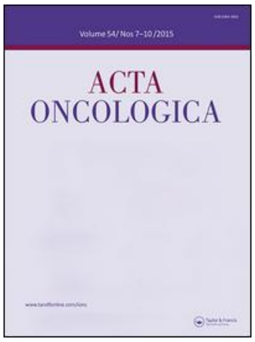

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REVIEW

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The effect of training during treatment with chemotherapy on muscle strength and endurance capacity: A systematic review

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ABSTRACT

Background Treatment of cancer with chemotherapy decreases endurance capacity and muscle strength. Training during chemotherapy might prevent this. There are no clear guidelines concerning which type of training and which training dose are effective. This review aims to gain insight into the different training modalities during chemotherapy and the effects of such training to improve endurance capacity and muscle strength in order to obtain the knowledge to compose a future training program which trains cancer patients in the most effective way. **Material and methods** A systematic search of PubMed was carried out. In total, 809 studies of randomized controlled trials studying the effects of training during chemotherapy on endurance capacity and muscle strength were considered. Only 14 studies met all the inclusion criteria. The studies were assessed on methodological quality by using Cochrane criteria for randomized controlled trials. **Results** The quality of the studies was generally poor and the study populations varied considerably as the training programs were very heterogeneous. Variables of endurance capacity reported beneficial effects in 10 groups (59%). Increases due to training ranged from 8% to 31%. Endurance capacity decreased in nine of 13 control groups (69%), which ranged from 1% to 32%. Muscle strength improved significantly in 17 of 18 intervention groups (94%), ranging from 2% to 38%. Muscle strength also improved in 11 of 14 control groups (79%), but this increase was only minimal, ranging from 1.3% to 6.5%. **Conclusions** This review indicates that training during chemotherapy may help in preventing the decrease in muscle strength and endurance capacity. It is important to know which training intensity and duration is the most effective in training cancer patients, to provide a training program suitable for every cancer patient. Training should be based on good research and should be implemented into international guidelines and daily practice. More research is needed.

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Ferlay et al. estimated 3.45 million new cases and 1.75 million deaths from cancer in Europe in 2012. In combination, cancers of the female breast, colorectal, prostate and lung represent almost half of the overall burden of cancer in Europe [1]. The survival rates have increased during recent years – nowadays 61% of the cancer patients will survive [2]. All these numbers show a future increase of the number of cancer survivors who have to deal with the side effects of cancer therapy.

A considerable number of cancer patients receive chemotherapy or radiotherapy. Side effects include both physical as well as psychological complications and have a huge impact on daily life. A frequently reported side effect from chemotherapy and radiation is cancer-related fatigue [3,4]. One study found that up to 82% of breast cancer patients experienced fatigue after their first chemotherapy cycle [5]. Cancer-related fatigue has a negative effect on muscle strength, endurance capacity, quality of life and return to work [6–9].

Chemotherapy may be myelotoxic, leading to anemia, which decreases the oxygen transport to the muscles [10]. In addition chemotherapy, particularly anthracyclines and irradiation of the mediastinum may result in myocardial damage and can therefore lead to a decrease in cardiac output or damage to the lungs [10]. Immunosuppressive agents may cause a marked loss of muscle mass [10]. Furthermore, anorexia and nausea caused by chemotherapy result in a reduced protein and calorie intake [10]. All these side effects may impair the physical performance in cancer patients [3,4]. Moreover, inactivity related to disease and/or treatment may cause deconditioning [5]. One study showed that in cancer patients, a maximum oxygen uptake (VO2max) of 14 ml/kg/min is not uncommon, which is even below the level of 15 ml/kg/min, which is the limit for activities for daily life [11,12].

In the past, patients were advised to rest and avoid physical effort. However, it is now well established that a decrease in

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physical activity results in severe deconditioning [10]. Physical exercise may have beneficial effects on reducing cancer-related fatigue, both during and following the administration of adjuvant therapies [7,13–16]. Research has shown that physical activity after chemotherapy increases muscle strength, quality of life and return to work. Furthermore, it decreases cancer-related fatigue. Physical activity is generally well tolerated and only a few adverse events, such as shoulder tendonitis, knee injury and syncope, during training occur [7,15,16].

The American College of Sports Medicine (ACSM) identifies types of exercise in their document 'General Principles of Exercise Prescription'. The types of exercise can be, among others, divided into aerobic exercise training and muscle exercise training. Aerobic exercise training improves body composition and cardiorespiratory fitness, while muscle exercise training improves muscle strength and muscle endurance. Any activity that uses large muscle groups can be maintained continuously and is rhythmical in nature can be regarded as an aerobic exercise. Muscle strengthening exercises enable muscles to do more work than they are accustomed. The aerobic intensity (training dose) can be expressed as a percentage of a person's VO2max/aerobic capacity or as a percentage of a person's maximum heart rate (HRmax), which could be measured by exercise tests. Moderate exercise is performed at 65–75% of HRmax and vigorous exercise is performed at 75–95% of HRmax. To approximate the appropriate limb-specific weight loads for resistance exercise (training dose), one can determine the one-repetition maximum (i.e. 1-RM) – the greatest resistance/weight that can be moved through the full range of motion for a single repetition in a controlled manner and then lift a defined percentage of that amount during each set of the exercise (i.e. % 1-RM) [17]. The ACSM advises a combination of aerobic training and progressive resistance training on moderate intensity for people training *after* chemotherapy. In concordance with the most recent literature the ACSM [18] also advises training during treatment with chemotherapy. Unfortunately, there is no guideline concerning which type of training and which training dose are effective.

Objectives

There is a lot of evidence that training *after* chemotherapy is very effective. There are guidelines providing training prescription after chemotherapy. Up to now it is not known what training program is the most effective in training patients during chemotherapy. The purpose of this paper is to gain insight in the different training modalities during chemotherapy, focusing on the most effective way to improve endurance capacity and muscle strength, using objectively measurable outcomes in order to compose a training program which trains cancer patients in the most effective way.

Materials and methods

Eligibility criteria

Inclusion criteria

(1) Randomized controlled trials.
(2) Studies involving adult patients (>18 years), diagnosed for malignancy and receiving chemotherapy.
(3) Articles prescribing a physical exercise program, regardless of which type of exercise was prescribed.
(4) Studies prescribing training *during* chemotherapy.
(5) Studies using objective measurements of muscle strength or endurance capacity.

Exclusion criteria

(1) Reviews, case reports, study protocols and animal studies.
(2) Studies with patients treated with palliative intention, for this is a very heterogeneous group of patients.
(3) Studies involving children.
(4) Studies prescribing training *after* chemotherapy.
(5) Studies measuring muscle strength or endurance capacity using questionnaires.

Database search

A database search of PubMed up to and including January 2015 was performed, limited to studies in English, German and Dutch languages. Also the reference lists of relevant papers were searched for additional articles. The search was performed using the following terms: neoplasms OR neoplasm* OR cancer OR tumor OR tumors OR tumor* AND chemotherapy OR chemotherap* AND exercise therapy OR exercise.

The effects of the studies were graded according to the best evidence of Steultjens et al. [19]. The quality of the evidence was categorized into strong evidence, moderate evidence, limited evidence, indicative findings or no evidence [19,20].

Methodological quality

Study quality was assessed based on "The Dutch Cochrane form for the assessment of randomized controlled trials" [21]. However, two of the three criteria for blinding procedures could not be rated, because in physical activity interventions it is impossible to blind patients and care providers to the treatment assignment. Therefore the following seven criteria were applied and were rated as follows: yes (+), no (-), partially (+/-) or unclear (?).

(1) Were subjects randomly allocated?
(2) Was allocation concealed?
(3) Was there blinding of outcome assessors?
(4) Were the groups similar at baseline?
(5) Is loss to follow-up less than 80%?
(6) Is an intention-to-treat analysis done?
(7) Were the two groups treated equally, except for the intervention?

Results

Study selection

The search resulted into 809 papers. The papers were screened for title and abstract by OH and CvM. In case of disagreement a third author was consulted. Twelve articles were selected for eligibility testing. Hand searching of the reference list of relevant reviews resulted in three additional articles. One article was excluded because it used the same data as another study, and focused mainly on hemoglobin changes during training [22]. In total 14 articles were included.

Quality assessment

Ratings of different quality criteria varied considerably (Table I). The median score for quality was 4.25, ranging from 1 to 7. Only one study met all the criteria. Only five studies (38%) had adequate allocation concealment. Blinding of the outcome assessors was fulfilled only in three studies. In most studies both study groups did not differ on baseline characteristic. Only a few studies took the drop-outs into account in their analyses and did an intention-to-treat analysis. In five studies the quality was very low, only scoring 1–3.5 of a maximum of seven criteria of the Cochrane Library Assessment forms. In these studies, besides the criteria mentioned in Table I, the outcome assessment was of low quality, the reasons for loss-to-follow-up were not mentioned [23], people trained in the control groups as well [24,25], or the training program was of very long duration [24].

Subjects

Eight (46%) studies involved a total number of 595 breast cancer patients. Six studies (46%) involved patients with hematologic malignancies, resulting in a total number of 317 patients. Four studies selected cancer patient receiving stem cell transplantations. Three studies involved a heterogeneous group of cancer patients (Table II).

The fitness level of the participants varied among the different studies. In the studies by Al-Majid, Hornsby and Campbell relatively young and fit breast cancer patients were recruited [26–28]. While Oechsle, Dimeo and Chang recruited relatively unfit patients, with hematological cancer types and Eastern Cooperative Oncology Group performance scores ranging from 0 to 3 [29–31]. Adherence among the different articles ranged from 66% to 82%.

The duration of the programs ranged from 3 to 52 weeks, with a median of 13.5 weeks. The frequency of the training sessions ranged from two to seven times per week, with a median of 5.5 sessions per week. Ten studies (71%) provided a supervised training program, three studies (23%) provided a home-based program and one study provided both (Table III).

In six studies (43%) a combination of resistance and aerobic training was applied. Six studies only focused on aerobic training. Only nine studies were accurate in describing the intensity of the training or the number of sets and repetitions. In the resistance exercises the intensity varied from 40% to 100% of 1-RM, and was mostly between 60% and 70% of 1-RM. All programs focused on large muscle groups and two studies used theraband exercises as training.

In the aerobic training stationary cycling and walking were prescribed most frequently. Three studies (23%) provided a walking program only [25,29,32]. The intensities varied from 50% to 100% of VO2max or HRmax. Several studies provided a high-intensity program with intensities ranging from 60% to 100% of HRmax or VO2peak [26,33–35], and others a more moderate program with intensities ranging from 50% to 70% of HRmax or VO2max [24,25,27,29,30,32]. The duration of the aerobic training was mostly between 10 and 30 minutes.

Endurance capacity

Variables of endurance capacity were assessed in 17 different intervention groups (14 articles) and reported beneficial effects in 10 groups (59%). Direct measurement of VO2max, which is the gold standard for measuring endurance capacity, was assessed in five intervention groups [25,27,31,32,34], indirect measurement of VO2max was measured in two intervention groups [27,28] (Table V). The studies reported significant increases due to training, which ranged from 8% to 31%. Endurance capacity decreased in nine of 13 control groups (69%), which ranged from 1% to 32% (Table VI). Effect sizes were very high in the papers of Al-Majid, and Campbell, 2, 7 and 2.3, respectively [26,28]. An effect size around 1 was calculated in the papers of Schwartz, Hornsby and Coleman [23,24,27] (Table IV).

Muscle strength

Muscle strength was assessed by means of a 1-RM test. Muscle strength improved significantly in 17 of 18 intervention groups (94%), ranging from 2% to 38%. Measures of upper body

Table I. Quality assessment of the studies.

	Randomization	Allocation concealment	Blinding	Baseline criteria	Follow-up	Intention-to-treat	Contamination	Total max = 7
Hornsby et al.	+	+	+	-	+	?	+	5
Coleman et al.	+	?	?	+	-	-	-	2
Lin et al.	-	+	?	+	?	+	+/-+	3,5
Oechsle et al.	+	?	?	+	+	-	+	4
Courneya et al.	+	+	?	+	+	+	+	6
Adamsen et al.	+	+	+	+	+	+	+	7
Dimeo et al.	+	?	+	+	+	+	+/-	5,5
Campbell et al.	+	?	?	+	+	+/-	+	4,5
Schwartz et al.	+	?	?	+	-	+	-	3
Baumann et al.	+	?	-	-	-	-	-	1
Segal et al.	+	+	?	+	+	+	+	6
Chang et al.	+	?	-	+	+	?	+	4
Griffith et al.	+	?	?	+	-	-	-	2
Al-Majid et al.	+	?	?	+	+	+	+	5

+ = 1 point, +/- = 0.5 point.

Table II. Overview of the study populations.

Primary author of the study	Number of participants	Cancer/stage	Age (meanyrs)	Male/female (number)	Treatment	Design of study
Hornsby et al., 2014	E = 10 C = 10	Breast, IIB-IIIC	E = 51 (+/−6) C = 46 (+/−11)	Females only	Ch	phase II RCT
Coleman et al., 2012	E = 95 C = 92	Multiple myeloma	E = 56 (+/−10) C = 56 (+/−9)	Male (109), female (78)	MC + PBST	repeated measures experimental design
Lin et al., 2013	E = 21 C = 24	Colorectal, II-III	E = 59 (+/−9) C = 54 (+/−10)	Male (26), female (19)	Ch	CT
Oechsle et al., 2014	E = 24 C = 24	AML, NHL, MM, germcelltumor	E = 52 (+/−13) C = 53 (+/−15)	Male (34) female (14)	Ch, MC + PBST	prospective pilot RCT
Courneya et al., 2007	AET = 78 RET = 82 C = 82	Breast, I-IIIA	AET = 49 RET = 50 C = 49	Females only	Ch	RCT
Adamsen et al., 2009	E = 135 C = 134	All	E = 47 (+/−10) C = 47 (+/−10)	Male (73) female (196)	Ch	RCT
Dimeo et al., 1997	E = 33 C = 37	Breast, germcell, sarcoma, (non)small cell lung cancer, adenocarcinoma, neuroblastoma	E = 39 (+/−10) C = 40 (+/−11)	Male (19) female (51)	Ch + PBST	RCT
Campbell et al., 2005	E = 12 C = 10	Breast	E = 48 (+/−10) C = 47 (+/−5)	Females only	Ch/R/combination	pilot RCT
Schwartz and Winters-Stone, 2009	AET = 34 RET = 34 C = 33	Breast, lymphoma, colon II-III	AET = 48 RET = 47 C = 48	Females only	Ch	RCT
Baumann et al., 2011	E = 17 C = 16	Hematologic malignancies	E = 41 (+/−12) C = 43 (+/−14)	Male (16) female (17)	Ch + HSCT	RCT
Segal et al., 2001	SD = 40 SV = 42 C = 41	Breast	SD = 51 (+/−9),SV = 51 (+/−9), C = 50 (+/−9)	Females only	Ch	RCT
Chang et al., 2008	E = 11 C = 11	AML	E= 49 (+/−15) C = 53 (+/−13)	Male(12) female (10)	Ch	RCT
Griffith et al., 2009	E = 68 C = 58	Breast, colorectal, prostate, other	E = 60 (+/−11) C = 61 (+/−11)	Male (49) female (77)	Ch/R	RCT
Al-Majid et al., 2015	E= 7 C = 7	Breast	E = 48 (+/−10) C = 53 (+/−11)	Females only	Ch	Pilot RCT

AET, aerobic exercise training group; AML, acute myeloid leukemia; C, control group; Ch, chemotherapy; CT, controlled trial; E, exercise group; HSCT, hematopoietic stem cell transplantation; MC, myeloablative chemotherapy; MM, multiple myeloma; NHL, non-Hodgkin lymphoma; PBST, peripheral blood stem cell transplantation; R, radiotherapy; RCT, randomized controlled trial; RET, resistance exercise training group; SD, self-directed exercise group; SV, supervised exercise group.

Table III. Overview of the training programs.

Primary author	Duration (weeks)	Frequency (session/week)	Supervised/ home-based
Hornsby et al., 2014	12	3	Supervised
Coleman et al., 2012	15	3–4	Home-based
Lin et al., 2013	12	2	Supervised
Oechsle et al., 2014	~3	5	Supervised
Courneya et al., 2007	18	3	Supervised
Adamsen et al., 2009	6	5	Supervised
Dimeo et al., 1997	Unspecified	7	Supervised
Campbell et al., 2005	12	2	Supervised
Schwartz and Winters-Stone, 2009	52	4	Home-based
Baumann et al., 2011	~2.5	7	Supervised
Segal et al., 2001	26	5	Supervised + home-based
Chang et al., 2008	3	5	Supervised
Griffith et al., 2009	13	5	Home-based
Al-Majid et al., 2015	9–12	5–6	Supervised

strength (chest press) and lower body strength (leg press) were measured in nine intervention groups [24,33–35], and showed an increase in eight groups. The increase on the leg press ranged from 4% to 33% and the increase in chest press ranged from 12% to 38%. Muscle strength also improved in 11 of 14 control groups (79%), but this increase was only minimal, ranging from 1.3% to 6.5%. An effect size of 0.3–0.8 was calculated in the papers of Courneya, Adamsen and Schwartz [24,33,34].

Discussion

Summary of evidence

This paper gains insight into the different training modalities during cancer treatment with chemotherapy and focuses on the most effective way to improve physical fitness and muscle strength. The objective was to compose a training program in which people undergoing chemotherapy could be trained in the most effective way. In total 14 papers could be identified in which a training program during chemotherapy was compared to a control group. In addition to earlier reported improvements in cancer-related fatigue [16] these papers provide evidence to suggest that an exercise intervention during treatment with chemotherapy is associated with significant improvements in muscle strength as well as endurance capacity. Although the purpose of this study was to find the most effective way to improve endurance capacity and muscle strength, the papers were too heterogeneous to draw a distinct conclusion. Also, there was a lack in a consistent methodological approach in the dose of the training.

Limitations

This review is based on a small number of papers (n = 14), their poor methodological quality suggests that not much research on this specific topic has been done so far. Most research has been done on quality of life or cancer-related fatigue [7,13–16]. Furthermore, there was a large diversity in the study populations which ranged from very fit to unfit patients. There was also a considerable heterogeneity in tumor types, tumor stage and outcome measures.

Table IV. Overview of training modalities and intensities of the different studies, including effect sizes (Cohen's *d*).

	Resistance training				Aerobic training			
Primary author	Resistance exercises	Sets and reps	Intensity	Effect size (Cohen's *d*) RET	Aerobic exercises	Duration (min)	Intensity/effect size (Cohens' *d*)	Effect size (Cohen's *d*) AET
(Hornsby et al., 2014)					Stationary cycling	15–30min	60–100% VO2max	1.1
(Coleman et al., 2012)	Biceps curl, triceps extension, chair stands, hamstring strengthening, therabands	Us	60–80% 1-RM	NA	Aerobic walking	Us	65–80% max HR	1.1
(Lin et al., 2013)	Arm, abdomen, thigh, gluteus, therabands, dumbbell	Us	Us	Knee: 0.2 Hand: −0.1	Stationary cycling	30–40 min	60–75% max HR	0.0
(Oechsle et al., 2014)	Bridging, sit-ups, back, arm, elastic band	2 sets, 16–25 rep	40–60% 1-RM	NA	Stationary cycling	10–20 min	Us	0.3
(Courneya et al., 2007)	Leg extension, leg press, chest press, leg curl, calf raises, seated row, triceps extension, biceps curl, curl ups	2 sets, 8–12 reps	60–70% 1-RM	Leg: 0.4 Chest: 0.8	Stationary cycling	15–45 min	60–80% VO2max	0.3
(Adamsen et al., 2009)	Leg press, chest press, pull down, abd crunch, lower back, knee ext	3 sets, 5–8 rep	70–100% 1-RM	Leg: 0,6 Chest: 0,3	Stationary cycling	15 min	85–95% max HR	0.2
(Dimeo et al., 1997)					In-bed cycling	30 min interval	50% cardiac reserve	0.3
(Campbell et al., 2005)					Walking, cycling, low-level aerobics, muscle strengthening exercises, circuits	10–20 min	60–75% age-adjusted max HR	2.3
(Schwartz and Winters-Stone, 2009)	Theraband	3 sets, 12 rep/2 sets 18–20 rep	Us	Leg: 0.5 Arm: 0.5	Walking, jogging, dancing	20–30 min	Us	1.3
(Baumann et al., 2011)					Stationary cycling, walking, stair climbing, coordination, strengthening	10–40 min	80% watt load WHO test	1.0
(Segal et al., 2001)					Walking	Us	50–60% predicted VO2max	NA
(Chang et al., 2008)					Walking	12 min	resting HR +30	0.65
(Griffith et al., 2009)					Walking	20–30 min	50–70% max HR	NA
(Al-Majid et al., 2015)					Treadmill walking	Us	50–80% max HR	2.7

AET, aerobic exercise training; HR, heart rate; NA, not applicable; 1-RM, one-repetition maximum; reps, repetitions; RET, resistance exercise training; us, unspecified.

Table V. Physical outcome measures of endurance capacity in the intervention groups and control groups.

Outcome measure	*Number of intervention groups assessed*	*Increase*	*Decrease*	*No-effect*	*Best evidence synthesis*
Intervention groups					
VO2max (ml/kg/min)	7	4	3	1	Moderate evidence
VO2max (l/min)	1	1	0	0	Low evidence
12MWT	4	4	0	0	Low evidence
6MWT	2	1	1	0	No evidence
Walking speed (km/h)	1	0	1	0	Limited evidence
Watt	1	0	0	1	No evidence
TOTAL	17	10	5	2	
Control groups					
VO2max (ml/kg/min)	6	0	4	2	Moderate evidence
VO2max (l/min)	1	1	0	0	Low evidence
12MWT	3	0	3	0	Low evidence
6MWT	2	1	0	1	No evidence
Walking speed (km/h)	1	0	1	0	Limited evidence
Watt	1	0	1	0	No evidence
TOTAL	14	2	9	3	

Table VI. Physical outcome measures of muscle strength in the intervention groups and control groups.

Outcome measure (1-RM)	*Number of intervention groups assessed*	*Increase*	*Decrease*	*No-effect*	*Best evidence synthesis*
Intervention groups					
Leg press	6	6	0	0	Moderate
Chest press	3	2	1	0	Strong
Hand grip strength	2	2	0	0	Indicative findings
Pull down	1	1	0	0	Low
Bridging	1	1	0	0	Indicative findings
Sit-ups	1	1	0	0	Indicative findings
Seated row	2	2	0	0	Indicative findings
Overhead press	2	2	0	0	Indicative findings
TOTAL	18	17	1	0	
Control groups					
Leg press	4	4	0	0	Moderate
Chest press	3	2	1	0	Strong
Hand grip strength	2	2	0	0	Indicative findings
Pull down	1	1	0	0	Low
Bridging	1	1	0	0	Indicative findings
Sit-ups	1	1	0	0	Indicative findings
Seated row	1	0	1	0	Indicative findings
Overhead press	1	0	1	0	Indicative findings
TOTAL	14	11	3	0	

The participation level in most papers was low. This suggests that only motivated patients participated in the studies. This is an important finding, it may have influenced the results, but is also a point of concern for future training programs, as unmotivated patients should be more encouraged and involved into training programs. As a result of the heterogeneity on several topics it was not possible to provide a meta-analysis. This was also the case in other reviews, focusing on the specific outcomes of objectively measured improvements in aerobic capacity and muscle strength [36,37]. Another limitation is the fact that only PubMed was searched, limiting the number of articles. Furthermore, we had to exclude some studies, e.g. a randomized controlled trial by Courneya et al. [38] in which no difference could be made between patients during and off treatment with chemotherapy.

Endurance capacity

Our review showed a general increase in endurance capacity. In people receiving chemotherapy for the treatment of lymphomas while not training, Vermaete et al. found a decrease of 7.8% in endurance capacity (VO2max) [39]. The magnitude of the improvement in our review, however, was inconsistent among the different groups. The improvement ranged from 4% to 33%. The greatest increase was seen in the study by Campbell et al. [26], which showed a 31% improvement on the 12-minute walking test after a follow-up of 12 weeks. Unfortunately, the sample size in this study was very small and the methodological quality was moderate. The calculated effect sizes were the highest in the papers by Campbell and Al-Majid, suggesting that the most effective training intensity ranges from 60% to 80% of maximum heart rate. The subjects in these papers were relatively fit breast cancer patients. In the paper by Courneya et al., lymphoma patients were provided with aerobic exercise training for 12 weeks. At post-intervention, the aerobic exercise training group was superior to the usual care group on all indicators of physical fitness, including VO2max [38]. This is comparable to the results of this review.

Muscle strength

Chemotherapy normally causes a severe decrease in muscle strength, especially in striated muscles [40]. Vermaete et al. showed a decrease of 5.6–14.6% in muscle strength in people not training and receiving chemotherapy for lymphoma [39]. In our review the muscle strength improved in the intervention groups as well as in the control groups, although the increase in the control groups was only minimal. A reason for the increase could be the high level of contamination. Many people in the control groups did a lot of training by themselves. This may have influenced the results. The calculated effect sizes were the highest in the papers of Courneya, Adamsen and Schwartz, the patients in these papers trained in 60–100% of 1-RM, in 2–3 sets of 5–12 repetitions. This suggests that the most effective training intensity is in that range. This is in concordance with De Backer et al., in which patients were trained after receiving chemotherapy. The patients trained at an intensity level of 65–80% of 1-RM in two sets of 10 repetitions, with an effect size of 1.3–2.7 [7]. This paper also showed long-term effects of a maintained muscle strength and quicker return to work [8].

Recent research suggests that cancer survivors experience participation in exercise-based rehabilitation as a means to fulfil their mental, social and physical well being independent of disease status [41]. Other papers suggest associations between lifetime and recent pre-diagnosis recreational physical activity and risk of all-cause death [42]. We continually need to raise awareness among health professionals to continue to suggest modifications to impact on fatigue and physical performance at all stages of cancer treatment and into survivorship and late effects [43].

It is important to know which training intensity and duration is the most effective in training cancer patients in order to provide a training program suitable for every cancer patient. Training should be based on good research and implemented into international guidelines. Furthermore, it should be implemented into daily practice.

Conclusion

This literature review focuses specifically on the objectively assessed outcome measures muscle strength and endurance capacity in training programs during chemotherapy. It shows that training during chemotherapy is an effective way to improve muscle strength and endurance capacity in cancer patients. The overall positive results of training may warrant a more active approach to incorporate training in standard care. Given the limited availability of studies and the lack of standardization it is currently still unclear what training modalities are the best way to improve muscle strength and physical fitness. Future research should specifically focus on finding the most effective exercise intensity with the aim to gain insight into the most effective way to improve both muscle strength and endurance capacity in different patient groups.

Suggestions for future research

Future research should use valid and reliable physical outcome measures, such as VO2peak and upper- and lower body strength measures (1-RM). Furthermore, it is important to blind the outcome assessors. Also, a detailed prescription of the exercise intervention in terms of duration, intensity and frequency should be provided.

Although it is important to compare an intervention group to a control group, the high level of contamination suggests that this is difficult in daily practice. Patients participating in a study who are allocated to a control group tend to start training by themselves. A fair approach is to use a different method of research, such as clinical comparative research which is more practice based and combines implementation of effective intervention with research aiming to optimize these interventions [44].

Conflict of interest

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

References

1. Ferlay J, Steliarova-Foucher E, Lortet-Tieulent J, Rosso S, Coebergh JW, Comber H, et al. Cancer incidence and mortality patterns in Europe: estimates for 40 countries in 2012. Eur J Cancer 2013;49:1374–403.
2. VIKC. PHnk Landelijke richtlijn oncologische revalidatie 2011 [cited 2014 23-01]. 1:Available from: http://www.oncoline.nl/oncologische-revalidatie.
3. Courneya KS. Exercise in cancer survivors: an overview of research. Med Sci Sports Exerc 2003;35:1846–52.
4. Courneya KS, Friedenreich CM. Physical exercise and quality of life following cancer diagnosis: a literature review. Ann Behav Med 1999;21:171–9.
5. Greene D, Nail LM, Fieler VK, Dudgeon D, Jones LS. A comparison of patient-reported side effects among three chemotherapy regimens for breast cancer. Cancer Pract 1994;2:57–62.
6. Schwartz AL. Fatigue mediates the effects of exercise on quality of life. Qual Life Res 1999;8:529–38.
7. De Backer IC, Van Breda E, Vreugdenhil A, Nijziel MR, Kester AD, Schep G. High-intensity strength training improves quality of life in cancer survivors. Acta Oncologica 2007;46:1143–51.
8. De Backer IC, Vreugdenhil G, Nijziel MR, Kester AD, van Breda E, Schep G. Long-term follow-up after cancer rehabilitation using high-intensity resistance training: persistent improvement of physical performance and quality of life. Br J Cancer 2008;99:30–6.
9. Thijs KM, de Boer AG, Vreugdenhil G, van de Wouw AJ, Houterman S, Schep G. Rehabilitation using high-intensity physical training and long-term return-to-work in cancer survivors. J Occup Rehabil 2012;22:220–9.
10. Dimeo F. Exercise for cancer patients: a new challenge in sports medicine. Br J Sports Med 2000;34:160–1.
11. Lucia A, Earnest C, Perez M. Cancer-related fatigue: can exercise physiology assist oncologists? Lancet Oncol 2003;4:616–25.
12. Irwin M. ACSM's Guide to Exercise and Cancer Survivorship. Champaign: Human Kinetics; 2010.
13. Cramp F, Byron-Daniel J. Exercise for the management of cancer-related fatigue in adults. Cochrane Datab Syst Rev 2012;11:CD006145
14. Mcneely ML, Campbell KL, Rowe BH, Klassen TP, Mackey JR, Courneya KS. Effects of exercise on breast cancer patients and survivors: a systematic review and meta-analysis. CMAJ 2006;175:34–41.
15. Mishra SI, Scherer RW, Snyder C, Geigle PM, Berlanstein DR, Topaloglu O. Exercise interventions on health-related quality of life for people with cancer during active treatment. Clin Otolaryngol 2012;37:390–2.
16. Velthuis MJ, Agasi-Idenburg SC, Aufdemkampe G, Wittink HM. The effect of physical exercise on cancer-related fatigue during cancer treatment: a meta-analysis of randomised controlled trials. Clin Oncol (R Coll Radiol) 2010;22:208–21.
17. WRTNFGLSP. ACSM's guidelines for exercise testing and prescription. American College of Sports Medicine. 2010;(3)(8th ed).
18. Schmitz KH, Courneya KS, Matthews C, Demark-Wahnefried W, Galvao DA, Pinto BM, et al. American College of Sports Medicine roundtable on exercise guidelines for cancer survivors. Med Sci Sports Exerc 2010;42:1409–26.
19. Steultjens EM, Dekker J, Bouter LM, van de Nes JC, Cup EH, van den Ende CH. Occupational therapy for stroke patients: a systematic review. Stroke 2003;34:676–87.
20. Atkins D, Best D, Briss PA, Eccles M, Falck-Ytter Y, Flottorp S, et al. Grading quality of evidence and strength of recommendations. BMJ 2004;328:1490
21. Library TDC. FORMULIER II voor het beoordelen van een RANDOMISED CONTROLLED TRIAL (RCT) [cited 2014 28-01]. Available from: http://dcc.cochrane.org/beoordelingsformulieren-en-andere-downloads.
22. Dolan LB, Gelmon K, Courneya KS, Mackey JR, Segal RJ, Lane K, et al. Hemoglobin and aerobic fitness changes with supervised exercise training in breast cancer patients receiving chemotherapy. Cancer Epidemiol Biomark Prev 2010;19:2826–32.
23. Coleman EA, Goodwin JA, Kennedy R, Coon SK, Richards K, Enderlin C, et al. Effects of exercise on fatigue, sleep, and performance: a randomized trial. Oncol Nursing Forum 2012;39:468–77.
24. Schwartz AL, Winters-Stone K. Effects of a 12-month randomized controlled trial of aerobic or resistance exercise during and following cancer treatment in women. Phys Sports Med 2009;37:62–7.
25. Griffith K, Wenzel J, Shang J, Thompson C, Stewart K, Mock V. Impact of a walking intervention on cardiorespiratory fitness, self-reported physical function, and pain in patients undergoing treatment for solid tumors. Cancer 2009;115:4874–84.
26. Campbell A, Mutrie N, White F, Mcguire F, Kearney N. A pilot study of a supervised group exercise programme as a rehabilitation treatment for women with breast cancer receiving adjuvant treatment. Eur J Oncol Nurs 2005;9:56–63.
27. Hornsby WE, Douglas PS, West MJ, Kenjale AA, Lane AR, Schwitzer ER, et al. Safety and efficacy of aerobic training in operable breast cancer patients receiving neoadjuvant chemotherapy: A phase II randomized trial. Acta Oncol 2014;53:65–74.
28. Al-Majid S, Wilson LD, Rakovski C, Coburn JW. Effects of exercise on biobehavioral outcomes of fatigue during cancer treatment: results of a feasibility study. Biol Res Nurs 2015;17:40–8.
29. Chang PH, Lai YH, Shun SC, Lin LY, Chen ML, Yang Y, et al. Effects of a walking intervention on fatigue-related experiences of hospitalized

acute myelogenous leukemia patients undergoing chemotherapy: a randomized controlled trial. J Pain Symptom Manage 2008;35:524–34.
30. Dimeo F, Fetscher S, Lange W, Mertelsmann R, Keul J. Effects of aerobic exercise on the physical performance and incidence of treatment-related complications after high-dose chemotherapy. Blood 1997;90:3390–4.
31. Oechsle K, Aslan Z, Suesse Y, Jensen W, Bokemeyer C, de Wit M. Multimodal exercise training during myeloablative chemotherapy: a prospective randomized pilot trial. Support Care Cancer 2014;22:63–9.
32. Segal R, Evans W, Johnson D, Smith J, Colletta S, Gayton J, et al. Structured exercise improves physical functioning in women with stages I and II breast cancer: results of a randomized controlled trial. J Clin Oncol 2001;19:657–65.
33. Adamsen L, Quist M, Andersen C, Moller T, Herrstedt J, Kronborg D, et al. Effect of a multimodal high intensity exercise intervention in cancer patients undergoing chemotherapy: randomised controlled trial. BMJ 2009;339:b3410.
34. Courneya KS, Segal RJ, Mackey JR, Gelmon K, Reid RD, Friedenreich CM, et al. Effects of aerobic and resistance exercise in breast cancer patients receiving adjuvant chemotherapy: a multicenter randomized controlled trial. J Clin Oncol 2007;25:4396–404.
35. Lin KY, Shun SC, Lai YH, Liang JT, Tsauo JY. Comparison of the effects of a supervised exercise program and usual care in patients with colorectal cancer undergoing chemotherapy. Cancer Nurs 2013;4.
36. Markes M, Brockow T, Resch KL. Exercise for women receiving adjuvant therapy for breast cancer. Cochrane Datab Syst Rev 2006:CD005001;37:21–29.
37. Bergenthal N, Will A, Streckmann F, Wolkewitz KD, Monsef I, Engert A, et al. Aerobic physical exercise for adult patients with haematological malignancies. Cochrane Datab Syst Rev 2014;11:CD009075.
38. Courneya KS, Sellar CM, Stevinson C, Mcneely ML, Peddle CJ, Friedenreich CM, et al. Randomized controlled trial of the effects of aerobic exercise on physical functioning and quality of life in lymphoma patients. J Clin Oncol 2009;27:4605–12.
39. Vermaete N, Wolter P, Verhoef G, Gosselink R. Physical activity and physical fitness in lymphoma patients before, during, and after chemotherapy: a prospective longitudinal study. Ann Hematol 2014;93:411–24.
40. Gilliam LA, St Clair DK. Chemotherapy-induced weakness and fatigue in skeletal muscle: the role of oxidative stress. Antioxid Redox Signal 2011;15:2543–63.
41. Midtgaard J, Hammer NM, Andersen C, Larsen A, Bruun DM, Jarden M. Cancer survivors' experience of exercise-based cancer rehabilitation - a meta-synthesis of qualitative research. Acta Oncol 2015;54:609–17.
42. Lahart IM, Metsios GS, Nevill AM, Carmichael AR. Physical activity, risk of death and recurrence in breast cancer survivors: A systematic review and meta-analysis of epidemiological studies. Acta Oncol 2015;54:635–54.
43. Minton O, Jo F, Jane M. The role of behavioural modification and exercise in the management of cancer-related fatigue to reduce its impact during and after cancer treatment. Acta Oncol 2015;54:581–6.
44. Horn SD, Dejong G, Deutscher D. Practice-based evidence research in rehabilitation: an alternative to randomized controlled trials and traditional observational studies. Arch Phys Med Rehabil 2012;93:S127–37.