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## Rehabilitation after lumbar disc surgery

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# 8

## **General discussion**

## General discussion

A substantial part of patients undergoing surgery for lumbar disc herniation suffer residual complaints. Recovery rates of 15-75% at 4-8 weeks post-surgery [1, 2] imply a poor outcome in 25-85% of the patients at short-term follow-up. The range in recovery rates is, amongst others, explained by differences in how recovery is operationalised. The group of patients with limited recovery highly contributes to the direct and indirect costs after lumbar disc surgery. In the Netherlands, two postoperative management strategies are commonly used: referral for early rehabilitation post-surgery or no referral [3]. An important aim of postoperative rehabilitation is to speed up return to daily activities and work and to prevent the development of chronic symptoms [4]. However, it is unclear if early rehabilitation (i.e., exercise therapy starting immediately after discharge from the hospital) is more effective than no referral. Healthcare decision makers are increasingly being faced with decisions about what treatment to implement with the limited resources available, but economic evaluations of postoperative management are scarce. Only two economic evaluations have been published and these both evaluated rehabilitation interventions that started 6 weeks after surgery [5, 6].

Evidence-based medicine requires clinicians to integrate the best external evidence with their individual clinical expertise, including 'compassionate use of individual patients' predicaments, rights, and preferences in making clinical decisions about their care' [7]. Best external evidence means clinically relevant research, amongst others into the efficacy of therapeutic interventions [7]. Randomised controlled trials yield stronger evidence of efficacy than any other design and systematic reviews and meta-analysis of RCTs provide the strongest evidence [8]. This implies that the most valuable recommendations for clinical practice, i.e., based on methods with highest rigor, come from systematically developed, evidence-based practice guidelines [9]. To generate evidence on the effectiveness and cost-effectiveness of rehabilitation after lumbar disc surgery we conducted several studies, amongst others: systematic reviews including meta-analyses and a randomised controlled trial with an economic evaluation alongside. This evidence should guide future guidelines or updates of existing guidelines on this topic.

## Rehabilitation after lumbar disc surgery and exercise therapy for acute non-specific low back pain: findings and methodological considerations of two systematic reviews

A Cochrane review published in 2008 on rehabilitation after lumbar disc surgery [10] was updated to summarise all available evidence (chapter 2). Rehabilitation after lumbar disc surgery was investigated in 22 trials. Most studies assessed the effectiveness of exercise therapy and only results of programs starting 4-6 weeks post-surgery could be pooled. Exercise seemed to lead to a faster decrease in pain and disability than no treatment, with small to medium effect sizes. High-intensity exercise programs seemed to lead to a slightly faster decrease in pain and disability than seen with low-intensity programs. No significant differences were noted between supervised and home exercise programs for pain or function. However, the overall quality of the evidence was only low to very low, indicating that further research is very likely to have an important impact on the confidence in the estimate of effect and is likely to change the estimate.

A second Cochrane review summarised 19 trials that assessed exercise therapy for acute non-specific low back pain (chapter 3). Exercise therapy was no better for pain relief or improvement in functional status compared with no treatment or other conservative therapies. In addition, there was no strong evidence that any particular form of exercise therapy was better than another. The evaluation was limited by the small number of studies for outcomes and time intervals for all comparisons, except for exercise therapy versus other conservative treatments. The last comparison included 10 trials.

In total 41 trials were included in the two systematic reviews. Many of these trials had a small sample size. Twelve trials included up to 25 participants per arm, with the two smallest trials including 10-14 participants, i.e., 5 or 7 per group. Notably, these were the two most recently published trials in each review (2012 and 2014). The largest trial included ( $n=710$ ), was a cluster randomised trial assessing effectiveness of an insurance medicine intervention after lumbar disc surgery. Only one trial assessing post-operative exercise therapy included  $>100$  participants per group. One trial assessing exercise therapy for acute low back pain included  $>100$  participants per group, and one trial compared two treatment groups including  $>100$  participants each and one smaller ( $n=66$ ) group. Although a small sample size is less

problematic when results of trials are to be pooled in meta-analyses, there is a risk of publication bias. Small studies are more likely to be published if they have positive results. Besides, these positive results may well be chance findings [11]. Roberts and colleagues dispute the usefulness of including small trials in systematic reviews [12]. Indeed, large high-quality trials are needed. Including small trials in systematic review may help creating awareness that large trials are needed in a specific area. Even if trial results were combined in a meta-analysis, in each of our systematic reviews, the total sample size did often not reach the, albeit arbitrary, threshold of  $n=400$  for continuous outcomes [13]. For trials assessing rehabilitation after disc surgery, none of the meta-analyses included at least 400 participants. For exercise therapy for acute low back pain, in 6 out of 10 meta-analyses the number of participants exceeded 400. The lack of sufficient sample size, amongst other quality items, was accounted for by the use of the GRADE system [14]. In the case of fewer than 400 participants for continuous outcomes, the quality of the evidence was downgraded.

An important prerequisite for pooling is methodological homogeneity amongst trials. Consistency in measuring outcomes is necessary to allow for statistical pooling. A proposed core outcome set for low back pain trials (which is deemed suitable for post-discectomy interventions, too) has been published in 1998 [15] and would facilitate consistency in measuring outcomes. The core set included the following measures: pain, back-related function, generic well-being and disability/social role (i.e., work absenteeism, cut down activities or bed rest). Recently the results of a Delphi study have been published, which can be considered as an update of this core set. This study proposes domains rather than outcome measures, which include the following: physical functioning, pain intensity and health-related quality of life (HRQoL) [16]. Of 20 trials included in one of the two reviews and published since 2000, 19 reported back-related physical functioning and 17 reported pain intensity. For pain and function, most trials used the instruments advised in the core set published in 1998, i.e., a VAS/NRS for pain and the Roland Morris Disability Questionnaire or Oswestry Disability Index for functioning. The consistency was far less for HRQoL. First of all it was only measured in five trials published since 2000. Secondly, the variety of instruments was larger as three different measurement tools were used: SF36 (two trials), EQ5D (two trials), Gothenburg Quality of Life Instrument. Three trials published before 2000 used a HRQoL measure: the SF36, Health Related Quality of Life Index and Nottingham Health Profile. The fact that only few studies measured HRQoL, and in such a diverse way, limited the possibilities to pool data.

Another prerequisite for pooling is clinical homogeneity amongst trials. However, in both reviews clinical heterogeneity often precluded pooling of results. Populations and interventions need to be similar. Gender and age did not limit homogeneity. In both reviews, trials recruited both men and women, who either underwent surgery for lumbar disc herniation or who suffered from acute low back pain. Studies usually included patients from 18 to approximately 60-70 years old. Clinical homogeneity was mainly limited by the variety in interventions. Specifically in trials assessing rehabilitation after disc surgery, interventions differed widely in content (e.g., multidisciplinary care, behavioural graded activity, various combinations of strength and stretching exercises), duration (from 10 times flexion of knee and hip and the advice to repeat this every 30 minutes during hospitalisation to a six-month progressive gym program) and starting point (2 hours post-surgery, several weeks or one year after surgery). Interventions were delivered in various settings: primary care, secondary care or occupational health. These limitations led to low to very low quality of evidence for all comparisons assessed in the review on rehabilitation for lumbar disc surgery. For exercise therapy for acute low back pain there was only high quality evidence that there is no difference between exercise therapy and other conservative therapies in pain and function. For all other comparisons there was low to very low quality evidence. This means that new trial results are likely to change the conclusions, and low to very low quality evidence is less likely to adequately inform clinicians. The clinical heterogeneity amongst trials reflects the large variety in interventions in clinical practice. The rationale for those interventions is not always clear, probably due to the lack of understanding of mechanisms that affect recovery. Large, high quality trials to test interventions based on plausible working mechanisms, which then could be used in clinical practice, might enhance the effectiveness of exercise therapy.

## **The REALISE trial: findings and methodological considerations**

We performed a randomised trial to compare two common strategies after surgery for lumbar disc herniation in the Netherlands (chapter 4). In this pragmatic trial the intervention group started their rehabilitation program, based on a current clinical guideline [17], immediately after discharge from the hospital. The control group was not referred to any treatment after discharge. For both groups, 6-8 weeks after discharge a follow-up consult with the neurosurgeon took place. Whether participants in the intervention

group continued rehabilitation or control group participants were referred for rehabilitation or other treatment after this follow-up consultation was left to the neurosurgeons' discretion. Alongside this RCT we conducted an economic evaluation. Chapters 5 and 6 describe the results of the REALISE trial, in terms of effectiveness and cost-effectiveness of early rehabilitation versus no referral for rehabilitation after lumbar disc surgery. There were no clinically relevant or statistically significant differences between the intervention (n=92) and control group (n=77) for any clinical outcome: global perceived effect, functional status, leg pain, back pain, physical function and mental health. At 26 weeks no significant differences were found in total costs. The maximum probability for the intervention to be cost-effective was 0.75 at a willingness-to-pay of €32,000/QALY. The maximum probabilities of cost-effectiveness for clinical outcomes varied between 0.68 and 0.70, regardless of the willingness-to-pay. These results show that referral for early rehabilitation after lumbar discectomy was not cost-effective compared with no referral.

Three aspects of this RCT warrant further discussion: the content of the rehabilitation program, selection of patients most likely to benefit postoperative treatment and methodological considerations of the cost-effectiveness analysis.

### **The content of the rehabilitation program**

Early rehabilitation consisted of 1-2 sessions of exercise therapy during 6-8 weeks, aiming to gradually extend activities of daily living from personal care to housekeeping tasks in the short term, and return to work and prepare for sports and leisure activities in the long term. Per treatment session, participating therapists were required to fill out a registration form including amongst others, treatment goals on both a global and more specific level. Ninety-two participants were allocated to the intervention group; 6 participants did not receive any treatment by a physiotherapist or exercise therapist. For 51 of 86 participants (59%) in the intervention group who received treatment, we obtained registration forms from the treating therapists. This trial aimed to investigate the effectiveness of an early functional training program, but the content of the intervention seemed to deviate from the protocol, with a focus on isolated exercises rather than the resumption of ADL activities. Exercise programs comprised stabilisation and coordination exercises (73% of the sessions), mobilising exercises (72%), strength (66%) and endurance exercises (54%). In 45% of the sessions instructions regarding lifestyle and posture were given. The intervention investigated in this trial might have been too generic



and this may have influenced effectiveness of the program. Interventions more specifically targeting mechanisms of pain chronification may be more effective as persistent post-surgical pain may be associated with central changes in pain processing, and related to comorbid chronic pain [18]. Pain education has been found to be an effective intervention in various chronic musculoskeletal disorders [19]. Pain education includes teaching patients about pain processing, inflammatory and immunologic response, peripheral and central sensitisation, and the effect of anxiety and stress on pain. Pain education prior to lumbar disc surgery was found to have a positive effect on beliefs regarding being prepared for surgery and surgery meeting expectations. It also led to far less utilisation of health care [20]. There were no clinically relevant differences in pain and function compared to usual preoperative care. Further research could focus on combining preoperative pain education for all patients scheduled for surgery with postoperative rehabilitation starting after follow-up consultation of the neurosurgeon for those with persisting pain. This postoperative rehabilitation could include pain education to increase the effects of exercise programs. This potentially optimises outcomes after lumbar disc surgery and reduces health care utilisation.

### **Selection of patients most likely to benefit from postoperative treatment**

In the REALISE trial, 68.8% of the participants in the control group were recovered (GPE-score 'completely' and 'much recovered') at 6-9 weeks follow-up. These time points coincide with the follow-up consultation of the neurosurgeon. Selection of patients who may benefit more from postoperative rehabilitation may enhance the effectiveness of these interventions. A prediction rule for limited recovery after lumbar discectomy has been developed in an earlier study [4]. This prediction rule has not been externally validated, and the variables in this rule were, apart from pain 3 days post-surgery, not confirmed in our trial. However, we tested whether variables were predictive of recovery 3 weeks postoperative, whereas the original prediction rule chose recovery at 6 months follow-up as the outcome, which may have influenced the results. Further research may contribute to the identification of subgroups with limited recovery at short-term follow-up. A high level of acute postoperative pain has consistently been found to be predictive of persisting postoperative pain [18]. It is likely that this variable will be found to predict limited recovery in future studies. Any potentially new interventions e.g., a rehabilitation program incorporating pain education as suggested previously,

could then be tested in further trials, targeting patients with expected limited recovery only.

## **Cost-effectiveness analysis**

For the cost-effectiveness study we followed recommendations for trial-based economic evaluations [21]. Sample size calculation for the REALISE trial was based on primary clinical effect measures rather than on economic outcomes, which might have underpowered it to detect relevant difference in these economic outcomes. As cost data tend to be right skewed (negative costs are impossible, and only a small proportion of the participants account for high costs) a larger sample size is required to detect relevant differences in economic outcomes. Underpowered studies lead to imprecise cost estimates. Therefore, the probability that early rehabilitation was cost-effective was calculated for different ceiling ratios rather than testing if costs statistically differed between groups and confidence intervals around costs, effects and ICERS were presented rather than p-values. There were no differences in clinical effects between the intervention and control groups, therefore differences in costs are not expected. Skewness of the cost data probably affected power, but the point estimates of the clinical effects are too small to consider these differences to be clinically relevant. Therefore, if we would have included a larger sample it is not likely that we would have drawn substantially different conclusions.

## **Adherence to early rehabilitation after lumbar discectomy: findings and methodological considerations**

Adherence to exercises and advice, which were components of the rehabilitation program, is expected to influence the effectiveness of this rehabilitation program [22, 23]. However, adherence to exercises [24] and recommendations regarding physical activity [25] is known to be problematic. A qualitative study was conducted to assess facilitators and barriers of treatment adherence amongst participants of the trial who received early rehabilitation. The results of this study are described in chapter 7. Surgery was often experienced as a major event by the patient, in contrast to the neurosurgeons who saw lumbar discectomy as a minor operation, according to the respondents. The main barriers of adherence to exercise and advice were fear of pain aggravation and subsequent activity avoidance immediately post-surgery and perceived poor practical skills to cope with all treatment

requirements. Opportunities to ask questions and receiving information and reassurance were welcomed and mentioned as helpful to overcome this fear of pain aggravation and activity avoidance. This emphasises the need for personalised, patient-centred care after lumbar disc surgery. Key facilitators to adherence were expected recovery and treatment efficacy; a decrease in pain or other symptoms and expected preventative effect, which were contributed to performing exercises or following advice regarding daily activities; perceived sufficient practical skills to perform home exercises and to follow advice; a strong belief that exercises were needed for recovery which enhanced skills to find solutions to any perceived time constraints. Finally, therapist involvement which was tailored to the participant's needs was an important facilitator. A first type of therapist involvement consisted of merely providing information and feedback for patients taking full responsibility for their own recovery. A more extensive therapist involvement offering a structured approach and supervision was the second type, needed for patients with perceived limited coping skills. Finally, the third type was described as a collaborative approach, suitable for those patients with sufficient practical skills. This type included providing information and advice, inquiring about the patient's experiences, providing feedback, being a motivator and enhancing practical skills if needed. In qualitative research, methods of sampling deserve attention. The purpose of sampling is not to draw a random sample as in quantitative research, but to include specific groups of people who are characteristic for or experience the circumstances relevant to the phenomenon that will be studied [26]. We used a purposive sampling method, based on 'a priori' defined criteria that were thought to represent characteristic features of patients receiving rehabilitation after lumbar disc surgery. Based on preliminary analysis further respondents with specific characteristics were included. Recommendations for sample size vary from '5 to 25' to 'at least 6', and the debate on when saturation is reached is ongoing [27]. We used a sample of 12 trial participants. No new themes came up in the last two interviews, respondent characteristics greatly differed and we captured a broad range of experiences. Despite the lack of clarity regarding saturation, this study seems to present a representative overview of factors influencing adherence after discectomy. Specifically the experiences with the involvement of the therapist in the rehabilitation process and consequences for adherence differed widely, which highlights the importance of tailoring the intervention to the needs of each individual patient.

## **Recommendations for research**

Based on the studies presented in this thesis, we suggest several options for further research. Trials assessing interventions for patients who underwent lumbar disc surgery or suffering acute low back pain often showed small effects, if any. For both groups only a part of the patients experienced limited recovery or chronification of pain. Identifying these subgroups is key, as is the unraveling of mechanisms influencing recovery. High pain scores three days post-surgery may be an indicator for limited recovery after lumbar disc surgery but other prognostic variables are yet to be assessed. To identify patients' preferences for the content and delivery of interventions, further qualitative research is needed. Pain education pre-operatively may be a potential effective intervention. This could be combined with post-operative exercise therapy including pain education for those with persistent pain after follow-up consultation with the neurosurgeon. Specifically when early return to work is a central element of this intervention, it may be cost-effective, as absenteeism is the main cost driver after lumbar disc surgery. Large high-quality RCTs are warranted to test these interventions, and to possibly test the implementation of these interventions in daily practice.

## **Recommendations for clinical practice**

Evidence-based medicine integrates evidence, clinical expertise and patient preferences for clinical decision making. For rehabilitation after lumbar disc surgery, an early rehabilitation intervention was neither effective nor cost-effective compared to no referral for early rehabilitation. Based on a systematic review of the literature, rehabilitation starting some 6 weeks after surgery was found to be slightly more effective than no treatment, with high-intensity exercise being more effective than low-intensity exercise. An initial watchful waiting policy might therefore be advised, with referral for rehabilitation in case of persisting complaints and possibly for patients with severe post-operative pain. For therapists providing this treatment it is important to take patient preferences for the level of therapist involvement into account to enhance adherence to home exercises and treatment advice.

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