Treatment of osteochondral defects of the talus
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Chapter 1

General introduction
Historical perspective

An osteochondral defect or lesion involves the articular cartilage and the subchondral bone. The challenge of treating osteochondral defects and cartilage diseases in general has been recognized for a long time. In 1743, Hunter stated that "From Hippocrates down to the present age, ulcerated cartilage is a troublesome disease; when destroyed, it is not recovered." In 1856, Monro first reported the presence of cartilaginous bodies. König in 1888 first used the term *osteochondritis dissecans* (dissecans, derived from the Latin word *dissec*, which means to separate) to describe loose bodies in the knee joint, theorizing that they were caused by spontaneous necrosis of bone or an inflammatory process.

In 1922, Kappis noted the similarity of lesions of the ankle to those found in the knee and referred to osteochondritis dissecans of the ankle. In 1932, Rendu reported an intra-articular fracture of the talus that appeared to be similar in nature to the lesion of osteochondritis dissecans. In 1953, Rödén et al. reported on 55 osteochondritis dissecans-like lesions of the talus. They concluded that almost all of the lesions occurring laterally in the talus were secondary to trauma. Conversely, a large percentage of the medial lesions in their series were not secondary to trauma. Berndt and Harty in 1959 demonstrated that both the medial and lateral lesions of osteochondritis dissecans of the talus were in reality transchondral (osteochondral) fractures caused by trauma. In their classic work, 43% of the lesions were noted to be in the lateral portion, usually the middle third of the talus, while 57% were noted to be in the medial portion, usually the posterior third.

Etiology

Nowadays, it is widely accepted that a traumatic insult is the most frequent etiologic factor in osteochondral defects (OCDs) of the talus. Trauma has been reported in 93% to 98% of lateral talar lesions and in 61% to 70% of medial lesions.

Ankle sprains cause intra-articular pressure impact and have a prominent role in the development of traumatic OCDs (Figure 1). The trauma causing the lesion can be a single event or a series of less intense (micro) traumas, which may remain unrecognized in some cases. Lateral lesions usually are deep and cup shaped and caused by a shear mechanism. In contrast, medial lesions usually are deep and oval and caused by torsional impaction.

Figure 1. During an ankle sprain, the talus twists inside the ankle mortise. Osteochondral talar defects can be caused by local high compression in the articulation during this movement and are typically localized on the medial or lateral talar dome (**).
and axial loading of the talocrural joint. Rotation of the talus inside the ankle mortise during an ankle sprain can damage the cartilage lining, leading to bruising and subsequent softening of the cartilage or cracking of the cartilage with subsequent delamination. Separation in the upper layer of the cartilage occurs as a result of shear stresses. 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 may remain partially attached and stay in position.

Yet, not all patients report a history of ankle injury. The etiology of nontraumatic, idiopathic lesions may involve ischemia, necrosis, or genetics. OCDs of the talus have been described in identical twins and siblings. Furthermore, the defect is bilateral in 4% to 7% of the patients. These facts suggest a nontraumatic origin and possibly a genetic predisposition.

Epidemiology

The most common site of osteochondral lesions is the knee, followed by the ankle and elbow. Symptomatic OCDs of the talus usually appear in the second or third decade of life. Men are affected more often than women. The exact incidence of these lesions in the general population is unknown. Approximately 1 in 10,000 people per day suffers an ankle injury. In athletes, this number can be as high as 9.4 per 10,000 athlete-exposures during active competition. Talar OCDs occur in 15% to 25% of these injuries. In the military, the overall incidence of OCDs has been reported 27 per 100,000 person-years. A cadaver study using 72 paired ankles found (osteo)chondral talocrural lesions in 58 (81%) specimens, of which two thirds were on the talus. These data suggest that OCDs are common but not always cause symptoms.

In light of increased awareness and continued evolution of imaging and treatment modalities, more attention has been given to the diagnosis of OCD during the past decades. In the 1990s and early 2000s, full thickness talar defects were found in 3% to 4% of patients with lateral ligament rupture or chronic ankle instability. Later, studies reported OCD rates of 19% to 21% in patients with chronic ankle instability. An incidence of up to 71% has been reported in patients with ankle fractures. OCDs of the talus have been described in identical twins and siblings. Furthermore, the defect is bilateral in 4% to 7% of the patients. These facts suggest a nontraumatic origin and possibly a genetic predisposition.

Cartilage physiology

Articular cartilage consists mainly of extracellular matrix and a sparse population of chondrocytes. The extracellular matrix consists of collagen, hyaluronic acid, proteoglycans, and a small quantity of glycoproteins. Chondrocytes lie in groups in the lacunae of the extracellular matrix they produce. Cartilage does not contain lymph vessels or nerves and has a slow metabolism. It is avascular and is nourished by diffusion from the intra-articular synovial fluid. Water accounts for approximately 75% of the total weight of the cartilage. It functions as a transport medium. The frictional resistance of the water through the pores of the extracellular matrix and the pressurization of the water are the basic mechanisms from which articular cartilage derives its ability to support very high joint loads.

The cartilage of the talar dome is thin when compared with that of other joint surfaces. The mean cartilage thickness of the talar dome is in the range 1.2 to 1.4 mm. In comparison, the average thickness of the cartilage in the hip and knee is 1.6 mm (range, 1.4 – 2.0 mm) and 2.2 mm (range, 1.7 – 2.6 mm), respectively.

The thickness of the cartilage appears to be related to the congruence of a joint. The
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ankle (with the thinnest articular cartilage) is a congruent joint, and the knee (with the thickest cartilage) is an incongruent joint. It has been hypothesized that congruent joint surfaces are covered only by thin articular cartilage because the compressive loads are spread over a wide area, decreasing local joint stresses. Incongruent joints are covered by thicker cartilage, which deforms more easily.

Cartilage is able to withstand compressive stress because of the interaction of its fluid and solid components. Its viscoelasticity is based on the electrostatic connections between collagen fibers and glycosaminoglycan (GAG) side chains of the proteoglycans, the flexibility and sliding qualities of the collagen fibers, and the displacement of water in cartilage. The water is a dialysate of synovial fluid. It is incompressible but able to flow. It is contained in the matrix by the negatively loaded GAGs. Furthermore, 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 and proteoglycan matrix components) offers considerable resistance to interstitial fluid flow. These characteristics provide adequate containment for the fluid to support the loads that joints sustain. Herberhold et al. studied the effect of patellofemoral compression during a 4-hour continuous static loading of 150% of body weight. The maximal thickness reduction was 57% in patellar cartilage. These findings suggest that more than 50% of the interstitial fluid can be displaced from the matrix. When one part of the joint is in compression, fluid flows from the loaded area to the unloaded area, thereby increasing the load-bearing area and decreasing the stress per unit area.

The load-bearing area of the ankle joint is relatively small compared to the forces it transmits. The load on the remaining cartilage increases when the contact surface area decreases in size, for example, after a malreduction of an ankle fracture or by an OCD. Ramsey and Hamilton found that a 1-mm lateral talar shift, as occurs after an ankle fracture malunion, reduces the contact area by 42%, and a 2-mm lateral shift reduces the contact area by 58%. A 1-mm shift generally is considered acceptable, while a 2-mm shift should be surgically corrected because of the high risk of degenerative changes. Apparently, the talar cartilage can adapt to an increase in contact stress as great as 42%. These findings concur with studies on contact stresses caused by OCDs. Christiansen et al. evaluated the effect of talar OCDs graduated in size. Significant changes in contact stresses were demonstrated only for larger lesions (diameter, ≥15 mm). Likewise, Hunt et al. studied progressively larger OCDs up to 12 mm and found no change in peak stress magnitude. It has been postulated by van Dijk that the increase in load caused by a small OCD probably is not large enough to cause damage to the remaining cartilage in a normally aligned ankle. However, any varus or valgus malalignment increases the likelihood of cartilage damage by high contact stresses.

Importance of the subchondral bone

Articular cartilage is supported by the subchondral bone plate. The subchondral bone is crucial for the load-bearing capacity of the joint and for survival of chondrocytes. It has been suggested that the release of soluble factors from subchondral bone may influence chondrocyte survival. Van Dijk has underlined the importance of the subchondral bone in talar OCDs. The morphologic features suggest that the main area of action is around the subchondral bone plate. Samples harvested from patients with OCDs of the knee all have (micro) fractured areas in the subchondral and underlying cancellous bone, besides a loss of GAGs from the damaged extracellular cartilage matrix and...
a decrease in the number of chondrocytes. A decrease in the number of chondrocytes is common. Damaged subchondral bone is less able to support the overlying cartilage, and cartilage that is not supported by the underlying bone plate loses proteoglycans and glycoprotein, which causes a decrease in water containment.

In a healthy joint, the cartilage fluid is not able to enter the subchondral plate. Van Dijk et al. have theorized that traumatic microfractures of the subchondral bone plate allow the fluid not only to flow within the cartilage but also to enter the subchondral bone through defects in the subchondral bone surface. 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. Similarly, the synovial fluid of the ankle joint may be pressed through the (micro) defect in the cartilage layer into the damaged area of the subchondral bone. Different investigations have supported the theory. The high local fluid pressure can lead to osteonecrosis, bone resorption, and formation of lytic areas, causing a cyst.

Clinical presentation

An OCD may not be recognized and therefore not adequately treated. The lack of recognition may be due to the fact that the symptoms resemble those of the previous trauma. The symptoms of a nondisplaced acute lesion often are masked by swelling and pain from the lateral ligament lesion. Swelling, limited range of motion, and pain on weight bearing may persist after the symptoms of the ligament injury have resolved. If the symptoms of deep ankle pain on weight bearing persist after 6 weeks, an OCD should be suspected.

The typical symptom of a chronic lesion is persistent or intermittent deep ankle pain during or after activity. Reactive swelling or joint stiffness may be present. Most patients have normal range of motion without swelling or tenderness on palpation. Locking and catching may be present in the case of a displaced fragment. However, the absence of swelling, locking, or catching does not rule out the presence of an OCD.

The pain probably does not arise from the cartilage but from the innervated subchondral bone. Patients usually feel deep ankle pain caused by the OCD. Increased intraosseous pressure has been reported as a cause of pain. The nerve endings in the subchondral bone are the most probable cause of this pain.

Imaging

Radiographs (weight-bearing anteroposterior mortise and lateral views) are the preferred initial investigation for a suspected OCD. The sensitivity and specificity of the combination of medical history, physical examination and radiography are 59% and 91%, respectively. An anteroposterior heel rise view with the ankle in a plantarflexed position may reveal a posteriorly located defect. The radiographs may show an area of detached bone or radiolucency. Initially, the damage may be too small to be visualized on routine radiography. By repeating the imaging in a later stage, the abnormality sometimes becomes apparent.

Computed tomography (CT) and magnetic resonance imaging (MRI) allow multiplanar and 3-dimensional evaluation. The sensitivity and specificity of CT to detect an OCD are 0.81 and 0.99, respectively; those of MRI are 0.96 and 0.96. In diagnosing a talar OCD, CT is as accurate as
MRI (p = 0.33).\textsuperscript{440} CT is useful in determining the size, location, shape and degree of displacement of osteochondral fragments, and is therefore valuable in preoperative planning.\textsuperscript{160,370,440,457} MRI offers the advantage of visualizing bone bruises, articular cartilage damage, and other soft tissue insults, but signal patterns in the talus may overestimate the severity of the bone injury.\textsuperscript{303}

Treatment

Treatment options for OCDs are numerous. There is worldwide debate on the optimal strategy. In our clinic, several systematic reviews of the literature have been performed through the years.\textsuperscript{393,439,458} The most recent update by Zengerink et al. included 52 studies with a total of 1361 patients.\textsuperscript{458} The highest success rates were reported for bone marrow stimulation (85%) and osteochondral autograft transfer (87%). Because osteochondral autograft transfer can cause knee morbidity, the conclusion was that debridement and bone marrow stimulation remains the treatment of choice for primary OCDs (i.e., those without previous surgery) up to 15 mm.\textsuperscript{458}

During debridement and bone marrow stimulation, the OCD is preferably approached by anterior ankle arthroscopy with the ankle in full plantar flexion for adequate exposure of the defect.\textsuperscript{424} Most lesions of the anterior and central talar dome can be accessed with this technique. However, the ankle is a congruent joint with limited surgical access. Some defects are located so far posteriorly that they may not be accessible by anterior ankle arthroscopy. Alternatively, the OCD is exposed by posterior arthroscopy with the patient in the prone position or by open surgery. Whether the OCD can be reached by anterior ankle arthroscopy may often be unclear preoperatively. A predictive modality is required that preoperatively identifies the accessibility of the defect by the arthroscope. Moreover, quantification of normative data of the arthroscopic reach of the talus may be helpful for the planning of the surgical approach. Identifying predictive factors of the arthroscopic reach (e.g., patient characteristics and ankle function) may further improve the preoperative planning process.

Many studies report good to excellent short- and mid-term outcomes of debridement and bone marrow stimulation.\textsuperscript{458} However, little is known about the long-term outcome. There are concerns that the fibrocartilage that is formed after this procedure may deteriorate over time, resulting in osteoarthritic changes.\textsuperscript{262,303} Therefore, a long-term follow-up study is required.

The rehabilitation after debridement and bone marrow stimulation for symptomatic OCDs may take up to 1 year postoperatively. Many patients aim to achieve resumption of sport activities. A potential solution to accelerate postoperative rehabilitation and shorten the period to sport resumption is the application of pulsed electromagnetic fields (PEMFs). PEMFs have been shown to suppress inflammation, promote tissue healing, and relieve pain.\textsuperscript{436} They have been used successfully in healing of nonunited fractures and in recovery after arthroscopic treatment of knee lesions.\textsuperscript{161,441,462} However, the effectiveness of PEMFs for talar OCDs is unknown.

Lesions after failed previous surgery or large lesions can be treated by various alternative surgical methods, including autologous cancellous bone grafting, osteochondral autograft transfer, and (matrix-associated) autologous chondrocyte implantation.\textsuperscript{457} Although successful results can be achieved, disadvantages of these secondary methods include pain at the donor site, limited availability of graft material, and two surgical procedures, i.e., one for harvesting the graft material and one for graft implantation.\textsuperscript{224,299,312,357} An alternative without these disadvantages would be desirable.
A 15-mm metal resurfacing inlay implant was developed for secondary OCDs of the medial talar dome. The implant set consists of 15 offset sizes that are based on the geometry of the medial talar dome. The aim is to provide a matching implant for each patient. The implant possibly is a viable treatment option for secondary OCDs because it can be implanted in one session without the risk of donor-site morbidity. In theory, it should be implanted slightly recessed relative to the adjacent cartilage, in order to prevent excessive contact pressure by the implant on the opposite tibial joint surface. Before the implant can be used safely in patients, it is important to know whether the spectrum of offset sizes is adequate, whether the implantation level is reproducible, and whether excessive contact pressures at the opposing tibial plafond are avoided. After these items have been elucidated, the implant can be used in patients. Naturally, thorough follow-up of these patients is required to evaluate the clinical effectiveness.

As stated above, the main target in the treatment of talar OCDs is repair of the subchondral bone. Ideally, the surgery involves a one-step, minimally invasive procedure. A healthy restored subchondral bone plate would decrease the pain, improve the load-bearing capacity of the ankle, and improve chondrocyte survival in the remaining cartilage.

Demineralized bone matrix (DBM) from donors is a possible alternative to autologous bone grafting. It has been successfully used in the treatment of OCDs of rabbit knees. DBM has been ascribed osteoconductive, osteoinductive, and osteogenic potential. Osteoconduction is a property of a matrix that supports the attachment of bone-forming cells for subsequent bone formation. Osteoinduction is a process that supports the mitogenesis of undifferentiated mesenchymal cells, leading to the formation of osteoprogenitor cells that form new bone. Osteogenic property can be defined as the generation of bone from bone-forming cells. Autologous platelet-rich plasma (PRP) contains concentrated growth factors, which may further improve the treatment effect of DBM. It is obtained by the centrifuge of venous blood. Neither the use of DBM nor PRP have been investigated in the treatment of talar OCDs.

Animal models are often essential in the testing of orthopaedic procedures prior to clinical use in humans. However, experimental animal studies of articular cartilage defects predominantly investigate the knee. These knee studies cannot reliably be extrapolated to patients with ankle defects, because the knee and ankle have clearly different properties. A large animal model specifically designed for the ankle would allow the investigation of DBM, PRP, and other alternatives before clinical application.
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Outcome assessment

The reporting of outcome after treatment requires reliable and valid outcome scores. The score preferably should be translated and validated in the target population. A large amount of outcome measures have been used for evaluation of OCDs. However, none of the outcome measures has been specifically designed or validated for OCDs. Because of the diversity of the outcome measures, comparison and pooling of studies may be unreliable. A clear guideline as well as the validation of existing outcome measures would enable more consistent reporting of outcomes.

Aims and outline of the thesis

This thesis investigates various aspects of talar OCDs that were introduced in the previous sections. Part I of the thesis describes the current concepts in the treatment of OCDs. Part II contains chapters on primary arthroscopic debridement and bone marrow stimulation. It aims to improve the preoperative planning of the arthroscopic approach, evaluate the long-term outcomes, and accelerate postoperative rehabilitation. Part III presents the biomechanical and clinical evaluation of a metal resurfacing inlay implant as a new secondary treatment method. It also aims to refine the medial malleolar osteotomy, which is used as a surgical approach to the talus. Part IV describes animal studies on an alternative treatment with DBM and PRP. Part V presents an overview and recommendations of outcome measures used for OCD treatment and the validation of the German Foot and Ankle Outcome Score. Part VI finalizes the thesis with a general discussion and a summary.

Part I – Current concepts

As described above, there are numerous management options and surgical strategies in the treatment of OCDs. Chapter 2 aims to provide an overview of treatment options. Based on the literature, a treatment algorithm is proposed. Chapter 3 describes the evolution and the various possibilities of anterior and posterior ankle arthroscopy.

Part II – Primary arthroscopic debridement and bone marrow stimulation

The optimal arthroscopic approach (i.e., anterior or posterior) can be unclear preoperatively. During anterior arthroscopic treatment of an OCD, the ankle is held in full plantar flexion to reach the defect. The purpose of chapter 4 is to determine whether preoperative CT of the ankle joint in full plantar flexion is a reliable and accurate tool to determine the anterior arthroscopic reach of talar OCDs. The dual purpose of chapter 5 is (1) to quantify the anterior arthroscopic reach with the ankle in full plantar flexion in a larger group of patients using CT scans, and (2) to identify predictive factors of the arthroscopic reach.

Although arthroscopic debridement and bone marrow stimulation is recommended as the primary treatment, long-term outcome data are scarce. The primary aim of chapter 6 is to assess the long-term clinical and radiographic outcomes of arthroscopic debridement and bone marrow stimulation for talar OCDs. The secondary aim is to identify prognostic factors that affect the long-term results.

Bone marrow stimulation can be achieved by drilling or microfracturing. Chapter 7 identifies a potential pitfall in the arthroscopic microfracturing technique.

Early sport resumption after treatment in the young and active population remains a challenge. Chapter 8 describes a detailed
study protocol of a randomized controlled trial, which investigates whether PEMF leads to earlier resumption of sports in a higher percentage of patients with an OCD of the talus after arthroscopic debridement and microfracturing.

Part III – Secondary surgical treatment with a metal resurfacing inlay implant

Because of the disadvantages of current secondary treatment methods, such as donor-site morbidity and limited availability, a metal resurfacing inlay implant was developed. Chapter 9 aims to investigate whether the offset sizes are adequate for various cadaveric tali, whether the device can be reproducibly implanted slightly recessed relative to the adjacent cartilage, and whether excessive contact pressures to the opposite cartilage can be avoided with this implantation level.

The goal of chapter 10 is to evaluate the clinical safety and efficacy of the metal implant in patients with an OCD of the medial talar dome after failed previous treatment.

A medial malleolar osteotomy is indicated for the surgical implantation of the metal device. To obtain a congruent joint surface after refixation, the osteotomy should be directed perpendicularly to the articular surface of the tibia at the intersection between the tibial plafond and medial malleolus. The purpose of chapter 11 is to determine this perpendicular direction in relation to the longitudinal tibial axis on radiographs for application during surgery. Chapter 12 describes the use of a right-angled aiming probe to facilitate identification of the optimal terminal point of the medial malleolar osteotomy.

Part IV – Alternative treatment

In the absence of an animal model for the investigation of alternative treatment of talar OCDs, we have developed a caprine model for the ankle joint. The aim of chapter 13 is to test the feasibility of the developed animal model in a small number of goats.

DBM and PRP possess properties that may enhance the repair of OCDs. Chapter 14 investigates whether DBM leads to more bone regeneration than control OCDs of the goat's talus, and whether PRP improves the effectiveness of DBM.

Part V – Outcome measures

Because a large amount of outcome measures are used in the literature for evaluation of OCDs, comparison of different studies may be unreliable. The objective of chapter 15 is to describe and discuss frequently used clinical and functional outcome scores, as well as postoperative imaging modalities, and provide directions for use.

The study protocol of chapter 10 has been designed as a multicenter study in cooperation with a German university hospital. An important outcome score of the study is the Foot and Ankle Outcome Score (FAOS). A Dutch version has been translated and validated. To also evaluate the German patients reliably, the objective of chapter 16 is to translate and validate a German version of the FAOS.

General discussion

Chapter 17 provides a general discussion and a summary of the thesis.