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Digital exercise interventions in low back pain – RCT with longitudinal evaluation of clinical outcome measures and MRI examinations

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Background

Low back pain is a major global health problem. It is one of the most common causes of disability (1,2) and leads to high costs for society (3). Most adults will suffer from low back pain at some point in their lives. The incidence is highest in people in working age and more common in women than in men (1).

Low back pain is defined according to European guidelines, as pain and discomfort localised in the lumbosacral region, with or without radiating leg pain (4). Historically, low back pain is classified according to diagnostic triage; nonspecific low back pain, nerve root pain or possible or confirmed serious pathology (4). Since a specific anatomical cause rarely can be identified either confirmed by clinical examination or imaging, most cases of low back pain are classified as nonspecific (1). Low back pain is also classified based on time duration, acute <6 weeks, subacute 6–12 weeks and long-term >12 weeks (4,5).

The condition is complex and is often described as a result of biological, psychological and social factors (1). Lifestyle factors such as smoking, obesity and low physical activity levels, which may lead to poorer overall health, are seen to be related to low back pain (1). Mental illness and psychological factors such as confidence in one's own ability and fear of movement are other factors that are related and may increase the risk of long-term problems (1,4,5).

Acute low back pain usually decreases over time, and the person can gradually return to previous activity level. However, recurrent episodes are common, about 30% experience having a new episode of low back pain within a year (1). For a small group, there is a risk of developing long-term problems (4). Long-term low back pain is seen as a condition where different patterns of pain may change over time (1,6).

According to World Health Organization (WHO), *physical activity* is defined as any body movement generated by skeletal muscles and requiring an increase in energy expenditure (7). *Physical exercise* is defined as a planned, structured and recurring physical activity aimed at maintaining or improving physical capacity such as fitness, mobility and strength (8). *Physical inactivity, or insufficient physical activity*, is defined as not meeting these recommendations (7). Studies have shown that patients with long-term low back pain have a low level of physical activity (9). There is no general definition of *Health-related quality of life* but refers to quality of life related to function and well-being in bad health, disease and treatment (10).

International guidelines focus on a biopsychosocial model when assessing and treating low back pain (11). This model includes information and advice on being physically active and, if possible, avoiding sick leave. It is also important to support self-care strategies. There is evidence for exercise training for patients with low back pain and physiotherapy is recommended as the first treatment option (11). However, there is still a lack of evidence which type of training has best effect (12,13). Both supervised and non-supervised training has been suggested to have effect on these patients well as daily physical activity such as Nordic walking (Hartvigsen et al-10, Matará-Peñarrocha et al-20, Quentin et al 21) (1,14,15). To reduce pain and increase functional capacity, patients with long-term low back pain are recommended daily physical activity. In addition, muscle strengthening exercise

and/or specific exercise for core stability[1] with or without the addition of aerobic exercise[2] is generally recommended (16). To achieve good adherence to exercise and training, patients with long-term low back pain demand better support from the healthcare, improved opportunities for supervised training and the use of new technology to visualize feedback (17).

The healthcare is facing major challenges and needs to be transformed. Health care closer to residents and more e-services are part of this transition. There is currently little knowledge about the effects of supervised digital physiotherapy training. Previous studies have shown that digital exercise training is as effective as traditional exercise for patients with long-term low back pain (18,19). Studies have also shown that digital training can contribute to increased accessibility and cost-effectiveness (20,21). However, there is a need to structurally evaluate supervised digital physiotherapy training in real time for patients with long-term low back pain.

During the pandemic, most training sessions were cancelled or performed at home, either on their own or via link. In Sweden, a daily home-training program on TV have had great impact during the pandemic, but also a large number of gym companies have offered supervised training via link both in real time and recorded during the last years. Digital training is an effective way to reach people and keep them interested to keep up with their training. It is therefore of interest to evaluate the effect of supervised training via link in this patient group.

Lack of reliable methods to determine what causes the pain (nonspecific back pain) makes it difficult to set a specific diagnosis. It is therefore of great importance that new methods are developed to improve the ability to the give a correct diagnose. Furthermore, the effect of different treatment on structural changes of the spine, e.g., different types of exercise, may guide how to best advice patients with different pathologies. With magnetic resonance imaging (MRI) an image of the spine can be obtained, but there is still a lack of evidence of its diagnostic benefit and knowledge if it can determine the origin of back pain. In a previous study using advanced MRI technology groups of individuals exposed to different exercise over a 3-month period demonstrated different disc patterns (22). Furthermore, new MRI techniques have demonstrated altered biodynamic properties on group level, when comparing patients with low back pain and control persons (23).

Purpose

The overall aim is to evaluate two different types of digital training interventions (aerobic, core stability) supervised by physiotherapists compared to daily physical activity in terms of clinical and patient-reported outcome (PROM) in patients with low back pain, both for short- and long-term. Furthermore, to evaluate whether new diagnostic MRI methods can identify longitudinal spine tissue changes and to analyse if there is an exercise-related difference (differences between the training groups). In addition, the ability to participate in the different exercise programs and their effect on pain in relation to baseline MRI findings will be evaluated.

Question / Hypothesis

- Do the clinical (muscle strength, conditioning, mobility, function/physical capacity) and PROM differ between patients with low back pain randomized to 3 different exercise interventions (aerobic, core stability, daily physical activity) after 6 and 12 months?

[1] the capacity of the lumbar-pelvic-hip muscle complex to control lower trunk movement and maintain stability of the vertebral column after skeletal perturbation.

[2] any activities that raise heart rate and make breathing somewhat harder

- Does patients' physical capacity change over time, and is there a difference between groups?
  Does the training effect persist 12 months after ending the training intervention (6 months)?
- Can new diagnostic MRI methods identify characteristic changes over time in back tissue (disc/vertebra/muscle) in patients with low back pain in the full cohort and/or after different types of exercise intervention (aerobic, core stability, daily physical activity) after 6 - 12 months?
- Are MRI-verified changes in the back detected at base line associated the ability to participate in the training interventions as well as associated with positive effect (pain relief, increased endurance and muscle strength, etc.) after participating in any of the training intervention?
- Is there a relationship between clinical changes (pain, activity level and quality of life/function) and longitudinal changes in MRI verified components of the spine tissues depending on what type of exercise intervention (aerobic, core stability, daily physical activity)?

Hypothesis 1: Supervised digital training (aerobic and/or core stability) led by physiotherapist gives better results regarding clinical and PROM compared to self-training (daily physical activity), and the effect persists after ending the intervention (6 months) in patients with low back pain.

Hypothesis 2: new MRI methods can identify exercise-related changes in the lumbar spine in patients with nonspecific low back pain after undergoing supervised physiotherapy digital training (aerobic and/or core stability).

Hypothesis 3: there is a relationship between identified changes in low back tissues and the effect of different types of exercise interventions in patients with low back pain.

Method & Materials

Patients seeking primary health care (primarily Vänersborg/Trollhättan/Uddevalla, Sweden) for lower back pain will be asked to participate. Inclusion criteria: low back pain> 3 months, 18-50 years, have access to computer/tablet/mobile

Exclusion criteria:

- Inadequate Swedish as the language is an obstacle to be able to fully understand written and oral information regarding the project and to follow training instructions
- Other ongoing treatment/exercise for their low back pain
- Age > 50 years
- Patients with radiating leg pain and other neurological symptoms
- Previous back/neck surgery
- Pregnancy
- Diagnosed systematic diseases engaging the spine as rheumatoid arthritis, ankylosing spondylitis
- Factors that prevent an MRI examination, such as claustrophobia, metal implants, etc.

Patients who meet the inclusion criteria and agree to participate in the study will undergo a thorough clinical low back examination according to standard routine, and assessment of function and physical capacity performed by an experienced physiotherapist.

Before start, the patient will undergo MRI examination (NÄL, Trollhättan, Sweden) and functional imaging methods without contrast agents (such as diffusion tensor imaging (DTI), DIXON[3], magnetic resonance spectroscopy (MRS) and T2 mapping[4]) will be obtained.

Sample size calculation regarding the training intervention: based on a p-value 0.05, power 0.85, SD 0.1 and a minimal clinical change in Visual Analog Scale (VAS)/pain 0.11 (Hawker et al-11) gives 23 people/group.
Sample size calculation regarding MRI: is based on the possibility of detecting a 0.5% difference (power size 0.041) regarding the T2 value between the three occasions with significance level 0.05 and power 0.8. Considering possible dropouts, we expect 30 patients in each group, a total of 90 patients.

Intervention

Training intervention

After completing the clinical low back examination, the patient will initially be randomized to either group 1 & 3, then 2 & 3 (see below). As more units will be included over time (Vänersborg/Trollhättan/Uddevalla, Sweden), we expect several training groups on-going at the same time.

Group 1 Aerobic
Group 2 Core stability
Group 3 Daily Physical Activity

Group 1 & 2 will be training according to the following program for 3 months: 45 minutes 3 times/week, 2 times digitally supervised by experienced physiotherapist and one-time un-supervised training. Then 3 months of un-supervised training with regular follow-up meetings with responsible physiotherapist.
Each training session includes warm-up, specific exercises with the ability adjust according to pain and function, and progression, then final relaxation exercises. Estimated number of participants/group (1&2): 10-12, inclusion rate about 35 patients first year, 35 patients 2nd year and 20 patients 3rd year (only preliminary calculation as we depend on the inclusion rate of patients and number of involved health care centre).

Group 3 (~10 patients will run concurrently with group 1or 2) will receive training instruction regarding daily physical activity equivalent to >150 min/week according to WHO recommendations (7) (11) (12) for 6 months. The activity will be recorded in a health app on the patient's mobile.

All patients (groups 1-3) will be able to continuously book a video appointment with the physiotherapist responsible for the training during the whole intervention period.

Any problems that cannot be solved during video consultation or at a follow-up examination will be referred back to the attending physician.

MRI scan

All included patients will be examined with MRI including T1- and T2-weighted sequences and functional imaging methods (such as DTI, DIXON and T2 mapping).

Data collection

Training intervention

[3] a chemical shift imaging method
[4] a magnetic resonance imaging technique used to calculate the T2 times of a certain tissue and display them voxel-vice on a parametric map.

Clinical examination of the low back will be performed according to standard routine (baseline – 6 months – 12 months) by an experienced physiotherapist. The examination will also include muscle strength tests and assessment of physical capacity.

At the same occasion, the patient will undergo MRI examination according to the protocol above. Responsible for the development of specific imaging methods and training of staff at the Imaging and Function Department is an experienced MRI physicist.

All clinical data will be recorded in the patient's medical record. All MRI scans will be archived as a medical record according to the hospital's regulations.

The patients will answer several questionnaires at the base line, 3 – 6 – 12 months. The questionnaires are registered in a web-based Survey & Reporting program (https://webropol.se/). The patients will receive mail or SMS with information when and how to answer the questionnaires.

The questionnaires include demographic data (based on questions included in SweSpine (https://www.swespine.se/), physical activity (https://www.socialstyrelsen.se/), as well as established and validated questionnaires regarding low back pain such as VAS (24), Oswestry Low Back Pain Disability Questionnaire (25), TAMPA scale of kinesiophobia (26), Hospital Anxiety and Depression Scale (HAD) (27), Swedish Version of the General Self-Efficacy Scale (28) and EQ-5D-5L. (29)

Analysis of MRI examination

Conventional radiological categorization schemes (identification of high intensity zones = HIZ in the intervertebral discs and Modic changes in the vertebrae), as well as advanced analysis methods (e.g. histogram analysis, shape/texture analysis and regional analysis) will be used for detailed characterization of the vertebrae/disc/muscle.

The MR images will be assessed according to clinical routine and in addition, when relevant, according to conventional classification systems for specific morphological changes such as Modic Types, Schmorls nodules, High-Intensity Zones. New objective tissue characteristic measures (histogram analysis, shape/texture analysis and regional analysis) in vertebrae/disc/muscle will be extracted by the software we previously have developed and validated based on artificial intelligence (histogram analysis, shape/texture analysis and regional analysis) (30)

Data analysis

All data will be documented in a separate database. This database will be password protected and only those directly involved in the study will have access to the database. In addition, all personal data will be pseudonymised according to EU general data protection rules (GDPR) before exported into SPSS (https://www.ibm.com/products/spss-statistics). Data will only be analysed at the group level.

The questionnaires in Webropol will be exported to SPSS for analysis.

Descriptive statistics will be presented as mean/standard deviation or median/range. Comparisons between and within groups will be conducted using either parametric or non-parametric statistical methods depending on data quality. Bonferroni correction will be performed when multiple comparisons are done. All statistical tests will be 2-tailed with statistical significance level of $p<0.05$.

Spearman rank correlation will be used analysing the association between specific morphological changes and clinical data. In addition, multiparametric prediction modelling will be performed (based on unsupervised/supervised machine-learning).

Expected result / Clinical relevance

By offering patients supervised training led by experienced physiotherapist, we hope for high compliance and thus improved chance for a high-quality study evaluating the result of the different training programs. Muscle strength exercises and specific exercise programs to improve trunk control as well as aerobic physical exercise to reduce pain and increase physical capacity and functional capacity are already well-established treatment methods for patients with long-term low back pain (14-16) (30,31,32). However, research has shown that patients demand better support from healthcare where patients wanted to use technology to visualize feedback and improved opportunities to be guided in their training (17). A previous randomised trial compared supervised physiotherapist-led exercise and "unsupervised" home exercise and found supervised training more effective regarding several patient-related outcome measures, such as pain, health-related quality of life, and function (7) (14). With a personal and regular contact with the physiotherapist digitally, the present study setup provides such support which in turn likely improves patient related outcomes.

To evaluate whether the effect of daily physical activity is comparable to more exercise-intensive programs is important since if this can be shown the likelihood that more people continuing being physically active increases which in turn contributes to also other health-promoting effects. The detailed longitudinal MRI evaluation deepen the knowledge regarding how different physical activity affect the spinal tissues and has the potential to provide improved diagnostics for patients with low back pain.

Our previous study regarding monitoring the effect of exercise in healthy subjects was for the first time able to objectively measure the effects of different types of exercise on the disk.

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