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Structural changes in the knee during weight loss maintenance after a significant weight loss in obese patients with osteoarthritis: a report of secondary outcome analyses from a randomized controlled trial

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SUMMARY

Objective: To compare structural knee joint changes in obese patients with knee osteoarthritis (OA) that after an intensive weight loss therapy were randomized to continuous dietetic support, a specialized knee exercise program, or 'no attention' for 1 year.
Methods: 192 obese individuals with knee OA underwent an intensive 16-week weight loss program with subsequent randomization to one of the three treatment groups. Changes in cartilage loss, bone marrow lesions (BMLs), synovitis, and effusion were assessed using semi quantitative assessments of magnetic resonance imaging (MRI) obtained at weeks 0 and 68 applying the BLOKS score.
Results: During the 52 weeks maintenance period the continuous dietary maintenance group support on average gained 1.1 kg (95% CI: −0.3:2.5) body mass, the exercise group gained 6.6 kg (95% CI 5.4:7.8) and the no-attention group gained 4.8 kg (95% CI: 2.9:6.7). There were no statistically significant between-group differences in changes in cartilage loss, synovitis or effusion at the follow-up (analysis of covariance; ANCOVA, $P > 0.16$), while there was an increased number of medial tibiofemoral BMLs in the exercise group (ANCOVA, $P = 0.015$) compared to both diet (difference: −0.21 [95%CI −0.40:−0.03]) and "no attention" (difference: −0.26 [95%CI −0.44:−0.07]) groups.
Conclusion: In this 1 year follow-up after weight-loss in obese knee OA patients, we found a potentially increased number of BMLs in the exercise group compared to the diet and no attention groups, with no between-group differences in changes in cartilage loss, synovitis or effusion. These findings should be interpreted with caution for exercise compliance, MRI methodology and follow-up time.
(ClinicalTrials.gov identifier: NCT00655941)

Introduction

The association between knee osteoarthritis (OA) and obesity is well known[1,2], and obesity is an important factor in the development of OA[2,3]. Accordingly, weight loss is recommended as treatment of choice[4] and the short-term results of weight loss on symptoms are comparable to that of a joint replacement[5]. There are no definitive data on whether weight loss is beneficial for reducing structural OA progression, but available data from different study designs support the notion that intensive dietary-induced weight loss and exercise interventions slow disease progression[4]. However, because knee OA is a slowly progressive disease it is generally agreed that structural disease modifying effects of an intervention should be assessed at the earliest after 1 year[6]. In relation to weight loss, this represents a challenge as maintaining weight loss is difficult.

Maintaining weight loss is typically achieved through continuous dietary counseling or exercise programs, which each

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and in combination have been shown to result in positive clinical long term (18 months) results in patients with knee OA[7]. While the evidence in favor of weight loss and weight loss maintenance with respect to symptomatic relief is indisputable, the effects of weight loss maintenance on structural disease progression are not well documented. Anandacoomarasamy *et al.*[8] showed that weight loss was associated with reduced loss of cartilage thickness and proteoglycan content over 12 months in a cohort of mixed OA and non-OA obese individuals. Other structural changes are also known to characterize OA such as bone marrow lesions (BMLs), cartilage loss, synovitis, and effusion. The effects of weight loss and weight loss maintenance on these structures are unknown.

The present study is a secondary report from a randomized trial and the present study purpose was to compare changes in magnetic resonance imaging (MRI) based assessments of multi-tissue changes in knee OA patients that after an intensive weight-loss therapy entered either (1) 1 year of continuous dietetic support from a dietician, (2) 1 year of a specialized knee exercise program or (3) a 1 year 'no attention' control group.

Patients & methods

Study design

This is a secondary report of MRI outcomes from the CAROT study – Influence of weight loss or exercise on CARtilage in Obese knee osteoarthritis patients Trial (ClinicalTrials.gov identifier: NCT00655941). The CAROT study was designed as a pragmatic randomized controlled trial, with pain and treatment response as primary outcomes and blinded outcome assessors[9]. In the CAROT study knee OA patients were included and were all given an initial 16 week intensive diet intervention, inducing a clinically significant weight loss, i.e., >10%[10–13]. Following the 16-week weight loss program the participants were enrolled in a 52-week maintenance program with random assignment to either (1) continued dietary consultancy, (2) knee exercise therapy, or (3) a no attention control group. Thus, the total study duration was 68 weeks (16 weeks weight loss phase + 52 weeks maintenance phase). The participant's most symptomatic knee at inclusion was designated as the target knee for assessments throughout the study.

Participants

CAROT participants were recruited from November 2007 to August 2008 from the outpatient clinic at the Department of Rheumatology, Frederiksberg Hospital, Denmark, through advertisements in newspapers and on the website of the Parker Institute. Additionally, local general practitioners were informed about the possibility of assigning patients to the project. All participants were prescreened *via* telephone using a series of standard questions concerning eligibility according to criteria of inclusion and exclusion.

Eligibility criteria for the CAROT study were age above 50 years, clinical knee OA confirmed by radiography (osteophytes and/or joint space narrowing assessed by a radiologist), and a BMI>30 kg/m^2. Exclusion criteria were: lack of motivation to lose weight, inability to speak Danish, planned anti-obesity surgery, or receiving pharmacologic therapy for obesity. The participants were asked not to change any medication or nutritional supplement during the study. The study was performed in compliance with the Helsinki Declaration, was approved by the ethics committee of the Capital Region of Denmark [H-B-2007-088], and all participants gave written informed consent.

Interventions and randomization

Initial weight loss program

The 16-week dietary program consisted of a low-energy-diet of normal food plus meal replacements (The Cambridge Weight plan, UK) and nutritional education. The details of the dietary program are described elsewhere[10,12]. Following the first 16 weeks of intensive dietary therapy, participants were randomly assigned with the use of minimization to one of three subsequent treatment groups with an equal allocation ratio (1:1:1). The concealed allocation was carried out on all patients entering the study at week 0 into blocks of 24 participants, consecutively enrolled by the recruiting staff at the Parker Institute, resulting in eight participants in each group per 24 enrolled. Thus, participants were randomly assigned at week 0 – independent of the first 16 weeks – to either (1) a continued dietary maintenance program, (2) exercise therapy lead by an experienced physical therapist, or (3) a no attention control group receiving no intervention for the 52 weeks maintenance period. For each block of patients enrolled, a randomization list was drawn up by the Biostatistician and given to the secretariat at the Parker Institute. After the patients had completed the first 16 weeks of dietary program, the secretariat informed the participants, when to meet with the dietician or physical therapist (i.e., securing concealed allocation), or if they did not have to meet until week 68. This way the random assignment prevented prior knowledge of forthcoming allocations by study participants and those recruiting them to the trial.

Continuous dietary program

The dietary maintenance intervention focused on long-term lifestyle modifications. Participants attended sessions lasting approximately 60 min. The participants were weighed and formula products were handed out (The Cambridge Weight Plan). Participants were advised to use one formula product a day to enhance weight loss. The educational themes in the sessions were: energy expenditure and energy balance, macronutrients, satiety, digestion, motivation, and diet planning. The group treatment provided a combination of empathy, social support, and friendly competition. The dietician aimed to maximize adherence by reinforcing positive dietary changes and addressing barriers to adherence. Attendance to the sessions was recorded.

Exercise program

The 3 days/week exercise program prescribed to each participant randomized to the exercise group consisted of a warm-up phase (10 min), a circuit training phase (45 min), and a cool down/stretching phase (5 min). The exercise intervention was divided into four periods of 12 weeks and one period of 4 weeks (total 52 weeks). The exercise program was designed to gradually transfer the intervention from supervised facility-based exercises to unsupervised home-based exercises. The participants alternated between attendance to exercise at the facility and performing exercises at home. During the first 12 weeks the intervention was facility-based 2 days/week, and concurrently the participants were encouraged to perform the exercises at home 1 day/week. In the second 12 weeks period the participants exercised at the facility 1 day/week and at home 1–2 days/week. During the third 12 weeks period the participants exercised at home 3 days/week, and attended one facility-based exercise session once every second week, substituting one home exercise session. In the fourth 12 weeks period the participants exercised at home 3 days/week, attended one facility-based exercise session once every 3 weeks, substituting one home exercise session,