A description of the proposed research

The CARE trial: CAsting and REhabilitation for osteochondral lesions of the talus in the skeletally immature: improved quality of life and protection towards early osteoarthritis

Literature review, purpose and hypothesis

Introduction

An osteochondral lesion (OCL) is a lesion of the articular cartilage and underlying subchondral bone. In the pediatric population the highest incidence of OCLs has been described in the knee joint followed by the ankle joint (1). There is a hypothesis that OCLs in the pediatric population are congenital and may be diagnosed by accident after trauma. Additionally, OCLs can occur after trauma or in patients with juvenile idiopathic arthritis (JIA) (2-4). The main complaint of an OCL is pain during weightbearing activities(5). Therefore, these lesions have significant impact on the health status of patients. Pediatric patients with an OCL assign an extremely low utility health state score of 0.15 to their symptomatic health state. To put this into perspective, studies have shown utility health state scores of 0.23 in pediatric patients with a diabetes-associated stroke, 0.39 in pediatric patients with cerebral palsy, 0.35 in pediatric patients with hearing impairment, and 0.48 in pediatric patients with visual impairment (6).

To reduce the invalidating symptoms of patients with an OCL, adequate treatment of OCLs is essential.

Current practice

To date, the current management can consist of conservative or surgical management. Surgical management is generally considered to be indicated after failure of conservative management. Conservative management is frequently focused on supervised neglect until skeletally maturity. This means that patients are advised to alter their physical activities during their growing period. Supervised neglect causes a decrease in physical possibilities which has major impact on the quality of life, and physical and mental development of the children. Additionally, adequate conservative management might protect patients from surgery for their OCL and thereby an increased risk on early osteoarthritis. Success rates of conservative management for OLTs in literature range from 8% to 100% (7, 8). This wide variation in success rate can partly be explained by the heterogeneity in study populations. Additionally, there is also lack of a standardized treatment protocol for the (conservative) management of OLTs. Previous research on OCLs in the knee of skeletally immature patients has shown improved radiological and clinical outcomes after a supervised immobilization- and rehabilitation protocol (9, 10). Additionally, it is shown that this protocol could lead to a 57% reduction of surgical interventions over the long term (10). This demonstrates that skeletally immature patients have a natural healing potential, in which an immobilization and supervised rehabilitation protocol can successfully support this potential. Healing of the lesion will likely resolve symptoms and therefore result in fewer physical restrictions, which will improve the quality of life.

However, as of yet, no studies describe the role of a standardized immobilization and supervised rehabilitation protocol in the conservative management of OCLs of the ankle in the skeletally immature population. For that reason, a Randomized Controlled Trial (RCT) will aid in directing the conservative treatment towards an evidence-based approach. The hypothesis of this study is that this evidence-based approach will improve the clinical and radiological outcomes in patients with an OLT and protect them from osteoarthritis over the long term.

Methodology

The study is designed as a multicenter randomized controlled trial. After the diagnostic process in the outpatient clinics, patients will be asked to participate in this RCT. If patients and their parents/caretakers agree with participation, randomization will be conducted. Subsequently, patients will be allocated to group 1 (intervention group) or group 2 (control group).

Treatment groups

Group 1: patients in the intervention group will undergo non-weightbearing immobilization with a cast for 6 weeks in phase one. At the end of phase one, patients must have shown clinical progression in order to go to phase 2. In phase 2, which starts between week 6 and 12 and ends between week 12 and 16, a supervised rehabilitation will be performed. If patients show clinical and radiological improvement at the end of phase 2, phase 3 can be started (figure 1)

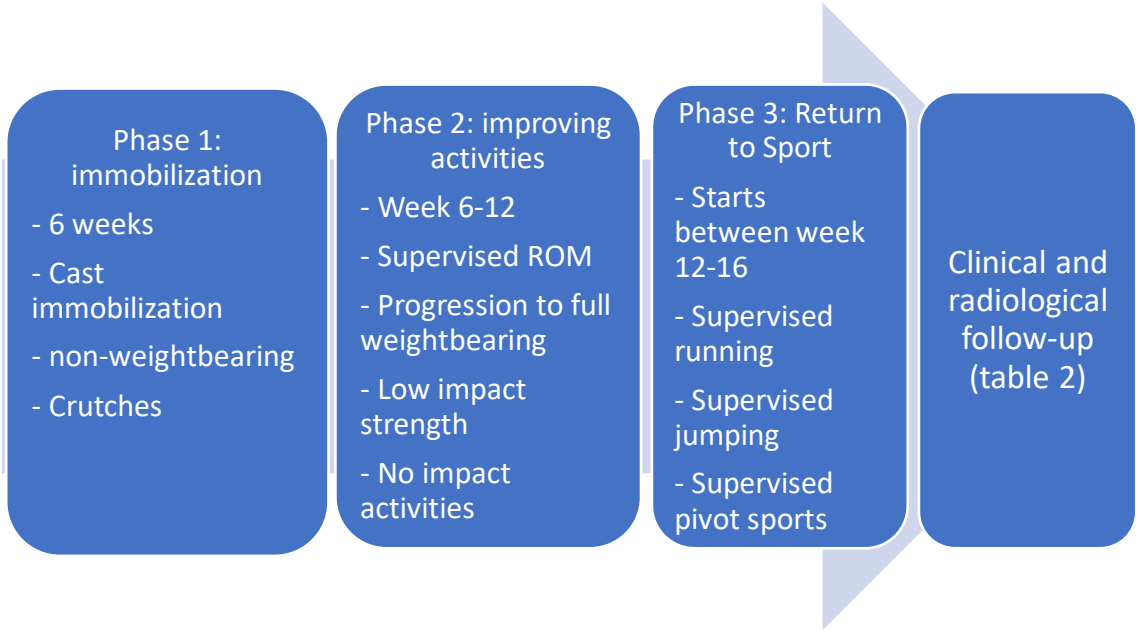

Figure 1: Immobilization and supervised rehabilitation

Group 2: Patients in the control group will undergo a ''supervised neglect'', which means that they adjust their activity level based on their complaints.

Inclusion criteria	Exclusion criteria
Symptomatic, stable osteochondral lesion of the talus	Acute lesions
Diagnosed on Computed Tomography (CT)	Unstable lesions
Open physes of the distal tibia	Surgically treated OLT
	Systemic diseases that can influence cartilage conditions such as hemophilia and JIA

Table 1: in- and exclusion criteria

Clinical and radiological follow-up

Follow-up moment	Clinical measurement	Radiological measurement
Baseline	Biographic information, history of sporting activities, NRS	X-ray, MRI, CT

	weightbearing, OxAFQ-C, PedsQL	
12-16 weeks	Return to sport questions, NRS WB, OxAFQ-C, PedsQL, CVS	
26 weeks	Returning to sport questions, NRS WB, OxAFQ-C, PedsQL, CVS	
52 weeks	Returning to sport questions, NRS WB, OxAFQ-C, PedsQL, CVS	X-ray, MRI
104 weeks	Returning to sport questions, NRS WB, OxAFQ-C, PedsQL, CVS	X-ray, MRI

Table 2: clinical and radiological follow-up. MRI= Magnetic Resonance Imaging, WB= WeightBearing, Ox-AFQ-C: Oxford Ankle Foot Questionnaire for Children, NRS=Nummeric Rating Scale, PedsQL=Pediatric Quality of Life Inventory(11), CVS=Child Vulnerability Scale(12).

Physical therapy

After the confirmation of participation in the study, patients will be informed about the rehabilitation process. In order to support the treating physical therapists, they will be provided with a detailed protocol, which is outlined in figure 1. Patients in the intervention group will receive physical therapy from week 6 onwards, two times a week.

Statistical analysis

Clinical results will be compared by means of the Oxford Ankle Foot Questionnaire for Children(13), Numeric Rating Scale (NRS) during weightbearing(14), and (time to) return to sport and (time to) return to pre-injury-level. Clinical and radiological measurement will be performed at time points as mentioned in table two. In addition to the clinical outcomes, conversion to surgery will be compared between the two groups by means of a survival analysis. An unpaired t-test will be used for the comparison between the group means in case of numerical data. In case of ordinal data, the non-parametric Mann-Whitney U test will be conducted to compare both groups. In both cases, a p-value less than 0.05 will be considered significant. The sample size is calculated based on a minimally important difference of 17% in the OxAFQ-C physical domain (13). A sample size of 35 patients in each group is needed for an 80% study power. To compensate for potential loss to follow up of 10%, 39 patients will be included in both groups.

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