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Systematic review

Is Knee joint distraction a viable treatment option for knee OA? - a literature review and meta-analysis

Abstract

Background: Knee joint distraction (KJD) is a new application of an established technique to regenerate native cartilage using an external fixator. The purpose of this study is to perform a systematic review and meta-analysis of the literature to determine whether KJD is beneficial for knee osteoarthritis and how results compare to established treatments.

Methods: Studies assessing the outcomes of KJD were retrieved, with three studies (one cohort, two randomized controlled trials), 62 knees, meeting inclusion criteria. The primary outcome was functional outcome, assessed using a validated outcome score, at one year. Secondary outcomes included: pain scores, structural assessment of the joint and adverse events.

Results: KJD is associated with improvements in WOMAC from baseline to one year as well as reductions in pain scores and improvements in structural parameters assessed radiographically and by MRI. KJD is not associated with decreased knee flexion, but is associated with a high risk of pin site infection. In patients aged 65 years or under at one year no differences in WOMAC or pain scores was detected between patients managed with KJD compared to high tibial osteotomy or total knee arthroplasty.

Conclusions: KJD may represent a potential treatments for knee arthritis though further trials with longer term follow up are required to establish its efficacy compared to contemporary treatments.

Keywords:

Knee osteoarthritis; knee joint distraction; total knee arthroplasty; high tibial osteotomy; outcomes; complications.

Level of evidence: Level I (systematic review and meta-analysis)

Introduction

Knee osteoarthritis (OA) is the most common musculoskeletal disease estimated to effect 3.8% of the world's population [1]. Considered a disease of the whole joint, knee OA is characterized by loss of cartilage, bone remodeling and inflammation. Cumulative joint degeneration eventually leads to substantial loss of function and quality of life, and represents a major cause of global disability [1,2]. The burden of OA is set to increase with rising obesity levels and an ageing population [1,3]. Gold standard treatment for OA of significant severity is joint arthroplasty after initial conservative treatment. Beyond arthroplasty, no other treatment is proven effective in halting or reversing disease progression. Globally, the prevalence of knee OA peaks at 50 years [1]. However, both patients and surgeons are reluctant to replace joints where the patient is expected to outlive the lifespan of the prosthesis as there is a greater risk of revision surgery [4-6].

Consequently, there is an increasing need for alternative treatments for this younger OA population. Not least because of the increased failure risk [5] but also because in some cases arthroplasty may result in poor clinical outcomes [7]. Following injury and osteoarthritis in the ankle, ankle joint distraction has provided a useful means of reducing pain, improving function and increasing radiological joint space [8]. Likewise basilar thumb arthritis has been effectively treated with joint distraction and debridement in small prospective studies [9]. There are a certain risks of infection at pin sites and related bone infection often observed in any surgical procedure using external frame and pins or wires, however, such joint sparing alternatives are useful for patients who wish to preserve the native joint.

A similar approach has been adopted to treat knee OA with knee joint distraction (KJD). KJD uses an external fixator to unload the joint by distracting the tibia and femur [10]. It is reported that this temporary mechanical unloading allows natural intrinsic repair processes to regenerate cartilaginous tissue evidenced by a sustained clinical benefit and increase in joint width space [11]. With KJD being a joint sparing procedure aimed at postponing a first prosthesis, successful clinical adoption could significantly improve patients' quality of life and thus reduce the long-term healthcare costs associated with knee OA.

The aims of this systematic review are to identify and examine the current evidence for the use of KJD focusing on clinical and radiological outcomes. This review will also help to identify gaps in our understanding and so inform future clinical and scientific studies.

Material and methods

Inclusion and exclusion criteria

Eligible studies included those involving patients aged 18 years or older with knee arthritis that compared surgical KJD against other surgical procedures for knee arthritis. There were no exclusions based study design or duration of distraction.

Information Sources and Search Strategy

Electronic databases (MEDLINE (Ovid), EMBASE (Ovid), Web of Science (ISI Web of Knowledge)) were searched from their inception until 25 February 2018 for studies meeting inclusion criteria. Searches were tailored to individual databases with the search strategy for MEDLINE shown in Appendix 1. In addition, reference lists of reviews and retrieved articles were assessed for further studies as were registers of controlled clinical trials (metaRegister of controlled trials (mRCT) (www.controlled-trials.com/mrct), clinicaltrials.gov (www.clinicaltrials.gov) and the World Health Organization (WHO) International Clinical Trials Registry Platform

(ICTRP) (http://apps.who.int/trialsearch/)). No restrictions were applied based on the publication status. Where necessary authors were contacted for additional information.

Studies were assessed independently in duplicate for eligibility and data from eligible studies extracted independently in duplicate into an electronic database (TT, TWH). A risk of bias assessment was performed on included studies.

Outcome measures assessed

To assess the outcome of KJD improvements from baseline to one year post intervention were assessed. To compare KJD with other surgical interventions outcomes at one year post intervention were assessed.

The primary outcome assessed was functional outcome, assessed using a validated outcome score, at one year following surgical intervention. Secondary outcomes included: pain scores, assessed using a validated pain score, structural assessment of the joint, both radiographic and with MRI and assessment of adverse events. All secondary outcomes were assessed at one year following surgical intervention.

Statistical analysis

Heterogeneity of included studies was assessed using the I2 statistic and in the event of substantial heterogeneity (I2>85%) a meta-analysis was not be performed. As a degree of variability was expected due to the subjectivity of the outcome measures a random-effects model was used in all cases. For continuous data the mean difference (MD) was calculated along with 95% confidence-intervals (95%CI), calculated using the inverse variance method. For dichotomous data the risk difference along with 95%CI was calculated using the Mantel-Haenszel method. Data analysis was performed using standard statistical techniques as described in the Cochrane Handbook for Systematic Reviews of Interventions, using Review Manager-5.3 (The Nordic Cochrane Centre, The Cochrane Collaboration, 2014).

Results

Three studies consisting of one cohort study and two randomized controlled trials were identified as meeting inclusion criteria [11-13]. Figure 1. The results of the cohort study were reported across three papers with relevant data extracted where reported [11,14,15]. Included studies are outlined in Table 1 with an assessment of risk of bias presented in Figure 2. All studies were considered at high risk of performance and detection bias as it was not possible to blind surgeons, participants or outcome assessors as to the treatment received. Attrition and reporting bias was assessed as low risk with no loss to follow up at one year reported. As all three studies originate from the same research group it was consider that this presented an unclear risk of bias.

Two studies were excluded as they reported the results of arthroscopic microfracture in combination with KJD and it was the authors opinion that, as microfracture is already an established treatment for cartilaginous loss, it would not be possible to delineate any treatment effect seen [16,17]. The first of these studies by Deie et al. (2007) reported the outcomes of six knees managed with KJD and microfracture and found at a mean 3 year follow up significant improvements in Japanese Orthopaedic Association Score, VAS pain score and radiographic joint space width [16]. The second, by Aly et al. (2011), reported the outcomes of 61 knees, 19 managed with KJD, joint debridement and microfracture and 42 managed with joint debridement and microfracture and found that at a mean follow up of 3 to 5 years the group managed with KJD, joint debridement and microfracture had significantly improved pain, walking capacity, stair climbing and radiographic joint space width compared to baseline whereas those treated with joint debridement and microfracture without KJD did not [17].

Outcomes of KJD improvement from baseline to one year post intervention

Primary Outcome

The Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) scores at baseline and one year post KJD were reported in all 3 studies, 62 patients, with a significant improvement in WOMAC scores, mean difference 28.7

points (p<0.001; 95%CI 22.6 to 34.8), between baseline and one year post surgery observed. Figure 3. Improvements were seen across all subdomains of WOMAC: pain (p=<0.001; MD 29.3 points 95%CI 21.9 to 36.5), stiffness (p=<0.001; MD 19.5 points 95%CI 8.4 to 30.6) and function (p=<0.001; MD 29.5 points 95%CI 23.6 to 35.4).

KOOS, ICOAP, EQ-5D and SF-36 were reported in 2 studies, 42 patients. Significant improvements between baseline and one year scores were observed for KOOS (p<0.001, MD 23.2 points 95%CI 15.4 to 31.1), ICOAP (p<0.001, MD 26.7 points 95%CI 17.0 to 36.4) and EQ-5D (p<0.001, MD 0.15 points 95%CI 0.06 to 0.23) and all subdomains. Significant improvements between baseline and one year SF-36 physical component score (p=0.009, MD 7.8 points 95%CI 1.9 to 13.7), but not mental component score (p=0.41, MD -1.5 points 95%CI -5.0 to 2.0) were observed.

Secondary outcomes

Pain score, assessed using a pain visual analogue score (VAS) 0 to 100 where 0 was equivalent to no pain, were reported in all 3 studies, 62 patients. Patients managed with KJD reported significant improvements in pain VAS of 33.3 points ($p=<0.001$; 95%CI 19.7 to 46.9) from baseline to one year post surgery. Figure 4.

Structural assessment of the joint was performed radiographically in all 3 studies, 59 patients, and by MRI in one study, 20 patients. Between baseline and one year following KJD the radiographic minimum joint space width increased by 0.8mm ($p<0.001$; 95%CI 0.5 to 1.0; Figure 5) and mean joint space width increased by 0.8mm ($p=0.003$; 95%CI 0.3 to 1.3). On MRI the mean cartilage thickness over the total subchondral bone area increased from 1.4mm (SD 0.3) to 1.6mm (SD 0.3; $p=0.03$) on the tibia and from 1.0mm (SD 0.4) to 1.4mm (SD 0.3; $p<0.001$) on the femur. The percentage of denuded subchondral bone decreased from 16.7% (SD 17.2) to 4.8% (SD 8.3; $p=0.006$) on the tibia and from 27.3% (SD 25.6) to 4.2% (SD 10.2; $p<0.001$) on the femur.

Adverse events

Knee flexion was reported in 2 studies, 42 patients. No change in knee flexion between baseline and one year following KJD was observed ($p=0.18$; MD 2.4° 95%CI

-1.1 to 5.9) from baseline to one year post surgery. Across all three studies, 62 patients, one patient was reported as requiring manipulation under anesthetic at 17 days following frame removal for stiffness.

Across all three studies, 62 patients, 42 patients developed single or multiple pin site infection requiring antibiotics. Overall, the risk of developing pin site infection was 69% (95%CI 51 to 87). Figure 6. The risk of developing pin site infection requiring oral antibiotics was 57% (95%CI 33 to 82). The risk of developing pin site infection requiring intravenous antibiotics was 10% (95%CI 1 to 18%). Overall two patients required surgical irrigation and debridement with one developing osteomyelitis three weeks following frame removal.

Additional adverse events reported with the use of KJD included pulmonary emboli (2 of 20 patients (10%) in one study), post-operative foot drop managed with ankle foot orthosis (1 patient), failure of the KJD distraction device (1 patient) and breaking of a bone pin during application (1 patient).

Outcomes of KJD compared to other treatments

Primary Outcome

Two randomized controlled trials assessed the outcomes of KJD against other treatments for arthritis, one against high tibial osteotomy, one against total knee arthroplasty. Both studies were conducted in patients aged 65 years and under. At one year no difference in total WOMAC score, or across subdomains, was seen between knees managed with KJD and those managed with HTO ($p=0.25$; MD -5.0 points, 95%CI -13.5 to 3.5) or TKA ($p=0.53$; MD -3.0 points, 95%CI -12.5 to 6.5). Figure 7. At one year no difference was seen in KOOS, ICOAP, EQ-5D or SF-36 between treatment groups.

Pain score, assessed using a pain VAS 0 to 100 were reported in both studies. At one year no difference in pain VAS was seen between knees managed with KJD and those managed with HTO ($p=0.17$; MD 9.0 points, 95%CI -3.8 to 21.8) or TKA ($p=0.13$; MD 10.0 points, 95%CI -3.0 to 23.0). Figure 8.

Adverse events

At one year no difference in knee flexion was seen between knees managed with KJD and those managed with HTO (p=0.05; MD 4.0 degrees, 95%CI -0.1 to 8.1) or TKA (p=0.07; MD 5.0 degrees, 95%CI -0.3 to 10.3). No difference in the rate of manipulation under anesthetic (MUA) was seen between KJD and HTO (p=0.40; RD 0.05 95%CI -0.1 to 0.2). A higher rate of MUA was seen with TKA compared to KJD (p=0.04; RD 0.14 95%CI 0 to 0.3).

The risk of developing infection requiring antibiotics was significantly higher following KJD compared to both HTO (p<0.01; RD 0.5 95%CI 0.3 to 0.8) and TKA (p<0.01; RD 0.6 95%CI 0.4 to 0.8). This is likely to be secondary to associated risks of using pins which provide a communication between the external environment and lower limb bones into which they are placed.

Discussion

The main findings of this systematic review are that KJD is associated in significant improvements in functional scores, pain scores and radiographic measures of cartilage thickness at one year post-operatively and in patients aged 65 years or younger has comparable functional outcomes to HTO and TKA. The main limitation of KJD is the occurrence of pin-tract infection was reported in 69% (95%CI 51 to 87) of patients and was significantly higher than that seen in HTO or TKA. At one year no difference in knee flexion, compared to baseline flexion and flexion one year following HTO and TKA, was seen. Whilst MUA following KJD has been reported (one case across three studies, 62 patients) the rate of MUA was found to be significantly lower than the rate observed following TKA.

Compared to older patients, in young patients managed with arthroplasty, the risk of implant failure, and subsequent revision burden is high and any intervention that can postpone or reduce the need for the index procedure in this group, and other groups at risk of poor outcomes, is worth considering. This review has found that KJD appears to be a potential alternative treatment option in managing knee OA, and in patients aged

65 years or younger the results appear to be as good as HTO and TKA at one year. Whilst these results are promising, the high rate of pin site infection following KJD is a concern because both HTO and TKA can give lower rate of post-operative infection. Despite in the majority of these cases resolution of infection was achieved with oral antibiotics. In very few instances, osteomyelitis has been reported, and surgeons may well have concerns about performing arthroplasty in these cases should KJD fail. However, Wiegant K, et al. [18] described the safety to perform TKA following KJD and concluded that it appears safe to treat patients several years following KJD with a TKA.

The mechanism by which KJD works is unclear. In the clinical studies of KJD increased radiographic JSW and coverage of denuded bone assessed by MRI were reported. Biomarker analysis has reported that following KJD a decrease in the collagen type II breakdown marker (CTXII) is observed coupled with an increase in the collagen type II synthesis marker (PIIANP) [14,15]. Whilst these findings would suggest that KJD changes the intra-articular environment to one that favors cartilage repair. It is likely that the conflicting results obtained in animal experiments are due to a variety of reasons such as differences in experimental set up, type of surrogate endpoints used to assess cartilage repair and limited follow up. Some studies have shown promising results with evidence of bone and cartilage repair whilst others have failed to demonstrate any advantage with KJD, with some even reporting adverse effect on the cartilage integrity. It is clear from these conflicting observations that more work is needed to establish indeed when and how joint distraction works and in which scenarios [19-26].

Alongside the mechanism of action of KJD there are several other areas of uncertainty around this treatment. In the present studies static distraction was applied using two 45 kg springs to permit some degree of joint loading. Whether this represent the optimum distraction force, and whether a hinged distractor, which has been demonstrated to be superior for ankle OA, still needs to be assessed [27,28]. Additionally, the patient population most likely to benefit from distraction and optimum duration of distraction remains to be defined. Early reports suggest that men with more severe arthritis are most likely to respond to treatment, and six weeks distraction provides equivalent clinical outcomes to eight weeks distraction however these findings are based on limited data, and appropriately powered trials comparing the outcomes of KJD to other treatments for knee OA are required [29,30]. Finally, further information on the long term efficacy of KJD is required. Current data suggests that, at five years the functional outcomes and structural assessments of joint remain improved compared to baseline, about 70% of the patients treated still have their own knee instead of the initially planned joint prosthesis [11]. At 9 years post distraction, still 50% of the patients continue to manage with their own knee and thereby the need for an artificial joint is avoided. Remarkably mostly women seem to drop out and opt for further intervention although there is no clear explanation for this gender difference [31].

The strengths of this systematic review are that is a comprehensive assessment of the efficacy of KJD for the treatment of knee arthritis. The weakness of this review is that it is limited by the data available, with only three studies available for inclusion, with all originating from the same research group.

This study has highlighted that KJD may be a valid alternative to HTO and TKA in the treatment of knee arthritis in the young, resulting in improvements in functional and pain as well as evidence of structural improvements within the joint lasting beyond one year. However, further work is required to optimize the technique of KJD, define the optimum population for its use as well as develop methods to reduce the risk of pin site infection, the major complication associated with this technique. Ultimately KJD needs to be assessed pragmatically through appropriately powered multi-center studies designed to assess its long term effectiveness and comparative efficacy against other established treatments for knee OA.

List of abbreviations

EF: External Fixator

EQ-5D: EuroQol five dimensions questionnaire

HTO: High Tibial Osteotomy

JOA: Japanese Orthopaedic Association

KJD: Knee Joint Distraction

KOOS: Knee Injury and Osteoarthritis Outcome Score

PRISMA: Preferred Reporting Items for Systematic reviews and Meta-Analyses

PROM: Patient Reported Outcome Measures

RCT: Randomized Controlled Trial

ROM: Range Of Motion

TKA: Total Knee Arthroplasty

VAS: Visual Analogue Scale

WOMAC: The Western Ontario and McMaster Universities Osteoarthritis Index

Conflict of interest

The authors have no financial conflict of interest in this study.

Funding

None.

Ethical approval

This is a systematic review so ethical approval was waived.

Written informed consent

Not applicable.

Appendix 1: MEDLINE (Ovid) Search Strategy

1. Knee joint/
2. distraction.mp. OR arthrodiatasis.mp
3. 1. AND 2.

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