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REVIEW

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Systematic review of the effect of aquatic therapeutic exercise in breast cancer survivors

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Abstract

Background: Aquatic therapeutic exercise can be equally effective or even superior to land-based exercise in improving several clinical variables. However, there is still a lack of knowledge on the effects compared to land-based interventions particularly in breast cancer (BC) patients.

Objective: The objective of this study is to examine the effects of aquatic therapeutic exercise on pain, shoulder mobility, lymphedema, cardiorespiratory fitness, muscle strength, body composition, pulmonary function, cancer-related fatigue (CRF) and health-related quality of life (HRQoL) and which parameters are effective compared to similar land-based interventions.

Methods: The databases used were PubMed, Scopus, Web of Science, Cochrane Library and CINAHL, retrieving 145 articles.

Results: Eleven studies were included. Aquatic therapeutic exercise is feasible, safe, well tolerated and achieved high percentages of adherence. As for the assessed outcomes, moderate to large improvements were found compared to usual care or to land-based physical exercise interventions in pain, shoulder range of motion, pulmonary function, HRQoL, cardiorespiratory fitness and muscle strength. Inconclusive results were found for lymphedema, body composition and CRF.

Conclusions: Aquatic therapeutic exercise interventions using a combination of endurance, strength, mobility, stretching and breathing exercises resulted in improvements in common side effects of BC and its treatments. More studies on CRF, body composition and lymphedema need to be done to further evaluate the impact of the intervention on these outcomes.

KEYWORDS
aquatic therapeutic exercise, breast cancer survivors, side effects

1 | BACKGROUND

Breast cancer (BC) is the second malignancy most commonly diagnosed in the world (first among women) (Bray et al., 2018). In 2018, one every four malignancies diagnosed in women were BC diagnosis (Bray et al., 2018). Thanks to the new advances especially in early diagnosis and targeted therapies, BC has an overall 5-year survival rate of 83.7% (Bray et al., 2018), which is one of the highest among all solid tumours. However, it is well-known that BC survivors experience a high burden due to the anti-cancer therapies received, leading to several impairments that can affect patients' functional capacity even years after treatment completion. Cancer-related persisting symptoms such as fatigue, musculoskeletal pain and feelings of anxiety or depression which commonly present as a cluster in survivors of BC can dramatically compromise patients' engagement in physical and social activities and decrease health-related quality of life (HRQoL) (Blaney et al., 2013; Bloom et al., 2007; Minton & Stone, 2008).

The effects of physical activity and exercise have been extensively studied in patients with cancer including BC survivors and are currently regarded as the best non-pharmacological treatment for several side-effect cancer-related therapies (CRT) (Ehlers et al., 2020). Both endurance and strength training have shown to be effective and safe in patients with cancer (during and after treatment) to improve not only physical capacity and symptom management but also to increase uptake of anti-cancer therapies (Bland et al., 2019) and to reduce the risk of recurrence and extend survival (Ammitzbøll et al., 2020; Hanson et al., 2016; Lopez et al., 2021; Madzima et al., 2017; Mctiernan et al., 2019; Meneses-Echávez et al., 2015; Sweegers et al., 2018).

Traditional physical exercise programmes in patients with cancer commonly include both strength and endurance training performed using fitness equipment (cycloergometers, treadmills, dumbbells, etc.) which is not always the patients' preference and frequently results in a reduction in overall attendance. For example, in a study published in 2011 among patients with breast and prostate cancer, almost 40% reported disliking exercise as a barrier to engage in physical activity (Ottenbacher et al., 2011). Adherence in patients with cancer is challenging and is influenced by cancer-related (anti-cancer therapies received, symptoms, stage of disease, etc.) and patient-related factors (co-morbidities, physical condition, age, socioeconomic status, education level etc.). In addition, in most cancer studies, adherence is poorly reported and/or achieves insufficient levels to yield expected results (Turner et al., 2018). Kim et al. (2020) pointed out the need to offer attractive interventions which could be more interesting or enjoyable for patients to ensure long-term adherence, especially among those who experience CRF who face greater barriers to exercise (Kim et al., 2020). In this sense, some studies have shown that water-based exercise can increase adherence comparing to other interventions because it is a comfortable environment, accessible in the community and has the extra beneficial effects of water immersion such as buoyancy (Cantarero-Villanueva et al., 2012; Dionne et al., 2018; Torres-Ronda & del Alcázar, 2014) which decreases joint stress and thus can especially benefit those with shoulder-neck mobility restrictions, pain and/or overweight (Kutzner et al., 2017; McIlroy et al., 2017; Torres-Ronda & del Alcázar, 2014). Furthermore, some studies have also found that water-based exercise can be equally effective or even superior to land-based exercise in improving muscle strength, balance, flexibility, symptom control and functional exercise capacity in different clinical populations (Bergamin et al., 2013; Bocalini et al., 2008; Siqueira et al., 2020; Zoheiry et al., 2017). Despite these initial investigations, there is still a lack of knowledge on the effects of water-based exercise compared to land-based interventions particularly in BC patients. Because there is large variation in the application of aquatic therapy among the studies published and its specific effects on different outcomes remain unknown, in this systematic review, we aimed to synthetize the existing evidence related to the effects of aquatic therapeutic exercise on the following outcomes associated with BC side effects: pain, shoulder mobility, lymphedema, cardiorespiratory fitness, muscle strength, body composition, pulmonary function, cancer-related fatigue and health-related quality of life, both compared to usual care or land-based exercise interventions. As secondary objectives, we aimed to (1) examine adherence to the aquatic therapeutic exercise interventions and (2) explore which exercise parameters (intensity, modality, frequency of training, etc.) may be more effective to improve the aforementioned outcomes in this population.

2 | METHODS

The protocol of the systematic review was registered prospectively in the PROSPERO International Prospective Register of Systematic Reviews (CRD42021236555) and can be consulted online. No changes to the protocol were made after registration. This systematic review follows the *Preferred Reporting Items for Systematic Reviews and Meta-Analyses* (*PRISMA*) statement (Liberati et al., 2009), and following this guideline, a specific question is proposed: 'Is an aquatic intervention effective to improve side effects compared to usual care or other physical interventions for patients who had breast cancer?'

2.1 | Eligibility criteria

To retrieve relevant papers, the search was organised using a PICO strategy (acronym for Patient, Intervention, Comparison and Outcome). The population were women diagnosed with BC, the intervention was any type of aquatic therapeutic exercise and there were no initial restrictions regarding the comparison group (usual care, other type of physical interventions) and the outcomes. The eligibility criteria for the inclusion of the studies are detailed in the Table 1. Records were excluded in the screening of titles and abstract if they were protocols with no outcomes, guidelines, reviews, case–control studies and cross-sectional studies books; if they had no aquatic intervention and the patients had other types of cancer or the intervention was not performed on humans or the studies were not relevant for the purpose of the review. In the full-text screening, records were

TABLE 1 Eligibility criteria

Inclusion criteria		
Acronym	**Definition**	
P	Patients	Women that had BC. >18 years
I	Intervention	Aquatic exercise intervention
C	Comparator	No restrictions
O	Outcomes	No restrictions
S	Study design and characteristics	RTCs Non-randomised trials. Single-arm pre-post studies.
-	Language	English or Spanish
Exclusion criteria		
Guidelines, reviews, opinions, editorials, commentaries, letters, conference abstracts, case–control and case series studies. Studies including patients with other types of cancer. Studies conducted in animals. Patients with secondary lymphedema.		

Abbreviations: BC, breast cancer; RCT, randomised controlled trials.

excluded if they fulfilled the previously mentioned characteristics, the intervention was of less than 1 session per week and the patients had other type of cancer or articles were not available.

2.2 | Search strategy

The following databases were used for conducting the search: Medline (via PubMed), Web of Science, Scopus, Cumulative Index to Nursing and Allied Health Literature (CINAHL) and the Cochrane Library. MeSH terms and keywords were used to make the query. Databases were accessed via The University of Granada, Spain and TecnoCampus University – UPF, Spain. No publication date was imposed or any other additional filters to the search, and the last search was conducted on 14 September 2020. Also, cross-references were additionally searched in eligible full-text articles. Table 2 shows the chosen search terms which were used for Pubmed that were subsequently modified to fit each database. Titles and abstract were identified and selected by two independent reviewers that were added to the set of eligible papers. To update the search, alerts in each database were set up.

2.3 | Databases' sensitivity and precision

To determine the quality of databases, an analysis of their sensitivity and precision was calculated.

2.4 | Selection of studies

The duplicates were removed using Mendeley (Version 1.13.8, Windows, Elsevier). Titles and abstracts were scanned by the independent reviewers to determine eligibility of the papers using Microsoft Office Excel 2019 (Version 2019 Windows, Microsoft Corporation) template to review the full-text studies and determine inclusion. The reasons for exclusion were recorded, and differences between reviewers were discussed, and where no agreement was reach, a third reviewer was consulted.

TABLE 2 Terms that compose the search strategy for PubMed

	Concept	Terms
#1	Intervention	((aquatic AND (exercise[MeSH Terms] OR exercis*[Text Word] OR physical activit*[tiab] OR physical exercis*[tiab] OR acute exercis*[tiab] OR isometric exercis*[tiab] OR aerobic exercis*[tiab] OR exercis* training[tiab] OR resistance training [MeSH Terms] OR resistance training [Text Word] OR strength* training[tiab] OR weight-lifting strength*[tiab] OR weight-lifting exercis* program[tiab] OR weight-bear* strength* program[tiab] OR weight bear* exercis* program[tiab] OR weight bear* exercis* program[tiab] OR exercise therapy[MeSH Terms] OR exercis* therap*[Text Word] OR remedial exercis*[tiab] OR rehabilitation exercis* [tiab])) OR aquatic exercis*[tiab] OR aquatic physiotherapy[tiab] OR aquatic therapy[tiab] OR aquatic physical therapy [tiab])
#2	Condition	(neoplasms[MeSH Terms] OR neoplasia* [tiab] OR neoplasm*[tiab] OR tumor* [tiab] OR cancer*[tiab] OR malignanc* [tiab] OR malignant neoplasm*[tiab] OR benign neoplasm*[tiab])
#1 AND #2		

TABLE 3 Characteristics of studies

Author/Year publication	Participants/Comparison or control group	Outcomes	Measured time points	Adverse effects	Main results
RCT studies					
Cantarero-Villanueva et al. (2012)	Women with BC. • Aquatic exercise intervention ($n = 33$) • Control group ($n = 33$).	• Pain (neck and shoulder) *Visual analogue scale* • Pressure pain threshold. *Electronic algometer* • Presence of trigger points*Criteria described by Simons* et al. (Sterne et al., 2019)	• Baseline • Post-intervention (8 wk)	Transient increase of edema ($n = 3$), increased fatigue in the first session ($n = 4$).	The aquatic exercise group showed benefits with large intergroup effect size for neck pain ($d = 1.1$, 95% CI 0.81–1.75), and moderate for shoulder-axillary ($d = 0.70$, 95% CI 0.14–1.40). For PPT in levels over C5-C6, the intergroup effect size was large ($d = 1.5$, 95% CI 0.21–2.77) and small for the rest PPT levels ($d < 0.11$). Also, a greater reduction of active TrPs than the control group ($p < 0.05$).
Cantarero-Villanueva, Fernández-Lao, Cuesta-Vargas, et al. (2013)	Women with BC. • Aquatic exercise intervention ($n = 34$) • Control group ($n = 34$).	• Strength (abdominal and leg) *Trunk curl static endurance test* *Multiple sit-to-stand test* • Cancer-related fatigue*Piper fatigue scale* • Mood state*Profile of mood states*	• Baseline • Post-intervention (8 wk) • 6-month follow-up	Discomfort or low-intensity pain/stiffness.	The aquatic exercise group showed benefits with a large intergroup size effect in trunk endurance ($d = 0.92$, CI 1.97–3.83), leg strength ($d = 1.10$; 0.55–2.76), and cancer-related fatigue ($d = 0.87$, CI 0.48–1.26). At the follow-up period of 6 months, small to large effect sizes regarding cancer-related fatigue, trunk and leg strength ($0.25 > d > 0.90$). The effect size for mood state were negligible ($d < 0.25$).
Johansson et al. (2013)	• Women with BC • Aquatic exercise intervention ($n = 15$) • Control group ($n = 14$)	• Range of motion (shoulder) *Goniometer* • Lymphedema*Bioimpedance spectroscopy*	• Baseline • Post intervention	No adverse effects	The aquatic exercise intervention had significant effect on the range of motion of the shoulder ($p < 0.05$) but had no effect on lymphedema compared with the control group. No effect sizes were reported

TABLE 3 (Continued)

Author/Year publication	Participants/Comparison or control group	Outcomes	Measured time points	Adverse effects	Main results
Odynets et al. (2018)	Women with BC with post mastectomy pain syndrome. • Intervention ($n = 115$): Aquatic exercise intervention ($n = 45$) Pilates intervention ($n = 40$) Yoga intervention ($n = 30$) • Healthy women ($n = 50$)	• Pulmonary function *Forced spirometry*	• Baseline • 12-months follow-up	Not reported	All groups improved pulmonary function compared with the group of healthy women ($p < 0.05$) (except for expiratory reserve volume and maximal voluntary ventilation).
Odynets, Briskin, and Todorova (2019)	Women with BC • Aquatic exercise intervention ($n = 45$) • Pilates intervention ($n = 40$) • Yoga intervention ($n = 30$)	• Quality of life *Functional assessment of Cancer therapy questionnaire, specific module for breast cancer patients (FACT-B).*	• Baseline • 6 months follow-up • 12 months follow-up	Not reported	All groups had significant improvement of quality of life at 6 months program ($p < 0.01$). After 12 months, the aquatic exercise intervention showed benefits in emotional ($d = 0.67$), physical ($d = 0.38$), social ($d = 0.42$) and functional well-being ($d = 0.10$) compared to the Pilates intervention as well as to a yoga intervention ($d = 0.10$ to 0.80). The BR subscale also showed moderate improvements ($d = 0.27$)
Odynets, Briskin, Zakharina, et al. (2019)	Women with BC • Aquatic exercise intervention ($n = 34$) • Pilates intervention ($n = 34$)	• Pulmonary function *Spirometry*	• Baseline • 3 months follow-up	No adverse effects	The aquatic exercise intervention was more effective improving pulmonary function parameters (vital capacity, forced vital capacity, maximal voluntary ventilation, and expiratory reserve volume) ($p < 0.01$) than a Pilates exercise program. No effect sizes were reported.

(Continues)

TABLE 3 (Continued)

Author/Year publication	Participants/Comparison or control group	Outcomes	Measured time points	Adverse effects	Main results
Tidhar and Katz-Leurer (2010)	• Women with BC and lymphedema. • Aquatic exercise intervention ($n = 16$) • Control group ($n = 32$)	• Lymphedema *Limb volume by a water displacement device.* • Quality of life*Upper limb lymphedema questionnaire (ULL27)*	• Before and after the first (baseline) and last session (12 wks).	No adverse effects	Aqua lymphatic therapy had a significant immediate ($p < 0.02$) but not long-term effect on limb volume. Quality of life improved in the emotional dimension ($p = 0.03$) and social dimension ($p = 0.001$) but not in the physical dimension ($p = 0.39$).
Non-RCT studies					
Broach and Norrell (2019)	Women with BC. Aquatic exercise intervention ($n = 12$) Usual care ($n = 7$)	• Cardiovascular fitness *12-minute walk test* • Body composition*Body mass index and bioimpedance* • Arm edema*Volumometer* • Fatigue*Multidimensional fatigue inventory short form* • Emotional distress level*Impact of event scale* • Quality of life.*Health-related quality of life (HRQoL)* scale developed by the Centers for Disease Control and Prevention	• Baseline • Post intervention (8wk)	Not reported	An aquatic exercise program improved body composition ($p = 0.03$), cardiovascular fitness ($p = 0.001$), emotional distress ($p = 0.002$) and fatigue ($p = 0.038$). No effects were found in arm edema or healthy day scores. No significant differences occurred in the control group. Effect sizes were not reported.
Cantarero-Villanueva, Fernández-Lao, Caro-Morán, et al. (2013)	Women with BC. Aquatic exercise intervention ($n = 20$) Control group ($n = 20$)	• Body composition *Body mass index and waist circumference.* • Pressure pain threshold (neck, shoulder, hand and leg)*Electronic algometer* • Cancer-related fatigue*Piper fatigue scale*	• Baseline • Post-intervention (8 wk)	No adverse effects	An aquatic exercise intervention showed benefits with large intergroup effect size for pressure pain threshold in cervical area ($d = 1.49$), unaffected hand area ($d = 1.15$) and leg area *($d > 1.15$); and moderate for affected shoulder* ($d = 0.82$). For waist circumference the intergroup effect size was moderate ($d = 0.580$). No effects were found in cancer-related fatigue and body mass index.

TABLE 3 (Continued)

Author/Year publication	Participants/Comparison or control group	Outcomes	Measured time points	Adverse effects	Main results
Fernández-Lao et al. (2013)	Women with BC. Aquatic exercise intervention ($n = 33$) Land-based intervention ($n = 31$) Control group ($n = 34$)	• Body composition. *Bioimpedance (weight, body mass index, fat and lean mass) and waist circumference.* • Secondary lymphedema. *Circumferential at 5 and 10 cm below the distal border of the lateral epicondyle of the humerus.* • Quality of life.*Spanish version of European Organization for Research and Treatment of Cancer Breast Cancer-Specific Quality of Life (EORTC QLQ-BR23) questionnaire*	• Baseline • Post-intervention • 6 months follow-up	Not reported	The land-based intervention showed greater decrease in fat percentage than the aquatic exercise intervention ($p < 0.001$), and shower a greater increase in lean body mass ($p = 0.008$). Both intervention groups showed a decrease in waist circumference compared with the control group ($p \leq 0.003$). There were no effects in body weight and body mass index. The land-based intervention also showed greater improvement in 5-cm forearm circumference than the aquatic exercise intervention ($p = 0.024$). The aquatic exercise intervention significantly improved breast symptoms compared to the land and control groups ($p < 0.001$). Effect sizes were not reported.
Single-arm pre-post study					
Siqueira et al. (2020)	Women with BC. Aquatic exercise intervention ($n = 21$)	Range of motion (shoulder) *Computerised, photogoniometer with image analysis.*	• Baseline • After 7 wks. • Post-intervention (12 wks)	No adverse events	The aquatic exercise program improved significantly the range of shoulder motion of abduction, flexion, external rotation, adduction ($p < 0.05$), but no extension nor internal rotation.

Abbreviations: BC, breast cancer; CI, confidence interval; PPT, pressure pain threshold; RCT, randomised controlled trial; ROM, range of motion; wk, week.

2.5 | Data extraction

One reviewer collected the data of the different studies covering the following aspects: characteristics of included studies (authors and year of publication), population characteristics (sample size and type of population included) intervention, comparison group, outcomes, assessment times and main results (Table 3). These items were discussed and agreed previously by all authors of the study. The detailed intervention from each study is summarised in Supporting Information S1.

2.6 | Assessment of the risk of bias

Two independent reviewers assessed the risk of bias. The instruments used were the Risk of Bias tool (RoB) 2.0 (Sterne et al., 2019) to assess a RCT design studies and the Risk Of Bias In Non-randomised Studies–of Interventions (ROBINS-I) (Sterne et al., 2016) to assess non-randomised studies. The kappa statistic index was used to determine interrater agreement (values of 0.4 or less, 0.4 to 0.75 and over 0.75, correlates with poor, fair or excellent agreement, respectively) (Fleiss, 1971). The score of the two reviewers was compared, and differences were discussed. If no agreement was reached, a third reviewer intervened. According to study quality, the studies were rated from low to high risk of bias in the ROB 2.0 scale and from low to critical bias in the ROBINS-I scale. There was not a cut point that studies had to reach to be included in the review, but this assessment was used for the solely purpose of classifying the quality of the evidence collected from each study.

2.7 | Data analysis

Due to heterogeneity in the type of aquatic therapeutic exercises, the outcomes included in the review and instruments used to assess them, a meta-analysis on the effect of the interventions was deemed inappropriate. Instead, a qualitative synthesis of the studies included was performed, and results from the interventions on each specific outcome of interest were summarised narratively in tables.

When available, results on each outcome of interest were expressed in terms of mean change or effect size. Statistical significance was also reported for each comparison. Details on the exercise interventions were presented in a table according to the FITT principle when reported by the studies. If available, results on adherence were expressed in percentage of sessions attended of those prescribed.

3 | RESULTS

3.1 | Search results

In the initial search, 145 potential articles were identified. After excluding duplicates and the ones which did not meet the inclusion

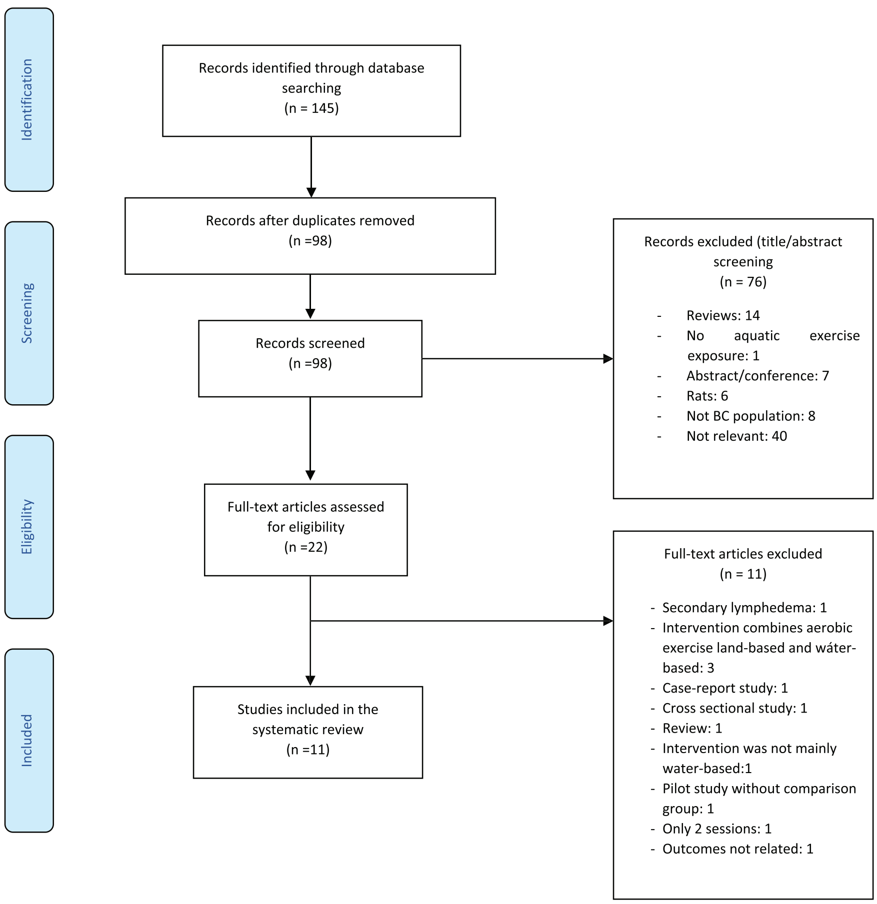

FIGURE 1 Diagram flow

criteria by screening titles and abstract, 22 studies were identified for full-text assessment. Finally, 11 articles were included in this review after excluding studies with patients with secondary lymphedema ($n = 1$), case-report ($n = 1$), cross-sectional ($n = 1$), reviews ($n = 1$), studies where a water intervention was a small part of the intervention ($n = 1$), the intervention combined land and water-based exercises ($n = 3$), a pilot study without comparison group ($n = 1$), intervention only consisted of two sessions ($n = 1$) or studies with outcomes not related ($n = 1$). The selection process appears in (Figure 1).

3.2 | Sensitivity and precision analysis

The result of the analysis is detailed in Table 4.

3.3 | Participants, study characteristics and design

The studies included in total 737 women (308 in the aquatic exercise intervention, 205 in a comparison intervention group with other intervention programmes and 224 in the usual care group) with a sample ranging from 19 to 165 participants.

Among the studies, six of them were RCTs (Cantarero-Villanueva et al., 2012; Cantarero-Villanueva, Fernández-Lao, Cuesta-Vargas, et al., 2013; Odynets et al., 2018; Odynets, Briskin, & Todorova, 2019; Odynets, Briskin, Zakharina, et al., 2019; Tidhar & Katz-Leurer, 2010), one was a randomised controlled pilot trial (Johansson et al., 2013) and three of them were controlled trials (Broach & Norrell, 2019; Cantarero-Villanueva, Fernández-Lao, Caro-Morán, et al., 2013; Fernández-Lao et al., 2013) and a single-arm pre-post trial (Siqueira et al., 2020). Studies were published from 2010 to 2020. Participants and study main characteristics are in Table 3. The intervention details are gathered in Supporting Information S1. The aquatic intervention was compared to usual care (Broach & Norrell, 2019; Cantarero-Villanueva et al., 2012; Cantarero-Villanueva, Fernández-Lao, Caro-Morán, et al., 2013; Cantarero-Villanueva, Fernández-Lao, Cuesta-Vargas, et al., 2013; Johansson et al., 2013; Tidhar & Katz-Leurer, 2010), to land exercise or usual care (Fernández-Lao et al., 2013), to a Pilates (Odynets et al., 2018; Odynets, Briskin, & Todorova, 2019; Odynets, Briskin, Zakharina, et al., 2019) or a Yoga programme (Odynets et al., 2018; Odynets, Briskin, & Todorova, 2019) and a group of healthy women (Odynets et al., 2018) or had no comparison group (Siqueira et al., 2020).

3.4 | Risk of bias of the studies

The summary of the assessment of risk of bias is included in Figure 2 and Table 5. The assessment was made by two independent assessors, and the interrater agreement was excellent (0.75 kappa index). The agreement of 100% was reached through discussion. The majority of the RCTs presented some methodological issues, especially in the randomisation process, deviations from intended interventions and selection of the reported results. As an overall risk of bias, most studies presented some concerns. In non-RCTs, the major methodological issue was bias due to confounding with a moderate to a serious risk, and the overall risk was moderate to critical.

4 | OUTCOMES

The outcomes and the instruments used to assess them are summarised in Table 3.

4.1 | Aquatic intervention programs characteristics

The total duration of the intervention was 8 weeks (Broach & Norrell, 2019; Cantarero-Villanueva et al., 2012; Cantarero-Villanueva, Fernández-Lao, Caro-Morán, et al., 2013; Cantarero-Villanueva, Fernández-Lao, Cuesta-Vargas, et al., 2013; Fernández-Lao et al., 2013; Johansson et al., 2013), 12 weeks (Odynets, Briskin, Zakharina, et al., 2019; Siqueira et al., 2020; Tidhar & Katz-Leurer, 2010) or 48 weeks (Odynets et al., 2018; Odynets, Briskin, &

TABLE 4 Sensitivity, precision, NNR and unique hits of the search

Databases	Total hits retrieved	Relevant hits retrieved	NNR	Unique hits	Sensitivity	Precision
Pubmed	26	8	3	0	73	31
Web of science	26	8	3	0	73	31
Scopus	36	11	3	1	100	31
CINAHL	46	10	5	0	91	22
Cochrane	11	2	6	0	18	18
TOTAL	145	11				

The number of hits is the remaining after duplicates were removed.
NNR: Number Needed to Read (total hits retrieved/relevant hits on a database).
Unique paper: relevant study retrieved from one database only.
Sensitivity: relevant hits retrieved/relevant hits retrieved TOTAL (%).
Note: Precision: relevant hits retrieved/total retrieved (%).

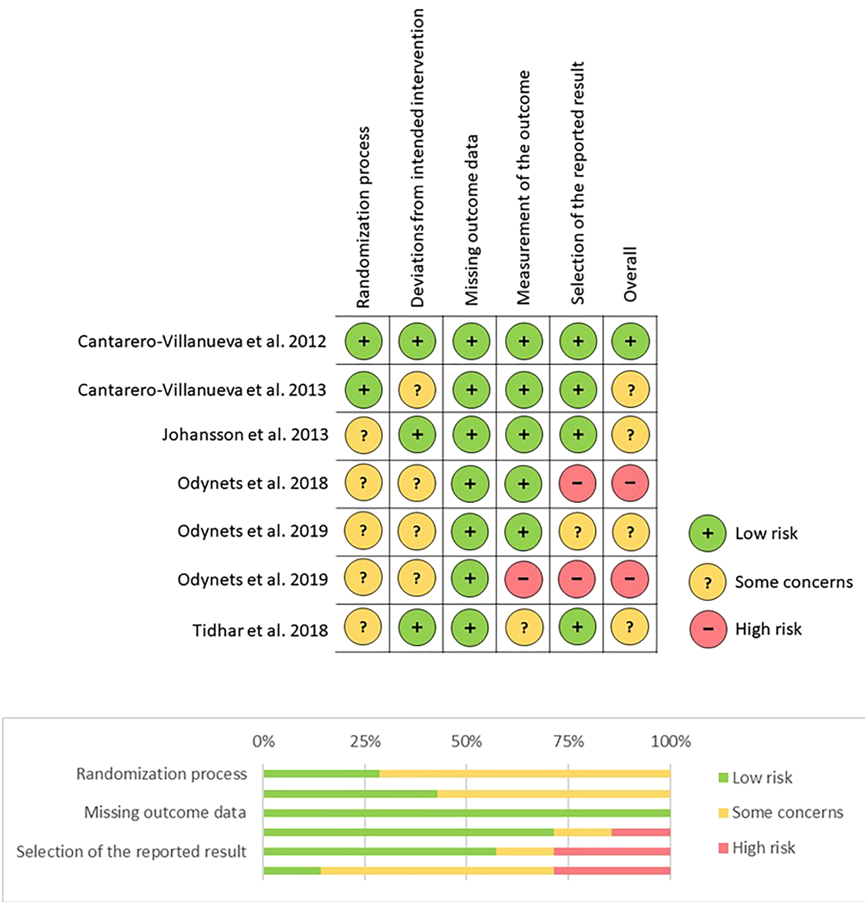

FIGURE 2 Assessment of the risk of bias scale risk of bias assessment of RCTs

TABLE 5 Robins-I scale for assessment of non-randomised studies' risk of bias

	D1	D2	D3	D4	D5	D6	D7	Overall Judgement
Broach and Norrell (2019)	Serious	Low	Low	Low	Low	Moderate	Moderate	Serious
Cantarero-Villanueva, Fernández-Lao, Caro-Morán, et al. (2013)	Moderate	Low	Low	Low	Low	Low	Low	Moderate
Fernández-Lao et al. (2013)	Moderate	Low	Low	Low	Low	Low	Low	Moderate
Siqueira et al. (2020)	Serious	Critical	Low	Low	Low	Serious	Moderate	Critical

Note: Domains. D1: Bias due to confounding. D2: Bias in the selection of participants into the study. D3: Bias in the classification of interventions. D4: Bias due to deviations from intended interventions. D5: Bias due to missing data. D6: Bias in the measurement of outcomes. D7: Bias in selection of the reported results.

Todorova, 2019). The frequency of the sessions were one session/week (Tidhar & Katz-Leurer, 2010), two sessions/week (Siqueira et al., 2020) and three sessions/week (Broach & Norrell, 2019; Cantarero-Villanueva et al., 2012; Cantarero-Villanueva, Fernández-Lao, Caro-Morán, et al., 2013; Cantarero-Villanueva, Fernández-Lao, Cuesta-Vargas, et al., 2013; Fernández-Lao et al., 2013; Johansson et al., 2013; Odynets et al., 2018; Odynets, Briskin, & Todorova, 2019; Odynets, Briskin, Zakharina, et al., 2019). The intensity of physical exercise in the programmes was low (Tidhar & Katz-Leurer, 2010), low-moderate (Cantarero-Villanueva et al., 2012), moderate (Cantarero-Villanueva, Fernández-Lao, Cuesta-Vargas, et al., 2013; Fernández-Lao et al., 2013; Johansson et al., 2013; Odynets et al., 2018; Odynets, Briskin, & Todorova, 2019), moderate-vigorous (Broach & Norrell, 2019) or not specified (Cantarero-Villanueva, Fernández-Lao, Caro-Morán, et al., 2013; Odynets, Briskin, Zakharina, et al., 2019; Siqueira et al., 2020). The total sessions' duration was 30 (Johansson et al., 2013), 45 (Tidhar & Katz-Leurer, 2010), 50 (Broach & Norrell, 2019) or 60 (Cantarero-Villanueva et al., 2012; Cantarero-Villanueva, Fernández-Lao, Caro-Morán, et al., 2013; Cantarero-Villanueva, Fernández-Lao, Cuesta-Vargas, et al., 2013; Fernández-Lao et al., 2013; Odynets et al., 2018; Odynets, Briskin, & Todorova, 2019; Siqueira et al., 2020) min duration or not specified (Odynets, Briskin, Zakharina, et al., 2019). The intervention consisted of aerobic (Broach & Norrell, 2019; Cantarero-Villanueva et al., 2012;

Cantarero-Villanueva, Fernández-Lao, Cuesta-Vargas, et al., 2013; Fernández-Lao et al., 2013; Johansson et al., 2013; Odynets et al., 2018; Odynets, Briskin, & Todorova, 2019; Odynets, Briskin, Zakharina, et al., 2019; Siqueira et al., 2020), strength (Broach & Norrell, 2019; Cantarero-Villanueva et al., 2012; Cantarero-Villanueva, Fernández-Lao, Cuesta-Vargas, et al., 2013; Fernández-Lao et al., 2013; Johansson et al., 2013; Odynets et al., 2018; Odynets, Briskin, & Todorova, 2019; Odynets, Briskin, Zakharina, et al., 2019; Siqueira et al., 2020; Tidhar & Katz-Leurer, 2010), core stability (Broach & Norrell, 2019; Cantarero-Villanueva et al., 2012; Odynets, Briskin, & Todorova, 2019), stretching (Broach & Norrell, 2019; Odynets et al., 2018; Odynets, Briskin, & Todorova, 2019), mobility (Cantarero-Villanueva, Fernández-Lao, Cuesta-Vargas, et al., 2013; Johansson et al., 2013), massage (Tidhar & Katz-Leurer, 2010), breathing exercises (Odynets, Briskin, & Todorova, 2019; Odynets, Briskin, Zakharina, et al., 2019; Tidhar & Katz-Leurer, 2010), recovery strategies (Broach & Norrell, 2019; Cantarero-Villanueva et al., 2012; Cantarero-Villanueva, Fernández-Lao, Cuesta-Vargas, et al., 2013; Fernández-Lao et al., 2013; Odynets, Briskin, Zakharina, et al., 2019), such as stretching (Cantarero-Villanueva et al., 2012; Cantarero-Villanueva, Fernández-Lao, Cuesta-Vargas, et al., 2013; Fernández-Lao et al., 2013) exercises, mobility (Fernández-Lao et al., 2013), massage (Cantarero-Villanueva, Fernández-Lao, Cuesta-Vargas, et al., 2013; Fernández-Lao et al., 2013), breathing (Cantarero-Villanueva et al., 2012; Fernández-Lao et al., 2013), relaxation (Odynets, Briskin, Zakharina, et al., 2019), visualisation techniques (Fernández-Lao et al., 2013) and lymph node massage. The modality was mainly supervised with the exception of a study that was supervised only in the first session (Johansson et al., 2013). The aquatic intervention programmes' characteristics will be summarised in Supporting Information S1.

4.2 | Feasibility, adherence and adverse events

The majority of the studies had a recruitment rate over 80% of the eligible participants, and follow-up was obtained for more than 80% of the participants in all of the studies included. Adherence was also very high when reported (ranging from 79 to 85%) (Cantarero-Villanueva et al., 2012; Cantarero-Villanueva, Fernández-Lao, Caro-Morán, et al., 2013; Fernández-Lao et al., 2013; Tidhar & Katz-Leurer, 2010). Some studies reported on adverse events (Cantarero-Villanueva et al., 2012; Cantarero-Villanueva, Fernández-Lao, Cuesta-Vargas, et al., 2013). In one study (Cantarero-Villanueva et al., 2012), three of the participants had a transient increase in their lymphedema, and one had an increase in fatigue after the first session. Another study (Cantarero-Villanueva, Fernández-Lao, Cuesta-Vargas, et al., 2013) reported some discomfort or low-intensity pain/stiffness while the rest reported no adverse events (Fernández-Lao et al., 2013; Johansson et al., 2013; Odynets, Briskin, Zakharina, et al., 2019; Siqueira et al., 2020; Tidhar & Katz-Leurer, 2010). Overall, these results indicate that aquatic therapeutic exercise interventions are well-tolerated and achieve high attendance rates.

4.3 | Aquatic exercise intervention effects

The studies included in the review found significant effects of aquatic therapeutic exercise interventions on cardiovascular fitness (Broach & Norrell, 2019), endurance of the abdominal muscles (Cantarero-Villanueva, Fernández-Lao, Cuesta-Vargas, et al., 2013), shoulder range of motion (Johansson et al., 2013; Siqueira et al., 2020), lower-body strength (Cantarero-Villanueva, Fernández-Lao, Cuesta-Vargas, et al., 2013), pain (Cantarero-Villanueva et al., 2012) and pressure pain thresholds (Cantarero-Villanueva et al., 2012; Cantarero-Villanueva, Fernández-Lao, Caro-Morán, et al., 2013), presence of trigger points (Cantarero-Villanueva et al., 2012), emotional distress (Broach & Norrell, 2019) and HRQoL (Odynets, Briskin, & Todorova, 2019; Tidhar & Katz-Leurer, 2010), all $p < 0.05$ compared to a control group. Pulmonary function was also improved compared to land-based interventions (Yoga or Pilates) (Odynets, Briskin, Zakharina, et al., 2019). Inconsistent results were found for body composition, with one study (Broach & Norrell, 2019) showing improvements in body mass index and another in waist circumference (Cantarero-Villanueva, Fernández-Lao, Caro-Morán, et al., 2013) compared to a control group, where no effect was found compared to a land-based exercise programme (Fernández-Lao et al., 2013). CRF and lymphedema also showed conflicting results, with studies reporting either no effect (Broach & Norrell, 2019; Johansson et al., 2013) or transient effects (Tidhar & Katz-Leurer, 2010).

In the long term, some benefits were maintained after 6 months (Cantarero-Villanueva, Fernández-Lao, Cuesta-Vargas, et al., 2013) in fatigue (Cantarero-Villanueva, Fernández-Lao, Cuesta-Vargas, et al., 2013) and leg (Cantarero-Villanueva, Fernández-Lao, Cuesta-Vargas, et al., 2013) and trunk endurance (Cantarero-Villanueva, Fernández-Lao, Cuesta-Vargas, et al., 2013) compared to a control group. No differences were found at 6-month post-intervention in terms of overall HRQoL when compared to other interventions (Odynets, Briskin, & Todorova, 2019). However, at 12 months, the aquatic intervention improved significantly the emotional well-being and diminished the negative symptoms associated with the treatment compared to the groups of Pilates and yoga interventions, while yoga was more effective in improving social/family well-being (Odynets, Briskin, & Todorova, 2019).

5 | DISCUSSION

This systematic review aimed to synthetize the current evidence regarding the effects of aquatic therapeutic exercise interventions on the most common sequelae associated with BC and its treatments. The results obtained showed that engaging in aquatic exercise is safe and elicits several benefits both compared to usual care (no exercise intervention) or to different types of land-based exercise interventions. Overall, patients included in the aquatic therapy groups showed moderate to strong improvements in pain, shoulder range of motion, pulmonary function, health-related quality of life and cardiorespiratory fitness and muscle strength, while conflicting results were found for lymphedema, body composition and CRF. In addition, adherence rates were very high (ranging from 79% to 85%), and very few minor adverse events were reported, suggesting that aquatic therapeutic exercise interventions are well-tolerated and enjoyable. Noteworthy, studies were quite heterogeneous in terms of exercise parameters such as duration, frequency, intensity and type of aquatic exercise, which precluded us from drawing any conclusion on the most effective exercise prescription (Figure 3 shows a graphic summary of findings).

The benefits of aquatic therapy are well established in the literature and are related to the physical properties of water (Becker, 2009; Denning et al., 2012) including buoyancy, hydrostatic pressure and viscosity among others which could be of great advantage for patients with BC (Becker, 2009; Cantarero-Villanueva, Fernández-Lao, Caro-Morán, et al., 2013; Castillo-Lozano et al., 2014; Lauer et al., 2018; Siqueira et al., 2020; Thein & Brody, 2000; Torres-Ronda & del Alcázar, 2014; Wilcock et al., 2006). Pain and decreased range of motion of the affected arm are two common consequences of BC treatment, especially after surgery, which can be associated to greater rates of depression, lower levels of function and greater symptoms (Lamino et al., 2011). Two studies (Cantarero-Villanueva et al., 2012; Cantarero-Villanueva, Fernández-Lao, Caro-Morán, et al., 2013) analysed the effects of the aquatic intervention on pain threshold and/or presence of trigger points, and both reported a significant positive effect of the intervention comparing to usual care, especially for neck and shoulder/axillary pain which achieved clinical importance. The analgesic effect of water immersion is well studied in the literature, and it is mediated by the effects of hydrostatic pressure (Becker, 2009; Gueita-Rodriguez et al., 2019), as well as water temperature and buoyancy (Kamioka et al., 2020). The presence of this analgesic effect would also explain the increase in range of motion reported by some studies (Castillo-Lozano et al., 2014; Thein & Brody, 2000) although compared to land-based exercise, differences were not significant (Dong et al., 2018).

Hydrostatic pressure during immersion also compresses the chest wall resulting in an increased work of breathing and altered respiratory dynamics (Becker, 2009). This effect could explain the improvements in pulmonary function obtained in two of the studies included (Odynets et al., 2018; Odynets, Briskin, Zakharina, et al., 2019) which reported that aquatic therapeutic exercise improved several parameters of pulmonary function to a greater extent than a Pilates or a Yoga intervention (Odynets et al., 2018), even when these encourage a specific breathing technique. Two parameters (expiratory reserve volume and maximal voluntary ventilation) were only enhanced when breathing exercises were added to the aquatic therapeutic exercise programme (Odynets, Briskin, Zakharina, et al., 2019). These results are of particular interest as different types of cancer can directly affect pulmonary function and lung dynamics, due to surgery or toxicity accumulated during chemo-radiotherapy in the area.

In line with the improvements in pulmonary function, the effects of water immersion on cardiac output and peripheral resistance (Wilcock et al., 2006) can lead to an increase in cardiorespiratory fitness and particularly in VO_2max, as observed in some populations (Bocalini et al., 2008; Zoheiry et al., 2017). In this systematic review, only one study assessed cardiorespiratory fitness using the 12-min walk test and reported a small increase in the distance walked after the aquatic exercise programme (Cohen's $d = 0.26$). Nevertheless, the majority of the studies in this systematic review included aerobic training in combination with strength training as part of their exercise regimen (Broach & Norrell, 2019; Cantarero-Villanueva et al., 2012; Fernández-Lao et al., 2013; Johansson et al., 2013; Odynets, Briskin, & Todorova, 2019; Odynets, Briskin, Zakharina, et al., 2019), but high heterogeneity was observed in terms of duration, intensity and frequency of training. For instance, intensity of the exercise ranged from

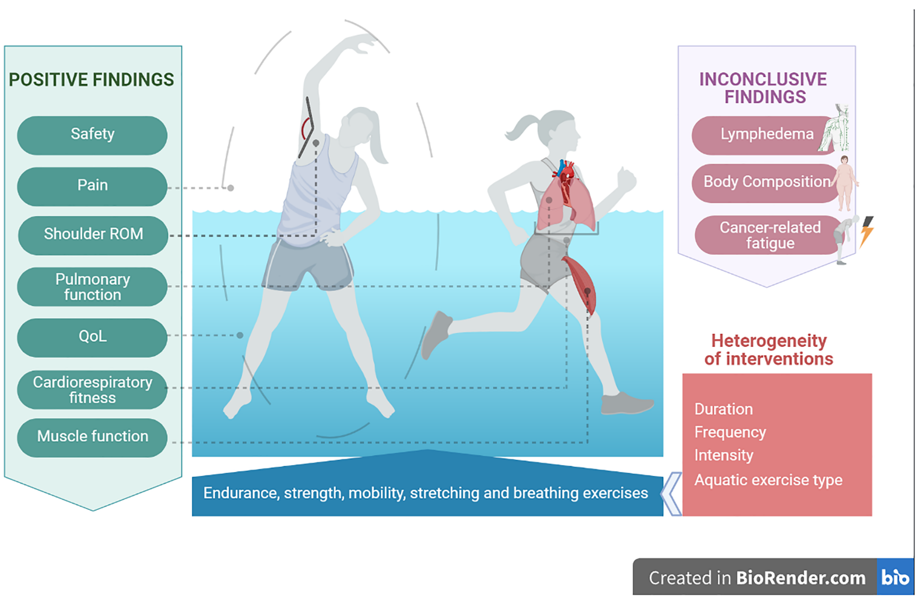

FIGURE 3 Summary of findings

low to moderate and lasted somewhere between 20 and 40 min, with a frequency of delivery of two or three sessions per week. Furthermore, more often than not, studies did not disclosure the percentage of the exercise session dedicated to endurance training; thus, cautious interpretation of the effects on cardiorespiratory fitness is needed. Both endurance and strength training in the water are enhanced thanks to its density which increases cardiovascular output and creates the perfect environment to progress resistance exercise, allowing easy adaptation of the load of an exercise to the patient's level of training (Torres-Ronda & del Alcázar, 2014). In a study published by Bocalini et al. (2008), older women who exercised in the water increased upper body strength and lower body flexibility compared to those randomised to a land-based programme. In the study by Cantarero-Villanueva, Fernández-Lao, Cuesta-Vargas, et al. (2013), a large effect was found on leg strength and trunk endurance (Cohen's $d = 1.10$ and $d = 0.92$) after an aquatic exercise intervention compared to a control group. In both studies, it seems that a combination of endurance and strength exercise at moderate intensity resulted in significant improvements in upper and lower-body muscle strength, which is consistent with the literature available in other clinical populations (Oh & Lee, 2021; Scheer et al., 2020).

Positive results of aquatic therapeutic exercise interventions on HRQoL were also found in this systematic review, which is a key outcome in people with cancer given its prognostic value in this population (Sim et al., 2020). As previously stated, exercising in the water can ameliorate pain and increase range of motion as well as decrease symptoms of depression and anxiety improving psychological wellbeing (Gueita-Rodriguez et al., 2019; Kojima et al., 2018). Studies in this systematic review showed indeed overall improvements in most dimensions of HRQoL, which is in line with previous research in BC (Cuesta-Vargas et al., 2014) as well as in other cancer populations (Gerritsen & Vincent, 2016). Nonetheless, some subscales of HRQoL might be further enhance with other type of exercises such as Pilates or Yoga, according to the study published by Odynets, Briskin, and Todorova (2019). These finding suggests that tailored-based interventions including different environments and exercise modalities should be offered to cancer survivors based on their particular needs and specific dimensions of HRQoL affected. Although this is true for most exercise interventions, evidence shows that it is of particular relevance for BC patients as they usually received a strong combination of highly disabling treatments (surgery, radiotherapy, chemotherapy, biological and hormonal treatments) predisposing them to a sedentary lifestyle.

In this systematic review, we also found some less consistent, small effects of aquatic exercise on outcomes such as lymphedema, body composition and CRF. First, although general improvements in body composition were observed in terms of body mass index (Broach & Norrell, 2019) and waist circumference (Cantarero-Villanueva, Fernández-Lao, Caro-Morán, et al., 2013), in another study (Fernández-Lao et al., 2013), total body fat and fat free mass only changed in the land-based group. The authors hypothesised that this lack of effect in the aquatic therapeutic exercise intervention could be related to the challenge of reproducing the same parameters of exercise prescription in the water than on land. Intensity and volume of the training are two major components of the exercise prescription that can influence the results obtained, and it is possible that in the study by Fernández-Lao et al. (2013), 8 weeks was insufficient to increase fat free mass and reduce body mass, given that positive results in body composition have been reported in water-based exercise programmes that lasted six or more months (Bergamin et al., 2013). As for the effects on lymphedema, exercise training has shown to be safe (Cheema et al., 2014; Hasenoehrl et al., 2020; Sánchez-Lastra et al., 2019), but most studies (Broach & Norrell, 2019; Johansson et al., 2013; Tidhar & Katz-Leurer, 2010) have found only a brief effect reducing arm volume which is consistent with a previous systematic review (Yeung & Semciw, 2018) probably because the improvement in venous and lymphatic circulation caused by hydrostatic pressure (Becker, 2009) is not sustained in time. Regarding CRF, the two studies included in the review reported conflicting findings, with Broach and Norrell (2019) showing that an aquatic therapeutic exercise improved CRF compared to a control group while Cantarero-Villanueva, Fernández-Lao, Caro-Morán, et al. (2013) found no effects. It is well known that exercise is the main non-pharmacological treatment to improve CRF, but specific exercise parameters of intensity, duration and frequency must be achieved in order for the intervention to be effective. In line with this, in the study by Cantarero-Villanueva et al., the authors acknowledged that the exercise protocol used was not designed to improve physical fitness but pain, as only 25% of the total time was dedicated to improve endurance which is key to reduce CRF.

Finally, regarding the quality of the databases for this search, Scopus recorded the highest sensitivity followed by CINAHL, having the lowest probability of missing relevant papers. Cochrane due to the lack of sensitivity and precision for this search was the most ineffective database for this topic. Researchers might consider this database in future searches related to aquatic therapeutic exercise in breast cancer survivors, given the lack of sensitivity and retrieval of the least number of relevant hits. In addition, the quality of the evidence was found to be low to moderate, as most studies exhibited some methodological concerns, especially non-RCTs. This highlights the need for future studies, preferably well-designed RCTs compared to other interventions to strengthen the evidence of aquatic therapeutic exercise for patients with BC before drawing solid conclusions.

In this systematic review, some limitations have occurred that need further discussion. First of all, we found large heterogeneity in the design of the water-based interventions, especially in terms of intensity, duration and type of exercise performed, which makes it difficult to draw solid conclusions, especially regarding the advantages of water-based interventions over land based. In addition, the outcomes assessed were also quite diverse and used different tools or instruments; thus, a meta-analysis was considered inappropriate. Even so, most studies found positive effects of the water-based intervention over a control group which should make us consider the adequateness of the water environment to deliver exercise programmes for BC survivors. Finally, we must acknowledge some restrictions during the search such as the language (English and Spanish only) which precluded us from finding other potential studies published in other languages. Based on these limitations, our results are to be interpreted cautiously.

In conclusion, this systematic review found that aquatic therapeutic exercise interventions for BC survivors using a combination of endurance, strength, mobility, stretching and breathing exercises resulted in moderate to large improvements in common side-effects of BC and BC treatments such as pain, decreased range of motion, impaired HRQoL and cardiorespiratory fitness. Unfortunately, large variations were found in terms of exercise prescription parameters as well as modality of aquatic exercise; thus, specific recommendations for clinical practice are unable to be made at this point. Further studies are needed to ascertain the effectiveness of these interventions on cancer-related fatigue, lymphedema and body composition as well as the optimal exercise parameters to boost the results obtained.

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CONFLICT OF INTEREST

The authors declare they have no conflict of interest.

AUTHOR CONTRIBUTIONS

EMG, ICV and RSG drafted the study. PPM and EMG collected the data. EMG, PPM, ICV and RSG analysed the data. EMG, PPM, ICV and RSG wrote the manuscript. EMG, PPM, ICV and RSG read, revised critically and approved the final the manuscript.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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