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REVIEW ARTICLE

# Resistance exercise and secondary lymphedema in breast cancer survivors—a systematic review

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**Abstract**
*Purpose* The aim of the present review was to determine effects of strength exercise on secondary lymphedema in breast cancer patients.
*Methods* Research was conducted by using the databases PubMed/Medline and Embase. Randomized controlled trials published from January 1966 to May 2015 investigating the effects of resistance exercise on breast cancer patients with or at risk of secondary lymphedema in accordance with the American College of Sports Medicine exercise guidelines for cancer survivors were included in the present study.
*Results* Nine original articles with a total of 957 patients met the inclusion criteria. None of the included articles showed adverse effects of a resistance exercise intervention on lymphedema status. In all included studies, resistance exercise intensity was described as moderate to high.
*Conclusions* Strength exercise seems not to have negative effects on lymphedema status or might not increase risk of development of lymphedema in breast cancer patients. Further research is needed in order to investigate the effects of resistance exercise for patients suffering from lymphedema.

**Keywords** Secondary lymphedema · Resistance exercise · Strength · Medical training therapy · Breast cancer

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## Introduction

Lymphedema (LE) is a relevant clinical problem of breast cancer patients. LE is a morbidity factor for breast cancer patients that causes limb swelling, lowers the function and mobility of the affected limb, and causes paresthesia. The prevalence rate of LE in the general population varies in a quite wide range [1, 2]. In patients suffering from cancer—particularly breast cancer—the prevalence and incidence rates of LE tend to be even higher [3–5].

Cancer-related LE reduces health-related quality of life (QoL) [6, 7]. As a consequence, breast cancer patients often do not use their affected arm, e.g., properly in their daily routine, as they fear this could worsen their condition [8, 9]. Additionally, LE causes a significant increase in healthcare costs [10].

Cancer-related LE can be caused not only by the disease itself but by necessary therapeutic measures such as radiation, chemotherapy, or lymphatic tissue destruction after surgery [3]. As an example, up to 30 % of breast cancer survivors (BCS) suffer from breast cancer-related LE (BCRL) after surgery [3]. This challenging problem of cancer-related LE is mainly addressed by interventions such as complex decongestive therapy as well as exercise and skin care [11]. Physical exercise is known to be useful not only for preventive goals but also as a therapeutic approach for a variety of medical, especially chronic, conditions such as cancer, hypertonia, osteoporosis, fat metabolism disorders, and many more [12–14]. Furthermore, literature shows beneficial effects of resistance exercise (RE) for cancer patients [15–17]. This furthers the question of exercise interventions for patients suffering from cancer-related LE, which is subject of intensive discussion in the current literature such as a recently published Cochrane review about BCRL and other articles show [18–20]. For example, Khwan et al. stated in a review that strong evidence is available on the safety of resistance exercise without an increase in risk of lymphedema for BCS [18]. Furthermore, Paskett et al. assumed even that exercise and physical activity reduce risk of LE [19]. In a Cochrane review, the authors assumed that progressive resistance exercise therapy does not increase the risk of developing lymphedema provided that symptoms are monitored and treated immediately if they occur. Nevertheless, due to the degree of heterogeneity, the limited precision, and the risk of bias across the reviewed studies, the authors concluded that the results should be interpreted with caution [20]. The aim of the present review was to investigate first, if RE increases the risk/causes the development specifically of BCRL and second, if patients with BCRL worsen, improve, or stay the same with RE.

## Methods

A systematic review of the existing scientific literature was performed including the databases PubMed, MEDLINE and EMBASE. Trials with the key words "lymphedema," respectively "lymphoedema," and "strength exercise," "resistance exercise," "resistance training," "weight training," "weight lifting," and "breast cancer" were extracted and considered for inclusion in the review. A total of 451 studies were found and screened for eligibility by title and abstract. Only English language studies were included. Four hundred and twenty-seven were rejected as non-includable and 24 studies were selected for full-text analysis (Fig. 1). Of these, nine fulfilled the inclusion criteria of being prospective randomized controlled studies investigating the influences of a RE intervention in accordance with the American College of Sports Medicine (ACSM) exercise guidelines for cancer patients [21] on the development of secondary lymphedema in breast cancer survivors [22–30]. The methodological quality of the included articles was assessed by implementing the risk of bias assessment tool of Downs and Black [31], which has been shown to be very helpful when comparing the quality of several trials [13, 32]. Both the systematic literature research and the risk of bias assessment were performed separately by two independent researchers. The integration of their individual findings was supervised by two senior researchers.

## Results

### Methodological quality

The risk of bias assessment revealed that the included studies ranged from 24 to 31 points of a maximum of 32 points (high score is a low bias) [31]. A weakness of all the included studies is that the participants could not be blinded to the interventions (Table 1, item 14 = internal validity—bias). On the other hand, all studies but Courneya et al. [26] reported an attempt to blind those measuring the main outcomes (Table 1, item 15). Further weaknesses are that only four studies recruited their patients from the same population (for example, patients for all comparison groups were recruited from the same hospital) [22, 23, 28, 29] (Table 1, item 21), only five provided a complete list of principal confounders [22, 23, 26, 29, 30] (Table 1, item 5), and three studies did not perform adequate adjustment for confounding in their analyses from which the main findings were drawn [23, 25, 28] (Table 1, item 25).

Eight of the nine included articles calculated a power analysis prior to the recruitment to reassure performing their exercise interventions with a sufficiently large sample [22, 24–30]. The detailed rating of the quality of included articles is presented in Table 1.

### Lymphedema

While some of the included articles focused on changes in BCS with preexisting LE [24, 25, 27, 29], some others observed the volume of the upper extremities in BCS at risk of LE [23, 28, 30] or included BCS both with or without preexisting LE [22, 26].

Arm volume was evaluated in all of the included studies [22–30]. One or more assessment methods were used in the different studies: Water displacement volumetry was used in four articles [23, 26, 29, 30], limb circumference measurements in six [22, 24, 25, 28–30], bioimpedance spectroscopy in four [24, 25, 27, 28], dual X-ray absorptiometry (DXA) in two [24, 25], and perometry in one [27] study. In the study by Ahmed et al., a validated survey for self-report of lymphedema diagnosis, symptoms, and treatment over the last 3 months was used additionally for limb circumference measurements [22, 33].

Schmitz et al. [30] used additionally (to water displacement volumetry and limb circumference measurements) the common toxicity criteria version 3.0 adverse events criteria as a clinical assessment method for LE, and lymphedema-related arm symptom presence and severity were reported using a validated and reliable survey for detecting prevalent lymphedema [33].

The other studies included validated self assessment tests to those methods listed before for LE development [23–25, 29]. Independent of assessment method, none of the studies reported significant detrimental effects of RE on LE status or risk of developing LE. On the contrary, Schmitz et al. [29] showed that during a 1-year weight-lifting program, the LE exacerbation rate was significantly lower in the exercise group than in

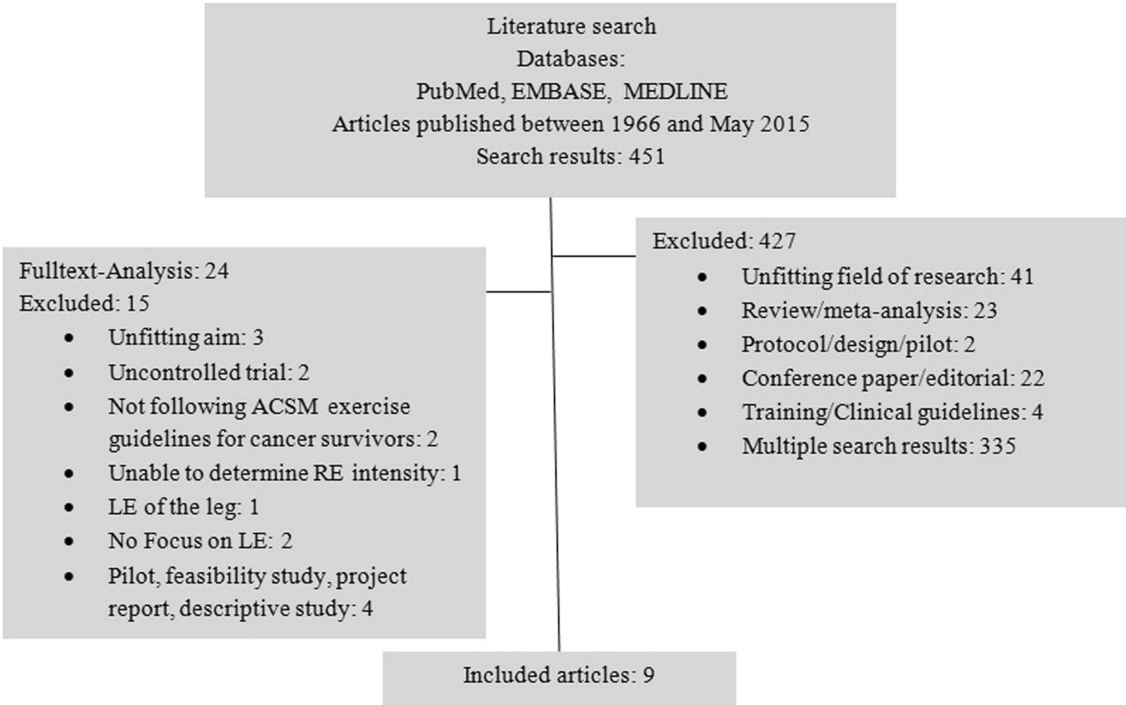


**Fig. 1** Flowchart of the systematic literature research and the selection process. *ACSM* American College of Sports Medicine, *RE* resistance exercise, *LE* lymphedema

the control group and Hayes et al. [27] even reported absence of signs of LE in two of 32 patients with preexisting LE by the end of the study.

## Physical performance and function

Physical performance or function testing was conducted by all authors but Cormie et al. [25], who primarily focused on LE exacerbation and Hayes et al. [27], whose main focus was on the safety and benefits of an exercise intervention on LE.

Strength testing was performed in six of the included studies [22, 24, 26, 28–30], endurance testing in one [26], flexibility tests in two [24, 28], and physical function tests in one article [23]. In all of the studies that conducted physical performance tests [22–24, 26, 28–30], significant increases in at least one performance parameter were reported. The detailed

**Table 1** Extended analyses from risk of bias assessment

| | | Risk of bias assessment of the included original studies | | | | | | | | | | | | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | Checklist items | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| | | Reporting | | | | | | | | | | External validity | | | Internal validity—bias | | | | | | | Internal validity—confounding (selection bias) | | | | | | Power | |
| Study | Year | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | 15 | 16 | 17 | 18 | 19 | 20 | 21 | 22 | 23 | 24 | 25 | 26 | 27 | Total |
| Ahmed [22] | 2006 | 1 | 1 | 1 | 1 | 2 | 1 | 1 | 0 | 1 | 1 | 1 | 0 | 1 | 0 | 1 | 1 | 1 | 1 | 1 | 1 | 0 | 1 | 1 | 1 | 1 | 1 | 5 | 28 |
| Anderson [23] | 2012 | 1 | 1 | 1 | 1 | 2 | 1 | 1 | 1 | 1 | 0 | 1 | 1 | 1 | 0 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 0 | 1 | 5 | 29 |
| Cormie [24] | 2013 | 1 | 1 | 1 | 1 | 0 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 0 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 5 | 29 |
| Cormie [25] | 2013a | 1 | 1 | 1 | 1 | 0 | 1 | 1 | 1 | 1 | 1 | 0 | 0 | 1 | 0 | 1 | 1 | 1 | 1 | 1 | 1 | 0 | 1 | 1 | 1 | 0 | 1 | 5 | 25 |
| Courneya [26] | 2007 | 1 | 1 | 1 | 1 | 2 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 0 | 0 | 1 | 1 | 1 | 1 | 1 | 0 | 1 | 1 | 1 | 1 | 1 | 5 | 29 |
| Hayes [27] | 2009 | 1 | 1 | 1 | 1 | 0 | 1 | 1 | 0 | 1 | 1 | 1 | 1 | 0 | 0 | 1 | 1 | 1 | 1 | 1 | 1 | 0 | 0 | 1 | 1 | 1 | 1 | 5 | 25 |
| Kilbreath [28] | 2012 | 1 | 1 | 1 | 1 | 0 | 1 | 1 | 0 | 1 | 1 | 1 | 0 | 1 | 0 | 1 | 1 | 1 | 1 | 1 | 1 | 0 | 0 | 1 | 1 | 0 | 1 | 5 | 24 |
| Schmitz [29] | 2009 | 1 | 1 | 1 | 1 | 2 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 0 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 5 | 31 |
| Schmitz [30] | 2010 | 1 | 1 | 1 | 1 | 2 | 1 | 1 | 0 | 1 | 1 | 1 | 1 | 1 | 0 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 5 | 30 |

results of the physical performance tests can be found in Table 2.

## Body composition

A pre-post comparison of the body composition after an exercise intervention was performed by three studies [26, 29, 30]. Both Courneya et al. [26] and Schmitz et al. [29] did not find any significant changes neither in body fat percentage nor fat mass, while Schmitz et al. [30] reported a lower body fat percentage in the exercise group after 12 months of weight lifting compared to the no exercise control group.

## Quality of life

Assessment of quality of life was performed by four studies [23, 24, 26, 28]. Anderson et al. [23] and Cormie et al. [24] used the FACT-B questionnaire, Courneya et al. [26] the FACT-Anemia-Scale, and Kilbreath et al. [28] the EORTC-BR23. In Courneya et al. [26], both exercise groups showed significantly higher self esteem values after the exercise intervention compared to the usual care group. The other studies did not report any significant differences between their exercise intervention and usual care groups [23, 24, 28].

Furthermore, Hayes et al. [27] recorded qualitative comments regarding the exercise program and the LE status and revealed the overarching concern that lymphedema impacts all facets of an individual's life.

## Safety

To show how safe RE programs have been in the included studies, we compiled an overview of the dropouts. In general, 44 dropped out of the 462 study participants (10 %) allocated to RE groups (Fig. 2). Not a single dropout was due to exercise-related LE complications. The adherence rate to strength exercise ranged in the majority of participants from 70 to 100 %. Details of drop out analysis are presented in Table 3.

# Discussion

Breast cancer is by far the most common malignancy among women, with nearly one and a half million affected women worldwide [34]. For example, one out of eight women in the USA will be diagnosed with breast cancer over her lifetime [35]. Of those, more than one in five women who survive breast cancer will develop secondary LE, which is associated with a number of major impairments in activities of daily living and a substantial loss of quality of life [3]. Historically, BCS suffering from or at risk of secondary LE were instructed to refrain from vigorous, repetitive, or excessive upper body exercise, because there was a mutual belief within health care professionals that such type of exercises might induce LE although this assumption has never been backed up by evidence-based research [35].

Stuiver et al. conducted a Cochrane review on the effects of conservative (non-surgical and non-pharmacological) interventions for preventing clinically detectable upper limb lymphedema after breast cancer treatment. The authors stated

**Table 2** Physical performance and function

| Author | Outcome measurement | Assessment | Results |
|---|---|---|---|
| Ahmed et al. [22] | Strength: upper lower | 1RM: bench press leg press | RE to Cont: ↑ RE to Cont: ↑ |
| Anderson et al. [23] | Physical function | 6-min walk test | RE to Cont: ↑ |
| Cormie et al. [24] | Muscular strength: grip strength major muscle groups: chest press seated row leg press muscular endurance upper body ROM: wrist shoulder elbow | Isometric hand dynamometer 1RM 70 % 1RM rep max. with chest press seated row leg press standard goniometer | (Low + high) RE to Cont: (↑) (low + high) RE to Cont: ↑ (low + high) RE to Cont: ↑ (low + high) RE to Cont: ↑ (low + high) RE to Cont: ↑ (low + high) RE to Cont: ↑ (low + high) RE+Cont:↓ |
| Courneya et al. [26] | Endurance strength | Peak oxygen consumption 8RM: bench press leg extension | AE to RE + Cont: ↑ RE to AE+Cont: ↑ RE to AE+Cont: ↑ |
| Kilbreath et al. [28] | ROM, shoulder, affected side strength upper limb, shoulder muscle | Digital inclinometer dynamometer | RE to Cont: ↑ RE to Cont: ↑ |
| Schmitz et al. [29] | Strength: upper lower | 1RM bench press leg press | RE to Cont: ↑ RE to Cont: ↑ |
| Schmitz et al. [30] | Strength: upper lower | 1RM bench press leg press | RE to Cont: ↑ RE to Cont: ↑ |

*RE* resistance exercise group, *ROM* range of motion, *Cont* control group, *1RM* one-repetition maximum, *70%1RM max rep* maximal possible amount of repetitions with 70 % 1RM, *8RM* eight repetition maximum, *AE* Aerobic exercise group, ↑ significant increase, ↓ significant decrease, (↑) trend in favor of

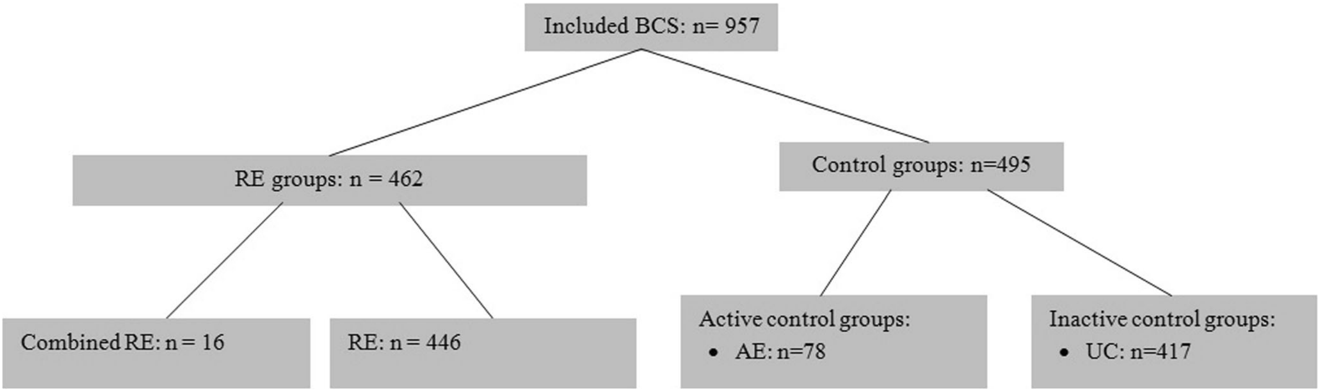


**Fig. 2** Summary of the allocations of all included participants. *BCS* breast cancer survivor, *RE* resistance exercise, *AE* aerobic exercise, *UC* usual care

that a progressive resistance exercise therapy does not increase the risk of developing lymphedema. These results of the Cochrane review are in accordance with the results of the present review. In contrast to Cochrane review, in the present systematic review, the effect of strength exercise on existing lymphedema was also considered. The results of this review revealed that strength exercise seems not to have negative effects on the existing lymphedema in breast cancer patients. As we have pointed out in this review, current literature does not support the assumption that a systematic RE program had detrimental effects on the development of secondary LE. On the contrary, we found that two studies even showed that individual patients experienced substantial improvements of their LE status [27, 29]. These results are far from being statistically significant but introduce the possibility that—under specific circumstances—RE might even preventative on the development of secondary LE. Therefore, it will be a major task for future research to identify those potentially beneficial factors. On the one hand, this means that future exercise programs will have to be evaluated in detail regarding RE intensity, volume, duration, frequency, and exercised muscle groups. As shown in Table 4, although all of the included

**Table 3** Dropout analysis and adherence

| Study | *n* in the RE group | Dropout | Dropout reason | Adherence |
|---|---|---|---|---|
| Ahmed et al. [22] | 23 | 0 | | All participants of the intervention group (but 1) attended 80 % of the sessions |
| Anderson et al. [23] | 52 | 9 | Feeling overwhelmed or a lack of time to participate (38 %), lost to follow-up (19 %), lack of interest (10 %), family issues (10 %), death (10 %), and other reasons (10 %). Dropout reasons were described for the whole population (RE + control group) | Majority (61 %) completed more than 75 % of the sessions whereas only 13 % completed less than 50 % of the sessions |
| Cormie et al. [24] | 43 | 3 | 3 participants in intervention groups did not complete all follow-up measurements due to "unrelated medical condition" (*n* = 1) or "time constraints" (*n* = 2) but finished the study | High exercise attendance rate with average 23.2 ± 1.9 out of 24 possible sessions |
| Cormie et al. [25] | 17 | 0 | | 100 % compliance |
| Courneya et al. [26] | 82 | 6 | Unreachable patient after multiple attempts | Average attendance to the exercise group was 70.2 % |
| Hayes et al. [27] | 16 | 1 | Recurrent disease | Average attendance more than 70 % of supervised sessions |
| Kilbreath et al. [28] | 81 | 8 | Disconnection due to time commitment (*n* = 4), unable to contact (*n* = 4) | 78 % average adherence (7 out of 8 sessions attended) |
| Schmitz et al. [29] | 71 | 6 | Lost to follow-up (*n* = 6) | Attendance decreased from 96 % in the first quarter of the year to 76 % in the last quarter |
| Schmitz et al. [30] | 77 | 11 | Recurrent disease (*n* = 5), no further details provided (*n* = 6) | Median attendance was 79 % |
| Overall | 462 | 44 | Dropouts due to LE-related symptoms: none | |

*LE* lymphedema, *RE* resistance exercise group

**Table 4** Patient details, lymphedema status, and exercise details of the 9 included studies

| Study | Year | Sample | Patient details/LE status | Exercise duration, frequency, intensity | Exercise details | Compression |
|---|---|---|---|---|---|---|
| Ahmed et al. [22] | 2006 | 45<br>RE: $n = 23$<br>Cont: $n = 22$ | Breast cancer survivors 4–36 months post treatment with axillary node dissection, women with LE ($n = 13$) and at risk of LE ($n = 32$) (LE defined as >2 cm interlimb difference) | Duration: 6 months<br>Frequency: 2×/week at 60 min<br>Intensity: start: no weight or half-pound wrist weight, increased by smallest increment<br>For lower body: participants lifted highest possible weight | Sets: 2–3<br>Rep/set: 8–10 (lower body) Muscle groups: arms, back, chest, buttocks, legs<br>Exercises used: variable resistance machines and free weights<br>Structure: warm up, weight training, cool down, and stretching exercises | Yes (women with known LE wore compression garment according to guidance of their LE specialist) |
| Anderson et al. [23] | 2012 | 104<br>RE: $n = 52$<br>Cont: $n = 52$ | Women with newly diagnosed TNM stage I–III breast cancer, at risk of LE (200-ml difference in volume between arms) | Duration: 12 months<br>Frequency: 2×/week at 60 min<br>Intensity: 50 % 1RM, slowly increasing | Sets: 1<br>Rep/set: 12<br>Muscle groups: upper body: chest, upper back, shoulders, arms lower body: legs, core: lower back<br>Exercises used: no detailed information<br>Structure: 5 min warm up, 30 min walking moderate to hard on RPE scale, 20 min strength exercise, 10 min stretching at the end | Yes. Additional instructions to wear it preventively during exercise, heavy arm use, and air travel |
| Cormie et al. [24] | 2013 | 62<br>RE (high): $n = 22$<br>RE(low): $n = 21$<br>Cont: $n = 19$ | Women with a histological diagnosis of breast cancer since at least 1 prior to the study<br>Women with clinical diagnosis of BCRL (>5 % interlimb difference) | Duration: 12 weeks<br>Frequency: 2×/week at 60 min<br>Intensity: 75–85 % 1RM (high load group)/10-6RM 55–65 % 1RM (low load group)/20-15RM | Sets: 1–4<br>Rep/set: variable, 12–16 on Borg Scale<br>Muscle groups: main upper + lower body muscles (chest, back, shoulders, upper arms and forearms)<br>Exercises used: chest press, seated row/lat. pulldown, shoulder press/lateral raise, bicep curl, tricep extension, wrist curl, leg press and squat<br>Structure: Warm-up + cool-down periods 5 min (low-level aerobic exercise and stretching) | Recommended, not obligatory (25 % of participants wore compression sleeve during intervention) |
| Cormie et al. [25] | 2013a | 17<br>RE: $n = 17$ | Women who had a histological diagnosis of breast cancer at least 1 year prior to the study<br>With BCRL diagnosis (defined by impedance ratio of at least 3 standard deviations greater than norm, interlimb volume difference ≥5 %) | Intervention details: One single exercise intervention applied twice (crossover design) with a washout phase of 1–2 weeks<br>Intensity: load was individually prescribed and progressed, intensity was low to high | Sets: 2<br>Rep/set: high: 6-8RM low: 15-20RM<br>Muscle groups: major muscle groups upper body Exercises used: chest press, lateral pulldown, biceps curl, triceps extension, lateral raise<br>Structure: Prior to experimental sessions, all participants completed 4 familiarization sessions over 2 weeks (sets: 1–2, rep/set: 6 to 20, 5 upper body resistance exercises) | Participants chose themselves whether or not to wear a compression garment, 3 of 17 chose to wear a compression garment |
| Courneya et al. [26] | 2007 | 242<br>AE: $n = 78$<br>RE: $n = 82$<br>Cont: $n = 82$ | Breast cancer patients stage I–IIIA receiving adjuvant chemotherapy<br>Patients at risk of and with preexisting LE (not exactly defined) | Duration: during chemotherapy (median: 17 weeks)<br>Frequency: 3×/week<br>Intensity: RE: 60–70 % 1RM, slowly increasing (+10 % when more than 12 | Sets: 2<br>Rep/set: 8–12<br>Muscle groups: main muscle groups upper + lower body | No recommendation |

**Table 4** (continued)

| Study | Year | Sample | Patient details/LE status | Exercise duration, frequency, intensity | Exercise details | Compression |
|---|---|---|---|---|---|---|
| | | | | repetitions could be completed by participant) AE: week 1–6: 60 % VO2max week 7–12: 70 % VO2max beyond week 12: 80 % VO2 max | Exercises used: leg extension, leg curl, leg press, calf raises, chest press, seated row, triceps extension, biceps curls, and modified curl-ups<br>Structure: warm-up + cool-down periods 5 min (light aerobic activity and stretching)<br>AE-structure: increasing duration, time starting at 15 min to 45 min+, using an ergometer, treadmill, or elliptical | |
| Hayes et al. [27] | 2009 | 32<br>RE: $n$ = 16<br>Cont: $n$ = 16 | Women who completed treatment for unilateral breast cancer<br>With unilateral upper limb LE<br>(diagnosed by a health professional) | Duration: 12 weeks<br>Frequency: weeks 1–4: 3×/week (1× supervised) at 20–30 min<br>Weeks 5–8: 4×/week (2× supervised) at 30–45 min<br>Weeks 9–12: 4×+/week (1× supervised) at 45 min+<br>Intensity: weeks 1–4: RPE 3-5<br>Weeks 5–8: RPE 4–6, Weeks 9–12: RPE 4-7 | Sets: 1<br>Rep/set: week 1–4: 20, week 5–8: 15, week 9–12: 10<br>Muscle groups: large and small upper limb muscles<br>Exercises used: no details provided<br>Structure: mixed type exercise:<br>Weeks 1–4: aerobic exercise + water-based resistance exercise<br>Weeks 5–8: aerobic exercise + water resistance exercise + free weight exercise<br>Weeks 9–12: aerobic exercise + machine weight resistance exercise | Participants chose themselves whether or not to wear a compression garment, 3 of 32 chose to wear a garment during exercise |
| Kilbreath et al. [28] | 2012 | 160<br>RE: $n$ = 81<br>Cont: $n$ = 79 | Women treated for early breast cancer 4–6 weeks after surgery, patients at risk of LE (an interlimb difference of >10 % or interlimb difference of >2 cm) | Duration: 8 weeks<br>Frequency: daily (1×/week supervised)<br>Intensity: 15 on Borg Scale | Sets: 2<br>Rep/set: 8–15<br>Muscle groups: shoulder muscles<br>Exercises used: free weights (supervised) + TheraBand® (at home)<br>Structure: participants were instructed to additionally stretch their shoulder muscles daily—according to given instructions | No recommendation |
| Schmitz et al. [29] | 2009 | 141<br>RE: $n$ = 71<br>Cont: $n$ = 70 | Breast cancer survivors (unilateral non- metastatic breast cancer 1 to 15 years before study entry), preexisting LE, (defined as 10 % interlimb volume or circumference difference, 5 % increase of interlimb volume was defined as LE exacerbation) | Duration: 12 months<br>Frequency: 2×/week at 90 min<br>Intensity: "little-to-no" weight, slowly increased by the smallest possible increment (no upper limit) | Sets: 2–3<br>Rep/set: 10<br>Muscle groups: main muscle groups for upper body + lower body<br>Exercises used: seated row, chest press, lateral or front raises, bicep curls, and tricep pushdowns. Lower body exercises included leg press, back extension, leg extension, and leg curl. Weight-lifting exercises were introduced with little-to-no resistance<br>Structure: stretching, cardiovascular warm-up, abdominal and back exercises, and weight-lifting exercises | Yes, a well-fitting compression garment was obligatory during weight lifting |
| Schmitz et al. [30] | 2010 | 154<br>RE: $n$ = 77 | Breast cancer survivors (unilateral non- metastatic breast cancer 1 | Duration: 12 months<br>Frequency: 2×/week at 90 min | Sets: 3<br>Rep/set: 10 | Yes (if LE occurred) |

**Table 4** (continued)

| Study | Year | Sample | Patient details/LE status | Exercise duration, frequency, intensity | Exercise details | Compression |
|---|---|---|---|---|---|---|
| | | Cont: $n = 77$ | to 5 years post treatment), at risk of LE (defined as 10 % interlimb volume or circumference difference, 5 % increase of interlimb volume was defined as LE onset) | Intensity: "little-to-no" weight, slowly increased by the smallest possible increment (no upper limit) | Muscle groups:<br>Main muscle groups for upper body + lower body<br>Exercises used: seated row, supine dumb bell press, lateral or front raises, bicep curls, and triceps pushdowns; leg press, back extension, leg extension, and leg curl<br>Structure: stretching, cardiovascular warm-up, abdominal and back exercises, and weight-lifting exercises | |

*AE* aerobic exercise group, *BCRL* breast cancer-related lymphedema, *Cont.* control group, *LE* lymphedema, *Rep/set* repetitions per set, *RE* resistance exercise group, *RPE* rating of perceived exertion scale, *TNM* TNM (tumor/nodes/metastasis) classification of malignant tumors, *RM* repetition maximum

studies complied with the exercise guidelines for breast cancer survivors [21], they still significantly differed between themselves. On the other hand, the current state of knowledge revealed that it will be necessary for future studies to thoroughly identify potential confounders. That is something that has not been done in all of the included studies, as was already shown in our risk of bias assessment (Table 1, items 5 and 25).

Ahmed et al. [22] noted that exercise might lead to physiological change in lymphatic structures and/or function. A possible pathway of how RE could positively influence the LE status in BCS could be deducted from the positive effects structured exercise has on the calf muscle pump in patients with chronic venous insufficiency [36]. RE of the upper extremities could have similar beneficial effects on the venous hemodynamics of the upper extremities, which in turn could support the lymphatic flow of the LE and then again lead to a reduction of swelling.

A major limitation of some of the reviewed articles was that not all of them used assessment methods for LE that would allow conclusions on the limb composition. Water displacement volumetry is described to be the gold standard for measuring limb volume [37, 38], and circumference measurements are inexpensive and, when correctly applied, also highly valid and reliable [39]. When conducting a structured RE program, it has to be considered that even without dietary monitoring, a positive muscle protein synthesis rate would most certainly be achieved in at least some of the participants [40]. Therefore, if the affected limb suffers from a LE-related swelling, by just measuring its volume or its circumference, potential increases in muscle cross-sectional area would not be detected. Nevertheless, indirect information about the LE status can be assessed by comparing the affected with the healthy arm, a method which also accounts for composition [22, 26, 29, 30]. Therefore, further studies are needed to improve our bulk of knowledge. In the discussion of definition and most appropriate assessment tool of LE, there is an absence of an agreed diagnostic definition of lymphedema due to its wide variation in different measurement techniques used in the literature and in daily routine. This might be to the fact that lymphedema assessment methods are concordant and reliable but not interchangeable. Furthermore, no consensus on golden standard of lymphedema measurement is available in the literature [19].

Another major concern regarding a RE intervention for BCS was mentioned by Hayes et al. [27], who recorded qualitative comments regarding the exercise program and the LE status. He found out that many patients sensed grief and frustration and became uncertain about the likely outcome of LE treatment because of conflicting advice from health professionals regarding the exercise intervention. It is therefore of substantial importance that, when planning a RE intervention study with BCS, all health professionals that may get in contact with the study participants receive sufficient information material about the current evidence ahead of time.

A limitation of the present systematic review is that due to the limited number of eligible studies and the heterogeneity of the RE interventions, we did not perform a meta-analysis. This narrow width of evidence-based scientific knowledge together with the presence of unbacked and out of date assumptions regarding RE and LE shows how important it is on the one hand to gain new evidence and on the other hand, to share the insights of this review about the current state of knowledge with health care professionals working with BCS. With this newly acquired knowledge, maybe more health care specialists will set aside their fear of performing RE with BCS. This would not only be beneficial for the patients but could also be very helpful in boosting the data collection process. We suggest that a minimum of about 20 high-quality RCTs would be necessary in total for being able to conduct a thorough meta-analysis.

It can be concluded that—at the moment—the scientific literature does not give any contraindications of RE for BCS suffering or at risk of BCRL when performed according to the ACSM guidelines for cancer survivors [21]. RE interventions seem to be safe, feasible, and beneficial regarding physical performance in patients with or at risk of BCRL. If RE could actually be beneficial for the LE status remains open for future research.

**Compliance with ethical standards**

**Conflict of interest** The authors declare that they have no competing interests.

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