

Chapter 7

General Discussion

The main focus of the current thesis was to investigate the long-term effectiveness of exercise therapy and the role of exercise adherence in patients with osteoarthritis of the hip or knee. It was hypothesized that the long-term effectiveness of exercise therapy declines after discharge and largely depends on the extent to which a person's behavior corresponds with agreed recommendations given by the patient's physical therapist (exercise adherence). Furthermore, it was investigated whether behavioral graded activity treatment improves adherence and the long-term effectiveness in patients with OA of the hip and/or knee. Data were used from a randomized controlled trial comparing behavioral graded activity (BGA) with usual exercise therapy (UC; exercise therapy according the Dutch guideline for physiotherapy) in patients with OA of the hip or knee. For the purpose of this thesis, an extra follow-up assessment was performed 5 years after inclusion. In this chapter, the main findings are put into perspective and will be discussed. Furthermore, implications for clinical physiotherapy practice, policy and future research are presented.

Main study findings

Long-term effectiveness of exercise therapy

This thesis includes a systematic review of the literature in which the long-term effectiveness of exercise therapy in patients with osteoarthritis was investigated (chapter 2).¹ No evidence was found for the long-term effectiveness of exercise therapy on pain and physical function in patients with osteoarthritis of the hip or knee. Beneficial long-term effects were only found for patients' self perceived effect. Based on these results it was concluded that after discharge the positive treatment effects of exercise therapy on pain and physical function decline over time and finally disappear in the long-term. Some of the included studies investigated the value of additional booster sessions in the period between discharge and long-term follow-up. It was concluded that the use of additional booster sessions after the treatment period has a positive influence on the maintenance of beneficial post-treatment effects on pain and physical function in the long term.

The role of exercise adherence

It was hypothesized that the beneficial effects of exercise therapy, both within and after the treatment period, depends on patients level of adherence to recommended exercise behavior. The results of chapter 4 show that adherence is an important predictor for the long-term effectiveness of exercise therapy. Not only within the period of treatment, but also after the treatment period adherence to the recommended exercises and a more physically active lifestyle was significantly associated with better outcome on pain, physical function and self-perceived effect. In chapter 5 it was investigated if integration of behavioral graded activity principles and additional booster sessions within exercise therapy can improve exercise adherence compared to usual exercise therapy. The results show that behavioural graded activity results in better exercise adherence and a higher level of physical activity than usual physiotherapy treatment according to the Dutch guideline for physiotherapy in patients with osteoarthritis of the hip or knee. Finally, the results described in chapter 6 show that psychological and treatment-related factors are associated with adherence within and after the treatment period. However, no consistent results were found for these factors across the different phases (within and after the treatment period) and between the different types of adherence measured (exercise and activity adherence).

Long-term effectiveness of behavioral graded activity

Because behavioral graded activity includes strategies to stimulate patients exercise behavior and the results described in chapter 4 showed that behavioral graded activity results in better adherence to the recommended exercise behavior (within and after the treatment period), it was expected that behavioral graded activity would result in better long-term effectiveness than usual exercise therapy following the Dutch physiotherapy guideline. To our surprise, both treatments showed beneficial within-groups effects in the long-term. No differences between the two treatments were found on the long-term, both in patients with knee OA and patients with hip OA. However, in patients with hip OA significant differences in favor of behavioral graded activity were found at 3 months (pain and physical performance) and 9 months follow-up (pain, physical function, patients self perceived effect and patient oriented physical function). Furthermore, in

patients with hip OA usual exercise therapy resulted in more joint replacement surgeries compared to behavioral graded activity. Based on these results it was concluded that both treatment groups show beneficial within groups results in the long-term. No significant differences between treatment groups were found in the long-term on pain, physical function and patients self perceived effect, both in patients with knee and hip OA. Although more research is needed to confirm the study findings, the results indicate that BGA reduces the risk for joint replacement surgeries compared to UC in patients with hip OA, which probably can be explained by better outcome in favor of BGA in the short- and mid-long-term.

Discussion

No difference between behavioral graded activity and usual exercise therapy in the long-term

Although the results described in chapter 4 show that behavioral graded activity results in better exercise adherence, no significant differences between behavioral graded activity and usual exercise therapy were found in the long-term effectiveness, both in patients with knee OA and patients with hip OA. Several possible explanations could be given for the absence of any difference between treatment groups in the long-term. A possible explanation in patients with hip osteoarthritis could be that the effect of usual exercise therapy is overestimated at the mid-long-term (15 months follow-up) and long-term (60 months follow-up). In patients treated with usual exercise therapy more patients underwent a joint replacement surgery compared to patients treated with behavioral graded activity. Because earlier research has shown that joint replacement surgery has a positive influence on pain and physical function in patients with osteoarthritis², it is possible that the results of UC on pain and physical function at 15 and 60 months follow-up were biased by patients who underwent joint replacement surgery during the study period. Some support for this explanation was found in a per-protocol-analysis, in which patients who underwent a joint replacement surgery during the study period were considered as lost to follow-up from operation date. The per-protocol analysis demonstrated that the differences between treatment groups increased considerably in favor of BGA on all outcome measures, due to a decline in effectiveness in patients treated with

UC in the mid-long-term and long-term. However, these differences between treatment groups at 15 and 60 months follow-up were not statistically significant, due to a lack of power.

A second possible explanation for the beneficial long-term effects could be the success of both treatments in maintaining or increasing the level of physical activity in the majority of patients. The results in chapter 4 show that although BGA results in a higher level of physical activity than UC, in both treatment groups 74.7% (UC) and 80.7% (BGA) of the patients maintained or increased their level of physical activity at 3 months follow-up. At 15 months follow-up respectively 75.6% and 72.7% of the patients' treated with UC and BGA maintained or increased their level of physical activity. A lack of regular physical activity is an important risk factor for functional decline³ and avoidance of activity induces muscle weakness, a reduced range of motion, and instability of joints.^{4,5} The success of UC in maintaining or increasing patients' level of physical activity can probably be explained by the paradigm shift within the field of physiotherapy in the Netherlands. Traditionally physiotherapy treatments are mainly focused on reducing impairments in body functions such as for instance pain, a reduced muscle strength, and range of joint motion. The last years the focus on reducing limitations in activities and participation, as advocated in the guidelines, gained more and more support in the physiotherapy profession.⁶⁻⁸ This paradigm shift was confirmed by the comparison of treatment goals and modalities as registered in the study of Van Baar^{9,10} and our trial. In the van Baar study, exercise therapy was mainly directed towards improvement of muscle strength (93% of treatments), improvement of range of motion (85%) and reduction of pain (80%). In our trial improvement of activities and decrease of limitations in activities was the most frequently mentioned treatment goal (84% of treatments) in the UC group.¹¹

Finally, a possible explanation could be that the contrast between both treatments was smaller than foreseen. Not all patients were treated according to the treatment protocol. It was expected that BGA patients would be treated at least 5 sessions more compared to the UC group, since BGA patients received additional booster sessions after the first 12 weeks of treatment. However, the average number of sessions was only slightly higher

in the BGA group than in the UC group (14.1 versus 11.7). A registration form was used to get insight in therapist compliance to the treatment protocol, which demonstrated that the baseline assessment to measure patients' physical capacity was performed for only 70% of the BGA patients, and a tailored exercise program was only made for 84% of the BGA patients. It is possible that also other specific elements of BGA, such as reinforcing feedback and extinction of pain behavior may not have been executed adequately.

Different effects in patients with hip versus knee osteoarthritis

Several studies in which the effectiveness of exercise therapy in patients with osteoarthritis was investigated established similar results for patients with hip OA and patients with knee OA.^{12;13} Surprisingly, in patients with hip OA the results were in favor of BGA and in patients with knee OA both treatments were equally effective. A possible explanation could be that prognostic biomechanical, psychological or clinical risk factors for functional decline differ between patients with hip and knee OA. For instance, in patients with knee OA a reduced muscle strength, range of joint motion, laxity of the knee joint, stability of joints and proprioceptive inaccuracy are important risk factors for functional decline.^{14;15} Because the hip is a different type of joint (ball and socket joint), it could be hypothesized that joint laxity and joint stability are less important in predicting functional decline in patients with hip OA and that other factors such as avoidance of activity and how patients cope with their disease (psychological factors) are more important in patients with hip OA. However, because existing studies on prognostic or risk factors are mainly carried out in patients with knee OA¹⁵, this possibility can not be fully evaluated. Therefore, more research on prognostic or risk factors for functional decline in patients with hip OA is needed. Due to the positive results in favor of BGA in patients with hip OA, it can be concluded that integration of more functional and task-oriented exercises, strategies directed at behavioral change and strategies directed at stimulation of exercise behavior are in particularly important for patients with hip OA.

How to stimulate exercise adherence

Since the positive post-treatment effects of exercise therapy decline after discharge and adherence was found to be an important predictor for the effectiveness of exercise therapy, integration of strategies directed at maintenance of exercise behavior (adherence to recommended exercises and a more physically active lifestyle) is important.

The current thesis provides evidence that integration of strategies directed at behavioral change and stimulation of exercise behavior improve adherence to the recommended exercise behavior, both within and after the treatment period. The results of chapter 2 demonstrated that behavioral graded activity including additional booster sessions results in better exercise adherence compared to usual exercise therapy according to the Dutch guideline for physiotherapy in patients with osteoarthritis of the hip or knee. The BGA treatment included several strategies which may have positively influenced adherence, such as personal (long-term) goal setting, education, gradually increasing exercise and activities based on patients' ability at baseline (individually tailored exercise scheme), positive reinforcement, a patients diary (by using a performance chart), and additional booster sessions. As a consequence of the design of our trial, it remains unclear which component contributed most to improving exercise adherence and patients level of physical activity. However, the results of this thesis underline the importance of integrating strategies directed at behavioral change and stimulation of exercise behavior. To a lesser extent, other treatment related factors and psychological factors seemed to be determinants of exercise adherence in patients with OA of the hip and/or knee. Based on the results of this thesis it can be concluded that - irrespectively of individual factors (e.g. age, gender) or illness related factors (e.g. radiographic and symptomatic disease severity) - adherence to recommended exercise behavior seems to depend mainly on how patients cope with their disease and how the exercise treatment is given by physiotherapists.

Adherence seems to be reasonable within the period of exercise therapy treatment, however after discharge it declines rapidly in the long-term. Stimulation of the maintenance of exercise behavior after discharge is one of the biggest challenges for sustaining the beneficial post-treatment effect of

exercise therapy in the long-term. Within the period of treatment the focus of a physiotherapy treatment is probably mainly directed at reducing limitations in functions which induce pain and limit the performance of activities, so that ultimately patients can better meet the demands of daily living and become more physically active.¹⁶ However, after the treatment period (after discharge), direct influence of the physiotherapist is minimal or absent and exercise behavior must literally be self-regulatory in nature in order to be maintained. An important determinant of adherence after discharge is the level of adherence within the period of treatment. So, stimulating adherence within the period of treatment is important. However, the within treatment period in which physiotherapists have partly a direct influence on patient's exercise behavior (which is approximately a two or three months period), is probably too short to ensure maintenance of behavioral change and/or exercise behavior in the long-term after discharge. A possible solution is the use of booster sessions after the treatment period. The results described in chapter 2 provide moderate evidence in favor of additional booster sessions for the maintenance of the positive post-treatment effect of exercise therapy on pain and physical function in the long-term. However, in the studies included in this systematic review compared exercise therapy including booster sessions with usual care. So, the surplus value of additional booster sessions remains unclear. In the current thesis, behavioral graded activity including additional booster sessions resulted in better adherence to the recommended exercise behavior than usual exercise therapy. It remains, however, unclear which component contributed most to improving exercise adherence. Although, up till now no studies have been performed specifically on the surplus value of additional booster sessions, we believe that additional booster sessions should be implemented within the physiotherapy treatment based on the current evidence in patients with OA of the hip or knee.

Is it possible to postpone joint replacement surgery by exercise therapy?

The results of this thesis demonstrate that BGA results in better short- and mid-long-term effects and a reduced risk for joint replacement surgery in patients with hip OA. It seems that the beneficial effects of BGA in the short- and mid-long-term are large enough to postpone joint replacement surgery. These findings are supported by earlier research from Deyle et al, who

concluded that a combination of manual physical therapy and supervised exercise yields functional benefits for patients with osteoarthritis of the knee and may delay or prevent the need for surgical intervention.¹⁷ Because we lacked a no-treatment control group in our study we can only conclude that BGA reduces the risk for joint replacement surgery compared to UC in patients with hip OA. However, these findings suggest that the reduction of the risk for joint replacement surgery is even bigger when it would be compared with only pharmacological treatment, which would put the importance of exercise therapy in an other perspective. Therefore, more research should be done on the influence of exercise therapy on the risk for joint replacement surgery.

On the other hand, our study was not specifically designed to investigate the effect of behavioral graded activity on the risk for joint replacement surgery (secondary outcome measure). So, it could be suggested that the difference in the number of patients undergoing joint replacement surgery between the two treatment groups can be attributed to bias, such as systematic differences between treatment groups in the region in which patients live (policy and the criteria used for indicating a joint replacement surgery could be different per region, hospital, and surgeon). However, the analyses were repeated on a multilevel basis in which the variation between physiotherapist (who are nested within different practices and regions) was taken into account. These analyses yielded similar results. Furthermore, it could be suggested that the difference in the frequency of joint replacement surgery between treatment groups was found by chance, because no differences were found in the long-term between treatment groups on the other primary and secondary outcome measures. We believe, however, that it is plausible to assume that the beneficial effects of BGA in the short- and mid-long-term on pain and physical function were probably large enough to postpone joint replacement surgery.

Implications for clinical practice and policy

Our study provides new insights in the long-term effectiveness of exercise therapy and the role of exercise adherence in treating patients with osteoarthritis of the hip or knee with exercise therapy. Based on these

findings, we will discuss our recommendations for clinical practice and policy below.

Booster sessions

As mentioned before, we recommend integration of booster sessions in exercise therapy to stimulate exercise behavior after discharge and ultimately better long-term effectiveness of exercise therapy. However, follow-up or booster sessions after discharge are currently no part of clinical physiotherapy practice. This is partly due to the current financing structure of physiotherapy in primary care. In the Netherlands, only physiotherapy in patients suffering from a chronic condition (specified on a list) is covered within the basic health care insurance; coverage starts at the tenth visit. People are able to obtain additional private insurance that covers also the first nine visits and physiotherapy when not suffering from a chronic condition. However, OA is not recognized as a chronic condition in terms of reimbursement of physiotherapy. Therefore, patients with OA need to have additional private insurance for having the costs for physiotherapy reimbursed. The implementation of additional booster sessions in physiotherapy in patients with OA will be difficult, since the covered number of treatment sessions in additional private insurances is often limited and varies between health insurance companies. Furthermore, physiotherapist should become more aware of the importance of maintenance of exercise behavior and skills they can use to stimulate maintenance of exercise behavior, such as communication skills, long-term monitoring, self-monitoring by means of a diary, positive reinforcement, or giving graphic feedback. Monitoring patients health status (e.g. important risk factors for functional decline such as for instance muscle strength, range of joint motion, stability of joints and patients' level of physical activity) within follow-up / booster sessions is also believed to be important. Early detection of deterioration of physical function can prevent relapse or further decline.¹⁸

Implementation of strategies directed at behavioral change and stimulation of exercise behavior

The results described in this thesis demonstrate that BGA results in better short- and mid-long-term effects and a reduced risk for joint replacement

surgery in patients with hip OA. Implementation of BGA in patients with hip OA is therefore recommended. In patients with knee OA both treatments, BGA and UC, seem to be equally effective. However, the use of BGA is preferable in patients who are expected to be non-adherent, avoid physical activity or have a relatively high level of limitations in activities. Behavioral graded activity results in better adherence to the recommended exercise behavior compared with usual exercise therapy and earlier research has shown that especially in patients with a relatively high level of impairments in activities benefit more from BGA compared to UC¹⁹. Identification of patients at the start of a treatment who tend to avoid activity and are expected to be non-adherent is difficult, since research on predictors of adherence shows conflicting results and research on predictors of avoidance of activity remains limited.²⁰ Furthermore, for a successful implementation of behavioral graded activity a post-graduate education program for physiotherapists should be developed and adoption of the recommendation in the Dutch guideline for physiotherapy in patients with OA of the hip or knee is needed.

Physical activity

Finally, for improving the long-term effectiveness of exercise therapy, we believe that besides stimulation of adherence to recommended exercises, stimulation of a more physically active lifestyle is very important in patients with OA of the hip or knee. Earlier research has shown that a lack of physical activity is an important risk factor for functional decline in patients with OA³ and our research shows that adherence to a more physically active lifestyle is associated with better outcome in the short and long-term. A more physically active lifestyle can prevent deterioration of important risk factors for functional decline (such as for instance muscle strength and range of joint motion) and has also important additional health and social benefits, such as a lower mortality risk and reducing health care costs.^{3,21}

Limitations

Some limitations of the presented studies should be considered. At first, a gold standard in measuring exercise adherence does not exist.²² In our studies exercise adherence was measured with a self-reported questionnaire. Although widely used, the quality of self-reported questionnaires to measure

exercise adherence is debatable. They are known to overestimate adherence and are susceptible to bias caused by patients memory, social desirability and social approval.²² A self-reported questionnaire has the advantage that it is a simple method to evaluate exercise adherence. Other possible measures include diaries, interviewing, or more objectively monitoring with an accelerometer. Compliance to diaries over time is poor and diary data have shown to be vulnerable to patient deceit and inaccuracies. Interviews increase the risk for socially desirable answers, while accelerometers or pedometers are reasonably accurate for measuring walking activities, but can not evaluate other types of physical activity. For these reasons we decided to use a self-reported questionnaire, in which patients were asked whether they performed the instructed home exercises or activities as recommended by their physiotherapist, assessed on a 5-point scale (1 = almost never; 5 = very often).²³ To prevent overestimation the ratings on exercise adherence were dichotomized more strictly, namely as 'adherence' (often adherent and very often adherent) versus non-adherence (regularly adherent, occasionally adherent, almost never adherent).

Secondly, the self-reported questionnaire to measure adherence to the recommended exercise and activities measured only the extent to which patients adhere to recommendations by their physical therapist. It is expected, however, that the relationship between adherence to recommended exercises or activities and patients' outcome also depends on the quality, dosage and intensity of recommended exercises. Because these aspects were not measured in the questionnaire, it was not possible to adjust in the analyses for these characteristics. This may have led to an underestimation of the association between adherence and patients' outcome on pain, physical function and patients self-perceived effect. For future research, it is therefore recommended to develop a self-reported questionnaire to measure adherence to recommended exercise and activities which takes the quality, dosage and intensity of recommended exercise behavior into account. For adequately measuring adherence in exercise therapy, information is needed from both the patient (information about the actual performance of exercises in terms of frequency, intensity and duration) and the physiotherapist (which exercises are recommended, including information about the recommended frequency, intensity and

duration). Exercise adherence can then be calculated as the ratio of actual performance versus the recommended amount of exercise. Furthermore, measuring adherence in terms of frequency, intensity and duration of the exercises can be helpful in determining the dose-response relation between exercise therapy and changes in health outcome in future research.

Thirdly, the loss to follow-up rate at 5 years after inclusion (26%) was higher than expected (20%). The sample of 149 patients which were followed until 5 years follow-up was smaller than the sample size required by our power analysis. To detect a small to medium effect-size (0.2-0.4) in the outcome measures pain and physical functioning (with a two-sided significance level of 0.05 and power of 80%) in the long term, the sample size needed to be at least 80 per group. However, a non-response analysis showed similar baseline characteristics for responders and non-responders. The power calculation was done based on the assumption that both treatments would show similar results in patients with knee and hip OA. Surprisingly, the location of OA seemed to be a modifier of the relationship between the allocated treatment and outcome. For this reason the data needed to be analyzed separately for patients with knee OA and patients with hip OA. Consequently, our study was theoretically underpowered to detect any between-group differences. However, statistically significant and clinically relevant effects in favor of behavioral graded activity were found in patients with hip OA on the outcome measures pain, physical function, and patients self perceived effect.

Recommendation for future research

Based on the findings of our study, several recommendations for future research can be made. First of all, future research should be done separately for patients with hip or knee OA, because the results of our study show that the location of OA is a modifier of the relationship between the allocated treatment and outcome. Up till now most research is conducted in patients with knee OA.²⁴ Therefore, more research on the effectiveness of exercise therapy in patients with hip OA is needed.

Secondly, the effectiveness of exercise therapy programs varies across patients and the course of pain and activity limitations varies considerably between-individuals.^{14;24-26} Therefore, the development of clinical decision

rules for physiotherapy in patients with OA of the hip or knee is needed. A clinical decision rule can be defined as a clinical tool that quantifies the individual contributions that various components of the history and physical examination results make toward the diagnostic, prognostic or likely response to treatment in an individual patient.²⁷ The development of a clinical decision rule in patients with OA of the hip and knee can improve decision making in physiotherapy practice by establishing a prognosis and matching patients to optimal interventions and give guidance to optimal monitoring within and after the treatment period.

Thirdly, future research should focus on physical activity in patients with OA of the hip and/or knee. Although earlier research has shown that a lack of regular physical activity is an important risk factor for functional decline, research in this field is limited. The aim of exercise therapy is to reduce impairments which limit the performance of activities, so that ultimately patients can better meet the demands of daily living and become more physically active. It is therefore important to know why patients tend to avoid physical activity and which determinants are associated with avoidance of physical activity. Earlier research has shown that a more passive coping strategy is associated with deterioration of muscle strength and more disability.⁵ It was hypothesized that patients with a more passive coping strategy or having fear for pain tend to avoid physical activity and consequently important body functions deteriorate (such as muscle strength, joint motion) which leads to disability. More insight in this mechanism is needed to improve treatment modalities in patients with OA of the hip and/or knee.

Furthermore, as mentioned before, more research should be done on the influence of exercise therapy on the risk for joint replacement surgery. The results of the current thesis and one earlier study from Deyle et al.¹⁷ suggest that exercise therapy can postpone joint replacement surgery. However, the evidence remains limited and these studies were not specifically designed to investigate the effect of exercise therapy on the risk for joint replacement surgery. Because the large (and growing) amount of patients with osteoarthritis and the impact of hip joint replacement for patients and the

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whole society (less medical costs), more research on the influence of exercise therapy on the risk for joint replacement surgery is needed.

Finally, a high quality instrument to measure exercise adherence does not exist. Furthermore, the existing self-reported questionnaires measure only the extent to which patients adhere to recommendations by their physical therapist. For adequately measuring adherence in exercise therapy, information is needed from both the patient (information about the actual performance of exercises in terms of frequency, intensity and duration) and the physiotherapist (which exercises are recommended, including information about the recommended frequency, intensity and duration). Therefore, a new questionnaire to measure adherence in exercise therapy needs to be developed.

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