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Prediction of cartilaginous tissue repair after knee joint distraction

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ABSTRACT

Background: For young patients (<65 years), knee joint distraction (KJD) may be a joint-saving treatment option for end-stage knee osteoarthritis. Distracting the femur from the tibia by five millimeters for six to eight weeks using an external fixation frame results in cartilaginous tissue repair, in addition to clinical benefits. This study is a first attempt to predict the degree of cartilaginous tissue repair after KJD.
Methods: Fifty-seven consecutive patients received KJD. At baseline and at one year of follow-up, mean and minimum joint space width (JSW) of the most-affected compartment was determined on standardized radiographs. To evaluate the predictive ability of baseline characteristics for JSW at one year of follow-up, multivariable linear regression analysis was performed.
Results: Mean JSW ± SD of the most affected compartment increased by 0.95 ± 1.23 mm to 3.08 ± 1.43 mm at one year ($P < 0.001$). The minimum JSW increased by 0.94 ± 1.03 mm to 1.63 ± 1.21 mm at one year of follow-up ($P < 0.001$). For a larger mean JSW one year after KJD, only Kellgren & Lawrence grade (KLG) at baseline was predictive (Regression coefficient (β) = 0.47, 95% CI = 0.18 to 0.77, $P = 0.002$). For a larger minimum JSW, KLG (β = 0.46, 95% CI = 0.19 to 0.73, $P = 0.001$) and male gender (β = 0.52, 95% CI = 0.06 to 0.99, $P = 0.028$) were statistically predictive. Eight weeks of distraction time neared significance (β = 0.44, 95% CI = −0.05 to 0.93, $P = 0.080$).
Conclusions: In our cohort of patients treated with KJD, males with higher KLG had the best chance of cartilaginous tissue repair by distraction.

1. Introduction

Knee osteoarthritis is a chronic joint disease, clinically characterized by pain and functional limitation. Structural changes associated with knee osteoarthritis are progressive degradation of cartilage, low-grade inflammation of synovial tissue, osteophyte formation and subchondral bone changes [1,2]. In the case of persistent, conservative-treatment-resistant pain accompanied by cartilage tissue damage, the treatment of choice is often a total knee replacement. However, in the case of relatively young patients (<65 years) knee joint distraction (KJD), being a joint-sparing treatment, should be considered an alternative, postponing arthroplasty for a prolonged time in at least three-quarters of patients [3,4]. This surgical procedure provides a six- to eight-week biomechanical joint homeostasis, by distracting the femur from the tibia by five millimeters with the use of an external fixation frame, which appeared to facilitate cartilage repair activity [5]. In the past, five studies [3,6–9] have been performed using knee distraction. Only one of those studies was based on prospective evaluation [3], although all showed significant increases in the radiographic joint space width (JSW). Most convincingly, Wiegant et al. [4] showed that the newly formed cartilage-like tissue was stable and mechanically resilient under weight-bearing conditions over two years of follow-up in 20 patients. However, cartilaginous tissue repair by use of joint distraction is still controversial, and it is not clear which patients are the most suitable for this treatment with regard to cartilage tissue repair. Knowledge in this respect may add to acceptance of distraction and may refine indications for treatment. Therefore, this paper is a first attempt to identify patient characteristics predicting cartilage tissue repair after KJD treatment.

2. Materials and methods

2.1. Patients

Fifty-seven consecutive patients received KJD between April 2006 and July 2013 (24 at the University Medical Center Utrecht and 33 at

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the Sint Maartenskliniek Woerden, The Netherlands). Twenty patients were included in an open prospective study and had end-stage knee osteoarthritis, were initially considered for total knee arthroplasty (TKA) and received eight weeks' distraction. The remaining 37 patients were included in ongoing randomized controlled trials (RCTs). These RCTs compare KJD with surgical alternatives (total knee arthroplasty (TKA) or high tibial osteotomy (HTO)) [10]. These patients were appropriate for TKA or for HTO (with a deviation of <10°) and received six weeks' distraction. In addition, all patients had to be below 65 years of age, have a body mass index (BMI) <35 kg/m^2, intact knee ligaments and a normal range of motion (minimum of 120° flexion). Exclusion criteria were primary patellofemoral osteoarthritis, severe knee malalignment (>10° varus or valgus), a history of inflammatory or septic arthritis, inability to cope with an external fixator, and post-traumatic fibrosis due to a fracture of the tibial plateau. The medical ethical review committee of the University Medical Center Utrecht approved all studies (Nos. 04/086, 10/359/E and 11/072), all patients gave written informed consent and all studies were performed in accordance with the ethical principles laid out in the Declaration of Helsinki.

Table 1
Baseline characteristics.

Characteristics	KJD (n = 57)
Male gender, n (%)	33 (58%)
Height, cm (±SD, range)	176 ± 9.4 (156–197)
Weight, kg (±SD, range)	86.8 ± 13.6 (55–117)
Body mass index, kg/m^2 (±SD, range)	27.9 ± 3.7 (19–36)
Affected knee, n left knees (%)	26 (46%)
Most affected compartment, n medial (%)	51 (90%)
Age at surgery, year (±SD, range)	52.1 ± 6.8 (32–65)
Kellgren & Lawrence, median	3
Grade 0, n (%)	0 (0%)
Grade 1, n (%)	9 (16%)
Grade 2, n (%)	9 (16%)
Grade 3, n (%)	27 (47%)
Grade 4, n (%)	12 (21%)
Tibio-femoral angle joint (±SD, range)	−6.1 ± 4.1 (−13.1–5.8)
Initial indication TKA/HTO	35/22
Duration of distraction 6/8	37/20

2.2. Distraction method

The applied distraction method has been described in detail previously [3]. In short: two dynamic monotubes were placed on either side of the knee joint, at both sides (lateral and medial) fixed to femur and tibia with two bone pins each. The knee joint was distracted by ~5 mm. Patients were allowed to fully load the distracted knee, supported by crutches, if needed. After a mean of 49 (±8) days of distraction, the frame and pins were removed, patients were discharged and rehabilitated in their own environments with the help of a physiotherapist and pain medication on demand.

2.3. Outcome

The outcome parameters (dependent variables) were, minimum (min) JSW and mean JSW of the most affected compartment (MAC) at one year after KJD [3,4]. Both radiographic parameters were determined at baseline and at one year follow-up on standardized weight-bearing, semi-flexed posterior–anterior radiographs. These were taken according to the protocol of Buckland–Wright (seven to 10° of knee flexion) [11]. This method has been proven to produce accurate and precise measurements and technicians are able to reliably and consistently place the knee in the correct position [12,13]. The digital radiographs were taken with an aluminum step wedge on the lateral side close to the knee, against the detector (film) within the field of exposure. Knee Images Digital Analysis (KIDA) software was used to determine mean JSW and min JSW [14]. This is a fully mathematical method of analyzing the mean JSW and min JSW of the knee. The aluminum step wedge reference (15 cm × 3 cm) is included in the analysis in order to correct for, e.g., magnification of the radiograph. The min JSW was measured as the smallest distance between the femur and the tibia. The mean JSW of the MAC was defined as the mean of four predefined locations in the most affected compartment. The tibio-femoral joint angle was defined as the angle between the femoral and tibial knee joint lines in the frontal plane. A negative angle indicates a medially converging joint line. The image analyses were performed blinded to the order of acquisition and patient characteristics. Interobserver reproducibility was high, and the intraobserver variation revealed good variability in the past [14,15]. Intraobserver variation, tested by random reanalyses of 29 radiographs in the present study showed good correlations between the two observations (Pearson's R, 0.97 and 0.91 for mean JSW and min JSW, respectively). Baseline (pre-treatment) patient characteristics assessed for their predictive ability for the outcome were gender, distraction time (six or eight weeks of distraction performed), HTO or TKA indication, age, BMI, min JSW, mean JSW of the MAC, and Kellgren & Lawrence grade (KLG). There were no statistical significant correlations between all those parameters. Clinical outcome was assessed using the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC, version 3.0 and 3.1), normalized to a 100-point scale; 100 being the best condition. Furthermore, a visual analog scale for pain (VAS-pain; 0 to 100 mm, 0 meaning no pain) was used.

2.4. Statistical analysis

Two-sided paired tests were used to evaluate whether outcome variables changed from baseline to one year post treatment. To obtain (a combination of) variables predictive for radiographic outcome, multivariable linear regression analyses were used. The effect of predictors on change in the outcome was assessed by using min JSW and mean JSW at one year as the dependent variable and adjusting the analysis for the respective baseline values. A stepwise selection procedure was used starting with all variables and removing them one-by-one based on P-value and change in explained variance of the model (R^2 change > 3%).

SPSS software version 22.0 was used for statistical analysis and a $P < 0.05$ was considered statistically significant.

3. Results

Baseline characteristics of the whole cohort are given in Table 1.

A mean ± SD clinical improvement of 28.3 ± 18.8 points, based on the WOMAC total was observed for this cohort. The WOMAC total increased from 50.0 ± 17.0 points at baseline, to 78.3 ± 17.7 points at one year ($P < 0.001$). In line with this, the VAS-pain decreased from 64.2 ± 18.7 mm to 30.9 ± 24.4 mm at one year ($P < 0.001$) after joint distraction.

For this cohort, on average the mean ± SD JSW of the MAC increased by 0.95 ± 1.23 mm, from 2.13 ± 1.62 mm at baseline to 3.08 ± 1.43 mm at one year ($P < 0.001$). Min JSW increased by 0.94 ± 1.03 mm, from 0.69 ± 1.08 at baseline to 1.63 ± 1.21 mm at one year of follow-up ($P < 0.001$). In the patients with a medially converging joint line at baseline, the tibio-femoral joint angle, changed from −6.98 ± 2.90° to −6.07 ± 3.18° at one year (n = 52, $P = 0.001$). In the patients with a laterally converging joint line at baseline, the tibio-femoral joint angle changed from 3.59 ± 1.65° to 2.38 ± 1.10° at one year (n = 5, $P = 0.010$). Multivariable linear regression analysis revealed that only higher KLG was predictive for a higher mean JSW (in addition to mean JSW at baseline; Table 2). For mean JSW, the regression coefficient (β) of KLG measured 0.47 mm (95% CI = 0.18 to 0.77, $P = 0.002$), meaning that the mean JSW after one year would be 0.47 mm higher if the patient had a higher KLG at baseline (e.g. grade IV instead of grade III). For min JSW,

Table 2
Multivariable linear regression analysis with mean joint space width (mm) as dependent variable.

	β (95% CI)	*P*
KLG	0.47 (0.18–0.77)	0.002
Mean JSW baseline value	0.72 (0.55–0.90)	<0.001