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EFFECTS OF RESISTANCE TRAINING AND AEROBIC TRAINING ON PHASE ANGLE IN BREAST CANCER SURVIVORS: A NARRATIVE REVIEW

EFEITOS DO TREINAMENTO RESISTIDO E DO TREINAMENTO AERÓBIO NO ÂNGULO DE FASE EM SOBREVIVENTES DE CÂNCER DE MAMA: UMA REVISÃO NARRATIVA

EFECTOS DEL ENTRENAMIENTO DE RESISTENCIA Y DEL ENTRENAMIENTO AERÓBICO SOBRE EL ÁNGULO DE FASE EN SUPERVIVIENTES DE CÁNCER DE MAMA: UNA REVISIÓN NARRATIVA

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ABSTRACT
Phase angle can be an indicator of membrane integrity and cell water distribution. Furthermore, phase angle can increase with training and, among women with breast cancer, it can be an indicator of survival. The aim of the study was to investigate the effects of resistance training and aerobic training on phase angle in breast cancer survivors. Searches were performed in the PubMed, Sicelo, and Google Scholar databases, considering publications between January 2014 and March 2024. Inclusion criteria were: clinical trials in English or Portuguese, which used resistance and/or aerobic training as an intervention for more than 8 weeks with breast cancer survivors and which measured the phase angle. Studies with other types of exercise, other chronic diseases, and other types of cancer were excluded. Five studies were included. These

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articles involved a total of 307 breast cancer survivors. No studies exclusively with aerobic training were found. Resistance or combined training was performed 2 to 5 times per week, mostly at moderate intensity and 30 to 90 minutes per session. Three of these studies showed significant increases in phase angle. Only one of the five studies reported being randomized and found no significant difference in phase angle. Conclusion: Resistance training and combined training may be effective in improving phase angle and cellular integrity in breast cancer patients or survivors.

Keywords: Breast cancer; phase angle; cell integrity; strength training; aerobic training.

RESUMO

O ângulo de fase pode ser um indicador da integridade da membrana e da distribuição de água das células. Além disso, o ângulo de fase pode aumentar com treinamento e, em mulheres com câncer de mama, pode ser um indicador de sobrevida. O objetivo do estudo foi investigar os efeitos do treinamento resistido e do treinamento aeróbio no ângulo de fase em sobreviventes de câncer de mama. As buscas foram realizadas nas bases de dados PubMed, Scielo e Google Acadêmico, considerando as publicações entre janeiro de 2014 e março de 2024. Os critérios de inclusão foram: ensaios clínicos em inglês ou português, que utilizaram como intervenção treinamento resistido e/ou aeróbico por mais de 8 semanas com sobreviventes de câncer de mama e que tenham mensurado o ângulo de fase. Foram excluídos estudos com outros tipos de exercício, outras doenças crônicas e outros tipos de câncer. Cinco estudos foram incluídos. Esses artigos envolveram ao todo 307 sobreviventes de câncer de mama. Não foram encontrados estudos exclusivamente com treinamento aeróbio. O treinamento resistido ou combinado foi realizado de 2 a 5 vezes por semana, principalmente em intensidade moderada e 30 a 90 minutos por sessão. Três desses estudos apresentaram aumento significativo no ângulo de fase. Apenas um dos cinco estudos relatou ter sido randomizado e não encontrou diferença significativa no ângulo de fase. Conclusão: o treinamento resistido e o treinamento combinado podem ser eficazes para melhorar o ângulo de fase e a integridade celular em pacientes ou sobreviventes de câncer de mama.

Palavras-chave: Câncer de mama; ângulo de fase; integridade celular; treinamento de força; treinamento aeróbio.

RESUMEN

El ángulo de fase puede ser un indicador de la integridad de la membrana y la distribución del agua celular. Además, el ángulo de fase puede aumentar con el entrenamiento y, en mujeres con cáncer de mama, puede ser un indicador de supervivencia. El objetivo del estudio fue investigar los efectos del entrenamiento de resistencia y el entrenamiento aeróbico sobre el ángulo de fase en sobrevivientes de cáncer de mama. Las búsquedas se realizaron en las bases de datos pubmed, scielo y google scholar, considerando publicaciones entre enero de 2014 y marzo de 2024. Los criterios de inclusión fueron: ensayos clínicos en inglés o portugués, que utilizaron entrenamiento de resistencia y/o aeróbico como intervención durante más de 8 semanas con supervivientes de cáncer de mama a las que se les ha medido el ángulo de fase. Se excluyeron los estudios con otros tipos de ejercicio, otras enfermedades crónicas y otros tipos de cáncer. Se incluyeron cinco estudios. Estos artículos involucraron a un total de 307 sobrevivientes de cáncer de mama. No se encontraron estudios exclusivamente con entrenamiento aeróbico. El entrenamiento de resistencia o combinado se realizó de 2 a 5 veces por semana, principalmente a intensidad moderada y de 30 a 90 minutos por sesión. Tres de estos estudios mostraron un aumento significativo en el ángulo de fase. Sólo uno de los cinco estudios informó haber sido aleatorio y no encontró diferencias significativas en el ángulo de fase. Conclusión: el entrenamiento de resistencia y el entrenamiento combinado pueden ser efectivos para mejorar el ángulo de fase y la integridad celular en pacientes o sobrevivientes de cáncer de mama.

Palabras clave: Cáncer de mama; ángulo de fase; integridad celular; entrenamiento de fuerza; entrenamiento aeróbico.

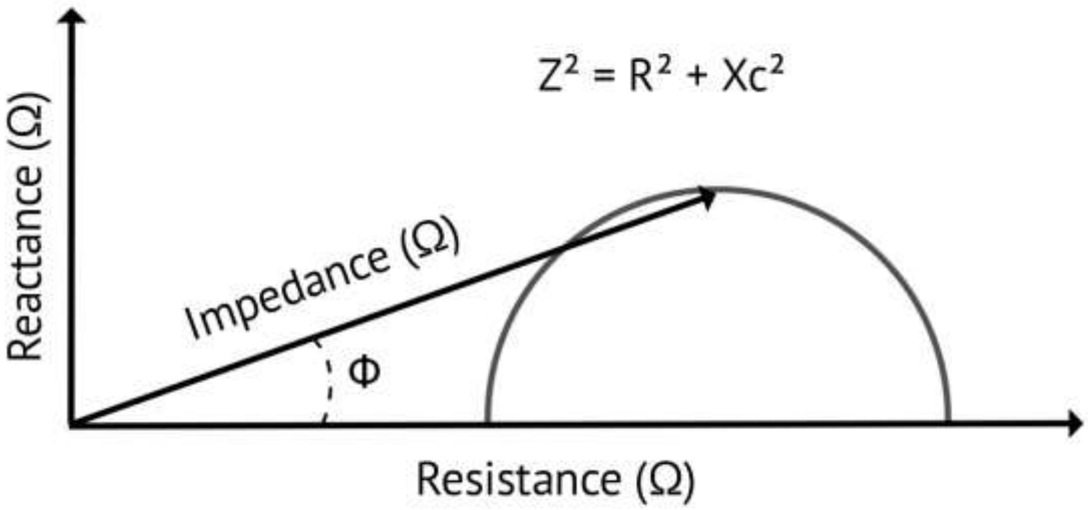
1. Introdução

Cancer refers to a set of more than 100 diseases and is considered a major public health problem (DeSantis *et al*., 2015). Among women, breast cancer is the most common cause of death by cancer in developing regions and the second cause of death in developed regions, after non-melanoma skin cancer. In Brazil, for each year of the 2023-2025 triennium, 73.610 new cases of cancer were estimated, which represents an adjusted incidence rate of 4,89 cases per 100.000 women (INCA, 2022).

Typical cancer treatment includes surgery to remove the tumor, chemotherapy, radiotherapy, hormone therapy and immunobiological agents (Figueiredo *et al*., 2014). Chemotherapy treatment is toxic for the body's normal cells, normally causing adverse events in patients, such as vomiting, alopecia, anemia and fatigue (Kirjner e Lima Pinheiro, De, 2007).

Bioelectrical impedance analysis (BIA) is a noninvasive, inexpensive, and portable method that has been used mainly for body-composition analysis over the past decade. This instrument is capable of measuring body composition from 2 bioelectrical parameters: body resistance (R), that is the opposition offered by the body tissues to the flow of an alternating electrical current, and reactance (Xc), that is related to the capacitance properties of the cell membrane, as shown on Figure 1. Therefore, those parameters can provide valuable data about the body tissues' integrity, function and composition (Baumgartner, Chumlea e Roche, 1988)

Figure 1. Representation of the relationship between reactance (Xc) and resistance (R) on bioelectrical impedance (Z) and phase angle (Φ).



Source: produced by the authors.

Nevertheless, phase angle (PhA) has been interpreted as an indicator of membrane integrity and water distribution between the intra and extracellular spaces (Barbosa-Silva *et al*., 2005). PhA is a derived measure obtained from the relation between the direct measures of resistance and reactance (Barbosa-Silva *et al*., 2005).

According to Champ *et al*. (2024), phase angle reflects the health of cellular membranes and muscle function and correlates with outcomes after the treatment for cancer. Moreover, individuals with cancer are expected to have PhA values lower than the average (Barbosa-Silva *et al*., 2005). Apparently, it happens due to a reduced Xc component with a preserved resistance component in cancer patients (Toso *et al*., 2003). Besides, PhA can be predictive of survival among women with breast cancer (Gupta *et al.*, 2008).

In context, Gupta *et al*. (2008) evaluated 259 breast cancer patients. 56 had stage I disease at diagnosis, 110 had stage II, 46 had stage III and 34 had stage IV. The median age at diagnosis was 49 years (range 25 – 74 years) and the median PhA score was 5.6 (range 1.5 – 8.9). The authors found that patients with PhA ≤ 5.6 had a median survival of 23.1 months, while patients with PhA > 5.6 had a median survival of 49.9 months.

Furthermore, a few studies have shown that mean PhA is higher in athletes compared to other populations, increases with age and is likely to be higher in male than female athletes. Besides, a previous study showed that an exercise-based rehabilitation program significantly increased PhA in breast cancer survivors (BCS) (Short; Teranishi-Hashimoto; Yamada, 2022).

However, despite the evidence of the practice of physical exercise to improve PhA, there are still few publications analyzing the effects of exercise on PhA, especially when using resistance training (RT) and aerobic training (AT), as well as comparisons between them at different periods of breast cancer treatment.

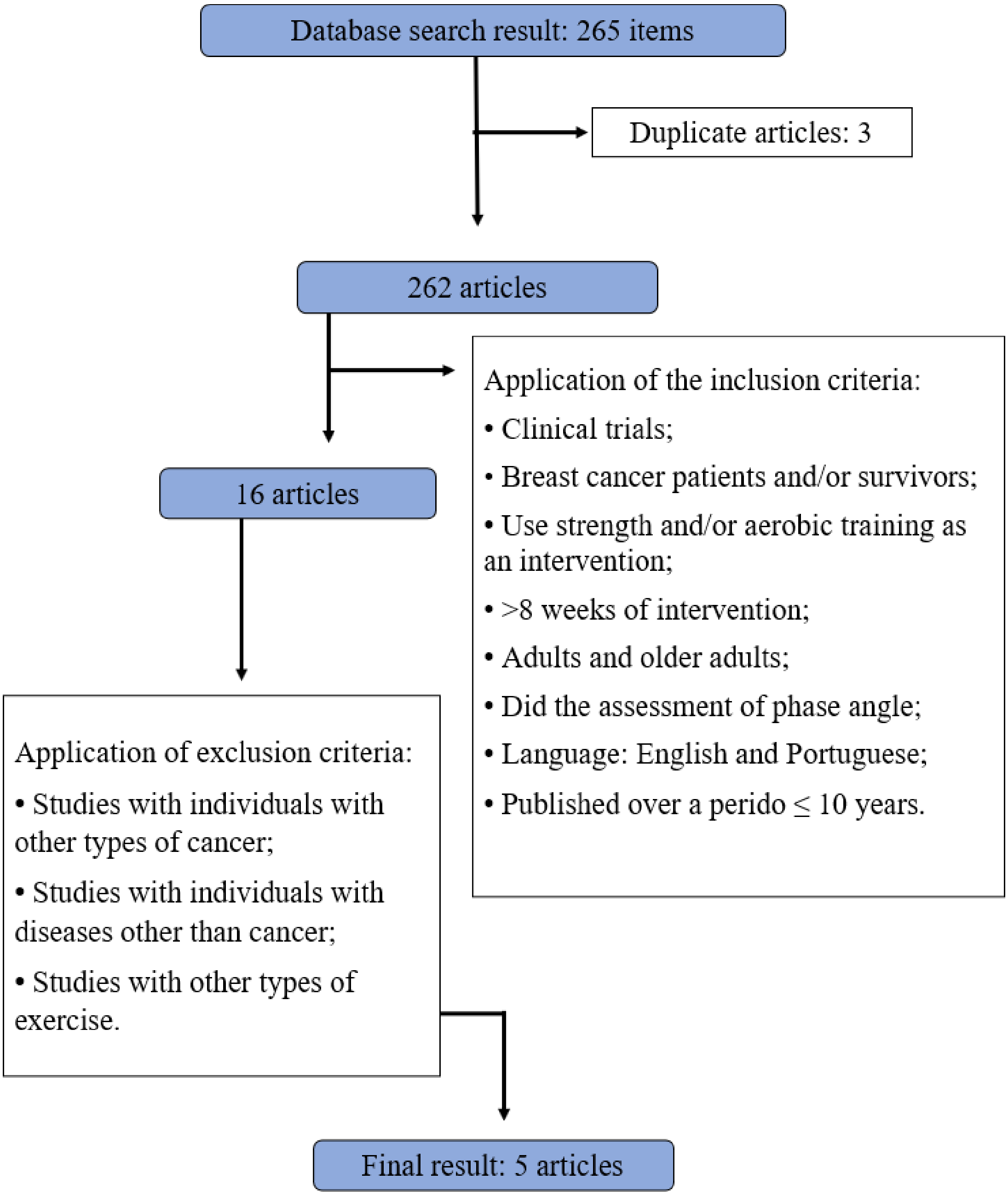
Therefore, the present study aimed to analyze the effects of both resistance and aerobic exercise on PhA in breast cancer survivors.

2. Methods

We conducted a narrative review of literature across the SciELO, Scholar Google and PubMed databases. The search terms included various combinations of “resistance training", “strength training”, "aerobic training", “endurance training”, "physical exercise", "physical activity", "phase angle" and “breast cancer”.

We included our scoped clinical trials published after 1 January 2014 that used RT and/or AT as intervention and evaluated PhA in breast cancer patients and/or survivors were included. To ensure the rigor and relevance of our review, we excluded book chapters and reports. Non-English and non-Portuguese language publications were omitted. Additionally, articles that did not have the keywords above in any fields of the text or that evaluated individuals with other types of cancer were excluded. As shown in Figure 2:

Figure 2. Flowchart of article selection.



Source: produced by the authors.

3. Results

The five studies included in this review have enrolled between 20 and 158 BCS and aimed to investigate the effects of physical exercise regimens on PhA, body composition, physical fitness, quality of life and other outcomes (Table 1).

Table 1. Characteristics of the studies included and their findings on phase angle (º).

Autors/year	Sample (age)	Objective	Protocol	Duration	Treatment	Dietary counseling	Randomization	Results
Stefani *et al*, 2017	28 BCS (59 ± 9 years)	To evaluate the impact of physical activity on body water distribution in BCS and control group (women without cancer)	AT: 60% of PHR, consisted primarily of walking. RT: 8 exercises targeting major muscle groups, with 3 sets and 10–15 repetitions, mainly with free weight or using body weight.	12 months	Post-chemotherapy treatment for approximately 1–2 years	Yes	No	PhA significantly increased compared pre intervention (5.4 ± 0.7) and post intervention: (5.9 ± 0.7) (p<0.05)
Champ *et al*, 2023	20 BCS (age 57 (41-74) years)	To assess body composition, strength, and balance in women treated for breast cancer.	RT: full body protocol, 3 times a week, 3 sets per exercise and 6 exercises.	3 months	Anti-estrogen therapy (73%), chemotherapy (14%), and radiotherapy (23%)	No	No	PhA significantly increased compared pre intervention (4.85 ± 0.11) and post intervention: (5.11 ± 0.12) (p=0.011)
Mascherini *et al*, 2020	42 BCS (52.0 ± 10.1 years)	(1) Evaluate the influence of adjuvant therapy and unsupervised exercise on fat loss. (2) Verify the effectiveness of an unsupervised exercise program on health-related QoL in BCS.	AT: 30 minutes, 5 times per week. In addition, a target of number daily step were provided. At the end of each AT sessions, flexibility exercise have been recommended. RT has been suggested twice per week with 8 exercises involving the main muscle groups,	6 months	Hormone therapy (36%), chemotherapy (21%), combined hormone therapy with chemotherapy (21%), and did not undergo any adjuvant cancer therapy (21%).	No	No	PhA did not increased significantly compared pre intervention (5.2 ± 0.7) and post intervention: (5.3 ± 0.7) (p>0.05)

			performed for 3 sets with 10 repetitions.					
Short, Hashimoto e Yamada, 2022	59 BCS (61 ± 9 years)	To assess the effect of ExCR on PhA in BCS.	90 minutes, 3 times a week, for 12 weeks. Training sessions included 45 minutes of RT (40-85% of 1RM with a RPE between 3-8), 30 minutes of AT (40-85% of heart rate reserve with an RPE between 3-8), and 15 minutes of flexibility training.	12 months	The subjects were post-chemotherapy treatment for 49 ± 29 months	No	No	PhA significantly increased compared pre intervention (4.56 ± 0.52) and post intervention: (4.64 ± 0.59) (p=0.0196)
Schmidt *et al*, 2023	158 BCS (55.5 ± 9 years)	(1) To investigate longitudinal associations between PhA and fatigue in BCS; (2) to explore if these associations might be moderated by other factors and (3) to investigate the effect of RT on PhA.	Progressive RT or muscle relaxation (control group). Both 2 sessions/week and 1h/session	3 months	Previous cancer treatment: neo-adjuvant (64.6%) adjuvant (20.9%) or no chemotherapy (14.6%).	No	Yes	PhA did not increased significantly compared pre intervention (4.82 ± 0.80) and post intervention: (4.95 ± 0.71) (p=0.82)

PhA = phase angle; **BCS** =breast cancer survivors; **RT** = resistance training; **AT** = aerobic training; **QoL** = quality of life; **PHR** = peak heart rate; **6MWT** = Six minute walk test; **ExCR** = exercise-based cancer rehabilitation programs; **1RM** = 1 repetition maximum; **RPE** = rate of perceived exertion.

Source: produced by the authors.

Three studies (Champ *et al.*, 2024; Mascherini *et al.*, 2020; Stefani *et al.*, 2017) reported cancer stage. Shimidt *et al*. (2023) described the stages between 0-3, with most women (51%) being diagnosed with stage 1 breast cancer. Still, Champ *et al.* (2024) classified cancer staging in five groups: biopsy-proven ductal carcinoma in situ (DCIS) (5%); early stage (45%), locally advanced (32%); locally recurrent (14%) and metastatic (5%). Mascherini *et al*. (2020) reported that all the volunteers had been diagnosed with stage IIIC breast cancer or inferior.

Stefani *et al*. (2017), Mascherini *et al*. (2020) and Short *et al*. (2022) used both resistance and aerobic exercise protocols as intervention. Although, Mascherini’s prescription was composed by unsupervised aerobic (such as walking, cycling or jogging), flexibility and RT (twice a week, with 8 exercises involving the main muscle groups, performed for 3 sets with 10 repetitions), based on general recommendations from the guidelines of the American College of Sports Medicine (ACSM).

Champ *et al*. (2024) used only resistance exercise, with a full body protocol, 3 times a week, 3 sets, 6 exercises and mainly closed kinetic chain exercises, using body weight and free weight. It was the only study that reported volunteers’ adherence and injuries. Subjects missed an average of 1.75 sessions (range 0–7), with all meeting adherence above 75 %. The only injuries or adverse events described was muscle soreness and 2 days of knee pain.

Schimidt *et al*. (2023) used a protocol that is described in another article (Morlino *et al.*, 2022). A total of 158 subjects were 1:1 randomized to a progressive strength training or muscle relaxation (control group), for 60 minutes, twice weekly for 12 weeks. The strength training sessions followed the ACSM exercise guidelines for cancer survivors.

They were composed by one to three sets, 8-12 repetitions (60-80% of 1RM) and one minute rest between sets. The sessions had eight different types of exercises for major upper and lower muscle groups: 1) leg extension; 2) leg curl; 3) leg press; 4) shoulder internal and external rotation; 5) seated row; 6) latissimus pull down; 7) shoulder flexion and extension; and 8) butterfly and butterfly reverse. If the participants were able to complete 3 sets of an exercise reaching 12 repetitions in three consecutive sessions, the weight were increased at least by 5%. (Potthoff *et al.*, 2013)

This study (Stefani *et al.*, 2017) was the only one that described arm symptoms (47.5% no/little, 41.3% moderate and 11.3% high) based on the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire for Breast Cancer (EORTC QLQ-BR23) (Limon-Miro *et al.*, 2019). Champ *et al*. (2024) just reported that 25% of the sample had lymphedema and it did not get worse during the study.

Only one study provided dietary counseling to the volunteers (10). Stefani *et al*. (2017) instructed the volunteers to follow a typical Mediterranean diet throughout the 12 months of intervention. Daily calories (50–60% carbohydrates; between 12% and 18% of vegetable and animal proteins; and the remaining 25–30% provided by lipids) were divided in three main meals and two snacks. The participants were oriented not to add too much salt to their meals and to eat vegetables, fruits, dry fruits, cereals, milk and dairy products, virgin olive oil, red and white fish, eggs, all in pre-determined quantities. Besides, they should also limit the percentage of carbohydrates coming from simple sugars and lipids composed of saturated fatty acids and consume 1.5-2 L of water every day, in small amounts.

Those studies diverged about the different types of cancer treatment. Stefani *et al*. (2017) recruited volunteers who had undergone chemotherapy 1-2 years ago. Short *et al*. (2022) enrolled BCS who had also undergone chemotherapy, approximately 4 years ago. Champ *et al*. (2024) classified the treatments in anti-estrogen therapy (73%), chemotherapy (14%), and radiotherapy (23%). Similarly, Mascherini's treatment groups were divided in hormone therapy (36%), chemotherapy (21%), combined hormone therapy with chemotherapy (21%), no adjuvant cancer therapy (21%). Shimidt *et al*. (2023) only selected BCS who had received breast surgery, 64.6% being neo-adjuvants, 20.9% being adjuvants and 14.6% did not undergo chemotherapy.

Significant increases on PhA were find in three studies (Champ *et al*., 2024; Short; Teranishi-Hashimoto; Yamada, 2022; Stefani *et al*., 2017). Two of these studies have in common that the volunteers were post-chemotherapy treatment for more than one year and they undergone a 12 months combined (aerobic and resistance) training intervention (Short, Teranishi-Hashimoto e Yamada, 2022; Stefani *et al*., 2017), which was the longest periods found in this review. These studies were also the only ones that provided dietary counseling. Although, Champ *et al. (2024)* also found significant increases on PhA with a 6 months RT protocol, but it is important to highlight that they monitored and progressed the load lifted across the study period. Still, the other two studies did not find statistic significant increases on PhA after the exercise protocol (Mascherini *et al.*, 2020; Schmidt *et al.*, 2023) .

Nevertheless, it is important to highlight that Schimidt *et al*. (2023) was the only study that reported to randomize volunteers into an intervention group and a control group. This may demonstrate a certain methodological weakness of the other studies.

4. Discussion

The present study aimed to analyze the effects of resistance and aerobic exercise on PhA in BCS. Three of five studies analyzed actually found significant and positive differences on PhA, with supervised resistance or combined (aerobic and resistance) training for at least 3 months.

Morlino *et al*. (2022) reviewed 16 observational and intervention studies and concluded that there is a great variability between studies and breast cancer patients at baseline, even though the PhA seems to decrease by 5-15% after completing chemotherapy. Besides, those effects might persist in long term and lifestyle changes like nutritional or exercise interventions can help improve PhA levels (Limon-Miro *et al.*, 2019; Morlino *et al.*, 2022; Stefani *et al.*, 2017).

All of the protocols reviewed used RT and not all of them reported increases on PhA, so it is difficult to conclude the potential role of RT to improve cellular integrity. However, no other clinical trials using exclusive RT to improve PhA were found in our research, based on our inclusion and exclusion criteria.

Furthermore, dietary counseling, long term exercise protocols, volunteers being post-chemotherapy for more than one year, supervision and progressive individualized workloads are all variables that might have influenced the increases found on PhA (Short, Teranishi-Hashimoto e Yamada, 2022; Stefani *et al*., 2017).

A recent systematic review with meta-analysis showed that RT promotes increases on bioelectrical PhA, by improving Xc and decreasing R in older adults, while physical inactivity results on reduction of PhA by decreasing Xc and increasing R (Campa *et al.*, 2023). A previous cross-sectional study has also found positive correlation between PhA, muscle strength and physical activity levels (Matias *et al.*, 2020).

Unlike RT, there are other studies that investigated the effects of AT alone on PhA in cancer patients. Grabenbauer *et al*. (2016) al tested the feasibility of a 12 months aerobic exercise intervention during and after radiation and chemotherapy in cancer patients, including breast (Grabenbauer *et al.*, 2016). They did not find improvement on bioelectrical PhA, but there was statistic significant decrease in median body mass index (BMI), from 27.4 ± 7.2 kg/m2 to 26.9 ± 6.7 kg/m2 ($p = 0.015$), and in fat mass, from 30.7 ± 15 kg to 29.5 ± 13 kg ($p = 0.017$). Also, peak oxygen consumption increased from 18.8 ± 6 ml/kg/min at baseline to 19.9 ± 5 ml/kg/min at 12 months ($p = 0.017$).

Nevertheless, Lira *et al*. (2019) aimed to determine if a short high-intensity interval training program leads to similar improvements in fasting blood lipoproteins and PhA than a continuous moderate-intensity program in healthy adult men. Results showed that PhA presented no significant differences in response to the training programs.

Other studies also look into the effects of alternative exercises and found no significant differences on PhA with activities like dragon boat (Moro *et al.*, 2024), Hatha yoga (Eyigör *et al.*, 2021) and adapted nordic walking (Morano *et al.*, 2024).

Despite the evidences showed about the effects of physical exercise on PhA, it remains unclear the effects of RT not combined with other exercise models. The only randomized controlled trial using exclusive RT was made by Schimidt *et al*. (2023) but they did not report RT intensity, exercise order, load and rest interval, so it is difficult to reproduce the protocol and to analyze the influence of each variable on the outcomes found. That study also highlighted that the subjects had not been asked for dietary restrictions before BIA and that a previous study showed that fasting could not be indispensable for BIA (Androutsos *et al.*, 2015). Notwithstanding, the authors pointed that a strict standard operating procedure for their BIA measurements was lacking, what could have influenced the PhA values in that study(Schmidt *et al.*, 2023).

Supervision is an important RT variable that has been studied for the past decades. Previous studies showed that supervision provides greater training intensities and might consequently lead to greater strength gains (Coutts, Murphy e Dascombe, 2004; Gentil e Bottaro, 2010; Mazzetti *et al.*, 2000). Since it was shown that PhA has a positive correlation with muscle strength, it is plausible to hypothesize that supervision ratio could influence changes in PhA values in a aerobic and/or RT program.

Despite the evidence demonstrating possible positive effects of RT or AT on cellular integrity during cancer treatment, the plausible physiological mechanisms for that improvement are still unclear, as are the influence of different training variables on that parameter in women with breast cancer.

5. Limitations

This study does not provide enough information about the topic to affirm that resistance, aerobic or combined training is the best intervention to improve phase angle. Nevertheless, it did not consider possible race, socioeconomic level and geographic differences that could be investigated and that may demonstrate variability in phase angle values.

6. Conclusions

Combined and resistance training are considerable non-pharmacological treatment strategies for breast cancer that can help improve PhA values in that population. However, the effectiveness of the exercise intervention may be influenced by previous cancer treatment intervention period, exercise modality (resistance, aerobic, combined or alternative activities), age, diet, strength levels and supervision. Given the relevance of PhA as mortality and prognostic predictor in BCS, it is very important for the clinical scope to investigate and try to find the best ways to prescribe exercise, and to manage its variables to reach greater improvements in PhA values in BCS.

Therefore, the effects of resistance and combined training on phase angle in breast cancer survivors are still unclear and future randomized control trials should clarify this topic. Moreover, future studies should also investigate the effects of training supervision, diet and exclusive aerobic training on phase angle in breast cancer survivors.

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