Resistance Training in Cancer Survivors: A Systematic Review

Authors I. C. De Backer[1], G. Schep[1], F. J. Backx[2], G. Vreugdenhil[3], H. Kuipers[4]

Affiliations
[1] Maxima Medical Centre, Sports Medicine, Veldhoven, Netherlands
[2] Department of Rehabilitation and Sports Medicine, University Medical Centre Utrecht, Utrecht, Netherlands
[3] Maxima Medical Centre, Internal Medicine, Veldhoven, Netherlands
[4] University Maastricht, Human Movement Sciences, Maastricht, Netherlands

Key words
- cancer
- rehabilitation
- exercise
- resistance training
- muscle strength

accepted after revision
April 28, 2009

Bibliography
DOI 10.1055/s-0029-1225330
Published online:
July 7, 2009
Int J Sports Med 2009; 30: 703–712 © Georg Thieme Verlag KG Stuttgart · New York
ISSN 0172-4622

Correspondence
I. C. De Backer, MSc
Maxima Medical Centre
Sports Medicine
De Run 4600
5500MB Veldhoven
Netherlands
Tel.: +0031/40/88 88 620
Fax: +0031/40/88 88 584
I.deBacker@students.uu.nl

Abstract

This systematic review summarizes the research of previous studies that used resistance training in the post-treatment phase of cancer patients with a focus on methodological quality, training methods and physical outcome measures. We found twenty-four studies (10 RCTs, 4 controlled clinical trials and 10 uncontrolled trials) that met all inclusion criteria. The studies were of moderate methodological quality. The majority of studies involved breast cancer patients (54%), followed by prostate cancer patients (13%). Most studies used a combination of resistance and aerobic training, which was mostly supervised. Resistance training involved large muscle groups, with 1–3 sets of 8–12 repetitions. The duration of the resistance training programs varied from 3–24 weeks, with a training frequency of 1–5 sessions per week. The training intensity ranged from 25% to 85% of the one-repetition maximum. Overall, positive training effects were observed for cardiopulmonary and muscle function, with significant increases in peak oxygen uptake (range: 6–39%), and in the one-repetition maximum (range: 11–110%). In general, there were no effects of training on body composition, endocrine and immune function, and haematological variables. No adverse effects of the resistance training were reported. Based upon these results, we recommend to incorporate resistance training in cancer rehabilitation programmes.

Introduction

Cancer treatment has made substantial progress in the last few decades, resulting in more survivors [22]. However, cancer and its treatment are still associated with adverse psychosocial and physical side effects. Physical side effects including fatigue, a decreased muscle strength, reduction of lean body mass, bone mass, and aerobic capacity, causes an overall decrease in the quality of life [7,8,37].

Regular physical exercise has been shown to counteract adverse side effects of cancer treatment by improving patient's health status. Post training effects comprise an increase in cardiopulmonary function, muscle strength, bone mineral density, and quality of life, with a reduction in body weight, fat mass and feelings of fatigue [44].

Despite the current physiological insight into cancer-related muscle wasting and the potential beneficial role of resistance training, which was discussed in the review of Al-Majid et al., most rehabilitation programmes use predominantly aerobic exercises [29]. However, recent randomized controlled trials (RCTs) showed that resistance training has a great potential to counteract the adverse side effects of cancer, such as muscle wasting [26,54]. Most resistance training studies in cancer patients have focused on quality of life and psychosocial outcome measures and less on physical outcome measures [44]. Furthermore, most resistance training studies involved breast cancer patients [4].

Therefore, the gap between the physiological knowledge about benefits of resistance training and the limited number of intervention studies with resistance training in cancer patients justifies a systematic review of current research in all cancer survivors with a focus on methodological quality, training methods and physical outcome measures.

The objectives of this review are:
- to systematically review the studies that use resistance training after cancer treatment;
- to give an overview of the different types of resistance training (type of exercises, intensity, and duration);

- to assess effects of resistance training;
- to make recommendations for future studies.

Methods

Database Search

Using database searches of PubMed and Embase, a literature review up to December 2008 was performed, limited to studies in English, German, French and Dutch languages. In addition, bibliographies of previous review articles about exercise and cancer were examined [4,6,19,30,31,42,50]. The search combined key words related to cancer (oncology, neoplasm, tumour, malignancy), cancer treatment (chemotherapy, radiotherapy, surgery, hormonal therapy) and exercise (exercise training, training, physical activity, rehabilitation, resistance training, aerobic training, strength training, lifestyle, endurance, resistance).

Inclusion and exclusion criteria

Study design

Included were randomized controlled designs (RCTs), but due to the limited number of studies, non-randomized controlled trials as well as uncontrolled trials published in peer-reviewed journals were also included. Abstracts and case reports were excluded.

Subjects

Included were studies involving adult patients (> 18 years), diagnosed for malignancy and treated with curative intention. Excluded were studies, in which patients were treated with palliative intention. Studies with children were excluded since in children prevalence of tumour types and treatment are very different as compared to adults.

Intervention

Included were studies prescribing resistance training alone or in combination with other training modalities (e.g. aerobic training).

Timing of the intervention

Only studies prescribing resistance training after chemotherapy were included. Studies prescribing resistance training during chemotherapy were excluded since other exercise targets are involved during treatment, and as a result, probably other intensities, frequencies and durations of exercise are warranted [27].

Outcome. measures

All outcome measures that were studied in the above selected studies were addressed. The observed effects in the intervention studies were graded according to the best-evidence synthesis of Steultjens et al. [55]. The quality of evidence was categorized into strong evidence, moderate evidence, limited evidence, indicative findings or no evidence [2,55].

Methodological quality

Study quality was assessed primarily based on the PEDro scale [38] However, two of the three criteria for blinding procedures could not be rated, because in physical activity interventions it is almost impossible to blind patients and care providers to the treatment assignment. Therefore, we applied ten quality criteria (see below), which were rated as follows: yes (+), no (−), partially (+/−), or unclear (?).

1) Were eligibility criteria specified?
2) Were subjects randomly allocated?
3) Was allocation concealed?
4) Were the groups similar at baseline?
5) Was there blinding of outcome assessors?
6) Was adherence to exercise greater than 70%?
7) Were there fewer than 15% drop-outs?
8) Was the analysis an intention-to-treat analysis?
9) Was there supervision of the exercise?
10) Was the type of resistance training specified?

Results

Database search

After selection of a total number of 135 papers, 34 papers were considered potentially relevant. Application of all desired inclusion criteria resulted in a final inclusion of 24 studies [1,5,10–12,21,24–26,28,32,34,36,40,41,43,45–47,49,51,52,54,56], consisting of 10 RCTs [25,26,36,40,41,43,45–47,54], 4 controlled clinical trials (CTs) [3,12,23,28], and 10 uncontrolled trials (Ts) [5,11,12,18,21,32,34,51,52,56]. Three RCTs randomized between two different exercise protocols [25,40,43], and four studies [21,24,47,54] resulted in several publications, but were considered as one study.

Subjects and timing of intervention

Table 1 shows the study population of the 24 included studies. Thirteen studies (54%) involved a total number of 586 breast cancer patients [5,25,26,28,32,34,36,41,45–47,52,56]. Most breast cancer patients received chemotherapy. As shown in **Table 1**, the timing of intervention in breast cancer patients varied considerably, ranging from 2 weeks to 60 months post-treatment.

Three studies (13%) involved prostate cancer patients, resulting in a total number of 196 patients [11,21,54]. All patients received androgen deprivation therapy (ADT), and the timing of interventions ranged from 29 to 47 months after diagnosis.

Six studies (25%) involved a heterogeneous group of cancer patients [3,12,13,18,23,40], with a timing of intervention that ranged from unspecified to 14 months post treatment. One study selected cancer patients after peripheral blood stem cell transplantation [23]. Latter patients started with a relatively fast intervention (on average 17 days after stem cell infusion).

Intervention

Table 2 shows an overview of the resistance training programmes. The duration of the programmes ranged from 3 to 24 weeks, with a median score of 12 weeks. Most training programmes prescribed 2 or 3 sessions per week. In 20 studies (83%) a combination of resistance and aerobic training was applied. Four studies only focused on resistance training [21,43,47,54]. Regarding the prescription of resistance training, only 9 studies (37%) were accurate in describing the number of sets and repetitions, or the intensity of the training [5,12,13,21,23,26,36,43,54]. In particular, the training intensity was rarely stated, or given in global terms, such as "as tolerated" or "moderate". Ten studies reported exercise intensities in percentages of one-repetition maximum (1-RM). For upper and lower body exercises and for the abdominal and lower back muscles training

Table 1 Overview of the study population.

Primary author of the study	Number of patients	Cancer	Stage	Age yrs (mean ± sd)	Treatment	Timing of intervention
Kolden [32]	40	breast	I–III	55 ± 8	100 %S, 60 %RT, 65 %C	83 % within 12 months after diagnosis, most during treatment
Turner [56]	10	breast	us	47 ± 8	100 % S, 100 %RT, 100 %C	4–60 months post-diagnosis
Lane [34]	16	breast	I–III	52 ± 7	100 %S, 100 %RT, ? %C	>6 months post-treatment
Cheema [5]	27	breast	I–III	58 ± 7	100 % S, 67 %RT, 52 %C	mean: 60 months post-treatment
Schneider [52]	113	breast	us	56 ± 10	us	85 % post-treatment, 15 % during treatment
Hutnick [28]	E = 28, C = 21	breast	I–III	50 ± 10*	100 %S, 71 %RT, 100 %C	2 weeks 2 months post-treatment
Nieman [46]	E = 6, C = 6	breast	us	56 ± 4*	100 % S, 100 %RT, 100 %C	mean: 36 months post-diagnosis
McKenzie [41]	E = 7, C = 7	breast	I–II	57 ± 9*	us	>6 months post-treatment
Ohira [47], Ahmed [1], Schmitz [49]	E = 43, C = 43	breast	I–III	53 ± 8*	70 %C	3–34 months post-treatment
Herrero [26]	E = 8, C = 8	breast	I–II	51 ± 8*	100 %S, 100 %RT, 100 %C	24–60 months post-treatment
Milne [45]	E = 29, C = 29	breast	I–III	55 ± 8*	? %S, 60 %RT, 71 %C	mean: 13 months post-treatment
Heim [25]	E_1 = 32, E_2 = 31	breast	us	31–70**	100 %S, 79 %RT, 63 %C	60 % within 12 months after diagnosis
Ligibel [36]	E = 40, C = 42	breast	I–III	52 ± 9*	100 %S, ? %RT, 72 %C	us
Galvao [20, 21]	10	prostate	us	70 ± 8	100 % ADT	mean: 47 months post-diagnosis
Culos-Reed [11]	31	prostate	us	65 ± 10	100 % ADT	mean: 34 months post-diagnosis
Segal [54], Courneya [10]	E = 82, C = 73	prostate	I–IV	68 ± 8*	100 % ADT, 61 % curative, 39 % palliative	mean: 29 months post-diagnosis
Schneider [51]	135	breast + prostate	us	59 ± 10	93 %S, 40 %RT, 47 %C	84 % post-treatment, 16 % during treatment
McNeely [43]	E_1 = 27, E_2 = 25	head + neck	I–IV	52 ± ?	100 %S, 85 %RT, 27 %C	median: 15 months post-surgery
De Backer [12]	57	diverse	us	50 ± 11	84 %S, 56 %RT, 100 %C	mean: 7 months post-treatment
Dimeo [18]	32	diverse	us	52 ± 7	? % S, 9 %RT, 68 %C	us
Berglund [3]	E = 30, C = 30	diverse	us	54 ± ?*	100 % S, 90 %RT, 25 %C	< 2 months post-treatment
De Backer [13]	E = 49, C = 22	diverse	us	49 ± 9*	89 %S, 68 %RT, 100 %C	mean: 7 months post-treatment
Hayes [23, 24]	E = 6, C = 6	diverse	us	47 ± ?*	100 % PBST	mean: 17 days post-stem cell infusion
May [40]	E_1 = 75, E_2 = 69	diverse	us	49 ± 11	86 %S, 57 %RT, 68 %C	mean: 14 months post-treatment

* Weighted mean of intervention and control group.** Range of age. us = unspecified; E = exercise group; E1, E2 = different exercise protocols; C = control group; ADT = androgen deprivation therapy; S = surgery; RT = radiation therapy; C = chemotherapy; PBST = peripheral blood stem cell transplantation

intensities varied mostly between 60–85 % and 30–60 % of 1-RM, respectively.

As shown in **Table 2**, outdoor or treadmill walking and stationary cycling were the most frequently prescribed aerobic exercises. In several training programmes patients could choose their aerobic activity. Intensities of aerobic exercises varied from 40 % to 90 % of maximal heart rate or maximal exercise capacity. Nine studies used a percentage of maximal heart rate to control the training intensity [5, 18, 23, 26, 36, 46, 51, 52, 56], while five studies prescribed the training intensity by using a percentage of maximal workload or aerobic capacity [12, 13, 28, 32, 34].

Physical outcome measures

Table 3 presents the different physical outcome measures of the studies.

Body composition

Body composition was assessed in 11 studies [5, 11, 12, 26, 28, 32, 34, 36, 49, 54, 56]. There was no evidence for significant effects of the training programmes on BMI, fat mass or waist circumference. Three studies reported significant effects of training on lean body mass, of which two are of high quality [26, 49] Schmitz et al. [49], using Dual-Energy X-ray Absorptiometry (DEXA), found a significant increase in lean body mass of 0.88 kg, and a decrease in percentage body fat of 1.15 % after a 6-months training programme. Herrero et al. [26] found a significant increase of 1 kg in muscle mass after an 8-weeks training programme. Muscle mass was indirectly estimated from anthropometrical data by the prediction equation of Lee et al. [35].

Cardiopulmonary function

Variables of cardiopulmonary function were assessed in 13 studies, and all studies reported beneficial effects in at least one variable. Peak oxygen uptake, the gold standard for measuring cardiopulmonary function, was assessed in 7 studies [5, 12, 13, 23, 26, 28, 40]. All studies reported significant post training increases from 6 % to 39 %. The largest increase was observed in a study with patients, who underwent stem cell transplantation. Three studies

Table 2 Training prescription in cancer survivors after medical treatment.

Primary author of the study	Duration (weeks)	Frequency sessions/week	Resistance training prescription			Aerobic training		
			Exercises	Sets and reps	Intensity	Exercise	Duration (min)	Intensity
Kolden [32]	16	3	resistance bands, dumbbells, variable resistance machines	us	us	walking, cycling, step, or dance	20	40–60 % max aerobic capacity
Turner [56]	8	3	us	2–3 sets 8–12 rep	moderate	aerobics, water-based exercises	40–60	70–90 % max HR
Lane [34]	20	3	seated row, bench press, lat pull-down, rowing, triceps extension, biceps curl	2–3 sets 10 rep	as tolerated	participants may choose	30–45	60 % max effort
Cheema [5]	8	2	bench press, leg press, lat pull-down, leg curl, shoulder press, split squat, biceps curl, calf raise, triceps press down, abdominal	1–3 sets	8–12 RM	treadmill walking, stationary cycling, aerobics	15–30	65–85 % max HR
Schneider [52]	24	2 or 3	us exercises	us	us	walking, cycling, stepping or underwater treadmill	40	40–75 % max of HRR
Hutnick [28]	12	3	4 upper body exercise, 4 lower body exercises	1–3 sets 8–12 rep	us	treadmill or outdoor running, walking	10–20	60–75 % functional capacity
Nieman [46]	8	3	7 us exercises	2 sets 12 rep	us	walking on indoor track	30	75 % max HR
McKenzie [41]	8	3	seated row, bench press, lat pull-down, rowing triceps extension, biceps curl	2–3 sets 10 rep	as tolerated	arm cycle ergometer	5–20	8.3–25W
Ohira [47], Ahmed [1], Schmitz [49]	24	2	9 exercises for muscles of the chest, back, shoulders, arms, buttocks, hips, thighs	1–3 sets 8–12 rep	as tolerated	–	–	–
Herrero [26]	8	3	chest press, shoulder press, leg extension, leg curl, leg press, calf raise, abdominal crunch, low back extension, arm curl, arm extension, lateral pull-down	1–3 sets	12–15 RM to 8–12 RM	ergometer cycling	30	70–80 % max HR
Milne [45]	12	3	chest press, chest extension, biceps curl, triceps extension, leg extension, leg curls, hip ab- and adduction, back extension, abdominal crunches, fly's, leg press	2 sets 10–15 reps	us	cycle and rowing ergometers, mini-trampoline, step-up blocks	20	us
Heim [25]	?	3	9 exercises for all large muscle groups	us	us	walking	30	us
Ligibel [36]	16	3	leg press, quadriceps extension, hamstring curl, hip adductor, abdominal crunch, calf press, leg lifts	2–4 sets 10 rep	80 % 1-RM	participants may choose	90	55–80 % max HR
Galvao [20, 21]	20	2	chest press, seated row, shoulder press, lat pull-down, triceps extension, biceps curl, leg press, squat, leg extension, leg curl, abdominal crunch, back-extension	2–4 sets	12–6 RM	–	–	–
Culos-Reed [11]	12	3–5	us exercises	us	us	walking	us	us
Segal [54], Courneya [10]	12	3	leg extension, calf raise, leg curl, chest press, lat pull-down, overhead press, triceps extension, biceps curl, curl-ups	2 sets 8–12 rep	60–70 % 1-RM	–	–	–
Schneider [51]	24	2–3	bench press, lat pull-down, leg press, shoulder press, curl-up crunch	2–3 sets 8–12 rep	RPE 1–5 (0–10)	walking, cycling, stepping or underwater treadmill	40	30–60 % of HRR
McNeely [43]	12	2–3	5–8 exercises for rhomboids/trapezius, levator scapula, biceps, triceps, deltoid, pectoralis major	2 sets 10–15 rep	25–70 % 1-RM	–	–	–

Table 2 Continued.

De Backer [12]	18	2	vertical row, leg press, bench press, lunge, pull over, abdominal crunch	2 sets 10 rep	65–80% 1-RM	stationary cycling	20	Interval: 30–65% of MSEC
Dimeo [18]	3	5	exercise with rubber bands, dumbbells for major muscle groups (arms, pectoral and abdominal muscles, lower back, tights, gluteus region)	20–30 reps or 45–60s static isometric	us	treadmill walking	30	80% of max HR
Berglund [3]	7	1	us exercises	us	us	water exercises, conditioning training	us	us
De Backer [13]	18	2	vertical row, leg press, bench press, lunge, pull over, abdominal crunch	2 sets 10 reps	65–80% 1-RM	stationary cycling	20	Interval: 30–65% of MSEC
Hayes [23,24]	12	3	seated bench press and shoulder press, lat pull-down, leg press, upright row, lunges	1 set 8–20 reps	15–20 RM to 8–12 RM	treadmill walking, stationary cycling	20–40	70–90% max HR
May [40]	12	2	upper and lower body exercises	us	30–60% 1-RM	cycling, swimming, badminton, soccer, walking	us	us

us = unspecified, HR = heart rate, HRR = heart rate reserve, 1-RM = one-repetition maximum, MSEC = maximal short exercise capacity

[32,45,56] estimated peak oxygen uptake by submaximal testing, and two studies [32,45,56] reported significant increases of 15%. The anaerobic threshold was determined in three studies [12,13,18], and the oxygen uptake, power output or heart rate at the anaerobic threshold increased significantly after training.

Muscle function

Most studies (71%) reported outcome measures evaluated by muscle strength and endurance tests, hand grip tests and flexibility tests. Muscle strength was generally assessed by means of a 1-RM test. To assess upper body and lower body muscle strength both bench press and leg press were mostly applied. As shown in ▸ **Table 3**, muscle strength improved significantly after training. In six studies muscle endurance was measured using the maximal number of repetitions at 60–70% of 1-RM [5,21,26,43,51,54]. ▸ **Table 3** showed that muscle endurance improved, except for the bench press in one study [26].

Lymphedema

Three studies with breast cancer patients focused on lymphedema, a possible complication after axillary node resection [1,41,56]. Lymphedema was assessed by measuring arm circumference, arm volume or bio-electric impedance. None of the studies found an increase in these parameters after training.

Immune system

Four studies were focused on the immune system [20,24,28,46]. None of the studies reported negative training effects. Hutnick et al. [28] even found in breast cancer survivors, who underwent an exercise programme, an improvement of the immune function as compared with control patients, who did not follow this programme [28].

Endocrine system

Three studies assessed endocrine parameters after training [20,36,49]. Schmitz et al. [49] and Ligibel et al. [36] used the variables fasting blood glucose, insulin levels in blood, and insulin resistance in their study. Ligibel et al. observed in a RCT with breast cancer survivors a significant decrease in insulin levels and a trend toward improvement in insulin resistance after an exercise intervention [36]. Schmitz et al. found a significant decrease in insulin-like growth factor-II after a 6-months training programme. Galvao et al. [20] examined in prostate cancer patients receiving ADT endocrine parameters in serum, including growth hormone (GH), dehydroepiandrosterone (DHEA), and testosterone. Their study showed that a 20-weeks resistance training programme did not compromise the testosterone suppression, whereas elevations in serum GH and DHEA contributed to improvement in physical function [20].

Haematological variables

Three studies measured Hb concentrations in blood before and after an exercise programme [18,20,26], and reported no change in Hb values after a 5-weeks, 8-weeks or 20-weeks exercise programme.

Quality of the studies

▼

Ratings of the different quality criteria varied considerably (see ▸ **Table 4**). The median score for quality was 4, ranging from 1 to 10. Three RCTs met all the quality criteria [26,43,54]. Eligibil-

Table 3 Physical outcome measures of resistance training in cancer survivors.

Outcome measure	Number of studies assessed	Effect post-training	Best-evidence synthesis[55]		
		Increase	Decrease	No effect	
body composition					
body weight	9	0	0	9 [5, 11, 12, 26, 28, 32, 49, 54, 56]	NE
BMI	6	0	0	6 [12, 28, 34, 49, 54, 56]	NE
fat mass	7	0	2 [5, 26]	5 [12, 28, 32, 49, 54]	NE
lean body mass	3	3 [26, 49, 56]	0	0	SE
bone mass	1	1 [21]	0	0	NE
waist or hip circumference	3	0	1 [5]	2 [10, 49]	NE
cardiopulmonary function					
systolic BP	2	0	2 [32, 52]	0	NE
diastolic BP	2	0	1 [52]	1 [32]	NE
VO_{2peak}	7	7 [5, 12, 13, 23, 26, 28, 40]	0	0	SE
peak power output	4	4 [12, 13, 26, 40]	0	0	SE
HR peak	5	3 [12, 13, 28]	0	2 [5, 26]	NE
VE peak	1	1 [26]	0	0	LE
RQ peak	1	0	0	1[5]	NE
VO2 AT	2	2 [12, 13]	0	0	IF
power output AT	1	1 [18]	0	0	NE
HR AT	1	1[12]	0	0	NE
submax power output	1	1 [45]	0	0	IF
estimated VO2 peak	3	2 [32, 52]	0	1 [56]	NE
HR rest	3	0	2 [11, 52]	1 [32]0	NE
muscle function					
muscle strength (1-RM)					
bench press	7	7 [1, 5, 12, 13, 23, 32, 34]	0	0	SE
chest press	2	2 [21, 43]	0	0	LE
chest extension	1	1 [45]	0	0	LE
seated row	4	4 [12, 13, 21, 43]	0	0	ME
biceps curl	3	2 [28, 45]	0	1 [25]	IF
triceps curl	1	1 [28]	0	0	IF
pull over	2	2 [12, 13]	0	0	IF
abdominal crunch	2	2 [12, 13]	0	0	IF
lunge	2	2 [12, 13]	0	0	IF
leg press	9	9 [1, 5, 12, 13, 21, 23, 32, 36, 45]	0	0	SE
leg extension	3	1 [36]	0	2 [25, 46]	NE
hamstrings curls	1	1 [36]	0	0	LE
hip ab- and adduction	1	1 [36]	0	0	LE
calf press	1	1 [36]	0	0	LE
muscle endurance (reps)					
bench press	3	2 [5, 51]	0	1 [26]	NE
chest press	2	2 [21, 54]	0	0	LE
lateral pull down	1	1 [51]	0	0	NE
seated row	1	1 [43]	0	0	LE
leg press	5	5 [5, 21, 26, 51, 54]	0	0	SE
shoulder press	1	1 [51]	0	0	NE
curl-up crunch	1	1 [51]	0	0	NE
sit-and-stand test (s)	1	0	1 [26]	0	LE

BP = blood pressure; VO_2 = oxygen uptake; W = Watt; HR = heart rate; VE = ventilation; RQ = respiratory quotient; AT = anaerobic threshold; Best-evidence synthesis: SE = strong evidence; ME = moderate evidence; LE = limited evidence; IF = indicative findings; NE = no evidence

ity criteria were presented in most studies. Seven RCTs (70 %) had an adequate allocation concealment [26, 40, 41, 43, 45, 47, 54]. Blinding of the outcome assessors was fulfilled in only four studies [26, 43, 47, 54]. Half of the studies reported adherence to exercise training and drop-outs. Only a few studies took the drop-outs into account in their analyses and did an intention-to-treat analysis. Most studies had qualified supervisors during the training programmes. The last criterion, specifying the resistance training, was met by 42 % of the studies [5, 12, 13, 21, 23, 26, 36, 43, 45, 51, 54].

Discussion

This review summarizes the research of previous studies that used resistance training in the post-treatment phase of patients with different types of cancer, by focussing on methodological quality, training methods and physical outcome measures.

Subjects and timing of intervention

Most studies involved patients, diagnosed with stage I to III breast cancer, who received adjuvant chemotherapy. Fatigue was

Table 4 Methodological quality of resistance training interventions in cancer survivors.

Study	Design	Criteria*										
		1	2	3	4	5	6	7	8	9	10	Total
Kolden et al. [32]	T	–	–	–	–	–	+	+	–	+	–	3
Turner et al. [56]	T	+	–	–	–	–	–	+	–	+/–	–	2
Lane et al. [34]	T	+	–	–	–	–	–	+	–	–	–	2
Cheema et al. [5]	T	+	–	–	–	–	+	+	–	+/–	+	4
Schneider et al. [52]	T	–	–	–	–	–	+	–	–	+	–	2
Hutnick et al. [28]	CT	+	–	–	+	–	+	+	–	+	–	5
Nieman et al. [46]	RCT	–	+	–	+	–	+	+	–	+	–	5
McKenzie et al. [41]	RCT	+	+	+	+	–	–	–	–	+/–	–	4
Ohira et al. [47] Ahmed et al. [1] Schmitz et al. [49]	RCT	+	+	+	+	+	+	+	–	+/–	–	7
Herrero et al. [26]	RCT	+	+	+	+	+	+	+	+	+	+	10
Milne et al. [45]	RCT	+	+	+	+	–	–	+	+	+	+	8
Heim et al. [25]	**RCT	+	–	–	–	–	–	–	–	–	–	1
Ligibel et al. [36]	RCT	+	+	–	+	+/–	+	+	+	+/–	+	7
Galvao et al. [20,21]	T	+	–	–	–	–	–	+	–	+	+	4
Culos-Reed et al. [11]	T	+	–	–	–	–	–	–	–	–	–	1
Segal et al. [54] Courneya et al. [10].	RCT	+	+	+	+	+	+	+	+	+	+	10
Schneider et al. [51]	T	–	–	–	–	–	+	+	–	+	+	4
McNeely et al. [43]	**RCT	+	+	+	+	+	+	+	+	+	+	10
De Backer et al. [12]	T	+	–	–	–	–	–	+	–	+	+	4
Dimeo et al. [18]	T	+	–	–	–	–	–	+	+	?	–	3
Berglund et al. [3]	CT	+	–	–	+	?	+	+	+	+	–	6
De Backer et al. [13]	CT	+	–	–	+	–	–	+	+	+	+	6
Hayes et al. [23,24]	CT	–	–	–	+/–	–	–	+	–	+	+	3
May et al. [40]	**RCT	+	+	+	+	–	+	+	+	+	–	8
Studies meeting criteria (n)		19	9	7	12	4	13	20	8	15	11	

RCT = Randomized controlled trial; CT = Non-randomized controlled trial; T = Uncontrolled trial

+ = yes; – = no; +/– = partially; ? = do not know

*1) Eligibility specified; 2) Randomization; 3) Allocation concealment; 4) Similarity at baseline; 5) Blinding outcome assessors; 6) Adherence rate greater than 70%; 7) Drop-outs fewer than 15%; 8) Intention-to-treat analysis; 9) Supervision of exercise; 10) Type of resistance training specified

** Both groups underwent exercise training

reported as the most prevalent and distressing side effect of chemotherapy [14]. Compliance to regular physical exercise has been shown to have the potential to break the cycle of fatigue and exercise avoidance [37]. It is obvious that in daily practice the timing of intervention with an exercise programme varied considerably. Some studies started their training programme weeks to months, and other studies months to years after the last treatment. However, starting *early* after diagnosis seemed to be most appropriate, since a significant decrease in interest in participating in lifestyle interventions has been noted when time elapsed after diagnosis [17]. Also during treatment, exercise has been shown to be successful in the improvement of physical fitness and thus the capacity for performing activities of daily life [39]. Even exercise before cancer treatment to prepare the body for a stressful event such as chemotherapy has been broached [15].

Intervention

In all included studies the duration of resistance training programmes lasted 3–24 weeks, contributing to a variable training response. In our hospital we observed that most progression in muscle strength could be achieved after the first 12 weeks [12]. In seven studies (29%) the training duration was shorter than 12 weeks, therefore, patients in these studies will probably not have attained their maximal performance level [3,5,18,26,41,46,56]. Also, the number of training sessions per week (frequency) may affect the response to resistance training. Numerous resistance training studies have demonstrated that at least 2–3 alternating days per week are necessary for an optimal progression in untrained individuals [33]. In fact, most training programmes prescribed 2 or 3 sessions per week.

It is of clinical relevance that in most studies exercises, targeting the large muscle groups, were applied, such as leg press and seated row. Since 71% of cancer survivors are overweight or obese [16], sufficient muscle mass involved in exercises is important to evoke metabolic demands that are necessary for reduction in body fat and improvement in lean body mass. No evidence was found for significant training effects on body composition or fat mass. Therefore, other strategies besides exercise training (e.g. dietary intervention) will be needed to manage body weight. This is of clinical relevance since excess body weight in cancer survivors may contribute to a high risk for cardiovascular disease and diabetes mellitus [16].

Most studies described training intensities between 60% and 85% of 1-RM, or 15-6 RM, which can be considered as moderate to high-intensity training [33]. Only in two studies patients trained at lower intensities between 25% and 70% of 1-RM [40,43]. It is well known that in healthy adult subjects a resistance training programme is more effective when relatively heavy loads (high intensity) are used. Substantial gains in maximal muscle strength and hypertrophy can only be achieved when the maximal number of motor units is recruited, which warrants high training loads [33]. In addition, other tissues such as bone also respond more favourably to such heavy loading, because strength training is beneficial in preventing further bone loss in patients at risk for osteoporosis [48]. This is clinically of importance especially in postmenopausal breast cancer survivors, who might have a lower than normal bone mineral density. The observed training intensities are remarkable high compared with the advised exercise intensities for cancer patients, which can be considered as low to moderate (50% of 1-RM with 2 or 3 sets of 3–5 repetitions building to 10–12 repetitions) [53]. Since none of the moderate to high-intensity training studies reported adverse effects, we conclude that moderate to high training intensities are well-tolerated in cancer survivors.

Physical outcome measures

Almost all included studies reported beneficial effects of resistance training on cardiopulmonary function and muscle function. However, since most studies used a mixed training programme, it is unclear whether these improvements could be attributed to the resistance training alone or to the combined resistance/aerobic exercise intervention. Post training improvements in cardiopulmonary function ranged from 6% to 39%, with the lowest improvement in studies with a short training duration. Post training increases in muscle strength ranged from 11% to 110%. This enormous range in improvement could be attributed to different causes, such as the contribution of a learning effect, the variability in strength exercises, intensities and duration of training programmes, and genetic differences. Only the study of Herrero et al. [26] described a familiarization session before the first assessment to eliminate learning effects. If learning effects could be eliminated, the observed range would be smaller. Also the variability in type and stage of cancer, the different cancer treatments and the different times elapsed since cancer diagnosis will contribute to the observed heterogeneity in training responses. Finally, there was general agreement in the absence of adverse effects of training on immunological, endocrinological, and haematological variables, or lymphedema, indicating that high training intensities were well-tolerated in cancer survivors.

Methodological quality

Since 10 out of 24 studies were uncontrolled trials, the median quality score of the studies was low (4 on a scale from 1–10). This was mainly due to the fact that in studies without a control group, a maximum of 7 out of 10 quality criteria could be fulfilled. Criteria of randomization, allocation concealment, and baseline similarity could not be applied. Three RCTs fulfilled all quality criteria [26,43,54], of which one randomized between two exercise interventions [43]. Therefore, the studies of Herrero et al. [26] and Segal et al. [54] could be considered an impetus for future studies.

It is obvious that a number of quality criteria were poorly achieved. It is remarkable that not all RCTs blinded their outcome assessors. This criterion is especially important in cases where maximal exercise tests are performed in order that encouragements at the end of the test may not differ between exercise and control group. Adherence rates were lacking in almost half of the studies. However, the extent to which an intervention group performs the exercise prescription should be an important topic in starting exercise intervention studies [9,10] to pursue optimal training outcomes. In three studies there was no supervision of the training [11,25,34]. Although regular exercise is generally considered a safe procedure, supervision is essential to prevent injuries and to safeguard patients from excessive risks. Finally, the criterion of specifying the type of resistance training was poorly described in most studies. However, for an optimal progression in performance benefits, individualization of the training prescription is essential. Based on the health status and needs of the patients, training goals must be determined, involving choices of which muscles must be trained and how injuries can be prevented. After that, the selection, order, and intensity (number of repetitions and sets) of each exercise, as well as the balance between physical activity and rest must be defined [33]. For example, a well-defined training programme to improve shoulder function is required in breast cancer patients, who might have specific post treatment limitations in the shoulder.

Recommendations and future directions

We conclude that resistance training is not only well-tolerated in cancer patients, but also a tool to counteract adverse effects of cancer and its treatment. Based on the findings of this systematic review we recommend the following for future studies:

- Since most of the research is focused on breast and prostate cancer survivors, future research should incorporate more patients with other types of cancer to determine whether the observed positive effects of physical training could be generalized for all cancer types.
- Expand the duration of training programmes to at least 12 weeks, with a training frequency of 2 to 3 times a week. Resistance training should be primarily focused on the large muscle groups, with intensities between 60–85% of 1-RM and 2–3 sets of 8–12 repetitions.
- Use valid and reliable physical outcome measures to improve comparability between effects of different training programmes (e.g. VO_2 peak, VO_2 AT, upper body strength (1-RM), lower body strength (1-RM)).
- Before starting an intervention, high levels of exercise adherence must be warranted.
- Before starting a randomized, controlled trial, adequate allocation concealment and blinding of outcome assessors must be warranted.
- When reporting the findings, a detailed prescription of the exercise intervention should be provided (frequency, duration, intensity and type of exercise).
- Future studies should pay more attention to additional strategies for improvement in body composition (decrease in fat mass and increase in lean body mass) in cancer survivors.

References

1 *Ahmed RL, Thomas W, Yee D, Schmitz KH.* Randomized controlled trial of weight training and lymphedema in breast cancer survivors. J Clin Oncol 2006; 24: 2765–2772
2 *Atkins D, Best D, Briss PA, Eccles M, Falck-Ytter Y, Flottorp S, Guyatt GH, Harbour RT, Haugh MC, Henry D, Hill S, Jaeschke R, Leng G, Liberati A, Magrini N, Mason J, Middleton P, Mrukowicz J, O'Connell D, Oxman AD, Phillips B, Schunemann HJ, Edejer TT, Varonen H, Vist GE, Williams Jr JW, Zaza S.* Grading quality of evidence and strength of recommendations. BMJ 2004; 328: 1490–1498
3 *Berglund G, Bolund C, Gustavsson UL, Sjoden PO.* Starting again – a comparison study of a group rehabilitation program for cancer patients. Acta Oncol 1993; 32: 15–21
4 *Cheema B, Gaul CA, Lane K, Fiatarone Singh MA.* Progressive resistance training in breast cancer: a systematic review of clinical trials. Breast Cancer Res Treat 2008; 109: 9–26
5 *Cheema BS, Gaul CA.* Full-body exercise training improves fitness and quality of life in survivors of breast cancer. J Strength Cond Res 2006; 20: 14–21

6 *Conn VS, Hafdahl AR, Porock DC, McDaniel R, Nielsen PJ.* A meta-analysis of exercise interventions among people treated for cancer. Support Care Cancer 2006; 14: 699–712
7 *Courneya KS.* Exercise in cancer survivors: an overview of research. Med Sci Sports Exerc 2003; 35: 1846–1852
8 *Courneya KS, Friedenreich CM.* Physical exercise and quality of life following cancer diagnosis: a literature review. Ann Behav Med 1999; 21: 171–179
9 *Courneya KS, Friedenreich CM, Quinney HA, Fields AL, Jones LW, Fairey AS.* Predictors of adherence and contamination in a randomized trial of exercise in colorectal cancer survivors. Psychooncology 2004; 13: 857–866
10 *Courneya KS, Segal RJ, Reid RD, Jones LW, Malone SC, Venner PM, Parliament MB, Scott CG, Quinney HA, Wells GA.* Three independent factors predicted adherence in a randomized controlled trial of resistance exercise training among prostate cancer survivors. J Clin Epidemiol 2004; 57: 571–579
11 *Culos-Reed SN, Robinson JL, Lau H, O'Connor K, Keats MR.* Benefits of a physical activity intervention for men with prostate cancer. J Sport Exerc Psychol 2007; 29: 118–127
12 *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 Oncol 2007; 46: 1143–1151
13 *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: 30–36
14 *de Jong N, Courtens AM, bu-Saad HH, Schouten HC.* Fatigue in patients with breast cancer receiving adjuvant chemotherapy: a review of the literature. Cancer Nurs 2002; 25: 283–297
15 *de Paleville DT, Topp RV, Swank AM.* Effects of aerobic training prior to and during chemotherapy in a breast cancer patient: a case study. J Strength Cond Res 2007; 21: 635–637
16 *Demark-Wahnefried W, Aziz NM, Rowland JH, Pinto BM.* Riding the crest of the teachable moment: promoting long-term health after the diagnosis of cancer. J Clin Oncol 2005; 23: 5814–5830
17 *Demark-Wahnefried W, Peterson B, McBride C, Lipkus I, Clipp E.* Current health behaviors and readiness to pursue life-style changes among men and women diagnosed with early stage prostate and breast carcinomas. Cancer 2000; 88: 674–684
18 *Schwartz S, Wesel N, Voigt A, Thiel E.* Effects of an endurance and resistance exercise program on persistent cancer-related fatigue after treatment. Ann Oncol 2008; 19: 1495–1499
19 *Galvao DA, Newton RU.* Review of exercise intervention studies in cancer patients. J Clin Oncol 2005; 23: 899–909
20 *Galvao DA, Nosaka K, Taaffe DR, Peake J, Spry N, Suzuki K, Yamaya K, McGuigan MR, Kristjanson LJ, Newton RU.* . Endocrine and immune responses to resistance training in prostate cancer patients. Prostate Cancer Prostatic Dis 2008; 11: 160–165
21 *Galvao DA, Nosaka K, Taaffe DR, Spry N, Kristjanson LJ, McGuigan MR, Suzuki K, Yamaya K, Newton RU.* Resistance training and reduction of treatment side effects in prostate cancer patients. Med Sci Sports Exerc 2006; 38: 2045–2052
22 *Ganz PA.* A teachable moment for oncologists: cancer survivors, 10 million strong and growing!. J Clin Oncol 2005 23: 5458–5460
23 *Hayes SC, Davies PS, Parker TW, Bashford J, Green A.* Role of a mixed type, moderate intensity exercise programme after peripheral blood stem cell transplantation. Br J Sports Med 2004; 38: 304–309
24 *Hayes SC, Rowbottom D, Davies PS, Parker TW, Bashford J.* Immunological changes after cancer treatment and participation in an exercise program. Med Sci Sports Exerc 2003; 35: 2–9
25 *Heim ME, Malsburg ML, Niklas A.* Randomized controlled trial of a structured training program in breast cancer patients with tumor-related chronic fatigue. Onkologie 2007; 30: 429–434
26 *Herrero F, San Juan AF, Fleck SJ, Balmer J, Perez M, Canete S, Earnest CP, Foster C, Lucia A.* Combined aerobic and resistance training in breast cancer survivors: A randomized, controlled pilot trial. Int J Sports Med 2006; 27: 573–580
27 *Humpel N, Iverson DC.* Review and critique of the quality of exercise recommendations for cancer patients and survivors. Support Care Cancer 2005; 13: 493–502
28 *Hutnick NA, Williams NI, Kraemer WJ, Orsega-Smith E, Dixon RH, Bleznak AD, Mastro AM.* Exercise and lymphocyte activation following chemotherapy for breast cancer. Med Sci Sports Exerc 2005; 37: 1827–1835
29 *Irwin ML, Ainsworth BE.* Physical activity interventions following cancer diagnosis: methodologic challenges to delivery and assessment. Cancer Invest 2004; 22: 30–50
30 *Jones LW, Demark-Wahnefried W.* Diet, exercise, and complementary therapies after primary treatment for cancer. Lancet Oncol 2006; 7: 1017–1026
31 *Knobf MT, Musanti R, Dorward J.* Exercise and quality of life outcomes in patients with cancer. Semin Oncol Nurs 2007; 23: 285–296
32 *Kolden GG, Strauman TJ, Ward A, Kuta J, Woods TE, Schneider KL, Heerey E, Sanborn L, Burt C, Millbrandt L, Kalin NH, Stewart JA, Mullen B.* A pilot study of group exercise training (GET) for women with primary breast cancer: feasibility and health benefits. Psychooncology 2002; 11: 447–456
33 *Kraemer WJ, Ratamess NA.* Fundamentals of resistance training: progression and exercise prescription. Med Sci Sports Exerc 2004; 36: 674–688
34 *Lane K, Jespersen D, McKenzie DC.* The effect of a whole body exercise programme and dragon boat training on arm volume and arm circumference in women treated for breast cancer. Eur J Cancer Care (Engl) 2005; 14: 353–358
35 *Lee RC, Wang Z, Heo M, Ross R, Janssen I, Heymsfield SB.* Total-body skeletal muscle mass: development and cross-validation of anthropometric prediction models. Am J Clin Nutr 2000; 72: 796–803
36 *Ligibel JA, Campbell N, Partridge A, Chen WY, Salinardi T, Chen H, Adloff K, Keshaviah A, Winer EP.* Impact of a mixed strength and endurance exercise intervention on insulin levels in breast cancer survivors. J Clin Oncol 2008; 26: 907–912
37 *Lucia A, Earnest C, Perez M.* Cancer-related fatigue: can exercise physiology assist oncologists? Lancet Oncol 2003; 4: 616–625
38 *Maher CG, Sherrington C, Herbert RD, Moseley AM, Elkins M.* Reliability of the PEDro scale for rating quality of randomized controlled trials. Phys Ther 2003; 83: 713–721
39 *Markes M, Brockow T, Resch KL.* Exercise for women receiving adjuvant therapy for breast cancer. Cochrane Database Syst Rev 2006; CD005001
40 *May AM, van WE, Korstjens I, Hoekstra-Weebers JE, van der Schans CP, Zonderland ML, Mesters I, van den BB, Ros WD.* Improved physical fitness of cancer survivors: a randomised controlled trial comparing physical training with physical and cognitive-behavioural training. Acta Oncol 2008; 47: 825–834
41 *McKenzie DC, Kalda AL.* Effect of upper extremity exercise on secondary lymphedema in breast cancer patients: a pilot study. J Clin Oncol 2003; 21: 463–466
42 *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
43 *McNeely ML, Parliament MB, Seikaly H, Jha N, Magee DJ, Haykowsky MJ, Courneya KS.* Effect of exercise on upper extremity pain and dysfunction in head and neck cancer survivors: a randomized controlled trial. Cancer 2008; 113: 214–222
44 *McTiernan A.* Physical activity after cancer: physiologic outcomes. Cancer Invest 2004; 22: 68–81
45 *Milne HM, Wallman KE, Gordon S, Courneya KS.* Effects of a combined aerobic and resistance exercise program in breast cancer survivors: a randomized controlled trial. Breast Cancer Res Treat 2008; 108: 279–288
46 *Nieman DC, Cook VD, Henson DA, Suttles J, Rejeski WJ, Ribisl PM, Fagoaga OR, Nehlsen-Cannarella SL.* Moderate exercise training and natural killer cell cytotoxic activity in breast cancer patients. Int J Sports Med 1995; 16: 334–337
47 *Ohira T, Schmitz KH, Ahmed RL, Yee D.* Effects of weight training on quality of life in recent breast cancer survivors: the Weight Training for Breast Cancer Survivors (WTBS) study. Cancer 2006; 106: 2076–2083
48 *Ott CD, Lindsey AM, Waltman NL, Gross GJ, Twiss JJ, Berg K, Brisco PL, Henricksen S.* Facilitative strategies, psychological factors, and strength/weight training behaviors at risk for osteoporosis. Orthop Nurs 2004; 23: 45–52
49 *Schmitz KH, Ahmed RL, Hannan PJ, Yee D.* Safety and efficacy of weight training in recent breast cancer survivors to alter body composition, insulin, and insulin-like growth factor axis proteins. Cancer Epidemiol Biomarkers Prev 2005; 14: 1672–1680
50 *Schmitz KH, Holtzman J, Courneya KS, Masse LC, Duval S, Kane R.* Controlled physical activity trials in cancer survivors: a systematic review and meta-analysis. Cancer Epidemiol Biomarkers Prev 2005; 14: 1588–1595
51 *Schneider CM, Hsieh CC, Sprod LK, Carter SD, Hayward R.* Cancer treatment-induced alterations in muscular fitness and quality of life: the role of exercise training. Ann Oncol 2007; 18: 1957–1962

52 *Schneider CM*, *Hsieh CC*, *Sprod LK*, *Carter SD*, *Hayward R*. Effects of supervised exercise training on cardiopulmonary function and fatigue in breast cancer survivors during and after treatment. Cancer 2007; 110: 918–925
53 *Schwartz AL*. Cancer. In Durstine JL, Moore GE, (eds.) ACSM's Exercise Management for Persons with Chronic Diseases and Disabilities. Champaign, Human Kinetics 2003; 166–173
54 *Segal RJ*, *Reid RD*, *Courneya KS*, *Malone SC*, *Parliament MB*, *Scott CG*, *Venner PM*, *Quinney HA*, *Jones LW*, *Slovenic D'Angelo ME*, *Wells GA*. Resistance exercise in men receiving androgen deprivation therapy for prostate cancer. J Clin Oncol 2003; 21: 1653–1659
55 *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: 676–687
56 *Turner J*, *Hayes S*, *Reul-Hirche H*. Improving the physical status and quality of life of women treated for breast cancer: a pilot study of a structured exercise intervention. J Surg Oncol 2004; 86: 141–146