Rehabilitation in cancer: Training *and* talking?
Effects of physical training versus physical training combined with cognitive-behavioural therapy

Anne May

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Oncologische revalidatie: Trainen *en* praten?
Effecten van fysieke training versus fysieke training gecombineerd met cognitieve gedragstherapie

(met een samenvatting in het Nederlands)

Krebsrehabilitation: Trainieren *und* Unterhalten?
Auswirkungen von physischem Training im Vergleich zu physischem Training in Verbindung mit kognitiver Verhaltenstherapie

(mit einer Zusammenfassung in deutscher Sprache)

Proefschrift

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Prof.dr. J. Passchier

Co-promotor: Dr. W.J.G. Ros

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Manuscripts based on the studies presented in this thesis

Chapter 2

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Chapter 3

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Chapter 4

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Chapter 5

May AM, Duivenvoorden HJ, Korstjens I, van Weert E, Hoekstra-Weebers JEHM, van den Borne B, Mesters I, van der Schans CP, Ros WJG. The effect of group cohesion on rehabilitation outcome in cancer survivors. *Psycho-Oncology, 2007, DOI: 10.1002/pon.1308.*

Chapter 6

May AM, van Weert E, Korstjens I, Hoekstra-Weebers JEHM, van der Schans CP, Zonderland ML, Mesters I, van den Borne B, Ros WJG. Maximal and submaximal exercise outcome following physical training in cancer survivors: a submaximal exercise test as an alternative for an exhaustive exercise test? *Submitted.*

Contents

1

General introduction

"After my very last radiation treatment for breast cancer, I lay on a cold steel table hairless, half-dressed, and astonished by the tears streaming down my face. I thought I would feel happy about finally reaching the end of treatment, but instead, I was sobbing. At the time, I wasn't sure what emotions I was feeling. Looking back, I think I cried because this body had so bravely made it through 18 months of surgery, chemotherapy, and radiation. Ironically, I also cried because I would not be coming back to that familiar table where I had been comforted and encouraged. Instead of joyous, I felt lonely, abandoned, and terrified. This was the rocky beginning of cancer survivorship for me."
- Elizabeth D. McKinley, MD, MPH[1]

Cancer epidemiology

Worldwide, there were 10.9 million new cases of cancer, 6.7 million deaths and 24.6 million people living with cancer (within three years of diagnosis) in 2002.[2,3] In the Netherlands, 73,000 people were newly diagnosed with cancer in 2003.[4] It is estimated that the number of new diagnoses will increase to 95,000 new cases in 2015, representing an increase of approximately 40%.[5]

Recent advances in diagnosis and treatment have resulted in an improvement in the survival rate of cancer patients. The 5-year survival rate for men increased from 30% in the 70s to 45% in 2001. As regards women, an increase in the 5-year survival rate from 45% in the 70s to 60% in 2001 has been reported. The increase in new cases, in combination with improved survival rates, has resulted in a serious increase in the prevalence of cancer (Figure 1). The expectation is that the number of people who currently have cancer or were successfully treated for cancer will increase from 366,000 in 2000 to 692,000 in 2015. This means that, within 15 years, the number of (ex-)cancer patients in the Netherlands will have almost doubled.

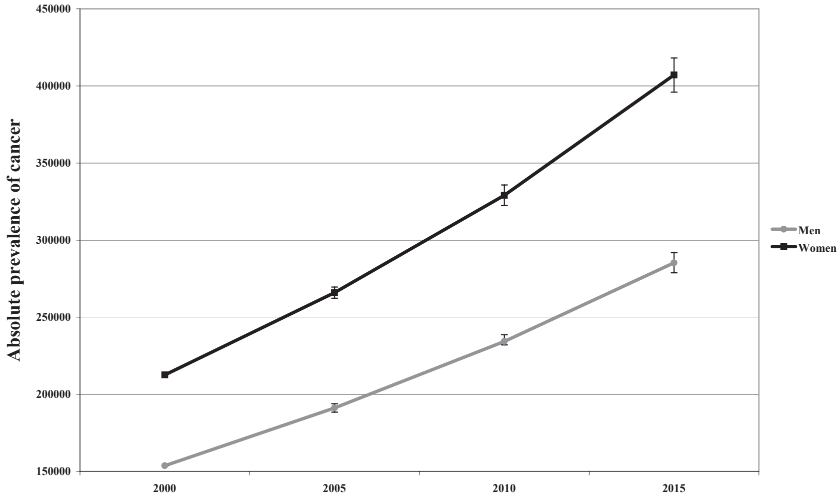

Figure 1. Absolute prevalence of cancer in the year 2000 and the estimated prevalence of cancer in the years 2005, 2010 and 2015 (with 95% confidence intervals) in the Netherlands.[5]

Cancer survivorship

One would expect the completion of primary curative cancer treatment to be a positive life event for cancer patients given that 'the battle against cancer has been won'. However, as the quotation above emphasises, the transition from cancer patient to survivor can be quite distressing.[6,7] Despite the fact that primary treatment has been successfully completed, cancer survivors often report long-lasting physical and psychological complaints.[8-12] Physical complaints include decreased cardiorespiratory capacity, decreased physical functioning, cancer-related fatigue, and a decreased quality of life.[13,14] Recent prospective studies showed that quality of life and physical functioning declined most soon after diagnosis, attenuated with the time since diagnosis, but remained at a lower level in the long-term.[8,15] The prevalence of long-term limitations might be explained by long-term effects of cancer treatment, such as fatigue, depression and decreased physical activity.[15] Persistent functional limitations in cancer survivors appear to be a general phenomenon that is not linked to one specific cancer site or stage of diagnosis.[15]

In the case of cancer survivors with long-lasting physical and psychological problems, it has been suggested that rehabilitation may help maintain or regain physical and psychological functions.[8,15] Moreover, survivors who reported a decreased quality of life indicated a need for rehabilitation.[16]

Cancer rehabilitation

Cancer rehabilitation is a concept that is defined by the patient and includes helping a person with cancer to obtain maximum physical, social, psychological, and vocational functioning within the limits imposed by the disease and its treatment.

In 1978, Lehmann et al.[17] were the first to pay attention to the rehabilitative needs of cancer patients. In their study of 805 cancer patients, 52% of the patients had psychological problems, 35% suffered from general weakness, 30% had problems with daily activities, 25% had ambulation difficulties, 7% had transfer deficits, and 7% had deficits relating to communication. The authors concluded that psychosocial support services are needed, but did not yet mention physical exercise as a possible rehabilitative tool. Up until the 1980s, cancer patients who reported fatigue and muscle weakness were told by their physicians to get more rest. Information on the beneficial results of exercise for cancer patients was published for the first time in 1981.[18] From then on, and especially in recent years, it became more and more evident that, besides psychosocial interventions, physical training also improves cancer patients' quality of life.

Physical training

Physical exercise has proven to be effective in many chronic diseases.[19,20] In the case of cancer survivors, recent meta-analyses and reviews documented the beneficial effects of physical exercise on physical fitness, physical functioning and quality of life. Recent observational reports suggested that increasing physical activity levels after cancer diagnosis may even reduce the risk of cancer recurrence and mortality in patients with breast[21], colon[22,23] or prostate cancer[24]. As yet, nothing is known about the mechanism by which physical activity may have a protective effect. Physical activity may decrease serum levels of hormones, such as androgen, oestrogen and insulin, which are associated with increased cancer risk.[21-24] Hence, exercise might be successful in increasing not only cancer survivors' quality of life but overall survival as well.

Psychosocial intervention

Psychosocial interventions that have been proven to be effective for cancer survivors typically include stress management and cognitive-behavioural therapy such as problem solving.[25] A recent meta-analysis demonstrated that cognitive-behavioural therapy effectively decreased depression and anxiety, and increased the quality of life of cancer survivors.[26] The authors concluded that cognitive-behavioural therapy might not be useful for improving physical functioning of cancer survivors.

Combination of physical training and psychosocial intervention

Physical training appears primarily to have a positive effect on the physical and functional aspects of quality of life[27-29], whereas cognitive-behavioural therapy has been shown to be beneficial for the psychosocial aspects[26]. Therefore, combining physical training with cognitive-behavioural therapy may lead to more intensive (within a domain) and broader (more domains) improvements in global quality of life by having benefits on both physical and psychosocial functioning.[27]

In the Netherlands, the rehabilitation programme for cancer survivors known as 'Recovery&Stability' (*Herstel&Balans)* was started in 1996. It combined a physical training module and a psycho-education module. With support from the Comprehensive Cancer Centres and 'Revalidatie Nederland', this programme is now offered in almost 60 centres throughout the Netherlands. Recent evaluations showed that quality of life and physical fitness improved and that fatigue decreased following the 12-week group-based 'Recovery&Stability' programme when compared with pre-intervention.[30,31] However, no conclusions could be drawn as to whether these changes were a result of the physical training, the psycho-education or a combination of both. Furthermore, there was no comparison group and it was therefore unclear whether these improvements resulted from the intervention or from natural recovery after primary treatment. As a result, the Comprehensive Cancer Centres and clinical practice took the initiative of setting up the OncoRev project.

The OncoRev project

The OncoRev project, which is financed by the Dutch Cancer Society (UU-2000-2585), Maastricht University and the Comprehensive Cancer Center North-Netherlands, was started in 2000. The OncoRev project group consists of researchers from the University Medical Center Utrecht, the Erasmus Medical Center Rotterdam, Maastricht University and the Comprehensive Cancer Centre North-Netherlands. The aim of this multicentre study was to determine the effects of a combined physical and cognitive-behavioural intervention on quality of life, fatigue and physical fitness in cancer survivors compared to physical training and a waiting list control group.

To this end, we developed a group-based multidisciplinary cancer rehabilitation programme combining physical training with cognitive-behavioural therapy, using experiences from earlier studies concerning multidisciplinary rehabilitation[30,31]. The programme development was based on Engel's bio-psychosocial model.[32] This model implies that physical interventions might affect physical problems as well as psychosocial problems, that psychosocial interventions have the potential to affect physical problems, and that dovetailed interventions may enhance the effect of the entire intervention. In order to dovetail the interventions, both the physical and the psychosocial component were based on the principles of self-management[33] that had beneficial effects on the health outcomes in a range of chronically ill patients and on the quality of life of cancer patients.[34,35] The chosen group format, which provided opportunities for social comparison[36], social support[37] and modelling[38], might have beneficial effects on quality of life[35].

Outline of the theses

The present thesis reports, in **Chapter 2**, on the effects of our physical training programme combined with cognitive-behavioural therapy (PT+CBT) on physical fitness compared to physical training alone (PT). **Chapter 3** describes the effects of PT+CBT on quality of life compared to PT and waiting list control. The effects described in chapters 2 to 3 relate to the direct effects of the intervention, namely cancer survivors' levels of physical fitness and quality of life immediately following the intervention. **Chapter 4** reports on the long-term effects of PT+CBT on quality of life compared to PT. The effect of group cohesion on rehabilitation outcome is studied in **Chapter 5**. The relationship between submaximal and maximal exercise outcome is investigated in **Chapter 6**. **Chapter 7** contains the general discussion. The results presented in this thesis are summarised in **Chapter 8**.

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2

Cancer survivors' physical fitness: effects of physical training versus physical training combined with cognitive-behavioural therapy

Abstract

Objectives

We compared the effect of a group-based 12-week supervised exercise programme, i.e. aerobic and resistance exercise, and group sports, with that of the same programme combined with cognitive-behavioural training on physical fitness and physical activity level of cancer survivors.

Methods

147 cancer survivors (all cancer types, medical treatment ≥3 months ago) were randomly assigned to physical training (PT, n=71) or PT plus cognitive-behavioural training (PT+CBT, n=76). Maximal aerobic capacity, muscle strength and physical activity were assessed at baseline and post-intervention.

Results

Analyses using multilevel linear mixed-effects models showed that cancer survivors' physical fitness increased significantly in PT and PT+CBT from baseline to post-intervention. Changes did not differ between PT and PT+CBT.

Conclusion

Physical fitness of cancer survivors was improved following an intensive physical training programme. Adding a structured cognitive-behavioural intervention did not enhance the effect.

Introduction

Many cancer survivors experience serious physical and psychological complaints caused by the disease and consequent treatment that may persist for many years.[1] Due to these complaints, the activity level of cancer survivors often diminishes. Inactivity itself leads to a progressive decline in physiological functioning characterised by decreased physical capacity, reduced muscle strength and rapid fatigue during exertion.[2,3] Several physical training programmes have been developed for cancer survivors aiming at breaking this vicious cycle. Reviews of the effectiveness of exercise interventions after cancer treatment demonstrate a beneficial effect on physical fitness.[4-6] Two shortcomings of available studies have been summarised.[4] Firstly, most research was performed in breast cancer survivors limiting generalization to other types of cancer. Secondly, the majority of exercise interventions focused on cardiovascular training. However, it is argued that muscle strength exercises should be included because such exercise may counteract cancer-related decreased muscle strength.[6] The few studies that combined aerobic and resistance exercise reported positive effects on muscle strength in cancer survivors[3,7-11], but only two[7,11] were randomised controlled trails.

Positive effects on physical outcomes were not only reported following exercise interventions, but also following psychosocial interventions. It is reported that physical activity increased after cognitive-behavioural interventions based upon principles of self-management in various diseases.[12-14] Moreover, Courneya and associates observed significant improvements in cardiovascular endurance in cancer survivors receiving cognitive-behavioural therapy.[15] Several authors suggested that adding a behavioural intervention to a structured exercise programme may help facilitate exercise adoption.[13,16] A cognitive-behavioural intervention might positively influence physical activity behaviour and exercise compliance by increasing self-efficacy and decreasing perceived barriers to exercise such as cancer-related distress and fatigue.[17] These favourable findings imply that adding a cognitive-behavioural intervention to physical training might enhance the effect on physical outcomes obtained by exercise alone.

Therefore, in the present randomised clinical trial we combined an extensive, supervised exercise programme including aerobic training, resistance exercise and group sports with a cognitive-behavioural intervention, which was aimed at solving cancer-related problems that limit patients to be physically active in everyday life. Patients were randomly assigned to physical training (PT) or PT plus cognitive-behavioural training (PT+CBT). We hypothesised that PT+CBT and PT participants would experience significant improvements in physical fitness and activity from baseline to post-intervention. We also expected PT+CBT participants to benefit more than PT participants.

Participants and Methods

A randomised clinical multicenter trial was conducted with four participating centres experienced in oncological rehabilitation: Erasmus University Medical Center, Rotterdam; University Medical Center Groningen, Groningen; Hilversum Hospital, Hilversum; and Rehabilitation Center De Hoogstraat, Utrecht, all in The Netherlands.

Inclusion criteria were: last cancer treatment completed at least three months before study entry; age ≥18 years; and estimated life expectancy at least one year. Moreover, subjects needed to be referred by a medical specialist or a general practitioner who judged whether rehabilitation was indicated. The latter meant a minimum of three positive findings on the following questions:

1. Physical complaints like aching muscles, problems with coordination, headache, nausea, heart palpitations, shortness of breath
2. Reduced physical capacity compared with before the illness, e.g., less able to walk or cycle
3. Psychological problems like increased anxiety level, depression, uncertainty, lack of energy or nervousness
4. Increased levels of fatigue
5. Sleep disturbances
6. Problems in coping with reduced physical and psychosocial functioning due to cancer

Patients were excluded if they had cognitive disturbances, serious psychopathology or emotional instability that might impede participation, or if they needed intensive medical treatment or rehabilitation. The medical ethics committee of the University Medical Center Utrecht and the local research ethics committees approved the study that was performed according to the Helsinki Declaration of 1975, as revised in 1983.

Recruitment and allocation

Cancer survivors were informed about the study by various methods, including leaflets handed out by oncologists and general practitioners, information in the local newspapers and through the website. Those expressing interest were sent an information letter, an informed consent form, an intake questionnaire and referral papers. After written consent, eligible subjects were scheduled for baseline measurements and randomised to either PT or PT+CBT. In each centre consecutive groups of eight to twelve eligible subjects were assigned to the randomly determined treatment to ascertain adequate numbers of participants in each group. An independent researcher randomly determined the sequence of interventions at each centre, using a randomisation list. The number of PT and PT+CBT groups were balanced in each centre. Figure 1 shows the flow of participants through the trial. Until the first session, participants were blinded to the intervention they were allocated to. A power analysis for a comparison between the randomised groups on the primary outcome maximal exercise capacity estimated a sample size of 64 participants in each group to detect a moderate effect-size (d=0.50) with a power of 0.80 and a two-tailed alpha of 0.05. Accounting for an estimated dropout of 10% 71 participants in each group were needed.

Intervention

Both components, PT and the cognitive-behavioural intervention were based on the principles of self-management: i.e. goal selection, information collection, information processing and evaluation, decision making, action and self-reaction.[18] Rehabilitation took place in groups of 8-12 cancer survivors. PT was supervised by two physical therapists and CBT by a psychologist and a social worker. All therapists were experienced professionals and in the field of cancer rehabilitation. The experience of PT therapists ranged from 2.5 to 6.3 years (median 5.1 years) and of CBT therapists from 2.4 to 11.3 years (median 4.4 years). All therapists received group training to apply the standardized protocols: PT therapists during one day, CBT therapists during two days.

Physical training (twice weekly, two hours per session)

In accordance with the principles of self-management, participants used heart rate monitors, the Borg Scale for dyspnea and fatigue and training logs to monitor and evaluate their performance, and received feedback, information and support from their therapists in regulating their performance.

***Bicycle training* (30 minutes)**. Patient's main baseline physical problems were defined by assessing aerobic capacity, testing muscle strength, and medical history. Based on these, participants chose, in cooperation with the therapists, their individual goals during the first four weeks, to be trained from week five onwards: i.e. (a) improving exercise capacity, (b) improving muscle strength, (c) coping with fatigue or (d) handling physical role limitations. Training intensity was determined using the Karvonen formula[19] that uses the peak heart rate (HR_{peak}) obtained from baseline graded exercise testing and the heart rate (HR) at rest (HR_{rest}) to calculate the training HR (HR_{tr}). During the first four weeks training was performed at a HR_{tr} of (HR_{rest}+40% to 50% of (HR_{peak}-HR_{rest})). Training intensity from Week 5-12 depended on the individual training goal as mentioned above. The training programme of participants who chose improvement of exercise capacity gradually increased to a HR_{tr} of (HR_{rest}+80% of (HR_{peak}-HR_{rest})) at Week 12, whereas the programmes of patients with other goals were aimed at a gradual increase to (HR_{rest}+70% of (HR_{peak}-HR_{rest})).

***Muscle strength training* (30 minutes).** Resistance exercise of lower and upper extremities was based on the baseline 1-Repetition Maximum (1-RM). Training intensity started at 30% of the 1-RM during the first week and was increased until 60% of 1-RM in week 12 for participants aiming at improving muscle strength and until 50% of 1-RM for patients with other goals.

***Group sport* (60 minutes).** Group sports, such as swimming, badminton and soccer, which were outlined in the training protocol, aimed at enjoying sports and overcoming any lack of confidence patients may have felt about exercising their body. Sports were performed while participants were still able to talk, which implicates a moderate intensity level.[20]

From week six on, the patients started a home-based walking programme as described in detail by Winningham[21] to provide an additional training stimulus. Based on performance status and age, subjects started walking for 5 to 20 minutes once per week increasing the walking time by 30 seconds to two minutes per week.

Walking speed was regulated by the subjects' heart rate depending on their age, e.g. the target pulse of persons aged between 40 and 50 years was from 110-120 beats per minute. Therefore, participants wore heart rate recorders or counted their pulse rate during walking.

Cognitive-behavioural training (once a week, two hours per session)

Cognitive-behavioural training aimed at training self-management skills to solve personal problems associated with physical and psychosocial consequences of cancer limiting patients to be physically active in daily living using a cognitive-behavioural problem-solving protocol for individual cancer patients[22] and a group problem-solving protocol[23]. The content of CBT is outlined in Table 1.

2

Table 1. Content of the cognitive-behavioural training*

	Content of the session
Session 1	Acquaintenance and introduction of the rationale and the aims of the training
Session 2	Information about stress and relaxation
Session 3	Information about fatigue and exercise physiology
Session 4	Information about the subsequent steps in the circular self-management process
Session 5	Problem orientation
Session 6	Problem definition and formulation
Session 7	Goal setting
Session 8	Generation of alternative solutions (brainstorming)
Session 9	Decision making
Session 10	Solution implementation and verification
Session 11	Recapitulation and practice of self-management process
Session 12	Retrospection on the training and anticipation to future functioning
Structure of each session	
	• Recapitulation of last weeks session and exchanging daily life experiences • Discussing home assignment • Introducing new topic or self-management skill • Practicing self-management skill • Introducing next homework assignment† • Relaxation exercise.

* *Duration of one session is two hours. A workbook is used containing an extensive summary of the training, self-management worksheets and assignments, and information on additional relevant topics for cancer patients.*

† *Homework with a maximum of half an hour per week.*

Outcomes

Socio-demographic and medical data were collected using a self-report questionnaire. Medical data were confirmed by the referring physicians. Information about pre-cancer and pre-recruitment activity levels were assessed at intake.

Cardiopulmonary outcomes were change in peak oxygen consumption (VO_{2peak}), peak power (W_{peak}) and exercise duration evaluated by a symptom limited graded exercise test. Changes in muscle strength were determined in all centres except one. All assessments were conducted at baseline (T0) and immediately after the 12-week rehabilitation (T1). T0 and T1 tests were consistently performed by the same assessor who was not involved in the intervention. Participants were asked not to eat or drink (except water) during the two hours before exercise testing.

Exhaustive graded exercise test.[24] Participants cycled at 60 rates per minute (rpm) with no workload for one minute to adapt to the cycle ergometer. The exercise test started with a workload of 20 Watt and the load was increased every minute by 10, 15 or 20 Watt (depending on the subject's fitness) until voluntary exhaustion. Increments were estimated using formulas provided by Wassermann et al.[24]. Subjects were encouraged during the test. The test ended when the patient was restricted by clinical symptoms, when the cycling rate was lower than 60 rpm, or by the physician's intervention. HR was recorded during the whole test (Polar S610i, Polar Electro Inc., Helsinki, Finland). Expired gases were analysed using Oxycon Delta, Oxycon Champion (Jäger, Höchberg, Germany), Metamax MMX (Cortex Biophysics GmbH), or K4b2 (Cosmed, Rome, Italy) in the four study centres, respectively. Differences in measured oxygen uptake and carbon dioxide output between analysis systems in the different centres were small (-3.4% to 2.4% difference from overall mean at 150 Watt) and fell within the range of day-to-day variability[25] (data not shown). VO_{2peak} was calculated as the mean of VO_2-values during the final 30 seconds of exercise. W_{peak} was defined as workload at exhaustion.

Muscle strength measurement. Maximum voluntary isometric muscle strength of elbow flexor and extensor muscles and the knee extensor muscles was determined using a hand-held dynamometer (Strength Evaluating & Testing (microFET), Hoggan Health Industries, USA). The 'break method' was applied: the examiner gradually overcomes the strength produced by the patient until the extremity gives way.[26] All measurements were performed three times, with recovery intervals of at least 10 s. Peak strength was recorded, and the mean values of three technically correct measurements were taken for analysis.

Physical activity was assessed through the 12-item Physical Activity Scale for the Elderly (PASE), a valid and reliable questionnaire.[27,28] Questions deal with physical activities, such as leisure, sports, occupational, housework, and gardening. The questionnaire records the frequency of participation in these activities over the preceding seven days. Scoring procedures were derived from motion sensor counts, physical activity diaries and a global activity self-assessment. The total PASE-score is computed by multiplying the amount of time spent in each activity by the item weights and summing over all activities. The PASE generates a single composite score of physical activity that ranges from 0-400.

Adherence to intervention

The exercise trainers and psychologists filled in a Case Record Form for each subject every session to monitor adherence to the intervention. Moreover, after each PT and CBT session, therapists filled in a general form to monitor whether the session was performed as described in the protocol.

Data analysis

Analyses (R software, version 2.3.1) were performed according to the intention-to-treat principle. Two-sided significance tests were used ($p < 0.05$). Missing values of outcome variables were imputed by the mean of the predicted distribution given the hierarchical structure and specific characteristics of the person (age, gender, weight, and group allocation) using Bayesian statistics. Subjects with missing baseline values were not taken into account (n=3; missing due to untreated hypertension, lymphedema in both legs, and claustrophobia caused by the mask covering nose and mouth). The reasons for these missing values were unrelated to non-compliance, withdrawal, or losses to follow-up and were not affected by the treatment these patients were assigned to. Therefore, post-randomisation exclusion was appropriate.[29]

The baseline status of the randomised participants was compared to that of those who discontinued intervention using independent Student's t-tests or Mann-Whitney tests for continuous data and Chi-square tests for categorical data. Differences in socio-demographic and medical characteristics of PT+CBT and PT were tested with ANOVA and Chi-Square tests.

Changes in outcome variables between study groups were compared using linear mixed-effects models while taking the different levels (centre, group and individual) into account. The Akaike Information Criterion was used as a measure of how well our different models fit the data. A lower value on the Akaike Information Criterion indicated a better model fit. Additionally, an analysis was performed for complete cases. Furthermore, presence or absence of breast cancer and its interaction with treatment allocation was included as covariate to investigate whether the effects of rehabilitation were different between breast cancer patients and others.

Results

Participant recruitment took place between February 2004 and December 2005. Measurements started in March 2004 and the last follow-up measurements were performed in April 2006 (Figure 1). Those who stayed in the study did not differ from the patients who discontinued with regard to age, sex, educational, marital status, type of cancer, type of treatment, time post-treatment, past physical activity and baseline values of graded exercise testing.

Baseline characteristics

Table 2 shows the baseline characteristics of the study participants. Groups were not different in socio-demographic, medical and past physical activity variables (all p-values>0.05). The majority of our participants were female, middle-aged, married, educated, employed and overweight. Pre-intervention, subjects' physical activity levels were decreased compared to their physical activity levels before the diagnosis of cancer ($p<0.0001$).

Adherence to the intervention

Both intervention groups completed 83.5% of 24 physical training sessions (PT+CBT 20±4.7 sessions; PT 20±5.2 sessions, $p>0.05$) and the PT+CBT group completed 82.4% of 12 cognitive-behavioural training sessions (9.9±2.4 sessions).

One participant, assigned to PT, collapsed during the intervention and deceased at the first-aid station. After autopsy, physicians judged this death to be unrelated to the intervention. No further adverse events were reported.

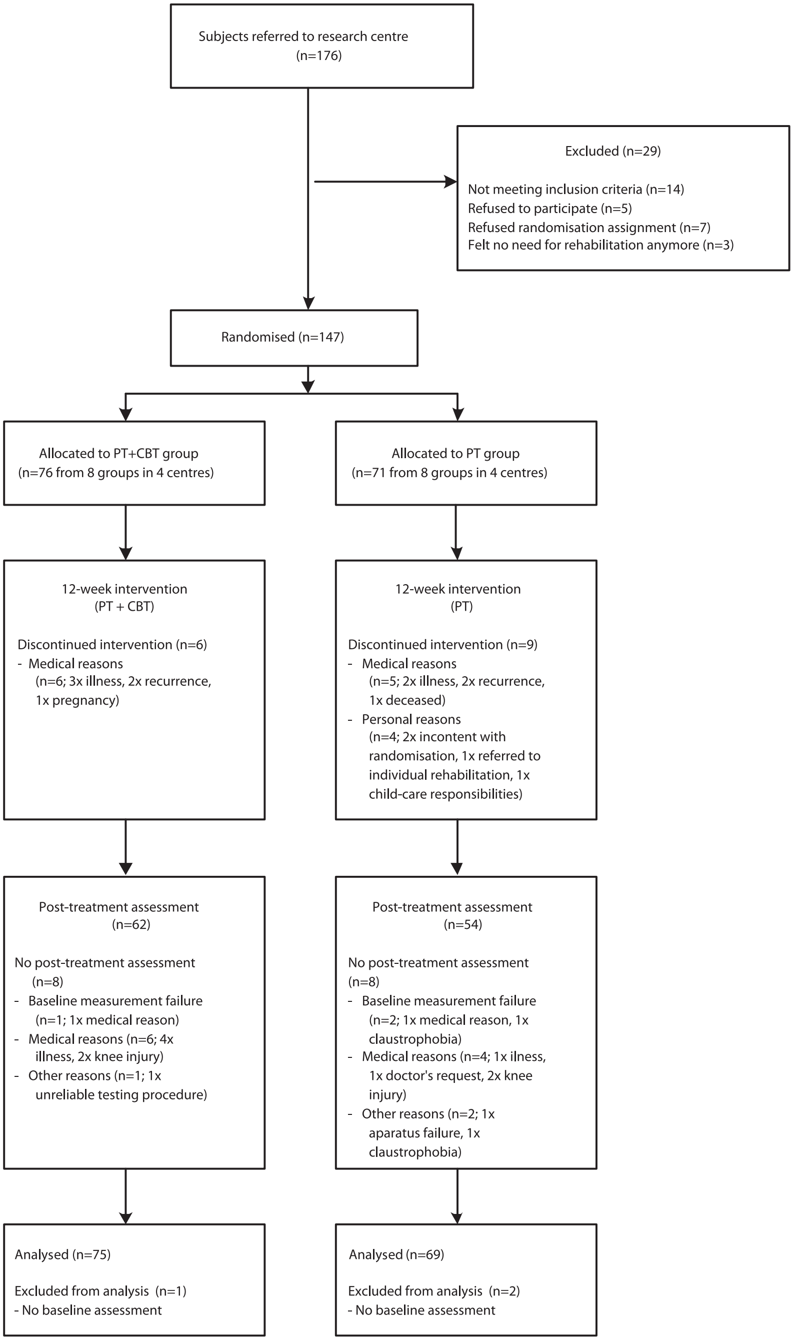

Figure 1. Flow of participants through the trial

Abbreviations: PT+CBT – physical training plus cognitive-behavioural training; PT – physical training

2

Table 2. Baseline characteristics*

Variable	Overall (n=147)	PT+CBT group (n =76)	PT group (n =71)
Age (years)	48.8 ± 10.9	47.8 ± 10.5	49.9 ± 11.3
Sex			
Female	123 (83.7)	66 (86.8)	57 (80.3)
Male	24 (16.3)	10 (13.2)	14 (19.7)
Educational level			
Low	23 (14.1)	6 (7.9)	14 (19.7)
Middle	80 (49.1)	40 (52.6)	32 (45.1)
High	60 (36.8)	30 (39.5)	25 (35.2)
Marital status			
Married/living together	117 (71.8)	53 (69.7)	51 (71.8)
Single	46 (28.2)	23 (30.3)	20 (28.2)
Employed at diagnosis	107 (72.8)	54 (71.1)	53 (74.6)
Body Mass Index (kg*m^2)	27.5 ± 6.2	27.4 ± 6.7	27.7 ± 5.8
Type of cancer			
Breast	82 (55.8)	48 (63.2)	34 (47.9)
Haematological	23 (16.6)	15 (19.7)	8 (11.3)
Gynaecological	17 (11.6)	6 (7.9)	11 (15.5)
Urogenital	9 (5.5)	3 (3.9)	6 (8.5)
Colon	3 (2.0)	1 (1.3)	2 (2.8)
Lung	4 (2.7)	2 (2.6)	2 (2.8)
Other	9 (6.2)	1 (1.3)	8 (11.3)
Type of treatment			
Surgery	126 (85.7)	64 (84.2)	62 (87.3)
Chemotherapy	100 (68.0)	55 (72.4)	45 (63.4)
Radiotherapy	84 (57.1)	43 (56.6)	41 (57.7)
Time post-treatment (years)	1.3 ± 1.7	1.2 ± 1.3	1.4 ± 2.1
Pre-cancer activity level†			
Sedentary	15 (10.2)	6 (7.9)	9 (12.7)
Walking and cycling for pleasure	50 (34.0)	31 (40.8)	19 (26.8)
Regular physical exercise (≥ 3h/w)	52 (35.4)	23 (30.3)	29 (40.8)
Intense regular physical training (≥ 4h/w)	30 (20.4)	16 (21.1)	14 (19.7)
Pre-rehabilitation activity level†			
Sedentary	39 (26.5)	15 (19.7)	24 (33.8)
Walking and cycling for pleasure	89 (60.5)	50 (65.8)	39 (54.9)
Regular physical exercise (≥ 3h/w)	17 (11.6)	10 (13.2)	7 (9.9)
Intense regular physical training (≥ 4h/w)	2 (1.4)	1 (1.3)	1 (1.4)

Data presented as mean ± standard deviation for continuous variables and frequency (percentage) for categorical variables.

† *Classification of activity level according to Saltin et al.*[30]

Abbreviations: PT+CBT – physical training plus cognitive-behavioural training; PT – physical training.

Physical fitness outcome variables

Changes in exercise capacity, muscle strength and physical activity from baseline to post-intervention were not significantly different between PT and PT+CBT (see Table 3 and Table 4).

VO_{2peak}, W_{peak}, exercise time, muscle strength of upper and lower limbs and physical activity improved significantly in PT+CBT and PT from baseline to post-intervention.

Additional analysis

Complete case analyses showed similar results for all outcome variables indicating that missing data had no impact on the results (data not shown).

Adding the covariate breast cancer yes/no and its interaction with treatment allocation to the model showed that results were not different between patients with breast cancer and patients with other types of cancer (data not shown).

Table 3. Maximal exercise performance and physical activity at baseline and post-intervention; and intra- and inter-group changes pre-intervention to post-intervention[a]

	Baseline (Mean ± SD)	**Post-intervention (Mean ± SD)**	**Within-group change (95% CI)**	**Between-group change (95% CI) (PT versus PT+CBT)**
VO_{2peak} ($mL \cdot kg^{-1} \cdot min^{-1}$)				
PT	23.3 ± 7.3	25.8 ± 7.8	2.1 (1.2 to 3.0) ***	Reference
PT+CBT	23.9 ± 6.7	25.9 ± 7.1	2.0 (1.1 to 2.9) ***	-0.1 (-1.5 to 1.3)
W_{peak} (Watt)				
PT	158.8 ± 50.7	173.1 ± 50.6	14.3 (9.7 to 19.0)***	Reference
PT+CBT	153.3 ± 44.1	170.8 ± 47.6	17.7 (13.2 to 22.2) ***	3.4 (-3.1 to 9.8)
Exercise time (seconds)				
PT	597.5 ± 157.2	656.5 ± 153.5	58.5 (40.6 to 76.5) ***	Reference
PT+CBT	581.4 ± 135.9	657.2 ± 149.4	76.2 (58.7 to 93.7) ***	17.7 (-7.1 to 42.5)
Physical activity				
PT	110.0 ± 57.4	136.9 ± 75.6	26.8 (12.2 to 41.5) **	Reference
PT+CBT	116.1 ± 60.5	139.9 ± 73.1	23.8 (9.6 to 37.9)**	-3.1 (-23.5 to 17.3)

Abbreviations: SD – standard deviation; CI – confidence interval; PT – physical training; PT+CBT – physical training plus cognitive-behavioural training; VO_{2peak} – peak oxygen uptake; W_{peak} – peak workload.
[a] *PT+CBT group (n=75). PT group (n=69). Change scores, between-group change scores and corresponding 95% CI using linear mixed-effects models. Physical activity was assessed by the Physical Activity Scale for the Elderly (PASE) questionnaire (range 0-400).*
**P≤0.01; ** P≤0.001, ***P<0.0001.*

Table 4. Muscle strength at baseline and intra-group and inter-group changes from pre-intervention to post-intervention[a]

	Baseline (Mean ± SD)	Post-intervention (Mean ± SD)	Within-group change (95% CI)	Between-group change (95% CI) PT versus PT+CBT
Muscle strength left elbow flexors (N)				
PT	198.3 ± 52.7	213.6 ± 48.2	15.8 (3.5 to 28.2)*	Reference
PT+CBT	172.6 ± 44.6	193.9 ± 38.8	21.1 (8.9 to 33.4)**	5.3 (-11.9 to 22.5)
Muscle strength right elbow flexors (N)				
PT	208.3 ± 57.8	221.6 ± 52.7	13.3 (3.6 to 23.1)*	Reference
PT+CBT	182.2 ± 44.5	201.7 ± 42.7	19.8 (10.2 to 29.3)***	6.4 (-7.2 to 19.9)
Muscle strength left elbow extensors (N)				
PT	140.5 ± 40.3	154.2 ± 38.6	13.7 (9.4 to 17.9)***	Reference
PT+CBT	130.2 ± 35.6	139.6 ± 29.9	9.4 (5.3 to 13.6)***	-4.2 (-10.1 to 1.7)
Muscle strength right elbow extensors (N)				
PT	139.6 ± 36.2	148.7 ± 34.7	9.2 (3.0 to 15.4)*	Reference
PT+CBT	124.6 ± 32.5	139.0 ± 27.1	14.3 (8.2 to 20.3)***	5.1 (-3.4 to 13.6)
Muscle strength left knee extensors (N)				
PT	266.5 ± 80.3	317.8 ± 65.9	51.2 (31.6 to 70.8)***	Reference
PT+CBT	244.9 ± 76.4	301.5 ± 67.1	55.9 (36.6 to 75.3)***	4.7 (-22.4 to 31.9)
Muscle strength right knee extensors (N)				
PT	255.6 ± 76.0	310.5 ± 67.6	55.6 (35.1 to 76.2)***	Reference
PT+CBT	241.0 ± 66.5	294.8 ± 65.0	53.3 (33.0 to 73.5)***	-2.4 (-30.8 to 26.1)

Abbreviations: SD – standard deviation; CI – confidence interval; PT – physical training, PT+CBT – physical training plus cognitive-behavioural training; N – Newton.

[a] PT+CBT group (n=53). PT group (n=50). Change scores, between-group change scores and corresponding 95% CI using linear mixed-effects models.

$^{*}P\leq0.01$; $^{**}P\leq0.001$, $^{***}P\leq0.0001$.

Discussion

The present randomised clinical trial showed that physical fitness improved following physical training consisting of aerobic training, resistance exercise, and group sports in survivors from different types of cancer. In the present study, participants received an intensive supervised physical training programme that incorporated principles of self-management. In addition, participants trained within exercise classes. This peer contact provided ample opportunities for social interaction, social comparison, group support and education that might improve self-efficacy and through that physical activity behaviour.[30] We showed that adding structured cognitive-behavioural training to our exercise programme did not add to the beneficial effect of physical training on physical fitness. Apparently, our theory-based group exercise programme seemed to be sufficient to improve exercise capacity. However, this conclusion might be premature because long-term effects might be different. CBT did not enhance the effect of PT on physical fitness in the short-term, but PT+CBT might be superior in the long-term because CBT might possibly enhance long-term adherence to an active lifestyle. Hence, long-term follow-up measurements in our study population are needed. Furthermore, as our PT was an intensive, group-based supervised programme that also included social cognitive components a ceiling effect might partly explain that adding structured CBT did not offer additional benefits.

We showed that the effect of the intervention in breast cancer survivors were not different to the effect in survivors of other types of cancer, which is consistent with findings of others.[15] Two pilot studies investigated the effect on physical fitness of a rehabilitation programme including aerobic training and resistance exercise in breast cancer survivors, and reported beneficial effects in the training group: W_{peak} and VO_{2peak} improved and the muscle strength of the lower limbs increased.[7,11] Our results confirm these findings and extend them to survivors from all types of cancer.

At baseline, our population's VO_{2peak} was 84.3±22.6% (mean ± standard deviation) of predicted VO_{2peak} based on height, weight, gender and age[31] and below 30 $mL \cdot kg^{-1} \cdot min$, which implies poor physical fitness. The enhancement of W_{peak} and VO_{2peak} found in the present study exceeds the day-to-day variability[25] and could, therefore, be considered as clinically relevant. The magnitude of change of W_{peak} and VO_{2peak} in our study is comparable to results of other studies evaluating oncological rehabilitation in survivors, which reported improvements in W_{peak} of almost 10% and increases of VO_{2peak} from 6.2% to 18.6%.[3,11,32]

At pre-intervention, physical activity levels of our participants were decreased compared to pre-diagnosis as is also reported by others.[33,34] At post-intervention, our participants reported an increase of physical activity levels compared to pre-intervention. According to Cohen[35], this increase implied a small treatment effect.

Muscle strength of the lower and upper limb increased in both PT and PT+CBT participants from pre- to post-intervention. Increases of the knee extensor muscles were of moderate to large effect size, whereas effect sizes for increases of elbow flexor and extensor muscles were small.[35] In contrast to upper limb muscles, lower limb muscles were not only trained during resistance training but also during bicycle exercise. Possibly, training of the upper limb muscles should be extended and, moreover, therapists should ensure careful implementation.

Strengths of the present study were the large sample size, the randomised controlled design with intention-to-treat analysis, the supervised, standardised and theory-based intervention, high attendance rates, and the validated measures of fitness. For feasibility reasons, our study did not include a control group. Since cancer rehabilitation is presently offered to cancer patients in 60 centres throughout the Netherlands, participants were not willing to run the risk of being randomised to a control situation in which they had to wait for an intervention. In addition, recent reviews and meta-analyses[4,5] reported that exercise is an effective intervention to improve cardiorespiratory fitness.

In conclusion, survivors of different types of cancer showed improved physical fitness following a supervised, self-management physical training programme which combines cardiorespiratory and resistance exercise with group sports. Adding a structured cognitive-behavioural intervention did not enhance the positive effects of physical training on physical fitness immediately following the intervention.

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APPENDIX

Effects on physical fitness of physical training and physical training combined with cognitive-behavioural therapy compared to waiting list control

The paper presenting the results of our intervention on physical fitness reported on the comparison between physical training (PT) and physical training combined with cognitive behavioural training (PT+CBT). However, in one centre we included, in addition to PT+CBT and PT groups, a waiting list control group (WLC) in the randomisation scheme. The results of changes of physical fitness from pre-intervention to post-intervention of PT+CBT and PT compared to changes of WLC are presented here.

RESULTS

Table 1 shows the characteristics of the participants. All 16 subjects randomised to WLC completed the 12-week waiting list control period.

Baseline characteristics

Physical fitness outcome variables

Peak exercise capacity and physical activity. Compared to the WLC group, significant differences in changes from pre-intervention to post-intervention of PT+CBT and PT participants were observed for W_{peak} and exercise time (Table 2). Physical activity levels increased (not significant, p=0.1) in PT+CBT and PT compared to WLC from pre- to post-intervention. Due to gas analysis system failure, only six of sixteen post-VO_{2peak} measures were available in the WLC group. Therefore, analysis of difference in changes between the intervention groups and WLC condition was not conducted.

Table 1. Baseline characteristics*

Variable	**Overall (n=163)**	**PT+CBT group (n =76)**	**PT group (n =71)**	**WLC group (n =16)**
Age (years)	48.8 ± 10.7	47.8 ± 10.5	49.9 ± 11.3	48.6 ± 8.5
Sex				
Female	136 (88.4)	66 (86.8)	57 (80.3)	13 (81.2)
Male	27 (16.6)	10 (13.2)	14 (19.7)	3 (18.8)
Educational level				
Low	23 (14.1)	6 (7.9)	14 (19.7)	3 (18.2)
Middle	80 (49.1)	40 (52.6)	32 (45.1)	8 (50)
High	60 (36.8)	30 (39.5)	25 (35.2)	5 (31.3)
Marital status				
Married/living together	117 (71.8)	53 (69.7)	51 (71.8)	13 (81.3)
Single	46 (28.2)	23 (30.3)	20 (28.2)	3 (18.8)
Employed at diagnosis	120 (73.6)	54 (71.1)	53 (74.6)	13 (81.3)
Body Mass Index (kg*m^2)	27.3 ± 6.1	27.4 ± 6.7	27.7 ± 5.8	25.1 ± 4.8
Type of cancer				
Breast	90 (55.2)	48 (63.2)	34 (47.9)	8 (50.0)
Haematological	27 (16.6)	15 (19.7)	8 (11.3)	4 (25.0)
Gynaecological	18 (11.0)	6 (7.9)	11 (15.5)	1 (6.3)
Urogenital	9 (5.5)	3 (3.9)	6 (8.5)	--
Colon	4 (2.5)	1 (1.3)	2 (2.8)	1 (6.3)
Lung	5 (3.1)	2 (2.6)	2 (2.8)	1 (6.3)
Other	10 (6.1)	1 (1.3)	8 (11.3)	1 (6.3)
Type of treatment				
Surgery	138 (84.7)	64 (84.2)	62 (87.3)	12 (75.0)
Chemotherapy	113 (69.3)	55 (72.4)	45 (63.4)	13 (81.3)
Radiotherapy	94 (57.7)	43 (56.6)	41 (57.7)	10 (62.5)
Time post-treatment (years)	1.3 ± 1.7	1.2 ± 1.3	1.4 ± 2.1	1.2 ± 1.9
Pre-cancer activity level†				
Sedentary	16 (9.8)	6 (7.9)	9 (12.7)	1 (6.3)
Walking and cycling for	52 (31.9)	31 (40.8)	19 (26.8)	2 (12.5)
pleasure	60 (36.8)	23 (30.3)	29 (40.8)	8 (50.0)
Regular physical exercise	35 (21.5)	16 (21.1)	14 (19.7)	5 (31.3)
(≥ 3h/w)				
Intense regular physical training (≥ 4h/w)				
Pre-rehabilitation activity level†				
Sedentary	43 (26.4)	15 (19.7)	24 (33.8)	4 (25.0)
Walking and cycling for	100 (61.3)	50 (65.8)	39 (54.9)	11 (68.8)
pleasure	18 (11.0)	10 (13.2)	7 (9.9)	1 (6.3)
Regular physical exercise	2 (1.2)	1 (1.3)	1 (1.4)	--
(≥ 3h/w)				
Intense regular physical training (≥ 4h/w)				

**Data presented as mean ± standard deviation for continuous variables and frequency (percentage) for categorical variables.*

† Classification of activity level according to Saltin et al. (1983).[32]

Abbreviations: PT+CBT – physical training plus cognitive-behavioural training; PT – physical training; WLC – waiting list control.

Table 2. Maximal exercise performance and physical activity at baseline and intra- and inter-group changes pre-intervention to post-intervention[a]

	Baseline (Mean ± SD)	**Post-intervention (Mean ± SD)**	**Within-group change (95% CI)**	**Between-group change (95% CI)**
W_{peak} (Watt)				
PT	158.8 ± 50.7	173.1 ± 50.6	14.3 (9.5 to 17.7) †††	13.9 (3.0 to 24.8)§
PT+CBT	153.3 ± 44.1	170.8 ± 47.6	17.7 (13.0 to 22.5) †††	17.3 (6.5 to 28.1)§§
WLC	144.7 ± 33.6	146.0 ± 31.0	0.4 (-9.4 to 10.3)	Reference
Exercise time (seconds)				
PT	597.5 ± 157.2	656.5 ± 153.5	58.4 (40.0 to 76.8) †††	48.8 (7.2 to 90.4)§
PT+CBT	581.4 ± 135.9	657.2 ± 149.4	76.3 (58.3 to 94.3) †††	66.7 (25.3 to 108.1)§§
WLC	514.4 ± 109.8	526.5 ± 105.4	9.6 (-28.0 to 47.3)	Reference
VO_{2peak} ($mL \cdot kg^{-1} \cdot min^{-1}$)*				
PT	23.3 ± 7.3	25.8 ± 7.8	2.1 (1.2 to 3.0) †††	--
PT+CBT	23.9 ± 6.7	25.9 ± 7.1	2.0 (1.1 to 2.9) †††	--
WLC (n=6)	19.3 ± 2.9	20.1 ± 3.5	0.8 (-1.5 to 3.2)	--
Physical activity				
PT	110.0 ± 57.4	136.9 ± 75.6	26.8 (12.2 to 41.5) †††	32.0 (-2.0 to 66.1)
PT+CBT	116.1 ± 60.5	139.9 ± 73.1	23.8 (9.6 to 37.9) †††	29.0 (-4.9 to 62.8)
WLC	126.0 ± 95.9	120.8 ± 77.2	-5.2 (-36.0 to 25.6)	Reference

Abbreviations: SD – standard deviation; CI – confidence interval; PT – physical training; PT+CBT – physical training plus cognitive-behavioural training; WLC – waiting list control; VO_{2peak} – peak oxygen uptake; W_{peak} – peak workload.

[a] *PT+CBT group (n=75). PT group (n=69). WLC group (n=16, if not stated otherwise). Change scores, between-group change scores and corresponding 95% CI using linear mixed-effects models. Physical activity was assessed by the Physical Activity Scale for the Elderly (PASE) questionnaire (range 0-400).*

* *No statistical testing was done due to gas analysis system failure in WLC group.*

†*$P<0.05$; ††$P<0.01$, †††$P\leq0.001$ for within-group changes (pre-intervention to post-intervention). §$P<0.05$; §§$P<0.01$, §§§$P\leq0.001$ for between-group changes with WLC as reference (pre-intervention to post-intervention).*

Table 3. Muscle strength at baseline and intra-group and inter-group changes from pre-intervention to post-intervention[a]

	Baseline (Mean ± SD)	**Post-intervention (Mean ± SD)**	**Within-group change (95% CI)**	**Between-group change (95% CI)**
Muscle strength left elbow flexors (N)				
PT	198.3 ± 52.7	213.6 ± 48.2	15.9 (3.2 to 28.5) *	16.9 (-8.3 to 41.9)
PT+CBT	172.6 ± 44.6	193.9 ± 38.8	21.1 (8.6 to 33.6) **	22.0 (-3.0 to 47.1)
WLC	198.4 ± 35.1	199.6 ± 33.1	-0.9 (-23.0 to 21.1)	Reference
Muscle strength right elbow flexors (N)				
PT	208.3 ± 57.8	221.6 ± 52.7	13.3 (3.8 to 22.8) **	8.4 (-10.6 to 27.4)
PT+CBT	182.2 ± 44.5	201.7 ± 42.7	19.8 (10.5 to 29.1) ***	14.8 (-4.1 to 33.8)
WLC	210.0 ± 42.1	215.2 ± 39.4	4.9 (-11.8 to 26.6)	Reference
Muscle strength left elbow extensors (N)				
PT	140.5 ± 40.3	154.2 ± 38.6	13.7 (9.2 to 18.1) ***	1.1 (-8.0 to 10.1)
PT+CBT	130.2 ± 35.6	139.6 ± 29.9	9.4 (5.1 to 13.8) ***	-3.2 (-12.2 to 5.8)
WLC	147.1 ± 38.6	159.7 ± 34.6	12.6 (4.7 to 20.5) **	Reference
Muscle strength right elbow extensors (N)				
PT	139.6 ± 36.2	148.7 ± 34.7	9.3 (2.4 to 16.3) **	7.7 (-6.3 to 21.6)
PT+CBT	124.6 ± 32.5	139.0 ± 27.1	14.2 (7.4 to 21.1) ***	12.5 (-1.3 to 26.4)
WLC	141.3 ± 36.5	143.7 ± 30.2	1.7 (-10.6 to 13.9)	Reference
Muscle strength left knee extensors (N)				
PT	266.5 ± 80.3	317.8 ± 65.9	51.1 (30.4 to 71.9) ***	72.4 (31.1 to 113.8) ††
PT+CBT	244.9 ± 76.4	301.5 ± 67.1	55.8 (35.3 to 76.3) ***	77.1 (35.9 to 118.3) ††
WLC	305.3 ± 61.1	287.2 ± 54.9	-21.3 (-57.6 to 15.0)	Reference
Muscle strength right knee extensors (N)				
PT	255.6 ± 76.0	310.5 ± 67.6	55.8 (33.4 to 78.1) ***	59.7 (15.0 to 104.3) †
PT+CBT	241.0 ± 66.5	294.8 ± 65.0	53.1 (31.0 to 75.3) ***	57.0 (12.5 to 101.5) †
WLC	281.0 ± 64.7	281.5 ± 50.0	-3.9 (-43.1 to 35.3)	Reference

Abbreviations: SD – standard deviation; CI – confidence interval; PT – physical training, PT+CBT – physical training plus cognitive-behavioural training; WLC – waiting list control; N – Newton.

[a] PT+CBT group (n=53). PT group (n=50). WLC group (n=16). Change scores, between-group change scores and corresponding 95% CI using linear mixed-effects models.

**P<0.05; **P<0.01, ***P≤0.001 for within-group changes (pre-intervention to post-intervention). †P<0.05; ††P<0.01, †††P≤0.001 for between-group changes with WLC as reference (pre-intervention to post-intervention).*

Muscle strength

When compared to the WLC group, the muscle strength of the knee extensor muscles improved significantly in PT+CBT and PT groups, whereas changes in muscle strength of the elbow flexor and extensor muscles were not different (Table 3).

Conclusion

In conclusion, compared to a WLC group our physical training programme improved physical fitness and tended to improve physical activity of cancer survivors.

3

Cancer survivors' quality of life: short-term effects of physical training versus physical training combined with cognitive-behavioural therapy and waiting list control

Abstract

Objective

A randomised clinical trial was conducted to compare the effects on cancer survivors' quality of life of a 12-week group-based multidisciplinary self-management rehabilitation program, combining physical training (twice weekly) and cognitive-behavioural training (once weekly) with those of a 12-week group-based physical training (twice weekly). In addition, both interventions were compared to no intervention.

Methods

Participants (all cancer types, medical treatment completed ≥3 months ago) were randomly assigned to multidisciplinary rehabilitation (n=76) or physical training (n=71). The non-intervention comparison group consisted of 62 patients on a waiting-list. Quality of life was measured using the RAND-36. The rehabilitation groups were measured at baseline, after rehabilitation, and 3-month follow-up, and the non-intervention group at baseline and 12 weeks later.

Results

The effects of multidisciplinary rehabilitation did not outperform those of physical training in role limitations due to emotional problem (primary outcome) or any other domains of quality of life (all $p>0.05$). Compared to no intervention, participants in both rehabilitation groups showed significant and clinically relevant improvements in role limitations due to physical problem (primary outcome; $p<0.01$, ES 0.66), and in physical functioning ($p<0.001$, ES 0.48), vitality ($p<0.001$, ES 0.54) and health change ($p<0.001$, ES 0.76) (all $p<0.01$).

Conclusion

Adding cognitive-behavioural training to group-based self-management physical training did not have additional beneficial effects on cancer survivors' quality of life. Compared to no-intervention, group-based self-management rehabilitation improved cancer survivors' quality of life.

Introduction

Since survival rates of cancer are growing[1] cancer must be managed as a chronic disease. Approximately 30% of cancer survivors report decreased quality of life (QoL) and express a need for professional support in managing physical and psychosocial problems following cancer diagnosis and its treatment.[2] Meta-analyses of randomised controlled trials of physical interventions[3,4] or psychosocial interventions[5,6] for cancer patients report small to large effect sizes (ES from 0.28 to 0.84) for QoL. Moreover, a meta-analysis of randomised clinical studies of cognitive-behavioural interventions in cancer survivors reports large effects (ES 1.45) on QoL.[7]

QoL is a multidimensional construct that includes physical as well as psychosocial dimensions. Therefore, acknowledging the bio-psychosocial model[8], combined physical and psychosocial interventions may enhance effects on QoL beyond those of single focused interventions. Indeed, combined interventions have also shown positive effects in cancer patients during medical treatment[9,10], and after medical treatment[11-13]. Yet, no ES were reported of these interventions compared to no intervention. To date, only one study has compared a combined intervention to a single focused intervention.[13] In that study the combination of group psychotherapy and home-based walking as compared to group-psychotherapy alone improved QoL in two domains; functional well-being and fatigue. This finding is consistent with other studies in cancer survivor groups, suggesting that exercise is associated primarily with the physical and functional aspects of QoL, rather than the social and emotional dimensions[14] and may have the most benefits in physical and functional domains[15]. The goal of multidisciplinary cancer rehabilitation is to improve participants' functioning in their daily roles by reducing physical as well as emotional problems. Therefore, we expect that adding a cognitive-behavioural intervention to physical training in multidisciplinary rehabilitation might show improvements in QoL beyond those of physical training, primarily in role functioning associated with emotional problems.

The present 4-center trial is the first study to compare combined physical training and cognitive-behavioural training (PT+CBT) to physical training (PT) in cancer survivors. Furthermore, this is the first study to include a 3-month follow-up of cancer patients in a combined intervention as compared to a single focused intervention. Additionally, we compare the rehabilitation groups (PT and PT+CBT combined) to a waiting-list comparison group (WLC). To this end, we developed a multidisciplinary cancer rehabilitation program, based on earlier studies concerning multidisciplinary rehabilitation.[11,12] In this program we integrated evidence-based[3,5-7,16] PT and CBT protocols according to a self-management approach[17,18]. PT focused on enhancing self-management in physical training and sports, while in CBT emphasis was placed on providing structural interactive psycho-education and training in self-management skills. Firstly, we hypothesized that PT+CBT would demonstrate more improvement in QoL than PT after rehabilitation and at 3-month follow-up, primarily in the domain of role limitations due emotional problem. Secondly, we hypothesized that after rehabilitation both rehabilitation groups would outperform WLC, primarily in reducing role limitations due to physical problem.

Participants and Methods

Study design

In this prospective controlled 4-center study, participants were randomly assigned to PT+CBT or PT, while participants awaiting rehabilitation elsewhere were assigned to WLC. Measurements were performed before and after rehabilitation (12 weeks after baseline), and at 3-month follow-up (6 months after baseline) in PT+CBT and PT. Participants in WLC filled out questionnaires at baseline and 12 weeks later (post-test).

Settings and participants

The centres involved were: two university medical centres, one general hospital and one rehabilitation centre, all of them located in the Netherlands. The medical ethics committee of the University Medical Center Utrecht and the local research ethics committees approved the study. Written informed consent was obtained from each participant. Eligible for the study were cancer patients (age ≥18 years) who completed curative cancer treatment at least three months ago, with a minimum estimated life expectancy of one year. They needed to be referred by a medical specialist or a general practitioner who then judged fulfilment of at least three of the following criteria: physical complaints, reduced physical capacity, psychological problems, increased fatigue, sleep disturbances, and problems in coping with reduced physical and psychosocial functioning due to cancer. Patients were excluded in case of restrictive side effects from medication, serious cognitive disturbances, psychopathology, or emotional instability that might impede participation in rehabilitation, or if they needed intensive medical treatment or rehabilitation. So, cancer survivors were eligible for the study when they were considered to be successfully treated for cancer, but still experienced physical and psychosocial problems.

Recruitment and allocation

Leaflets handed out by general practitioners or by medical professionals in hospitals, local newspapers, radio and television, and a website (www.oncorev.nl) informed cancer patients about the study. Patients who contacted a study centre received a study information package, containing an information letter, an informed consent form, an intake questionnaire and referral papers for their medical specialists or general practitioners. Each centre delivered one group at a time. In each centre consecutive groups of 8-12 eligible subjects were assigned to PT+CBT or PT and were scheduled for baseline measurements. Randomization at group level was applied; prior to enrolment of participants in the study, the sequence of PT+CBT and PT groups at each centre was determined by an independent researcher from the University Medical Center Utrecht using a randomization list. After randomization, the sequence of treatments in each centre was fixed and could not be influenced by research centres or researchers. Until the first session, participants were blinded to the rehabilitation group they were allocated to. Centre 1 (n=15) delivered one PT+CBT and one PT group, Centres 2 (n=44) and 3 (n=39) each delivered two PT+CBT and two PT groups, and Centre 4 (n=49) delivered three PT+CBT and three PT groups. Eligible patients were invited to participate in WLC if they had to wait at least three months for 12-week group-based multidisciplinary cancer rehabilitation programmes in other Dutch centres using the same inclusion criteria. This population was expected to be highly comparable to participants in the rehabilitation groups. Interested WLC patients received the study information package and, after written consent, filled out questionnaires.

Recruitment and assessments of participants occurred between February 2004 and September 2006 (Figure 1).

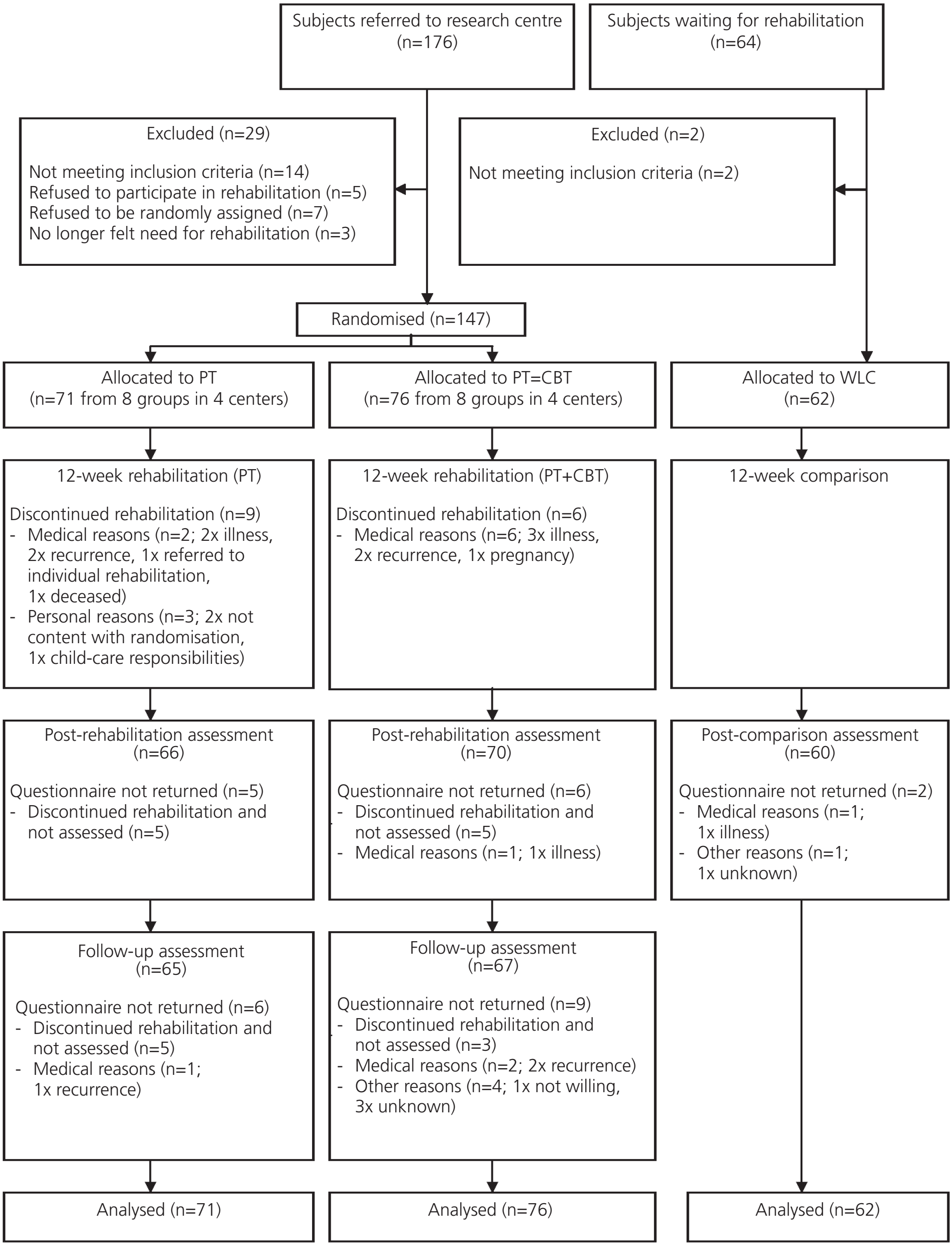

Figure 1. Flow of the participants through the study
Abbreviations: PT+CBT – physical plus cognitive-behavioural training; PT – physical training; WLC – waiting-list comparison.

The interventions

The two interventions compared in this study were 1) a 12-week (twice weekly, 2-hour sessions) physical training programme (PT), and 2) the same 12-week physical training programme plus a cognitive-behavioural training programme (CBT) (weekly, 2-hour sessions). Both programmes aimed at improving participants' role functioning and other aspects of QoL and supporting patients in coping with the physical and psychosocial consequences of cancer, with a primary focus on illness perceptions and self-management. The programmes focused on patients' illness perceptions because coping strategies are guided by patients' perceptions of their illness and perceived identity (label and symptoms of illness), perceived causes, time-line (duration and course), and perceived consequences, controllability and curability.[18] Therefore, awareness or even adaptation of these perceptions might influence coping and support self-management. Self-management theory describes how patients cope with the consequences of their disease and their treatment by means of a circular process of goal selection, information collection, information processing and evaluation, decision-making, action and self-reaction.[17] Both programmes were purposely developed as group-wise interventions to enhance fellow patient contacts.

The group format and specially included refreshment breaks in both PT and CBT provided opportunities for social comparison[19], social support[20] and modelling[21]. Also, PT as well as CBT were tailor-made to individual participants through personalized exercises. PT was guided by two physiotherapists and CBT was guided by a psychologist, and a nurse, physiotherapist or social worker. All therapists were experienced in their profession and in the field of cancer rehabilitation. The experience of PT therapists in this field ranged from 2.5 to 6.3 years (median 5.1 years) and CBT therapists were working in cancer rehabilitation between 2.4 to 11.3 years (median 4.4 years). All therapists received group training to apply the standardized protocols: PT therapists for one day, CBT therapists for two days.

Physical training

PT included personalized physical exercise to improve exercise capacity, muscle strength, to reduce physical limitations and fatigue and to increase daily activity. Each session consisted of individual aerobic bicycle training (0.5 hours), based on baseline graded exercise testing, muscle strength training (0.5 hours), and group sports and games (1 hour). Sports and games, such as badminton, soccer, swimming and balancing games, were aimed at promoting enjoyment in sports and improving self-efficacy in order to incorporate sporting activities into daily life and to adopt a physically active lifestyle. Additionally, patients received information on exercise physiology, illness perceptions and self-management to support them in regulating their physical training. Participants learned to use by themselves heart rate sport testers, the Borg Scale for dyspnea and fatigue[22] and training logs to monitor and evaluate their performance, and they received feedback, information and support from their therapists in regulating their performance. During the first four weeks participants followed a tailor-made basic training programme, based on individual baseline testing. Then, in cooperation with the therapists, participants determined their personal goals for training from Week 5 onwards. They could choose one of four modules: improvement of physical condition, improvement of muscular strength, coping with fatigue, or handling limitations.

Cognitive-behavioural training

CBT included interactive psycho-education and structured self-management skills training. This training was formatted in line with a cognitive-behavioural problem-solving therapy protocol for individual cancer patients[23] and a group problem-solving protocol successfully applied in patients with non-specific low back pain[24,25]. CBT aimed to enable participants to effectively solve their personal problems associated with cancer. To this end, they learned to apply self-management skills in striving for personal goals (e.g., in work, household, hobbies, physical activity, family relations and social contacts). Generalization to daily life during and after rehabilitation was promoted by practicing activities during sessions and by homework assignments (maximally 0.5 hours weekly). Every session was structured in: 1) recapitulation of the previous week's session and exchanging daily life experiences; 2) discussing home assignments; 3) introducing new topics or self-management skills; 4) practicing self-management skills; 5) introducing the next homework assignments; and 6) relaxation exercises. Participants used a workbook containing a summary of the training, self-management worksheets and assignments, as well as information on additional topics relevant to cancer patients. The first three weeks focused primarily on exchanging participants' experiences with cancer, psycho-education about stress, relaxation, fatigue, exercise physiology, illness perceptions, as well as on promoting optimism and self-efficacy for self-management. From Week 4 onwards participants were primarily trained in applying self-management skills to realize personal goals by practicing the following steps in the circular problem-solving process: 1) problem orientation; 2) problem definition and formulation, and goal setting; 3) generation of alternative solutions (brainstorming); 4) decision-making; and 5) solution implementation and verification.

Measures

Socio-demographic and medical variables were assessed using self-report questionnaires, with confirmation of medical data by the referring physicians.

General health-related QoL was measured using the RAND 36-item Health Survey.[26,27] This multidimensional self-report questionnaire consists of four functional scales: role limitations due to physical problem (four items), role limitations due to emotional problem (three items), physical functioning (ten items), social functioning (two items); three well-being scales: mental health (five items), vitality (four items) and pain (two items), and a global scale: general health perception (five items). The two role limitations subscales measure problems with work or other daily activities, either as a result of physical health problems, or due to emotional problems. One last item, health change, assesses the perceived change over the last year in general health status. After applying linear transformation according to the manual, scores of the scales ranged from 0–100 with a higher score reflecting better health. The RAND-36 is a reliable and valid instrument widely used in patients with different somatic diseases. Cronbach's α of the subscales range from 0.71 to 0.92.[26,28] The Cronbach's α in the present study ranged from 0.74 to 0.89 at baseline, from 0.75 to 0.87 at post-test, and from 0.77 to 0.90 at 3-month follow-up, indicating adequate to good internal consistency of all subscales. The Dutch RAND-36 manual provides reference scores of a random sample (n=1063, 65% females, mean age 44.1, range 18-89) of the general Dutch population (notes Table 3).[26]

Primary outcome in the comparison between both rehabilitation groups was role imitations (emotional), and the primary outcome in the comparison between both rehabilitation groups and WLC was role limitations (physical).

Data analysis

A priori power analysis for a comparison between the randomised groups on the primary outcome role limitations (emotional) estimated a sample size of 64 participants in each group to detect a moderate effect-size (*d=0.50*) with a power of 0.80 and a two-tailed alpha of 0.05. Accounting for an estimated dropout of

10% 71 participants in each group were needed. Statistical analysis was performed using SPSS statistical software, version 13.0, 2004.

Longitudinal intention-to-treat analyses were conducted, using mixed linear regression models[29]. In these analyses the programme accounts for missing data based on the observed data. Firstly, the rehabilitation effect on QoL was tested in PT+CBT as compared to PT after rehabilitation and at 3-month follow-up. Level 1 was time; level 2 was participant. A factor "centre" was also included because of the 4-center study design. Because of the group format in rehabilitation we considered to see group as level 3. However, after incorporating group, in most subscales the analyses failed, probably due to small sample sizes (16 groups) at this higher level[30] and small differences in QoL between groups, while in the subscales in which the analyses were successfully conducted, incorporating group level did not influence the results. Secondly, the same method of analysis was performed to test the rehabilitation effect on QoL in the rehabilitation groups as compared to WLC at post-test, except that the factor "centre" was not included, because WLC was not nested in the four centres. In these longitudinal analyses we corrected for any baseline differences between the rehabilitation groups and WLC.

ES were calculated according to Cohen as indices measuring the magnitude of a treatment effect. An ES <0.2 reflects "no effect," ES ≥ 0.2, ≤ 0.5 "small effect," ES ≥ 0.5, ≤ 0.8 "moderate effect" and ES ≥ 0.8 "large effect".[31]

Differences were explored in baseline socio-demographic and medical characteristics between included patients and those who met the inclusion criteria but refused participation or no longer felt a need for rehabilitation at baseline as well as between participants who stayed in the study and those who discontinued rehabilitation. In addition, differences were tested in socio-demographic and medical characteristics and in baseline QoL scores between the rehabilitation groups and WLC. ANOVA was used for continuous data and Chi-Square tests were used for categorical data.

Results

No differences were found in baseline socio-demographic and medical characteristics between the 209 included patients (Table 1) and the 15 patients who met the inclusion criteria but refused participation or no longer felt a need for rehabilitation at baseline. Differences were found between the 194 participants who stayed in the study and the 15 participants who discontinued rehabilitation. Participants who stayed in the study were significantly more often working at baseline than were those who discontinued rehabilitation (39.7% versus 13.3%) and they reported more often co-morbidity (47.4% versus 20%) (p-values <0.05). Participants with co-morbidity reported to receive medical treatment for one or more of the following problems: cardiac problems, vascular problems, diabetes, asthma, rheumatic problems, musculoskeletal problems, psychological problems or other complaints.

Patient characteristics

Table 1 shows participants' baseline characteristics. Groups were well balanced in almost all socio-demographic and medical variables. However, as compared to participants in both rehabilitation groups WLC participants were less educated, more often married and more of them had experienced a cancer recurrence more than 3 months before rehabilitation (p-values <0.05). All participants, including those who had experienced a recurrence, had completed curative medical treatment at least 3 months before rehabilitation and had a minimum estimated life expectancy of one year.

Attendance and adverse events

Both rehabilitation groups completed 83.5% of 24 physical training sessions (PT+CBT 20±4.7; PT 20±5.2) and PT+CBT completed 82.4% of 12 cognitive-behavioural training sessions (9.9±2.4). One participant in PT collapsed during rehabilitation and died at the first-aid station, which, after autopsy, the physician diagnosed as not related to the intervention. No further adverse events were reported.

Table 1. Baseline characteristics

	PT n=71	PT+CBT n=76	Rehabilitation groups n=147	WLC n=62	Overall n=209
Age (years)	49.9 ± 11.3	47.8 ± 10.5	48.8 ± 10.9	51.3 ± 8.8	49.5 ± 10.4
Sex					
Female	57 (80.3)	66 (86.8)	123 (83.7)	56 (90.3)	179 (85.6)
Educational level [b]					
Low	14 (19.7)	6 (7.9)	20 (13.6)	16 (25.8)	36 (17.2)
Middle	32 (45.1)	40 (52.6)	72 (49.0)	32 (51.6)	104 (49.8)
High	25 (35.2)	30 (39.5)	55 (37.4)	14 (22.6)	69 (33.0)
Marital status [b]					
Married/living together	51 (71.8)	53 (69.7)	104 (70.7)	55 (88.7)	159 (76.1)
Employment status					
Employed at diagnosis	53 (74.6)	54 (71.1)	107 (72.8)	46 (74.2)	153 (73.2)
Actually working at baseline	23 (32.4)	32 (42.1)	55 (37.4)	24 (38.7)	79 (37.8)
Cancer type					
Breast	34 (47.9)	48 (63.2)	82 (55.8)	38 (61.3)	120 (57.4)
Haematological	8 (11.3)	15 (19.7)	23 (15.6)	10 (16.1)	33 (15.8)
Gynaecological	11 (15.5)	6 (7.9)	17 (11.6)	7 (11.3)	24 (11.5)
Urologic	6 (8.5)	3 (3.9)	9 (6.1)	-	9 (4.3)
Lung	2 (2.8)	2 (2.6)	4 (2.7)	4 (6.5)	8 (3.8)
Colon	2 (2.8)	1 (1.3)	3 (2.0)	2 (3.2)	5 (2.4)
Other	8 (11.3)	1 (1.3)	9 (6.1)	1 (1.6)	10 (4.8)
Recurrence >3months ago [b]					
Yes	7 (9.9)	7 (9.2)	14 (9.5)	15 (24.2)	29 (13.9)
No	57 (80.3)	61 (80.3)	118 (80.3)	45 (72.6)	163 (78.0)
Unknown	7 (9.9)	8 (10.5)	15 (10.2)	2 (3.2)	17 (8.1)
Metastases >3 months ago					
Yes	15 (21.1)	16 (21.1)	31 (21.1)	12 (19.4)	43 (20.6)
No	55 (77.5)	59 (77.6)	114 (77.6)	49 (79.0)	163 (78.0)
Missing	1 (1.4)	1 (1.3)	2 (1.4)	1 (1.6)	3 (1.4)
Treatment >3 months ago					
Surgery	62 (87.3)	64 (84.2)	126 (85.7)	51 (82.3)	177 (84.7)
Chemotherapy	45 (63.4)	55 (72.4)	100 (68.0)	39 (62.9)	141 (67.5)
Radiotherapy	41 (57.7)	43 (56.6)	84 (57.1)	41 (66.1)	123 (58.9)
Time since treatment (years)	1.4 ± 2.1	1.2 ± 1.3	1.3 ±1.7	1.9 ± 2.7	1.5 ± 2.1

Table 1 continued

Co-morbidity at start					
Yes	32 (45.1)	36 (47.4)	68 (46.3)	27 (43.5)	95 (45.5)
No	39 (54.9)	40 (52.6)	79 (53.7)	34 (54.8)	113 (54.1)
Missing	--	--	--	1 (1.6)	1 (0.5)
Hormonal therapy at start					
Yes	20 (28.2)	31 (40.8)	51 (34.7)	19 (30.6)	70 (33.5)
No	51 (71.8)	45 (59.2)	96 (65.3)	43 (69.4)	139 (66.5)
Other medication at start					
Yes	52 (73.2)	53 (69.7)	105 (71.4)	42 (67.7)	147 (70.3)
No	19 (26.8)	20 (26.3)	39 (26.5)	18 (29.0)	57 (27.3)
Missing	--	3 (3.9)	3 (2.0)	2 (3.2)	5 (2.4)
Contacts < 2 months ago					
Specialist	2.2 ± 2.1	2.1 ± 1.8	2.2 ± 1.9	2.1 ± 4.2	2.1 ± 2.8
General practitioner	1.7 ± 1.9	1.3 ± 1.2	1.5 ± 1.6	1.3 ± 1.5	1.4 ± 1.6
Physiotherapist	2.2 ± 4.3	2.1 ± 3.9	2.2 ± 4.1	2.5 ± 3.8	2.2 ± 4.0
Psychologist	0.3 ± 0.7	0.2 ± 0.7	0.3 ± 0.7	0.4 ± 1.5	0.3 ± 1.0

Abbreviations: SD – standard deviation; PT – physical training; PT+CBT – physical training plus cognitive-behavioural training; WLC – waiting-list comparison.
[a] *Continuous data: mean ± SD; categorical data: frequency (percentage).*
[b] *Significant differences between rehabilitation groups and WLC: p < 0.05.*

Quality of life

At baseline no significant differences in QoL subscales were found between both rehabilitation groups and WLC. Participants in the study reported significantly lower QoL than did the general Dutch population (note Table 3) in all domains (p-values <0.05), except for PT+CBT and WLC in health change and PT in pain.

Table 2 shows participants' QoL changes in PT+CBT as compared to PT after rehabilitation and at 3-month follow-up. The primary outcome was role limitations (emotional). PT+CBT showed no significant changes beyond those in PT, neither in role limitations (emotional), nor in the other domains of quality of life.

Table 3 shows participants' QoL changes in the rehabilitation groups as compared to the WLC between baseline and post-test. The primary outcome was role limitations (physical). Compared to WLC, both rehabilitation groups showed significant improvements in role limitations (physical) (ES 0.66), representing a moderate treatment effect. Additionally, both rehabilitation groups showed significant improvements in physical functioning (ES 0.48), vitality (ES 0.54) and health change (ES 0.76), representing small to moderate treatment effects. Furthermore, all significant improvements were larger than a five-point difference and a 10% change of scores, which are considered to be clinically relevant changes in the RAND-36.[32,33] Lastly, within-group improvements in the rehabilitation groups were significant in all domains of QoL (p-values <0.001), except in pain (data not shown).

Discussion

Our hypothesis that multidisciplinary rehabilitation would demonstrate a greater improvement in role limitations (emotional) than would physical training was not supported. Furthermore, multidisciplinary rehabilitation did not outperform physical training in any other domains of quality of life. Our hypothesis that both rehabilitation groups would outperform a waiting-list comparison group was confirmed by a significant, clinically relevant improvement in role limitations (physical). Additionally, significant and clinically relevant improvements were found in physical functioning, vitality and health change (subjective health improvement). No improvements were found in general health perception, social functioning, role limitations (emotional), mental health, and pain. As participants did not report substantial pain at baseline, improvements in this domain were not likely to appear. The improvements in the rehabilitation groups, compared to WLC, were predominantly found in the physical domains. This might well be due to the physical training component in both rehabilitation groups as physical training may have most benefits in physical and functional domains, whereas psychosocial functioning is less likely to be considerably improved by physical training.[4,13-15]

Our randomised controlled study was the first study to compare combined cancer rehabilitation to physical training and, at the same time, it was the first trial to include a 3-month follow-up of participants in comparing combined to single focused cancer rehabilitation. Our study showed that group-based cognitive-behavioural training had no effects on role limitation (emotional) or any other domains of quality of life beyond those of group-based self-management physical training after rehabilitation and at 3-month follow-up.

Table 2. Quality of life RAND-36 mean scores (range 0-100) at baseline, post-rehabilitation and 3-month follow up and between-group changes (pre to post-rehabilitation and pre to 3-month follow-up) in PT and PT+CBT (PT is reference)[a]

	Baseline Mean (SD)		**Post-rehabilitation Mean (SD)**		**3-month follow-up Mean(SD)**		**Pre to post Between-group change PT+CBT compared to PT**			**Pre to 3-month follow-up Between-group change PT+CBT compared to PT**		
	PT	PT+CBT	PT	PT+CBT	PT	PT+CBT	Change (95% CI)	*p*	*ES*	Change (95% CI)	*p*	*ES*
Role limitations (physical)	27.1 (35.8)	18.8 (27.1)	54.9 (40.0)	47.1 (40.1)	46.5 (40.7)	44.3 (41.6)	0.9 (-12.8 to 14.5)	.900	*0.03*	6.6 (-7.2 to 20.5)	.345	*0.21*
Role limitations (emotional)	52.3 (43.7)	49.3 (46.5)	71.1 (39.4)	69.2 (43.3)	73.1 (41.2)	66.5 (44.7)	-0.1 (-15.9 to 15.7)	.986	*0.00*	-5.6 (-21.6 to 10.3)	.486	*-0.12*
Physical functioning	62.2 (20.7)	60.8 (19.0)	76.5 (17.6)	77.1 (16.2)	76.2 (20.8)	73.3 (20.4)	1.2 (-4.2 to 6.5)	.666	*0.06*	-1.2 (-6.7 to 4.2)	.654	*-0.06*
Social functioning	63.0 (23.8)	60.5 (19.6)	74.6 (20.9)	72.0 (18.3)	70.2 (26.0)	71.0 (20.7)	-0.1 (-7.0 to 6.9)	.986	*0.00*	3.2 (-3.8 to 10.3)	.368	*0.15*
Mental health	66.6 (17.4)	63.6 (17.8)	74.7 (13.7)	70.7 (15.3)	71.9 (18.8)	72.1 (15.1)	-1.4 (-6.3 to 3.5)	.568	*-0.08*	2.5 (-2.5 to 7.4)	.324	*0.14*
Vitality	43.5 (18.2)	43.7 (18.8)	61.4 (16.4)	59.1 (16.7)	56.3 (19.8)	57.2 (18.5)	-2.2 (-7.9 to 3.4)	.442	*-0.12*	1.0 (-4.7 to 6.7)	.735	*0.05*
Pain	75.2 (23.9)	70.3 (23.8)	75.3 (21.6)	77.7 (20.9)	74.3 (24.3)	74.2 (22.6)	6.9 (-0.4 to 14.2)	.065	*0.29*	4.2 (-3.2 to 11.6)	.262	*0.18*
General health perception	50.5 (18.1)	49.2 (16.5)	58.9 (20.3)	55.6 (16.3)	57.5 (19.2)	52.3 (18.4)	-1.1 (-6.2 to 4.1)	.683	*-0.06*	-3.4 (-8.7 to 1.8)	.198	*-0.20*
Health change	43.2 (35.3)	45.0 (33.4)	75.4 (27.6)	82.3 (23.1)	74.2 (30.0)	80.3 (25.0)	5.1 (-7.6 to 17.9)	.428	*0.15*	4.7 (-8.1 to 17.6)	.468	*0.14*

Abbreviations: SD – standard deviation; CI – confidence interval; p – p-value; ES - effect size; PT – physical training; PT+CBT – physical training plus cognitive-behavioural training.

[a] PT n=71; PT+CBT n=76; higher scores reflect better health, mean (SD) based on observed data, between-group changes based on mixed linear regression models.

3

Table 3. Quality of life RAND-36 mean scores (range 0-100) at baseline and post-rehabilitation and between-group changes pre- to post-rehabilitation) in the rehabilitation groups and WLC (WLC is reference)[a]

	Baseline Mean (SD)		**Post-rehabilitation Mean (SD)**		**Pre to post Between-group change Rehabilitation compared to WLC**		
	Rehabilitation groups	WLC	Rehabilitation groups	WLC	Change (95% CI)	*p*	*ES*
Role limitations (physical)	22.8 (31.7)	25.0 (31.7)	50.9 (40.1)	32.9 (39.7)	20.8 (8.9 to 32.7)	.001	*0.66*
Role limitations (emotional)	50.7 (45.1)	59.0 (42.7)	70.1 (41.3)	66.7 (41.6)	12.2 (-2.4 to 26.8)	.100	*0.27*
Physical functioning	61.5 (19.7)	62.5 (19.7)	76.8 (16.8)	68.2 (20.2)	9.4 (5.1 to 13.6)	.000	*0.48*
Social functioning	61.7 (21.7)	64.7 (19.8)	73.3 (19.6)	71.6 (20.1)	4.5 (-1.4 to 10.4)	.132	*0.21*
Mental health	65.0 (17.6)	64.9 (15.9)	72.7 (14.6)	68.0 (17.0)	3.8 (-0.2 to 7.8)	.063	*0.22*
Vitality	43.6 (18.5)	45.3 (16.9)	60.2 (16.5)	51.7 (18.7)	9.8 (5.3 to 14.3)	.000	*0.54*
Pain	72.7 (23.9)	70.0 (27.6)	76.5 (21.2)	73.3 (26.1)	0.3 (-5.8 to 6.5)	.916	*0.01*
General health perception	49.8 (17.2)	53.6 (21.5)	57.2 (18.3)	56.3 (19.4)	3.6 (-0.7 to 8.0)	.097	*0.19*
Health change	44.1 (34.2)	45.2 (32.6)	78.9 (25.5)	55.4 (32.6)	25.7 (16.8 to 34.5)	.000	*0.76*

Abbreviations: SD – standard deviation; CI – confidence interval; p – p-value; ES - effect size; WLC – waiting-list comparison.

[a] *Rehabilitation groups n=147; WLC n=62; higher scores reflect better health, mean (SD) based on observed data, between-group changes based on mixed linear regression models.*

Reference scores Dutch general population: mean (SD) (24): role limitations (physical) 79.4 (35.5); role limitation (emotional) 84.1 (32.3); physical functioning 81.9 (23.2); social functioning 86.9 (20.5); mental health 76.8 (18.4); vitality 67.4 (19.9); pain 79.5 (25.6); general health perception 72.7 (22.7); health change 52.4 (19.4).

To date, one study, comparing combined rehabilitation (group-psychotherapy plus home-based walking) to group-psychotherapy only, suggested the additive value of physical training in two domains of quality of life, functional well-being and fatigue.[13] These findings, combined with our results, imply that physical training should be included in cancer rehabilitation. Moreover, our study showed that up to 3-month follow-up combined cancer rehabilitation did not improve quality of life beyond the effects of physical training.

Although our findings suggest that cognitive-behavioural training has no unique additive value for quality of life above and beyond physical training, such a conclusion would be premature. Cognitive-behavioural problem-solving interventions showed substantial beneficial effects on quality of life in cancer patients in the longer term.[7,34] Moreover, positive long-term effects were reported of a group-based problem-solving intervention added to physical training in non-specific low back pain patients.[24] Therefore, a long-term follow-up measurement in our two rehabilitation groups is needed.

It should be noted that our physical training should not be regarded as being exercise-only. First, the physical training purposely applied a group-format that included opportunities for fellow patient contacts to enhance social comparison[19], social support[20] and modelling[21]. Second, a self-management approach was applied to improve participants' self-efficacy in the physical training. By including self-management in rehabilitation our study also distinguishes from earlier studies on group-based multidisciplinary cancer rehabilitation in patient populations similar to ours[11,12] and from the group-based multidisciplinary programme of Courneya et al.[13]. A meta-analysis of randomised controlled studies of physical interventions reported an ES of 0.30 for QoL in cancer patients after medical treatment.[4] The larger effects in our study (ES up to 0.76) in both rehabilitation groups as compared to no intervention might be explained by the group-format and self-management. At the same time, including these elements in physical training may have prevented that cognitive-behavioural training could improve participants' QoL beyond the benefits of physical training.

A process analysis of both interventions showed high attendance in sessions and low dropout. This indicates that participants, who on average reported a low level of quality of life at baseline, were highly motivated and that both rehabilitation programmes were highly feasible in these cancer survivors. Hence, our findings can be generalized to cancer survivors experiencing physical and psychosocial problems

that apply for rehabilitation on their own initiative.
Strengths of the present study were the randomised controlled design with intention-to-treat analyses, the 3-month follow-up, the supervised, standardized and theory-based intervention, large sample size, high attendance and low dropout rates.

A limitation of our study was that participants could not be randomly assigned to a waiting-list comparison condition and that participants in the waiting-list comparison group could not be assessed at 3-month follow-up. The reason for this was that cancer patients prefer to start rehabilitation as soon as possible after medical treatment. Nevertheless, as the comparison group participants were waiting for 12-week group-based multidisciplinary cancer rehabilitation programmes in other Dutch centres using the same inclusion criteria, the comparison group was expected to be highly comparable to the rehabilitation groups. Indeed, the groups showed to be well balanced in baseline quality of life scores, while at the same time we corrected for any differences in socio-demographic and medical variables. Furthermore, we evaluated our tailor-made programme at group level, but to further improve tailoring, additional research on predictors of successful treatment should show who profits most from what. Further research should focus on, for example, exercise capacity, muscle strength, anxiety and depression.

To conclude, our study was the first to compare multidisciplinary cancer rehabilitation, combining physical and cognitive-behavioural training, to physical training. Up to 3-month follow-up, multidisciplinary cancer rehabilitation did not outperform physical training, neither in role limitation (emotional), nor in other domains of quality of life. Compared to a waiting-list comparison condition the rehabilitation groups showed significant, clinically relevant improvements in role limitations (physical) and in several other domains of quality of life.

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4

Cancer survivors' quality of life: long-term effects of physical training versus physical training combined with cognitive-behavioural therapy

Abstract

Objective

We compared the effect of physical exercise with that of physical exercise combined with a cognitive-behavioural intervention on quality of life of cancer survivors over a 1-year period.

Methods

147 survivors (48.8±10.9 years (mean±SD), all cancer types, medical treatment ≥3 months ago) were randomly assigned to either 12-week group-based physical training (twice weekly, PT n=71) or to 12-week group-based physical training (twice weekly) plus cognitive-behavioural therapy (once weekly; PT+CBT, n=76). Quality of life was measured before and immediately after the intervention, and at three and nine months post-intervention using the EORTC-QLQ-C30 questionnaire.

Results

Analyses using multilevel linear mixed-effects models revealed no differential pattern in change between PT and PT+CBT. In both PT and PT+CBT, quality of life was significantly and clinically relevantly improved immediately following the intervention and also at three and nine months post-intervention compared to pre-intervention ($p<0.001$).

Conclusion

Physical training had substantial and durable positive effects on cancer survivors' quality of life. Combining physical training with a cognitive-behavioural intervention does not add to these beneficial effects of physical training neither in the short-term nor in the long-term.

Introduction

The short-term benefits of physical training on cancer survivors' quality of life (QoL) are well established.[1,2] However, evidence for the durability of these beneficial effects is lacking.[1] One randomised clinical trial examining the effects of a 12-week exercise programme on QoL in cancer survivors who completed primary cancer treatment showed promising results: QoL was improved immediately following the intervention and remained higher from post-intervention to 3-month follow-up.[3] Daley et al.[4] recently reported a beneficial effect on breast cancer survivors' QoL directly following an 8-week physical training programme compared to control, but differences between experimental and control disappeared at 4-month follow-up. To date, only one study investigating the effect of a 7-week group rehabilitation programme on cancer survivors' QoL included a one-year follow-up.[5] However, this particular intervention consisting of physical training, information and training of coping skills did not lead to improvements in QoL neither in the short-term nor in the long-term.

QoL is a multidimensional construct including physical as well as psychosocial dimensions.[6] Studies on the effect of physical training in cancer survivors suggest that physical training is primarily associated with improved physical and functional aspects of QoL, rather than the social and emotional domains.[7-9] A recent meta-analysis reported that cognitive-behavioural therapy had positive effects on mental health of cancer survivors.[10] Hence, combining physical training with cognitive-behavioural therapy could lead to greater improvements in global QoL by having benefits for both physical and psychosocial functioning. Therefore, we developed a cancer rehabilitation programme that integrated physical training and cognitive-behavioural therapy, both based on principles of self-management[11], and investigated the effects of that programme on QoL.

We recently showed that adding cognitive-behavioural therapy to physical training does not enhance the positive effects of physical training on quality of life and physical fitness at the short-term.[12,13] However, long-term effects may be different. Physical training may have early effects on QoL, while cognitive-behavioural therapy, that at first confronts patients with personal worries and possibly increases distress[14,15], might have especially long-term benefits[16-18]. Hence, the long-term effects of physical training combined with cognitive-behavioural therapy on QoL may be greater compared to the effects of physical training. Therefore, the aim of the present study was to compare the long-term effects on QoL of a 12-week self-management physical training intervention (PT) with that of the same physical training intervention combined with cognitive-behavioural therapy (PT+CBT). Furthermore, we investigated whether effects on quality of life persist over time.

Participants and Methods

A prospective, randomised multicentre trial was conducted from February 2004 through January 2007. Four Dutch centres experienced in oncological rehabilitation participated in the trial: two university medical centres, one general hospital and one rehabilitation centre. Patient inclusion criteria were: age ≥18 years; last curative cancer treatment completed at least three months before study entry; estimated life expectancy at least one year. Referral by a medical specialist or a general practitioner was needed who judged fulfilment of at least three of the following criteria to ascertain the need for rehabilitation: i.e. physical complaints, reduced physical capacity, psychological problems, increased levels of fatigue, sleep disturbances, and problems in coping with reduced physical and psychosocial functioning. Patients were excluded if they had cognitive disturbances, serious psychopathology or emotional instability that may impede participation, or if they were in need of intensive medical treatment or rehabilitation. The medical ethics committee of the University Medical Center Utrecht and the local research ethics committees approved the study.

Recruitment and allocation

Cancer survivors were informed about the study by various methods, including leaflets handed out by oncologists and general practitioners, information in the local newspapers and through the website. After written consent, eligible subjects were scheduled for baseline measurements and randomised to PT or PT+CBT. By design, PT and PT+CBT were balanced in each centre. Each centre delivered one group at a time. Randomisation at group level was applied; in each centre consecutive groups of eight to twelve eligible subjects were assigned to the randomly determined treatment to ascertain adequate numbers of participants in each group. Prior to enrolment of participants in the study, an independent researcher randomly determined the sequence of interventions at each centre, using a randomisation list. Until the first session, participants were blinded to the rehabilitation group they were allocated to. Figure 1 shows the flow of participants through the trial.

Intervention

The present intervention has been described in more detail elsewhere.[12]

Both components, PT and CBT, were based on the principles of self-management[11]: i.e. goal selection, information collection, information processing and evaluation, decision making, action and self-reaction. Rehabilitation took place in groups of 8-12 cancer survivors. PT was supervised by two physical therapists and CBT by a psychologist and a social worker. All the therapists involved were trained to apply the standardised intervention protocol. All therapists were experienced in their profession and in the field of cancer rehabilitation.

Physical training (twice weekly, two hours per session) consisted of a personalised exercise program based on baseline exhaustive exercise testing. Each session consisted of individual exercise (aerobic bicycle training (30 minutes) and muscle strength training (30 minutes)) followed by group sports (60 minutes). During the training, the participants used heart rate monitors, the Borg Scale for dyspnea and fatigue[19] and training logs to monitor and evaluate their performance, and received feedback, information and support from their therapists in regulating their performance. The physical training was supervised by two physical therapists.

Aerobic bicycle training: Intensity was determined using the Karvonen formula[20] that uses the peak heart rate (HR_{peak}) obtained from baseline exhaustive exercise testing and the heart rate at rest (HR_{rest}) to calculate the training HR (HR_{tr}). Exercise training was performed at a HR_{tr} of $(HR_{rest}+40\%$ *to* 50% *of* $(HR_{peak}-HR_{rest}))$ during the first four weeks and was gradually increased to $(HR_{rest}+70\%$ *to* 80% *of* $(HR_{peak}-HR_{rest}))$ in Week 12.

Muscle strength training: Resistance exercise of lower and upper extremities was based on the baseline 1-Repetition Maximum (1-RM). Training intensity started at 30% of the 1-RM during the first week and was increased until 50 to 60% of 1-RM in Week 12.

Group sports: Sports, such as badminton, soccer, swimming and balancing games were performed with the aim being to promote enjoyment of sports and overcome any lack of confidence patients may have felt about exercising.

Cognitive-behavioural intervention (once a week, two hours per session) was based on a cognitive-behavioural problem-solving protocol for individual cancer patients[21] and a group problem solving protocol[22]. During CBT, the participants learned to apply self-management skills[11] in striving for personal goals (e.g., in physical activity, work, household, hobbies, family relations and social contacts). Generalisation to daily life during and after rehabilitation was promoted by practicing activities during sessions and by homework assignments (maximally 0.5 hours weekly). The first three weeks focused primarily on exchanging participants' experiences with cancer, psycho-education about stress, relaxation, fatigue, exercise physiology, illness perceptions, as well as on promoting optimism and self-efficacy for self-management. From Week 4 onwards participants were primarily trained in applying self-management skills to realise personal goals by practising the following steps in the circular problem-solving process: 1) problem orientation; 2) problem definition and formulation, and goal setting; 3) generation of alternative solutions (brainstorming); 4) decision-making; and 5) solution implementation and verification. The cognitive-behavioural intervention was supervised by a psychologist and a social worker.

Outcomes

Socio-demographic and medical data were collected using a self-report questionnaire. Medical data were confirmed by the referring physicians.

Quality of life was assessed by the multidimensional European Organization for Research and Treatment of Cancer Quality of Life Questionnaire C30 (EORTC QLQ-C30)[6], which assessed cancer-specific QoL. The 30-item EORTC QLQ-C30 incorporates a global QoL scale and five functional scales: namely, physical functioning, social functioning, role functioning, emotional functioning, cognitive functioning; and three symptom scales: fatigue, pain and nausea and vomiting. In this study we report the results of the global scale, the functional scales, and one symptom scale (i.e., fatigue) since these scales are most relevant for participants who have already completed primary treatment for cancer. The raw scores were transformed linearly into scores ranging from 0 to 100. A higher score represents a higher QoL, a higher level of functioning, and a higher level of fatigue. The Cronbach's alphas in the present study were high for each of the seven scales (0.7-0.9) at all measurement occasions.

Differences of at least 10 points were classified as a minimum clinically meaningful change. Changes of less than 10 points were regarded as clinically irrelevant, and changes of more than 20 points were classed as large effects.[23]

Data analysis

The effect of PT+CBT compared to PT on QoL was tested at three, six and twelve months post-enrolment according to the intention-to-treat principle. Longitudinal analyses were conducted, using linear mixed-effects models while taking the different levels (training group, participant, and time) into account. The Akaike Information Criterion was used as a measure of how well our different models fit the data. A lower value on the Akaike Information Criterion indicated a better model fit. To determine whether changes of QoL were maintained from post-intervention to 9-month post-intervention statistical testing was performed as to whether the regression coefficients were different. In these analyses the program accounts for missing data based on the observed data. Statistical analysis was performed using R software, version 2.4.1. (www.r-project.org). Two-sided significance tests were used ($\alpha < 0.05$).

Results

Table 1 presents the baseline characteristics of the study participants. The groups were balanced on all socio-demographic and medical variables. Both rehabilitation groups completed 83.5% of 24 physical training sessions (PT+CBT 20±4.7 (mean±SD); PT 20±5.2) and PT+CBT participants completed 82.4% of 12 cognitive-behavioural sessions (9.9±2.4). Of PT+CBT participants 92.1%, 88.2% and 85.5% completed the assessments at post-intervention and 3-month and 9-month post-intervention, respectively. Of PT participants 93.0%, 91.5% and 81.7% completed the assessments at post-intervention and 3-month and 9-month post-intervention, respectively (Figure 1).

Table 1. Baseline characteristics*

Variable	**Overall (n=147)**	**PT+CBT group (n =76)**	**PT group (n =71)**
Age (years)	48.8 ± 10.9	47.8 ± 10.5	49.9 ± 11.3
Sex			
Female	123 (83.7)	66 (86.8)	57 (80.3)
Educational level			
Low	20 (13.6)	6 (7.9)	14 (19.7)
Middle	72 (49.0)	40 (52.6)	32 (45.1)
High	55 (36.8)	30 (39.5)	25 (35.2)
Marital status			
Married/living together	104 (70.7)	53 (69.7)	51 (71.8)
Employed at diagnosis	107 (72.8)	54 (71.1)	53 (74.6)
Body Mass Index (kg·m^2)	27.5 ± 6.2	27.4 ± 6.7	27.7 ± 5.8
Type of cancer			
Breast	82 (55.8)	48 (63.2)	34 (47.9)
Haematological	23 (16.6)	15 (19.7)	8 (11.3)
Gynaecological	17 (11.6)	6 (7.9)	11 (15.5)
Urogenital	9 (5.5)	3 (3.9)	6 (8.5)
Lung	4 (2.7)	2 (2.6)	2 (2.8)
Colon	3 (2.0)	1 (1.3)	2 (2.8)
Other	9 (6.2)	1 (1.3)	8 (11.3)
Type of treatment (>3 months ago)			
Surgery	126 (85.7)	64 (84.2)	62 (87.3)
Chemotherapy	100 (68.0)	55 (72.4)	45 (63.4)
Radiotherapy	84 (57.1)	43 (56.6)	41 (57.7)
Time post-treatment (years)	1.3 ± 1.7	1.2 ± 1.3	1.4 ± 2.1

**Data presented as mean ± standard deviation for continuous variables and frequency (percentage) for categorical variables.*

Abbreviations: PT+CBT – physical training plus cognitive-behavioural therapy; PT – physical training.

Changes in QoL

Table 2 shows the descriptive study measures over the 1-year study period. Multilevel linear mixed-effects models revealed no significant differences in changes over time in global QoL between PT+CBT and PT (Figure 2). The physical, role, emotional, cognitive and social functioning subscales and the fatigue subscale all demonstrated the same pattern of change (Table 3).

Significant improvements ($p<0.001$) in global QoL and in the other domains of QoL were found in the PT group as well as in the PT+CBT group immediately following the intervention, and at 3- and at 9-month post-intervention compared to pre-intervention. Almost all of these improvements were larger than ten points, which is considered to be clinically relevant.[23]

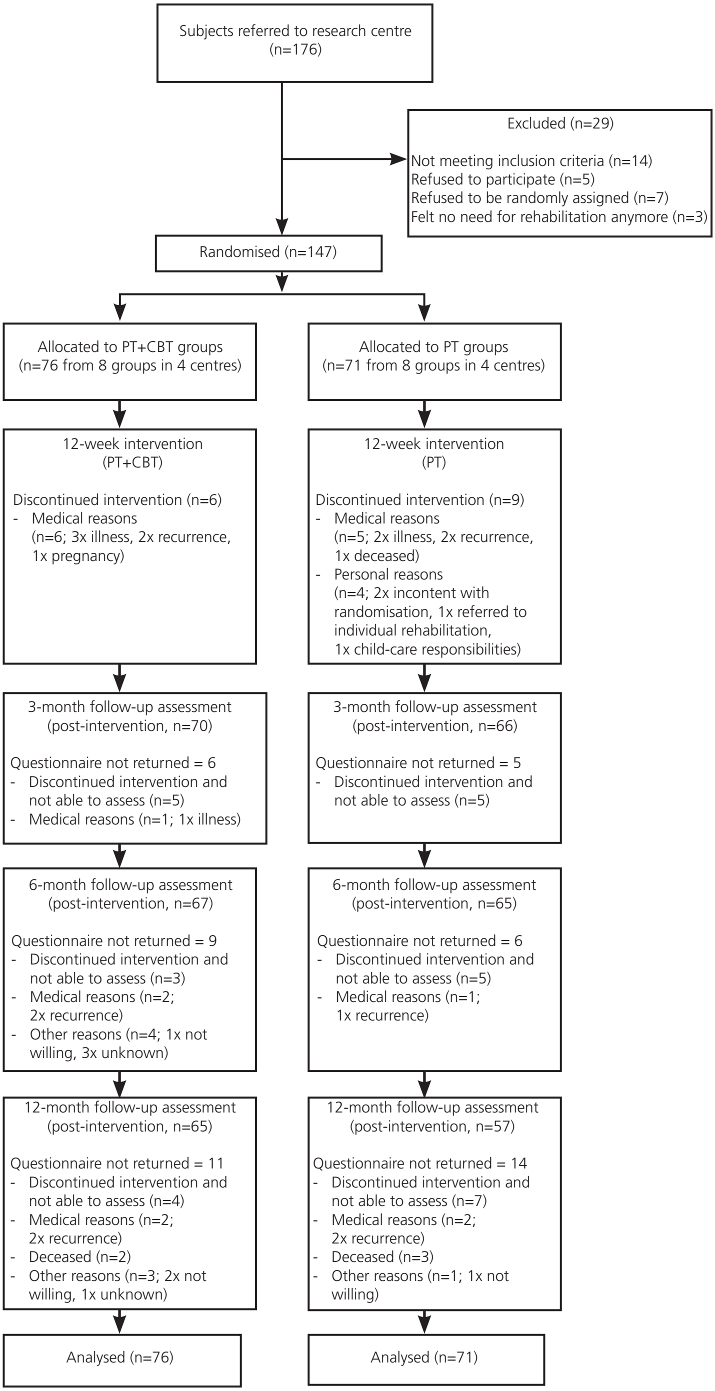

Figure 1. Flow of the participants through the study

Abbreviations: PT+CBT – physical training plus cognitive-behavioural therapy; PT – physical training.

4

In both PT and PT+CBT, the short-term improvements in all domains of QoL were maintained from post-intervention to 9-month post-intervention except that global QoL had decreased significantly but not clinically relevant in PT participants (p=0.04, 3.9-point difference).

Table 2. Descriptives of quality of life (EORTC-QLQ-30) over the 1-year study period[a]

	Baseline Mean (SD)	**Post-intervention* Mean (SD)**	**3-month post-intervention Mean (SD)**	**9-month post-intervention Mean (SD)**
Global quality of life				
PT	57.7 (16.7)	74.1 (14.8)	71.1 (18.7)	70.2 (18.2)
PT+CBP	56.5 (18.4)	71.3 (16.4)	66.5 (20.7)	67.9 (19.6)
Physical functioning				
PT	73.9 (14.2)	84.1 (12.0)	83.6(16.3)	85.2 (14.6)
PT+CBP	71.7 (13.3)	85.5 (10.5)	83.8 (13.3)	82.5 (15.6)
Role functioning				
PT	59.6 (24.2)	74.0 (24.3)	74.9 (23.4)	77.0 (24.5)
PT+CBP	55.0 (24.2)	75.2 (20.0)	67.4 (24.0)	70.8 (26.2)
Emotional functioning				
PT	63.6 (21.0)	76.0 (19.4)	76.4 (21.0)	75.3 (23.2)
PT+CBP	60.7 (22.1)	75.8 (18.9)	73.6 (19.2)	70.6 (22.5)
Cognitive functioning				
PT	66.9 (24.6)	76.5 (21.9)	76.7 (21.8)	79.0 (21.1)
PT+CBP	62.3 (27.0)	72.4 (21.0)	72.9 (24.2)	73.3 (22.6)
Social functioning				
PT	64.5 (26.4)	83.8 (20.5)	81.8 (24.4)	82.8 (23.3)
PT+CBP	61.4 (27.4)	81.2 (19.6)	75.6 (23.3)	80.0 (24.5)
Fatigue				
PT	49.0 (22.0)	31.0 (18.6)	33.3 (20.6)	35.6 (22.7)
PT+CBP	52.8 (24.5)	34.8 (17.5)	37.5 (24.1)	36.2 (25.3)

Abbreviations: EORTC- QLQ-30 - European Organization for Research and Treatment of Cancer Quality of Life Questionnaire C30; SD – standard deviation; PT – physical training; PT+CBT – physical training plus cognitive-behavioural therapy.

[a] *PT: n=71 at baseline, n=66 at 3 months, n=65 at 6 months and n=58 at 12 months; PT+CBT: n=76 at baseline, n=70 at 3 months, n=67 at 6 months and n=65 at 12 months.*

* *The intervention period comprised twelve weeks.*

Table 3. Intra- and inter-group mean changes in quality of life outcomes (EORTC-QLQ-30) at post-intervention and three and nine months post-intervention[a]

	Baseline to post-intervention		Baseline to 3-month post-intervention		Baseline to 9-month post-intervention	
	Within-group change Mean (95% CI)	**Between-group change Mean (95% CI)**	**Within-group change Mean (95% CI)**	**Between-group change Mean (95% CI)**	**Within-group change Mean (95% CI)**	**Between-group change Mean (95% CI)**
Global quality of life						
PT	16.0 (11.7 to 20.4)***	reference	12.9 (8.5 to 17.3)***	reference	11.1 (6.5 to 15.7)***	reference
PT+CBP	14.2 (10.0 to 18.4)***	-1.8 (-7.9 to 4.2)	8.8 (4.5 to 13.1)***	-4.1 (-10.2 to 2.0)	10.5 (6.2 to 14.8)***	-0.6 (-6.8 to 5.7)
Physical functioning						
PT	10.4 (7.4 to 13.3)***	reference	9.8 (6.8 to 12.7)***	reference	10.3 (7.2 to 13.4)***	reference
PT+CBP	13.1 (10.3 to 15.9***	2.7 (-1.4 to 6.8)	11.4 (8.5 to 14.3)***	1.6 (-2.5 to 5.7)	10.2 (7.3 to 13.1)***	-0.1 (-4.3 to 4.1)
Role functioning						
PT	14.1 (8.0 to 20.3)***	reference	14.9 (8.7 to 21.0)***	reference	15.6 (9.1 to 22.0)***	reference
PT+CBP	19.5 (13.6 to 25.5)***	5.4 (-3.2 to 13.9)	11.7 (5.7 to 17.8)**	-3.1 (-11.8 to 5.5)	14.6 (8.5 to 20.7)***	-1.0 (-9.8 to 7.9)
Emotional functioning						
PT	12.3 (7.3 to 17.3)***	reference	12.4 (7.4 to 17.4)***	reference	10.4 (5.2 to 15.7)***	reference
PT+CBP	14.4 (9.6 to 19.3)***	2.1 (-4.9 to 9.0)	11.7 (6.8 to 16.6)***	-0.7 (-7.7 to 6.3)	9.4 (4.4 to 14.4)**	-1.0 (-8.3 to 6.2)
Cognitive functioning						
PT	9.6 (4.5 to 14.8)**	reference	10.5 (5.4 to 15.7)***	reference	12.5 (7.2 to 17.9)***	reference
PT+CBP	9.3 (4.3 to 14.2)**	-0.4 (-7.5 to 6.7)	10.1 (5.0 to 15.1)***	-0.4 (-7.6 to 6.7)	9.6 (4.5 to 14.7)**	-2.9 (-10. to 4.4)
Social functioning						
PT	19.1 (13.3 to 24.8)***	reference	17.5 (11.7 to 23.3)***	reference	16.4 (10.3 to 22.4)***	reference
PT+CBP	18.9 (13.1 to 24.3)***	-0.4 (-8.4 to 7.6)	13.4 (7.7 to 19.1)***	-4.1 (-12.2 to 4.0)	17.0 (11.3 to 22.7)***	0.6 (-7.7 to 8.9)
Fatigue						
PT	-18.4 (-23.9 to -12.8)***	reference	-15.8 (-21.4 to -10.2)***	reference	-13.0 (-18.8 to -7.2)***	reference
PT+CBP	-17.2 (-22.6 to -11.9)***	1.1 (-6.6 to 8.9)	-14.6 (-20.0 to-9.1)***	1.2 (-6.6 to 9.0)	-15.5 (-21.0 to -10.0)***	-2.5 (-10.5 to 5.5)

Abbreviations: EORTC-QLQ-30 – European Organization for Research and Treatment of Cancer Quality of Life Questionnaire C30; CI – confidence interval; PT – physical training; PT+CBT – physical training plus cognitive-behavioural therapy.

[a] PT+CBT group (n=76). PT group (n=71). Change scores, between-group change scores and corresponding 95% CI using linear mixed-effects models. $^{*}P \leq 0.01$; $^{**}P \leq 0.001$, $^{***}P < 0.0001$. *The intervention period comprised twelve weeks.*

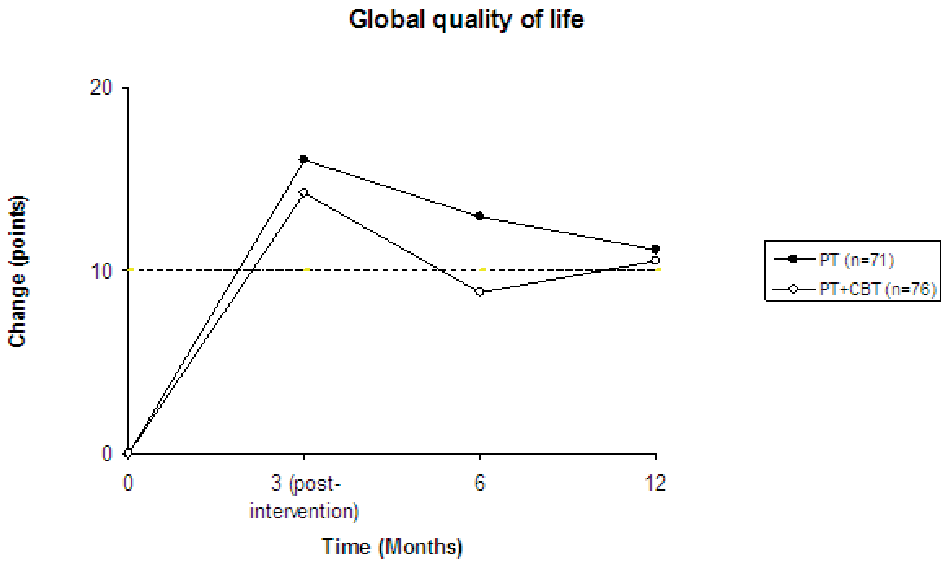

Figure 2. Change of global quality of life measured using the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire C30 from baseline to twelve months by intervention assignment. The dashed line represents the minimally clinically-important difference.
Abbreviations: PT – physical training; PT+CBT – physical plus cognitive-behavioural therapy

Discussion

The present randomised clinical trial showed that combining a self-management physical training programme for cancer survivors with structured CBT did not add to the beneficial effects of physical training neither in the short-term nor in the long-term. In contrast to our expectations based on several authors reporting that the effect of CBT may become more prominent over longer follow-up times[16,17], our results did not demonstrate significant differences between PT and PT+CBT for any of the outcomes from pre-intervention to 9-month post-intervention. An explanation may be that our physical training intervention integrated a self-management approach. It has been shown that including social cognitive components, such as self-management, in an intervention had positive effects on QoL in cancer patients.[24] Furthermore, PT was offered in group-format that provides opportunities for social interaction, social comparison and group support that might improve self-efficacy and through that QoL.[24] Apparently, our self-management group-based exercise programme is sufficient to improve cancer survivor's QoL in the short- and in the long-term. The present results showed that QoL was improved following 12-week self-management physical training consisting of aerobic training, resistance exercise, and group sports in cancer survivors. Nine months after the intervention, improvements in global QoL, physical, role, emotional, cognitive and social functioning and fatigue were maintained and were clinically relevant. Only participants in the PT group reported a decrease in global QoL from post-intervention to 9-month post-intervention. However, this small decrease was not clinically relevant and the improvement in global QoL at 9-month post-intervention was still clinically relevant compared to pre-intervention. Moreover, global QoL at 9-month post-intervention of PT participants was comparable to that of PT+CBT participants.

Three other studies[3-5] reported long-term results following an exercise intervention for cancer survivors. Similar to our findings in a mixed group of cancer survivors, Milne et al.[3] showed that QoL of breast cancer survivors was improved directly after and three months following a 12-week combined aerobic and resistance exercise intervention. Contrary to us, they reported that QoL still increased from post-intervention to 3-month post-intervention. This effect may be partly due to the attention given to the participants during regularly telephone calls (every three weeks) during follow-up, whereas we did not approach our participants during follow-up. Daley et al.[4] showed a beneficial effect on breast cancer survivors' QoL directly following an 8-week physical training programme when compared to control that was not maintained at 4-month follow-up. To date, only one study included a 1-year follow-up.[5] This 7-week group rehabilitation programme, however, did not lead to improvements in QoL on the short-term and the long-term. This could well reflect the short duration of the intervention and the low intensity of the programme which included only four information sessions, three coping skills training sessions and four light-intensity physical training sessions.

Strengths of the present study were the length of follow-up, the use of intention-to-treat analyses, the supervised, standardised self-management intervention, the large sample size, high attendance rates and low drop-out rates. A limitation of the study was the lack of a control group for the long-term effect. We included a waiting-list comparison group for the evaluation of the effects immediately after our intervention, and showed significant improvements in QoL in the intervention condition compared to control.[13] However, for feasibility reasons, due to the facts that cancer survivors are highly motivated to attend an exercise intervention[25] and that alternatives are available in the Netherlands, a control group could not be assessed at 3-month and 9-month post-intervention. Therefore, we cannot definitely conclude that the maintained improvements in QoL are specific to our intervention. Nonetheless, considering that QoL was significantly improved directly following the intervention compared to waiting-list control patients and that these improvements were maintained at 9-month post-intervention, some evidence is provided that the beneficial long-term effects are not simply attributable to the passage of time and may likely be a consequence of the intervention. Furthermore, we showed that physical fitness was improved following our intervention.[12] As long-term physical fitness measurements were not feasible, we were not able to investigate whether the sustained improvements of QoL were related to those of physical fitness.

The changes of QoL in PT+CBT and PT were of a similar magnitude. It is unlikely that including more subjects in the study would have changed the conclusion that CBT did not add to the beneficial effects of PT. A post-hoc power analysis using the change scores found in the present study revealed that more than 1100 participants per group would have been required to show statistically significant differences in improvement of QoL between PT+CBT and PT. A study of this size would not be feasible, and it is also doubtful wither a significant difference here would have sufficient clinical relevance.

In conclusion, adding cognitive-behavioural therapy to structured and supervised self-management physical training did not further enhance the beneficial effects of physical training on QoL, neither on the short-term nor on the long-term. Cancer survivors showed improved QoL immediately following physical training and also at three and nine months post-intervention.

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5

Group cohesion in cancer rehabilitation

Abstract

Objective

Group-based physical training interventions have been shown to be effective in increasing quality of life in cancer survivors. Until now, however, the impact of cohesion within the group on intervention outcome has not been investigated. The present aim was to explore the relationship between group cohesion and intervention outcome.

Methods

We examined self-reported individual group cohesion ratings collected in the first half of a 12-week rehabilitation programme for cancer survivors (n=132). Four dimensions of group cohesion were measured, i.e. the bond with the group as whole, the bond with other members, cooperation within the group and the instrumental value. Quality of life, physical functioning and fatigue were assessed before and after the intervention using European Organization for Research and Treatment of Cancer Quality of Life Questionnaire-C30. Linear multiple multivariate regression analysis was conducted to explore the relationship between group cohesion and intervention outcome.

Results

The relationship between group cohesion and outcome was significantly modified by gender. Higher ratings of cooperation within the group predicted better post-intervention quality of life and physical functioning and less fatigue in men, and better quality of life and physical functioning in women. Additionally, women who reported a stronger bond with other members showed a lower quality of life after the intervention. No relationship was found between the instrumental value and the outcome variables.

Conclusion

Some dimensions of group cohesion seem to be associated with intervention outcome. The underlying mechanisms need to be unravelled.

Introduction

Recent reviews and meta-analyses have revealed the physical and psychological benefits of exercise programs in cancer patients.[1,2] Several of these programs were offered to individuals in group format and these reported improvement in quality of life, physical functioning and fatigue in cancer patients during primary treatment[3-10] and after completion of initial treatment[11-14]. Recently, interest has been growing in patients' experience with training within groups. Several authors explored the relevance of group processes by means of in-depth interviews and focus groups.[8,15-17] Cancer patients and survivors emphasized the importance of exercising in groups. Participants felt motivated by others to overcome their physical limitations and they experienced reciprocal upwards comparison.[8,17] By exercising in groups, patients were encouraged and challenged to attain physical peak performance.[8] It is suggested that these group processes may have a positive effect on intervention outcome, that is an improvement in the quality of life of cancer patients.[4] In group therapy, one supposed mechanism of change is that of group cohesion.[18] Two components of cohesion were described, namely social cohesion and task cohesion.[19] Group cohesion as defined by Yalom[18] primarily refers to social-emotional cohesion since group cohesion is conceptualised as the intimacy, reciprocity and emotional disclosure that is felt amongst the group members. In sport psychology, the definition was expanded by integrating the component of task cohesion: Group cohesion is defined as "a dynamic process that is reflected in the tendency of a group to stick together and remain united in the pursuit of its instrumental objectives and/or for the satisfaction of member affective needs".[20] Cohesiveness is a multidimensional concept that refers to cooperation within the group to achieve a common therapeutic aim.[21] Group cohesion has been described as a bonding force consisting of four factors, namely attraction to the group as a whole and to individual members of the group, risk taking, and instrumental value of the group.[22] It is presumed that when cohesion is high, the group is motivated to perform well and is more able to coordinate activities for successful performance.[23]

The role of cohesion within a group has been extensively investigated in psychotherapy and it has been shown that higher group cohesion predicted better treatment outcome.[24-26] In the case of sedentary adults involved in exercise classes, it has been demonstrated that groups that reported high cohesiveness

5

were characterized by mutual support for exercise activities which then facilitated the development of self-efficacy beliefs and improved mastery expectation with regard to exercise.[27] This is supposed to have a positive effect on physical activity behaviour.[10] Hence, the implication is that cohesion is a putative mechanism of change during group interventions and is therefore expected to be related to intervention outcome.

Research in cancer self-help groups revealed differences in the needs of men and women within groups.[28,29] Men emphasised the importance of giving and seeking information, whereas women emphasised the importance of intimacy, mutual support and emotional disclosure. It may therefore be conceivable that men and women would experience the cohesion within the group differently.

To date, the impact of group cohesion on the effectiveness of group-based physical exercise interventions for cancer survivors has not been explored.[30] The present study is part of a randomised controlled trial which evaluates the effect of group-based rehabilitation among cancer survivors. Our aim was to explore the relationship between group cohesion and intervention outcome. We expected the perception of higher group cohesion to be significantly related to better quality of life, physical functioning and less fatigue. We also explored the differences between men and women as regards their perception of group cohesion and the relationship between group cohesion and intervention outcome.

Participants and Methods

Procedure

The sample of the current study is a subset of the sample in a prospective, randomised multicenter trial conducted at four Dutch centres, namely at the rehabilitation units of two university medical centres and one general hospital and at one rehabilitation centre.[31] The study was approved by the medical ethics committee of the University Medical Center Utrecht and the local research ethics committees.

Cancer survivors were informed about the study by their treating physician, information in the local newspapers or via the Internet. After written consent, eligible subjects were scheduled for baseline measurements and allocated randomly to either physical training (PT) based on principles of self-management or physical training plus cognitive-behavioural training (PT+CBT). In each centre consecutive groups of 8-12 eligible subjects were assigned to PT or PT+CBT to ascertain adequate numbers of participants in each group. Randomisation at group level was applied; prior to enrolment of participants in the study, the sequence of PT and PT+CBT groups at each centre was determined by an independent researcher using a randomisation list. Until the first session, participants were blinded to the rehabilitation group they were allocated to. Following the intervention, participants in both intervention groups showed significant improvements in global quality of life, physical functioning and fatigue compared to control.[32,33] No differences in any outcome variable were found between PT and PT+CBT groups from pre-intervention to post-intervention. Also, group cohesion ratings were not different between PT and PT+CBT (data not shown). The two intervention groups were therefore combined into one group in the present study.

Participants

Inclusion criteria were: age ≥18 years; last cancer treatment completed at least three months before study entry; estimated life expectancy at least one year (i.e., based on medical evaluation of each individual by the referring physician); and referred for rehabilitation by medical specialist or general practitioner on the basis of at least three out of the following six criteria: physical complaints, reduced physical capacity, psychological problems, increased levels of fatigue, sleep disturbances, and problems coping with reduced physical and psychosocial functioning. Cancer survivors were excluded if they had cognitive disturbances (e.g., cancer survivors who were unable to be instructed, to think in three dimensions, to complete questionnaires), serious psychopathology or emotional instability that might impede participation in the rehabilitation program (e.g., being in the process of a divorce at the moment or a recent death of a loved one), or if they needed intensive medical treatment or rehabilitation (i.e., having a low level of activity, e.g., less than 50% of their daytime ambulant, rapid fatigue appearance on performance of low physical activity, and activity of daily living dependency).

Recruitment and assessments of cancer survivors occurred between February 2004 and April 2006. One hundred and seventy-six cancer survivors were referred to the research centres. 29 subjects were excluded before randomisation due to not meeting the inclusion criteria (n=14), refusing to participate in the rehabilitation (n=5), refusing to be randomly assigned (n=7), and feeling no need for rehabilitation anymore (n=3). There were no significant differences between subjects who were randomised and those who were excluded before randomisation with regard to age, gender, educational level, marital status, type of cancer, type of treatment, and time post-treatment.

Because the focus of the present study was the relationship between group cohesion and intervention effects, we limited the analyses to 132 of 147 participants who completed the intervention. Reasons for discontinuing the intervention were medical (n=11) and personal (n=4). There were no significant differences in demographic variables and pre-intervention scores on the outcome variables between those who completed the intervention and those who dropped out.

Intervention

The intervention took place in mixed-gender groups of 8-12 participants and approximately 80% of each group were women. Participants in PT (n=62 from eight groups) followed 24 sessions of physical training and participants in PT+CBT (n=70 from eight groups) followed 24 sessions of PT combined with 12 CBT sessions. Both components, PT and the CBT, were based on principles of self-management: i.e. goal selection, information collection, information processing and evaluation, decision-making, action and self-reaction.[34]

Physical training (twice weekly, two hours per session): Each session consisted of individual training performed within the group (aerobic bicycle training (30 minutes) and muscle strength training (30 minutes)) followed by group sports (60 minutes). The training sessions were supervised by two physical therapists and were performed according to a standardised protocol taking cancer survivor's baseline physical fitness into account. Group sports included badminton, soccer, swimming, balancing games, and aimed, firstly at promoting enjoyment in sports and improving self-efficacy in order to incorporate sporting activities into daily life and to adopt a physically healthy lifestyle, and at the same time to enhance cohesiveness by stimulating interaction. Self-management skills[34] were trained to stimulate exercise motivation and execution.

Cognitive-behavioural training (once a week, two hours per session): The intervention was based on a cognitive-behavioural problem-solving protocol for individual cancer patients[35] and a group problem solving protocol for low back pain patients[36]. During the intervention self-management skills[34] were trained to enable participants to solve present and future problems associated with the physical and psychosocial consequences of cancer. A psychologist and a social worker supervised the intervention.

Measures

Outcome measures

Global quality of life, physical functioning and fatigue were assessed using subscales of the *European Organization for Research and Treatment of Cancer Quality of Life Questionnaire-C30* (EORTC-QLQ-C30)[37]. Two, five and three items measured global quality of life, physical functioning and fatigue, respectively. Raw scores of the EORTC-QLQ-C30 were transformed linearly into scores ranging from 0 to 100. A higher score represents a higher quality of life and physical functioning, and a higher level of fatigue. In our sample, the Cronbach's α of the used subscales ranged from 0.64 to 0.81 at baseline, and from 0.60 to 0.80 post-intervention. The EORTC-QLQ-C30 was administered pre-intervention and directly after the 12-week intervention at the study site.

Predictive measures

Socio-demographic and medical data were obtained at baseline using a self-report questionnaire. The referring physician confirmed medical data.

Group Cohesion was assessed using the ***Group Cohesion Questionnaire*** (GCQ-22)[38] which is based on the Group Attitude Scale[39] and the Three Factor Group Questionnaire[40]. The GCQ-22 compromises 22 items across four scales: Bond-Group – the bond with the group as total (7 items, e.g. "I feel involved about what happens in the group"); Bond-Member – the bond with other members of the group (4 items, e.g. "After the last session I would like to stay in contact"); Cooperation (4 items, e.g. "Generally, everybody is actively involved"); and Instrumental Value (7 items, e.g. "I feel supported by the group as regards achieving my goals"). Each item is rated from 1 (totally disagree) to 6 (totally agree). The lowest score is 1, meaning an absence of group cohesion, and the highest score is 6, meaning very high group cohesion. The internal consistency of all scales was reported to range from adequate to good (0.66 to 0.88).[38] We discarded one item from the cooperation-subscale resulting in an increase of the Cronbach's alpha from 0.57 to 0.62. For the assessment of early group cohesion the GCQ-22 was completed at the centre at the end of sessions 4 (s-4), 8 (s-8) and 12 (s-12) of the physical training program. The Cronbach's α of the subscales ranged from 0.62 to 0.80 at s-4, from 0.67 to 0.82 at s-8, and from 0.65 to 0.83 at s-12.

Data analysis

If not stated otherwise, analyses were performed using the R software (version 2.4.1, http://www.r-project.org).

Socio-demographic and medical data of the participants who dropped out and who stayed in the study, and data on men and women were compared using independent Student's t-tests for continuous data and Chi-square tests for categorical data.

Spearman rank correlation coefficients for continuous data and Chi-square tests for categorical data were calculated in order to investigate the relationship between group cohesion scores and socio-demographic data and medical data. Group cohesion ratings of men and women and changes over time were analysed using linear mixed-effects models. Effect sizes (ES) were calculated according to Cohen as indices measuring the magnitude of change[41]. Changes in outcome variables among and between men and women were compared using multilevel (i.e. centre, group and individual) linear mixed-effects models taking the baseline values as covariates into account.

Linear multiple multivariate regression analysis (Mplus version 4.1[42]) was conducted with quality of life, physical functioning, and fatigue at post-intervention as dependent variables and the four GCQ-subscales as predictor variables. Owing to the fact that results were not different for GCQ measurements at s-4, s-8 and s-12 the mean of these three measurements for each subscale was used in the model. The model was adjusted for pre-intervention levels of the outcome variables, intervention modality (i.e., PT+CBT or PT), attendance rate and age. Model fit was assessed using the chi-square test for model fit ($p>0.05$) and the Standardized Root Mean Square Residual (SRMR<0.05). Between-group intra-class correlations ($ICCs_{group}$) for the GCQ-subscales were estimated in order to examine the interdependence of data due to nesting within groups. These $ICCs_{group}$ appeared to be low (0.001-0.058). The non-standardised regression coefficients (raw importance of predictor variables) and the standardised regression coefficients (relative importance of predictor variables) were presented as a measure of the performance of the individual predictive variables. In order to determine whether the relationship between group cohesion and outcomes was modified by gender, statistical testing was performed to establish whether the regression coefficients were different ($p<0.05$).

In these analyses, the models accounted for missing data (EORTC-Q-30 n=1; GQC s-4 n=6, s-8 n=8, s-12 n=4) based on the observed data. Only two-sided significance tests were used ($\alpha<0.05$).

Results

Study participants

Table 1 shows the baseline characteristics of the study participants. There was no statistical difference between men and women as regards socio-demographic variables and time post-intervention. The prevalence of type of cancer was distributed differently because breast and gynaecological cancers are predominantly diagnosed in women. Surgery was reported more often in women and this may be due to the types of cancer (breast and gynaecological) for which surgery is needed. PT+CBT subjects completed 89% of 24 PT sessions and 87% of 12 CBT sessions. PT subjects completed 91% of 24 PT sessions. There was no significant difference in the attendance rate of men and women. Table 2 provides characteristics of the sixteen intervention groups. Each group consisted of eight to twelve participants except for four groups in which subjects cancelled participation at short notice.

Outcome measures

Pre-intervention outcome measures did not differ between men and women. Quality of life and physical functioning increased significantly and fatigue decreased significantly from baseline to post-intervention in both men and women (Table 3). Changes were not different between men and women ($p>0.05$).

Group cohesion ratings

Group cohesion scores were unrelated to socio-demographic and medical data, i.e. age, education, marital status, type of cancer, primary cancer treatment, time post-treatment. Cohesion scores were also unrelated to intervention group (PT or PT+CBT) and the number of sessions attended.

Table 4 shows the group cohesion scores. Scores were not significantly different between men and women with the exception of higher scores for women on Bond-Member at the three measurement times ($p=0.0001$).

Table 1. Baseline characteristics*

Variable	Overall (n=132)	Men (n=21)	Women (n=111)	P-value†
Age (years)	48.6 ± 10.8	45.9 ± 11.8	49.2 ± 10.6	0.31
Educational level				0.60
Low	17 (12.9)	4 (19.0)	13 (11.7)	
Middle	62 (47.0)	10 (47.6)	52 (46.8)	
High	53 (40.2)	7 (33.3)	46 (41.4)	
Marital status				0.11
Married/living together	94 (71.2)	18 (85.7)	76 (68.5)	
Single	38 (28.8)	3 (14.3)	35 (31.5)	
Type of cancer				<0.0001
Breast	77 (58.3)	1 (4.8)	76 (68.5)	
Haematological	20 (15.2)	7 (33.3)	13 (11.7)	
Gynaecological	14 (10.6)	1 (4.8)	13 (11.7)	
Colon	3 (2.3)	3 (14.3)	--	
Urogenital	8 (6.1)	6 (28.6)	2 (1.8)	
Other	10 (7.6)	3 (14.3)	7 (6.3)	
Type of treatment				
Surgery	115 (87.1)	13 (61.9)	103 (91.9)	<0.0001
Chemotherapy	76 (57.6)	12 (57.1)	64 (57.7)	0.97
Radiotherapy	93 (70.5)	13 (61.9)	80 (72.1)	0.35
Time post-treatment (years)	1.3 ± 1.8	1.2 ± 0.9	1.4 ± 1.9	0.60

**Data are presented as mean±standard deviation for continuous variables and frequency (percentage) for categorical variables.*

† P-value for differences between men and women.

Table 2. Outcome variables at baseline, post-intervention and changes from baseline to post-intervention assessed using the European Organization for Research and Treatment of Cancer QLQ-C30 (range 0-100)

	Baseline (Mean ± SD)	Post-intervention (Mean ± SD)	Change score (95% CI)	P-value*
Quality of life				
Overall	58.2 ± 16.4	73.4 ± 15.0	15.2 (11.5 to 18.9)	0.0002
Men	63.9 ± 15.7	79.0 ± 12.2	15.2 (7.4 to 22.9)	< 0.0001
Women	57.1 ± 16.3	72.3 ± 15.3	15.2 (11.3 to 19.1)	< 0.0001
Physical functioning				
Overall	73.4 ± 13.2	85.4 ± 10.7	12.0 (10.2 to 13.7)	< 0.0001
Men	75.2 ± 14.2	87.0 ±15.0	11.7 (7.3 to 16.2)	< 0.0001
Women	73.1 ± 13.1	85.1 ± 9.8	12.0 (10.0 to 14.0)	< 0.0001
Fatigue				
Overall	50.0 ± 22.6	31.8 ± 17.2	-18.3 (-22.5 to -14.1)	< 0.0001
Men	43.9 ± 22.6	29.6 ± 19.0	-14.3 (-23.7 to -4.9)	0.003
Women	51.2 ± 22.5	32.2 ± 16.9	-19.0 (-23.5 to -14.6)	< 0.0001

Abbreviations: SD – standard deviation; CI – confidence interval.

** P value for change from baseline to post-intervention using linear mixed-effects model.*

Bond-Group and Cooperation within the group did not change significantly over time between s-4, s-8 and s-12. Instrumental Value increased significantly from s-4 to s-8 (p=0.02, ES=0.18), but not from s-8 to s-12. A significant interaction effect of gender and time was found in Bond-Member. In women, Bond-Member at s-8 and s-12 was higher than at s-4 (p=0.01, ES=0.19 and 0.0001, ES=0.25, respectively). In men, Bond-Member decreased from s-4 to s-8 (p=0.03, ES=0.28) and then increased from s-8 to s-12 (0.04, ES=0.26) to a level comparable to s-4.

Table 3. Group cohesion ratings assessed using the Group Cohesion Questionnaire-22 (range 1-6)

	Session 4 (Mean ± SD)	Session 8 (Mean ± SD)	Session 12 (Mean± SD)	Mean of all sessions* (Mean ± SD)
Bond-Group				
Overall	4.90 ± 0.56	4.94 ± 0.50	4.95 ± 0.47	4.92 ± 0.47
Men	5.02 ± 0.40	5.05 ± 0.48	4.92 ± 0.38	4.99 ± 0.38
Women	4.88 ± 0.59	4.92 ± 0.50	4.95 ± 0.49	4.91 ± 0.48
Bond-Member				
Overall	4.00 ± 0.80	4.07 ± 0.85	4.15 ± 0.83	4.06 ± 0.76
Men	3.61 ± 0.94†	3.34 ± 0.97†, ‡	3.58 ± 0.93†, §	3.50 ± 0.90
Women	4.07 ± 0.75	4.21 ± 0.75‡	4.26 ± 0.76‡	4.17 ± 0.69
Cooperation				
Overall	4.60 ± 0.83	4.56 ± 0.83	4.50 ± 0.86	4.54 ± 0.66
Men	4.72 ± 0.87	4.76 ± 0.70	4.44 ± 0.88	4.64 ± 0.57
Women	4.57 ± 0.82	4.52 ± 0.85	4.52 ± 0.85	4.53 ± 0.68
Instrumental value				
Overall	4.59 ± 0.68	4.71 ± 0.64‡	4.65 ± 0.65	4.64 ± 0.58
Men	4.69 ± 0.68	4.76 ± 0.64	4.66 ± 0.49	4.69 ± 0.52
Women	4.57 ± 0.68	4.70 ± 0.64	4.65 ± 0.68	4.64 ± 0.59

Abbreviations: SD – standard deviation.
** Ratings are the mean of group cohesion scores assessed after 4, 8, 12 of 24 sessions.*
† Indicating a significant difference between men and women.
‡ Indicating a significant change compared to session 4.
§ Indicating a significant change compared to session 8.

Relationship between group cohesion rating and outcome measures

The relationship between group cohesion and outcome was significantly modified by gender (p=0.0005). Table 5 shows that higher cooperation within the group predicted higher post-intervention quality of life, physical functioning and lower fatigue in men, and higher quality of life and physical functioning in women. Women who reported a stronger bond with other members showed lower post-intervention quality of life. There was no relationship between Instrumental Value and any outcome variable.

5

Table 4. Regression coefficients for group cohesion score predicting outcome variables for men and women*

	Quality of life			Physical functioning			Fatigue		
	B	CI	β	B	CI	β	B	CI	β
Male participants									
GCQ subscales									
Bond-Group	2.9	(-11.1 to 17.0)	0.01	-4.6	(-16.1 to 7.0)	-0.13	12.2	(-3.5 to 34.1)	0.26
Bond-Member	-1.0	(-6.2 to 4.2)	-0.07	-0.8	(-5.0 to 3.4)	-0.06	1.8	(-6.8 to 11.0)	0.09
Cooperation	**13.2**	**(4.4 to 21.9)**	**0.64**	**8.6**	**(1.4 to 15.8)**	**0.37**	**-18.7**	**(-38.6 to -2.7)**	**-0.60**
Instrumental Value	0.5	(-9.5 to 10.6)	0.02	-2.0	(-10.3 to 6.2)	-0.08	-8.0	(-21.1 to 6.1)	-0.23
Female participants									
GCQ subscales									
Bond-Group	6.1	(-2.2 to 14.4)	0.19	2.8	(-1.8 to 7.4)	0.15	-3.1	(-12.6 to 5.5)	-0.09
Bond-Member	**-6.5**	**(-11.3 to -17)**	**-0.30**	-0.6	(-3.3 to 2.1)	-0.05	4.4	(-0.9 to 10.0)	0.18
Cooperation	**4.0**	**(-0.1 to 8.1)**	**0.18**	**2.5**	**(0.2 to 4.8)**	**0.17**	0.6	(-3.6 to 7.3)	0.02
Instrumental Value	0.2	(-6.4 to 6.8)	0.01	-2.5	(-6.1 to 1.2)	-0.16	-2.4	(-10.6 to 3.8)	-0.08

* *Linear multiple multivariate regression model adjusted for pre-intervention levels of outcome variables, intervention group (physical training; physical training plus cognitive-behavioural therapy), age and attendance.*

Abbreviations: B – unstandardised regression coefficient; β – standardised regression coefficient; GCQ – Group Cohesion Questionnaire; Bond-Group – bond within the group as a whole; Bond-Member – bond with the other members of the group.

Discussion

The present study examined cancer survivors' cohesion in group-based rehabilitation and its relationship to intervention outcomes, i.e. global quality of life, physical functioning and fatigue. We expected group cohesion to be related to better intervention outcomes. Indeed, higher cooperation within the group predicted better quality of life, physical functioning and less fatigue. This is in accordance with the findings of others who reported that mainly task-commitment was positively related to performance.[43] Unexpectedly and in contrast to the findings of others[24], we found that a higher bond between individual members predicted lower post-intervention outcome in women. One explanation could be altruism, that is a mechanism of support previously observed in cancer patients with metastatic disease during supportive group meetings.[44] Cancer survivors who felt that they were not making progress discovered that they could be useful to others and, therefore possibly rate the relationship with other members as high. Possibly, cancer survivors 'hided behind' the group. Being involved with other members of the group probably caused cancer survivors to avoid working on their own problems. A different mechanism might be downward social comparison[45,46], which means that participants who did not experience improvement compared themselves to others who performed worse in order to enhance their self-esteem. The reverse may also be the case, namely that these participants compared themselves to other participants who were making progress and bond to them because their progress was proof that improvement was possible. The latter implies that group cohesion might be influenced by the development of the outcome. The development of group cohesion and intervention outcome may be a reciprocal process during the course of the intervention[25]. By design we were able to answer the question of whether group cohesion predicted outcome, but not of whether the development of outcome influenced the development of group cohesion. The directionality of this relationship needs to be investigated in the future. By measuring group cohesion and the outcome variables at same time points over the course of the intervention statistical analytical techniques are possible to examine the causal direction.

Interestingly, there was no relationship between instrumental value and intervention outcomes. We have no clear explanation for this finding. Instrumental value can be understood as being the extent to which the group mediates goals for its members. A possible explanation could be that our Instrumental Value-subscale did not specify which goals were mediated by the group. Questions concerning goals that are related specifically to physical training would probably reveal a relationship between instrumental value and outcome.

The present results illustrated that the perception of group cohesion did not differ between men and women, with the exception that Bond-Member scores were lower among men. Men seemed to be less interested in contact with individual members of the group during and after the intervention. Also we cannot rule out the possibility that lower Bond-Member rates in men were due to the fact that women were in the majority in each group. The role of cooperation within the group was related to better outcome for men as well as for women. However, it seemed to be more important for men. This might be explained by gender-specific coping styles. Men might prefer problem-focused coping strategies while women possibly prefer coping through mutual support and emotional disclosure within the group.[28,29] However, one should again note that women were in the majority. Men might have experienced cohesion within a group differently if there had been more men in the group. Future research is needed in groups with more or only men attending.

For the purpose of the present study we chose to measure group cohesion during the first half of the intervention to reveal the effect of early aspects of group cohesion on intervention outcome. Identifying these aspects might be important because the sooner possible difficulties in a group are recognised, the more time there is available for the therapists to address them. It might be important for clinicians to be sensitive to the different aspects of early group cohesion. Our results propose that cooperation within the group ought to be stimulated. Attention might be paid to participants who are engaged particularly with the other members and the reasons for their engagement should be clarified to ensure profit from the intervention. However, it would be premature to conclude that bonding between group members impedes individual profit since the directionality of the relationship is not yet investigated.

Our results suggest that group cohesion developed early during the intervention. Bond-Group and Cooperation within the group did not change in time between session 4, 8 and 12. Bond-Member and Instrumental Value changed significantly over time. However, effect sizes of these changes ranged from 0.10 to 0.28 indicating either no effect or a small effect.[41] This early development might be due to the fact that cancer survivors felt connected by being in the same situation of having cancer and fighting against the consequences of cancer.[16]

In conclusion, the present study was the first that investigated the relationship between group cohesion and rehabilitation outcome in cancer survivors. The results showed that cooperation within the group was related to better outcome, while a higher bond with individual members was negatively related. This suggests that it might be beneficial for therapists to pay attention to the different dimensions of cohesion within oncological rehabilitation groups.

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6

Relationship between maximal and submaximal exercise outcome following physical training in cancer survivors

Abstract

Objective

To compare the changes of maximal and submaximal exercise capacity after physical training for cancer survivors to determine whether submaximal testing could be used as an evaluation tool for physical fitness in daily clinical practice.

Methods

147 cancer survivors (all cancer types, medical treatment ≥3 months ago) attended a 12-week supervised exercise programme. Exercise testing was performed before and after the intervention. Outcome measures were peak oxygen consumption, peak power output (both determined during exhaustive exercise testing) and submaximal heart rate (determined during submaximal testing).

Results

Peak oxygen consumption and peak power output increased and submaximal heart rate decreased significantly from baseline to post-intervention (p-values<0.0001). Changes in submaximal heart rate were only weakly correlated with changes in peak oxygen consumption and peak power output. Subgroup analyses revealed that changes in submaximal heart rate in the group cycling with moderate to high intensity (i.e., heart rate ≥140 beats per minute) were clearly related to changes in peak oxygen consumption and peak power output.

Conclusion

In daily clinical practice, a submaximal exercise test of moderate to high intensity might be an alternative to exhaustive exercise testing for the evaluation of physical fitness and progress during and after an oncological physical training programme.

Introduction

While the prognosis of cancer patients has improved, a substantial number of patients continue to report physical and psychological complaints.[1] Exercise became increasingly recognized as beneficial to cancer patients and seemed to be associated with less severe side-effects during and after cancer treatment.[1-3] Consequently, interest in the effect of physical training on physical fitness in cancer patients has been growing. Generally, the best direct indicator or the gold standard for physical fitness is peak oxygen uptake (VO_{2peak}).[4,5] VO_{2peak} is assessed by means of respiratory gas analysis during graded exercise testing up to exhaustion. However, such exhausting exercise test may be unpleasant for patients and requires experienced personnel and medical supervision as well as the use of expensive equipment. Performing an exhaustive test frequently during physical training might put a serious burden on patients. Hence, for monitoring physical progress throughout the training programme, a submaximal exercise test, which is easily performed, inexpensive and well accepted by patients, and that provides information about the effect of physical training on the circulatory capacity comparable to maximal exercise testing, would have greater applicability in daily clinical practice.[6] In cardiac and pulmonary rehabilitation moderate to high correlations between submaximal and maximal exercise capacity were reported.[7-10] To date, no submaximal measures have been validated in cancer survivors. Cancer patients often experience fatigue of which the physiologic basis is still poorly understood.[11] It is therefore conceivable that cancer patients might react differently to submaximal exercise testing.

In the present study an exhaustive exercise test was used to evaluate the effect of a 12-week supervised physical training programme in cancer survivors. In addition, all participants performed a 10-minute submaximal cycle ergometer test at a constant power output. This allowed us to validate the submaximal exercise test in an oncological setting.

Our present objectives were first to determine whether cancer survivors' submaximal heart rate, VO_{2peak} and peak power output (W_{peak}) changed after our 12-week physical training programme. Furthermore, we investigated the relationship between changes in outcomes of submaximal and exhaustive exercise testing from pre- to post-intervention. We expected the change in submaximal exercise capacity, i.e. a decreased heart rate, to be negatively associated with the change in maximal exercise capacity, i.e. an increased VO_{2peak} and W_{peak}.

Participants and Methods

The present study is part of a prospective, randomised multicentre trial that was conducted in four Dutch centres: two university medical centres, one general hospital and one rehabilitation centre. The medical ethics committee of the University Medical Center Utrecht and the local research ethics committees approved the study that was performed according to the Helsinki Declaration of 1975, as revised in 1983.

Participants

Inclusion criteria were: age ≥18 years; last cancer treatment completed at least three months before study entry; estimated life expectancy at least one year; and referred for rehabilitation by medical specialist or general practitioner on the basis of at least three out of the following six criteria: physical complaints, reduced physical capacity, psychological problems, increased levels of fatigue, sleep disturbances and problems coping with reduced physical and psychosocial functioning. Patients were excluded if they had cognitive disturbances, serious psychopathology or emotional instability that might impede participation in the rehabilitation programme, or if they needed intensive medical treatment or rehabilitation.

After written consent, eligible subjects were scheduled for baseline measurements and randomised to physical training (n=76) or the same physical training combined wit cognitive-behavioural therapy (n=71). Changes of physical fitness appeared not to be different between these two intervention groups.[12] Therefore, for the present objective, participants were combined into one group.

Intervention

The present intervention has been described in more detail elsewhere.[12]

Physical training (twice weekly, two hours per session) consisted of a personalised exercise programme based on baseline graded exercise testing. Each session consisted of individual exercise (aerobic bicycle training (30 minutes) and muscle strength training (30 minutes)) followed by group sports (60 minutes). The physical training was supervised by two physical therapists and was performed according to a standardised protocol.

Aerobic bicycle training: Intensity was determined using the Karvonen formula[13] that uses the peak heart rate (HR_{peak}) obtained from baseline exhaustive exercise testing and the heart rate at rest (HR_{rest}) to calculate the training HR (HR_{tr}). Exercise training was performed at a HR_{tr} of $(HR_{rest}+40\%\ to\ 50\%\ of\ (HR_{peak}\ -HR_{rest}))$ during the first four weeks and was gradually increased to $(HR_{rest}+70\%\ to\ 80\%\ of\ (HR_{peak}\ -HR_{rest}))$ in week 12.

Muscle strength training: Resistance exercise of lower and upper extremities was based on the baseline 1-Repetition Maximum (1-RM). Training intensity started at 30% of the 1-RM during the first week and was increased until 50 to 60% of 1-RM in week 12.

Group sports: Sports, such as badminton, soccer, swimming and balancing games were performed with the aim being to promote enjoyment of sports and overcome any lack of confidence patients may have felt about exercising.

Cognitive-behavioural intervention (once a week, two hours per session) was based on a cognitive-behavioural problem-solving protocol for individual cancer patients[14] and a group problem solving protocol.[15] During the intervention self-management skills[16] were trained to enable participants to solve problems associated with physical and psychosocial consequences of cancer. The cognitive-behavioural intervention was supervised by a psychologist and a social worker.

Outcomes

At baseline, socio-demographic and medical data were collected using a self-report questionnaire. Medical data were confirmed by the referring physicians.

6

Physical fitness was assessed at baseline (T0) and post-intervention (T1). T0 and T1 tests were consistently performed by the same assessor who was not involved in the intervention. Participants were asked to refrain from food and beverage (except water) during the two hours before exercise testing.

Exhaustive exercise test. Participants cycled at 60 revolutions per minute (rpm) with no workload for one minute to adapt to the cycle ergometer. The exercise test started with a workload of 20 Watt and the load was increased every minute by 10, 15 or 20 Watt until voluntary exhaustion. Increments were estimated using formulas provided by Wassermann et al.[17] Subjects were encouraged during the test. The test ended when the patient was restricted by volitional exhaustion or clinical symptoms, or when the cycling rate was lower than 60 rpm. Heart rate (HR) was recorded during the whole test (Polar S610i, Polar Electro Inc., Helsinki, Finland). Expired gases were analyzed using Oxycon Delta, Oxycon Champion (Jäger, Höchberg, Germany), Metamax MMX (Cortex Biophysics GmbH), or $K4b^2$

(Cosmed, Rome, Italy) in the four centres, respectively. The differences in measured oxygen uptake and carbon dioxide output between analysis systems in the different centres were small (-3.4% to 2.4% difference from overall mean at 150 Watt) and fell within the range of day-to-day variability[18] (data not shown). VO_{2peak} was calculated as the mean of VO_2-values during the final 30 seconds of exercise. W_{peak} was defined as workload at exhaustion.

Submaximal exercise test. Also the submaximal exercise test was performed on a cycle ergometer. Subjects completed the submaximal test within one week and at least two days after the exhaustive exercise test. Before the test, subjects remained at quiet rest in supine position for ten minutes with no distractions. Then, participants cycled at 60 rpm for ten minutes at 50% of W_{peak} obtained during baseline graded exercise testing. Using that workload, all patients were expected to be able to finish the test without being exhausted and without developing an adverse event. The test phase was preceded by a 1-minute warming-up and followed by a 3-minute cooling-down, both at 25% of W_{peak}. The test was performed in a quiet environment and subjects were not allowed to talk during cycling. HR was recorded during the test using Polar S610i (Polar Electro Inc., Helsinki, Finland). Mean HR was defined as the mean of all recorded HRs from minute 3-10. A decreased mean HR from baseline to post-intervention during cycling at the same fixed workload indicated improved aerobic fitness.

Data analysis

Analyses (R software, version 2.3.1, http://www.r-project.org) were performed according to the intention-to-treat principle. Only two-sided significance tests were used ($\alpha < 0.05$).

In order to retain power and to prevent bias from missing values in a selected group of respondents, missing values of outcome variables were imputed by the mean of the predicted distribution given the hierarchical structure and specific characteristics of the person (age, gender, weight, and group allocation) using Bayesians statistics. Subjects with missing baseline values were not taken into account (exhaustive graded exercise testing: n=3 due to untreated hypertension, lymphedema in both legs, and claustrophobia caused by the mask covering nose and mouth; submaximal exercise testing: n=3 due to logistics). The reasons for these missing values were unrelated to non-compliance, withdrawal, or losses to follow-up and were not affected by the treatment these patients were assigned to. Therefore, post-randomisation exclusion was appropriate.[19]

Changes in outcome variables from baseline to post-intervention were analysed using linear mixed-effects models.

With a view to examine the interrelation between change in submaximal HR and change in VO_{2peak} and W_{peak} Spearman rank correlation coefficients were calculated. It has been suggested that a submaximal test is predictive of maximal aerobic capacity when a HR of at least 140 bpm is reached.[20] Therefore, correlations were also determined for two subgroups: namely, for participants who performed baseline submaximal exercise testing with a HR of either below or above 140 beats per minute (bpm; HR_{low} group and HR_{high} group, respectively). The reason for this distinction was that a HR below 140 bpm is regulated by both, the parasympathic nervus vagus and the sympathic nervi accelerantes, whereas the HR above 140 bpm is regulated solely by the nervi accelerantes, after which a linear relationship is assumed between HR and oxygen uptake [20,21]. A t-test for independent correlation coefficients was performed to determine whether correlations differ between the HR_{low} group and HR_{high} group. Independent Samples t-tests were used to compare the subjects' characteristics and the percentage of peak HR reached during baseline submaximal testing between these two groups.

Results

One hundred and forty-seven cancer survivors were included in the study. Table 1 shows the baseline characteristics of the study participants. Fifteen patients discontinued the intervention due to medical reasons or personal reasons (n=11 and n=4, respectively). Participants completed 20 (SD 4.9) of 24 physical training sessions.

Table 1. Baseline characteristics of study subjects (n=147)*

Characteristics	**Value**
Age (years)	48.8 ± 10.9
Sex	
Female	123 (83.7)
Male	24 (16.3)
Weight (kg)	79.8 ± 17.6
Body Mass Index ($kg \cdot m^2$)	27.5 ± 6.2
Type of cancer	
Breast	82 (55.8)
Haematological	23 (16.6)
Gynaecological	17 (11.6)
Urogenital	9 (5.5)
Colon	3 (2.0)
Lung	4 (2.7)
Other	9 (6.2)
Type of treatment	
Surgery	126 (85.7)
Chemotherapy	100 (68.0)
Radiotherapy	84 (57.1)
Time post-treatment (years)	1.3 ± 1.7
Resting heart rate ($beats \cdot min^{-1}$) †	71.4 ± 12.2

* *Data presented as mean ± standard deviation for continuous variables and frequency (percentage) for categorical variables.*
† *Variable obtained preceding submaximal exercise testing at baseline after subjects remained at quiet rest in supine position for ten minutes with no distractions.*
Abbreviations: PT+CBT – physical training combined with cognitive-behavioural therapy; PT – physical training.

Effects on maximal and submaximal exercise capacity

VO_{2peak} and W_{peak} improved significantly from pre-intervention to post-intervention (Table 2). HR during submaximal exercise testing at a fixed workload decreased significantly from baseline to post-intervention. No adverse events occurred during both submaximal and exhaustive exercise testing.

Association between changes in submaximal and maximal exercise outcomes

Table 3 shows that change in submaximal HR is weakly correlated with change in W_{peak} from baseline to post-intervention and tended to be weakly correlated with change in VO_{2peak} (p=0.08).

Table 2. Exercise performance at baseline and post-intervention and change from baseline to post-intervention

	Baseline (Mean ± SD)	**Post-intervention (Mean ± SD)**	**Change score (95% CI)**	**P-value***
VO_{2peak} ($mL \cdot min^{-1}$) †	1831.6 ± 559.2	1995.2 ± 582.9	158.6 (110.2 to 207.0)	< 0.0001
W_{peak} (Watt) †	155.9 ± 47.3	171.9 ± 48.9	16.1 (12.9 to 19.3)	< 0.0001
Submaximal heart rate (beats$\cdot min^{-1}$) ‡	125.4 ± 16.7	120.4 ± 14.9	-5.0 (-6.6 to -3.3)	< 0.0001

Abbreviations: SD – standard deviation; CI – confidence interval.
* *P value for change from baseline to post-intervention using linear mixed-effects model (n=144).*
† *Assessed during exhaustive graded exercise testing.*
‡ *Assessed during submaximal exercise testing.*

Table 3. Correlation of change from baseline to post-intervention of submaximal exercise outcome variables with change in outcome variables of graded exercise testing

	Overall (n-141)	**BL submaximal HR <140 beats$\cdot min^{-1}$ (n-114)**	**BL submaximal HR ≥140 beats$\cdot min^{-1}$ (n-27)**
	Change in submaximal HR (beats$\cdot min^{-1}$)	Change in submaximal HR (beats$\cdot min^{-1}$)	Change in submaximal HR (beats$\cdot min^{-1}$)
Change in VO_{2peak} ($ml \cdot min^{-1}$) Correlation coefficient (p-value)	-0.15 (0.08)	-0.10 (0.31)	-0.51 (0.006)
Change in W_{peak} (Watt) Correlation coefficient (p-value)	-0.18 (0.04)	-0.05 (0.57)	-0.69 (<0.001)

Abbreviations: BL – baseline; HR – heart rate; VO_{2peak} – peak oxygen uptake; W_{peak} – peak power output.

6

Subgroup analyses

We also performed the analyses for two subgroups: HR_{low} group and HR_{high} group. Participants of the HR_{low} group and HR_{high} group did not differ in gender, educational level, marital status, type of cancer, type of treatment, time post-treatment, body mass index and baseline VO_{2peak} and W_{peak} (p>0.05). Subjects of the HR_{high} group were younger compared to the subjects of the HR_{low} group (43.3±10.7 years and 50.0±10.6 years, respectively; p=0.004).

Table 4 specifies that the HR_{high} group cycled at a higher percentage of their peak HR compared to the HR_{low} group during baseline submaximal exercise testing. Workload of the submaximal exercise test tended to be higher in the HR_{high} group. The change in HR from pre- to post-intervention was larger in the HR_{high} group

($p<0.0001$; Cohen's effect sizes [22] were 0.26 and 1.47 for the HR_{low} group and HR_{high} group, respectively and 0.43 for the total group).

Correlational analyses revealed that in the HR_{high} group changes in submaximal HR were clearly related to changes in VO_{2peak} and W_{peak} (r=-0.51 and -0.69, respectively), whereas the relationship in the HR_{low} group was not significant (Table 3). Indeed, the correlation coefficient in the HR_{high} group was significantly different from the coefficient in the HR_{low} group (p=0.04).

Table 4. Characteristics for the group cycling with a heart rate of below 140 beats per minute and above 140 beats per minute during submaximal exercise testing at baseline

	BL submaximal HR <140 beats·min⁻¹ (n=114) (mean±SD)	**BL submaximal HR ≥140 beats·min⁻¹ (n=27) (mean±SD)**	**P-value***
Baseline maximal exercise testing			
VO_{2peak} ($mL \cdot min^{-1}$)	1820.7 ± 580.7	1946.8 ± 541.1	0.29
VO_{2peak} ($mL \cdot kg \cdot min^{-1}$)	23.3 ± 6.9	25.3 ± 7.5	0.19
W_{peak} (Watt)	153.4 ± 46.4	171.7 ± 48.8	0.07
Baseline submaximal exercise testing			
Percentage HR_{peak} †	75.9 ± 6.7	82.2 ± 6.4	< 0.0001
Workload (Watt)	76.3 ± 33.8	85.4 ± 25.4	0.06
Change in heart rate ($beats \cdot min^{-1}$) ‡	-3.4 ± 9.2	-10.8 ± 8.2	< 0.0001

Abbreviations: BL – baseline; HR – heart rate; HR_{peak} – peak (HRpeak - peak heart rate).
** P value for between-group differences using linear mixed-effects model.*
† HR_{peak} was assessed during pre-intervention exhaustive graded exercise testing.
‡ Change in heart rate response during submaximal exercise testing from pre- to post-intervention.

Discussion

In the present study we used an exhaustive exercise test and a submaximal exercise test to evaluate the effect of a physical training programme in cancer survivors. We showed that VO_{2peak} and W_{peak} significantly increased from baseline to post-intervention in the present study population. The decline in HR response to a constant submaximal power output is in line with these findings. By performing two separate exercise tests we were able to investigate the responsiveness of the submaximal exercise capacity compared to the change in maximal exercise capacity, which is supposed to be the gold standard. Our results revealed that only changes in submaximal HR while cycling with a HR above 140 bpm were associated with changes in VO_{2peak} and W_{peak} indicating that, during submaximal testing, an exertion of moderate to high intensity is necessary.

The strengths and limitations of this study need to be addressed before discussing the results. The strengths of the present study were the large sample size, the supervised and standardised intervention, low dropout rates, and the validated measure of fitness. A limitation of the present study was the small number of participants in the HR_{high} group (n=27) and that this group consisted of younger subjects compared to the HR_{low} group. Future research should include more cancer survivors all cycling with a submaximal HR of above 140 bpm to further reveal the relationship between changes of submaximal and maximal exercise testing outcomes. All participants in the present study completed the exhaustive exercise test and this suggests that all were capable of completing a submaximal test with moderate to high intensity.

The improvements of VO_{2peak} and W_{peak} reported in the present study are in accordance with the findings of others [3,12,23]. De Backer et al.[23] also used a submaximal and an exhaustive exercise test for the evaluation of an 18-week oncological physical training programme.[23] Contrary to our results, the authors reported that the HR at 50%, 60% and 70% of W_{peak} did not decrease in their participants from pre- to post-intervention, whereas VO_{2peak} and W_{peak} improved significantly. A possible explanation of these opposite finding might be the submaximal testing protocol they used: the test started at 50% of W_{peak} and was increased by 10% every three minutes sampling the HR in the last 15 seconds of each stage. A duration of three minutes might be too short in this deconditioned population to achieve a true steady state that is needed for a valid monitoring of a HR response to submaximal exercise. In the present study, the participants cycled during ten minutes at a fixed workload. This duration is in line with recommendations of Astrand and Rodahl[20] who reported that a period of about four to five minutes is necessary to reach a steady state.

Our findings that only changes in submaximal HR while cycling with a HR above 140 bpm were associated with changes in VO_{2peak} and W_{peak} might be explained by the findings of Davies et al.[24] who observed that higher intensity work produced intra-individual variations in HR of 2%, while intra-individual variations at lower intensities were higher and ranged from 3-8% when using the Astrand-

Ryhming test[25], which is a comparable submaximal cycle ergometer test. Moreover, Astrand and Rodahl[20] also recommend a HR up to or above 140 bpm to generate the best estimate of aerobic capacity. At lower heart rates fear, excitement and emotional stress may cause a marked elevation of HR at a submaximal work rate without either VO_{2peak} or performance capacity being affected. Thus, the submaximal test seems to be more accurate at higher intensities.[26]

Beforehand, we expected that when cycling at 50% of W_{peak} the relative HR response would be comparable for all participants. However, in the HR_{high} group the relative HR was higher compared to the HR_{low} group indicating that the intensity was higher for the HR_{high} group. During exhaustive graded exercise testing, the obtained level of W_{peak} was determined by aerobic as well as anaerobic (production of lactate) capacity. Possibly, the contribution of the anaerobic system was larger in the HR_{high} group. As a consequence in this group, cycling at 50% W_{max} implies cycling at a higher % VO_{2peak} and, therefore, a higher % HR_{peak} than in the HR_{low} group.

Do the present results implicate that our submaximal test could replace the exhaustive exercise test? The answer is no, as far as it concerns the assessment of VO_{2peak} that is only accurately determined by an exhaustive exercise test using gas exchange measurements.[20] Moreover, as is also proposed by others[23], an exhaustive exercise test using gas exchange measurements should be used as a diagnostic tool before the start of the training programme to detect cardiac or pulmonary limitations. Cancer survivors are at risk for developing cardiovascular complications caused by cardiotoxic or pulmotoxic medication or radiation therapy to the breast, which can occur immediately, but also may not manifest themselves until months or years after treatment.[27] However, our submaximal exercise test seemed suitable for the evaluation of fitness and its progress during the training programme or thereafter. The present study showed that submaximal testing at a moderate to high intensity was feasible and no complaints were reported. Compared to an exercise test until exhaustion, the submaximal test has several advantages. The test is simple to administer and avoids the expenses, patient discomfort and increased risk of maximal exercise testing. Taking these advantages and the shown responsiveness to change following physical training into account, we think that this test might be an appropriate tool to evaluate fitness changes in daily clinical practice of an oncological physical training programme. However, the testing procedure should be modified. We chose a workload of 50% of W_{peak} to avoid the risk of overstraining in our deconditioned population. That intensity of 50% of W_{peak} appeared to be too low to reach an appropriate HR response of above 140 bpm in all participants. Our results indicate that the procedure described by Astrand and Rodahl[20] can be used to select the appropriate workload for reaching a HR above 140 bpm.

In conclusion, our supervised, structured exercise programme had positive effects on cancer survivors' maximal and submaximal exercise capacity. Changes of submaximal and maximal exercise capacity were only weakly related to each other; possibly because of the insufficient high strain of the submaximal exercise test. However, when the intensity of the submaximal exercise test is sufficiently high, changes in submaximal HR were clearly correlated with changes in VO_{2peak} and W_{peak}. We recommend using an exhaustive exercise test as a diagnostic tool at the start of a physical training programme and for the assessment of the initial fitness state. For the evaluation of training progress in daily clinical practice a submaximal exercise test that is performed with moderate to high intensity might be an alternative to an exhaustive exercise test.

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7

General discussion

Is more always better?

Intuitively, '*more often seems better*, yet in life, *more is often not better*'.[1]

The above statement originates from the domain of behavioural sciences and marketing. However, it might also be applicable to oncological rehabilitation. The main question around which the present thesis is oriented is, 'Does adding cognitive-behavioural therapy to physical training enhance the positive effects of physical training on cancer survivors' quality of life and physical fitness?'
Translating the statement to the present area under discussion, it becomes, *intuitively, combining physical training with cognitive-behavioural therapy seems better*, yet in life, *physical training combined with cognitive-behavioural therapy does not outperform physical training alone*.

In this chapter, we discuss whether the statement is indeed valid for cancer survivors' rehabilitation.

'More often seems better'

Van Weert and colleagues[2] allowed 40 cancer survivors to choose either a complete rehabilitation programme consisting of four components, namely individual exercise, sports, psycho-education and information, or to drop one or more of these components. Thirty-two participants (80%) chose the total programme. Seven participants dropped one component that still results in a programme that combines physical training with a psychosocial intervention. Only one participant dropped both psycho-social components. Hence, before the start of the rehabilitation and without having the experience of physical training and a psychosocial intervention, '*more often seemed better'* as far as the patients were concerned. In the OncoRev study, we asked the participants at the end of the intervention whether physical training would have been enough for them. Only 17.4% of the participants in the PT+CBT group indicated that physical training would have been enough. Although we know that our physical training intervention was effective, almost 40% of participants in the PT group stated at the end of the intervention that they would have preferred the combination of physical training and cognitive-behavioural therapy (unpublished data). Consequently, '*more still seemed better'* after the interventions as well.

The starting point of the OncoRev project was also that '*more seemed better*'. Cancer survivors suffer from a wide range of problems which include physical as well as psychosocial complaints. Physical training is known primarily to affect physical functioning and cognitive-behavioural therapy had beneficial effects on psychosocial functioning. We hypothesised that combining both would lead to greater improvements in quality of life and physical fitness in comparison to physical training alone.

'More is often not better'

In the present study the combination of physical training and cognitive-behavioural therapy did not outperform physical training alone since we did not find any additional effect of cognitive-behavioural therapy on the beneficial effect of physical training on quality of life and physical fitness. There is one other study that is complementary to ours. Courneya and colleagues[3] compared the effect of the combination of physical training and psychotherapy on cancer survivors' physical and psychological functioning to the effect of psychotherapy alone. The authors reported that the combination of physical training and psychotherapy resulted in a significant increase of functional well-being, fatigue status and sum of skin folds and a borderline significant increase of physical well-being, satisfaction with life and flexibility, whereas psychotherapy alone had no effects on any of these outcomes. Moreover, both the combination of physical training with psychotherapy and of psychotherapy alone revealed comparable beneficial effects on emotional well-being, spiritual well-being and anxiety. Taking all this together we can conclude that physical training makes a valuable contribution to cancer patients' aftercare, but that the addition of cognitive-behavioural therapy does not lead to further improvement. Therefore, in the case of cancer survivors' rehabilitation, '*more is not better*', but this conclusion does need some consideration.

First, with respect to the effects of our physical training it should be noted that this training intervention integrated a self-management approach. It has been shown that including social cognitive components, such as self-management, in an intervention had positive effects on cancer patients' quality of life.[4] Furthermore, physical training was offered in a group format and that provides opportunities for social interaction, social comparison, social support[5] and modeling[6] that might improve self-efficacy and, therefore, quality of life.[4] We cannot distinguish these effects from the effects of solely performing physical exercise. Possible differential effects between physical training and cognitive-behavioural therapy might be diminished by integrating social cognitive components into the physical training in a standardised way.

Second, our results do not imply that cognitive-behavioural therapy is ineffective. Since we did not use a full factorial design, we can only conclude that adding cognitive-behavioural therapy to physical training does not enhance the beneficial effects of physical training. Other research and a meta-analysis revealed the positive effects of cognitive-behavioural interventions in cancer survivors.[7-9] Nezu et al.[8] used a cognitive-behavioural intervention comparable to ours that proved to be effective in decreasing distress and improving the quality of life of cancer survivors with clinically significant levels of psychological distress. Recently, Gielissen et al.[9] reported that cognitive-behaviour therapy had clinically relevant effects in reducing fatigue and functional impairments in a Dutch sample of severely fatigued cancer survivors. Furthermore, as mentioned above, Courneya et al.[3] showed that psychotherapy increased emotional and spiritual well-being and decreased the anxiety of cancer survivors and also that adding physical training did not result in further enhancements.

Third, in the past, the cognitive-behavioural intervention we used was shown to be effective mainly in highly distressed cancer patients.[8] We may, therefore, wonder whether an additional effect of cognitive-behavioural therapy could be demonstrated in a subgroup of distressed patients. However, preliminary analyses involving a subgroup of our participants who were highly distressed, as assessed by the Hospital Anxiety and Depression Scale[10], revealed no differential effects of physical training combined with cognitive-behavioural therapy compared to physical training as regards quality of life, anxiety and depression (unpublished data).

Lastly, the participants in the present study are a subgroup of all cancer survivors. Our population consisted of cancer survivors who applied voluntarily for a physical training programme (whether or not combined with cognitive-behavioural therapy). This may imply that cancer survivors who are primarily attracted by psychosocial interventions did not apply for the training. We assume that our subjects were highly motivated to participate in the intervention since they applied for rehabilitation on their own initiative and their attendance rates were high during the intervention. Moreover, their quality of life and physical fitness appeared to be low at baseline. Therefore, the results of our study can only be generalized to cancer survivors who experience physical and/or psychosocial problems who apply for a physical training programme on their own initiative.

Physical training: 'Is more always better?'

In the previous paragraph, we concluded that cognitive-behavioural therapy does not enhance the beneficial effects of our physical training programme. The content and delivery of this physical training programme was based on the best available evidence and addressed cancer survivors' main problems, namely decreased aerobic capacity, decreased muscle strength, fatigue and impaired quality of life.[11] The 12-week intervention consisted of two weekly sessions of 30 minutes of aerobic exercise, 30 minutes of muscle force training and one hour of group sports. Moreover, a self-management approach including goal setting, monitoring, norms and decision making, action and self-reflection was integrated into the training. At the end of the OncoRev project, the question remained as to whether all those components are necessary to gain improvements in physical fitness and quality of life of cancer survivors. Did we offer the most optimal intervention or would '*less (or fewer components) be better*'?

The future: More research or other research?

At present, physical training has proven to be effective in improving cancer survivors' quality of life. Therefore, in our opinion, there seems to be no need for *more* research that addresses solely the effectiveness of physical training. Future research should focus on the optimal content of a physical training programme. Which components should be maintained `which should be left out? Does an integrated self-management approach add to the effects of physical exercise? What is the optimal training modality? Is it aerobic exercise, resistance exercise or a combination of both? Is there an optimal training modality at all which can be applied to all cancer survivors? Cancer survivors are a heterogeneous group and they may well have different rehabilitation needs. Possibly, rehabilitation should be individually tailored by offering different components from which cancer patients can choose depending on their needs. However, their choice should be evidence-based to avoid the pitfall of '*more often seems better*'.

Furthermore, research should aim at the optimal extent of the physical training programme. What is the optimal number of training sessions needed per week to accrue health benefits? And what is the optimal duration of a physical

training intervention?
Moreover, more research is needed concerning the target group for a physical training intervention. What are the characteristics of cancer survivors who benefit most from the different components of rehabilitation?

Finally, there is one issue that has not yet been addressed at all namely, detailed assessment is lacking of the cost-benefit ratio of physical training following primary cancer treatment?

Conclusion

In conclusion, doing more is not always better in spite of its intuitive appeal. Improving the quality of cancer patients' rehabilitation does not necessarily imply providing as much as possible. The results of the present thesis suggest that cognitive-behavioural therapy does not add to the beneficial effects of physical training. After completing the physical training intervention, cancer survivors demonstrate a considerable increase in quality of life and a considerable reduction in the degree of fatigue. These findings support the notion that physical training is a useful, beneficial and clinically relevant approach which should be implemented within the framework of standard care for cancer survivors.

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8

Summary
Samenvatting
Zusammenfassung
Dankwoord
Curriculum Vitae

Summary

As a result of recent advances in diagnosis and treatment, the number of people surviving cancer is increasing. A subgroup of these cancer survivors report long-lasting physical and psychological complaints including decreased cardiorespiratory capacity, decreased physical functioning, cancer related fatigue, and decreased quality of life. Physical and psychological rehabilitation had beneficial effects on cancer survivors' physical fitness and quality of life. Physical training appeared to have a primarily positive effect on the physical and functional aspects of quality of life, whereas cognitive-behavioural therapy was shown to be beneficial for the psychosocial aspects. Therefore, compared to a single intervention, combining physical training with cognitive-behavioural therapy may lead to greater improvements in quality of life by having benefits on both physical and psychosocial functioning. To this end, the OncoRev project was started in 2000 with the aim being to determine the effects of a group-based combined physical and cognitive-behavioural intervention (PT+CBT) on the physical fitness and quality of life of cancer survivors compared to group-based physical training (PT) and a waiting list control group (WLC).

The OncoRev study is a cooperation of the University Medical Centre Utrecht, the Erasmus Medical Centre Rotterdam, Maastricht University and the Comprehensive Cancer Centre North-Netherlands. The study population consisted of survivors of all types of cancer who had completed their primary cancer treatment at least three months ago and had a life expectancy of at least one year. All the participants were referred by their medical specialist or general practitioner who assessed the need for rehabilitation. The medical ethics committee of the University Medical Centre Utrecht and the local research ethics committees approved the study.

Between February 2004 and January 2007, a total of 209 cancer survivors were recruited and participated in PT+CBT (n=76), PT (n=71) or WLC (n=62). Furthermore, PT+CBT and PT participants were followed during a nine month post-intervention period. The sample compromised 179 women and 30 men. The age of participants ranged from 18 to 74 years with a mean of 49.9 years. 57.4% survivors were diagnosed with breast cancer, 15.8% with haematological cancer, 11.5% with gynaecological cancer and 15.3% with other types of cancer. In terms of treatment, 84.7% had surgery, 67.5% received chemotherapy and 58.9% received radiation therapy. The participants completed their last cancer treatment 1.5 years (standard deviation 2.1) before study entry.

The two group-based interventions compared in the present study were a 12-week (twice weekly 2-hour sessions) physical training programme and the same 12-week physical training programme (twice weekly 2-hour sessions) combined with cognitive-behavioural therapy (weekly 2-hour sessions). Both interventions were offered at the following centres, namely Rehabilitation Centre De Hoogstraat in Utrecht, Rehabilitation Department Zonnestraal of Hilversum Hospital, Rehabilitation Department and Department of Psychosocial Services of the Erasmus Medical Centre Rotterdam and the Centre for Rehabilitation at the University Medical Centre Groningen. In each centre, after written consent had been obtained, participants were randomly assigned to PT+CBT or PT. Patients who had to wait at least three months for cancer rehabilitation in other Dutch centres using the same inclusion criteria as used in the OncoRev study were invited to participate in the WLC group.

Both PT and CBT integrated principles of self-management: i.e. goal selection, information collection, information processing and evaluation, decision making, action and self-reaction. Each physical training session consisted of individual aerobic bicycle exercise (30 minutes) and muscle strength training (30 minutes) and group sports (60 minutes). During the first three weeks, the cognitive-behavioural therapy focused primarily on exchanging participants' experiences with cancer, and psycho-education on stress, relaxation, fatigue, exercise physiology, illness perceptions, as well as on promoting optimism and self-efficacy for self-management. From Week 4 onwards, participants were primarily trained in applying self-management skills to realize personal goals (e.g., in work, hobbies, physical activity, family and social relations).

Physical fitness testing, i.e. maximal and submaximal bicycle exercise testing and muscle force measurements, were performed before and after the 12-week intervention. In addition, at pre-intervention, post-intervention, and 3- and 9-month post-intervention participants filled in questionnaires designed to measure quality of life (RAND 36-item Health Survey and European Organization for Research and Treatment of Cancer Quality of Life Questionnaire C30 (EORTC-QLQ-C30)) and physical activity (Physical Activity Scale for the Elderly (PASE)). Group cohesion (Group Cohesion Questionnaire (GCQ-22)) was measured after the forth, eighth and twelfth PT session. WLC participants filled in questionnaires at baseline and 3-month post-baseline. Additionally, a subgroup of WLC participants performed at the same time points an exhaustive exercise test and muscle force measurements.

Main results

This thesis reports on the effects of PT+CBT when compared to PT on maximal exercise capacity, muscle force and physical activity (**Chapter 2**), and on quality of life (**Chapter 3**). All these outcome measures increased significantly in PT and PT+CBT from baseline to 12-week post-intervention. There was no difference in changes between PT and PT+CBT indicating that adding cognitive-behavioural therapy to physical training did not enhance the effects of physical training. We concluded that our intensive, supervised, group-based physical training programme that integrated the principles of self-management and the advantages of peer contact was sufficient to improve cancer survivors' physical fitness and quality of life. In the **appendix to Chapter 2** and in **Chapter 3** the effects of both interventions were also compared with a waiting list control group to control for natural recovery. Participants in both intervention groups exhibited significant and clinically relevant improvements in role limitations due to physical problems, physical functioning, vitality and health change compared to control. Furthermore, peak exercise capacity and muscle strength of the lower limb of PT+CBT and PT participants were increased after the intervention in comparison to the control subjects.

In the short-term, we did not observe an additional effect of cognitive-behavioural therapy on cancer survivors' quality of life. However, long-term effects may be different. Increased physical fitness may have early effects on quality of life, while cognitive-behavioural therapy that at first might increase distress by confronting patients with personal worries, is known to have long-term benefits. Hence, in **Chapter 4** we investigated the effects of PT+CBT on quality of life nine month post-intervention compared to the effects of PT. Our results showed that the short-term beneficial effects were maintained since quality of life had increased, in clinically relevant terms, at 9 month post-intervention compared to baseline in both PT+CBT and PT. However, we did not detect any additional effect of cognitive-behavioural therapy. We therefore concluded in **Chapter 7** that doing more is not always better: cognitive-behavioural therapy does not add to the beneficial effects of physical training in the short- and in the long-term. Physical training appeared to be a useful, beneficial and clinically relevant approach, which should be implemented in cancer survivors' aftercare. However, we noted that our results do not suggest that cognitive-behavioural therapy alone is not effective. Moreover, our physical training intervention integrated psychosocial components as well, i.e. a self-management approach and peer contact that possibly diminished the difference in effect between PT+CBT and PT. Our participants applied for the intervention voluntarily and exhibited a low quality of life and low physical functioning at pre-intervention. Therefore, the results of our study can be generalized to cancer survivors experiencing physical and psychosocial problems who apply for a physical training programme on their own initiative.

Additional results

In **Chapter 5** we explored the effect of group cohesion on rehabilitation outcome. Group-based physical training interventions have been shown to be effective in increasing quality of life in cancer survivors. Until now, however, the impact of cohesion within the group on intervention outcome has not been investigated. We examined self-reported individual group cohesion ratings collected in the first half of the 12-week intervention. Four dimensions of group cohesion were measured, i.e. the bond with the group as whole, the bond with other members, cooperation within the group and the instrumental value. Quality of life, physical functioning and fatigue were assessed before and after the intervention. Our results showed that higher ratings of cooperation within the group predicted better post-intervention quality of life and physical functioning and less fatigue in men, and better quality of life and physical functioning in women. Additionally, women who reported a stronger bond with other members showed a lower quality of life after the intervention. One explanation for this unexpected finding might be that patients who felt that they were not making progress discovered that they could be useful to other members of the group and, therefore possibly rated the relationship with other members as high. A different mechanism might be downward social comparison, which means that participants who do not experience improvement compare themselves to others who perform worse in order to enhance their self-esteem. The reverse may also be true, namely that these patients compare themselves to other patients who are making progress and bond to them because their progress is proof that improvement is possible. No relationship was found between the instrumental value and the outcome variables. Thus, some dimensions of group cohesion seem to be associated with intervention outcome. However, the underlying mechanisms need to be clarified.

Evaluating changes of physical fitness following physical training is not only important for research purposes, since appropriate evaluation tools are also needed in daily clinical practice. Peak oxygen uptake (VO_{2peak}) measured by means of a maximal exercise test is considered the gold standard for determining the effects of physical training on fitness. However, maximal exercise testing may not be feasible with all populations or at all facilities. Therefore, submaximal testing could have greater applicability in daily clinical practice. To date, no submaximal measures have been validated in oncological rehabilitation. Therefore, the relationship between submaximal and maximal exercise outcome is investigated in **Chapter 6**. We examined the association between changes from pre-intervention to post-intervention of submaximal heart rate and changes of maximal aerobic capacity (i.e., peak oxygen consumption or peak power output). Our results suggested that changes in submaximal heart rate only in the group cycling with moderate to high intensity (i.e., heart rate ≥140 beats per minute) were strongly related to changes in maximal aerobic capacity. We concluded that in daily clinical practice, a submaximal exercise test of moderate to high intensity might be an alternative to exhaustive exercise testing for the evaluation of physical fitness and progress during and after an oncological physical training programme. However, an exhaustive exercise test using gas exchange measurements should be used for the assessment VO_{2peak} and as a diagnostic tool at the start of a physical training programme.

Samenvatting

Dankzij recente verbeteringen in diagnostiek en behandeling is het aantal mensen dat kanker overleeft toegenomen. Een subgroep van de overlevenden van kanker heeft langdurig fysieke en psychische klachten zoals een verlaagde cardiorespiratoire capaciteit, een verminderd fysiek functioneren, kankergerelateerde vermoeidheid, en een verminderde kwaliteit van leven. Fysieke en psychologische revalidatie heeft positieve effecten op de fysieke fitheid en de kwaliteit van leven van de overlevenden van kanker. Fysieke training heeft vooral een positief effect op de fysieke aspecten van de kwaliteit van leven; cognitieve gedragstherapie daarentegen heeft met name effect op de psychische aspecten. Daarom werd verondersteld dat een combinatie van fysieke training en cognitieve gedragstherapie tot grotere verbeteringen in kwaliteit van leven en fysieke fitheid zou leiden dan één van deze twee interventies afzonderlijk. Om deze aanname te onderzoeken is in 2000 de OncoRev studie gestart. Het doel van de OncoRev studie was het bepalen van het effect van fysieke training gecombineerd met cognitieve gedragstherapie (PT+CBT) op de kwaliteit van leven en fysieke fitheid van overlevenden van kanker vergeleken met het effect van fysieke training alleen (PT) en een wachtlijst controle groep (WLC).

In de OncoRev studie is samengewerkt tussen het Universitair Medisch Centrum Utrecht, het Erasmus Medisch Centrum Rotterdam, de Universiteit Maastricht en het Integraal Kankercentrum Noord-Nederland Groningen. De deelnemers aan dit onderzoek waren patiënten met verschillende vormen van kanker met een levensverwachting van meer dan één jaar die hun primaire kankergerelateerde behandeling minstens drie maanden voor begin van het onderzoek hadden afgerond. Alle deelnemers hadden een verwijzing van hun huisarts of medische specialist met een indicatie voor revalidatie. De medisch ethische toetsingscommissies van het Universitair Medisch Centrum Utrecht en van alle participerende centra hebben hun toestemming voor het uitvoeren van de OncoRev studie gegeven.

In de periode van februari 2004 tot februari 2007 werden 209 kankerpatiënten geïncludeerd. 76 patiënten namen deel aan PT+CBT, 71 aan PT en 62 patiënten maakten deel uit van de WLC groep. Deelnemers aan PT+CBT en PT werden gevolgd tot negen maanden na beëindiging van de interventie. De totale studiepopulatie bestond uit 179 vrouwen en 30 mannen. De leeftijd van de deelnemers varieerde van 18 tot 74 jaar (gemiddeld 49.9 jaar). Van de

deelnemers was 57.4% gediagnosticeerd met borstkanker, 15.8% met kanker aan het lymfestelsel, 11.5% met gynaecologische kanker en 15.3% met een andere soort kanker. 84.7% van de deelnemers was chrirugisch behandeld, 67.5% was behandeld met chemotherapie en 58.9% met radiotherapie. De tijd sinds de laatste kankergerelateerde behandeling was gemiddeld 1.5 jaar (standaard deviatie 2.1) bij aanvang van dit onderzoek.

De twee groepsinterventie die in deze studie werden onderzocht, waren een twaalf weken durend fysiek trainingsprogramma (twee keer per week, twee uur per sessie) en hetzelfde fysieke trainingsprogramma (twee keer per week, twee uur per sessie) gecombineerd met cognitieve gedragstherapie (één keer per week, twee uur per sessie). Beide interventies werden aangeboden in vier centra: Revalidatiecentrum De Hoogstraat in Utrecht, Universitair Medisch Centrum Groningen, locatie Beatrixoord in Haren, Erasmus Medisch Centrum in Rotterdam en Ziekenhuis Hilversum, locatie Landgoed Zonnestraal in Hilversum. Nadat de deelnemers hadden ingestemd met deelname aan het onderzoek werden zij door loting ingedeeld in PT+CBT of PT. Overlevenden van kanker die langer dan drie maanden moesten wachten op deelname aan oncologische revalidatie in een ander centrum in Nederland dat dezelfde in- en exclusie criteria hanteerde, werden gevraagd om aan de WLC groep deel te nemen.

Zowel in het fysieke trainingsprogramma als ook in de cognitieve gedragstherapie waren de principes van zelfmanagement en problem solving geïntegreerd. In het zelfmanagement proces worden zes stappen onderscheiden, namelijk probleemoriëntatie (hoe te denken over problemen/hindernissen), probleemdefinitie (wat is er aan de hand), doelen stellen (wat wil je bereiken), bedenken van oplossingen (welke oplossingen bedenk je), beslissingen nemen (welke oplossing kies je en waarom), oplossing uitvoering en evaluatie (wat heb je gedaan en heb je je doel bereikt).

Elke fysieke trainingssessie bestond uit individuele aerobe training (30 minuten), spierkrachttraining (30 minuten) en groepssport (60 minuten). De focus van de cognitieve gedragstherapie lag de eerste drie weken op het uitwisselen van ervaringen met de ziekte kanker, op psycho-educatie over stress, ontspanning, vermoeidheid, inspanningsfysiologie en ziekte percepties, en op het versterken van gevoelens van optimisme en vertrouwen in eigen kunnen (self-efficacy) voor het uitvoeren van zelfmanagement activiteiten. Vanaf de vierde week werden de deelnemers vooral getraind in het toepassen van zelfmanagement vaardigheden om persoonlijk relevante doelen te bereiken (zoals op het gebied van werk, vrijetijdsbesteding, fysieke activiteit, contacten met familie en vrienden).

Voor de start en aan het eind van de interventie werden maximale en submaximale inspanningstesten en spierkrachttesten uitgevoerd en werden vragenlijsten afgenomen. Deelnemers aan PT+CBT en PT vulden de vragenlijsten ook drie en negen maanden na beëindiging van de interventie in. De WLC groep vulde de vragenlijsten in op baseline en drie maanden later. Een subgroep van de WLC groep onderging op deze tijdstippen ook een maximale inspanningstest en spierkrachttesten. Met behulp van de vragenlijsten werd de kwaliteit van leven (EORTC-QLQ-30 en RAND-36) en fysieke activiteit (PASE) bepaald. In de interventiegroepen werd daarnaast ook na de vierde, achtste en twaalfde trainingssessie de groepscohesie (GCQ-22) gemeten.

Primaire uitkomsten

Dit proefschrift rapporteert de effecten van PT+CBT op de maximale inspanningscapaciteit, spierkracht en fysieke activiteit (**Hoofdstuk 2**) en op de kwaliteit van leven (**Hoofdstuk 3**) vergeleken met de effecten van in PT. Na de interventie werden significante verbeteringen gevonden op al deze uitkomstmaten, zowel in PT+CBT als ook in PT. De veranderingen waren niet verschillend tussen PT+CBT en PT. Dit impliceert dat de toevoeging van cognitieve gedragstherapie aan fysieke training de effectiviteit van het fysieke trainingsprogramma niet verhoogt. Wij concludeerden dat het intensieve, fysieke op zelfmanagement gerichte trainingsprogramma dat onder begeleiding en in groepsverband aangeboden werd, voldoende was om de fysieke fitheid en kwaliteit van leven van overlevenden van kanker te verbeteren. In de **Appendix van Hoofdstuk 2** en in **Hoofdstuk 3** werden de effecten van beide interventies vergeleken met een wachtlijstcontrole groep om voor natuurlijk herstel te controleren. De deelnemers aan beide interventies verbeterden vergeleken met de controlegroep significant en klinisch relevant ten aanzien van beperkingen in rol functioneren op grond van fysieke problemen, fysiek functioneren, vitaliteit en verandering in gezondheid. Bovendien was de piek inspanningscapaciteit en de spierkracht van de strekspieren van de bovenbenen van de deelnemers aan PT+CBT en PT verbeterd in vergelijking met de controlegroep.

Op de korte termijn werd geen toegevoegd effect gevonden van de cognitieve gedragstherapie op de kwaliteit van leven van onze onderzoekspopulatie. De lange-termijn effecten zouden echter anders kunnen zijn. Bekend is dat fysieke training al op korte termijn effectief kan zijn. Van cognitieve gedragstherapie daarentegen is aangetoond dat effecten ook op latere termijn zichtbaar kunnen worden. Bovendien kan niet uitgesloten worden dat de cognitieve gedragstherapie in eerste instantie een stressverhogend effect heeft doordat patiënten in die fase nadrukkelijk uitgenodigd worden om hun problemen te benoemen. Daarom hebben wij in **Hoofdstuk 4** de effecten van PT+CBT op de kwaliteit van leven negen maanden na de interventie onderzocht en deze vergeleken met de effecten van PT. Onze resultaten lieten zien dat de positieve korte-termijn effecten behouden bleven: negen maanden na de interventie was de kwaliteit van leven nog steeds klinisch relevant hoger dan voor de interventie in zowel PT+CBT als PT. Wij hebben echter ook op lange termijn geen toegevoegde waarde van de cognitieve gedragstherapie gevonden. Daarom concludeerden wij in **Hoofdstuk 7** dat meer niet altijd beter is: cognitieve gedragstherapie heeft geen additief effect op de positieve effecten van fysieke training op de kwaliteit van leven, noch op de korte, noch op de lange termijn. We stelden vast dat fysieke training (groepsgewijs, onder begeleiding en gebaseerd op de principes van zelfmanagement) een nuttige, effectieve en klinisch relevante interventie is die standaard in de nazorg van kankerpatiënten geïmplementeerd zou moeten worden.

Wij merken echter wel op dat onze resultaten niet impliceren dat cognitieve gedragstherapie alleen niet effectief zou zijn. Bovendien waren in ons fysieke trainingsprogramma ook psychosociale componenten geïntegreerd, zoals het zelfmanagement benadering en het lotgenoten contact. Daardoor zou het verschil in effect tussen PT+CBT en PT kleiner kunnen uitvallen dan wanneer vergeleken werd met een puur fysieke training. Tenslotte is dit onderzoek uitgevoerd bij de specifieke groep deelnemers die zichzelf voor de interventie hebben opgegeven, wat kan wijzen op een hoge motivatie. Bovendien hadden zij aan het begin van de interventie een lage kwaliteit van leven en een laag fysiek functioneren. Onze resultaten kunnen dus gegeneraliseerd worden naar overlevenden van kanker die fysieke en psychische problemen hebben en die zich op eigen initiatief aanmelden voor een fysiek trainingsprogramma.

Additionele resultaten

De effecten van groepscohesie werden in **Hoofdstuk 5** gerapporteerd. Fysieke trainingsprogramma's in groepsverband bleken effectief te zijn voor het verbeteren van de kwaliteit van leven van kanker patiënten en overlevenden van kanker. Tot op heden is de impact van de cohesie in de groep op het effect van de interventie echter nog niet onderzocht. Wij onderzochten het effect van zelfgerapporteerde individuele groepscohesie in de eerste helft van de interventie. Vier dimensies van groepscohesie werd gemeten, namelijk de band met de groep als geheel, de band met individuele groepsleden, de samenwerking en de instrumentele waarde. Kwaliteit van leven, fysiek functioneren en vermoeidheid werden voor en na de interventie gemeten. Onze resultaten laten zien dat hogere scores voor de samenwerking in de groep bij mannen een hogere kwaliteit van leven, een beter fysiek functioneren en verminderde vermoeidheid na de interventie voorspelden en bij vrouwen een hogere kwaliteit van leven en een beter fysiek functioneren. Bij vrouwen was de kwaliteit van leven na de interventie afgenomen als zij een sterke band met de anderen groepsleden rapporteerden. Wij gaven als verklaring voor dit onverwachte resultaat dat de deelnemers die voelden dat zij geen vooruitgang boekten ontdekten dat zij nuttig voor andere deelnemers zouden zijn en dat zij daarom hun relatie met anderen hoger waarderen. Als alternatieve verklaring suggereerden wij de sociale vergelijking naar beneden kunnen zijn. Dit houdt in dat deelnemers die niet verbeteren zich vergelijken met deelnemers die slechter presteren waardoor hun eigenwaarde toeneemt. Een alternatieve verklaring zou kunnen zijn, dat deze patiënten zich vergelijken met anderen die wel vooruitgaan en zich met hen verbonden voelen omdat hun vooruitgang het bewijs is dat vooruitgang mogelijk is. Er werd geen relatie tussen instrumentele waarde en een van de uitkomstmaten gevonden. Wij concludeerden dat sommige dimensies van groepscohesie van invloed lijken op het resultaat van de interventie maar dat de onderliggende mechanismen nog nader onderzoek verdienen.

Het evalueren van veranderingen in fysieke fitheid na een trainingsprogramma, is niet alleen wetenschappelijk van belang, maar heeft ook betekenis voor de klinische praktijk van alledag. De piek zuurstofopname ($VO_{2peak)}$ die tijdens een maximale inspanningstest wordt bepaald, geldt als de gouden standaard om de effecten van fysieke training op de fitheid te bepalen. Maximale inspanningstesten zijn echter niet haalbaar voor alle patiëntpopulaties en op alle locaties. Een submaximale inspanningstest is in dergelijke situaties beter toepasbaar in de dagelijkse klinische praktijk. Tot op heden zijn geen submaximale inspanningstesten gevalideerd bij oncologische patiënten. Daarom komt in **Hoofdstuk 6** de relatie tussen de uitkomsten van submaximale en maximale inspanningtesten aan bod.

Wij onderzochten het verband tussen veranderingen in de submaximale hartslag en de maximale inspanningscapaciteit (piek zuurstofopname en piek vermogen). Onze resultaten wezen uit dat alleen in de groep die de submaximale inspanningstest met een gemiddelde tot hoge intensiteit uitvoerden (met een hartslag ≥ 140 slagen per minuut) veranderingen in submaximale hartslag sterk gecorreleerd waren met veranderingen in maximale test. Wij concludeerden dan ook dat een submaximale inspanningstest die met een gemiddelde tot hoge intensiteit wordt uitgevoerd een bruikbaar alternatief voor de maximale inspanningstest in de dagelijkse klinische praktijk kan zijn. Wij bevelen echter wel aan om een maximale inspanningstest te gebruiken als screeningsinstrument om inspanningsgerelateerde cardiopulmonaire beperkingen vast te stellen en om de VO_{2peak} te bepalen bij het begin van het fysieke trainingsprogramma.

Zusammenfassung

Als Ergebnis neuester Fortschritte in der Diagnose und Behandlung nimmt die Zahl Krebsüberlebender zu. Eine Untergruppe dieser Krebsüberlebenden berichtet von langanhaltenden körperlichen und psychischen Beschwerden wie verminderter kardiorespiratorischer Leistung, verminderter physischer Funktionsfähigkeit, durch den Krebs hervorgerufener Müdigkeit und verminderter Lebensqualität. Physische und psychologische Rehabilitation wirkte sich fördernd auf die körperliche Fitness und die Lebensqualität Krebsüberlebender aus. So stellte sich heraus, dass physisches Training einen hauptsächlich positiven Effekt auf die physischen und funktionellen Aspekte der Lebensqualität ausübt, während sich kognitive Verhaltenstherapie in psychosozialen Aspekten als fördernd erwies. Daher könnte das Kombinieren von physischem Training mit kognitiver Verhaltenstherapie, im Vergleich zur Anwendung von nur einer der Methoden, zu größeren Verbesserungen der Lebensqualität führen, da es sowohl in der physischen als auch in der psychologischen Funktionsfähigkeit fördernd wirkt. Zu diesem Zwecke begann im Jahr 2000 das OncoRev Projekt mit dem Ziel, die Auswirkungen der Anwendung von Gruppen basiertem, physischen Training in Verbindung mit kognitiver Verhaltenstherapie (PT+CBT) auf die körperliche Fitness und die Lebensqualität von Krebsüberlebenden im Vergleich zu Gruppen basiertem, physischen Training (PT) und einer Wartelisten-Kontrollgruppe zu bestimmen.

Die OncoRev Studie ist eine Zusammenarbeit der Universitätsklinik in Utrecht, der Erasmus Universitätsklinik in Rotterdam, der Universität Maastricht und dem Comprehensive Cancer Center der Nordniederlande in Groningen. Die Teilnehmergruppe der Studie bestand aus Überlebenden aller Arten von Krebs, die ihre Krebsbehandlung mindestens drei Monate zuvor beendet und eine Lebenserwartung von mindestens einem Jahr hatten. Alle Teilnehmer waren durch ihren Facharzt oder Allgemeinarzt aufgrund einer von ihnen attestierten Notwendigkeit der Rehabilitation überwiesen worden. Die Medizinische Ethik-Kommission der Universitätsklinik Utrecht und die Ethikkommissionen aller teilnehmenden Zentren genehmigten die Studie.

Von Februar 2004 bis Januar 2007 wurden im Ganzen 209 Krebsüberlebende angeworben. Von ihnen nahmen 76 an PT+CBT, 71 an PT und 62 an der Wartelisten-Kontrollgruppe teil. Die Teilnehmer an PT+CBT und PT wurden bis zu neun Monaten nach der Intervention gefolgt. Die Auswahl verglich 179 Frauen und 30 Männer.

Das Alter der Teilnehmer bewegte sich von 18 bis 74 Jahren mit einem Mittelwert von 49,9 Jahren. Bei 57,4% der Überlebenden war Brustkrebs, bei 15,8% hämatologischer Krebs, bei 11,5% gynäkologischer Krebs und bei 13,5% andere Arten von Krebs diagnostiziert worden. Der Krebs wurde bei 84,7% operativ, bei 67,5% mit Chemotherapie und bei 58,9% mit Strahlentherapie behandelt. Die Teilnehmer beendeten ihre letzte Behandlung eineinhalb Jahren vor Studienbeginn (Standardabweichung 2,1).

Die zwei Gruppen basierten Interventionen, die in der vorliegenden Studie verglichen werden, bestanden aus einem 12-wöchigen (zweimal pro Woche eine zweistündige Sitzung) physischen Trainingsprogramm und aus demselben 12-wöchigen physischem Trainingsprogramm (zweimal pro Woche eine zweistündige Sitzung) in Verbindung mit kognitiver Verhaltenstherapie (wöchentlich eine zweistündige Sitzung). Beide Interventionen wurden in den folgenden Zentren angeboten: Rehabilitationszentrum De Hoogstraat in Utrecht, Rehabilitationsabteilung Zonnestraal des Krankenhauses Hilversum, Rehabilitationsabteilung und Abteilung für Psychologischen Service der Erasmus Universitätsklinik Rotterdam und Rehabilitationszentrum Beatrixoord der Universitätsklinik Groningen in Haren. In jedem Zentrum wurden die Teilnehmer, nachdem eine schriftliche Einwilligung vorlag, ad random PT+CBT oder PT zugeteilt. Patienten, die in anderen holländischen Zentren, in denen die gleichen Aufnahmekriterien wie zur OncoRev-Studie gelten, mindestens drei Monate auf Krebsrehabilitation warten mussten, wurden zur Teilnahme an der Wartelisten-Kontrollgruppe eingeladen.

Sowohl das physischen Training als auch die kognitiver Verhaltenstherapie integrierten die Prinzipien von Selbstmanagement. Selbstmanagement ist ein Prozess, der aus sechs Phasen besteht, nämlich die Wahl eines Zieles, Sammlung von Informationen, Bearbeitung und Auswertung der Informationen, Treffen von Entscheidungen, Handlung und Selbstreaktion. Jede physische Trainingssitzung bestand aus individuellem aeroben Training (30 Minuten), Muskelaufbautraining (30 Minuten) und Gruppensport (60 Minuten). In den ersten Wochen konzentrierte sich die kognitive Verhaltenstherapie hauptsächlich auf den Austausch von Erfahrungen der Teilnehmer mit Krebs, auf Psychoeducation im Umgang mit Stress, Entspannung, Ermüdung, Leistungsphysiologie und Krankheitswahrnehmung und auf die Verbreitung von Optimismus und Selbstvertrauen in der Durchführung von Selbstmanagementfähigkeiten. Von der vierten Woche an wurden die Teilnehmer hauptsächlich darauf geschult, Selbstmanagementfähigkeiten auf die Verwirklichung ihrer persönlichen Ziele anzuwenden.

Physische Fitnesstests, die aus dem Testen der maximalen und submaximalen Leistung beim Fahrrad fahren und dem Messen der Muskelstärke bestanden, wurden vor und nach der 12-wöchigen Intervention durchgeführt. Zusätzlich füllten die Teilnehmer bei der Voruntersuchung, Nachuntersuchung sowie drei und neun Monate nach der Intervention Fragebögen aus, die zur Messung der Lebensqualität (RAND-36 und EORTC-QLQ-30) und der physischen Aktivität (PASE) konzipiert waren. Der Grupenzusammenhalt (GCQ-22) wurde nach der vierten, achten und zwölften physischen Trainingssitzung gemessen. Teilnehmer der Wartelisten-Kontrollgruppe füllten zu Beginn und drei Monate nach Beginn Fragebögen aus. Eine Untergruppe der Kontrollgruppe führte dann auch einen maximalen Leistungstest und Muskelstärkemessungen aus.

Hauptergebnisse

Diese Doktorarbeit stellt die Wirkung von PT+CBT im Vergleich zu PT auf die maximale Leistungsfähigkeit, Muskelstärke und physische Leistung (**Kapitel 2**) und auf die Lebensqualität (**Kapitel 3**) dar. Alle Endwerte nahmen sowohl bei PT als auch bei PT+CBT vom Beginn bis nach der zwölfwöchigen Intervention wesentlich zu. Die Änderungen unterschieden sich von PT zu PT+CBT nicht, was bedeutet, dass das Hinzufügen von CBT zu PT die Wirkung von PT nicht verbessert. Daraus schlossen wir, dass unser intensives, beaufsichtigtes, Gruppen basiertes, physisches Trainingsprogramm, das die Prinzipien des Selbstmanagement und die Vorteile des Kontakts mit Personen in der gleichen Situation beinhaltet, für die Verbesserung der physischen Fitness und der Lebensqualität Krebsüberlebender ausreichend ist. Im **Anhang zu Kapitel 2** und in **Kapitel 3** wurden die Wirkungen beider Interventionen mit einer Wartelisten-Kontrollgruppe verglichen, um für natürliche Genesung zu kontrollieren. Teilnehmer beider Interventionsgruppen zeigten im Vergleich zur Kontrollgruppe in der körperlichen Rollenfunktion und einer veränderten Lebensfreude und Gesundheit bedeutende und klinisch relevante Verbesserungen. Außerdem waren physische Höchstleistungsfähigkeit und die Muskelstärke der unteren Gliedmaße der PT+CBT und PT-Teilnehmer nach der Intervention im Vergleich zu den Teilnehmern der Kontrollgruppe erhöht.

Auf kurze Sicht konnten wir keine zusätzliche Wirkung der kognitiven Verhaltenstherapie auf die Lebensqualität Krebsüberlebender erkennen. Dennoch könnte die Langzeitwirkung anders ausfallen. Eine gesteigerte physische Fitness kann früh Wirkung auf die Lebensqualität haben, während man von kognitiver Verhaltenstherapie, die anfangs die Sorgen des Patienten durch die Konfrontation mit persönlichen Ängsten verstärken kann, weiß, dass sie auf lange Sicht Nutzen für den Patienten hat. Daher untersuchten wir in **Kapitel 4** die Wirkung von PT+CBT auf die Lebensqualität neun Monate nach der Intervention und verglichen diese mit der Wirkung von PT. Unsere Ergebnisse zeigten, dass die kurzfristigen positiven Wirkungen sowohl bei PT+CBT und PT erhalten blieben, da die Lebensqualität neun Monaten nach der Intervention im Vergleich zum Beginn noch immer mit klinischer Relevanz zugenommen hatte. Eine zusätzliche Wirkung der kognitiven Verhaltenstherapie konnten wir aber nicht erkennen. Wir kamen daher in **Kapitel 7** zu dem Schluss, dass mehr nicht immer gleich besser ist: Kognitive Verhaltenstherapie trägt weder auf kurze noch auf lange Sicht zur positiven Wirkung des physischen Trainings bei. Physisches Training stellte sich als nützliche, fördernde und klinisch relevante Methode heraus, die in der Nachsorgebehandlung Krebsüberlebender angewendet werden sollte.

Wir stellten fest, dass unsere Ergebnisse nicht belegen, dass kognitive Verhaltenstherapie allein nicht wirkungsvoll ist. Vielmehr integrierte unsere physische Trainingsintervention auch psychosoziale Elemente, wie die Methode de Selbstmanagement und der Kontakt mit Personen in der gleichen Situation, die möglicherweise den Unterschied in Wirkung zwischen PT+CBT und PT verringerten. Unsere Teilnehmer meldeten sich freiwillig zur Intervention an und zeigten bei der Voruntersuchung eine geringe Lebensqualität und eine geringe physische Funktionsfähigkeit. Daher können die Ergebnisse unserer Studie auf Krebsüberlebende verallgemeinert werden, die unter physischen und psychosozialen Problemen leiden und sich aus eigener Initiative für ein physisches Trainingsprogramm bewerben.

Zusätzliche Ergebnisse

In **Kapitel 5** erforschten wir die Wirkung des Gruppenzusammenhalts auf das Rehabilitationsergebnis. Gruppen basierte physische Trainingsinterventionen gelten als wirkungsvoll in der Verbesserung der Lebensqualität von Krebspatienten und Krebsüberlebender. Bisher war der Einfluss des Zusammenhalts innerhalb der Gruppe auf das Ergebnis der Intervention noch nicht untersucht worden. Wir untersuchten selbst verfasste, individuelle Bewertungen des Gruppenzusammenhalts, die in der ersten Hälfte der zwölfwöchigen Intervention gesammelt worden waren. Vier Dimensionen des Gruppenzusammenhaltes waren bewertet worden: Die Bindung mit der Gruppe als Ganzem, die Bindung mit anderen Mitgliedern, Zusammenarbeit innerhalb der Gruppe und der instrumentelle Nutzen. Lebensqualität, physische Funktionsfähigkeit und Müdigkeit wurden vor und nach der Intervention beurteilt. Unsere Ergebnisse zeigten, dass eine höhere Bewertung der Kooperation innerhalb der Gruppe bei Männern eine bessere Lebensqualität und physische Funktionsfähigkeit und geringere Müdigkeit nach der Intervention vorhersagte, bei Frauen eine besser Lebensqualität und physische Funktionsfähigkeit. Zusätzlich zeigte sich bei Frauen, die eine enge Bindung mit anderen Mitgliedern angegeben hatten, nach der Intervention eine niedrigere Lebensqualität. Eine Erklärung für dieses unerwartete Ergebnis könnte sein, dass Patienten, die das Gefühl hatten, keinen Fortschritt zu machen, entdeckten, dass sie für andere Mitglieder der Gruppe nützlich sein können und daher möglicherweise die Beziehung zu anderen Mitgliedern als eng bewerteten. Ein anderer Mechanismus könnte der soziale Vergleich nach unten sein, indem Teilnehmer, die keine Verbesserung erleben, sich mit anderen vergleichen, denen es noch schlechter geht, um ihr Selbstvertrauen aufzubauen. Das Gegenteil könnte auch der Fall sein, nämlich, dass diese Teilnehmer sich mit anderen Teilnehmern vergleichen, die Fortschritte machen, und sich an diese halten, da ihr Fortschritt Beweis dafür ist, dass Verbesserung möglich ist. Zwischen dem instrumentellen Nutzen und dem Rehabilitationsergebnis wurde keine Beziehung gefunden. Einige Dimensionen des Gruppenzusammenhalts scheinen also mit dem Ergebnis der Intervention zusammenzuhängen. Dennoch müssen die zu Grunde liegenden Mechanismen geklärt werden.

8

Die Auswertung der Änderungen der physischen Fitness nach physischem Training ist nicht allein für Forschungszwecke wichtig, da geeignete Beurteilungsmittel auch in der alltäglichen klinischen Praxis benötigt werden. Das Messen der maximalen Sauerstoffaufnahme (VO_{2max}) durch einen maximalen Leistungstest gilt als der grundlegende Maßstab zur Bestimmung der Wirkung des physischen Trainings auf die Fitness. Maximale Leistungstest können jedoch möglicherweise nicht mit allen Populationen oder in allen Einrichtungen durchgeführt werden. Daher könnten submaximale Tests für die alltägliche klinische Praxis besser geeignet sein. Bis heute wurden keine submaximalen Messungen in der onkologischen Rehabilitation auf Validität untersucht. Deshalb erforschten wir die Beziehung zwischen dem Ergebnis submaximaler und maximaler Leistung in **Kapitel 6**. Wir untersuchten die Verbindung zwischen Änderungen der submaximalen Herzfrequenz und

Änderungen der maximalen aeroben Kapazität (d.h. VO_{2max} oder maximale Leistung) von der Voruntersuchung bis zur Nachuntersuchung. Unsere Ergebnisse zeigten, dass Änderungen in der submaximalen Herzfrequenz bei den Teilnehmern, die den submaximalen Leistungstest bei mäßiger bis hoher Intensität (d.h. Herzfrequenz ≥140 Schläge pro Minute) ausgeführt hatten, eng mit Änderungen in der maximalen aeroben Kapazität verbunden waren. Wir kamen zu dem Schluss, dass in der alltäglichen klinischen Praxis ein submaximaler Leistungstest bei mäßiger bis hoher Intensität eine Alternative zu einem vollständigen Leistungstest zur Bewertung der physischen Fitness und des Fortschritts während und nach einem onkologischem physischen Trainingsprogramm sein könnte. Dennoch sollte ein maximaler Leistungstest, einschließlich der Messungen des Gaswechsels, zur Bewertung des VO_{2max} und als diagnostisches Mittel am Anfang eines physischen Trainingsprogramms angewendet werden.

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Curriculum Vitae

Anne Maria May was born on 1 October 1973 in Gräfelfing, Germany. In 1993, after graduating from secondary school at the Siebold Gymnasium in Würzburg, Germany, she studied Physical Therapy at the University of Professional Education, Faculty of Health Care in Utrecht, the Netherlands. After obtaining her Bachelor of Science (cum laude) in 1997, she studied Sciences of Human Movement at the Free University in Amsterdam, the Netherlands and obtained her Master of Science degree (cum laude) in 2001. As part of her traineeship two research projects were conducted. Her first project was conducted at the department of Sciences of Human Movement of the Free University (supervised by Prof. Arnold de Haan, PhD, and Jo de Ruiter, PhD) concerning muscle function during repetitive moderate-intensity muscle contractions in myoadenylate deaminase-deficient Dutch subjects. The second project was performed at Numico Research B.V. in Wageningen, the Netherlands, on 'Heart failure ex vivo'. From June 2001 to December 2002 she worked as a Scientist (Sport-)Nutrition at Numico Research. In January 2003 she started her PhD research described in this thesis at the Julius Center for Health Sciences and Primary Care, University Medical Center Utrecht, the Netherlands under supervision of Prof. Rick Grobbee, MD, PhD, Prof. Wim Trijsburg, PhD, Prof. Jan Passchier, PhD and Wynand Ros, PhD. She obtained her Master of Science in Epidemiology at the Netherlands Institute of Health Sciences, Erasmus Medical Center Rotterdam in August 2006. Since March 2007 she has been a postdoctoral fellow at the Julius Center for Health Sciences and Primary Care and has been working as the scientific coordinator of an international EC-funded research project investigating the relationship between physical activity, nutrition, alcohol, cessation of smoking, eating out of home and obesity (PANACEA) within the European Prospective Investigation into Cancer and Nutrition (EPIC) cohort.