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Exercise training is associated with reduced pains from the musculoskeletal system in patients with type 2 diabetes

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ABSTRACT

Aims: To investigate the effect of exercise training on musculoskeletal pain in patients with type 2 diabetes.

Methods: The intervention was exercise twice weekly for 12 weeks. The primary outcome was musculoskeletal pain assessed using a 0–10 Numeric Rating Scale (NRS) in 11 body sites. Secondary outcomes were use of analgesics, glycaemic control and body weight.

Results: The participants (n = 69) were 66 ± 10 years old, 38 were men and 50 completed the intervention. Pain in the limbs was more frequently reported by the participants compared to a matched general population (80.9% vs 65.3%, p = 0.007). The participants who had any pain at baseline (NRS > 0) and severe pain (NRS > 3) reported significantly decreased pain in the feet, calf muscles, knees, thighs, hips, lower back and arms after the training period. Use of analgesics was unchanged, HbA1c (mmol/mol) decreased from 60 ± 15 to 54 ± 11, p < 0.001 and body weight (kg) decreased from 100.5 ± 19.1 to 98.6 ± 17.7, p = 0.005.

Conclusions: The participants with type 2 diabetes reported more frequent pain than a matched general population. The training intervention was associated with reduced musculoskeletal pain. Reduced pain may together with a positive impact on glycaemic control be an important motivational factor in patients with type 2 diabetes to perform exercise training.

1. Introduction

Combined with dietary changes and medication, exercise training is a cornerstone in type 2 diabetes mellitus (T2DM) treatment and self-management [1]. Several systematic reviews have shown that exercise training has the potential to improve glycaemic control with mean effects varying from −0.3 to −0.8% of HbA_{1c} [2–6]. The recommendations of

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exercise training to patients with T2DM include aerobic training and resistance training [1,7]. Thus, in Denmark the ambition is to systematically offer exercise training programs to patients with T2DM, as part of the rehabilitation program in the municipalities and hospitals [7].

Whilst exercise training may improve glycaemic control in patients with T2DM, the effect of exercise training on musculoskeletal pain in these patients is unknown. A previous study indicated that patients with T2DM report musculoskeletal pain twice as often compared to a gender and age matched general population, and the pain was associated with lower levels of physical activity [8]. The pain may be a symptom of osteoarthritis which is not a contraindication to exercise training [9], and in the general population these symptoms may even be reduced with exercise training [10]. In diabetes, other musculoskeletal manifestation may arise from specific diabetes related changes as a result of advanced glycation end-products [11].Whether exercise interventions reduce the pain in patients with T2DM and musculoskeletal pain correspondingly has not been investigated. If a positive effect on pain reduction can be detected, it may contribute to increased motivation for physical activity in patients with T2DM.

The purpose of this study was to investigate the effect of exercise training on musculoskeletal pain in patients with T2DM. It was hypothesized that a 12-week exercise training program would decrease musculoskeletal pain in participants with T2DM.

2. Subjects, materials and methods

2.1. *Study setting*

The study was a clinical intervention study conducted during the implementation of an exercise training programme in patients with T2DM in The Capital Region, Denmark. The participants were consecutively recruited from a hospital (Nordsjællands Hospital) and a municipality (Hørsholm), where the intervention was delivered. The participants were recruited from February 2015 to December 2017. The data from the study were collected in another unpublished study which was stopped because of problems with recruitment of a projected number of participants.

The study protocol was approved by the local scientific ethical committee (ID: H-1-2014-122), registered at the Danish Data Protection Agency and on Clinicaltrials.gov (ID: NTC02366416), and it was performed in accordance with the Helsinki Declaration. Prior to the intervention the participants received oral and written information and gave oral and written consent.

2.2. *Inclusion, exclusion criteria*

The inclusion criteria were 18 years of age or older, diagnosed with T2DM and able to perform exercise training. The exclusion criteria were type 1 diabetes and other types of diabetes, dementia, psychiatric disorders or inability to understand Danish, pregnancy, participation in a structured exercise training programme within the last three months of inclusion, not having regular visits to the hospital or a general practitioner, hypoglycaemic events or unawareness, treatment by an ophthalmologist, known severe autonomic neuropathy, acute or untreated heart diseases, acute infections, other acute conditions with patients discomfort.

The participants were tested at baseline and after the 12-week intervention period.

2.3. *Data collection*

The primary outcome was self-reported musculoskeletal pain from 11 body sites during the last 14 days (feet, calf muscles, knees, thighs, hips, lower back, upper back, shoulders, neck, arm, and hands) assessed using a self-report 0–10 Numeric Rating Scale (NRS) with higher scores indicating more pain [12].

The secondary outcomes included glycaemic control, HbA1c, measured using a Tosoh G8 HPLC Analyzer (Tosoh Bioscience Inc., San Francisco, CA, USA), body weight and self-reported use of any type of analgesics, reported as 'number of tablets'. At baseline, the participants' musculoskeletal pains were compared to an age-, gender- and county-matched general population. The comparison of musculoskeletal pain between the participants and the general population was performed using three questions from the Danish Health and Morbidity Survey from 2017 [13] ('Have you during the last 14 days had pain in the i) shoulder/neck, ii) back/low-back, and iii) upper or lower limbs'). The participants' answers were compared with answers from a general population sample ($n \sim 58{,}000$) living in the Capital Region with the same age and gender as the participants'.

Gender, age, employment status and complications were registered at baseline in questionnaires and supplemented by information from patient records.

2.4. *The applied exercise training*

The exercise training was provided twice weekly for 12 weeks in groups of up to 10 participants. At baseline all study participants had an individual session with a physiotherapist, where the participants were tested according to the outcome measures and questionnaires were handed out. The intervention included one hour of exercise training of approximately 10 min warm-up, 15 min aerobic interval exercises on ergometer bikes and 30 min circuit training entailing aerobic exercises and resistance training. The resistance training was performed using elastic band with different resistance, dumb bells with weights ranging from one to 10 kilos, a leg press equipment (with up to 250 kilos resistance), and a knee extension equipment (with up to 100 kilos resistance). All resistance training exercise were dynamic. The training also included a short break and it was finished with stretching of the major muscle groups. The intensity during the aerobic exercises was aimed to correspond to 14–16 on Borgs 'rating of perceived exertion' [14], which was used to subjectively monitor the intensity. The resistance training was aimed at an intensity of 8–12 repetition maximum [15]. Before the exercise sessions, the participants measured their blood glucose. If the blood glucose was below 6 mmol/l or above 17 mmol/l, the participant's medical condition was examined before any exercises were allowed. If exercises were allowed with a low blood glucose level, a glucose supplement was given. If a participant had a high blood glucose level, exercises were only allowed if no acute disease was reported by the participant. In any doubts about the safety of exercises and low or high blood glucose levels, the participants were not allowed to perform the exercise session.

2.5. Statistical analyses

The present study was exploratory, and no power calculation was performed in relation to the primary outcome. Data were normally distributed and parametric statistics were used on continuous data. Welch's *t*-tests were used to test for significant differences in musculoskeletal pain from baseline to post-intervention in participants with any pain (NRS > 0) and severe pain (NRS > 3) (19). Welch's *t*-test was also used to test for significant differences between the participants who completed the intervention and those who dropped out, and to test for differences in changes in pain between participants who performed exercise in the hospital and the municipality and between men and women. Wilcoxon's test was used to compare the use analgesics before and after the intervention period. A chi squared test was used to test the difference in reported pain in the participants and the general population. Pearson's test was used to test the correlation between changed BMI and changes in pain. Data are presented as number and percentages, mean ± standard deviation (SD), mean (95% confidence interval (CI)) or median (range). The analyses were performed using SPSS Statistics version 22 and p-values below 5% were considered statistically significant.

3. Results

A total of 123 patients were screened for inclusion, 41.5% were excluded or declined participation and 69 participants were enrolled in the study. The characteristics of the participants are presented in Table 1. A total of 50 participants completed the intervention. The mean exercise attendance among the completers were 21.6 ± 2.4 (89.9% ± 10.2) exercise sessions. One HbA_{1c} test was missing at baseline and blood pressure was missing 27 participants.

When the levels of pain reported by the participants were compared to the general population as presented in Table 2, there was no difference between the two samples' pain in the shoulder/neck, whereas the participants more often reported pain in the back/low-back and upper or lower limbs.

In Fig. 1 the level of musculoskeletal pain after the intervention in those participants who reported any pain at baseline (NRS > 0) is presented. The pain decreased in the feet, n = 26 (−2.3 (−3.4; −1.1)), calf muscles, n = 18 (−2.1 (−3.7; −0.4)), knees, n = 30 (−1.4 (−2.1; −0.6)), thighs, n = 17 (−1.7 (−2.6; −0.8)), hips, n = 19 (−2.0 (−3.0; −1.0)), lower back, n = 31 (−1.0 (−2.0; −0.1)), arms, n = 17 (−1.8 (−2.8; −0.8)), and hands, n = 19 (−1.5 (−2.8; −0.2)).

Musculoskeletal pain in those participants who reported severe pain at baseline (NRS > 3), decreased in the feet, n = 16 (−2.8 (−4.7; −1.0)), calf muscles, n = 8 (−3.8 (−7.0; −0.5)), knees, n = 17 (−1.5 (−2.8; −0.2)), thighs, n = 6 (−2.8 (−5.4; −0.2)), hips, n = 9 (−3.0 (−4.8; −1.2)), lower back, n = 15 (−2.0 (−3.4; −0.6)) and arms, n = 9 (−2.0 (−4.0; −0.0)) after the 12 weeks exercise training intervention (Fig. 2).

Table 1 – Baseline characteristics of the included participants with type 2 diabetes.

Variables	N = 69
Gender (m/f)	38/31
Age (years)	66 ± 10
Weight (kg)	101.7 ± 19.3
BMI (kg/m^2)	34.3 ± 5.7
HbA_{1c} (mmol/mol)	60 ± 15
Diastolic blood pressure (mmHg)	83 ± 11
Systolic blood pressure (mmHg)	148 ± 17
Employed (yes/no)	13/56
Complications	
Nephropathy	16 (32.2%)
Arthritis	20 (29.0%)
Neuropathy	24 (34.8%)
Cardiovascular disease	30 (43.5%)
Location (hospital/municipality)	43/26

Data are presented as the mean ± SD or as frequencies and proportions. m male; f female; kg kilos; m meters.

There were no differences in the changes of pain between hospital and municipality sites and between men and women (data not shown). Changes in BMI were not associated with changes in pain (data not shown).

The use of analgesics was unchanged during the study (Table 3), HbA1c decreased by −6 (−9; −3) mmol/mol, and body weight decreased by −1.9 (−3.2; −0.6) kg.

Nineteen participants (27.5%) dropped out of the intervention. The reasons to drop out were 'increased back pain after the first exercise session' (n = 1); 'unchanged baseline pain' (n = 1); 'other disease' (n = 6); 'distance to the exercise centre' (n = 1); 'personal problem' (n = 1); 'time consuming' (n = 2); and 'unknown' (n = 7). The participants who dropped out reported more pain located in the hands at baseline compared to the completers (drop-outs vs completers 3.2 ± 3.0 vs 1.3 ± 2.2, p = 0.025) (Fig. 3). There were no differences between drop-outs' and completers' age (62 ± 11 vs 67 ± 10 years, p = 0.129), gender (53% vs 56% males, p = 0.802), HbA1c at baseline (66 ± 21 vs 60 ± 15 mmol/mol, p = 0.368) and BMI at baseline (35 ± 6 vs 34 ± 6 kg/m^2, p = 0.500).

No serious adverse events were reported in those who completed the training program or dropped out.

4. Discussion

To our knowledge, this study is the first to investigate the effect of an exercise intervention on musculoskeletal pain in patients with T2DM. The main result was that musculoskeletal pains were decreased with a 12 weeks exercise training program in participants with T2DM. The participants' use of analgesics remained unchanged.

Previous studies have shown that patients with T2DM report pains from the musculoskeletal system more often than the general populations [8,16] and this was also true in the present study. The improvement in musculoskeletal pain in this study was achieved with only two exercise sessions per week, whilst most other exercise trials have used three

Table 2 – Musculoskeletal pains during the last 14 days assessed using questions from the Danish Health and Morbidity Survey 2017. The included participants with type 2 diabetes at baseline compared to an age and gender matched general population.

Variables	T2DM	General population	p
Pain in shoulder/neck	50.8%	49.6%	0.898
Pain in back/low-back	67.7%	54.4%	0.030
Pain in upper or lower limbs	80.9%	65.3%	0.007

Data are presented as percentages. T2DM type 2 diabetes mellitus.

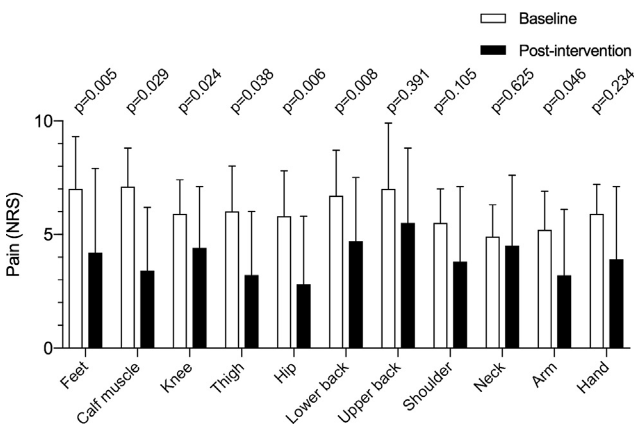

Fig. 1 – Change in self-reported pain of all participants who completed the intervention and reported pain >0 on Numeric Rating Scales (NRS) at baseline.

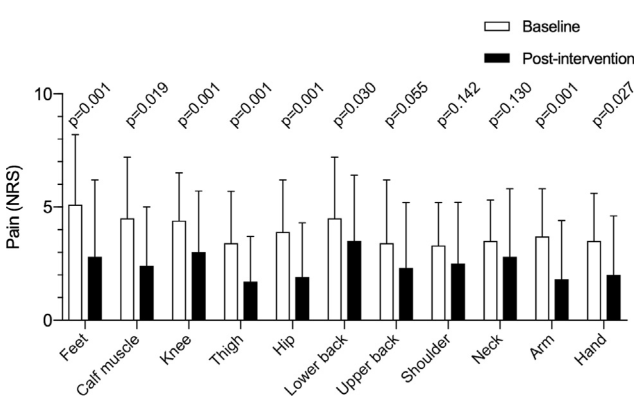

Fig. 2 – Change in self-reported pain of all participants who completed the intervention and reported pain >3 on Numeric Rating Scales (NRS) at baseline.

Table 3 – HbA1c, body weight and analgesics usage before and after the 12 weeks exercise training program.

Variables	Baseline	Re-test	p
HbA1c (mmol/mol)	60 ± 15	54 ± 11	<0.001
Body weight (kg)	100.5 ± 19.1	98.6 ± 17.7	0.005
Analgesics (n)	0 (0–6)	0 (0–5)	0.363

Data are presented as mean ± SD or median (range).

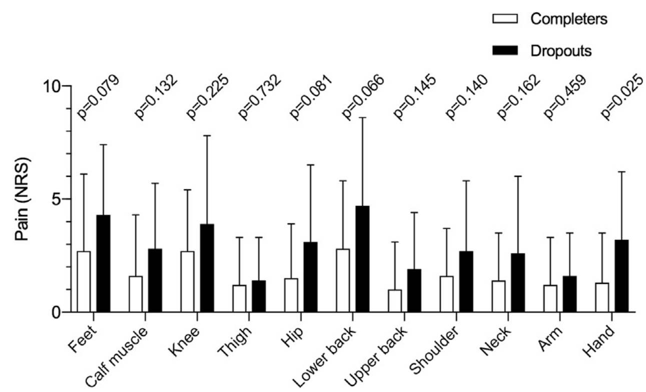

Fig. 3 – Self-reported pain at baseline in completers and dropouts. NRS Numeric Rating Scale.

exercise sessions weekly to achieve effects on other parameters. The participants' overall level of physical activity may also have increased during the intervention period and could therefore have affected this study's outcomes.

The reported pains may arise from osteoarthritis and musculoskeletal manifestations caused by diabetes specific pathogenesis including advanced glycation end-products or as a manifestation of diabetes related peripheral neuropathy. Indeed, symptoms from peripheral neuropathy in patients with T2DM have been suggested to be reduced after exercise training [17,18]. However, the pains may also arise from general rheumatic diseases including osteoarthritis [19]. Regardless of the underlying reasons for the reported pain, it may be associated with barriers to increase levels of physical activity and adherence to exercise training programs. The physiological mechanism in the pain relief after exercise training was not investigated in this study. It has been suggested that the musculoskeletal pain may be reduced by a positive adaptation in the cartilage after exercise training [20]. Another explanation may be, that exercises have a systemic effect on musculoskeletal pain, and the exercises have effects on other body sites than the those who are involved in the exercises [21].

The most pronounced effects were reported in the low back and in the different anatomical areas of the legs. The positive effects on pains in the lower limbs may reflect that the exercises primarily included the legs. The results are in line with studies of exercise training to patients with osteoarthritis, where exercise training is associated with reduced pain [22]. Further studies are needed to determine the underlying reasons to the musculoskeletal pains in patients with T2DM and how they are affected by exercise training.

Reduced pain with exercise training may be an important motivational factor for patients to elevate the level of physical activity and continue exercise training. Whilst an effect of exercise training on glycemic control is crucial, the potential additive effect on musculoskeletal pain may have another motivational factor associated to daily living. Pains in the hands at baseline were the only pain, that was associated with an elevated dropout rate, and this finding could most likely be found by chance. It could be speculated that if participants with musculoskeletal pains participate in supervised exercise training programs, they may experience a decrease in pain, and their chances to complete the program and gradually adopt a more physically active lifestyle may increase.

The present results should be interpreted with caution as the study was performed without a control group. In addition, it was not possible to register intake of glucose-lowering medication among the participants during the intervention and control for one such co-intervention to improve the glycaemic control. Likewise, the potential impact of diabetic complications and comorbidities, including osteoarthritis, was not considered in the present study, as the validity of these information obtained from questionnaires and medical records were considered low and subject to severe underreporting. The study also suffered from severe retention challenges as more than one fourth of the included participants dropped out of the study. Despite a relatively large number of dropouts, the attendance in the group of participants who completed the intervention was high (~90%).

This study may have important clinical implications in terms of positive effects of exercise training on musculoskeletal pain in parallel with decreased HbA1c and body weight. Indeed, a pain relief may be an important motivational aspect of exercise training in patients with T2DM, who have lower levels of physical activity compared to a non-diabetes population [23].

In conclusion, exercise training in 12 weeks was associated with reduced musculoskeletal pain in patients with T2DM and this effect may be an important motivational factor to the patients' initiation and adherence to exercise training.

Declaration of Competing Interest

None.

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