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Resistance Exercise for Breast Cancer Patients? Evidence from the Last Decade

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Abstract
Background: Breast cancer is associated with many therapy-induced side effects that impact patients' lives from diagnosis to long-term survivorship. Physical activity has become an important and proven supportive measure in treating side effects like loss of muscle strength, fatigue, chemotherapy-induced peripheral neuropathy, lymphedema, and loss of quality of life. Resistance training (RT) is an established exercise intervention for breast cancer patients, but the correct type, timing, intensity, and duration of exercise remain unclear. It is necessary to investigate different resistance training interventions and their effects on breast cancer patients by covering all stages of treatment, beginning with prehabilitation, through the period of acute therapy, to long-term survivorship. ***Conclusion:*** Upon evaluation of randomized controlled trials (RCTs) from the past decade, RT was found to be feasible and safe. Furthermore, there is evidence on the impact of RT on muscle strength, CRF and QoL amongst other factors. Studies implementing mixes of aerobic and strength exercises are rather common, but RCTs of RT-only protocols remain scarce. Different strength training protocols at distinct stages of breast cancer treatment have been conducted, but with the complexity of treatments and the variety of training styles, a large field of study remains. ***Key Messages:*** Although the overall data on RT for breast cancer patients has increased, there are many different methodological approaches and testing measures as well as gaps in study documentation. There is still very little of the evidence that would facilitate the compilation of standardized and individualized guidelines.

Introduction

Breast cancer is still the most common cancer diagnosis in women worldwide, and it is associated with many therapy-induced side effects which can remain a challenge for breast cancer patients for months, years, and even decades [1]. Exercise has been proven to benefit breast cancer patients in many ways, and it improves patients' physical condition and reduces treatment-associated impairments [2]. Both aerobic and resistance training (RT) are recommended as they involve different mechanisms. Even though RT is considered more promising in the domains of muscle mass, strength, and countering some side effects of therapy, the limited availability and lack of clarity of reported data mean that the ideal modalities, timing, intensity, and modes of RT have not yet been established.

The purpose of this review was to evaluate the findings of randomized-controlled trials (RCTs) regarding the impact of RT on breast cancer patients over the last 10 years, and differentiate between phases of medical treatment. Furthermore, the review will focus on cancer and treatment-associated impairments such as reduced muscle strength, secondary lymphedema, body weight and composition changes, reduced bone mineral density, fatigue, and a poorer quality of life (QoL). The literature search was conducted

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in PubMed early in March 2020 and articles were screened for RCTs examining the effects of RT only on breast cancer patients in the period 2010–2020. Additionally, the reference lists of original articles and the reviews of related articles were checked for further eligible studies.

Prehabilitation

In recent years, evidence has accumulated to suggest that physical fitness prior to breast cancer surgery influences the process of physical recovery [3]. A meta-analysis revealed the potential effects on length of hospital stay (although it was not cancer-specific) [4]. Surprisingly, not many RCTs have been published about prehabilitation of breast cancer patients, and none focused on RT [5]. Most studies discuss combinations of education, aerobic exercise, and mobility exercises [6, 7]. Strength exercises are positively associated with muscle strength, providing a satisfactory rationale to including RT as a preoperative exercise method. However, to our knowledge, there are no published reports of RCTs only investigating the effects of RT prior to surgery.

Acute Therapy

Acute treatment options for breast cancer range from surgery, to chemotherapy, hormonal therapy, targeted therapy, immunotherapy, and radiation therapy, often in combination. While there has been a call for targeted studies to determine the correct type, timing, intensity, and duration of exercise [8–10], so as to formulate exercise guidelines for breast cancer patients during acute treatment [11], we only found 4 RCTs and 3 studies with active control groups (Table 1).

Muscle Strength

RT was found to be safe and effective at improving upper- and lower-body muscular strength in women with breast cancer undergoing acute therapy [12]. The RCTs in the past 10 years have shown beneficial effects on strength parameters during acute therapy.

Ammitzbøll et al. [13] documented increased muscle strength in patients undergoing chemotherapy, by utilizing a progressive, whole-body training protocol that was split into a supervised phase and a longer-term self-administered phase. It is worth mentioning that posttesting was conducted 50 weeks after baseline.

Other mixes of supervised and unsupervised protocols reported positive effects on muscular strength too. Kilbreath et al. [14] trained patients after surgery in a mixed setting comprising a supervised session and a home-based session.

Unsurprisingly, high-intensity training protocols also led to significant strength gains. One study focusing on only 1 machine (the leg-press) and using intensities as high as 85–90% of the h1RM ([hypothetical 1-repetition maximum], extrapolated hypothetical resistance that the patient is able to overcome once), documented significant strength gains in the lower limbs [15, 16]. Of this collective, 92% were designated to undergo chemotherapy, 85% to have radiation therapy, and 78% to have hormone therapy, but it is unclear how many patients were actually under treatment during the intervention.

Wiskemann et al. [17] discussed progressive whole-body training and documented significant increases in muscle strength for patients undergoing radiation therapy. A similar approach was documented by Schmidt et al. [18] for patients undergoing chemotherapy, with significant strength gains being reported. Mijwel et al. [19] compared an RT group to an aerobic exercise group, and both collectives also did the same high-intensity interval training (HIIT). They reported significant strength gains for the upper body in the RT group.

BMI/Body Composition

Neither a high-intensity 12-week program [15, 16] nor a 16-week combination program of RT and HIIT [19] found significant changes in BMI or body composition, even though significant increases in strength were reported for the intervention group with both approaches. Mijwel et al. [19] point out that RT was as efficient as aerobic exercise in maintaining body composition during treatment.

Secondary Lymphedema

RT has been found to be safe for women surgically treated for breast cancer and does not worsen breast cancer-related lymphedema (BCRL) symptoms [11]. A recent study [13] found no evidence of a preventive effect of RT on BCRL development and no relevant intergroup differences for interlimb volume and mass. Another study [14] using an 8-week RT intervention 4–6 weeks after surgery could not find significant differences between the intervention and control group immediately after the intervention or at the 6-month follow-up. The findings support the safety of RT for patients suffering from BCRL, in accordance with the exercise guidelines [8], suggesting moderate intensities and starting exercise programs in a supervised setting.

Cancer-Related Fatigue

The exercise guidelines published by Campbell et al. [8] added RT as an effective method for treating cancer-related fatigue (CRF). A recent study comparing progressive RT and a relaxation group [17, 20] during radiation therapy found significant between-group differences for

Table 1. Resistance exercise in breast cancer patients – RCTs

First author [ref.], year	Supervised vs. unsupervised; machines vs. free weights	Duration	Intensity	Outcome vs. control
↓ Acute treatment ↓				
Ammitzbøll [13], 2019	1st 20 weeks, supervised group training + unsupervised free weights and resistance bands 2nd 30 weeks unsupervised	50 weeks, 3×/week	Whole body, progressive, 10–20 reps, 3 sets	↑ Muscle strength ↔ BCRL volume ↔ BCRL symptoms
Cešeiko [15], 2019	Supervised, leg-press machine	12 weeks, 2×/week for 20 min	Leg-press, progressive, 4 reps, 4 sets at 85–90% h1RM	↑ Muscle strength ↔ BMI ↑ QoL (EORTC-QLQ C30, BR23)
Kilbreath [14], 2012	Supervised + unsupervised Free weights, resistance bands	8 weeks, 1×/week + home program, 24-week follow-up	Shoulder muscles, exercises unspecified progressive, 8–15 reps	↑ Muscle strength ↔ BCRL ↑ BCRL symptoms
Mijwel [19], 2018	RE + HIIT: supervised, machines AE + HIIT: supervised	RE/AE: 16 weeks during chemotherapy, 2×/week	RE: 8–12 reps, 2–3 sets 80% h1RM 3 × 3 min HIIT AE: 20 min steady state, 13–15 BORG Scale 3 × 3 min HIIT	RE+HIIT vs. AE+HIIT: ↑ Muscle strength ↔ BMI ↑ Pressure-pain threshold
Schmidt [21], 2015	RE: group training, supervised RELX: group training, supervised	12 weeks, 2×/week during chemotherapy	Whole body, progressive, 3 sets/ 12 rep max Progressive muscle relaxation	RE vs. RELX ↑ CRF ↔ QoL
Schmidt [18], 2015	Supervised, machines	12 weeks, 2×/week during chemotherapy	Whole body, progressive, 20 reps, 1 set at 50% h1RM	↑ Muscle strength ↔ CRF ↑ QoL
Steindorf [20], 2014/ Wiskemann [17], 2017	RE: machines unsupervised RELX: group training, supervised	12 weeks, 2×/week	RE: whole body, progressive, 3 sets/12 rep max RELX: PMR	RE vs. RELX ↑ Muscle strength ↔ CRF
↓ Survivors ↓				
Schmitz [28], 2010/ Brown [27], 2012	1st 3 months supervised; 2nd 9 months unsupervised Machines and free weights	1 year, 2×/week for 90 min	Whole body, progressive, 10 reps, 3 sets	↑ Muscle strength ↑ BCRL onset ↔ BMI ↔ Lean mass
Winters-Stone [35], 2014	As above	As above	As above	↔ BMD
Hagstrom [24], 2019	Supervised; 1st 8 weeks machines, 2nd 8 weeks free weights	16 weeks, 3×/week for 60 min	Whole body, progressive, 8–10 reps, 3 sets	↑ Muscle strength
Hagstrom [23], 2016/ Hagstrom [41], 2016	As above	As above	As above	↑ Muscle strength ↔ BMI ↑ QoL (FACT-G) ↑ Fatigue (FACIT)
Dos Santos [26], 2019	Supervised, Machines and free weights	8 weeks, 1×/week	Whole body, progressive, 8–12 reps, 3 sets	↑ Muscle strength ↔ BMI ↔ Lean mass
Jeffs [31], 2013	Unsupervised Gravity resistive exercises	6 months, 7×/week for 10–15 min	Upper body, no intensities reported	↔ BCRL volume ↔ QoL (LYMQOL) ↔ BMI
Waltman [36], 2010	Unsupervised, 1st 9 months: free weights 2nd 15 months: machines	24 months, 2×/week	Whole body, progressive 8–12 reps, 2 sets	↔ BMD
Santagnello [37], 2020	Supervised, machines	12 weeks, 3×/week	Lower body, progressive, 8–12 reps, 3 sets	↑ Muscle strength ↑ Lean mass ↑ Fatigue
Buchan [34], 2016	RE: 1/3 supervised and 2/3 unsupervised, machines and free weights AE: 1/3 supervised and 2/3 unsupervised	RE/AE: 12 weeks + 12-week follow-up, 3×/week for 50 min	RE: Whole body, progressive, 8–12 reps, 2 sets AE: intensities according a MET-level of 5	RE vs. AE: ↑ Muscle strength ↔ BCRL ↔ Lean mass ↔ QoL (FACT-B)

Table 1 (continued)

First author [ref.], year	Supervised vs. unsupervised; machines vs. free weights	Duration	Intensity	Outcome vs. control
Musanti [25], 2012	Unsupervised RE: free weights (resistance bands) AE: walking REAE: combination of both	12 weeks, RE: 3×/week AE: 3×/week for15–30 min REAE: RE 2×/week + AE 4–5×/week	RE: whole body, progressive, 10–12 reps, 1 set AE: 40–65% (up to 85%) of HRmax Combination of both, intensities as above	RE and REAE vs. AE and controls: ↑ Muscle strength
Cormie [29], 2013	Supervised; machines and free weights RE intense RE moderate	12 weeks 2×/week for 60 min	Whole body, progressive, RE intense: 6–10 reps with 75–85% of 1RM, 1–4 sets RE moderate: 15–20 reps with 55–65% of 1RM, 1–4 sets	RE HIGH and MOD vs. controls: ↔ BCRL volume ↔ BCRL symptoms ↑ Muscle strength

Overview of strength exercise RCT studies in acute breast cancer therapy and in breast cancer survivors over the last 10 years. AE, aerobic exercise; BCRL, breast cancer-related lymphedema; BMD, bone mineral density; BMI, body mass index; CRF, cancer-related fatigue; HIIT, high-intensity interval training; HRmax, maximum heart rate; MET, metabolic equivalent of task; PMR, progressive muscle relaxation; RE, resistance exercise; REAE, resistance + aerobic exercise; RELX, relaxation training; reps, repetitions; QoL, quality of life.

self-reported CRF using the Fatigue Assessment Questionnaire (FAQ), especially concerning physical fatigue, but both interventions led to improvements in total and affective scores. Muscular fatigue worsened from baseline to postintervention in the relaxation group, but there was no deterioration in the RT group. Using comparable training designs with collectives undergoing chemotherapy, a study on lower-intensity RT [18] did not associate RT with improvements in CRF; a study on higher-intensity RT [21] found a favorable tendency for RT compared to relaxation training.

Quality of Life

QoL has been reported to be affected positively by RT during adjuvant therapy [22], and Campbell et al. [8] recommend 2–3 sets of 8–15 repetitions at 60–75% of the 1RM for cancer patients. In the recommended supervised setting, but using higher intensities, Češeiko et al. [15] reported positive effects for several scales in the EORTC QLQ C30 and BR23 questionnaires. One study on using low intensities during chemotherapy [18] found significant improvements in QoL, while a comparable design utilizing moderate intensities suggests slight improvements for role and social function, and a maintenance of global QoL measures. During radiotherapy, another study [20] reported significant increases in global QoL, again using a comparable training protocol.

Breast Cancer Survivors

Muscle Strength

Strength training is widely known to be beneficial in breast cancer survivors especially due to its effects on muscle function. Clinical trials in the last 10 years substantiated this assumption with conclusive findings of improvements of muscle strength following strength exercise interventions (Table 1) [23–29, 37].

Three RCTs [23, 24, 26] showed improved muscle strength due to machine-based and free-weight strength exercise programs of 16 and 8 weeks, respectively. The latter exercise program [26] was conducted as a 1:1 patient-trainer supervision, suggesting the ideal exercise support, whereas Hagstrom et al. [23, 24] used a small-group setting. An equivalent strength training protocol, with machine-based exercises of the lower body only, led to improved muscle strength after 12 weeks [37]. The Physical Activity and Lymphedema (PAL) trial showed that an initial 3 months of supervised strength exercise, followed by 9 months unsupervised, improved muscle strength by using comparable exercise protocols.

In comparison to aerobic exercise, strength exercise seems to be crucial for muscle strength improvements. Twelve weeks of mixed home-based and supervised RT showed superior muscle strength improvements in the upper body than 12 weeks of mixed home-based and supervised aerobic exercise [34]. The combination of aerobic exercise and RT does not seem to be more effective than RT only. The trial of Musanti [25] reported similar significant increases of muscle strength in breast cancer survivors who performed strength training or combined strength and aerobic training compared to aerobic- or mobility-exercised groups.

The study of Cormie et al. [29] showed that moderate RT was sufficient to improve muscle strength in the same way as intense strength training, with significant improvements in both groups compared to a control group. It should be mentioned that their study did not explicitly list completed treatment as an inclusion criterion, but the mean time since cancer diagnosis of the study population was given as approximately 6 years.

BMI/Body Composition

Both short- and long-term exercise durations did not change the BMI in a significant manner using RT protocols that lasted 1 year [25], nor did daily gravity-resistive exercise for 6 months [28]. Likewise, short- and mid-term strength exercise led to no changes after 16 weeks of strength exercise [23] and only small increases in BMI following 8 weeks of personal training [28]. Despite improved muscle strength, only 1 of 4 studies showed an impact of RT on lean body mass [34].

Secondary Lymphedema

Current reviews conclude that resistance exercise is safe and does not exacerbate BCRL [29, 30]. The strength studies of the last 10 years are in line with these conclusions. The PAL trial [25] reported a significantly reduced number of women experiencing a BCRL incident or onset in the weight-lifting group after 1 year of exercise. However, 2 studies with shorter exercise duration reported no effects of exercise on the volume [29, 31], number of symptoms, or severity of BCRL [29]. Comparison of 12 weeks of aerobic and strength exercise did not reveal differences in BCRL domains [34].

Bone Health

Two trials investigated the effects of RT only on bone mineral density (BMD). Neither study found any significant changes in BMD in breast cancer survivors after 1 or 2 years of strength exercise [35, 36]. However, small and nonsignificant trends in both studies suggested a potential osteogenic effect of RT in postmenopausal women.

Cancer-Related Fatigue

Two recent studies on breast cancer survivors evaluated the effects of progressive RT on CRF. Subjectively perceived fatigue improved in survivors who undertook RT compared to the control group [37, 41].

Quality of Life

Whereas the study of Jeffs and Wiseman [31] did not show increases of lymphedema-related QoL after 6 months of daily gravity-resistive exercises, the trial of Hagstrom et al. [41] improved breast cancer survivors' QoL (according to the functional assessment of cancer therapy-general [FACT-G] scale) following whole-body strength training over the same period. When the 12-week strength and aerobic exercise were compared, no differences were observed [34].

Discussion

In the current national guidelines, RT is an established supportive treatment during adjuvant therapy and for long-term survivors, and it is recommended for use during chemotherapy, antihormone treatment, and in the presence of BCRL in the German Breast Cancer Guidelines [42]. It is considered a flexible, proven, and powerful tool to treat muscle loss, reduced strength, CRF, lymphedema, and several aspects of QoL [8, 38, 39]. Furthermore, RT was found to be safe even utilizing high loads during adjuvant treatment [12]. However, current recommendations for cancer patients are vague. There is not enough evidence to provide guidelines for individualized, standardized, and targeted interventions that take into account therapy stage and other factors that influence the goals of interventions.

The listed studies underline the efficacy of RT for breast cancer patients during treatment and aftercare with regard to muscle strength. Supervised and unsupervised settings proved to be efficient as well as a broad range of intensity and length of periods of exercise. The studies of the past decade were generally useful in showing the positive impact of several factors on patients' QoL. RT as a treatment for CRF is now implemented in the exercise guidelines for cancer patients [8] despite the scarcity of pure RT studies in the past 10 years; effect sizes apparently depend on training intensity [18, 20]. The findings on RT and the development and symptomatology of lymphedemas vary, conclusively only suggesting the feasibility and safety but no distinct benefits of RT in patients with lymphedemas. Considering changes in BMI, aerobic exercise seems to be more beneficial for cancer patients, although the possible impact of RT on body composition is not reflected in the cited studies.

However, these studies cannot do justice to the complexity of breast cancer treatment and the diversity of RT. The lack of studies examining RT in prehabilitation, and the small number of RT-only protocols in adjuvant therapy was especially surprising, as surgery is associated with a loss of muscular strength and a reduced range of motion.

Comparability of the studies included was extremely limited due to different testing techniques, different questionnaires, different (and often not clearly outlined) training protocols, and a lack of information about the timing of inclusion and testing.

RT can be carried out indoors and outdoors in supervised, group, or home-based settings that utilize machines, free weights, and other equipment. Lund et al. [40] documented that supervision and support is crucial for adherence in untrained and overweight patients. RT can be considered a highly flexible therapeutic tool.

The measurability of RT exercises through resistance, range of motion, repetitions, and sets predestines this modality for systematic study designs. Simple tools for training control need to be established to meet target intensity and to create safe and efficient guidelines.

Regular physical activity is associated with reduced breast cancer-specific mortality and recurrence [43]. New data suggest that RT may lower chronic inflammation, thereby highlighting its potential to influence one major driver of cancer progression or recurrence [44]. Such perspectives emphasize the importance of a higher output of studies in the field of RT for breast cancer, studies that focus on the promising effects of RT on inflammation, bone health, and long-term survival. Currently, there is too little information comparing RT to other interventions to be able to determine which patients can benefit most from each type of exercise intervention.

Conclusion

Breast cancer patients are a very heterogeneous collective and the goals at every stage of therapy vary. The RCT of the last decade emphasised the beneficial impact of RT on muscle strength, CRF, QoL and possibly lymphedema in breast cancer patients during medical treatment and in survivorship with differing evidence levels. Therefore, a need for individualized guidelines for breast cancer patients exists, that will take into account therapy stage, medication, fitness, and other parameters. The studies of the past decade have found evidence for RT only in the supportive care of breast cancer, but there is room for specifically targeted study designs that will facilitate the compilation of individualized recommendations.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

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Author Contributions

L.G., F.T.B., and T.N.: study conceptualization, methodology, and writing the paper. L.G. and T.N.: investigation.

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