiographic outcomes of conservative and primary surgically treated osteochondral talar defects in skeletally immature children.

Methods: Thirty-six (97%) of 37 eligible patients with a symptomatic primary osteochondral talar defect were evaluated after a median follow-up of 4 years (range 1–12 years). Clinical assessment included the Berndt and Harty outcome question, Ogilvie-Harris score, Visual Analog Scale pain score (at rest, during walking and during running), the American Orthopaedic Foot and Ankle Society (AOFAS) ankle-hindfoot score, and the SF-36. Weight-bearing radiographs were compared with preoperative radiographs with the use of an ankle osteoarthritis classification system.

Results: Ninety-two per cent of the initially conservatively treated children [mean age 13 years (SD 2)] were eventually scheduled to undergo surgery. After fixation of the fragment, seven cases (78%) reported a good Berndt and Harty outcome, and two cases (22%) a fair outcome; the median AOFAS score was 95.0 (range 77–100). After debridement and bone marrow stimulation, 13 cases (62%) reported a good Berndt and Harty outcome, three cases (14%) a fair outcome, and five cases (24%) a poor outcome; the median AOFAS score was 95.0 (range 45–100). No signs of degenerative changes were seen in both groups at follow-up.

Conclusions: Fixation and debridement and bone marrow stimulation of an osteochondral talar defect are both good surgical options after failed conservative treatment.

INTRODUCTION

An osteochondral defect (OCD) of the talus is a lesion involving articular cartilage and subchondral bone. Several descriptive terms exist for this type of lesion, including osteochondritis dissecans, osteochondral fracture, transchondral fracture, osteochondral lesion, and flake fracture. OCDs differ in severity depending on the amount of separation and displacement of the fragment. Berndt and Harty[24] developed the classification of OCDs that is currently most frequently used.

Treatment strategies for primary OCDs of the ankle have substantially increased over the last decade[273]. Conservative treatment is the first step in the treatment of symptomatic OCDs and may consist of non-steroidal anti-inflammatory drugs (NSAIDs), restriction of (sporting) activities, rest, and/or cast immobilization. Surgical treatment for OCDs of the talus includes (arthroscopic) debridement and bone marrow stimulation, fixation, osteochondral autologous transplantation, and autologous chondrocyte implantation[161, 273]. Indications for each of these types of treatment depend on several factors, such as the size of the defect and whether it concerns a primary or secondary lesion[191].

Currently, the best available treatment in adults consists of arthroscopic debridement and bone marrow stimulation, which has a success rate of 85%[273]. During this procedure, loose fragments are removed, the defect is debrided, and in the underlying subchondral bone small holes are drilled or punctured to promote revascularization. Consequentially, bone marrow cells migrate to the defect, and new fibrous cartilage is formed[250].

OCDs of the talus are rare in children. Several studies have included children in series of predominant adults[23, 34, 76, 127, 128, 207]. Few studies have investigated OCDs of the talus exclusively in children[98, 135]; however, these series are small and also include skeletally mature children. The purpose of this study was to evaluate the clinical and radiographic outcomes of conservative and primary surgically treated osteochondral talar defects in skeletally immature children.

MATERIALS AND METHODS

This study was approved by the local Medical Ethics Committee at the University of Amsterdam and performed in accordance with current ethical standards (declaration of Helsinki). Forty-five children (girls ≤15 years and boys ≤16 years) who presented themselves at the outpatient clinic with an OCD of the talus were identified between 1990 and 2010. The selection criteria were based on the study of Karrholm et al.[114]. They found a mean growth arrest of the distal tibia at an age of 15 years in girls and 16 years in boys. On the basis of the inclusion and exclusion criteria, 37 children were invited to participate in this study (Fig. 1). The stages of the invitation process

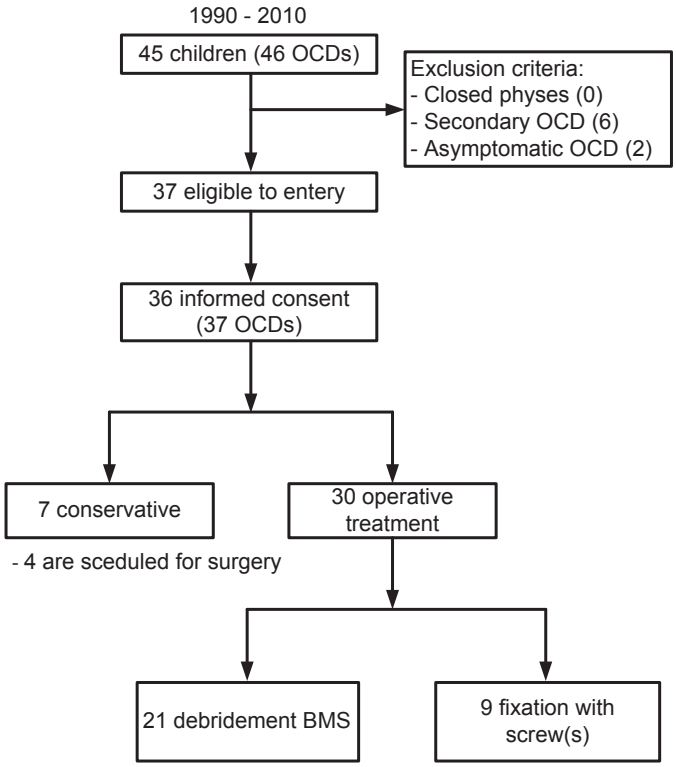

Figure 1: Flow chart of study inclusion and treatment of osteochondral talar defects of children between 1990 and 2010.

consisted of mailing a letter requesting permission to telephone the patient, making an appointment for follow-up visit at the hospital, and mailing the patient information, informed consent forms, and questionnaires. Thirty-six (97%) of the eligible patients provided informed consent and were included. Two patients preferred to refrain from visiting the hospital and completed the questionnaire by mail.

Patient evaluation included a chart review, interview, physical examination, and radiographic evaluation. One author not involved in the surgical procedures assessed the patients and completed custom-designed case report forms. The completed case report forms were entered into a digital database.

Clinical outcome measures

The primary outcome measure was the subjective patient outcome as assessed with the use of the Berndt and Harty[24] outcome question. Secondary clinical outcome measures were the Ogilvie-Harris[166] score, the Visual Analog Scale (VAS) pain score (at rest,

during walking, and during running), the American Orthopaedic Foot and Ankle Society (AOFAS) ankle-hindfoot score[118], and the Short-Form 36 (SF-36)[2, 266].

The Berndt and Harty[24] outcome question is a single question with three possible answers; the patient categorizes the ankle as good, fair, or poor. Good results are characterized by occasional symptoms without loss of function, fair results by decreased symptoms with persisting pain, and poor results by no change in symptoms. The Ogilvie-Harris[166] scale consists of five items each of which the patient grades as excellent, good, fair, or poor, with the lowest evaluation of each item determining the final outcome. The VAS pain score is an 11-point scale that represents the whole spectrum of no pain (0 points) up to the worst pain imaginable (10 points). The AOFAS score is a combined objective and subjective clinical rating system ranging from 0 to 100 points, which is subdivided into three categories: pain (40 points), function (50 points), and alignment (10 points)[118]. It is frequently used in the assessment of foot and ankle therapy, and the subjective component has been validated[104]. The SF-36 is a well known and extensively validated outcome measure to assess quality of life[2, 266]. It is divided into a physical and a mental component scale; the normative value of the Dutch population is 50.0 ± 10.0 for both components[2].

Imaging

The original size of the defects and the presence of open physis were assessed on the preoperative images by a pediatric orthopedic surgeon. Computed tomography (CT) was the first-choice imaging modality for measuring the size of the defect and was used in 32 patients. The size of the defect was determined in mm with an accuracy of one decimal. If CT scans were unavailable, the defect size was measured with the use of magnetic resonance imaging (MRI) (used in 4 patients) or conventional radiography (used in one patient). The preoperative defect condition was classified according to the modified Berndt and Harty's[24] staging system. On the original scale, defects were divided into four stages (I–IV) according to the amount of detachment and displacement of the OCD. The addition of stage V by Scranton and McDermott[210] was used to classify cystic defects. At final follow-up visit, weight-bearing radiographs of the affected ankles (mortise, lateral, and a 4-cm heel rise) were made of all patients. Osteoarthritic changes were scored by an orthopedic surgeon based on the van Dijk[253] classification.

RESULTS

The study group consisted of 24 girls (67%) and 12 boys (33%). The mean age at initial presentation was 13 years (SD 2 years). The median time follow-up was 4 years (range 1–12 years). The right talus was affected in 18 cases (49%), the left in 19 cases

(51%), with one child having bilateral involvement. A history preceding trauma was present in 18 children (49%). The mean duration of symptoms till diagnosis was 10 months (SD 12 months). Thirty-one out of 36 patients were referred by another hospital.

Treatment

Non-operative management was the initial treatment of choice for all patients for at least 6 months and could consist of restriction of (sports) activities (n = 37) combined with physiotherapy (n = 1), taping (n = 2), or treatment with a plaster cast (n = 14). Currently, seven patients continue conservative treatment; however, four of them are scheduled to undergo surgery. In total, 30 cases required surgical treatment and two cases had their primary surgical treatment in a referral hospital (1 fixation and 1 arthroscopic debridement and bone marrow stimulation). In nine cases (30%), fixation of the fragment was the first surgical treatment. Fixation of the fragment was only performed in Berndt and Harty[24] stage II–IV lesions. An arthrotomy without an osteotomy was the approach of this procedure. Debridement and bone marrow stimulation was performed in 21 cases (70%) (19 arthroscopy and 2 arthrotomy).

Post-operative treatment of debridement and bone marrow stimulation consisted of partial weight bearing for 4 weeks with progression to full weight bearing within 6 weeks. After fixation, a short-leg, non-weight-bearing cast was applied for 6 weeks post-operatively. After these 6 weeks, physical therapy was prescribed to assist in functional recovery and extend to full weight bearing in approximately 2 weeks. Screw removal was performed in all patients after fixation of the OCD because of the young age.

Clinical outcome

The Berndt and Harty[24] clinical outcome after fixation of the fragment was good in seven cases (78%) and fair in two cases (22%). After debridement and bone marrow stimulation, the Berndt and Harty[24] clinical outcome was good in 13 cases (62%), fair in three cases (14%), and poor in five cases (24%). Table I shows the Ogilvie-Harris[166] score, the VAS pain score, the AOFAS score, and the SF-36 scales of both treatment options. In both groups, the mean SF-36 physical and mental component scales were in the normal range of the Dutch population[2] (Table I).

Table I: Clinical outcome after surgical treatment of an OCD

BH-score	OH- score	VAS-rest	VAS-walking	VAS-running	AOFAS	SF-36 PC	SF-36 MC
Fixation of an osteochondral fragment (n = 9)							
7 good	4 excellent	0.0 median	1.0 median	1.5 median	95.0 median	47.6 mean	47.6 mean
2 fair	3 good	(range 0–6)	(range 0–7)	(range 0–4)	(range 77–100)	(8.3 SD)	(13.9 SD)
0 poor	2 fair						
	0 poor						
Debridement and bone marrow stimulation (n = 21)							
13 good	9 excellent	0.0 median	1.0 median	2.0 median	95.0 median	48.8 mean	55.9 mean
3 fair	3 good	(range 0–6)	(range 0–9)	(range 0–10)	(range 45–100)	(12.3 SD)	(6.3 SD)
5 poor	6 fair						
	3 poor						

BH, Berndt and Harty; OH, Olgilvie Harris; PC, physical component; MC, mental component

Imaging

Open physis of the distal tibia was found in all preoperative imaging. Preoperative radiographs of the ankle joint (mortise, lateral, and 4-cm heel rise) were generally sufficient for diagnosing the OCD. The mean preoperative size of the defects was 13.8 mm (SD 5.8) in the anteroposterior direction, 9.5 mm (SD 4.2) in the mediolateral direction, and 4.1 mm (SD 2.4) in the craniocaudal direction. Twenty-eight (76%) defects were located on the medial talar dome, and nine (24%) defects were located on the lateral talar dome. Three defects were classified as Berndt and Harty[24] stage I, 1 as stage II, 25 as stage III, 5 as stage IV, and 3 as stage V lesions[210]. On the final radiographs, there were no progressive degenerative changes seen in all patients (Figs. 2, 3).

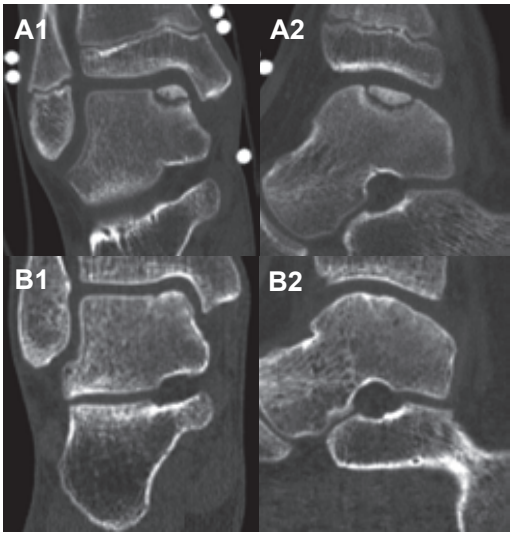

Figure 2A: Preoperative coronal (**A1**) and sagittal (**A2**) CT of a medial osteochondral talar defect (Berndt and Harty stage III) of a right ankle. **B**: Post-operative coronal (**B1**) and sagittal (**B2**) CT of the same ankle after fixation of the fragment with two screws and removal of the screws at 1-year follow-up. Good clinical and radiological results were observed at 8-year follow-up.

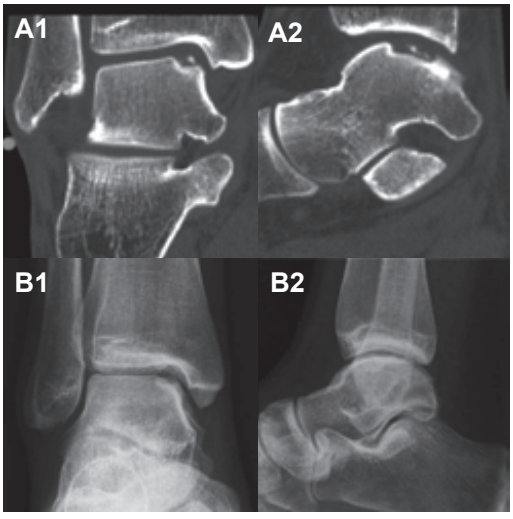

Figure 3A: Preoperative coronal (**A1**) and sagittal (**A2**) CT of a medial osteochondral talar defect (Berndt and Harty stage III) of a right ankle. **B**: Post-operative mortise (**B1**) and lateral (**B2**) weight-bearing radiographs of the same ankle after debridement and bone marrow stimulation with a good clinical outcome after 5 years.

Complications and reoperations

Complications of surgery occurred in four patients. An area of numbness around the scar was reported in one patient after fixation of the fragment and two patients after arthroscopic debridement and bone marrow stimulation. One other patient developed a superficial wound infection after arthroscopic debridement and bone marrow stimulation, which was effectively treated with oral antibiotics.

Two patients required a second surgical procedure because of persistent symptoms. Repeat arthroscopic debridement and bone marrow stimulation was performed in both patients. Times from the initial surgery to the second surgery were 27 and 35 months. One patient had a good Berndt and Harty[24] clinical outcome, while the other patient had a poor score at the time of final follow-up.

DISCUSSION

The most important findings of the present study were that 92% of the initially conservatively treated children were eventually scheduled to undergo surgical treatment. Fixation of the fragment, and debridement and bone marrow stimulation reported both a good clinical Berndt and Harty[24] outcome of 78 and 62%, respectively.

The etiology of OCDs of the talus in children is not entirely clear. A traumatic event is widely accepted as the most important etiologic factor of an OCD of the talus in adults. However, as not all patients report a history of ankle injury[66], a subdivision can be made in the etiology of traumatic and non-traumatic defects. In non-traumatic OCD ischaemia, subsequent necrosis and genetics are possible etiological factors[2, 62, 204, 271]. In this series, a history of trauma is described in 49% of the osteochondral talar defects. However, the true incidence is difficult to examine because children could easily forget a history of trauma. Furthermore, repeated microtraumas are often not associated as a traumatic event by patients.

Conservative treatment is the first step in the treatment of symptomatic OCDs in children, except in acute Berndt and Harty[24] type IV lesions. In this study 92% of the initially conservatively treated children were unhappy with the conservative treatment results and were treated surgically eventually. Different opposite results of conservative treatment in children are reported in literature. Letts et al.[135] found good results in 39% of the 23 conservatively treated children, while Higuera et al.[98] found 91% excellent/good results in 11 children (Table II). The poor results of conservative therapy found in this study can be explained through the high percentage of patients (86%) referred to us by other hospitals. In these patients previous conservative treatment had already failed.

In this study primary OCDs treated with debridement and bone marrow stimulation resulted in a good Berndt and Harty[24] clinical outcome in 13 cases (62%), fair in three

cases (14%), and poor in five cases (24%). Similar results are reported in smaller series in children. Letts et al.[135] published a good Berndt and Harty[24] clinical outcome in six of 12 cases (50%), fair in five (42%) cases, and poor in one case (8%) (Table II). Benthien et al.[23] reported a good Berndt and Harty[24] clinical outcome in four of six cases (66%) and poor in two cases (33%) (Table II).

Internal fixation is described as an alternative technique in the treatment of an OCD with a large avulsion fragment. Schuh et al.[207] reported a success rate of 100% in 11 cases using K-wires fixation in children (Table II). In this study the Berndt and Harty[24] clinical outcome was good in seven cases (78%) and fair in two cases (22%). No failures were reported in this group.

Fixation of the fragment and arthroscopic debridement and bone marrow stimulation are both good surgical options after failed conservative treatment. Arthroscopic debridement and bone marrow stimulation has a short surgery time, a low complication rate, and a fast rehabilitation[275]. However, fixation of a large fragment has the advantages of restoration of the natural congruency and subchondral bone of the talus and to maintain hyaline cartilage. Furthermore, after failed treatment with fixation, debridement and bone marrow stimulation is still feasible. The indication of fixation depends on the stage, size, and the location of the lesion. Berndt and Harty[24] stage II–IV are lesions in which fixation could be considered. However, there is no evidence in current literature to suggest that the classification of the lesions according to the system described by Berndt and Harty[24] should determine treatment[230]. In this series 84% of the defects were Berndt and Harty[24] stage II–IV lesions. However, not all defects were large enough to consider fixation. Furthermore, in case of skeletal immaturity, a malleolar osteotomy is a relative contraindication. However, the ankle joint of children is mostly very flexible, and therefore, most defects can be reached without an osteotomy. In case of doubt, a preoperative CT of the ankle in plantar flexion is useful to determine the possibility of fixation without a medial malleolar osteotomy[241]. If the approach is only possible with a malleolar osteotomy, surgery could be performed in a later stage when the patient is skeletally mature.

No degenerative changes in radiographs at a median time follow-up of 4 years (range 1–12 years) were found. However, in this analysis we included eight patients with a follow-up of less than 2 years. Bruns et al.[34] also reported no degenerative changes in 13 children after the surgical treatment of osteochondral talar defects at a mean follow-up of 55 months (range 8–134 months). In adults, progressive degenerative changes after debridement and bone marrow stimulation of the talus are also rare[208, 239]. The low incidence of degenerative changes might be the result of the high congruency of the ankle joint[250] and the relatively low percentage of a history of trauma in this series of patients.

Table II: Overview of reported cases of operative treatment of OCD of the talus in children

Study	No (♀ ≤ 15 yrs; ♂ ≤ 16 yrs)	Treatment	Outcome (Scoring system; follow-up)
Higuera J et al.[98]	11	Conservative	10 Excellent/good; 1 poor (OSS; 13–101 months)
Letts M et al.[135]	23	Conservative DB (1 arthroscopy, 11 arthrotomy): 12	9 good; 2 fair; 12 poor (BH; 1–44 months) 6 good; 5 fair; 1 poor (BH; 1–44 months)
Benthien RA et al.[23]	6	DB (arthroscopic)	4 good; 2 poor (BH; 3–27 months)
Hunt SA et al.[101]	2	DB (arthroscopic)	1 good; 1 fair (BH; 94–129 months)
Baker CL et al.[15]	2	DB (arthroscopic)	2 good (OSS; 8.8–11.7 yrs)
Kumai T et al.[127]	10	Transmalleolar drilling	10 good (BH; 30–114 months)
McCullough CJ et al.[146]	2	Conservative: 1 D (arthrotomy): 1	1 excellent (OSS; 24 months) 1 excellent (OSS; 43 months)
Bruns J et al.[34]	13	CBG: 9 Fixation: 3 DB: 1	CBG: 6 good; 3 fair. Fixation: 2 good; 1 fair. DB: 1 good (BH; 8–134 months)
Schuh A et al.[207]	11	Fixation with K-wire	11 excellent/good (OH; 18–93 months)
Kumai T et al.[128]	6	Fixation with cortical bone pegs	6 Good (BH; 3.5–10.5yrs)
Gautier E et al.[74]	1	OATS	90 (AOFAS; 13 months)
Raikin SM[181]	2	Osteochondral Allograft Transp.	100 (AOFAS; ≥24 months)
Giannini S et al.[76]	5	ACI	1: 90, 2: 95, 2: 100 (AOFAS 24 months)

DB, debridement and bone marrow stimulation; D, debridement; CBG, cancellous bone grafting; OATS, osteochondral autograft transfer; ACI, autologous chondrocyte implantation; BH, Berndt and Harty; OH, Ogilvie-Harris; OSS, own scoring system

This study does have limitations. It is a retrospective case series, with a great range of follow-up. Furthermore, different treatment modalities of fixation and debridement were used in our study; however, the number of patients in each treatment group was not sufficient to perform meaningful statistical analysis. Therefore, we were unable to identify differences in outcomes between the various treatment groups. Next, the decision-making between fixation and debridement of the fragment was based on surgeon preference. However, since 2007, fixation of a large fragment (>15 mm) is the primary treatment of choice in children in our clinic.

Little is known about the treatment and clinical outcome of OCDs of the talus in children. This study is useful as it suggests that fixation and debridement and bone marrow stimulation of an OCD of the talus are both good surgical options.

CONCLUSIONS

This study represents the largest exclusive study of OCDs of the talus in skeletally immature children. Fixation and debridement and bone marrow stimulation of an osteochondral talar defect are both good surgical options after failed conservative treatment.

CHAPTER 9

HemiCAP for secondary treatment for osteochondral talar defects

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ABSTRACT

The optimal treatment for large osteochondral defects of the talus or secondary defects has to be determined yet. A metal implant with a diameter of 15 mm has been developed for treatment of these lesions of the medial talar dome. We prospectively studied 20 consecutive patients for a mean of 4.5 years (3 to 5) post-surgery. There was statistically significant reduction of pain in rest, walking, and stair climbing ($p \leq 0.01$). The median American Orthopaedic Foot and Ankle Society ankle-hindfoot score improved from 62 (interquartile range (IQR), 46 to 72) preoperatively to 85 (IQR, 75 to 99) at final follow-up ($p < 0.001$). The Foot and Ankle Outcome Score improved on subscale pain, function, sports, and quality of life ($p \leq 0.01$). The mean Short-Form 36 physical component scale improved from 36 (SD 8.2) preoperatively to 45 (SD 9.4) at final follow-up ($p = 0.001$); the mental component scale did not change significantly. On radiographs, progressive joint space narrowing of the ankle was observed in two patients. One patient required additional surgery for the osteochondral defect. The mid-term results show that a metal implant is a promising treatment for osteochondral defects of the medial talar dome after failed previous surgery.

INTRODUCTION

In the eighteen century, Monro[153] was the first to report the presence of cartilaginous bodies. In 1888, König[123] used the term osteochondritis dissecans to describe loose bodies in the knee joint and suggested that these were the result of spontaneous necrosis. It was not until 1922 that the first report on osteochondritis dissecans in the ankle was published[113]. Since then, several etiologies for these lesions have been suggested. Trauma is known to be the most important etiologic factor[250], but ischemia and idiopathic osteochondral ankle lesions do occur[204]. The most common location of osteochondral defects (OCDs) is in the knee, followed by the talar dome[274]. OCDs of the talus are located in 62% on the medial talar dome[60]. These medial defects are generally deep and cup shaped[39]. An OCD may sometimes heal and stabilize, but often progresses to a cystic lesion causing deep ankle pain on weight bearing, prolonged swelling, diminished range of motion, and synovitis[190, 250].

Arthroscopic debridement and bone marrow stimulation is considered the primary treatment and yields 85% success[273], lasting over the years to have a 76% satisfactory outcome at the long term[239]. In case of failure of the primary treatment, current secondary treatment options include osteochondral autograft transfer (OATS), autogenous bone graft, and autologous chondrocyte implantation[17, 74, 88, 237]. However, these techniques are sometimes associated with donor-site morbidity, involve two-stage surgery or poor graft integration[12, 163, 171, 185].

For treatment of large lesions of the medial talar dome or after failed primary treatment, a contoured articular inlay implant (HemiCAP®, Arthrosurface Inc., Franklin, MA, USA) with a fixed diameter of 15 mm has been developed[245]. Its goals are to offer relief of pain, return to activity, and prevent degeneration/further cyst formation. There are two components: a cobalt-chromium articular component and a titanium screw. Fifteen articular component offset sizes are available, based on the surface geometry of the medial talar dome. The offset sizes have been found appropriate for a variety of talar specimens in a cadaveric study[245]. Since October 2007, this implant has been used in our institution in patients with persistent complaints more than one year after primary surgical treatment of a large OCD of the medial talar dome (anterior-posterior or medial-lateral diameter >12 mm on CT)[244]. Contraindications of this procedure are age <18 years, OCD size >20 mm, ankle osteoarthritis grade II or III[253], concomitant ankle pathology (tibial OCD, instability, fracture less than six months old, tendonitis), diabetes mellitus, advanced osteoporosis, infection, and a known allergy to the implant material. However, these indications/contraindications are not strict because the HemiCAP is still in the experimental stage.

SURGICAL TECHNIQUE

The procedure is carried out under general or spinal anesthesia. The patient is placed in the supine position with a tourniquet applied around the upper leg and a rolled-up apron underneath the lateral malleolus to facilitate eversion of the foot and improve exposure of the talus. A curved skin incision of approximately 7 cm is made over the medial malleolus. The anterior skin is mobilized using a scalpel and forceps, and a skin retractor is placed to retract the skin. A Hohmann retractor is placed over the distal tibia. A small anterior arthrotomy exposes the anteromedial talar dome. The level of this anterior superior border of the talar dome will later in the procedure act as a guide to identify the level of the posterior ankle joint. Next, the sheath of the posterior tibial tendon is incised, and another Hohmann retractor is placed posterior to the medial malleolus and anterior to the posterior tibial tendon. The posterior capsule of the ankle joint can be visualized now and incised. The posterior intersection between the medial malleolus and tibial plafond is identified using an arthroscopic probe. The surgeon carefully inserts the 5-mm tip of the probe in the posteromedial joint space by sliding along the posterior aspect of the distal tibia at the intersection with the medial malleolus and gently pulls in an oblique craniomedial direction[242]. This maneuver identifies the posterior part of the intersection between the tibial plafond and medial malleolus. The periosteum at the level of the intended osteotomy is marked. Next, the probe is placed in the anteromedial tibial notch and pulled in an oblique craniomedial direction, identifying the anterior part of the intersection. The anterior intersection is marked, and this is connected to the posterior intersection as a reference guide to the osteotomy. Before creating the osteotomy, two screw holes are predrilled and tapped in the medial malleolus, using a cannulated drill. An oscillating saw is placed on the incised periosteum and directed at the marked intersection of the tibia plafond and medial malleolus. The osteotomy is created up to approximately 2 mm above the articular cartilage, while two Hohmann retractors protect the adjacent soft tissue. The optimal angle for the osteotomy has determined to be at a mean angle of 30 degrees relative to the long tibial axis[243]. The osteotomy is completed with the use of an osteotome. This way, the surgeon controls the osteotomy of the articular surface and minimizes the risk of damaging the talar cartilage. After the osteotomy has been completed, the surgeon manually retracts and everts the medial malleolus using gauze. Optionally, the distal part is temporarily transfixed by retrograde drilling a 2.5 mm diameter K-wire into the talus through one of the predrilled holes. Exposure of the talar dome is improved by forced eversion of the heel. The fibula is hereby used as a fulcrum (take care not to use too much force), and the talus is tilted.

The necrotic fragment of the defect can now be identified and debrided (Fig. 1A). Utilizing a drill guide, a guide pin is placed into the center of the defect, perpendicular

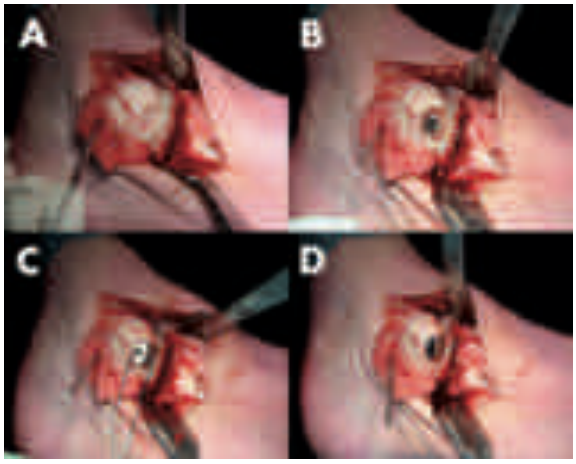

Figure 1: Intraoperative photographs of a right ankle showing (**A**) the OCD debrided following a medial malleolar osteotomy. **B**: The screw inserted in the center of the OCD. **C**: A trial articular component in place on the screw. **D**: The definitive resurfacing implant engaged on the screw.

to the curvature of the medial talar dome. The guide pin ensures that a perpendicular direction is maintained throughout the procedure. The titanium screw of the metal implant is inserted after drilling a pilot hole (Fig. 1B). A contact probe is used to determine the radius of curvature in the sagittal and coronal planes to allow for a precise fit of the articular component to the existing articular surface. A matching reamer prepares the site for placement of the articular component. The reamer is a cannulated instrument used over the guide pin with a diameter of 15 mm. A sizing trial with corresponding offsets allows for final verification of proper fit (Fig. 1C). The selected articular component is oriented into the correct planes and is placed on the screw. It is impacted with a gentle hammer stroke on an instrument with a plastic tip, thereby engaging the taper interlock (Fig. 1D). After the confirmation of slightly recessed implant edges, the osteotomy is reduced. Initially, large diameter K-wires are placed through the predrilled screw holes to confirm correct alignment. A Weber compression forceps can be placed for initial compression. Placement of the proximal leg of the Weber compression forceps is facilitated by creating a small hole in the distal tibial cortex proximal to the osteotomy using a 2.5-mm drill. We routinely use two 3.5-mm cancellous lag screws with a length of 40 or 45 mm. The posterior tibial tendon sheath is not repaired, and the wound is closed with Ethilon 3.0 sutures using a vertical mattress (Donati) technique.

RESULTS

We prospectively studied 20 consecutive patients with a mean age of 38 years (20 to 60) after failed prior surgical treatment of a large OCD of the medial talar dome[244]. The patients were assessed preoperatively and at two and six weeks, three and six months, and annually postoperatively. Various outcome measures were recorded prospectively, including numeric rating scales (NRS) of pain at rest, walking, climbing stairs, and running[199], American Orthopaedic Foot and Ankle Society (AOFAS) ankle-hindfoot score[104, 118], Foot and Ankle Outcome Score (FAOS)[196], and Short-Form 36 (SF-36)[2]. Weight-bearing radiographs (anteroposterior (AP) mortise and lateral views) were obtained at all follow-up visits including and after six weeks post-surgery.

Statistical analyses were performed with the use of SPSS software v19.0 (SPSS Inc., Chicago, Illinois). One-way repeated-measures analyses of variance (ANOVA) were performed to determine differences in mean scores at different time points for the outcomes with a normal distribution. When a p-value <0.05 was found, *post hoc* pairwise comparisons were performed using a Bonferroni correction. The assumptions of normality and sphericity were checked with use the of the Shapiro-Wilk test and Mauchly's test, respectively. Skewed distributions were analyzed using the Friedman's two-way analysis of variance by ranks. *Post hoc* pairwise comparisons of these outcome measures were performed with the use of Wilcoxon signed-rank tests with Bonferroni correction to adjust for multiple comparisons. The SF-36 scales were compared with the normative data for the Dutch population with the use of the Student's *t*-test.

Currently, the mean duration of follow-up is 4.5 years (3 to 5). No patients were lost to follow-up.

The mean defect size was 15 mm (SD 3.5) in the AP direction, 10 mm (SD 1.9) in the mediolateral direction, and 9 mm (SD 3.3) in depth. Radiologically, one defect was classified according to the modified Berndt and Harty[24] classification as stage III (complete avulsion of a fragment), one as stage IV (displaced fragment), and 18 as stage V (cystic lesion)[209]. Sixteen defects were located on the centromedial talar dome and four on the posteromedial talar dome.

The NRS pain improved significantly during walking, climbing stairs, and running (Table I and Fig. 2). Repeated-measures ANOVA determined that the mean NRS walking differed significantly between time points ($F_{(4, 76)} = 13.5$, $p < 0.01$). *Post hoc* pairwise comparisons using Bonferroni correction revealed that the NRS-walking was significantly decreased at all postoperative time points compared with the preoperative situation ($p < 0.001$ to $p = 0.05$).

The median AOFAS improved from 62 (IQR, 46 to 72) preoperatively to 75 (IQR, 68 to 87) at six months, 87 (IQR, 76 to 94) at one year, and 85 (IQR, 75 to 99) at final follow-up ($p < 0.001$; Friedman's two-way analysis of variance by ranks). *Post hoc*

Table I: Numeric rating scale (NRS) for pain (IQR, interquartile range)

	Mean (standard deviation)						Median (IQR)	
Time point	**NRS-rest**	***p*-value***	**NRS-walking**	***p*-value***	**NRS-strair climbing**	***p*-value***	**NRS-running**	***p*-value‡**
Pre-operative	3.6 (2.8)		6.7 (1.3)		6.6 (1.6)		10.0 (9–10)	
Three months	2.4 (2.2)	1.0	4.4 (2.4)	0.05	4.6 (2.7)	0.24	7.0 (5–10)	0.10
Six months	1.7 (1.9)	0.09	3.3 (2.4)	0.001	2.8 (2.4)	0.001	6.0 (3–10)	0.04
One year	1.3 (1.8)	0.01	2.3 (2.1)	<0.001	2.2 (2.0)	<0.001	3.0 (0–10)	0.005
Final	2.1 (2.6)	0.50	2.8 (2.7)	<0.001	3.0 (2.9)	0.001	6.0 (0–10)	0.004
p-value	$F_{(4, 76)} = 3.6$; $p = 0.01$†		$F_{(4, 76)} = 13.5$; $p < 0.01$†		$F_{(4, 72)} = 13.0$; $p < 0.01$†		$p = 0.08$§	

* Bonferroni-adjusted p-value of pairwise comparison with the preoperative NRS
† Repeated-measures analysis of variance
‡ Wilcoxon signed-rank test
§ Friedman's two-way analysis of variance by ranks

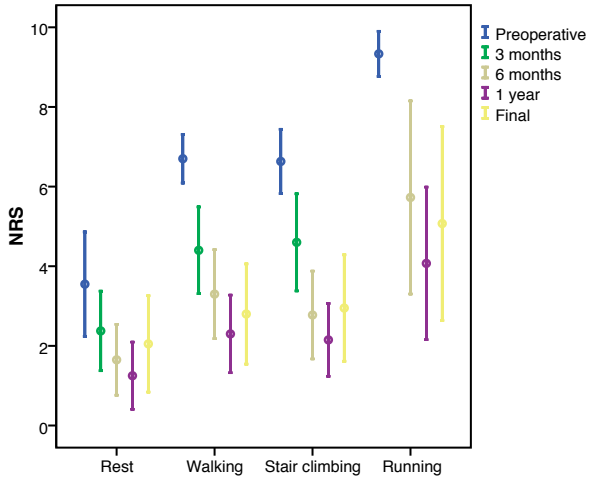

Figure 2: Graph showing the mean numeric rating scale (NRS) for pain in rest, walking, stair climbing, and running situations across the follow-up. *P*-values for comparisons across time points are given in table I. The error bars denote the 95% confidence intervals.

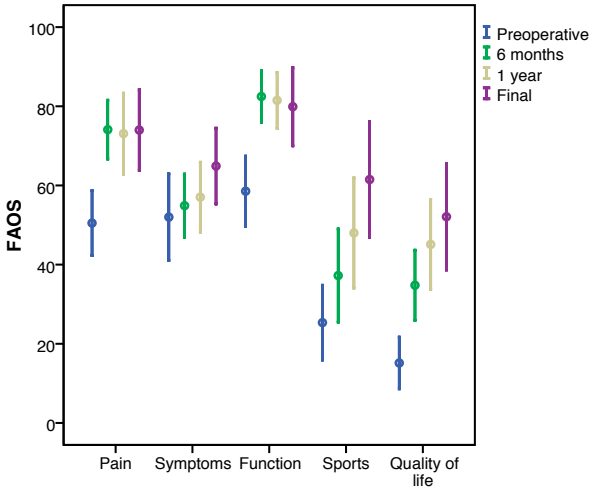

Figure 3: Graph showing the mean Foot and Ankle Outcome Score (FAOS) by subscore across the follow-up. *P*-values for comparisons across time points are given in table II. The error bars denote the 95% confidence intervals.

Table II: Foot and Ankle Outcome Score (FAOS) (ADL, activities of daily living)

	Mean FAOS subscore (standard deviation)									
Time point	**Pain**	***p*-value***	**Symptoms**	***p*-value***	**Function (ADL)**	***p*-value***	**Sport**	***p*-value***	**Quality of life**	***p*-value***
Pre-operative	50.5 (17.5)		52.0 (23.4)		58.6 (18.9)		25.4 (20.2)		15.2 (14.0)	
Six months	74.1 (15.4)	0.001	54.9 (16.5)	1.0	82.5 (13.5)	0.001	37.2 (24.4)	0.20	34.8 (18.4)	0.001
One year	73.1 (21.8)	<0.001	57.1 (18.8)	1.0	81.5 (15.1)	<0.001	48.0 (29.8)	0.002	45.1 (24.3)	<0.001
Final	74.0 (21.7)	<0.001	64.9 (20.5)	0.16	79.9 (21.2)	0.01	61.5 (31.3)	<0.001	52.1 (28.7)	<0.001
p-value	$F_{(3, 54)} = 10.1$; $p < 0.01$†		$F_{(3, 54)} = 2.3$; $p = 0.09$†		$F_{(3, 54)} = 11.2$; $p < 0.01$†		$F_{(3, 54)} = 9.5$; $p < 0.01$†		$F_{(3, 54)} = 18.6$; $p < 0.01$†	

* Bonferroni-adjusted p-value of pairwise comparison with pre-operative score
† Repeated-measures analysis of variance

tests revealed significant differences at one year ($p < 0.001$) and at the final follow-up ($p = 0.001$) compared with pre-operatively.

The FAOS improved significantly on subscale pain, function, sports, and quality of life (Fig. 3). *Post hoc* pairwise Bonferroni-adjusted comparisons revealed statistically significant differences between preoperative scores and most postoperative scores (Table II).

The mean SF-36 physical component improved from 36.2 (SD 8.2) preoperatively to 42.2 (SD 9.0) at six months ($p = 0.05$), 44.0 (SD 10.3) at one year ($p = 0.01$), and 45.1 (SD 9.4) at final follow-up ($p = 0.004$) ($F_{(3, 51)} = 6.4$, $p = 0.001$; one-way repeated-measures ANOVA). The SF-36 mental component did not change significantly; the mean score was 53.0 (SD 9.9) preoperatively, 50.6 (SD 7.9) at six months, 52.8 (SD 5.7) at one year, and 54.1 (SD 9.7) at final follow-up ($F_{(3, 51)} = 2.5$, $p = 0.07$). Neither the final physical nor the mental component differed significantly from the population norm[73].

There were four minor complications that resolved within the study period. Three patients reported an area of numbness about the scar, which resolved within the postoperative year. Another patient had a superficial wound infection, which was effectively treated by oral antibiotics. The medial malleolar osteotomy healed in all cases, and no signs of prosthetic loosening were seen on radiographs (Fig. 4). In two patients joint space narrowing was seen during follow-up. Eleven reoperations were performed in eight patients. Hardware removal was performed in seven patients and arthroscopic removal of anterior impingement in three patients, and one patient had

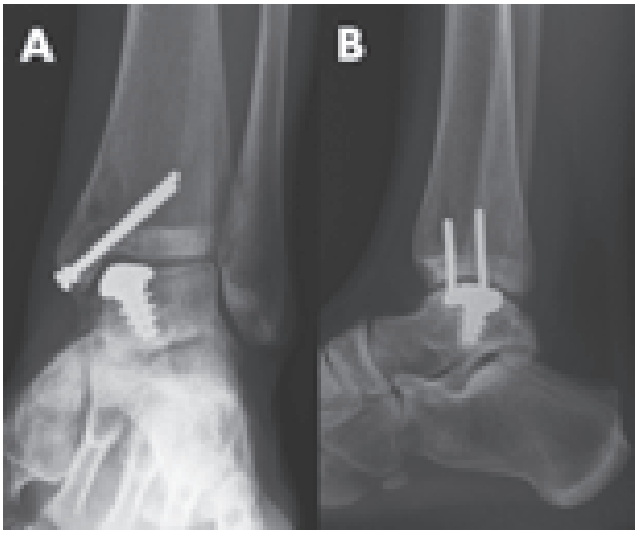

Figure 4: Mortise (**A**) view and lateral (**B**) weight-bearing radiographs of a left ankle five years post-operatively showing correct positioning of the implant.

a lateralizing calcaneus osteotomy to unload the medial facet of the ankle because of persisted deep ankle pain.

POSTOPERATIVE MANAGEMENT AND REHABILITATION

The postoperative management consists of a plaster cast for one week. A functional non-weight-bearing brace (Walker) or a detachable plaster cast can be applied for another five weeks. During this period, non-weight-bearing sagittal range-of-motion exercises are allowed, i.e., 15 minutes twice daily. After these, six weeks radiographs of the operated ankle are obtained to confirm consolidation of the malleolar osteotomy. Subsequently, physical therapy is prescribed to assist in functional recovery and facilitate the return to full weight bearing over approximately one month. Return to normal weight bearing and walking should thus be accomplished ten weeks after surgery. Impact activities, such as running, are allowed when no signs of prosthetic loosening and migration are seen after six months of follow-up. Non-contact sports are allowed after nine months of follow-up and contact sports one year after surgery. However, the risk of periprosthetic fracture during contact sports should be discussed with the patient. We reported the first clinical case report of the talus implant in which the patient was able to play korfball (contact sports) at the preinjury level after one year and continued to play at this level at four years follow-up[240].

DISCUSSION

Treatment of OCDs or osteonecrosis by means of metal resurfacing implants is relatively new[50, 93, 234, 256]. Two biomechanical cadaveric studies provided foundations for the use of a metal resurfacing implant in the talus[9, 245]. The results of our prospective case series show that patients with talar OCDs generally benefit from the procedure. Almost all outcomes demonstrated statistically significant improvements. Satisfaction was high, with 18 patients indicating that they would undergo the procedure again.

We believe that the effectiveness of the resurfacing implant is simply based on the mechanism of filling and coverage of the defect. Increased fluid pressure from the joint into the subchondral bone has been described as the cause of pain and subchondral cyst formation[186, 250]. Filling and resurfacing the defect will possibly stop this process.

Alternative current treatment methods for large or secondary lesions are OATS, cancellous bone grafting, osteochondral allograft transplantation, ankle arthrodesis, or ankle arthroplasty. Although excellent results of OATS have been published[209], the risk of donor-site morbidity in the knee is worrisome[235]. An additional disadvantage of

osteochondral autografts is difficulty in matching the talar surface geometry and poor graft integration[163]. Limited availability and donor-site pain are also disadvantages of cancellous bone grafting[12]. Osteochondral allografts can be used for massive defects but are not recommended for localized OCDs because of the loss of viability and stability in approximately one-third of the grafts[83]. Ankle arthrodesis or prosthesis is a definite solution for a recurrent OCD but is not preferable in young patients.

The surgical approach is an important part of the implantation technique because the accuracy of implantation of this device strongly depends on the approach and quality of exposure. If the osteotomy is created too medially, i.e., in the articular facet of the malleolus, exposure of the talar dome may be insufficient for adequate treatment. Furthermore, a small distal fragment may be prone to fracture when fixed at the end of the procedure. Conversely, if the osteotomy is created too laterally, it will exit in the tibial plafond. This is undesirable because the medial tibial plafond directly articulates with the medial talar dome[151, 245], and damage to this weight-bearing area might lead to secondary osteoarthritis[73]. We therefore routinely use a probe to determine the intersection of the tibial plafond and the articular facet of the medial malleolus when performing the osteotomy[242].

The surface of the prosthetic device should be placed slightly recessed relative to the surrounding surface of the talar cartilage because talar cartilage deforms during weight bearing while the implant does not. Wan et al.[264] measured a peak cartilage deformation of 34.5% ± 7.3% under full body weight in persons with a medial talar dome cartilage thickness of 1.42 ± 0.31 mm. We therefore aim at an implantation level of 0.5 mm below the adjacent cartilage. This implantation level was found appropriate in a previous cadaveric study[245]. When the prosthetic device is correctly implanted, excessive contact pressures of the implant on the tibial plafond are avoided[245].

In conclusion, this technique is a promising treatment for OCDs of the medial talar dome after failed previous treatment. Although the results of this study are encouraging, more patients, longer follow-up, and preferably a control group may determine the place of this implant in the treatment of these defects.

PART III

General discussion and summary

CHAPTER 10

General discussion

Osteochondral defects (OCDs) of the talus often have a severe impact on the quality of life of patients. Worldwide there is still debate on the optimal treatment strategy for a symptomatic talar OCD. Numerous treatment options are available, each with pros and cons. This thesis aimed to evaluate the etiology of (cystic) OCDs, and to analyze and improve surgical treatment of talar OCDs.

PART I NATURAL HISTORY AND SUBCHONDRAL BONE CYSTS

The natural history of OCDs of the talus is complicated and still not fully understood. Why do some OCDs remain asymptomatic, while others develop deep ankle pain and form subchondral bone cysts? Understanding the natural history of OCDs may lead to the development of strategies for preventing progressive joint damage.

In **chapter 2**, a review of literature on the natural history of talar OCDs is presented[250]. An ankle trauma is widely accepted as the most important etiological factor of a talar OCD[24, 68, 261]. The development of a symptomatic OCD depends on various factors, including the damage and insufficient repair of the subchondral bone plate[177]. Pain is most probably caused by an intermittent local rise in intra-osseous fluid pressure which occurs on every step[13, 14, 247]. This increased fluid pressure will result in local macrophage activation and osteolysis. Chronic macrophage activation and vascular derangements lead to low pH, local bone demineralization (acid attack), and H^+-mediated stimulation of the primary afferent nociceptive nerve fibers[131].

In some OCDs a subchondral bone cyst develops over time. Fluid pressure forced through a fissure in the subchondral bone plate has been proposed to play an important role in this pathogenesis[250]. In a computer simulation study it was found that pressurized fluid as a mechanical stimulus can indeed be responsible for cyst growth[48]. In this scenario, an irregularly shaped cyst developed which became rounded and obtained a sclerotic bone rim after removal of the pressurized fluid. The aim of **chapter 3** was to evaluate and compare the cyst morphology of human cadaveric tali by using microCT with the morphological simulation results previously reported. Six tali out of 66 were found to have a single cyst. Irregular and rounded cysts were found as were seen in the previous simulation study. In four of the six cysts a clear opening through the subchondral bone plate was found. This finding suggests that the subchondral bone plate plays an important role in cyst growth by pressurized fluid. When a subchondral fissure is detected in an early stage, treatment by reconstruction or closure of the subchondral plate might theoretically prevent cyst development. On the other hand, it is still unknown what percentage of these fissures will recover without development of a cyst. Furthermore, not all subchondral bone cysts are symptomatic[61, 119, 188]. On the basis of the present-day knowledge it seems not jet justified to screen for subchondral bone

fissures after a severe ankle sprain with (micro)CT, MRI or ultrasound[200]. More research in the early stage after a severe ankle sprain is necessary to gain knowledge about the incidence of subchondral bone fissures and subchondral bone cyst development.

PART II SURGICAL TREATMENT AND SUBCHONDRAL BONE HEALING

Chapter 4 provides an overview of the current treatment options. Conservative treatment is the first step in the treatment of symptomatic OCDs and may consist of non-steroidal anti-inflammatory drugs (NSAID's), restriction of (sporting) activities, rest and/or cast immobilization[261]. The success rates vary between 20 to 69%[261, 273].

There is still no consensus on an optimal surgical treatment regimen. Different surgical techniques include debridement and bone marrow stimulation[67], fixation[115], retrograde drilling[226], autologous chondrocyte implantation (ACI)[161], osteochondral autologous transplantation (OATS)[210], osteochondral allograft transplantation[59, 257], and metal resurfacing inlay implant[244]. Although these techniques differ significantly, success rates around 85% are reported in most cases[273]. This is perhaps not surprising because in all these techniques one similarity exists: the debridement of the defect. As described in **chapter 2** nerve endings are located in the subchondral bone and not in cartilage[142, 250]. Debridement will destroy these nerve endings and denervation is then achieved. Comparably, denervation of the Achilles tendon and patella is also reported to be successful in Achilles tendinopathy and anterior knee pain[136, 255]. The key to success is likely due to adequate debridement. However, we still have to ask ourselves why 15% of the patients have a poor outcome. Possible factors are body mass index, defect size and type, malalignment, ankle instability and technical failure by the surgeon. A defect size of approximately 1.5 cm^2 has a risk of clinical failure after arthroscopic bone marrow stimulation techniques[44]. Malalignment increases edge loading and this may lead to defect expansion[81, 82]. In ankle instability abnormal load distribution due to shifting of the center of pressure results in locally increased stresses on the articular cartilage[92, 167, 232]. Technical failure by the surgeon can also occur. For example, we found in **chapter 6** that not all OCDs (45 of 58) are fully debrided during ankle arthroscopy.

However, arthroscopic debridement and bone marrow stimulation has still been considered the primary surgical treatment of choice 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[273, 275]. However, little is known about the healing of the subchondral bone after debridement and microfracture of talar OCDs. An irregular subchondral bone plate may affect cartilage repair and thus plays a role in the development of

osteoarthritis[125, 141, 169, 177]. Progression of ankle osteoarthritis is seen in 33–34% of the patients following arthroscopic debridement and bone marrow stimulation at long term follow-up[67, 239]. **Chapter 6** describes the dimensional changes and bone healing of talar OCDs after arthroscopic debridement and microfracture. Fifty-eight patients were analyzed with computed tomography (CT) preoperatively, two weeks postoperatively and one year postoperatively. As a result of debridement of the defect, the size of the defect initially increased on the direct postoperative CT scan but returns to its original, preoperative size at one year follow-up. Twenty-one of the 58 OCDs were poorly healed, as judged by the incomplete filling of the defect by bone. However, no clinical differences were found at one year follow-up between a well and poorly healed defect. Expect the incomplete filling of bone, Lee et al.[133] reported on second-look arthroscopies that 35% of the defects were incompletely healed with fibrocartilage at one year follow-up. However, 90% of the ankles had still good to excellent functional outcomes. Although the knee joint differs from the ankle joint, the biological characteristics and response to microfracture techniques are similar. Mithoefer et al.[152] analyzed on magnetic resonance imaging the repair of knee OCDs after microfracture. At an average of 12 months after the index procedure, a good fill (volume filling of 67% to100%) of the defect was reported in 13 of 24 patients (54%), moderate fill (volume filling of 34% to 66%) in 7 (29%), and poor fill (volume filling of 0% to 33%) in 4 patients (17%). Only after 24 months poor fill grade was associated with limited improvement and decreasing functional scores[152]. It is therefore possible that a longer follow-up of our study may show the correlation between the degree of defect healing and the clinical outcome.

Pulsed electromagnetic fields (PEMF) has been suggested to improve bone healing[162]. It acts as adenosine A2a agonists, leading to an increase of transforming growth factor β-1, thereby improving bone development, reducing cartilage damage and increasing chondrocyte proliferation[1, 27, 47, 168, 198]. The study described in **chapter 5** evaluates in a randomized placebo controlled trial the effects of PEMF on return to sports and bone healing after arthroscopic debridement and microfracture of osteochondral talar defects. Sixty-eight patients were randomized to either PEMF (n=36) or placebo (n=32). To assess bone repair, computed tomography (CT) scans were obtained at 2 weeks and 1 year postoperatively. No differences were found in bone repair and return to sports between the groups[189]. Likewise, Hannemann et al.[91] concluded that PEMF does not accelerate bone healing as observed on CT scans in the conservative treatment of acute scaphoid fractures. Furthermore, a meta-analysis of randomized controlled trials showed no differences in time to radiological union between PEMF and placebo after surgical treatment in acute fractures[90]. So it may be concluded that PEMF in a clinical setting does not accelerate bone healing.

In the case of an OCD where a fragment is present, the fixation of the fragment is a good alternative technique to debridement and bone marrow stimulation[128, 207].

The loose fragment is not removed but fixed to the underlying bone by a screw[143, 187], Kirschner wires[207], absorbable fixation[115], or fibrin glue[5, 112]. Advantages of this technique are that it restores the natural congruency of the subchondral bone and preserves the hyaline cartilage. Good to excellent functional outcomes of 89 to 100% have been reported[128, 207]. However, until now, a medial or lateral arthrotomy often combined with a malleolar osteotomy had to be performed to allow proper visibility and working access[128, 207]. **Chapter 7** describes a new arthroscopic fixation technique for primary osteochondral talar defects, named by the subsequent procedures as lift, drill, fill, and fix (LDFF). All seven patients in the study improved significantly from preoperative to one year postoperative. On the one year postoperative radiographs we found that five of seven defects showed remodeling and bone ingrowth after arthroscopic LDFF. However, the interpretation should be made with caution because on plain radiographs over-projection of bone is present. This prospective study will continue with more patients, longer follow-up and CT evaluation.

Although arthroscopic fixation of a talar OCD is new, this surgical technique has been around longer for the knee. Din et al.[56] reported after arthroscopic fixation of 12 OCDs with bioabsorbable pins excellent results. After a mean follow up of 32 months all fragments had MRI evidence of union and all patients returned to sporting activities within 8 months of operation[56]. Millington et al.[150] reported less promising results with bioabsorbable fixation. In their retrospective study they included 18 patients who were treated with open or arthroscopic fixation of osteochondritis dissecans lesions of the knee. Fragment fixation methods included eleven bioabsorbable nails, three pins, two darts, one screw, and one combined screw and dart. After a minimum follow-up of one year fragment union occurred in 12 knees (67%) while the remaining 6 knees (33%) required removal of the loose fragment. The authors suggested that failure with unthreaded fixation devices may be caused by inadequate compression and not necessarily be related to bioabsorbability[150].

Fixation, and debridement and bone marrow stimulation in talar OCDs have both good clinical outcomes in adults. However, little is known about the treatment and clinical outcome of OCDs in children. Children have a higher healing potential. Therefore a better clinical and radiological outcome is expected. The purpose of **chapter 8** was to evaluate the clinical and radiographic outcomes of osteochondral talar defects in skeletally immature children. Seven of nine patients (78%) reported a good outcome after fixation of the fragment and 13 of 21 patients (62%) reported a good outcome after debridement and bone marrow stimulation[187]. In comparison with adults, the subjective clinical outcome is inferior. A possible explanation is that children have higher demands on their musculoskeletal function.

Different treatment modalities are available when the primary surgical treatment fails[59, 76, 161, 210, 257]. In **chapter 9**, the mid-term (3 to 5 years) results are described of a

metal resurfacing inlay implant (HemiCAP®, Arthrosurface Inc., Franklin, MA, USA) for the treatment of OCDs of the medial talar dome after failed previous surgery. Twenty patients were prospectively studied[240, 244]. Almost all outcomes demonstrated statistically significant improvements from baseline. Eighteen of the twenty patients indicate that they would undergo the procedure again. On radiographs, no signs of implant loosening were seen. Progressive joint space narrowing of the ankle was observed in two patients. Promising results are also reported with resurfacing prosthesis in other joints after failed previous surgery[25, 55, 120]. Although mid-term results of the resurfacing prosthesis are good, should this be the gold standard in secondary talar OCDs? Interesting is that biological options also have excellent results. Recently, Petersen et al.[173] reported in 20 patients an osteochondral transplantation from the posterior femoral condyles for the treatment of talar OCDs. Similar to our study the surgical approach was by means of a medial malleolar osteotomy. The authors included large defects. The visual analog scale (VAS, 10 always pain, 0 never pain) decreased significantly when walking from 5 to 0 and climbing stairs from 6 to 1 after a follow-up of 2 years. Furthermore, no significant donor site morbidity was reported. With the HemiCAP similar results were found after a follow-up of 4.5 years, with no obvious donor site morbidity. However, loosening of the implant is a potential risk in the long-term. As the study with the HemiCAP lacks a control group, a randomized controlled trial is required to draw the definite conclusion on the outcome of the procedure.

CONCLUSIONS AND FUTURE DIRECTIONS

Treatment options for talar OCDs are numerous. Multiple systematic reviews of the literature have been performed throughout the years with the aim to identify the best treatment protocol[139, 161, 230, 261, 273]. In recent years there has been an increased interest and awareness of the importance of the subchondral bone. The articular cartilage and its supporting bone are tightly coupled and should be viewed as a connected osteochondral unit[80]. With this in mind, we must remain critical to improve our surgical techniques. For a long time arthroscopic debridement and microfracture has been considered the primary surgical treatment for chronic OCDs. Although the clinical outcome is good, the quality of fibrocartilage is inferior. Furthermore, little is known about the healing of the subchondral bone, which has an important role in cartilage repair[125, 141, 169, 177].

This thesis has contributed to the treatment of OCDs of the talus in various ways, with special focus on the subchondral bone. The literature was reviewed and the development of subchondral bone cysts as a result of fluid pressure has been hypothesized. MicroCT scans of human cadaveric tali have shown subchondral fissures to support this hypothesis. CT scans after arthroscopic debridement and microfracture showed

poor healing in 36% of the talar defects at one year follow-up. However, no differences were found between the clinical outcomes and defect healing. The effects of PEMF on return to sports after arthroscopic debridement and microfracture was investigated. Addition of PEMF does neither lead to a higher percentage of patients to resume sports nor to earlier resumption of sports. A new arthroscopic fixation technique (LDFF) for primary OCDs was investigated. In a pilot study, all seven patients had good clinical and radiological outcomes at a mean follow-up of one year. The treatment of talar OCDs in skeletally immature children was evaluated and showed that fixation, and debridement and bone marrow stimulation are both good surgical options. Finally, a novel metal implant for secondary OCDs was prospectively investigated. Most patients had good clinical outcomes at a mean follow-up of 4.5 years. Eighteen of 20 patients indicating that they would undergo the procedure again.

Several recommendations can be made for the treatment of talar OCDs on the basis of this thesis and literature. Fixation of an OCD with a bony fragment should be considered as the primary treatment. Advantages of this technique are that it restores the natural congruency of the subchondral bone and preserves the hyaline cartilage. When an OCD is not fixable, arthroscopic debridement and microfracture is a good option in defects up to 1.5 cm in diameter[46, 239, 273]. If the primary treatment fails, several secondary treatment options are available, including bone grafting, OATS, ACI, and metal resurfacing implant. The choice depends on defect and patient characteristics as well as the preference of the surgeon.

Still there are many possibilities for future research to improve treatment strategies. Prevention of the development of an OCD is the most profitable goal. Research in the early stage after a severe ankle sprain is necessary to gain knowledge in this field. Early and targeted surgical treatment can be performed if we could predict which defect will heal and which defect will become symptomatic. An untreated OCD can grow in the course of time[61, 119], which is associated with an inferior surgical outcome[44]. Arthroscopic debridement and microfracture has been proven to be effective over the years[239] but a poor subchondral bone healing is often seen[188]. Although, no differences were found between the short-term clinical outcomes and level of subchondral bone healing, longer follow-up is necessary to see if these results remain. Furthermore, the short-term result of arthroscopic LDFF seems promising. However, a high quality randomized trial is recommended between the current primary treatment (arthroscopic debridement and microfracture) and this new technique. The metal resurfacing implant was found to be a good treatment option for secondary OCDs of the medial talar dome. However, a longer follow-up with more patients, and a control group will better determine the value of this implant.

CHAPTER 11

Summary in English and Dutch

Chapter 1

General introduction

An osteochondral defect (OCD) is a lesion in a joint involving the articular cartilage and its subchondral bone. In the development and treatment the integrity of the subchondral bone seems crucial. Fluid pressure through a subchondral fissure has been proposed to play an important role in the pathogenesis of a subchondral cyst. An irregular subchondral bone plate after treatment may affects cartilage repair and plays a role in pathogenesis of osteoarthritis. The general aim of this thesis was to evaluate the etiology of (cystic) OCDs, and to analyze and improve surgical treatment of talar OCDs.

PART I NATURAL HISTORY AND SUBCHONDRAL BONE CYSTS

Chapter 2

Osteochondral defects in the ankle; why painful?

In this chapter a narrative review of literature on the natural history of OCDs of the talus is presented. OCDs of the ankle can either heal and remain asymptomatic or progress to deep ankle pain on weight bearing and formation of subchondral bone cysts. The development of a symptomatic OCD depends on various factors, including the damage and insufficient repair of the subchondral bone plate. The ankle joint has a high congruency. During loading, compressed cartilage forces its water into the microfractured subchondral bone, leading to a localized high increased flow and pressure of fluid in the subchondral bone. This will result in local osteolysis and can explain the slow development of a subchondral cyst. The pain does not arise from the cartilage lesion, but is most probably caused by repetitive high fluid pressure during walking, which results in stimulation of the highly innervated subchondral bone underneath the cartilage defect. Understanding the natural history of OCDs could lead to the development of strategies for preventing progressive joint damage.

Chapter 3

Morphological analysis of subchondral talar cysts on microCT

The purpose of chapter 3 was to evaluate and compare the cyst morphology of human cadaveric tali by using microCT with the morphological simulation results previously reported. In the previous simulation study we found that pressurized fluid can be responsible for cyst growth. In this scenario, an irregularly shaped cyst developed which

became rounded and obtained a sclerotic bone rim after removal of the pressurized fluid. Sixty-six fresh-frozen human cadaveric tali were screened in a regular computed tomography (CT) for subchondral bone cysts, radiologically defined as unexpected rounded radiolucent area. Subsequently, the tali with a cyst were scanned in a microCT. The shape of the cysts, the presence of an opening through the subchondral bone plate, and the bone volume fraction around and next to the cyst were analyzed. In total, six tali were found to have a single cyst. Four cysts had an irregular shape, and two cysts were rounded. A clear opening from the cyst through the subchondral bone plate was found (diameter 0.5–1.7 mm) in four cysts. The bone volume fraction was higher ($p=0.025$) around the cyst then next to the cyst. This study showed that the morphological findings that we found are compatible with the previously reported simulation results. It is therefore most likely that pressurized fluid plays a role in the pathofysiology of cyst growth. A better understanding of cyst growth may improve treatment and prevent further cyst formation.

PART II SURGICAL TREATMENT AND SUBCHONDRAL BONE HEALING

Chapter 4

Diagnosis and treatment of osteochondral defects of the ankle

An OCD of the talus is a lesion involving talar articular cartilage and subchondral bone. It is frequently caused by a traumatic event. The lesions may heal, stabilize or progress to subchondral bone cysts. The subchondral cysts may develop due to the forcing of cartilaginous or synovial fluid with every step. Malalignment of the hindfoot plays an important role in the development of further degeneration. Plain radiographs may disclose the lesion. Modern imaging technology has enhanced the ability to fully evaluate and accurately determine the size and extent of the lesion, which are fundamental for proper treatment. Asymptomatic or low-symptomatic lesions are treated nonoperatively. For surgical treatment the following types of surgery are in clinical use: debridement and bone marrow stimulation, retrograde drilling, internal fixation, cancellous bone grafting, osteochondral autograft transfer, autologous chondrocyte implantation, and allograft transplantation. Although these are often successful, malalignment may persist with these treatment options. Calcaneal correction osteotomy may be suitable for OCDs in selected cases.

Chapter 5

Effects of pulsed electromagnetic fields on return to sports after arthroscopic debridement and microfracture of osteochondral talar defects: a randomized, double-blind, placebo-controlled, multicenter trial

The purpose of chapter 5 was to evaluate if the use of pulsed electromagnetic fields (PEMF) after arthroscopic debridement and microfracture of an OCD of the talus leads to earlier resumption of sports, and an increased number of patients that resume sports. Sixty-eight patients were randomized to either PEMF (n = 36) or placebo (n = 32) after arthroscopic treatment of an OCD of the talus. The primary outcomes, i.e., the number of patients that resume sports and time to resumption of sports, were analyzed using Kaplan-Meier curves, Mann-Whitney *U*, Chi-Square and log-rank tests. Secondary functional outcomes were assessed with questionnaires (American Orthopaedic Foot and Ankle Society (AOFAS) ankle-hindfoot score, Foot and Ankle Outcome Score (FAOS), EuroQol, and numeric rating scales (NRS) for pain and satisfaction) at multiple time points up to 1 year follow-up. To assess bone repair, CT scans were obtained at 2 weeks and 1 year postoperatively. Almost all outcome measures improved significantly in both groups. The percentage of sport resumption (PEMF, 79%; placebo, 80% ($p = 0.95$)) and time to resumption of sports (PEMF, median 17 weeks; placebo, 16 weeks ($p = 0.69$)) did not differ significantly between the treatment groups. Likewise, there were no significant between-group differences with regard to the secondary functional outcomes and the CT results. This study shows that PEMF does neither lead to a higher percentage of patients that resume sports nor to earlier resumption of sports after arthroscopic debridement and microfracture of talar OCDs.

Chapter 6

Computed tomography analysis after arthroscopic debridement and microfracture of osteochondral defects of the talus

The purpose of chapter 6 was to evaluate the dimensional changes and bony healing of talar OCDs after arthroscopic debridement and microfracture. Fifty-eight patients with a talar OCD were treated with arthroscopic debridement and microfracture. CT scans were obtained at baseline, two weeks postoperatively and one year postoperatively. Three-dimensional changes and bony healing were analyzed on CT scans. Additionally, clinical outcome was measured with the AOFAS score and NRS for pain. Average OCD size increased significantly ($p < 0.001$) in all directions from 8.6 (SD 3.6) × 6.3 (SD 2.6)× 4.8 (SD 2.3) mm (anterior–posterior × medial–lateral × depth) preoperatively

to 11.3 (SD 3.4) × 7.9 (SD 2.8) × 5.8 (SD 2.3) mm two weeks postoperatively. At one year follow-up, average defect size was 8.3 (SD 4.2) × 5.7 (SD 3.0) × 3.6 (SD 2.4) mm. Only average defect depth decreased significantly ($p<0.001$) from preoperative to one year postoperative. Fourteen of the 58 OCDs were well healed. No significant differences in the AOFAS and NRS-pain were found between the well and poorly healed OCDs. This study showed that arthroscopic debridement and microfracture of a talar OCD leads to an increased defect size on the direct postoperative CT scan but restores at one year follow-up. Only fourteen of the 58 OCDs were filled up completely but no differences were found between the clinical outcomes and defect healing at one year follow-up.

Chapter 7

Lift, drill, fill and fix (LDFF): a new arthroscopic treatment for talar osteochondral defects

The purpose of chapter 7 was to describe the short-term clinical outcome of a new arthroscopic fixation technique for primary talar OCDs: lift, drill, fill and fix (LDFF). Seven patients underwent an arthroscopic LDFF surgery for talar OCDs; the mean follow-up was 12 months (SD 0.6). Pre- and postoperative clinical assessment included the AOFAS score and NRS of pain at rest and during walking. Remodelling and bone ingrowth after LDFF were analyzed on weight-bearing radiographs during follow-up. In all patients, LDFF led to an improvement of the AOFAS and NRS-pain. The AOFAS significantly improved from 63 to 99 ($p<0.001$). The NRS-pain at rest significantly improved from 2.9 to 0.1 ($p=0.004$), and pain during walking significantly improved from 7.6 to 0.1 ($p<0.001$). On the final radiographs, five of seven patients showed remodelling and bone ingrowth after LDFF. This study showed that LDFF of a talar OCD appears to be a promising arthroscopic treatment option for primary defects. Although the clinical and radiological results of 1-year follow-up are encouraging, more patients and longer follow-up are needed to draw any firm conclusions and determine whether the results stand the test of time.

Chapter 8

Treatment of osteochondral defects of the talus in children

The purpose of chapter 8 was to evaluate the clinical and radiographic outcomes of conservative and primary surgically treated talar OCDs in skeletally immature children. Thirty-six (97%) of 37 eligible patients with a symptomatic primary talar OCD were

evaluated after a median follow-up of 4 years (range 1–12 years). Clinical assessment included the Berndt and Harty outcome question, Ogilvie-Harris score, Visual Analog Scale pain score (at rest, during walking and during running), the AOFAS score, and the SF-36. Weight-bearing radiographs were compared with preoperative radiographs with the use of an ankle osteoarthritis classification system. Ninety-two per cent of the initially conservatively treated children [mean age 13 years (SD 2)] were eventually scheduled to undergo surgery. After fixation of the fragment, seven cases (78%) reported a good Berndt and Harty outcome, and two cases (22%) a fair outcome; the median AOFAS score was 95.0 (range 77–100). After debridement and bone marrow stimulation, 13 cases (62%) reported a good Berndt and Harty outcome, three cases (14%) a fair outcome, and five cases (24%) a poor outcome; the median AOFAS score was 95.0 (range 45–100). No signs of degenerative changes were seen in both groups at follow-up. This study showed that fixation and debridement and bone marrow stimulation of a talar OCD are both good surgical options after failed conservative treatment.

Chapter 9

HemiCAP for secondary treatment for osteochondral talar defects

The optimal treatment for large OCDs of the talus or secondary treatment after failed surgery has to be determined yet. A metal implant with a diameter of 15 mm has been developed for the treatment of these lesions of the medial talar dome. We prospectively studied 20 consecutive patients for a mean of 4.5 years (3 to 5) post-surgery. There was statistically significant reduction of pain in rest, walking, and stair climbing ($p \leq 0.01$). The median AOFAS score improved from 62 (interquartile range (IQR) 46 to 72) pre-operatively to 85 (IQR 75 to 99) at final follow-up ($p < 0.001$). The FAOS improved on subscale pain, function, sports, and quality of life ($p \leq 0.01$). The mean SF-36 physical component scale improved from 36 (SD 8.2) pre-operatively to 45 (SD 9.4) at final follow-up ($p = 0.001$); the mental component scale did not change significantly. On radiographs, progressive joint space narrowing of the ankle was observed in two patients. One patient required additional surgery for the OCD. The mid-term results showed that a metal implant is a promising treatment for OCDs of the medial talar dome after failed previous surgery.

PART III GENERAL DISCUSSION AND SUMMARY

Chapter 10

General discussion

OCDs of the talus often have a severe impact on the quality of life of patients. Worldwide there is an ongoing debate on the optimal strategy in treating a symptomatic talar OCD. This thesis has contributed to the treatment of OCDs of the talus in various ways, with special focus on the subchondral bone. The literature was reviewed and the development of subchondral bone cysts as a result of fluid pressure has been hypothesized. MicroCT scans of human cadaveric tali have shown subchondral fissures which supports this hypothesis. CT scans after arthroscopic debridement and microfracture showed poor healing in 36% of the talar defects at one year follow-up. However, no differences were found between the clinical outcomes and defect healing on CT scan. PEMFs after arthroscopic debridement and microfracture do not accelerate the rehabilitation and bone repair. A new arthroscopic fixation technique for primary osteochondral talar defects led to good clinical outcomes in all seven patients at a mean follow-up of one year. Fixation and debridement and bone marrow stimulation of a talar OCD are both good surgical options in skeletally immature children. Finally, a novel metal implantation technique led to good clinical results in most patients at a mean follow-up of 4.5 years.

Several recommendations can be made for the treatment of talar OCDs on the basis of the thesis and current literature. Fixation of an OCD with a bony fragment should be considered as the primary treatment. Advantages of this technique are that it restores the natural congruency of the subchondral bone plate and preserves the hyaline cartilage. When an OCD is not fixable, arthroscopic debridement and microfracture is a good option in defects up to 1.5 cm in diameter.

In the current era of evidence based medicine, there is still no optimal surgical treatment in OCDs of the talus. The same type of OCD is often treated differently by the preference of the surgeon caused by great diversity and variability between studies. It is therefore important to base our knowledge on randomized controlled trials with uniform methodology and validated outcome measures.

Nederlandse samenvatting

Hoofdstuk 1

Algemene inleiding

Een osteochondraal defect (OCD) is een laesie van het kraakbeen en het subchondrale bot. In de ontwikkeling en behandeling van een OCD is een belangrijke functie weggelegd voor het subchondrale bot. Vloeistofdruk door een subchondraal fissuur lijkt een belangrijke rol te spelen in de pathogenese van subcondrale botcysten. Daarnaast kan een onregelmatige subchondrale botplaat na een chirurgische behandeling een negatief effect hebben op kraakbeenherstel en het ontwikkelen van arthrose. Het algemene doel van dit proefschrift was om de etiologie van (cysteuze)osteochondraal defecten te evalueren en verschillende chirurgische behandelopties te analyseren en verbeteren.

DEEL I – NATUURLIJKE HISTORIE EN SUBCHONDRALE BOTCYSTEN

Hoofdstuk 2

Osteochondraal defecten in de enkel; waarom pijnlijk?

In dit hoofdstuk wordt een literatuuroverzicht gegeven van osteochondraal defecten in de enkel. Deze defecten kunnen asymptomatisch blijven of leiden tot diepe enkelpijn tijdens belasten. Of een OCD symptomatisch wordt hangt van verschillende factoren af, waaronder de schade en insufficiënte herstel van de subchondrale botplaat. Het enkelgewricht heeft een hoge congruentie. Indien er een fissuur door het subchondrale bot aanwezig is kan er tijdens de belasting water vanuit het kraakbeen worden geperst. Dit kan tot een vergrote vloeistofdruk leiden in het subchondrale bot, wat resulteert in plaatselijke osteolyse en de ontwikkeling van een subchondrale botcyste. Pijn ontstaat niet van de kraakbeenlaesie maar wordt waarschijnlijk veroorzaakt door de repeterende hoge vloeistofdruk tijdens lopen. De drukopbouw zorgt voor de stimulatie van het sterk geïnnerveerde subchondrale bot onder het kraakbeen. Inzicht in de natuurlijke historie van osteochondraal defecten kan leiden tot preventietechnieken van enkelschade.

Hoofdstuk 3

Morfologische analyse van subchondrale botcysten in de talus met microCT

Het doel van hoofdstuk 3 was om de morfologie van humaan kadaver tali te evalueren met behulp van microCT en deze te vergelijken met de resultaten van een eerder morfologische simulatie studie. In een eerder simulatiestudie bleek dat vloeistofdruk verantwoordelijk is voor de groei van cysten. De groei ging gepaard met een onregelmatige cystevorm. Na het verwijderen van de vloeistofdruk werd de cyste rond en sclerotisch. Zesenzestig vers bevroren humaan kadaver tali werden met computertomografie (CT) gescreend op subchondrale cysten, radiologisch gedefinieerd als een radiolucent rond gebied. Vervolgens werden tali met een cyste gescand in een microCT. De vorm van de cysten, de aanwezigheid van een opening door de subchondrale botplaat en het botvolume rond en naast de cysten werden geanalyseerd. In totaal werden zes tali gevonden met een cyste. Vier cysten hadden een onregelmatige vorm, en twee cysten hadden een ronde vorm. Een duidelijke opening door de subchondrale botplaat werd in 4 cysten gevonden (diameter 0.5–1.7 mm). Het botvolume rond de cysten was hoger dan naast de cysten ($p=0.025$). Deze studie toonde aan dat de morfologische bevindingen vergelijkbaar zijn met de resultaten van een eerde gerapporteerde simulatiestudie. Het is daarom zeer waarschijnlijk dat vloeistofdruk een rol speelt in de pathofysiologie van cyste vorming. Meer inzicht over de groei van cysten kan de behandeling verbeteren en de groei stoppen.

DEEL II – CHIRURGISCHE BEHANDELING EN SUBCHONDRALE BOTGENEZING

Hoofdstuk 4

Diagnose en behandeling van osteochondraal defecten in de enkel

Een OCD van de talus is een laesie van het kraakbeen en het subchondrale bot. Het wordt vaak veroorzaakt na een enkeltrauma. Deze laesies kunnen genezen, stabiel blijven of leiden tot subchondrale botcysten. Subchondrale cysten ontstaan door de druk van kraakbeen- of synoviaal-vloeistof die tijdens elke stap in het defect wordt geperst. Een verkeerde uitlijning van de achtervoet speelt een belangrijke rol in de ontwikkeling van enkelarthrose. Een OCD kan zichtbaar zijn op routine röntgenfoto's. Moderne beeldvormende technologie heeft de mogelijkheid om een laesie nauwkeurig te evalueren. De grootte van de laesie is namelijk fundamenteel voor de juiste behandeling. Asymptomatische of mild symptomatische laesies worden conservatief behandeld.

Chirurgische behandelingen bestaan uit: uitruimen en beenmerg stimulatie, retrograad opboren, interne fixatie, spongieus botgraft, osteochondrale autologe transplantatie, autologe chondrocyten implantatie, en allograft transplantatie. Hoewel deze chirurgische opties vaak succesvol zijn, wordt er bij een verkeerde uitlijning niets aan de stand gedaan. Een calcaneus osteotomie is daarom geschikt voor specifieke gevallen.

Hoofdstuk 5

Effecten van gepulste elektromagnetische velden op sporthervatting na arthroscopisch uitruimen en microfracturing van osteochondraal defecten van de talus: een gerandomiseerde, dubbelblinde, placebo-gecontroleerde, multicenter trial.

In hoofdstuk 5 werd onderzocht of gepulste elektromagnetische velden (PEMF) na arthroscopisch uitruimen en microfracturing van een OCD van de talus tot een versnelde sporthervatting en een groter aantal patiënten dat sport hervat leidt. Achtenzestig patiënten werden gerandomiseerd naar PEMF (n = 36) of placebo (n = 32) na een arthroscopische behandeling van een OCD van de talus. De primaire uitkomsten, d.w.z. het aantal patiënten dat weer sport hervat en de tijd tot sporthervatting, werden geanalyseerd met Kaplan-Meier curven, Mann-Whitney *U*, Chi-kwadraat en log-rank testen. Secundaire functionele uitkomsten werden gemeten met vragenlijsten (American Orthopaedic Foot and Ankle Society (AOFAS) ankle-hindfoot score, Foot and Ankle Outcome Score (FAOS), EuroQol, en numerieke schalen (NRS) voor pijn en tevredenheid) op verschillende tijdstippen tot 1 jaar follow-up. Om botherstel te beoordelen, werden CT-scans 2 weken en 1 jaar postoperatief gemaakt. Bijna alle uitkomsten verbeterden significant in beide groepen. Het percentage van sporthervatting (PEMF, 79%, placebo 80% ($p = 0.95$)) en de tijd tot sporthervatting (PEMF, mediaan 17 weken, placebo 16 weken ($p = 0.69$)) verschilden niet significant tussen beide groepen. Ook waren er geen significante verschillen tussen de groepen wat betreft de secundaire functionele uitkomsten en de CT-scans. Deze studie toont aan dat PEMF niet leidt tot een versnelde sporthervatting, noch tot een hoger percentage van patiënten dat sport hervat na arthroscopisch uitruimen en microfracturing van een OCD van de talus.

Hoofdstuk 6

Computertomografie analyse na arthroscopisch uitruimen en microfracturing van osteochondraal defecten van de talus.

In hoofdstuk 6 werd de dimensionele veranderingen en bot genezing van osteochondraal defecten van de talus na arthroscopisch uitruimen en microfracturing onderzocht. Achtenvijftig patiënten met een OCD van de talus werden middels arthroscopisch uitruimen en microfracturing behandeld. CT-scans werden preoperatief, 2 weken postoperatief en 1 jaar postoperatief gemaakt. Driedimensionale veranderingen en bot genezing werden geanalyseerd op de CT-scans. Daarnaast werden klinische uitkomsten gemeten met behulp van de AOFAS score en NRS voor pijn. De gemiddelde grootte van het OCD steeg significant ($p<0.001$) in alle richtingen van preoperatief 8.6 (SD 3.6) x 6.3 (SD 2.6) x 4.8 (SD 2.3) mm (anterior – posterior × mediaal – lateraal × diepte) naar 2 weken postoperatief 11.3 (SD 3.4) × 7.9 (SD 2.8) × 5.8 (SD 2.3) mm. Na één jaar follow-up was het gemiddelde defect grootte 8.3 (SD 4.2) x 5.7 (SD 3.0) × 3.6 (SD 2.4) mm. Alleen de diepte van het defect was na één jaar follow-up significant ($p<0.001$) kleiner geworden in vergelijking tot preoperatief. Veertien van de 58 osteochondraal defecten waren goed genezen. Er werden geen significante verschillen gevonden in de AOFAS en NRS-pijn tussen goed en slecht genezende osteochondraal defecten. Deze studie toont aan dat arthroscopisch uitruimen en microfracturing van een OCD van de talus leidt tot toename van defect grootte op de direct postoperatieve CT-scan. Na één jaar follow-up herstelt het defect weer naar zijn oorspronkelijke grootte. Slechts veertien van de 58 osteochondraal defecten waren volledig opgevuld. Er werden geen verschillen gevonden tussen de klinische uitkomsten en de mate van botgenezing.

Hoofdstuk *7*

Liften, opboren, vullen en fixeren (LDFF): een nieuwe arthroscopische behandeling voor osteochondraal defecten van de talus

In hoofdstuk *7* werden de korte termijn resultaten van een nieuwe arthroscopische fixatietechniek (LDFF) voor primaire osteochondraal defecten van de talus beschreven. Zeven patiënten ondergingen een arthroscopische LDFF operatie voor osteochondraal defecten van de talus. De gemiddelde follow-up was 12 maanden (SD 0.6). Pre- en postoperatieve klinische uitkomsten werden gemeten met behulp van de AOFAS score en NRS voor pijn in rust en tijdens het lopen. Remodelering en botingroei na LDFF werden geanalyseerd op conventionele belaste röntgenfoto's tijdens de follow-up. Alle patiënten hadden een verbetering van de AOFAS en NRS-pijn na de LDFF procedure. De AOFAS verbeterde significant van 63 naar 99 ($p<0.001$). NRS-pijn in rust verbeterde significant

van 2.9 naar 0.1 ($p=0.004$), en NRS-pijn tijdens het lopen verbeterde significant van 7.6 naar 0.1 ($p<0.001$). Bij vijf van de zeven patiënten werd remodelering en botingroei gezien op de postoperatieve röntgenfoto's. Deze studie toont aan dat LDFF een veelbelovende arthroscopische behandeling lijkt voor primaire osteochondraal defecten van de talus. De klinische en radiologische resultaten van 1 jaar follow-up zijn bemoedigend. Echter zullen er meer patiënten met een langere follow-up nodig zijn om krachtige conclusies te kunnen trekken en vast te stellen of de resultaten stand houden.

Hoofdstuk 8

Behandeling van osteochondraal defecten van de talus bij kinderen

In hoofdstuk 5 werden de klinische en radiologische resultaten van conservatief en operatief behandelde osteochondraal defecten van de talus in niet uitgegroeide kinderen beschreven.

Zesendertig (97%) van de 37 patiënten met een symptomatische primaire OCD van de talus werden geëvalueerd na een mediane follow-up van 4 jaar (bereik 1–12 jaar). Klinische uitkomsten omvatten de Berndt en Harty uitkomst vraag, Ogilvie-Harris score, visueel analoge schaal voor pijn (in rust, tijdens het lopen en tijdens het hardlopen), de AOFAS score, en de SF-36. Belaste röntgenfoto's werden vergeleken met de preoperatieve röntgenfoto's en gescoord middels het enkelarthrose classificatiesysteem. Tweeënnegentig procent van de aanvankelijk conservatief behandelde kinderen [gemiddelde leeftijd van 13 jaar (SD 2)] werden uiteindelijk gepland voor een operatie. Na fixatie van het fragment, rapporteerde zeven gevallen (78%) een goede Berndt en Harty uitkomst, en twee gevallen (22%) een redelijke uitkomst; de mediane AOFAS score was 95,0 (bereik 77–100). Na uitruimen in combinatie met beenmerg stimulatie, rapporteerden 13 gevallen (62%) een goede Berndt en Harty uitkomst, drie gevallen (14%) een redelijke uitkomst, en vijf gevallen (24%) een slechte uitkomst; de mediane AOFAS score was 95,0 (bereik 45–100). In beide operatieve groepen werden geen degeneratieve veranderingen waargenomen bij follow-up. Deze studie toonde aan dat zowel fixatie als uitruimen in combinatie met beenmerg stimulatie van een OCD van de talus goede operatieve opties zijn na gefaalde conservatieve therapie bij kinderen.

Hoofdstuk 9

HemiCAP als secundaire behandeling voor osteochondraal defecten van de talus

De optimale behandeling van een groot of primair operatief gefaalde OCD van de talus moet nog worden bepaald. Een metalen implantaat met een diameter van 15 mm is ontwikkeld voor de behandeling van mediale laesies van de talus. We hebben 20 opeenvolgende patiënten prospectief onderzocht met een gemiddelde follow-up van 4.5 jaar (3–5). Statistisch significante vermindering van de pijn in rust, wandelen en traplopen ($p \leq 0.01$) werd gevonden. De mediane AOFAS score verbeterde van 62 (interkwartiel bereik (IQR) 46–72) preoperatief naar 85 (IQR 75–99) bij de laatste follow-up ($p < 0.001$). De subschalen pijn, functie, sport, en de kwaliteit van leven verbeterde ($p \leq 0.01$) op de FAOS. De gemiddelde SF-36 fysieke component schaal verbeterde van 36 (SD 8.2) preoperatief naar 45 (SD 9.4) bij de laatste follow-up ($p = 0.001$); de mentale component schaal veranderde niet significant. Op röntgenfoto's werd progressieve gewrichtvernauwing bij 2 patiënten geconstateerd. Eén patiënt kreeg additionele chirurgie in verband met pijnklachten aan het OCD. De middellange termijn resultaten van een metalen implantaat bij een OCD van de mediale talus na gefaalde chirurgie lijkt veelbelovend.

DEEL III – ALGEMENE DISCUSSIE EN SAMENVATTING

Hoofdstuk 10

Algemene discussie

Osteochondraal defecten van de talus hebben regelmatig een negatief effect op de kwaliteit van leven van patiënten. Wereldwijd is er nog steeds discussie over de optimale behandelstrategie van symptomatische osteochondraal defecten van de talus. Dit proefschrift heeft op verschillende manieren bijdrage geleverd aan de behandeling van OCD van de talus, met extra aandacht voor het subchondrale bot. Literatuuronderzoek is verricht waarbij de ontwikkeling van subchondrale botcysten als gevolg van vloeistofdruk werd gesuggereerd. Op microCT-scans van humaan kadaver tali werden subchondrale fissuren gevonden wat de vloeistofdruk hypothese ondersteunt. Op CT-scans na één jaar follow-up werd in 36% van de osteochondraal defecten van de talus een slechte botgenezing gezien na arthroscopisch uitruimen en microfracturing. Echter werden geen verschillen gevonden tussen de klinische uitkomsten en de mate van botgenezing op CT-scans. PEMF na arthroscopisch uitruimen en microfracturing leidt niet tot een versnelde sporthervatting en botherstel. Een nieuwe arthroscopische fixatie techniek

voor primaire osteochondraal defecten van de talus liet goede klinische uitkomsten zien bij alle 7 patiënten met een gemiddelde follow-up van één jaar. Zowel fixatie als uitruimen in combinatie met beenmerg stimulatie van een OCD zijn goede operatieve opties bij kinderen. Tenslotte werden goede resultaten in de meeste patiënten gevonden met een nieuwe metaal implantatietechniek na een gemiddelde follow-up van 4.5 jaar.

Verschillende aanbevelingen in de behandeling van een OCD kunnen worden gegeven op basis van dit proefschrift en huidige literatuur. Fixatie van een OCD met een benig fragment moet worden beschouwd als de primaire behandeling. De voordelen van deze techniek zijn het herstel van de natuurlijke congruentie van de subchondrale botplaat en het behoudt van hyalien kraakbeen. Arthroscopisch uitruimen en microfracturing is een goede optie voor defecten tot 1.5 cm in diameter indien een OCD niet fixeerbaar is.

Er is nog steeds geen optimale chirurgische behandeling voor een OCD van de talus op basis van de huidige evidence-based medicine. Hetzelfde type OCD wordt vaak anders behandeld door de voorkeur van de chirurg als gevolg van grote diversiteit en variatie tussen de studies. Het is daarom belangrijk om onze kennis te baseren op gerandomiseerde gecontroleerde studies met een uniforme methodiek en gevalideerde uitkomstmaten.

PART IV

Addendum

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PhD portfolio

Name M.L. Reilingh
PhD period 2008 – 2011
Promotores Prof. dr. C.N. van Dijk
Prof. dr. G.M.M.J. Kerkhoffs
Copromotor Dr.ir. L. Blankevoort

1. PHD TRAINING

Courses	Year
Scientific writing in English for publication	2009
Evidence based searching	2009
Practical biostatistics	2009
BROK ('Basiscursus Regelgeving Klinisch Onderzoek')	2009
Oral presentation	2010

Podium presentations	Year
Return to competition after injury. Dutch Soccer Academy (NVA) 2010 May 3, Hoenderloo, Netherlands	2010
Fluid pressure may lead to subchondral bone cyst development via mechanoregulated bone remodeling. ASME Summer Bioengineering Conference 2010 June 16-19, Naples, USA	2010
Mechanoregulated bone remodeling may explain bone structural changes in osteoarthritis. Congress of the European Society of Biomechanics 2010 July 5-8, Edinburgh, United Kingdom	2010
Metal implantation resurfacing for secondary osteochondral defects of the talus: first results of a prospective clinical study. EFFORT Congress 2011 June 1-4, Copenhagen, Denmark	2011
The optimal calcaneal osteotomy angle based on a simplified static force analysis. International Society of Biomechanics Congress 2011 July 3-7, Brussels, Belgium	2011
Postoperatieve losse fragmenten na arthroscopische nettoyage en microfracturing van osteochondraal defecten van de talus. NOV congres 2011 Oktober 6-7, Noordenwijk, Netherlands	2011
Een nieuwe methode om het verschil in botvolume te meten na nettoyage en microfracturing van een osteochondraal defect. NOV congres 2011 Oktober 6-7, Noordenwijk, Netherlands	2011
Metal implantation for secondary osteochondral defects of the talus: a prospective study. BOFAS conference 2011 November 2-4, Old Windsor, England	2011

Metal implantation for secondary osteochondral defects of the talus: a prospective study. AAOS 2012 February 7-11, San Francisco, USA	2012
The influence of foot geometry on the calcaneal osteotomy angle based on two-dimensional static force analysis. AAOS 2012 February 7-11, San Francisco, USA	2012
Metal implantation resurfacing for secondary osteochondral defects of the talus. ESSKA-AFAS 2012 April 13, Moscow, Russia	2012
Metal implantation resurfacing for secondary osteochondral defects of the talus. ESSKA 2012 May 2-5, Geneva, Switzerland	2012
Metallic resurfacing for the treatment of secondary defects of the talus: preliminary results of a prospective clinical study. XXXII Congresso Nacional de Orthopedia a Traumatologia 2012 October 17-19, Marina Vilamoura, Portugal	2012
Influence of basal support and early loading on bone cartilage healing in press-fitted osteochondral autografts. EFORT 2013 June 5-8, Istanbul, Turkey	2013
Fixation of osteochondral talar defects. ESSKA-AFAS 2014 April 11-12, Prague, Czech Republic	2014
Metal resurfacing inlay implant for osteochondral defects of the talus after failed previous surgery: a prospective study. ESSKA 2014 May 14-17, Amsterdam, Netherlands	2014
Metal resurfacing inlay implant for osteochondral talar defects after failed surgery: a prospective study. AAOS 2015 March 24-28, Las Vegas, USA	2015
Effects of pulsed electromagnetic fields on return to sports after arthroscopic debridement and microfracturing of osteochondral talar defects: a randomized, double-blind, placebo-controlled, multicenter trial. NVA 2015 May 21-22, Noordwijk, Netherlands	2015
Lift, drill, fill and fix (LDFF): A new arthroscopic treatment for talar osteochondral defects. ESSKA 2016 May 4-7, Barcelona, Spain	2016
Pulsed electromagnetic fields after arthroscopic treatment for OCD of the talus: a randomized, double-blind, multicenter trial. ESSKA 2016 May 4-7, Barcelona, Spain	2016

Poster presentations	**Year**
De optimale calcaneus osteotomie hoek middels een krachten analyse. SEOHS 2010 November 19, Rotterdam, Netherlands	2010
Novel metal implantation technique for secundary osteochondral defects of the talus: preliminary results. ESSKA Congress 2010 June 9-12, Oslo, Norway	2010
Second-look arthroscopic findings after metal implantation for osteochondral defects of the talus. NVA 2014 April 4, Den Bosch, Netherlands	2014

2. TEACHING

Supervising	**Year**
Summer course: Hindfoot geometry. Stephanie Klein Ikkink, Medical student Academic Medical Center, Amsterdam, Netherlands	2010

Summer course: Force analyses of the hindfoot. Eveline Verheij, Medical student Academic Medical Center, Amsterdam, Netherlands	2010
Summer course: Bone volume measurements after debridement and microfracture of osteochondral talar defects. Rogier Gerards, Medical student Academic Medical Center, Amsterdam, Netherlands	2011
Summer course: Loose bodies analysis after arthroscopic debridement and microfracture of osteochondral talar defects. Rogier Gerards, Medical student Academic Medical Center, Amsterdam, Netherlands	2011
Master thesis: Treatment of osteochondral defects of the talus in children. Caroline Telkamp, Medical student Academic Medical Center, Amsterdam, Netherlands	2011

Other	**Year**
Guest lecture at TU Delft: treatment in osteochondral talar defects	2010
Guest lecture at college art school: human anatomy	2010
Guest lecture at TU Delft: treatment in osteochondral talar defects	2011
Guest lecture at college art school: human anatomy	2011
Guest lecture at AMC department Trauma Surgery: hamstring injuries	2016
Faculty and Instructor of the Amsterdam Foot and Ankle Course	2012-2016
Reviewer for the journal Knee Surg Sports Traumatol Arthrosc	2014-2016

3. PARAMETERS OF ESTEEM

Awards and Prized	**Year**
Metallic resurfacing for the treatment of secondary defects of the talus: preliminary results of a prospective clinical study. XXXII Congresso Nacional de Orthopedia a Traumatologia 2012 October 17-19, Marina Vilamoura, Portugal ***(Winner of the best free paper)***	2012
Effects of pulsed electromagnetic fields on return to sports after arthroscopic debridement and microfracturing of osteochondral talar defects: a randomized, double-blind, placebo-controlled, multicenter trial. NVA 2015 May 21-22, Noordwijk, Netherlands ***(Winner of Dr. Eikelaar award)***	2015

4. PUBLICATIONS

Peer reviewed	**Year**
Reilingh ML, Kuijpers T, Tanja-Harfterkamp AM, van der Windt DA. Course and prognosis of shoulder symptoms in general practice. Rheumatology 2008;47:724-730	2008
Reilingh ML, Kuijpers T, Tanja-Harfterkamp AM, van der Windt DA. Het beloop en de prognose van schouderklachten: verschillen tussen acute en chronische klachten. Huisarts Wet 2008;51:542-548	2008

Reilingh ML, van Sterkenburg MN, de Leeuw PAJ, van Dijk CN. Ankle arthroscopy, indications, technique and complications. South Afr Orthop J 2009;8:51-58 — 2009

Reilingh ML, van Bergen CJ, van Dijk CN. Diagnosis and treatment of osteochondral defects of the ankle. South Afr Orthop J 2009;8:44-50 — 2009

Reilingh ML, Hartemink KJ, Hoksbergen AWJ, Saouti R. Occlusion of the common femoral artery by cement: case report. J Med Case Reports 2009;3:86 — 2009

Reilingh ML, de Leeuw PAJ, van Sterkenburg MN, van Dijk CN. Tendoscopy of posterior tibial and peroneal tendons. Tech Foot Ankle Surg 2010;9:43-47 — 2010

Reilingh ML, Beimers L, Tuijthof GJM, Stufkens SAS, Maas M, van Dijk CN. Measuring hindfoot alignment radiographically: the long axial view is more reliable than the hindfoot alignment view. Skeletal Radiol 2010;39:1103-1108 — 2010

van Dijk CN, **Reilingh ML**, Zengerink M, van Bergen CJ. Osteochondral defects in the ankle; why painful? Knee Surg Sports Traumatol Arthrosc 2010;18:570-580 — 2010

van Dijk CN, **Reilingh ML**, Zengerink M, van Bergen CJ. The natural history of osteochondral lesions in the ankle. Instr Course Lect 2010;59:375-386 — 2010

van Ooij B, Kaas L, **Reilingh ML**, van Dijk CN. Osteochondral defects of the talus: surgical treatment and rehabilitation. Archivio di Orthopedia e Reumatologia 2010;141:17-18 — 2010

Trof RJ, Danad I, **Reilingh MW**, Beukers RM, Groeneveld ABJ. Cardiac filling volume versus pressures for predicting fluid responsiveness after cadiovascular surgery: the role of systolic cardiac function. Crit Care 2011;15:R73 — 2011

van Bergen CJ, **Reilingh ML**, van Dijk CN. Tertiary osteochondral defect of the talus treated by a novel countoured metal implant. Knee Surg Sports Traumatol Arthrosc 2011;19:999-1003 — 2011

Wiegerinck JI, **Reilingh ML**, de Jonge MC, van Dijk CN, Kerkhoffs GM. Injection technique of platelet-rich plasma into and around the Achilles tendon: a cadaveric study. Am J Sports Med 2011;39:1681-1686 — 2011

Reilingh ML, van Dijk CN. Comments on: "osteochondral lesions of the talus: current concept" by O. Laffenêtre published in Orthop Traumatol Surg Res 2010;96: 554-66. Orthop Traumatol Surg Res 2011;97:461-462 — 2011

Reilingh ML, Tuijthof GJM, van Dijk CN, Blankevoort L. The influence of foot geometry on the calcaneal osteotomy angle based on two-dimensional static force analyses. Arch Orthop Trauma Surg 2011;131:1491-1497 — 2011

Cox LGE, Lagemaat MW, van Donkelaar CC, van Rietbergen B, **Reilingh ML**, Blankevoort L, van Dijk CN, Ito K. The role of pressurized fluid in subchondral bone cyst growth. Bone 2011;49:762-768 — 2011

Nosewicz TL, **Reilingh ML**, van Dijk CN, Duda GN, Schell H**.** Weightbearing ovine osteochondral defects heal with inadequate subchondral bone plate restoration: implications regarding osteochondral autograft harvesting. Knee Surg Sports Traumatol Arthrosc 2012;20:1923-1930 — 2012

Reilingh ML, van Bergen CJ, van Dijk CN. Novel Metal implantation technique for osteochondral defects of the medial talar dome. Tech Foot Ankle Surg 2012;11:45-49	2012
van Eekeren IC, **Reilingh ML**, van Dijk CN. Rehabilitation and Return-to-Sports Activity after Debridement and Bone Marrow Stimulation of Osteochondral Talar Defects. Sports Med 2012;42:857-870	2012
van Bergen CJ, Tuijthof GJ, **Reilingh ML**, van Dijk CN. Clinical tip: aiming probe for a precise medial malleolar osteotomy. Foot Ankle Int 2012;33:764-766	2012
Reilingh ML, Blankevoort L, van Eekeren IC, van Dijk CN. Morphological analysis of subchondral talar cysts on microCT. Knee Surg Sports Traumatol Arthrosc 2013;21:1409-1417	2013
van Bergen CJ, van Eekeren IC, **Reilingh ML**, Sierevelt IN, van Dijk CN. Treatment of osteochondral defects of the talus with a metal resurfacing inlay implant after failed previous surgery: a prospective study. Bone Joint J 2013;12:1650-1655	2013
Nosewicz TL, **Reilingh ML**, Wolny M, van Dijk CN, Duda GN, Schell H**.** Influence of basal support and early loading on bone cartilage healing in press-fitted osteochondral autografts. Knee Surg Sports Traumatol Arthrosc 2014;22:1445-1451	2014
Reilingh ML, Kerkhoffs GM, Telkamp CJ, Struijs PA, van Dijk CN. Treatment of osteochondral defects of the talus in children. Knee Surg Sports Traumatol Arthrosc 2014;22:2243-2249	2014
Nieuwe Weme R, **Reilingh ML**, van der Vis H. Trekkebenen na een rugoperatie. Medisch Contact 2014;10:481	2014
van Bergen CJ, van Eekeren IC, **Reilingh ML**, Gerards RM, van Dijk CN. The use of HemiCAP for the treatment of osteochondral lesions. Oper Tech Orthop 2014;24:190-194	2014
Kerkhoffs GM*, **Reilingh ML***, Gerards RM, de Leeuw PA. Lift, drill, fill and fix (LDFF): a new arthroscopic treatment for talar osteochondral defects. Knee Surg Sports Traumatol Arthrosc 2016;24:1265-1292,**(* both authors share first authorship)**	2016
Reilingh ML, van Bergen CJ, Blankevoort L, Gerards RM, van Eekeren IC, Kerkhoffs GM, van Dijk CN. Computed tomography analysis of osteochondral defects of the talus after arthroscopic debridement and microfracture. Knee Surg Sports Traumatol Arthrosc 2016; 24:1286-1292	2016
van Eekeren IC, van Bergen CJ, Sierevelt IN, **Reilingh ML**, van Dijk CN. Return to sports after arthroscopic debridement and bone marrow stimulation of osteochondral talar defects: a 5- to 24-year follow-up study. Knee Surg Sports Traumatol Arthrosc 2016;24:1311-1315	2016
Sierevelt IN, van Eekeren IC, Haverkamp D, **Reilingh ML**, Terwee CB, Kerkhoffs GM. Evaluation of the dutch version of the Foot and Ankle Outcome Score (FAOS): responsiveness and minimally important change. Knee Surg Sports Traumatol Arthrosc 2016;24:1339-1347	2016

Reilingh ML, van Bergen CJ, Gerards RM, van Eekeren IC, de Haan RJ, Sierevelt IN, Kerkhoffs GM, Krips R, Meuffels DE, van Dijk CN, Blankevoort L. Effects of Pulsed Electromagnetic Fields on Return to Sports After Arthroscopic Debridement and Microfracture of Osteochondral Talar Defects: A Randomized, Double-Blind, Placebo-Controlled, Multicenter Trial. Am J Sports Med 2016;44:1292-1300	2016

Book chapters	**Year**
van Dijk CN, **Reilingh ML**, Zengerink M, van Bergen CJ. The natural history of osteochondral lesions in the ankle. In: O'Connor MI, Egol KA, editors. Instructional course lectures. 1st ed. Rosemont: American Academy of Orthopaedics Surgeons; 2010. p. 375-386	2010
Reilingh ML, de Leeuw PAJ, van Sterkenburg MN, van Dijk CN. Posterior ankle arthroscopy and tendoscopy. In: Fu F, Schreiber VM, editors. Master techniques in orthopaedic surgery. 1st ed. Philadelphia: Lippincott Williams & Wilkins; 2010. p. 575-588	2010
van Eekeren ICM, **Reilingh ML**, van Dijk CN. Calcaneal osteotomy for retrocalcaneal bursitis. In: Calder J, Karlsson J, Maffulli N, Thermann H, van Dijk CN, editors. Disorders of the Achilles tendon insertion.1st ed. Guildford: DJO Publications; 2012. p. 131-136	2012
Reilingh ML, van Dijk CN. Talar Dome Resurfacing with the HemiCAP Prosthesis. In: van Dijk CN, Kennedy JG, editors. Talar osteochondral defects. 1st ed. Würzburg: Springer; 2014. p. 145-150	2014
Reilingh ML, Kerkhoffs GMMJ. Lift, drill, fill, fix (LDFF): a cartilage preservation technique in osteochondral talar defects. In: Canata GL, van Dijk CN, editors. Cartilage lesions of the ankle. 1st ed. Berlin: Springer; 2015. p. 77-85	2015
Reilingh ML, van Bergen CJ, Gerards RM, van Eekeren IC, van Dijk CN. HemiCAP for secondary treatment for osteochondral talar defects. In: Randelli P, Dejour D, van Dijk C.N, Denti M, Seil R, editors. Arthroscopy. 1st ed. Berlin: Springer; 2016. p. 1013-1022	2016

Curriculum Vitae

Mikel Reilingh was born (1983) in Purmerend and raised in Amsterdam, the Netherlands. After graduating from high school (VWO, Caland Lyceum, Amsterdam) in 2002, he studied medicine at the VU University Medical Center. During his study he was a student assistant in physiology, clinical education and medical ethics. In the final year of study, a clinical internship at the department of orthopedic surgery of the Slotervaart Medical Center (prof. dr. R.G. Pöll) and the VU University Medical Center (prof. dr. B.J. van Royen) made him enthusiastic to continue in this working field. After obtaining his medical degree in 2008 he started to work as a PhD student at the department of orthopedic surgery of the Academic Medical Center in Amsterdam (prof. dr. C.N. van Dijk & prof. dr. G.M.M.J. Kerkhoffs), which resulted in this thesis. During the 3-year period, he organized the 10th and 11th Amsterdam Foot and Ankle Course and presented his research at national and international congresses. In 2011, he started his orthopedic residency at the department of general surgery of the Diakonessenhuis in Utrecht (dr. G.J. Clevers). He continued his residency at the departments of orthopedic surgery of the Slotervaart Medical Center (dr. H. van der Vis) and the Academic Medical Center (prof. dr. C.N. van Dijk & prof. dr. G.M.M.J. Kerkhoffs). He will continue at the Amphia Ziekenhuis Breda (prof. dr. D. Eygendaal) and finish his training at the Slotervaart Medical Center at the end of 2017. In 2007 Mikel married Nadia al Maach, with whom he has two sons and one daughter. Faisel was born in 2010, followed by Nouri in 2013, and Sara in 2014.