Arthritis patients show long-term benefits from 3 weeks intensive exercise training directly following hospital discharge

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Objective. To examine the efficacy of short-term intensive exercise training (IET) directly following hospital discharge.

Methods. In the Disabled Arthritis Patients Post-hospitalization Intensive Exercise Rehabilitation (DAPPER) study, patients with rheumatoid arthritis or osteoarthritis were eligible when they needed hospitalization for either a flare-up in disease, elective hip or knee arthroplasty. The intervention group received IET for 3 weeks immediately after discharge; the control group was treated with the usual care (UC). The intensive exercise was provided in a resort. Outcomes were assessed at baseline, after 3, 13, 26 and 52 weeks. Range of motion was measured using the Escola Paulista de Medicina–Range of Motion scale (EPM-ROM), disability was measured using the HAQ and the McMaster Toronto Arthritis Patient Preference Disability Questionnaire (MACTAR), and for health-related quality of life (HRQoL), the Research and Development 36-item Health Survey (RAND-36) was used.

Results. The IET showed a better and faster improvement than UC on all outcome measures except for HRQoL. Up to 52 weeks after baseline, the EPM-ROM and the MACTAR remained favourable in IET compared with UC. At 3 weeks, the MACTAR improved significantly more in the IET compared with the UC: mean difference −5.5 (95% CI −8.4 to −2.2). At 26 weeks, the mean difference remained significant (−5.2; 95% CI −10.0 to −0.34). At 52 weeks, the effect was not significant; however, the mean difference in improvement between the groups can be considered clinically relevant. At 3 weeks, the IET had improved significantly more on the HAQ walking and rising subscales.

Conclusion. Intensive short-term exercise training of arthritis patients, immediately after hospital discharge results in improved regain of function. The DAPPER programme has a direct effect, which lasts up to 52 weeks.

Key words: Exercise therapy, Outcome assessment, Rheumatoid Arthritis, Osteoarthritis, Randomized controlled trial, Arthroplasty.

Introduction

Despite different pathophysiological processes, patients suffering from either rheumatoid arthritis (RA) or osteoarthritis (OA) experience pain and a gradual decline in muscle strength, eventually resulting in loss of function and quality of life. Hospitalization is required for arthritis patients who have a flare-up in disease activity or those requiring elective joint replacement. Especially during hospitalization, a rapid decline of function is observed [1]. Increasing evidence shows that physical exercise improves function and prevents loss of function in both RA and OA [2–6].

In hospitalized patients suffering from arthritis (OA as well as RA), the ability to regain function is retarded [7, 8]. Although, inpatient exercise is shown to be beneficial, the effects of intensive training directly following discharge has never been studied in these patients. Since risk factors for arthritis such as senescence and obesity in the population will increase, more arthritis patients will require hospitalization for joint replacement. Therefore, research into an optimal strategy to regain function and quality of life is warranted.

In RA patients, several exercise programmes have been investigated. Long-term high-impact exercise has been shown to be effective in patients with low disease activity in an outpatient setting. In contrast to the earlier belief, exercise did not increase disease activity [6, 9, 10]. In RA patients with active disease, an inpatient programme with frequent exercise therapy was found to be superior to usual care (UC) regarding disease activity as well as muscle strength [9]. However, inpatient interventions are costly. Physical exercise in a resort might be more acceptable to patients, and might be as effective as an inpatient hospital programme at lower costs.

Exercise was also found to have beneficial effects in OA patients. Positive effects were found in function, pain and muscle strength [11–18]. In patients with moderate functional limitations, early mobilization after arthroplasty resulted in improved functional ability [19, 20]. Even elderly, frail patients admitted for joint replacement were able to tolerate early intensive inpatient exercise therapy resulting in faster attainment of functional ability [21]. However, studies reporting the long-term effects of exercise following joint replacement are lacking [22].

We hypothesize that the recovery of function in arthritic patients improves with a short-term intensive exercise programme in a resort following hospital discharge. To test this hypothesis, the Disabled Arthritis Patients Post-hospitalization Intensive Exercise Rehabilitation (DAPPER) study was designed to investigate the short- and long-term effects of an intensive short-term exercise programme on function and health-related quality of life (HRQoL) in arthritis patients directly following hospital discharge.

Methods

Patients

Patients were recruited from four hospitals (Medisch Spectrum Twente, Enschede; Twenteborg Ziekenhuis, Almelo; Sint Maartenskliniek, Nijmegen and Isala Klinieken, Zwolle). Patients were eligible when they were admitted either due to a flare-up of their disease or for elective knee or hip replacement.
Additional inclusion criteria were: (i) age over 18 yrs, and (ii) RA (according to American College of Rheumatology criteria 1987) [23] or polyarticular OA.

Exclusion criteria were: (i) presence of serious cardiac disease (NYHA class III and IV) [24], (ii) incapacitating pulmonary disease Gold stage IV [25], (iii) serious hypertension (diastolic blood pressure >110 mmHg (during treatment), (iv) pregnancy, (v) insufficient understanding of the Dutch language and (vi) functional incapacity (Steinbrocker functional class 4) [26]. A signed consent form was obtained from all participants. Ethical approval was given before the start of the study by the medical ethical revision board of the Medical Spectrum Twente.

In the power calculation, we used the equation for sample size required per group using the t-test to compare means of continuous variables. In order to have an 80% chance of detecting a significant (at one-sided 5% level) 0.3 point difference in mean HAQ score between the two groups, assuming an s.d. of 0.57, 45 patients were needed per arm.

Design

The DAPPER study is a randomized controlled, clinical trial. In all participating centres, consecutive eligible patients were informed of the study by their treating physician. Those who agreed to participate were randomized. We performed a permuted blocked (blocks of 4) randomization with stratification for centre and reason for admission (flare/joint replacement), made up by a random digit generator to allocate the patient to either intensive exercise treatment (IET) or UC to prevent unbalanced distribution. The allocation was only disclosed to physician and patient after inclusion into the study.

During hospitalization, all patients were treated at the discretion of the attending physician. Directly following discharge patients in the IET group were sent to a dedicated resort, to receive a 3-week IET. Thereafter, the IET group received regular follow-up assessments ranges from 21 to 77 points. Lower scores reflect better functional ability. The MACTAR has been validated in Dutch patients [34]. An improvement of 3 points can be argued to be clinically significant [35].

Assessments

The primary outcome was recovery of function as measured by the HAQ. The secondary outcomes were range of motion as measured by the Escola Paulista de Medicina–Range of Motion scales (EPM-ROM) for the recovery of function from the patients’ perspective as measured by the McMaster Toronto Arthritis Patient Preference Disability Questionnaire (MACTAR). The Research and Development 36-Item Health Survey (RAND-36) was used as a quality of life measurement.

Functionality. This was measured with both the HAQ and the MACTAR. The HAQ is an independent patient-reported outcome questionnaire containing 20 questions, regarding eight domains of daily living activities. The total score as well as each sub-score range from 0 (no disability) to 3 (severe disability). The Dutch version of the HAQ has been validated [30]. To assess functional disability of the lower extremities, the subcategories ‘walking’ and ‘rising’ (items 6–8 and 12) were used [31]. An improvement of 0.26 is considered to be clinically relevant [32]. For the MACTAR [33], an interviewer assesses at baseline which activities are most impaired and which are considered most important by the individual patient (maximum 5). The follow-up assessments focus on change in ability to perform this set of impaired activities. The second part of the MACTAR evaluates the patient's health status by asking questions on general health, quality of life and physical, social and emotional well-being. The baseline score ranges from 39 to 59. The weighted MACTAR at follow-up assessments ranges from 21 to 77 points. Lower scores reflect better functional ability. The MACTAR has been validated in Dutch patients [34]. An improvement of 3 points can be argued to be clinically significant [35].

Range of motion. This was measured with the EPM-ROM scale. This scale evaluates 10 distinct movements of small and large joints and is based on movements and degrees of motion that are important in the performance of basic activities of daily living (ADL). The score for each movement can vary from 0 (no limitation) to 3 (severe limitation). The sum of the left and right side is divided by 2. The total score varies from 0 to 30 [36].

Health-related quality of life. This was measured using the RAND 36-Item Health Survey 1.0 (RAND-36). The RAND-36 uses the same health-status assessment questionnaire as the Short Form 36 (SF-36) [37]. Scores from the eight subscales of the RAND-36 are aggregated into two summary scores: Physical Component Summary (PCS) and Mental Component Summary (MCS) [38]. Raw scale score of the RAND-36 were transformed into z-scores, using Dutch means and s.d. which were multiplied with the US factor score coefficients and summed over all eight subscales. US factor scores were used to facilitate international comparisons. Finally, z-scores were calculated by multiplying the obtained PCS and MCS sums by 10 and adding 50 to the product to obtain transformed summary scores that are normally distributed with a mean of 50 and an s.d. of 10 [39]. This generic
Statistical analysis

Comparison of the baseline scores was done using either the Mann–Whitney test or the independent Student’s t-test, where appropriate. Evaluations were done according to the intention-to-treat method.

Between both groups, the changes of the follow-up scores compared with baseline were analysed. To control for baseline differences, analyses of covariance (ANCOVAs) were performed with the change scores as dependent variables, the group as independent variable and the baseline scores of each outcome measure as covariates. In addition, to adjust for confounding, diagnosis, age and disease duration were included as covariates. To test if the assumption of homogeneity of regression slopes for ANCOVA was satisfied, we tested whether there was an interaction between the independent variable and the covariates for each outcome measure. To evaluate the importance of the differences between the groups the effect size was calculated. An effect size of 0.10 is considered a small effect, 0.30 represents a moderate effect and 0.50 a large effect [41].

All statistical analyses were performed using the statistical package SPSS and utilizing two-tailed tests with a significance level of $\alpha = 0.05$.

The Institutional Review Boards of the hospitals approved the study.

Results

Between July 2002 and January 2004, 114 patients gave signed consent and were randomized (60 IET, 54 UC; Fig. 1). Sixteen patients were lost during follow-up (16.3%). Within the first 3 weeks, four patients withdrew consent (1 IET; 3 UC) and 2 UC patients stopped due to unexpected, non-related medical conditions. Ten patients (1 IET; 9 UC) withdrew consent during the course of the follow-up. Ninety-eight patients completed the study (58 IET, 40 UC). No significant differences were found at baseline between the completers and the non-completers or between the IET and UC groups.

The demographic and baseline characteristics of the evaluable patients are presented in Table 1. The mean age of the patients was 68 yrs (s.d. = 11), with a mean disease duration of 12.4 yrs (s.d. = 11.5). Fifty-two patients were admitted for total hip arthroplasty (53%, 13 RA/39 OA). Thirty-five patients were admitted for total knee arthroplasty (36%, 9 RA/26 OA) and only 11 patients were admitted because of flare (11%, 11 RA/0 OA). Comorbidities beside the diagnosed RA or OA were present in 81% of the patients. The most frequent comorbidities were hypertension (45%) and heart failure (30%), and 33% of all patients have had a joint replacement in the past.

The assumption for ANCOVA of homogeneity of regression slopes was met for all outcome measures [i.e. ANCOVAs showed no significant interactions ($P > 0.05$) between the groups (IET/UC) and all covariates].

Functional ability

Compared with baseline the IET group improved more than the UC group on the HAQ subscales for walking and rising. At 3 weeks this difference was statistically significant (Table 2 and Figs 2A and B).

![Diagram](image-url)

**Fig. 1.** Flow chart of participants in the DAPPER trial, in which arthritis patients were treated with either IET or UC directly following hospital discharge.
Compared with baseline the IET group showed better improvement in functional ability than the UC group, as measured with the MACTAR (Table 2 and Fig. 2C). The difference was significant at 3, 13 and 26 weeks with an effect size of 0.82, 0.46 and 0.50, respectively. At 52 weeks, the effect was not significant [−11 (s.d. 11) vs −8.6 (s.d. 12.7)]. However, the mean difference in improvement between the groups of 4.3 can be considered clinically relevant. The effect was moderate (effect size 0.36).

**Range of motion**

Compared with baseline, the improvement of range of motion (EPM-ROM) in the IET group exceeded the improvement in the UC group. The difference was significant at 3, 13 and 26 weeks (Table 2 and Fig. 3). The effect sizes were 0.46, 0.6 and 0.6, respectively.

**Health-related quality of life**

The effects on the RAND-36 physical component were not different between the groups (Table 2 and Fig. 4A and B).

**Discussion**

The DAPPER study shows improved recovery of function in arthritis patients due to a 3 week IET programme directly following hospital discharge. The patients in the IET group showed a quicker and significantly better recovery in all physical measures (HAQ, MACTAR and EPM-ROM). HRQoL (RAND-36) did not show a beneficial effect with the IET compared with UC. The improvements observed in the IET group lasted up to 12 months.

Before the DAPPER study, superiority of such a brief intensive exercise programme has never been demonstrated in an outpatient setting. Moreover, the DAPPER study encompassed RA patients among OA patients. The DAPPER study used a 3-week intensive exercise programme compared with other outpatient programmes lasting from 6 weeks up to 24 months [42, 43]. Despite the short duration of the DAPPER programme, the immediate effects were long-lasting. Due to the limited number of patients in each arm, the differences did not reach significance at 52 weeks; however, the difference between the groups could still be considered clinically relevant.

The DAPPER study used an intensive exercise programme in an outpatient setting in contrast to comparable programmes on an inpatient basis. The effects are comparable but the friendly resort dedicated to arthritis patients costs considerably less compared with hospital care. The DAPPER programme was not limited to exercise only. The beneficial effects might be explained by the combination of intensive exercise, excellent arthritis-dedicated facilities, the presence of care givers and group-based patient education.

Although the differences between the groups with respect to change in mobility and functional capacity as measured with the MACTAR were significant, the question whether the differences are relevant remains to be solved. To the best of our knowledge, the minimal clinically important change on the EPM-ROM and MACTAR still have to be established. However, since the weighted MACTAR score on average assigns 3 points to an individually selected impaired activity, the mean difference between the intervention and control group range from four to six. This outcome could be interpreted as at least one less relevant problem and thus clinically relevant.

Limitation of the current study was that the assessments were not blinded. Obviously, taking the informed consent obligation seriously, blinding is nearly impossible in clinical trials other than drug trials. Therefore, in this type of study, assessor bias is almost impossible to prevent. Disproportionately, UC patients were lost for follow-up due to withdrawal of informed consent. However, statistically, there is no indication for bias by selective dropout.

Although the intervention took place in a resort dedicated to arthritis patients, we feel that the main finding of our study, that intensive training directly following discharge quickly improved function, can be generalized. The setting in which the study took place is unique; however, the facilities of rehabilitation centres and nursing homes could be used for the implementation of this programme. The primary study question of the DAPPER study was to study the effects of intensive short-term exercise therapy on...
function as measured with the HAQ. We operationalized this by choosing the clinical problem of deterioration of function in hospitalized patients. Both patients with RA and OA who suffered deterioration in function were included in this study representing daily rheumatology practice.

The results of the DAPPER study have implications for the care of arthritis patients. In many studies, intensive training has been found to improve function in arthritis patients and also after arthroplasty. It is expected that increasing numbers of patients will need arthroplasty whereas at the same time the availability of inpatient facilities will decline, so effective recovery strategies on an outpatient basis are needed. The DAPPER study indicates that intensive training in a resort with arthritis-dedicated facilities and trained staff might be a very good alternative.

In conclusion, the DAPPER study supports the hypothesis that recovery of function in arthritis patients benefits from a 3-week intensive exercise programme directly following discharge from the hospital. In accordance with earlier research on IET on an inpatient basis, the importance of intensive exercise in arthritis patients has gained strength. Moreover, we consider it likely that the gained benefits of the DAPPER protocol outweigh the costs compared with UC. Obviously this has to be demonstrated by a health economical analysis.

**Rheumatology key message**

- Recovery of function of arthritis patients benefits from a 3-week intensive exercise programme directly following discharge from the hospital.
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References