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Sustained clinical and structural benefit after joint distraction in the treatment of severe knee osteoarthritis

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SUMMARY

Background: Treatment of severe osteoarthritis (OA) in relatively young patients is challenging. Although successful, total knee prosthesis has a limited lifespan, with the risk of revision surgery, especially in active young patients. Knee joint distraction (KJD) provides clinical benefit and tissue structure modification at 1-year follow-up. The present study evaluates whether this benefit is preserved during the second year of follow-up.

Methods: Patients included in this study presented with end-stage knee OA and an indication for total knee replacement (TKR); they were less than 60 years old with a VAS pain ≥60 mm ($n = 20$). KJD was applied for 2 months (range 54–64 days) and clinical parameters assessed using the WOMAC questionnaire and VAS pain score. Changes in cartilage structure were measured using quantitative MRI, radiography, and biochemical analyses of collagen type II turnover (ELISA).

Results: Average follow-up was 24 (range 23–25) months. Clinical improvement compared with baseline (BL) was observed at 2-year follow-up: WOMAC improved by 74% ($P < 0.001$) and VAS pain decreased by 61% ($P < 0.001$). Cartilage thickness observed by MRI (2.35 mm (95%CI, 2.06–2.65) at BL) was significantly greater at 2-year follow-up (2.78 mm (2.50–3.09); $P = 0.03$). Radiographic minimum joint space width (JSW) (1.1 mm (0.5–1.7) at BL) was significantly increased at 2-year follow-up as well (1.7 mm (1.1–2.3); $P = 0.03$). The denuded area of subchondral bone visualized by MRI (22% (95%CI, 12.5–31.5) at BL) was significantly decreased at 2-year follow-up (8% (3.6–12.2); $P = 0.004$). The ratio of collagen type II synthesis over breakdown was increased at 2-year follow-up ($P = 0.07$).

Conclusion: Clinical improvement by KJD treatment is sustained for at least 2 years. Cartilage repair is still present after 2 years (MRI) and the newly formed tissue continues to be mechanically resilient as shown by an increased JSW under weight-bearing conditions.

Introduction

Osteoarthritis (OA) is a slowly progressive joint disorder clinically characterized by pain, stiffness, and functional disabilities. Structural characteristics comprise cartilage damage and loss, changes in subchondral bone, and secondary synovial inflammation. These tissue changes are only partially associated with the clinical characteristics[1–3].

The incidence of OA is increasing, due to an aging population and a rise of obesity[4,5]. There is no cure for OA, and the first step in current treatment is conservative, predominantly focused on pain relief, minimizing functional disability, and limiting progression of structural joint changes. New treatments include cell transplantation techniques and disease modifying OA drugs (DMOADs)[6]. When conservative treatment fails and joint preserving surgery is not or no longer indicated, total knee replacement (TKR) of the affected joint is recommended. It is questionable, however, whether all options are routinely considered before replacement surgery is performed[7–9].

TKR is a final option and although expensive, considered effective in relieving pain and regaining function[10,11]. The total number of TKRs is increasing, as is the rate of revisions. It is remarkably that over 40% of all knee replacements and up to 44% of all total knee revisions are performed in patients ≤65 years of age[11], considering the known problems of limited lifespan of TKRs. This constitutes a

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costly healthcare problem[12,13]. Therefore, development of alternative treatment strategies for end-stage knee OA is necessary in order to preserve a patient's joint.

For certain disease specific indications, joint preserving surgery is an option; these include arthroscopic debridement, subchondral bone stimulation, osteotomy, and more recently, knee joint distraction (KJD). Joint distraction has been effectively applied in ankle OA with prolonged clinical benefit and indications of tissue structure modification[14–16]; there has also been a report of clinical benefit in the hip, published already years ago[17], although this has not been further explored. Recently, joint distraction was applied for severe end-stage knee OA, and a study by Deie M *et al.* reported positive clinical results with the use of hinged knee distraction over time[18]. These treatment approaches are discussed in detail in a review that was recently published by our group[19].

In 2006, our group started the first prospective evaluation of knee distraction in 20 patients with severe end-stage OA, who were considered for a TKR. In addition to evaluating clinical benefit, we also measured tissue structural repair using various imaging and biochemical markers. Analysis of the 1-year follow-up revealed positive clinical benefit and signs of cartilage repair[20]. This paper examines whether these beneficial effects are preserved over the second year of follow-up.

Materials and methods

Patient selection

Twenty-three successive patients with end-stage OA (average age 49 ± 1 years, range 32–57 years), indicated for TKR surgery due to persistent loss of function and pain, not adequately responding to conventional treatments were selected at the Department of Orthopedics, University Medical Center Utrecht. In short, inclusion criteria were age <60 years, Visual Analogue Scale (VAS) of pain ≥60 mm, and radiographic signs of primarily tibio-femoral OA joint damage. Exclusion criteria were severe symptoms in both knees, primary patella-femoral OA, a history of inflammatory or septic arthritis, severe knee malalignment (>10°) requiring surgical correction and inability to cope with an external fixator for 2 months. Patients had been referred from peripheral hospitals for a second opinion because the patient refused the indicated TKR for personal reasons mostly related to young age. Detailed clinical history of all patients has been previously described[20]. Of the 23 successively selected patients, three were excluded: one based on bilateral OA; one because of remaining metal in the knee after anterior cruciate ligament (ACL) reconstruction; and one withdrew the informed consent directly after treatment. The 20 included patients had predominantly medial compartmental OA ($n = 18$; most affected compartment (MAC) is medial), stable joints (despite three previous ACL ruptures), and an average K&L grade of 3 (Table I). Baseline (BL) characteristics of individual patients are given in Table I. This study was approved by the medical ethics review committee of the University Medical Center Utrecht (No.04/086), and all patients gave written informed consent.

Distraction method

The distraction method was applied as previously described by Intema *et al.*[20]. In short, an external fixation frame (Fig. 1) consisting of two monotubes with internal coil springs was placed, bridging the knee joint. Each monotube was fixed to two bone pins on each end and, in stages, distracted for 5 mm (confirmed by X-ray). After instructions about pin site care, daily exercise, and physical therapy, the patients were discharged from the hospital. Patients were allowed and encouraged to load the distracted joint with full weight-bearing capacity, supported with crutches. In case of superficial (skin) pin tract infections, treatment with oral antibiotics for 5–7 days was provided (Flucloxacillin). Every 2 weeks the patients returned to the hospital and the monotubes were temporarily removed. The knee was bent, for 3–4 h, in a continuous passive motion device, with pain at the pin sites determining the maximum degree of flexion; on average, 25° (15–80°) flexion and full extension was reached. The monotubes were replaced and sufficient distraction was confirmed by X-ray examination and adjusted if needed.

After 2 months (average duration 60 days, range 54–64 days), the tubes and pins were surgically removed and patients went home without imposed functional restrictions. After both surgeries, patients were treated with acetaminophen and NSAID as needed, according to the standard analgesia protocol of the UMCU. Upon discharge, pain medication, along with daily exercise and physical therapy, were regulated by the patient and not documented.

Follow-up

Patients visited the outpatient clinic twice before treatment (BL) and at 3 and 6 months, and subsequently every 6 months post-treatment. At these time points the WOMAC questionnaire[21] and VAS pain score were assessed. For evaluation of structural improvement, blood and urine samples were collected at BL and at six, 12 and 24 months after distraction therapy and stored at −80°C. Standardized weight-bearing X-ray images according to the knee images digital analyses (KIDA) protocol[22] and MRIs according to the Eckstein protocol[23] were taken at BL, and at 1 and 2 years of follow-up.

Clinical outcome

To score clinical improvement, the WOMAC (version 3.0, normalized to a 100-point scale for total and subscales; 100 being the best score) was used as primary outcome parameter. The secondary clinical outcome parameter was the VAS pain score (0–100 mm; "0" meaning no pain). To identify actual responders, we used the Osteoarthritis Research Society International (OARSI) defined OARSI-OMERACT responder criteria, validated for drug-therapies[24] and TKR[25] in case of diagnosed knee OA.

Structural outcome

Quantitative MRI analysis

MRI acquisition was performed with a 1.5 T Philips Achieva, using a 3D spoiled gradient recalled (SPGR) sequence with fat suppression (repetition time 20 ms; echo time 9 ms; flip angle 15°; slice thickness 1.5 mm; in-plane resolution 0.3125 × 0.3125 mm), which has been previously validated for the purpose of quantitative measurement of cartilage thickness and volume[23]. Coronal images were used to segment the tibio-femoral cartilage plates and bone surface, including denuded areas. The operator (SC) and quality control reader (FE) were blinded to the sequence of the BL and the 1-year follow-up images[19]; 2-year follow-up images were segmented independently, without reference to the BL or 1-year follow-up images, in order to exclude reading bias, and prevent overestimation of results. Cartilage parameters in the medial and the lateral compartment were computed using custom software (Chondrometrics GmbH., Ainring, Germany). The primary structural outcomes were cartilage thickness over the total subchondral bone area (ThCtAB; cartilage thickness with areas of denuded bone included, counting as 0 mm thickness) and the percentage of denuded subchondral bone area (dABp)[26]. The secondary structural outcome parameter was cartilage thickness over cartilaginous area of subchondral bone (ThCcAB; cartilage thickness with areas of