How Resistance Training Load Affects Breast Cancer Patients: Systematic Review

Master's degree dissertation

Miguel Ângelo Santos Moreno Calado

Trabalho realizado sob a orientação de Professor Morouço

Pedro Morouço, orientador

Rita Santos Rocha, coorientador

Raul Antunes, coorientador

Leiria, Novembro 2021

Mestrado em Prescrição do Exercício e Promoção da Saúde

ESCOLA SUPERIOR DE EDUCAÇÃO E CIÊNCIAS SOCIAIS

POLITÉCNICO DE LEIRIA

POLITÉCNICO DE LEIRIA | ESCOLA SUPERIOR DE EDUCAÇÃO E CIÊNCIAS SOCIAIS

AGRADECIMENTOS

Agradeço aos meus pais pelo apoio, familiares e amigos.

RESUMO

Objetivo: O objetivo desta revisão sistemática era identificar e rever a literatura que testou especificamente os efeitos do treino de resistência pesada em doentes com cancro da mama e investigar a viabilidade de prescrever.

Métodos: Foi realizada uma ampla pesquisa nas bases de dados eletrónicas PubMed, Scopus, SPORTDiscus, e British Journal of Sport Medicine para estudos relevantes publicados em revistas com revisão por pares até Maio de 2021, e foram seguidas as diretrizes PRISMA. Os critérios de inclusão foram que um estudo tinha de ser (a) escrito em inglês, (b) publicado numa revista com revisão por pares, e (c) excluído se combinar treino aeróbico, treino simultâneo ou ausência de comparadores, sem resultados relacionados, estudos não randomizados, e intervenção não supervisionada.

Resultados: Foi identificado um total de 5 estudos, que foram incluídos nesta revisão. A maioria dos estudos concluiu que o treino de resistência pesada é benéfico para as doentes com cancro da mama.

Conclusões: Esta revisão concluiu que o treino de resistência pesada em geral parece ter o potencial de melhorar o treino psicológico, físico e funcional, mas são necessários futuros estudos de alta qualidade.

Palavras-chave: Cancro da mama; treino de resistência; Alta intensidade; Carga pesada; oncologia; Linfedema.

ABSTRACT

Aim: The purpose of this systematic review was to identify and review the literature that has specifically tested the effects of heavy resistance training in breast cancer patients and to investigate the viability of prescribing.

Methods: A broad search of electronic databases PubMed, Scopus, SPORTDiscus, and British Journal of Sport Medicine for relevant studies published in peer-reviewed journals through May 2021 was conducted, and PRISMA guidelines were followed. Inclusion criteria were that a study had to be (a) written in English, (b) published in a peer-reviewed journal, and (c) excluded if combine aerobic training, concurrent training or absence of comparators, no outcomes related, non-randomized studies, and non-supervised intervention.

Results: A total of 5 studies were identified and were included in this review. The majority of studies concluded that heavy resistance training is beneficial for breast cancer patients.

Conclusions: This review found that overall, heavy resistance training seems to have the potential to improve psychological, physical, and functional, but future high-quality studies are needed.

Keywords

Breast cancer; Resistance training; High-intensity; Heavy-load; oncology; Lymphedema.

Índice Geral

ÍNDICE DE FIGURAS

ÍNDICE DE TABELAS

Background

It is estimated that the number of people diagnosed with cancer worldwide has been increasing, reaching 19.3 million in 2020. Of these, about 2.3 million (11.7%) will be breast cancer, which has now supplanted lung cancer as the leading cause of global cancer incidence (Sung et al., 2021). The aging population, the excessive consumption of alcoholic beverages, smoking, incorrect eating habits, and physical inactivity are considered potentiating agents in the development of the disease (Jemal et al., 2011).

Medical advances in treatment, coupled with early diagnosis and counseling, have led to an increase in the number of breast cancer survivors. The pathology is now diagnosed at earlier stages, making more treatment options available, such as mastectomy, radiation therapy, hormone therapy, chemotherapy, or immunotherapy. Despite these advances, the side effects are still felt in the quality of life (Tomás & Fernandes, 2012). The marked decrease in functionality and physical fitness is one of these effects and results in decreased functional independence, leading to a state of fatigue that requires the reduction or impossibility of performing activities of daily living. Thus, survival implies living with cancer as a chronic condition or with its persistent long-term effects, and therefore, it is important to adopt strategies to combat and mitigate the influence of these consequences on the body(AC et al., 2016; Clifford et al., 2018; Panchik et al., 2019).

The literature has shown robust evidence of the positive psychological, physical, and functional effects of physical exercise in cancer survivors. However, most people do not comply with the general recommendations for physical activity (Riebe et al., 2018). Although these recommendations reference the general population, cancer survivors have an increased need due to the impact the disease brings. Among the reasons for non-physical practice is a lack of clarity on the part of those working in cancer clinical settings and their role in counseling patients to exercise (Clifford et al., 2018; Lugo et al., 2019; Ruiz-Casado et al., 2017; Schmitz et al., 2019). It is of utmost importance that physicians refer patients to perform exercise where it is properly adapted based on the type of cancer, treatment, side effects, and potential risks. An exercise follow-up will allow better control over technique and effort resulting in better rehabilitation, taking into account people's level of physical fitness. This will require a good interdisciplinary intervention for the patient to benefit from the best possible monitoring to ensure optimal adaptation to individual needs (Chen et al., 2011; Musanti et al., 2019; Schmitz et al., 2019).

The use of resistance training together with aerobic training during treatment and after breast cancer surgery as an intervention strategy is feasible, producing beneficial effects on strength, cardiorespiratory levels, body composition, reduction of fatigue and depressive symptoms, post-operative recovery, and may help reduce the risk of recurrence (Betof et al., 2013; Blanchard et al., 2015; Kwan et al., 2011).

Aerobic training is important in the management of mental health, general well-being, and improving physical fitness in cancer patients (AC et al., 2016). However, low-to-moderate intensity activities such as walking or stationary cycling are more likely to be used, since they cause less "fatigue". This is counterproductive since is less muscle mass will be retained which will cause a decline in day-to-day life tasks due to muscle sarcopenic (Demmelmaier et al., 2021). Muscle sarcopenic originates from a sedentary lifestyle and increased inactivity time. In breast cancer patients the side-effects of treatments and medication makes it more likely to happen since the skeletal muscle structure and function happens to be affected (De Backer et al., 2007; Klassen et al., 2017; Villaseñor et al., 2012)

Resistance training has the potential of targeting muscles increasing muscle mass and strength which may contribute to complete participation in daily life tasks and consequently better quality of life. Furthermore, in breast cancer patients bone mineral density is lower due to postmenopausal. Thus, resistance training is suitable for preventing further bone loss (De Backer et al., 2007). There is increasing evidence highlighting the benefits of heavy-load resistance (high-intensity) exercise for clinical populations with improvements in physical or psychosocial capacity compared to moderate-load resistance (moderate-intensity) exercise (Christensen et al., 2014). However, the majority of the interventions use a combination of aerobic training or other forms of training with strength training making it difficult to evaluate the effect of heavy-load resistance training alone.

Thus, our purpose was to review supervised randomized control trials that evaluate the effect of heavy-load resistance training alone in breast cancer patients, in comparison with low- or moderate loads.

METHODS

The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) checklist was followed for this systematic review (Moher et al., 2016). Cochrane Collaboration guidelines for evaluation of the risk of bias in randomized studies (Higgins et al., 2011; Sterne et al., 2019).

Search

The search strategy was designed to identify existing, published articles. Search terms were formulated using the PICO structure. Participants (P) included women (over 18 years old) with breast cancer. Intervention (I) included heavy resistance training. Comparisons (C) were the comparisons between the control and intervention groups. Outcomes (O) included functional gains such as function, improvement in physical impairment, functional measures, overall quality of life, psychological and psychosocial gains.

The PICO strategy covers a larger number of articles and is recommended when searches are made in a variety of databases, this strategy was used according to the methodology of Preferred Report Items for Systematic Reviews and Meta-analyzes (PRISMA), considered relevant for the construction of systematic reviews. The PubMed, Scopus, SPORTDiscus, and British Journal of Sport Medicine databases were searched for significant articles. Only articles published in English were included; the keywords used were “breast cancer”, “resistance training”, “training intensity” which were crossed with the Boolean operator AND. Similar terms were used to ensure a more complete initial search thereby preventing an overly narrow scope. Studies that included breast cancer and heavy strength training and evaluated its effects on health were searched, and only randomized clinical trials were selected.

Eligibility criteria

Studies of original research or replication published in peer-reviewed journals were suitable, only if published in English. Based on scope, P.I.C.O.S., Table 1 cite the inclusion and exclusion criteria. Since randomized control trials are the holy grail of research data into clinical practice (Spieth et al., 2016) as the risk of bias is reduced with this study design. The clinical population requires mandatory supervision of a qualified professional to accommodate and assess all exercise interventions to minimize the risks of injury and drop-out.

TABLE 1 – Inclusion and exclusion criteria based on scope, PICOS

Rule	Inclusion criteria	Exclusion criteria
Study type	Original research or replication studies published in peer-reviewed journals. No limitations are imposed regarding language or publication date.	Conference abstracts, books and book chapters, editorials, letters to the editor, feasibility and pilot studies, trial registrations, reviews, essays, or original research in non-peer-reviewed journals.
Participants	Participants of any age, sex, health, and training status.	Non-human animals (e.g., rats).
Interventions	Heavy resistance training in breast cancer.	HITT, Aerobic training, concurrent training.
Comparators	Heavy vs low- or moderate resistance training. Heavy vs daily activities.	Absence of comparators.
Outcomes	Improvements on cardiorespiratory levels, body composition, reduction of fatigue, and depressive symptoms. OR Positive effect on psychological, physical, and functional function (e.g., strength, cardiorespiratory function, fatigue, etc.).	No outcomes related.
Study design	Supervised randomized control trials (parallel or cross-over).	Non-randomized studies. Non-supervised intervention. Case reports, case series, observational studies (e.g., case-control and cohort studies).

The flow diagram, in Figure 1, describes the procedure of study selection. Initial search reported 5364 results [PubMed: 207; Scopus: 4,909; SPORTDiscus: 7; British Journal of Sport Medicine: 345]. A total of 43 studies were identified in search results from the four databases. by which studies were included or excluded. Manual removal of additional 13 duplicates resulted in 30 studies to be screened. The first stage of screening titles and abstracts was based on interventions (third inclusion criteria) and resulted in the exclusion of 21. The second and last stage with 9 studies was applied the PICOS criteria, and further excluded 4 studies. The final selection of studies can be observed in Table 2

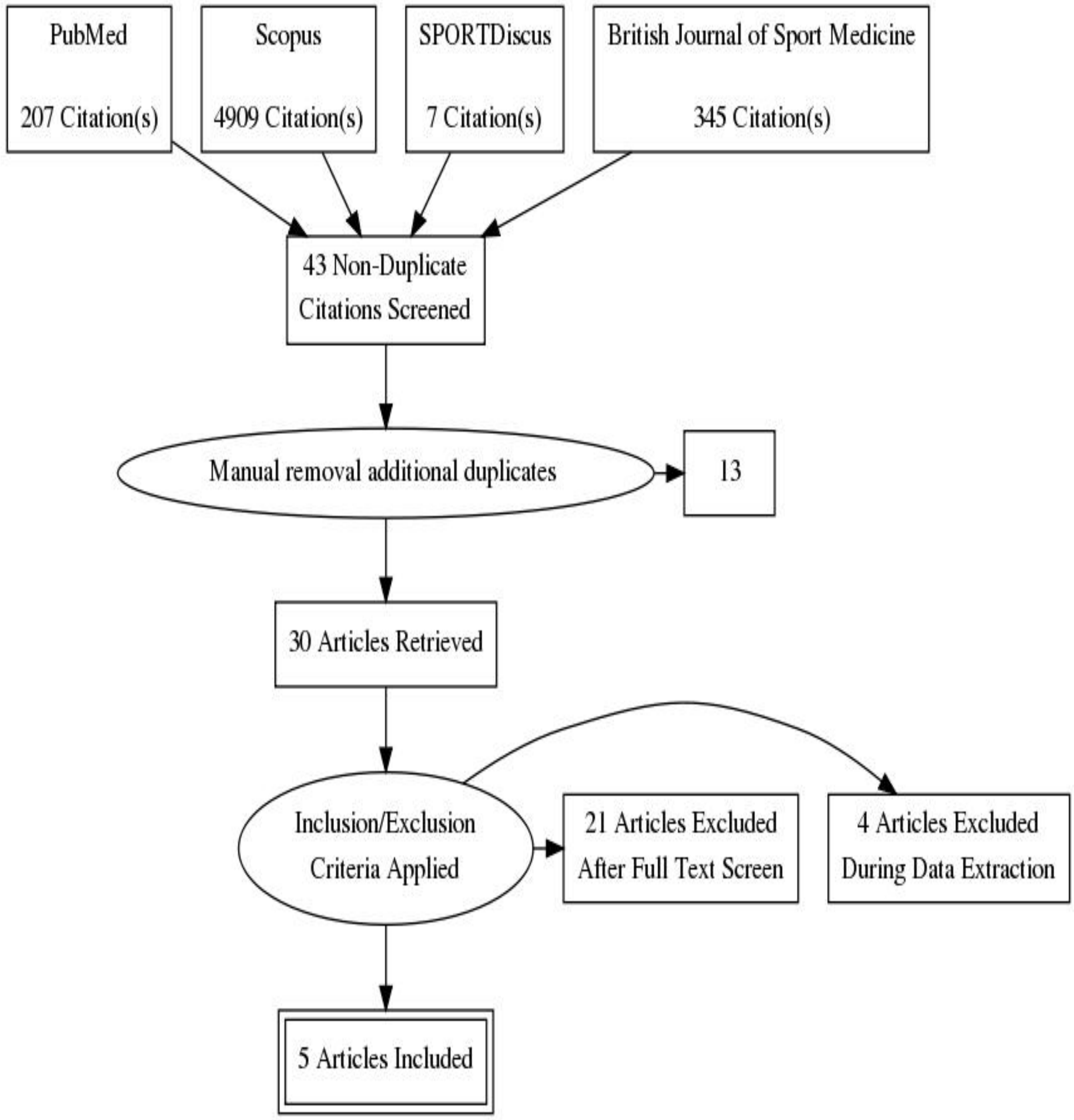

Figure 1 – Flow diagram

Risk of Bias

Bias refers to systematic errors that can threaten the internal validity of an RCT (Spieth et al., 2016). RoB was assessed using the revised Cochrane risk-of-bias tool for randomized trials (RoB 2) (Sterne et al., 2019), which consists of five dimensions, i.e., bias arising due to: (i) the randomization process; (ii) deviations from intended interventions; (iii) missing outcome data; (iv) measurement of the outcome; and (v) selection of the reported result. The author independently assessed RoB for all studies. For assessing RoB in parallel trials, the Excel tool ROB2_IRPG_beta_v9 (Cochrane) was used (Higgins et al., 2011).

The results of the methodological quality assessment of the studies included in this review are summarized in figure 2.

	D1 – Randomization process	D2 – Deviations from the intended interventions	D3 – Missing outcome data	D4 – Measurement of the outcome	D5 –Selection of the reported result	Overall
(Cormie, Galvão, et al., 2013)	+	+	+	+	+	+
(Bloomquist et al., 2018)	!	+	+	+	!	!
(Cešeiko et al., 2019)	+	+	+	!	+	+
(Cešeiko et al., 2020)	+	+	+	!	+	!
(Cormie, Pumpa, et al., 2013)	+	+	!	+	+	!

+ Low risk
! Some concerns
- High risk

Figure 2 - Summary of the Cochrane risk of bias tool

TABLE 2 – Characteristics of the included studies

Study	Sample size	Control group	Intervention	Duration	Supervision	Funding and potential conflicts of interest
(Cormie, Pumpa, et al., 2013)	62 women High load – 56.1±8.1 Low load – 57.0±10.0 Control – 58.6±6.7	Yes	Heavy load performed 10-6 repetitions from 75-85% of 1RM Heavy load performed 15-20 repetitions from 55-65% of 1RM.	12 weeks	Yes, by an exercise physiologist.	No conflict of interest. Funded by Edith Cowan University and the University of Canberra. Clinical trials registration ACTRN12610000788077.
(Cormie, Galvão, et al., 2013)	17 women 61.2 ± 9.1	No	Heavy load performed 6-8 1RM Heavy load performed 15-20c1RM.	10-12 day wash-out period	Yes, by an exercise physiologist.	No potential conflicts of interest in the publication of this article. Funded by Edith Cowan University. Prue Cormie is supported by the Cancer Council Western Australia Postdoctoral Research Fellowship.
(Bloomquist et al., 2018)	21 women (45.3 ± 9.2)	No	85-90% 1RM 3 sets of 5-8 repetitions with 60-90 seconds rest.	7-day wash-out period	Yes, by the author. Physical therapist.	Reported no conflicts of interest. Funded by the University Hospitals Centre for Health Research (UCSF), Copenhagen University Hospital, Rigshospitalet
(Cešeiko et al., 2019)	55 women High load 48.2 ± 6.7 Control group - 49.0 ± 8.0	Yes	85-90% 1RM 4 sets of 4 repetitions with 180 seconds rest.	12 weeks	Yes, by an exercise physiologist.	Not funded financially. conflicts of interest to disclose. No conflicts of interest regarding the publication of this paper.
(Cešeiko et al., 2020)	55 women High load 48 ± 7 Control group - 49 ± 8	Yes	85-90% 1RM 4 sets of 4 repetitions with 180 seconds rest.	12 weeks	Yes, by an exercise physiologist.	No conflicts of interest regarding the publication of this paper.

RESULTS

The results of outcomes were expressed in Table 3 on the form of means ± SD, except for the Scale pain in Bloomquist et al. (2018). Short-term effects were reported for breast cancer-related lymphedema in two studies (Bloomquist et al., 2018; Cormie, Galvão, et al., 2013).

In the study of Cormie, Pumpa, et al. (2013) all five outcomes variables at baseline moment no significant differences existed between groups except for shoulder extension range of motion where the high load was significantly lower than both low load (45±8°, 54±15°, and 54±10°). After the 12 weeks of intervention, the "Extent of swelling" and "Symptom severity" outcome measures did not change between all three groups.

Changes were observed in the other outcome measures, in Physical Function for both resistance groups when compared with the control group with an alteration in 1RM. Chest press RM test also showed differences between groups and the seated row RM test compared with the control group, exhibiting a change in upper body muscle endurance. Shoulder flexion range of motion in the low-load group exhibit differences compared with group control. Last but not least grip strength of the resistance groups also perceived tendencies to superior improvement.

Differences in "Quality-of-life" outcome measures occur only in the physical functioning domain between the low-load and control groups. This comes in compliance with some alteration in "Symptom severity can that explain this event.

The study of Cormie, Galvão, et al. (2013) analyses outcomes with points in time pre-exercise, post-exercise, 24 hours post-exercise, and 72 hours post-exercise. Observed the outcome "Extent of Swelling" the volume of the circumference of the affected arm was fairly even during all points in time. As far as the high-load and low-load groups no differences were observed between all points. When comparing both arms (affected and non-affected arm) in all domains no significant differences were observed between them. Differences were observed in arm circumference at 72 hours post-exercise in the high-load group being significantly lower than pre-exercise. There were no clear trends in terms of the impact of the resistance exercise, with individual responses being variable. The other outcome "Symptom Severity" reported differences in the affected arm for

Visual analogue scale and Brief Pain Inventory. The interference score of the Brief Pain Inventory was significantly lower than pre-exercise at 24 hours post-exercise, and 72 hours post–low load exercise. No significant differences in the severity of pain, heaviness, or tightness during all points in time. The affected and non-affected arms don't show a modification in symptom severity at all points. No noteworthy alterations were observed between the high load and low load exercise conditions across all of the time points examined. No clear trends existed in the symptom response to the exercise conditions with individual responses being variable following the exercise sessions

The author Bloomquist et al. (2018) defined to be overserved as the primary outcome "Extracellular Fluid" and as secondary outcomes "Inter arm Volume % difference" and "Breast cancer-related lymphedema symptoms". Low- and heavy-load intensities were used. These outcomes were analyzed in points of points in time being pre-exercise, post-exercise, 24 hours post-exercise, and 72 hours post-exercise. L-Dex presented normal values scores pot-exercise and 24 hours post-exercise representing equivalence between intensities. However, 72 hours post-exercise a difference between low- and heavy-load intensities was observed, backing heavy-load resistance exercise.

Interarm volume difference and breast cancer-related lymphedema symptoms showed similarities between low- and heavy-load intensities in all four points in time. In the study performed by Cešeiko et al. (2019) using maximal strength training with just one exercise, the aim was to observe muscle strength and improvements in quality of life. To assess these outcomes 1RM teste was used and The European Organization for Research and Treatment of Cancer Core Quality of Life Questionnaire-C30 and the supplement Breast Cancer Module.

After the intervention, the 1RM of the training group showed improvements compared with pre-test and statistical differences to control group. The questionnaire evidence improved quality of life in the training group showing significant changes between groups. In the other two domains training group keep improving while the control group worsened. Differences were observed in emotional and social functioning. In the domain fatigue training group reduced this symptom whereas control group it became worse. The supplement for breast cancer showed differences between groups in post-test in symptom scale and a decrease in body image whilst in training group staid altered.

The last article also from Cešeiko et al. (2020) where mostly physical capacities were assessed such as Walking economy and time to exhaustion, Maximal muscle strength, Functional performance. As far as maximal muscle strength was observed an increase in 1RM for the heavy-load group whilst the group control suffered a reduction in 1RM. This results in 1RM being superior in the heavy-load group compared to the control group at post-intervention. In walking economy and time to exhaustion also was observed changes having the heavy-load groups better results. At functional performance changes occur for the 6- minutes walking test, chair rising, and stair climbing. Post-intervention the heavy-load group exhibit improvements whereas group control got worst results. This translates to a difference between groups post-intervention. These results could be due to an increment in 1RM for the heavy-load group.

All five studies had an intervention with heavy resistance training but three (Bloomquist et al., 2018; Cormie, Galvão, et al., 2013; Cormie, Pumpa, et al., 2013) of the selected studies were focused on the upper body in specific with breast cancer-related lymphedema. Two of the three only performed movements for the upper body and one (Cormie, Pumpa, et al., 2013) also included exercise for the lower-body extremities. The other two (Cešeiko et al., 2019, 2020) were focused on lower-body extremities. As far as adverse events there were no reports related to the training intervention itself. The reported withdrew reason was due to time constraints (n=2) and an unrelated medical condition (n=1) (Cormie, Pumpa, et al., 2013) and because of logistical considerations (n=1) (Bloomquist et al., 2018). The five studies had the same duration of 12 weeks, Toohey et al. (2018) suggested that high-intensity programs must last at least four weeks in cancer survivors. Interventions with longer times get stronger results.

TABLE 3 – Results of the included studies

Studies	Outcomes	Pre- Intervention			Post - Intervention			Main findings
		Extent of swelling			**Extent of swelling**			
		BIS (L-Dex score):			BIS (L-Dex score):			
(Cormie, Pumpa, et al., 2013)	The extent of swelling in the affected arm. Symptom severity, physical function, and quality of life.	18.8±23.0	13.9±14.2	17.2±15.6	18.5±21.8	12.4±14.8	16.2±16.9	Women with breast cancer-related lymphedema can safely lift heavy weights during upper body resistance exercise without fear of lymphedema exacerbation or increased symptom severity with breast.
		Affected arm volume (mL):			Affected arm volume (mL):			
		4279.7±1134.3	4173.1±1055.7	3916.7±1100.0	4227.8±109	4272.1±1157.5	3916.0±1164.3	
		Interlimb arm volume difference (%):			Interlimb arm volume difference (%):			
		12.7±16.1	9.1±9.0	10.9±11.0	10.7±12.5	7.6±7.2	9.3±12.4	
		Affected arm circumference (cm):			Affected arm circumference (cm):			
		372.6±54.8	346.8±51.1	342.6±60.0	371.3±52.7	347.3±49.0	341.0±60.6	
		Interlimb arm circumference difference (%):			Interlimb arm circumference difference (%):			
		16.3±9.4	12.7±7.2	13.5±7.1	14.6±9.8	12.0±6.0	13.6±8.6	
		Symptom severity DASH (score):			Symptom severity DASH (score):			
		19.5±15.3	18.0±13.2	16.0±15.4	15.7±15.0	12.6±10.0	17.1±16.0	
		BPI-severity (score):			BPI-severity (score):			
		2.1±2.0	1.7±1.8	1.7±1.8	1.7±1.8	1.4±1.2	1.6±1.7	
		BPI-interference (score):			BPI-interference (score):			
		2.2±2.2	1.6±2.1	2.0±2.2	1.5±1.9	1.2±1.4	1.9±2.3	
		FACT-B+4-arm function (score):			FACT-B+4-arm function (score):			
		12.7±4.7	14.6±3.6	13.9±3.4	14.0±4.9	.2±2.7	14.4±4.3	
		QLQ-BR-23-arm symptoms (score):			QLQ-BR-23-arm symptoms (score):			
		38.3±25.42	32.3±17.2	32.7±16.9	30.0±24.2	20.6±10.1	33.3±22.2	
		Muscle strength Grip strength-affected arm (kg):			Muscle strength Grip strength-affected arm (kg):			
		25.9±5.5	25.1±5.6	25.6±5.4	27.6±7.2	27.0±5.9	26.7±6.3	
		Chest press 1RM (kg):			Chest press 1RM (kg):			
		43.4±9.5	41.3±12.0	41.2±11.6	30.0±7.4	28.4±8.1	22.7±5.6	
		Seated row 1RM (kg):			Seated row 1RM (kg):			
		43.4±9.5	41.3±12.0	41.2±11.6	49.8±12.5	49.3±11.8	41.9±12.6	

Leg press 1RM (kg):			Leg press 1RM (kg):			
94.9±39.1	98.6±56.7	79.8±51.8	133.4±55.8		135.6±68.7	86.0±45.7
Muscle endurance Chest press RM test (volume-load):			Muscle endurance Chest press RM test (volume-load):			
155.2±61.7	146.1±99.0	133.5±59.1	208.3±103.3	251.2±137.6	133.1±73.9	
Seated row test (volume-load):			Seated row test (volume-load):			
400.3±163.4	347.6±180.9	361.7±165.5	522.2±296.7		497.8±177.6	371.4±195.7
Leg press test (volume-load):			Leg press test (volume-load):			
1036.9±655.4	1017.3±959.7	726.7±538	1770.4±1243.6 1809.		1809.9±1478.9	944.0±605.1
Range of motion (affected arm)			**Range of motion (affected arm)**			
Wrist flexion (degrees):			Wrist flexion (degrees):			
65.3±11.0	65.4±8.9	66.6±9.5	68.7±9.4	68.2±7.1	64.1±7.4	
Wrist extension (degrees):					Wrist extension (degrees):	
56.4±10.1	58.3±8.4	58.4±8.4	58.8±8.9	63.1±7.7	59.6±9.8	
Elbow flexion (degrees):			Elbow flexion (degrees):			
142.5±6.9	140.8±5.4	142.6±4.9	143.9±6.3	142.1±6.3	144.5±5.2	
Elbow extension (degrees):			Elbow extension (degrees):			
171.7±6.0	172.8±4.5	175.4±4.3	172.6±4.8	174.5±4.4	174.6±3.6	
Shoulder flexion (degrees):			Shoulder flexion (degrees):			
140.4±17.5	141.3±14.0	144.3±16.7	146.2±18.1	153.0±11.1	147.6±15.6	
Shoulder extension (degrees):			Shoulder extension (degrees):			
45.1±8.0	54.4±15.3	53.9±9.6	48.2±10.7	56.8±11.7	54.2±11.9	
Shoulder abduction (degrees):			Shoulder abduction (degrees):			
150.1±24.3	154.1±16.4	156.7±17.0	150.0±22.	158.9±11.5	158.3±16.9	
Quality of life Physical functioning (NBS):			Quality of life Physical functioning (NBS):			
45.4±8.3	45.2±6.6	46.2±8.8	48.5±7.8	49.2±5.8	45.4±9.7	
Role physical (NBS):			Role physical (NBS):			
44.6±9.3	46.7±9.6	46.9±9.3	49.8±7.8	51.5±8.0	48.1±10.5	
Bodily pain (NBS):			Bodily pain (NBS):			
47.2±8.8	47.0±9.7	50.9±8.3	49.9±9.1	51.7±8.7	52.8±9.6	
General health (NBS)			General health (NBS)			
45.9±7.5	48.3±9.5	44.5±11.0	50.4±8.2	50.8±10.0	47.0±12.3	
Vitality (NBS):			Vitality (NBS):			
46.8±10.4	49.9±8.4	45.2±12.8	48.6±9.4	54.3±7.3	46.2±13.9	
Social functioning (NBS):			Social functioning (NBS):			
45.7±8.6	49.3±8.9	45.9±10.6	48.2±8.4	53.5±7.8	48.5±12.1	

		Role emotional (NBS):		
		42.5±11.5 47.4±8.0 41.4±13.9	44.6±11.7 53.3±4.1 44.7±12.3	
		Mental health (NBS):	Mental health (NBS):	
		47.8±11.2 54.4±7.8 48.4±12.6	47.8±11.2 54.4±7.8 48.4±12.6	
		Physical health composite (raw score):	Physical health composite (raw score):	
		47.3±8.7 46.3±9.3 48.3±9.2	50.8±7.5 49.5±7.9 48.8±9.5	
		Mental Health composite (raw score):	Mental Health composite (raw score):	
		44.1±12.1 49.6±9.5 44.1±14.7	46.5±12.2 55.3±6.9 46.7±13.5	
(Cormie, Galvão, et al., 2013)	Observe the acute impact of upper body resistance exercise on the amount of swelling and severity of symptoms in women with breast cancer-related lymphedema and compared these effects between resistance exercise involving high and low loads.	**Bioimpedance Spectroscopy:** High load = 22.9 ± 22.2 Low load = 24.5 ± 21.8; **Affected arm volume (mL):** High load = 4283.8 ± 1163.3 Low load = 4253.6 ± 1103.6; **Volume difference between affected and non-affected arms (mL):** High load = 601.4 ± 571.5 Low load = 604.8 ± 559.4; **Affected arm circumference (cm):** High load = 195.0 ± 34.5 Low load = 192.6 ± 28.7; **Circumference difference between affected and non-affected arms (cm):** High load = 15.2 ± 11.6 Low load = 15.2 ± 10.8; **VAS—Pain (score):** High load = 0.7 ± 1.3 Low load = 1.0 ± 2.2; **VAS—Heaviness (score):** High load = 1.3 ± 1.8 Low load = 1.3 ± 2.4; **VAS—Tightness (score):** High load = 1.3 ± 1.5 Low load = 1.3 ± 2.0; **BPI_—Pain (score):**	**Bioimpedance Spectroscopy:** High load = 22.6 ± 20.9 Low load = 24.4 ± 22.9; **Affected arm volume (mL):** High load = 4306.3 ± 1150.0 Low load = 4269.1 ± 1105.3; **Volume difference between affected and non-affected arms (mL):** High load = 645.2 ± 593.9 Low load = 628.8± 551.5; **Affected arm circumference (cm):** High load = 194.7 ± 33.8 Low load = 192.2 ± 28.5; **Circumference difference between affected and non-affected arms (cm):** High load = 15.1 ± 11.2 Low load = 14.9 ± 11.0; **VAS—Pain (score):** High load = 1.2 ± 1.5 Low load = 1.8 ± 2.0; **VAS—Heaviness (score):** High load = 1.2 ± 1.5 Low load = 1.8 ± 2.0; **VAS—Tightness (score):** High load = 1.6 ± 2.1 Low load = 1.7 ± 1.9; **BPI_—Pain (score):**	Women with breast cancer-related lymphedema can perform moderate- to high-intensity upper body resistance exercise with both low and high loads without fear of exacerbation. Furthermore, this type of exercise was well tolerated, and we report no adverse events. The clear potential for resistance exercise to aid in the long-term management of breast cancer-related lymphedema through enhanced muscular strength and endurance as well as improved functional ability.

		High load = 1.6 ± 2.0 Low load = 1.9 ± 2.0;	High load = 1.8 ± 1.6 Low load = 2.2 ± 1.5;	
(Bloomquist et al., 2018)	Observe acute changes in extracellular fluid, arm volume, and associated breast cancer-related symptoms after a session of low- and heavy-load resistance exercise in women who had undergone axillary lymph node dissection and were receiving taxane-based chemotherapy.	**L-Dex score:** Heavy load 1.7 ± 3.3 Low load 0.8 ± 5.0 **% interarm difference:** Heavy load 0.5 ± 4.4 Low load 1.3 ± 4.1 **Pain:** Heavy load 0 (-1, 6) Low load 0 (0, 5) **Heaviness:** Heavy load 0 (0, 2) Low load 0 (0, 5) **Tightness:** Heavy load 0 (0, 6) Low load 0 (0, 7) **Swelling:** Heavy load 0 (0, 2) Low load 0 (0, 2)	**L-Dex score:** Heavy load 1.9 ± 3.4 Low load 1.9 ± 5.1 **% interarm difference:** Heavy load 1.0 ± 4.0 Low load 1.6 ±4.8 **Pain:** Heavy load (-1, 2) Low load 0 0 (-1, 1) **Heaviness:** Heavy load 0 (0, 4) Low load 0 (0, 3) **Tightness:** Heavy load 0 (0, 5) Low load 0 (0, 8) **Swelling:** Heavy load 0 (0, 3) Low load 0 (-1, 3)	The acute lymphatic response was similar irrespective of whether low- or heavy-load resistance exercise was undertaken in women with breast cancer-related lymphedema. with axillary node dissection during adjuvant taxane-based chemotherapy.
(Cešeiko et al., 2019)	Muscle strength and improved overall quality of life.	**Weight (kg)** Exercise = 77.0 ± 15.2 Control = 72.3 ± 17.4; **1RM (kg)** Exercise = 106.8 ± 22.8 Control = 98.9 ± 20.7 **Global health status:** Exercise = 67.2 ± 15.6 Control = 66.3 ± 16.5;	**Weight (kg):** Exercise = 76.7 ±14.5 Control = 73.3 ±16.5; **1RM (kg):** Exercise = 127.2 ± 26.4 Control = 89.9 ± 20.9 **Global health status:** Exercise = 76.2 ± 14.3 Control = 63.5 ± 14.7;	Improvement in muscle strength, QoL, and reduction of fatigue after a 12-week high-intensity strength training program in breast cancer patients. Recommendation in incorporating high-intensity strength training in cancer rehabilitation, accompanied by careful screening and supervision

				of patients during the training period.
(Cešeiko et al., 2020)	Improvements in lower extremity maximal muscle strength, walking economy, muscle mass, and functional performance.	**Walking economy:** HR± 140; RPE ±12 **Graded walking test:** Time to Exaustion ± 536; HR_{max} ± 172; E_{speed} ± 4.8; $E_{inclination}$ ±11; RPE ± 17;	**Walking economy:** HR± 128; RPE ±10 **Graded walking test:** Time to Exaustion ± 571; HR_{max} ± 172; E_{speed} ± 5.1; $E_{inclination}$ ±12; RPE ± 18;	The major findings were that three months of MST yielded large improvements in lower extremity maximal muscle strength, walking economy and functional performance, and maintained muscle mass. Conversely, patients assigned to the control group displayed reductions in all assessed variables.

Discussion

This systematic review aimed to evaluate the effects of heavy resistance training in breast cancer patients. Resistance training interventions during or after breast cancer treatment have been aimed at preventing or reducing the effects of the disease and treatments. Few studies investigated the resistance training effects without other types of training. The main findings of this review are that heavy resistance training interventions for breast cancer patients during treatment are feasible and could use upper-body and lower-body extremities. The risk of exacerbating lymphedema was showed that it didn't occur even with high loads. A possible reason for the insecurity to expose breast to higher loads could be due to injuries and psychological and physical stress. Kraemer & Ratamess (2004) stated that essential benefits in maximal strength and the subsequent hypertrophy can only be achieved by recruiting the highest number of motor units, ensuring high training loads.

Therefore, the current data demonstrate that breast cancer patients can profit from heavy resistance training during treatments without the fear of getting injured. These interventions were always supervised by an exercise physiologist. The clinical population should always get monitored since they get special needs (Schmitz et al., 2019). As far as upper-body changes in 1RM were an observed and even better range of motion of the shoulder. All of this happens without compromising the symptom severity extent of swelling or the severity of symptoms. These changes in strength and endurance mean that activities of daily living are easy to perform. That can explain the alteration in the domain "physical functioning" which translates to improvements in quality of life (Kirkham et al., 2016).

The studies that focus more on lower-body extremities also found relevant information. The 1RM also got improvements that translated into higher values in the post-intervention functional tests. Meaning that enhanced muscle function (Serra et al., 2018; Villaseñor et al., 2012) due to avoiding loss of muscle mass and muscle functionality caused by the disease and the treatments (Klassen et al., 2017). A reduction in fatigue was noticeable, and also in other domains as symptom scale and body image. This means that patients could be were more active during the treatment period since the side-effects of the disease and treatment affected less. These improvements all combined give breast cancer patients better well-being and quality of life.

Despite the observed advantages, there are some limitations to note. The relatively short duration of the studies also represents a limitation, as information on long-term effects would have provided a better understanding of resistance exercise in breast cancer patients. Another limitation noteworthy was that it would also have been advantageous to include musculoskeletal measurements, as breast cancer patients may suffer from diminished bone health. (De Backer et al., 2007). Not all studies used The European Organization for Research and Treatment of Cancer Core Quality of Life Questionnaire-C30 (Giesinger et al., 2016) or the supplement Breast Cancer Module (Sprangers et al., 1996) and Functional Assessment of Chronic Illness Therapy – Fatigue (FACIT-F) (Butt et al., 2008). These questionnaires are almost the gold standard to assess the quality of life, fatigue and well-being in breast cancer patients because it gives good feedback on how the resistance exercise interacts with breast cancer patients. Lastly, breast cancer-related lymphedema studies allowed the use of compression clothes which is a limiting agent of the research.

Nevertheless, it’s a good point of start and offers good insight and perspective for future studies to be realized and provide more feedback to be available for this population.

Conclusion

All studies on heavy resistance training for breast cancer patients have reported benefits to a variety of extents both physically and psychologically. A well-tailored and supervised heavy resistance training method for breast cancer patients is a must. To perceive the reality of the benefits further research is necessary to determine its effects on other outcomes such as health-related quality-of-life, fatigue, muscle function, and cardiovascular function because few studies have assessed those outcomes. Additional studies should be conducted to assess the extent of those effects in breast cancer patients during treatment and also after treatment.

BIBLIOGRAFIA

AC, F., Menig, M., & MH, M. (2016). Exercise for women receiving adjuvant therapy for breast cancer (Review). *Cochrane Database of Systematic Reviews*, *9*, 1–126. https://doi.org/10.1002/14651858.CD005001.pub3.

Betof, A. S., Dewhirst, M. W., & Jones, L. W. (2013). Effects and potential mechanisms of exercise training on cancer progression: A translational perspective. *Brain, Behavior, and Immunity*, *30*, 75–87. https://doi.org/10.1016/j.bbi.2012.05.001

Blanchard, C., Howes, J., Keats, M., Purcell, J., Shelton, E., Strang, R., Urquhart, R., Woodside, H., & Younis, T. (2015). Physical Activity & Exercise Benefits Cancer Patients and Survivors. *Cancer Care Nova Scotia*, *5*(1), 1–8.

Bloomquist, K., Oturai, P., Steele, M. L., Adamsen, L., Mkller, T., Christensen, K. B., Ejlertsen, B., & Hayes, S. C. (2018). Heavy-load lifting: Acute response in breast cancer survivors at risk for lymphedema. *Medicine and Science in Sports and Exercise*, *50*(2), 187–195. https://doi.org/10.1249/MSS.0000000000001443

Butt, Z., Lai, J., Rao, D., Heinemann, A. W., Bill, A., & Cella, D. (2008). Measurement of Fatigue in Cancer, Stroke, and HIV Using the Functional Assessment of Chronic Illness Therapy – Fatigue (FACIT-F). *Bone*, *74*(1), 64–68. https://doi.org/10.1016/j.jpsychores.2012.10.011.Measurement

Cešeiko, R., Eglitis, J., Srebnijs, A., Timofejevs, M., Purmalis, E., Erts, R., Vetra, A., & Tomsone, S. (2019). The impact of maximal strength training on quality of life among women with breast cancer undergoing treatment. *Experimental Oncology*, *41*(2), 166–172. https://doi.org/10.32471/exp-oncology.2312-8852.vol-41-no-2.13249

Cešeiko, R., Thomsen, S., Tomsone, S., Eglītis, J., Vētra, A., Srebnijs, A., Timofejevs, M., Purmalis, E., & Wang, E. (2020). Heavy Resistance Training in Breast Cancer Patients Undergoing Adjuvant Therapy. In *Medicine and science in sports and exercise* (Vol. 52, Issue 6). https://doi.org/10.1249/MSS.0000000000002260

Chen, X., Lu, W., Zheng, W., Gu, K., Matthews, C. E., Chen, Z., Zheng, Y., & Shu, X. O. (2011). Exercise after diagnosis of breast cancer in association with survival.

Cancer Prevention Research, *4*(9), 1409–1418. https://doi.org/10.1158/1940-6207.CAPR-10-0355

Christensen, J. F., Jones, L. W., Andersen, J. L., Daugaard, G., Rorth, M., & Hojman, P. (2014). Muscle dysfunction in cancer patients. *Annals of Oncology*, *25*(5), 947–958. https://doi.org/10.1093/annonc/mdt551

Clifford, B. K., Mizrahi, D., Sandler, C. X., Barry, B. K., Simar, D., Wakefield, C. E., & Goldstein, D. (2018). Barriers and facilitators of exercise experienced by cancer survivors: a mixed methods systematic review. *Supportive Care in Cancer*, *26*(3), 685–700. https://doi.org/10.1007/s00520-017-3964-5

Cormie, P., Galvão, D. A., Spry, N., & Newton, R. U. (2013). Neither heavy nor light load resistance exercise acutely exacerbates lymphedema in breast cancer survivor. *Integrative Cancer Therapies*, *12*(5), 423–432. https://doi.org/10.1177/1534735413477194

Cormie, P., Pumpa, K., Galvão, D. A., Turner, E., Spry, N., Saunders, C., Zissiadis, Y., & Newton, R. U. (2013). Is it safe and efficacious for women with lymphedema secondary to breast cancer to lift heavy weights during exercise: A randomised controlled trial. *Journal of Cancer Survivorship*, *7*(3), 413–424. https://doi.org/10.1007/s11764-013-0284-8

De Backer, I. C., Van Breda, E., Vreugdenhil, A., Nijziel, M. R., Kester, A. D., & Schep, G. (2007). High-intensity strength training improves quality of life in cancer survivors. *Acta Oncologica*, *46*(8), 1143–1151. https://doi.org/10.1080/02841860701418838

Demmelmaier, I., Brooke, H. L., Henriksson, A., Mazzoni, A. S., Bjørke, A. C. H., Igelström, H., Ax, A. K., Sjövall, K., Hellbom, M., Pingel, R., Lindman, H., Johansson, S., Velikova, G., Raastad, T., Buffart, L. M., Åsenlöf, P., Aaronson, N. K., Glimelius, B., Nygren, P., … Nordin, K. (2021). Does exercise intensity matter for fatigue during (neo-)adjuvant cancer treatment? The Phys-Can randomized clinical trial. *Scandinavian Journal of Medicine and Science in Sports*, *January*, 1–16. https://doi.org/10.1111/sms.13930

Giesinger, J. M., Kieffer, J. M., Fayers, P. M., Groenvold, M., Petersen, M. A., Scott, N.

W., Sprangers, M. A. G., Velikova, G., & Aaronson, N. K. (2016). Replication and validation of higher order models demonstrated that a summary score for the EORTC QLQ-C30 is robust. *Journal of Clinical Epidemiology*, *69*, 79–88. https://doi.org/10.1016/j.jclinepi.2015.08.007

Higgins, J. P. T., Altman, D. G., Gøtzsche, P. C., Jüni, P., Moher, D., Oxman, A. D., Savović, J., Schulz, K. F., Weeks, L., & Sterne, J. A. C. (2011). The Cochrane Collaboration's tool for assessing risk of bias in randomised trials. *BMJ (Online)*, *343*(7829), 1–9. https://doi.org/10.1136/bmj.d5928

Jemal, A., Bray, F., & Ferlay, J. (2011). Global Cancer Statistics: 2011. *A Cancer Journal for Clinicians*, *61*(2), 69–90. https://doi.org/10.3322/caac.20107

Kirkham, A. A., Bland, K. A., Sayyari, S., Campbell, K. L., & Davis, M. K. (2016). Clinically Relevant Physical Benefits of Exercise Interventions in Breast Cancer Survivors. *Current Oncology Reports*, *18*(2), 1–9. https://doi.org/10.1007/s11912-015-0496-3

Klassen, O., Schmidt, M. E., Ulrich, C. M., Schneeweiss, A., Potthoff, K., Steindorf, K., & Wiskemann, J. (2017). Muscle strength in breast cancer patients receiving different treatment regimes. *Journal of Cachexia, Sarcopenia and Muscle*, *8*(2), 305–316. https://doi.org/10.1002/jcsm.12165

Kraemer, W. J., & Ratamess, N. A. (2004). Fundamentals of Resistance Training: Progression and Exercise Prescription. *Medicine and Science in Sports and Exercise*, *36*(4), 674–688. https://doi.org/10.1249/01.MSS.0000121945.36635.61

Kwan, M. L., Cohn, J. C., Armer, J. M., Stewart, B. R., & Cormier, J. N. (2011). Exercise in patients with lymphedema: A systematic review of the contemporary literature. *Journal of Cancer Survivorship*, *5*(4), 320–336. https://doi.org/10.1007/s11764-011-0203-9

Lugo, D., Pulido, A. L., Mihos, C. G., Issa, O., Cusnir, M., Horvath, S. A., Lin, J., & Santana, O. (2019). The effects of physical activity on cancer prevention, treatment and prognosis: A review of the literature. *Complementary Therapies in Medicine*, *44*(March), 9–13. https://doi.org/10.1016/j.ctim.2019.03.013

Moher, D., Shamseer, L., Clarke, M., Ghersi, D., Liberati, A., Petticrew, M., Shekelle, P., Stewart, L. A., & PRISMA-P. (2016). Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015 statement. *Systematic Reviews*, *20*(2), 148–160. https://doi.org/10.1186/2046-4053-4-1

Musanti, R., Chao, Y.-Y., & Collins, K. (2019). Fitness and Quality of Life Outcomes of Cancer Survivor Participants in a Community Exercise Program. *Journal of the Advanced Practitioner in Oncology*, *10*(1), 24–37. https://doi.org/10.6004/jadpro.2019.10.1.2

Panchik, D., Masco, S., Zinnikas, P., Hillriegel, B., Lauder, T., Suttmann, E., Chinchilli, V., McBeth, M., & Hermann, W. (2019). Effect of Exercise on Breast Cancer-Related Lymphedema: What the Lymphatic Surgeon Needs to Know. *Journal of Reconstructive Microsurgery*, *35*(1), 37–45. https://doi.org/10.1055/s-0038-1660832

Riebe, D., Ehrman, J. K., Liguori, G., & Magal, M. (2018). *ACSM's Guidelines for Exercise Testing and Presciption - Tenth Edition*.

Ruiz-Casado, A., Martín-Ruiz, A., Pérez, L. M., Provencio, M., Fiuza-Luces, C., & Lucia, A. (2017). Exercise and the Hallmarks of Cancer. *Trends in Cancer*, *3*(6), 423–441. https://doi.org/10.1016/j.trecan.2017.04.007

Schmitz, K. H., Campbell, A. M., Stuiver, M. M., Pinto, B. M., Schwartz, A. L., Morris, G. S., Ligibel, J. A., Cheville, A., Galvão, D. A., Alfano, C. M., Patel, A. V., Hue, T., Gerber, L. H., Sallis, R., Gusani, N. J., Stout, N. L., Chan, L., Flowers, F., Doyle, C., … Matthews, C. E. (2019). Exercise is medicine in oncology: Engaging clinicians to help patients move through cancer. *CA: A Cancer Journal for Clinicians*, *69*(6), 468–484. https://doi.org/10.3322/caac.21579

Serra, M. C., Ryan, A. S., Ortmeyer, H. K., Addison, O., & Goldberg, A. P. (2018). Resistance training reduces inflammation and fatigue and improves physical function in older breast cancer survivors. *Menopause: The Journal OfThe North American Menopause Society*, *25*(2), 211–216. https://doi.org/10.1097/GME.0000000000000969

Spieth, P. M., Kubasch, A. S., Penzlin, A. I., Illigens, B. M. W., Barlinn, K., & Siepmann,

T. (2016). Randomized controlled trials – A matter of design. *Neuropsychiatric Disease and Treatment*, *12*, 1341–1349. https://doi.org/10.2147/NDT.S101938

Sprangers, M. A., Groenvold, M., Arraras, J. I., Franklin, J., te Velde, A., Muller, M., Franzini, L., Williams, A., de Haes, H. C., Hopwood, P., Cull, A., & Aaronson, N. K. (1996). The European Organization for Research and Treatment of Cancer breast cancer-specific quality-of-life questionnaire module: First results from a three-country field study. *Journal of Clinical Oncology*, *14*(10), 2756–2768. https://doi.org/10.1200/JCO.1996.14.10.2756

Sterne, J. A. C., Savović, J., Page, M. J., Elbers, R. G., Blencowe, N. S., Boutron, I., Cates, C. J., Cheng, H. Y., Corbett, M. S., Eldridge, S. M., Emberson, J. R., Hernán, M. A., Hopewell, S., Hróbjartsson, A., Junqueira, D. R., Jüni, P., Kirkham, J. J., Lasserson, T., Li, T., … Higgins, J. P. T. (2019). RoB 2: A revised tool for assessing risk of bias in randomised trials. *The BMJ*, *366*, 1–8. https://doi.org/10.1136/bmj.l4898

Sung, H., Ferlay, J., Siegel, R. L., Laversanne, M., Soerjomataram, I., Jemal, A., & Bray, F. (2021). Global Cancer Statistics 2020: GLOBOCAN Estimates of Incidence and Mortality Worldwide for 36 Cancers in 185 Countries. *CA: A Cancer Journal for Clinicians*, *71*(3), 209–249. https://doi.org/10.3322/caac.21660

Tomás, M. T., & Fernandes, M. B. (2012). Physical exercise and breast cancer: a review. *Saúde & Tecnologia*, 60–64.

Toohey, K., Pumpa, K., McKune, A., Cooke, J., & Semple, S. (2018). High-intensity exercise interventions in cancer survivors: a systematic review exploring the impact on health outcomes. *Journal of Cancer Research and Clinical Oncology*, *144*(1), 1–12. https://doi.org/10.1007/s00432-017-2552-x

Villaseñor, A., Ballard-Barbash, R., Baugartner, R., Bernstein, L., McTiernan, A., & Neuhouser, M. (2012). Prevalence and prognostic effect of sarcopenia in breast cancer survivors: the HEAL Study Adriana. *Journal of Cancer Survivorship*, *6*(4), 398–406. https://doi.org/10.1007/s11764-012-0234-x.Prevalence

ANEXOS

ANEXO 1

ANEXO 2