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The efficacy of 12 weeks non-surgical treatment for patients not eligible for total knee replacement: a randomized controlled trial with 1-year follow-up

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SUMMARY

Objective: To compare the efficacy of a 12-week non-surgical treatment program with usual care in patients with knee osteoarthritis (OA) not eligible for total knee replacement (TKR).
Method: This two-arm parallel group assessor-blinded randomized controlled trial (RCT) included 100 adults from secondary care with knee OA, confirmed by radiography (Kellgren–Lawrence grade $\geq$1), but not eligible for a TKR. The 12-week non-surgical treatment program consisted of individualized progressed neuromuscular exercise, patient education, insoles, dietary advice and prescription of pain medication if indicated, while usual care comprised two leaflets with information and advice on knee OA and recommended treatments. The primary outcome was the change from baseline to 12 months in the Knee injury and Osteoarthritis Outcome Score ($KOOS_4$) defined as the average score for the KOOS subscales of pain, symptoms, activities of daily living (ADL), and quality of life (QOL).
Results: 91% of the patients completed the 12 months follow-up on the primary outcome. Compared with usual care, patients undergoing the treatment program improved more in $KOOS_4$ (adjusted mean difference (95% CI) of 9.6 (4.4–14.8)) with no serious treatment-related adverse events (AE). The number needed to treat (NNT), defined as the number of patients needed to treat for one person to improve 15% was 7.2. Secondary outcomes supported the primary findings.
Conclusion: In patients with mostly moderate to severe knee OA not eligible for TKR, a 12-week individualized, non-surgical treatment program is more efficacious at 12 months compared with usual care and has few treatment-related AE.
Trial registration: ClinicalTrials.gov (NCT01535001).

Introduction

Guidelines from the European League Against Rheumatism (EULAR)[1] and the Osteoarthritis Research Society International (OARSI)[2] recommends a multimodal, individualized non-surgical treatment program as first line treatment for knee osteoarthritis (OA). The core treatment is exercise, weight management (if indicated) and education, while biomechanical interventions (such as insoles) and pharmacological treatment are recommended if indicated[1,2].

While the effects from exercise or diet alone were less convincing, the Arthritis, Diet, and Activity Promotion Trial (ADAPT) showed that the combination of exercise and weight loss improves pain, function[3] and health-related quality of life (QOL)[4] more than healthy lifestyle advice after 18 months, indicating an additive effect when combining treatments. This was confirmed by a

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subsequent trial, demonstrating that the combination of exercise and diet is more effective than either exercise or diet alone in improving pain and function[5]. However, both trials were performed in obese community dwelling adults, and no similar high quality trials have been conducted in OA patients with more severe disease who are seen in secondary health care. Such information would provide clinically relevant support for non-surgical treatment as a viable treatment option for those with more advanced disease.

The purpose of this randomized controlled trial (RCT) was to investigate whether a 12-week treatment program of neuromuscular exercise, education, diet, insoles and pain medication (the MEDIC treatment)[6] results in greater improvement in pain, function and QOL compared with usual care (information and advice on knee OA and recommended treatments) in patients with knee OA seen in secondary health care by an orthopedic surgeon but found to be not eligible for a total knee replacement (TKR).

We hypothesized that the treatment program would result in greater pain reduction, functional improvement and increase in QOL than usual care at the 12-month follow-up.

Method

Trial design

This was a parallel group assessor-blinded RCT (1:1 treatment allocation) with follow-ups at 3, 6, and 12 months conforming to the CONSORT statement for reporting RCTs[7,8]. The study was designed to follow the principles of the Declaration of Helsinki, approved by the local Ethics Committee of The North Denmark Region (N-20110085), and registered at ClinicalTrials.gov (NCT02091830).

Details of the recruitment process, full eligibility criteria, the process of randomization and allocation concealment have been published previously in the study protocol[6].

Patients and recruitment process

In the North Denmark Region, patients potentially eligible for a TKR are referred to one of two specialized, public outpatient clinics by their general practitioner. Patients for our study were recruited from this population by an orthopedic surgeon from either of the two clinics (50 patients from each clinic) between April 3, 2012 and July 12, 2013. We enrolled 100 patients with symptomatic and radiographically-confirmed knee OA, found not eligible for TKR by an orthopedic surgeon (decision among others factors based on pain, function and radiographic severity[9]), but experiencing more than mild limitations. Major exclusion criteria were less than mild limitations (a score above 75 on a 0–100 worst to best scale in the self-report questionnaire Knee injury and Osteoarthritis Outcome Score $(KOOS)_4$ defined as the average score for the subscale scores for pain, symptoms, activities of daily living (ADL) and QOL); previous ipsilateral knee replacement; and a mean knee pain intensity in the previous week greater than 60 mm on a 100 mm visual analog scale (VAS).

Randomization and allocation concealment

A priori, the randomization schedule was generated in permuted blocks of eight, stratified by clinic. The allocation numbers were concealed in opaque envelopes prepared by a staff member independent of the study. The envelopes were accessible to one research assistant at each clinic, only opening them after informed consent and baseline measures had been obtained.

Study treatments

The MEDIC treatment

The 12-week MEDIC treatment consisted of five components: education, exercise and insoles were prescribed to everyone in the MEDIC group, with weight loss and/or pain medication prescribed if indicated. The MEDIC treatment was delivered by physiotherapists and dieticians trained in delivering the treatment to ensure proper standardization of the treatment.

Education. The education consisted of two 60-min sessions focusing on disease characteristics, treatment and assistance to support self-help by actively engaging the patients in the sessions and in the treatment. The education included in this study, in combination with neuromuscular exercise, has previously demonstrated to be feasible and efficacious in improving pain, function and QOL[10].

Neuromuscular exercise. The NEuroMuscular EXercise training program (NEMEX), previously found feasible in patients with moderate to severe knee OA[11], was undertaken by patients twice a week for 12 weeks with each session lasting 60 min. The exercise program is based on neuromuscular and biomechanical principles[11]. It aims at restoring neutral functional alignment of the lower extremities by obtaining compensatory functional stability and improving sensorimotor control. It consists of warm-up and cool-down periods with a circuit program with four exercise circles in between. Key elements are core stability/postural function; postural orientation, muscle strength and functional exercises. Each participant was monitored individually with regard to pain intensity during the exercise session. Progression was allowed if the quality of the exercise could be maintained[11]. Details of the program are provided elsewhere[11]. Following the 12 weeks of supervised exercise, there was a transition period of 8 weeks, where the program was increasingly performed at home to improve long-term adherence.

Diet. Patients with a Body Mass Index (BMI) $\geq$25 at baseline underwent a 12-week dietary weight loss program consisting of four 60-min sessions aimed at reducing the body weight by at least 5% and sustaining this weight loss to reduce symptoms[12]. The dietary intervention was based on principles from motivational interviewing with instructions and guidance relevant to the individual participant[13].

Insoles. Patients in the MEDIC group received an individually fitted full-length Formthotics System insole with medial arch support (Foot Science International, Christchurch, New Zealand). Additionally, patients with a knee-lateral-to-foot position (the knee moves over or lateral to the fifth toe in three or more of five trials) using the valid and reliable single limb mini squat test[14], had a 4° lateral wedge added to their insole.

Medicine. The patients were offered pain medication if the orthopedic surgeon considered it necessary for participation in the exercise. If no contraindications were evident, they were prescribed 1 g paracetamol four times, 400 mg ibuprofen three times, and 20 mg pantoprazol daily. The prescription was reassessed every 3 weeks. The patients were instructed to contact the physiotherapist if they questioned the continuation of the medicine.

Booster sessions. After the 12-week MEDIC treatment and the 8-week transition period but prior to the 12-month follow-up, the physiotherapist contacted the patients monthly by telephone to support the continuation of exercise and physical activity.

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