



# The effects of exercise on the quality of life of patients with breast cancer: a systematic review and meta-analysis based on the QLQ-C30 quality of life scale

Lijie Chen, Puchao Peng, Zhouming Xu, Xiufang Ding

Department of Breast Surgery, Huzhou Maternity & Child Health Care Hospital, Huzhou, China

*Contributions:* (I) Conception and design: L Chen, X Ding; (II) Administrative support: P Peng; (III) Provision of study materials or patients: L Chen, X Ding; (IV) Collection and assembly of data: All authors; (V) Data analysis and interpretation: All authors; (VI) Manuscript writing: All authors; (VII) Final approval of manuscript: All authors.

*Correspondence to:* Xiufang Ding, BD. Department of Breast Surgery, Huzhou Maternity & Child Health Care Hospital, 2 East Street, Huzhou 313000, China. Email: dx01100214@163.com.

**Background:** Studies have reported that exercise can effectively improve the quality of life of breast cancer (BC) patients. However, considering the differences in exercise form and intensity, it is difficult to quantify and unify the improved outcomes, and there are contradictions in the conclusions. This meta-analysis aimed to quantitatively evaluate the effects of exercise on the quality of life (QoL) of patients with BC based on the European Organization for Research and Treatment of Cancer QoL Questionnaire-C30 (QLQ-C30) scale, to provide optimization suggestions for the treatment plan of BC survivors.

**Methods:** The literature were extracted from the databases of PubMed, Embase, Cochrane Library, Wanfang, and China National Knowledge Infrastructure. The main outcomes were extracted from the final included literature and chi square tests and  $I^2$  statistics were used to evaluate the heterogeneity among the included studies. Statistical analysis was performed by Stata/SE 16.0 software and Review Manager 5.4 software. The funnel plot was used to test for evaluation publication bias.

**Results:** All 8 included articles were original studies. The risk bias evaluation showed that 2 articles had low risk of bias and 6 articles had uncertain risk of bias. The results of meta-analysis revealed the following: (I) exercise significantly improved the overall health status of BC patients [mean difference (Hedges's  $g$ ) =0.81, 95% confidence interval (CI): 0.27, 1.34]; (II) exercise significantly improved the physiological function of patients (Hedges's  $g$  =0.78, 95% CI: 0.34, 1.22), daily life function (Hedges's  $g$  =0.45, 95% CI: 0.13, 0.77), emotional function (Hedges's  $g$  =0.52, 95% CI: 0.20, 0.84); (III) exercise significantly reduced the fatigue symptoms (Hedges's  $g$  =-0.51, 95% CI: -0.84, -0.19), nausea and vomiting symptoms (Hedges's  $g$  =-0.35, 95% CI: -0.60, -0.10), insomnia symptoms (Hedges's  $g$  =-0.59, 95% CI: -0.91, -0.26), and economic difficulties (Hedges's  $g$  =-0.48, 95% CI: -0.78, -0.18) of patients.

**Conclusions:** Exercise can significantly improve the overall physical health and body functions of BC survivors. Exercise can also significantly reduce the symptoms of fatigue, nausea, vomiting, and insomnia in BC patients. Different levels of exercise have significant effects on improving the quality of life of BC survivors, which is worth being widely advocated.

**Keywords:** Breast cancer; exercise; quality of life (QoL); Quality of Life Questionnaire-C30 scale (QLQ-C30 scale)

Submitted Mar 09, 2023. Accepted for publication May 18, 2023. Published online May 26, 2023.

doi: 10.21037/gs-23-126

**View this article at:** <https://dx.doi.org/10.21037/gs-23-126>

## Introduction

Breast cancer (BC) is one of the most common cancers worldwide. Its morbidity and mortality are very high (1). BC ranks first in the incidence of female malignant tumors in China (2), and the incidence rate is still on the rise (3). It has become the main cause of cancer death in women under the age of 45 in China (2). BC prognosis has improved dramatically over the past few decades alongside improvements in medical care (4,5). However, many survivors experience long-term adverse physical and psychological effects of surgery, chemotherapy, and radiation, such as fatigue, vasomotor symptoms, and psychosocial distress (6). It has become an inevitable trend to observe the recovery of the quality of life (QoL) of these BC survivors. Efforts to improve the QoL of BC patients are among the most important endeavors in women's health care today.

Studies have shown that exercise is a major means of rehabilitation. It can improve the rate of complications during BC treatment (7-9), and reduce breast cancer-specific mortality and all-cause mortality (10,11). Exercise can effectively improve the cardiopulmonary function of BC survivors, improve negative emotions (such as anxiety and depression), and promote their physical and mental health (12,13). The effectiveness of exercise rehabilitation in BC survivors has been demonstrated (9,11,14-16).

However, there is considerable heterogeneity in the form, time, intensity, frequency, intervention period, location, and

effect evaluation indicators used in various studies. Moreover, it is difficult to unify and quantify the outcome indicators for the improvement effect of BC patients. In addition, due to differences in ethnicity and medical habits in different regions, these can indirectly affect the quality of life and the impact of exercise on BC patients in different regions. The European Organization for Research and Treatment of Cancer Quality of Life Questionnaire-C30 (EORTC QLQ-C30) is the most widely used method to measure the QoL of cancer patients worldwide. It enables a quantitative assessment of the QoL of cancer patients (17-19).

Some studies have proposed that rehabilitation exercise can reduce the cardiopulmonary adverse reactions, bone loss and incidence rate of fractures caused by cancer surgery or chemotherapy, and improve the quality of life of patients (14-16). However, there is currently heterogeneity in the research on rehabilitation exercise and BC quality of life, and the results are also contradictory. Our aim is to quantitatively assess the impact of rehabilitation exercise on the quality of life of BC patients through meta-analysis, in order to provide a reference for improving the prognostic factors of their quality of life during rehabilitation. A pooled analysis of randomized controlled trials (RCTs) of exercise rehabilitation in BC survivors was performed. The relevant data of the QLQ-C30 QoL scale for the improvement of exercise in BC patients were extracted. A quantitative meta-analysis was performed on the effect of exercise on the improvement of QoL in patients with BC. These findings may provide a strong reference for the formulation of exercise rehabilitation programs for BC survivors. We present this article in accordance with the PRISMA reporting checklist (available at <https://gs.amegroups.com/article/view/10.21037/gc-23-126/rc>) (20).

## Methods

### *Literature search strategy*

This study extracted English and Chinese literature published until December 2022 from the databases of PubMed, Embase, Cochrane Library, Wanfang, and China National Knowledge Infrastructure (CNKI). The literature search primarily employed a combination of subject terms and unrestricted search to ensure comprehensive coverage. The search terms used in both Chinese and English included “breast cancer”, “QLQ-C30”, “exercise”, and “lifestyle”. Additionally, this study conducted a thorough review of citation indexes and reference lists of retrieved articles to identify any relevant studies that may have been missed in the original database search.

### Highlight box

#### Key findings

- In this study, meta-analysis showed that exercise can significantly improve the overall physical health and physical function of BC survivors.

#### What is known and what is new?

- Exercise can effectively improve heart and lung function, improve negative emotions (such as anxiety and depression), and promote physical and mental health in BC survivors.
- Meta-analysis revealed that exercise did not significantly improve cognitive function. Exercise did not significantly improve symptoms of pain, loss of appetite, constipation, or diarrhea.

#### What is the implication, and what should change now?

- The results showed that daily physical activity, using one's own equipment, in a safe and hygienic home environment, away from a hospital setting, improved the BC patients' QoL and reduced depression. Therefore, follow-up research can further investigate the implementation site of the exercise program for patients, so as to optimize the therapeutic effect.

### *Inclusion and exclusion criteria*

#### **Inclusion criteria**

(I) Type of study design: RCTs; the full text was available. (II) Participants: all cases were adults aged over 18 years. (III) Comparison: the “intervention group” was defined as BC patients who exercised at a certain intensity, time, and frequency (exercise for more than 30 minutes per day, lasting for more than 1 month); the “control group” was defined as BC patients who did not exercise (no regular exercise plan). (IV) Outcomes: studies including the scores of the 3 dimensions of EORTC QLQ-C30, namely: overall health status score, functional scores (physical function, role function, emotional function, cognitive function, social function), and clinical symptom scores (drowsiness, nausea and vomiting, pain, dyspnea, insomnia, loss of appetite, constipation, diarrhea, financial difficulties). It was also required that there were no missing data.

#### **Exclusion criteria**

(I) Exclusion of duplicate articles or those without full-text availability; (II) exclusion of studies with incomplete or erroneous data that cannot be rectified; (III) exclusion of studies lacking the necessary outcome indicators relevant to this study; (IV) exclusion of non-randomized controlled trials (non-RCTs); (V) exclusion of letters, case reports, comments, practical guidelines, and similar publication types; (VI) exclusion of studies that did not clinically diagnose breast cancer according to international standards.

#### **Outcome indicators**

EORTC QLQ-C30 scores in 3 dimensions: health status score, functional score (physical function, role function, emotional function, cognitive function, social function), and clinical symptom score (drowsiness, nausea and vomiting, pain, dyspnea, insomnia, loss of appetite, constipation, diarrhea, financial difficulties).

#### **Data extraction**

The following data were collected for analysis: article title, first author, year of publication, country of study, study design type, sample sizes in the experimental and control groups, mean age of participants in the experimental and control groups (along with standard deviation if provided), and scores of the EORTC QLQ-C30 scale in the control and experimental groups.

### *Quality evaluation*

The quality assessment of the included literature was conducted by two independent researchers using the Cochrane risk of bias assessment tool, which is integrated into the Review Manager 5.4 software (The Nordic Cochrane Center, Copenhagen, Denmark). This tool consists of seven domains that evaluate different aspects of bias. When all entries are met, the literature has a low risk of bias, when some entries are met, it has an uncertain risk of bias, and when all entries are not met, it has a high risk of bias. When opinions differed, the researchers entered discussion with a third party to reach agreement.

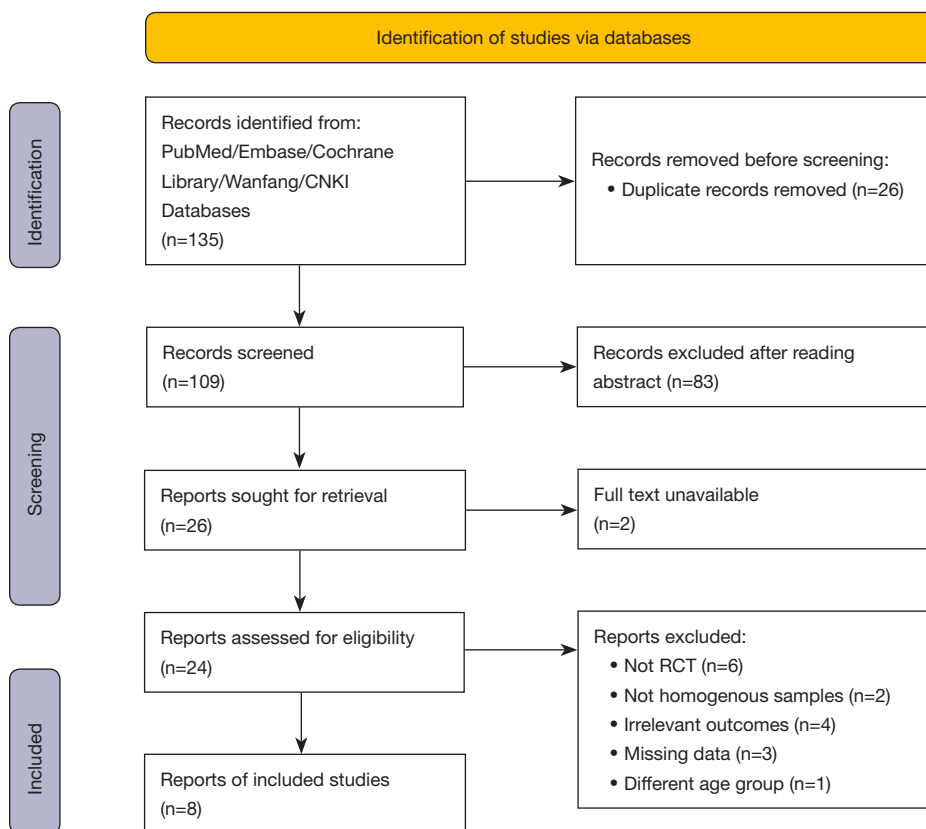
### *Statistical analysis*

This study used Stata/SE 16.0 software (StataCorp. LLC, College Station, TX, USA) and Review Manager 5.4 software based on the EORTC QLQ-C30 scale. Overall health status score, functional scores (physical function, role function, emotional function, cognitive function, social function), and clinical symptom scores (drowsiness, nausea and vomiting, pain, dyspnea, insomnia, loss of appetite, constipation, diarrhea, financial difficulties) of BC patients were analyzed in the “exercise intervention experimental group” and “no exercise control group”. The outcome indicators in this study were continuous variables, reported as mean values with their corresponding 95% confidence intervals (CI). Heterogeneity among the included studies was assessed using the Q test. If the  $I^2$  statistic was less than 50% and the P value was above 0.1, it indicated low heterogeneity, and the fixed-effect model was employed. Otherwise, the random-effects model was used to calculate the combined effect size. The results of the meta-analysis were presented using forest plots. Publication bias was assessed through a funnel plot, and a significance level of  $P < 0.05$  was considered statistically significant for detecting publication bias.

## **Results**

### *Literature search and screening results*

A total of 135 studies were retrieved from 5 databases using the described search methods. After removing duplicate articles, 109 original studies were identified. By reviewing abstracts, 26 studies were initially considered potentially relevant to the research topic. We obtained the full text of these 26 studies and ultimately included 8 studies (21-28)



**Figure 1** Flow chart of literatures screening. CKNI, China National Knowledge Infrastructure; RCT, randomized controlled trial.

in the meta-analysis, following the application of inclusion and exclusion criteria. The literature screening process is visually represented in *Figure 1*.

### **Basic characteristics of the included studies**

All eight included studies (21-28) were original studies. The total sample size comprised 1,248 breast cancer (BC) patients, with 639 cases in the exercise intervention experimental group and 609 cases in the non-exercise control group (*Table 1*).

### **Quality assessment of included literature**

The quality of the literature was evaluated based on the Cochrane risk of bias assessment tool, and the quality evaluation results of the included literature are shown in *Figures 2,3*. Among the 8 included literatures, 6 literatures had uncertain risk of bias and 2 literatures had low risk of bias, meeting the requirements of this meta-analysis.

### **Meta-analysis results and sensitivity analysis**

#### **The effect of exercise on the overall health status of BC patients**

The results of the heterogeneity test for the included studies are presented below:  $I^2=94.31\%$ ,  $P<0.001$ . Therefore, a random effects model was used for meta-analysis. The results showed that after a period of time and intensity of exercise, the overall health score of BC patients was significantly higher than that of control group patients who did not exercise (Hedges's  $g=0.81$ , 95% CI: 0.27, 1.34, *Figure 4*). The sensitivity analysis indicated that the exclusion of individual studies did not significantly alter the overall effect size, suggesting that the results of the meta-analysis were relatively stable.

#### **Physical function improvement of exercise in patients with BC**

The results of the heterogeneity test of the included studies were  $I^2=91.21\%$ ,  $P<0.001$ . Therefore, a random effects model was used for meta-analysis. The results showed

**Table 1** Basic characteristics of the included studies

Study (year)	Country	Type of study	Intervention	Experimental group		Control group	
				Sample size	Age, years	Sample size	Age, years
Shobeiri 2016	Iran	Prospective, randomized controlled trial	A supervised group exercise program two times per week for approximately 40–60 min per session for 10 weeks	27	42.70±9.60	26	43.50±8.60
Saarto 2012	Finland	Prospective, non-blinded randomized two-arm phase III trial	Supervised training was organized for the exercise group once a week in groups of 5 to 15 individuals for 12 months	263	52.3 [36–68]	237	52.4 [35–68]
Aydin 2021	Turkey	Prospective, randomized controlled trial	A 12-week aerobic exercise program at the fitness club and home-based resistance exercise program	24	45.0±2.2	24	45.0±2.2
Montagnese 2020	Italy	An ongoing multicenter randomized controlled trial	Daily brisk walking	227	52.3±9.3	227	52.3±9.3
Pasyar 2019	Iran	A randomized controlled trial study	Yoga exercise program plus the basic routine care. The duration of yoga exercise program was 8 weeks (3 sessions each week)	20	51.6±10.46	20	51.8±11.4
Zhu 2020	China	A randomized controlled trial study	Resistance training and aerobic exercise for 3 months	18	63.2±7.1	18	66.6±9.6
Schmidt 2015	Germany	A prospective, randomized, controlled intervention trial	Interventions were performed for 60 min twice weekly over 12 weeks together with other cancer patients under the supervision and guidance of experienced therapists in specific training facilities	49	52.2±9.9	46	53.3±10.2
Moros 2010	Spain	A prospective, randomized, controlled intervention trial	60 min exercise for 18–22 weeks	11	49±7	11	49±7

Data are presented as number, mean ± SD, or median [range]. SD, standard deviation.

that after exercising for a period of time and intensity, the physical function scores of patients with BC were significantly higher than those of the control group who did not exercise (Hedges's  $g = 0.78$ , 95% CI: 0.34, 1.22, *Figure 5*). The sensitivity analysis revealed that the exclusion of each study individually did not significantly impact the overall effect size, indicating that the results were relatively stable.

#### The effect of exercise on improving the daily life function of patients with BC

The heterogeneity test conducted on the included studies yielded significant results, indicating substantial variation among the studies ( $I^2 = 82.58\%$ ,  $P < 0.001$ ). Therefore, a random effects model was used for meta-analysis. The

results showed that after a period of time and intensity of exercise, the daily life function score of BC patients was significantly higher than that of the control group who did not exercise, and the difference was statistically significant (Hedges's  $g = 0.45$ , 95% CI: 0.13, 0.77, *Figure 6*). The sensitivity analysis revealed that the removal of individual studies did not have a significant impact on the overall effect size, indicating the stability of the results.

#### The effect of exercise on the improvement of emotional function in patients with BC

The included studies exhibited considerable heterogeneity, as evidenced by the results of the heterogeneity test ( $I^2 = 83.13\%$ ,  $P < 0.001$ ). Therefore, a random effects model

	Random sequence generation (selection bias)	Allocation concealment (selection bias)	Blinding of participants and personnel (performance bias)	Blinding of outcome assessment (detection bias)	Incomplete outcome data (attrition bias)	Selective reporting (reporting bias)	Other bias
Aydin 2021	+	+	?	+	+	?	?
Montagnese 2020	+	+	?	+	+	+	+
Moros 2010	-	+	+	+	+	?	?
Pasyar 2019	+	+	+	+	+	+	+
Saarto 2012	?	+	+	+	+	+	?
Schmidt 2015	?	+	+	+	+	+	+
Shobeiri 2016	+	?	-	+	?	+	?
Zhu 2020	+	+	+	+	+	+	+

**Figure 2** Quality assessment of included studies. Low risk of bias (represented by green “+”), high risk of bias (represented by red “-”), uncertain risk of bias (represented by yellow “?”).

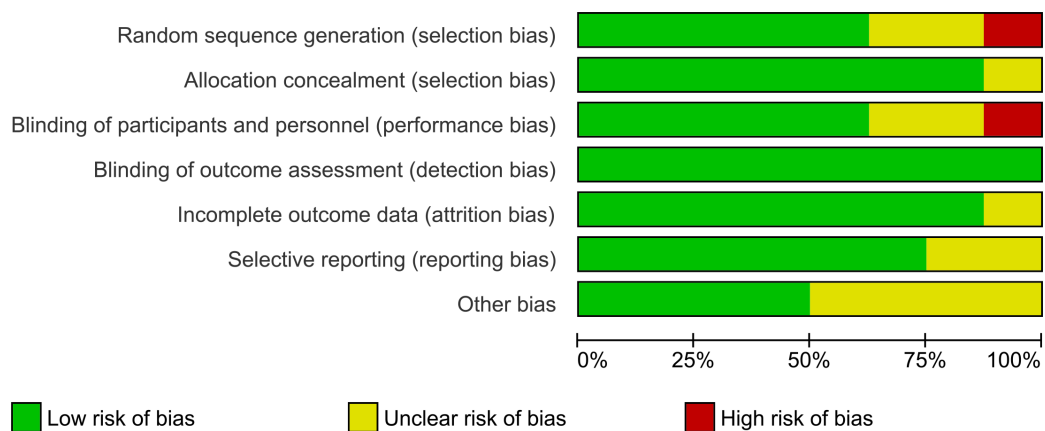
was used for meta-analysis. The results showed that after a period of time and intensity of exercise, the emotional function score of BC patients was significantly higher than that of the control group who did not exercise (Hedges’s  $g = 0.52$ , 95% CI: 0.20, 0.84, *Figure 7*). The sensitivity analysis demonstrated that the exclusion of individual studies had minimal impact on the overall effect size, indicating the robustness and stability of the results.

**Exercise improves the cognitive function of BC patients**

The heterogeneity test conducted on the included studies revealed moderate heterogeneity ( $I^2 = 67.95\%$ ,  $P = 0.01$ ). Therefore, the random effect model was used for meta-analysis. The results showed that after a period of time and intensity of exercise, there was no significant difference in cognitive function scores between patients with BC and those in the control group who did not exercise (Hedges’s  $g = 0.17$ , 95% CI: -0.06, 0.41, *Figure 8*). The sensitivity analysis demonstrated that the incremental removal of individual studies had minimal impact on the overall effect size, indicating that the results remained relatively stable and consistent.

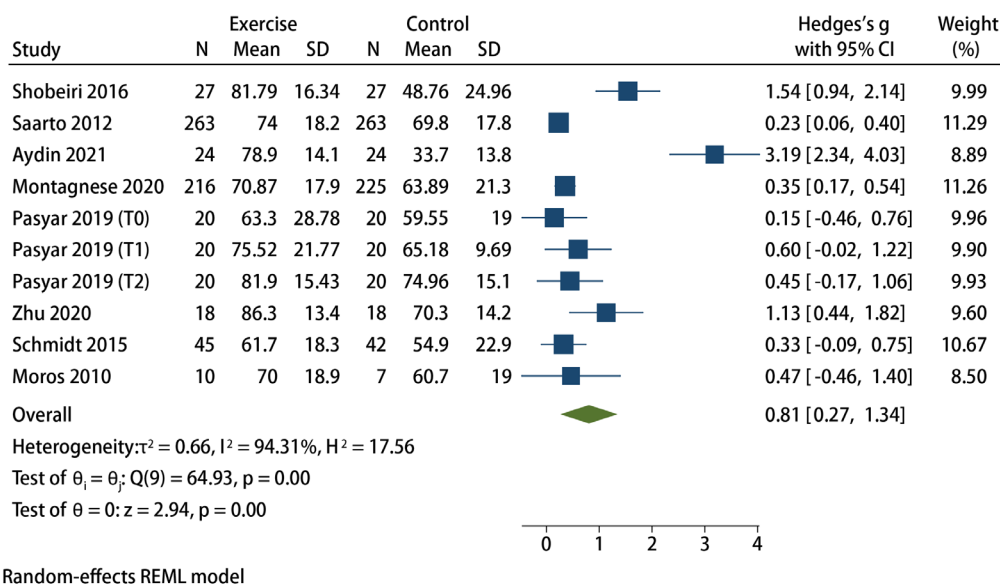
**The improvement of social function of BC patients by exercise**

The results of the heterogeneity test of the included studies were  $I^2 = 28.19\%$ ,  $P = 0.18$ . Therefore, a fixed-effects model was used for meta-analysis. The results showed that after a period of time and intensity of exercise, the social function score of BC patients was significantly higher than that of the

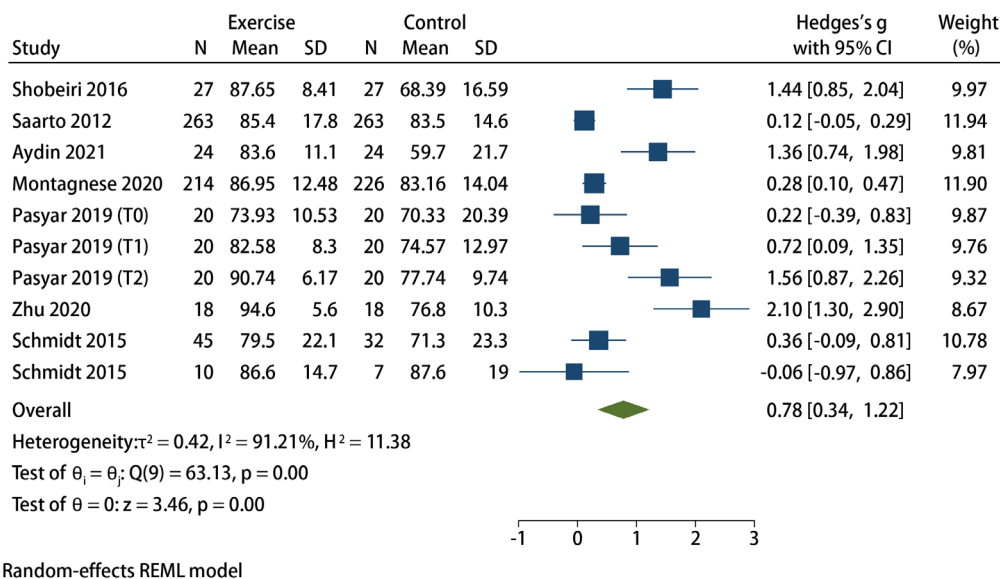


**Figure 3** Quality assessment of included studies.





**Figure 4** Forest plot of the improvement of overall health status of breast cancer patients after exercise. SD, standard deviation; CI, confidence interval; REML, restricted maximum likelihood.

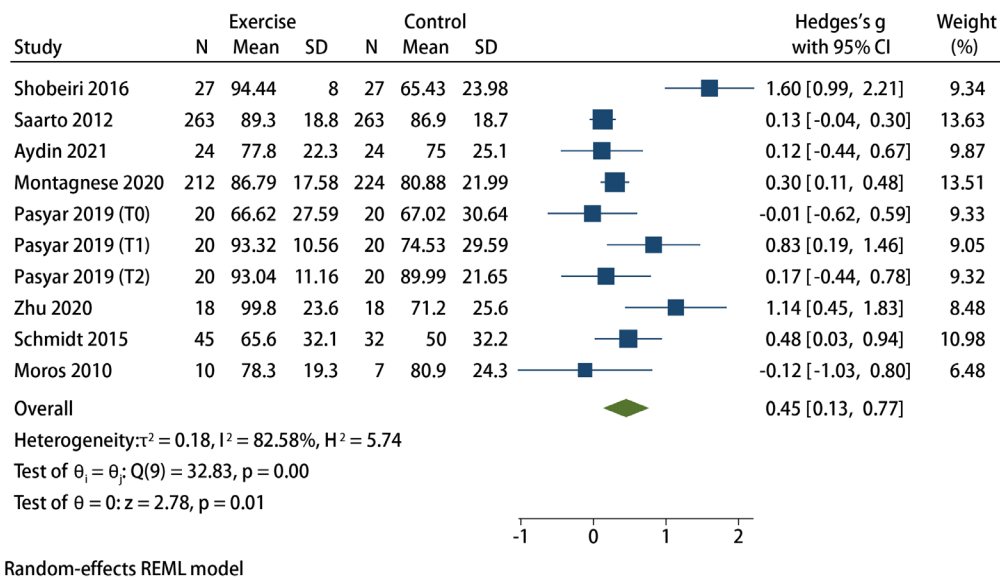


**Figure 5** Forest plot of physical function improvement in patients with breast cancer after exercise. SD, standard deviation; CI, confidence interval; REML, restricted maximum likelihood.

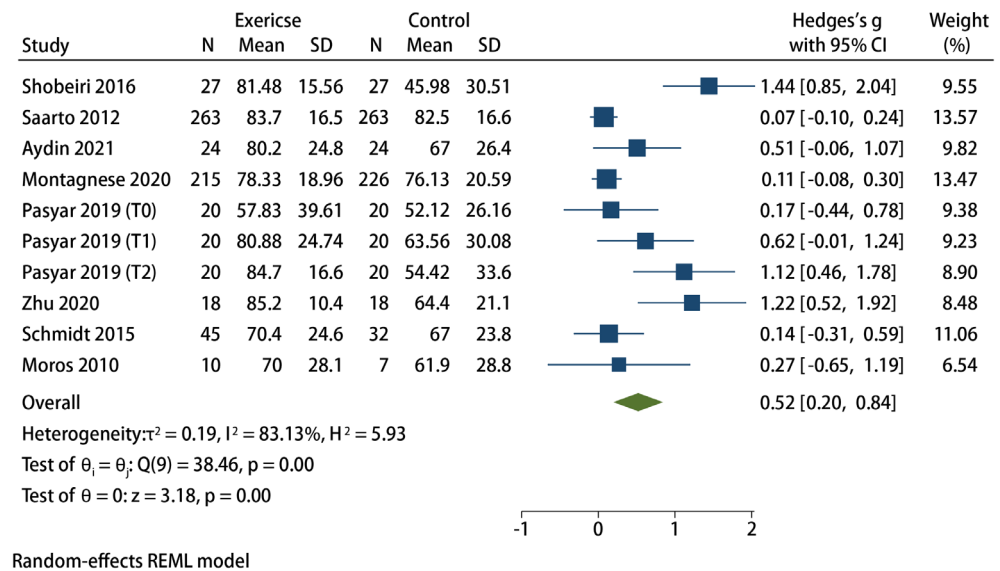
control group who did not exercise (Hedges's  $g = 0.42$ , 95% CI: 0.31, 0.53, *Figure 9*). The sensitivity analysis performed by systematically excluding studies one by one indicated that the overall effect size remained largely unchanged, suggesting that the results were stable and consistent.

**The effect of exercise on the improvement of fatigue symptoms in patients with BC**

The results of the heterogeneity test of the included studies were  $I^2 = 67.18\%$ ,  $P = 0.01$ . Therefore, a random effects model was used for meta-analysis. The results showed that



**Figure 6** Forest plot of the improvement in daily life function of patients with breast cancer after exercise. SD, standard deviation; CI, confidence interval; REML, restricted maximum likelihood.



**Figure 7** Forest plot of the improvement of emotional function in patients with breast cancer after exercise. SD, standard deviation; CI, confidence interval; REML, restricted maximum likelihood.

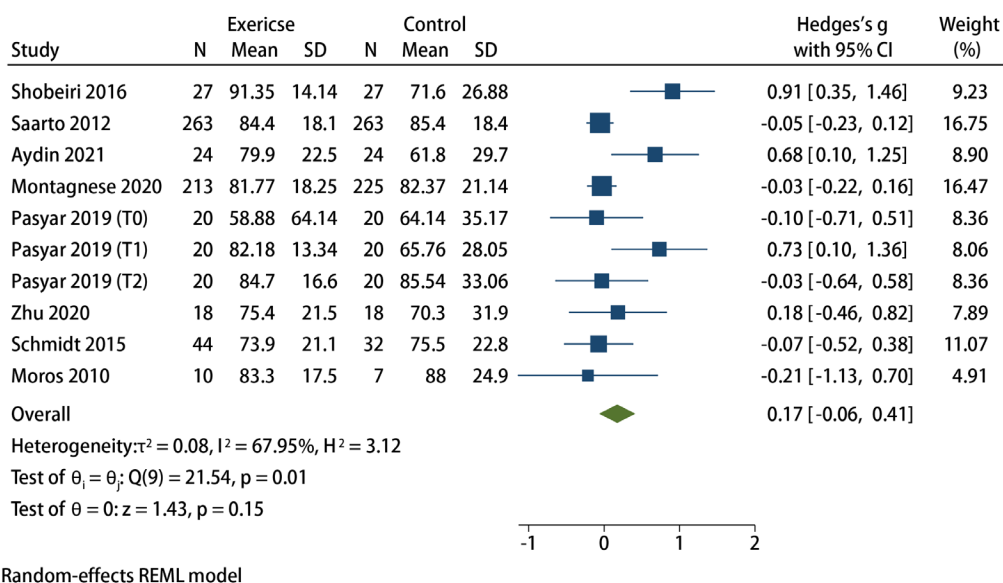
after a period of time and intensity of exercise, the fatigue symptoms of BC patients were significantly lighter than those of the control group who did not exercise (Hedges's  $g = -0.51$ , 95% CI:  $-0.84, -0.19$ , *Figure 10*). The sensitivity analysis demonstrated that the sequential removal of individual studies did not produce significant changes in the overall effect size,

indicating the stability and consistency of the results.

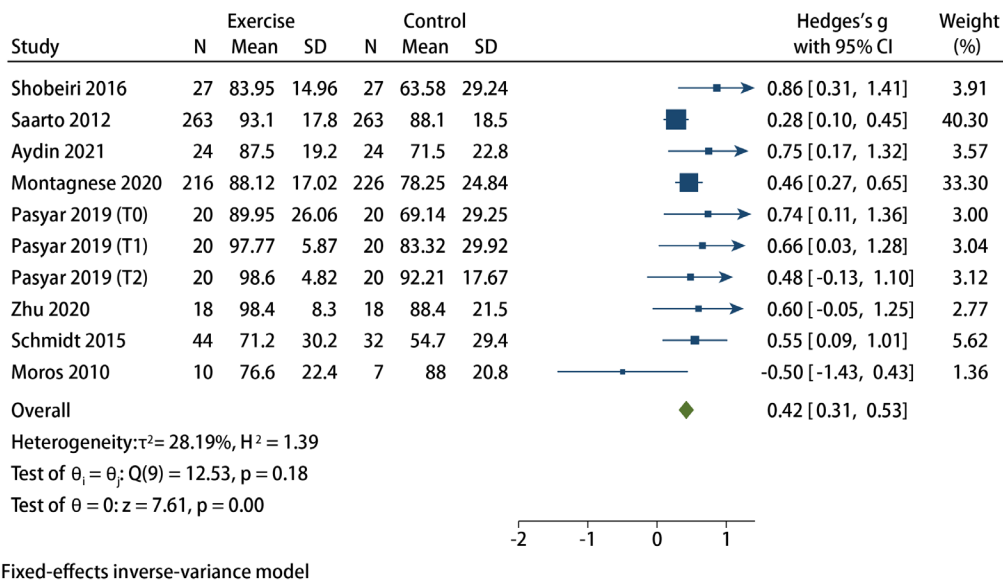
**The effect of exercise on the improvement of nausea and vomiting symptoms in patients with BC**

The results of the heterogeneity test of the included studies were  $I^2 = 45.79\%$ ,  $P = 0.01$ . The results showed that after a





**Figure 8** Forest plot of the cognitive function improvement in patients with breast cancer after exercise. SD, standard deviation; CI, confidence interval; REML, restricted maximum likelihood.



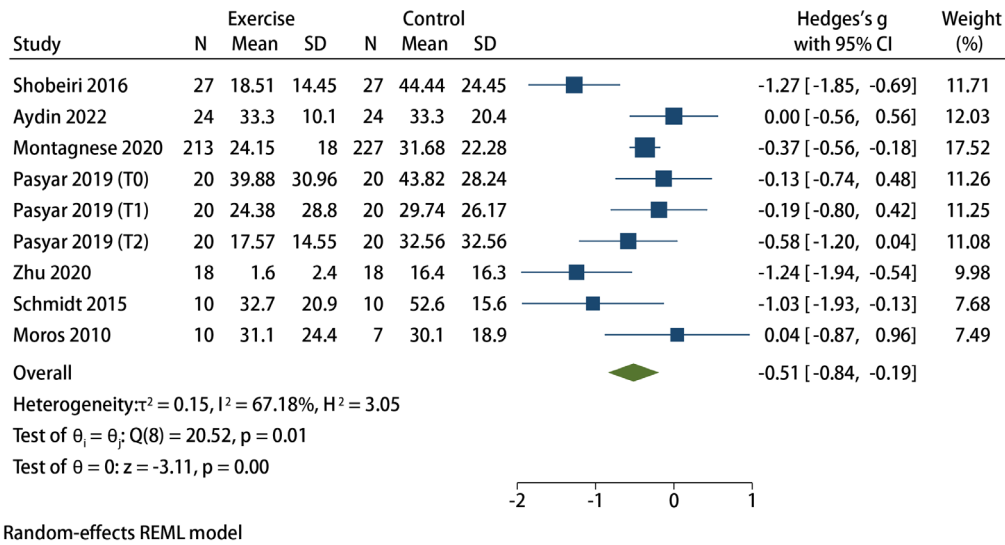
**Figure 9** Forest plot of the improvement of social function of breast cancer patients after exercise. SD, standard deviation; CI, confidence interval.

period of exercise and intensity, the symptoms of nausea and vomiting in patients with BC were significantly lighter than those in the control group who did not exercise (Hedges's  $g = -0.35$ , 95% CI:  $-0.60, -0.10$ , *Figure 11*). The sensitivity analysis revealed that the stepwise removal of individual studies did not lead to significant alterations in the overall

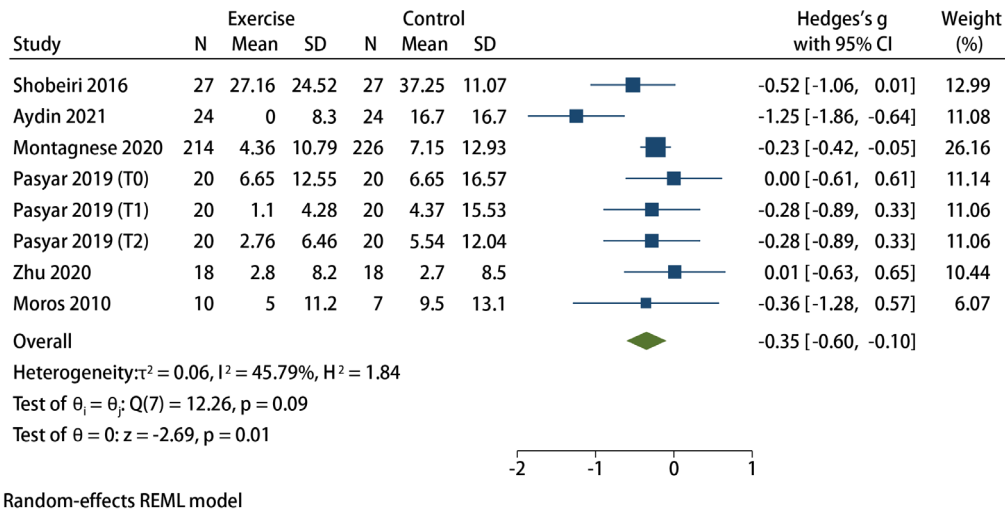
effect size. This indicates that the results remained relatively stable and consistent throughout the analysis.

**The effect of exercise on the improvement of pain symptoms in patients with BC**

The results of the heterogeneity test of the included studies



**Figure 10** Forest plot of the improvement of fatigue symptoms of breast cancer patients after exercise. SD, standard deviation; CI, confidence interval; REML, restricted maximum likelihood.



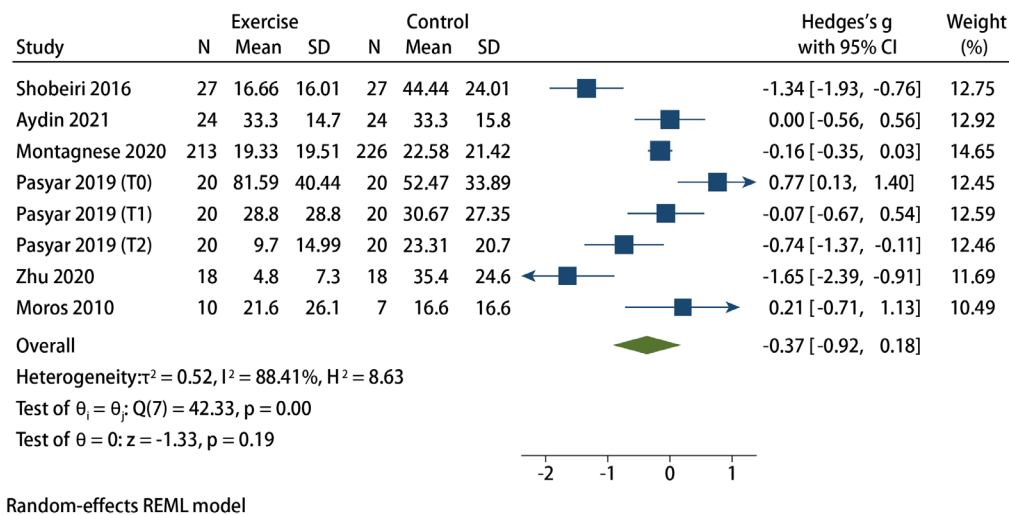
**Figure 11** Forest plot of the improvement of nausea and vomiting symptoms of breast cancer patients after exercise. SD, standard deviation; CI, confidence interval; REML, restricted maximum likelihood.

were  $I^2=88.41\%$ ,  $P<0.001$ . Therefore, a random effects model was used for meta-analysis. The results showed that after a period of time and intensity of exercise, there was no significant difference in pain symptoms between BC patients and control patients who did not exercise (Hedges's  $g = -0.37$ , 95% CI:  $-0.92, 0.18$ , *Figure 12*). The sensitivity analysis indicated that the exclusion of studies one by one did not have a substantial impact on the overall effect size,

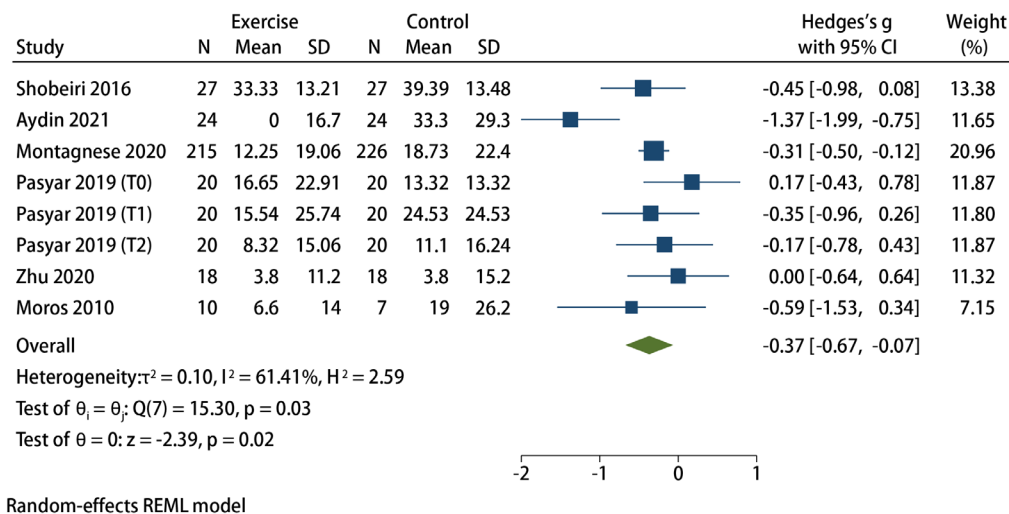
suggesting that the results remained relatively stable and consistent.

**The effect of exercise on the improvement of dyspnea symptoms in patients with BC**

The results of the heterogeneity test of the included studies were  $I^2=61.41\%$ ,  $P=0.03$ , so the random effect model was used for meta-analysis. The results showed that after a



**Figure 12** Forest plot of the improvement of pain symptoms in patients with breast cancer after exercise. SD, standard deviation; CI, confidence interval; REML, restricted maximum likelihood.

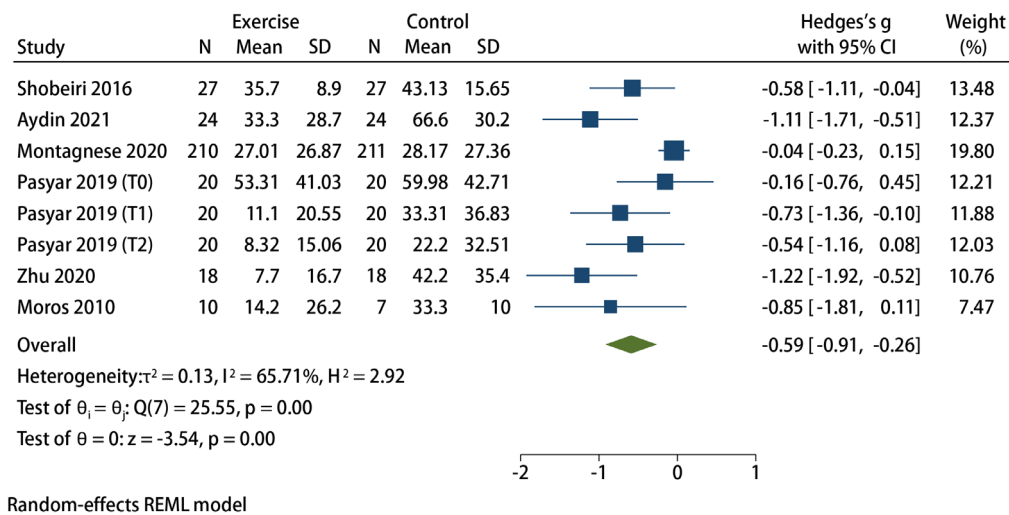


**Figure 13** Forest plot of the improvement of dyspnea symptoms of breast cancer patients after exercise. SD, standard deviation; CI, confidence interval; REML, restricted maximum likelihood.

certain period of exercise and intensity, the symptoms of dyspnea in patients with BC were significantly lighter than those in the control group who did not exercise (Hedges's  $g = -0.37$ , 95% CI:  $-0.67, -0.07$ , Figure 13). The sensitivity analysis indicated that the systematic removal of studies individually did not result in significant changes to the overall effect size, highlighting the stability and consistency of the findings.

**The effect of exercise on the improvement of insomnia symptoms in patients with BC**

The results of the heterogeneity test of the included studies were  $I^2 = 65.71\%$ ,  $P < 0.001$ . Therefore, a random effects model was used for meta-analysis. The results showed that after a certain period of exercise and intensity, the symptoms of insomnia in patients with BC were significantly lighter than those in the control group who did not exercise



**Figure 14** Forest plot of the improvement of insomnia symptoms in patients with breast cancer after exercise. SD, standard deviation; CI, confidence interval; REML, restricted maximum likelihood.

(Hedges's  $g = -0.59$ , 95% CI:  $-0.91, -0.26$ , *Figure 14*). The sensitivity analysis conducted by systematically excluding studies one by one demonstrated that the overall effect size remained largely unaffected, suggesting the robustness and stability of the results.

#### The effect of exercise on improving the symptoms of loss of appetite in patients with BC

The results of the heterogeneity test of the included studies were  $I^2 = 96.69\%$ ,  $P < 0.001$ . Therefore, a random effects model was used for meta-analysis. The results showed that after a period of time and intensity of exercise, there was no significant difference in the symptoms of loss of appetite between BC patients and control patients who did not exercise (Hedges's  $g = -0.71$ , 95% CI:  $-1.76, 0.34$ , *Figure 15*). The sensitivity analysis revealed that the incremental removal of individual studies did not have a substantial impact on the magnitude of the overall effect value. These findings indicate that the results remained relatively stable and consistent across the analysis.

#### The effect of exercise on the improvement of constipation symptoms in patients with BC

The results of the heterogeneity test of the included studies were  $I^2 = 0.00\%$ ,  $P = 0.77$ . The results showed that after a period of time and intensity of exercise, there was no significant difference in constipation symptoms between BC patients and control patients who did not

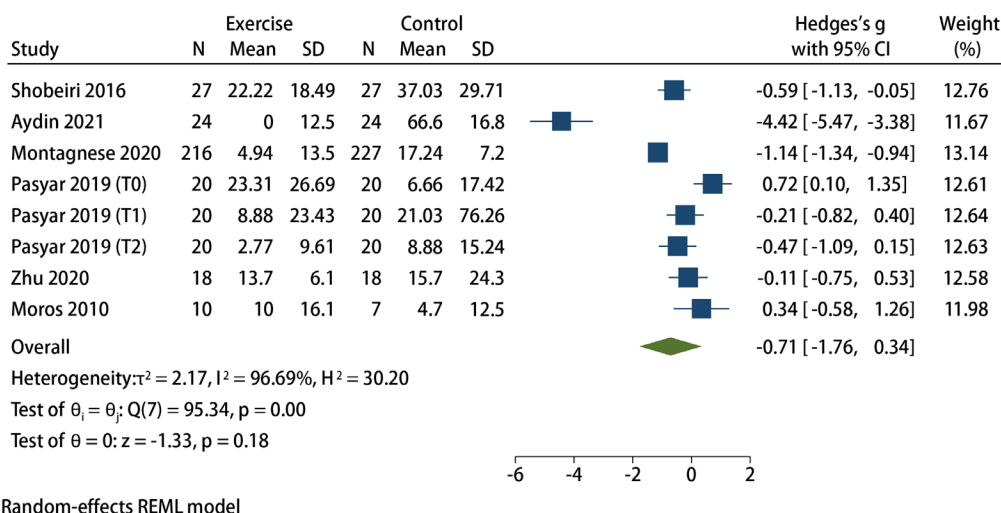
exercise (Hedges's  $g = -0.13$ , 95% CI:  $-1.28, 0.02$ , *Figure 16*). The sensitivity analysis indicated that the exclusion of individual studies, performed in a stepwise manner, had minimal influence on the overall effect size. This suggests that the results remained stable and consistent throughout the analysis.

#### The effect of exercise on the improvement of diarrhea in patients with BC

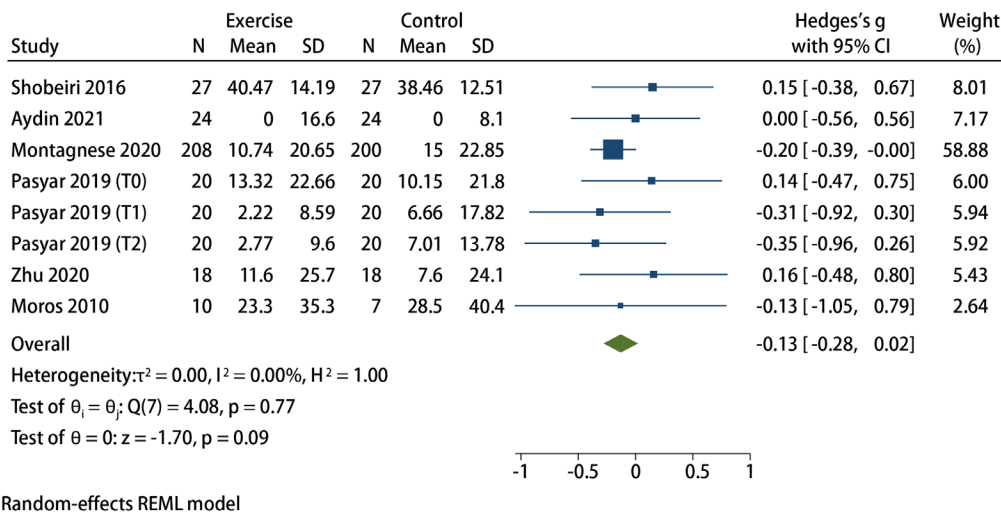
The heterogeneity test conducted on the included studies demonstrated a negligible level of heterogeneity ( $I^2 = 0.00\%$ ,  $P = 0.59$ ). The results showed that after exercise, there was no significant difference in diarrhea symptoms between BC patients and control patients who did not exercise (Hedges's  $g = -0.10$ , 95% CI:  $-0.26, 0.06$ , *Figure 17*). The sensitivity analysis demonstrated that the removal of individual studies had negligible impact on the overall effect size, suggesting the stability and consistency of the results.

#### Exercise improves the economic status of BC patients

The heterogeneity test conducted on the included studies revealed moderate heterogeneity ( $I^2 = 60.54\%$ ,  $P = 0.02$ ). Therefore, a random effects model was used for meta-analysis. The results showed that after a period of time and intensity of exercise, the economic difficulties of BC patients were significantly lighter than those of the control group who did not exercise, and the difference was statistically significant (Hedges's  $g = -0.48$ , 95% CI:  $-0.78$ ,



**Figure 15** Forest plot of the improvement of the symptoms of loss of appetite in breast cancer patients after exercise. SD, standard deviation; CI, confidence interval; REML, restricted maximum likelihood.



**Figure 16** Forest plot of the improvement of constipation symptoms in breast cancer patients after exercise. SD, standard deviation; CI, confidence interval; REML, restricted maximum likelihood.

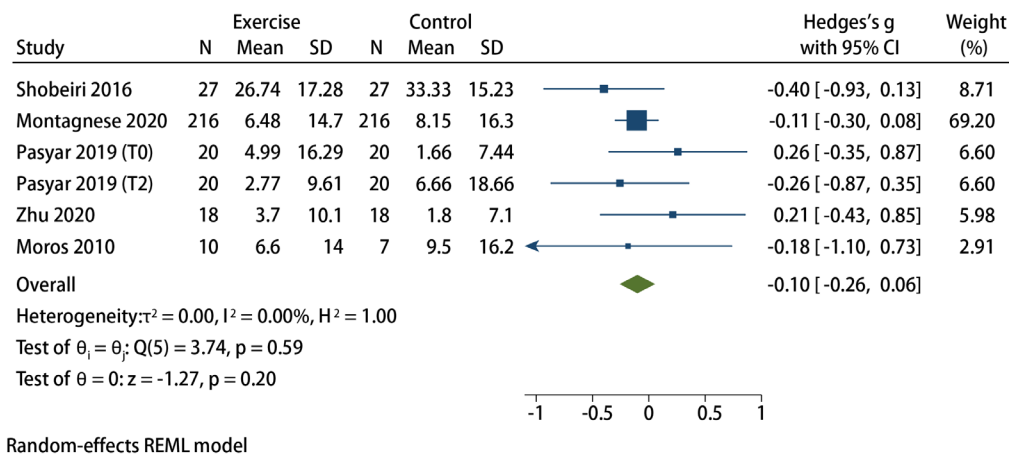
-0.18, Figure 18). The sensitivity analysis revealed that the exclusion of individual studies did not substantially alter the magnitude of the overall effect, indicating the stability and robustness of the results.

**Publication bias**

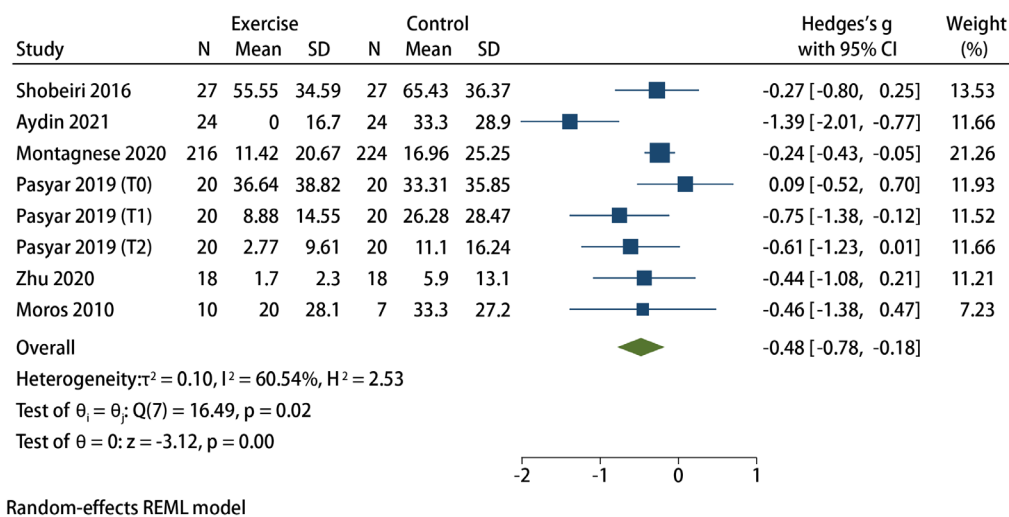
The funnel plot showed slight asymmetry (Figure 19). We speculated that there may be some publication bias, but it was difficult to quantify.

**Discussion**

BC is the tumor type with the highest incidence worldwide and the leading cause of cancer death in women (3,29). The incidence and mortality of BC have increased globally over the past decade (2,5,29). In 2015, there were approximately 303,600 new BC cases and 70,400 breast cancer deaths in China. The incidence and mortality of BC in China are expected to continue to increase by 2030 (2). With the advancement of modern medicine, early diagnosis of cancer,



**Figure 17** Forest plot of the improvement of diarrhea symptoms of breast cancer patients after exercise. SD, standard deviation; CI, confidence interval; REML, restricted maximum likelihood.



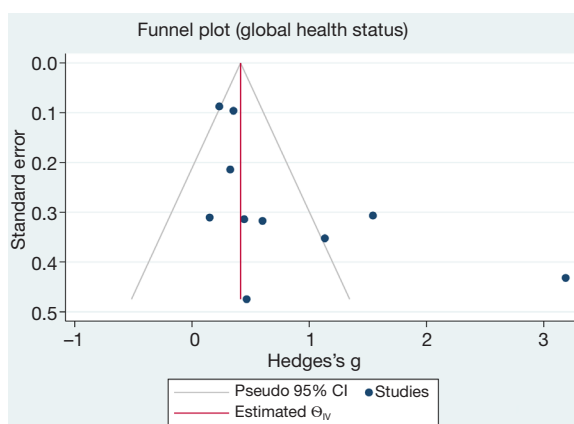
**Figure 18** Forest plot of the improvement of the economic status of breast cancer patients after exercise. SD, standard deviation; CI, confidence interval; REML, restricted maximum likelihood.

drug treatment, radiotherapy, and surgical intervention have increased the survival time of BC patients (6). However, along with improving prognosis, health-related QoL has become even more important.

The increasing incidence of BC and the high survival rates of BC patients suggest the importance of targeting health-related quality of life (HRQoL) and understanding its relationship to lifestyle, including diet and physical activity. A healthy lifestyle is associated with a better QoL. In turn, it promotes good prognosis and low mortality (13). Exercise represents a healthy way of life.

Studies have found that exercise can moderately improve cardiovascular fitness during cancer treatment. In addition, resistance exercise can also increase muscle strength (9,12,13,30,31). Exercise appears to be a feasible, well-tolerated, and promising strategy for improving physical and psychological outcomes in BC survivors. A study showed that low- to moderate-intensity exercise programs could relieve some symptoms in BC patients and could be considered as part of recovery (8). Other studies have shown that implementing a regular exercise program for patients during or after cancer treatment can improve QoL. Exercise





**Figure 19** Funnel plot (global health status). CI, confidence interval.

could lead to optimal body weight, cardiorespiratory fitness, decrease fatigue, neuromuscular integrity, increased muscle strength and flexibility, and improved psychosocial functioning (8,9,11,13-16,30,32-34).

BC patients enter a long recovery period after undergoing surgery, radiation therapy, chemotherapy, and endocrine therapy. BC rehabilitation includes three aspects: physiological, psychological, and social life. The physiological rehabilitation of BC patients determines the level of psychological rehabilitation and social activity participation. Rehabilitation exercise is the easiest way for BC patients to obtain exercise. Rehabilitation exercise during the recovery period of BC patients plays a decisive role in their quality of life, so it is necessary to conduct rehabilitation exercise after BC surgery.

Numerous studies have confirmed the positive effects of exercise for BC survivors. However, we still lack a systematic quantitative standard to further conduct in-depth research on the improvement of the QoL of BC patients by exercise. HRQoL evaluation has become the focus of medical workers. EORTC QLQ-C30 is one of the commonly used scales to evaluate the HRQoL of cancer patients (17). The scale consists of 30 questions, comprising 5 functions (physiological, daily life, cognitive, emotional and social functions), 3 symptoms (fatigue, pain, nausea and vomiting), overall health status, overall QoL, and another 6 separate items (sleep quality, appetite, diarrhea, constipation, dyspnea, and economic status) were used to measure the patient's QoL. All measurements are calculated into a score. The score is directly proportional to the patient's QoL (17,19).

Therefore, this meta-analysis conducted a summary and

in-depth analysis of RCTs on the improvement of the QoL of BC patients by exercise based on the EORTC QLQ-C30 scale. This study hoped to explore the improvement of the QoL of BC patients through exercise from a quantitative point of view, and to propose optimization suggestions for the treatment plan of BC survivors, so as to further improve the QoL of BC patients.

The results of this meta-analysis showed that exercise could significantly improve the overall health status of BC patients (Hedges's  $g = 0.81$ , 95% CI: 0.27, 1.34). In terms of improving the function of BC patients by exercise, we found that exercise could significantly improve the physiological function (Hedges's  $g = 0.78$ , 95% CI: 0.34, 1.22), the function of daily life (Hedges's  $g = 0.45$ , 95% CI: 0.13, 0.77), emotional function (Hedges's  $g = 0.52$ , 95% CI: 0.20, 0.84), and social function (Hedges's  $g = 0.42$ , 95% CI: 0.31, 0.53). However, exercise had no significant effect on the improvement of cognitive function of patients (Hedges's  $g = 0.17$ , 95% CI: -0.06, 0.41).

In terms of improving the symptoms of BC patients with exercise, we found that exercise could significantly reduce fatigue (Hedges's  $g = -0.51$ , 95% CI: -0.84, -0.19), nausea and vomiting (Hedges's  $g = -0.35$ , 95% CI: -0.60, -0.10), insomnia symptoms (Hedges's  $g = -0.59$ , 95% CI: -0.91, -0.26) and financial difficulties (Hedges's  $g = -0.48$ , 95% CI: -0.78, -0.18). However, the effect of exercise on pain symptoms (Hedges's  $g = -0.37$ , 95% CI: -0.92, 0.18), anorexia symptoms (Hedges's  $g = -0.71$ , 95% CI: -1.76, 0.34), constipation symptoms (Hedges's  $g = -0.13$ , 95% CI: -1.28, 0.02), and diarrhea symptoms (Hedges's  $g = -0.10$ , 95% CI: -0.26, 0.06) were not significantly improved.

We believe that exercise has a significant effect on improving the QoL of BC patients. It has a significant effect on improving the overall health status and functional status of the body. Exercise can effectively relieve various discomfort symptoms of patients, such as fatigue, nausea and vomiting, and insomnia. However, we found that exercise did not significantly improve the cognitive function of patients. Cognition is the process in which the human brain receives external information, processes it, and converts it into internal mental activities, thereby acquiring knowledge or applying knowledge. It includes aspects such as memory, language, visuospatial, executive, calculation, and comprehension judgments.

We speculate that cognitive enhancement is due to regeneration and repair of damaged neural tissue, increased intrasynaptic transmission, and activation of excitability in the ascending reticular system of the brain. However, there

are currently no reliable studies showing that exercise has a reparative effect on cranial nerves. We also believe that the effect of exercise on improving cognitive function in cancer patients can be further explored. Our study showed that exercise did not significantly improve pain symptoms, appetite loss symptoms, constipation, or diarrhea symptoms. This may be due to limitations of the current study, or because the studies we included were not comprehensive enough. Therefore, we believe that relevant research should further clarify the relationship between exercise and the improvement of the above symptoms.

A study have indicated that exercise programs (aerobic and/or other resistance training programs) are believed to be more effective when performed at home (35). Because daily physical activity, using one's own equipment, in a safe and hygienic home environment, and away from the hospital environment can improve patient QoL and reduce depression. Therefore, follow-up research can further explore the implementation site of the patient's exercise program to obtain better treatment effects.

Based on the QLQ-C30 scale, we can explain the great benefits of exercise for BC patients from the perspective of QoL improvement. However, we believe that its effect on improving the QoL of BC patients still needs further research.

There are some limitations to this study. We found that relevant studies had relatively small trial sizes and focused on different outcomes. The measures employed, as well as the timing, type, and duration of the intervention, also varied across studies. In particular, there is a lack of long-term large RCTs in this area (36-41). There are some publication biases in the funnel plot, so further subgroup analysis and larger scale experiments are necessary. In conclusion, we still need more definitive clinical evidence before routinely incorporating physical activity interventions into general rehabilitation guidelines for BC patients.

## Conclusions

In summary, this study quantitatively analyzed the improvement of exercise QoL in BC patients according to the QLQ-C30 QoL scale. The findings indicated a significant positive impact of exercise on the overall physical health and various functions of the body (including physiological function, daily life function, emotional function, and social function) among breast cancer survivors. Exercise also significantly reduced the symptoms

of fatigue, nausea and vomiting, and insomnia.

We suggest that exercise can be used as an adjuvant therapy for BC survivors, thereby substantially improving the QoL of patients. Adopting exercise is a cost-effective and effective way for recovering BC patients, including running, brisk walking, Tai Chi, and other exercise activities. It is not only easy to control, but also helps to improve the quality of life of BC patients.

## Acknowledgments

*Funding:* This study was supported by Huzhou Science and Technology Plan Project (No. 2020GYB29).

## Footnote

*Reporting Checklist:* The authors have completed the PRISMA reporting checklist. Available at <https://gs.amegroups.com/article/view/10.21037/gc-23-126/rc>

*Peer Review File:* Available at <https://gs.amegroups.com/article/view/10.21037/gc-23-126/prf>

*Conflicts of Interest:* All authors have completed the ICMJE uniform disclosure form (available at <https://gs.amegroups.com/article/view/10.21037/gc-23-126/coif>). The authors have no conflicts of interest to declare.

*Ethical Statement:* The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

*Open Access Statement:* This is an Open Access article distributed in accordance with the Creative Commons Attribution-NonCommercial-NoDerivs 4.0 International License (CC BY-NC-ND 4.0), which permits the non-commercial replication and distribution of the article with the strict proviso that no changes or edits are made and the original work is properly cited (including links to both the formal publication through the relevant DOI and the license). See: <https://creativecommons.org/licenses/by-nc-nd/4.0/>.

## References

1. Dai Y, Liang P, Yu J. Percutaneous Management of Breast Cancer: a Systematic Review. *Curr Oncol Rep* 2022;24:1443-59.

2. Li T, Mello-Thoms C, Brennan PC. Descriptive epidemiology of breast cancer in China: incidence, mortality, survival and prevalence. *Breast Cancer Res Treat* 2016;159:395-406.
3. Bhardwaj PV, Abdou YG. Germline Genetic Testing in Breast Cancer: Systemic Therapy Implications. *Curr Oncol Rep* 2022;24:1791-800.
4. Barroso-Sousa R, Jain E, Cohen O, et al. Prevalence and mutational determinants of high tumor mutation burden in breast cancer. *Ann Oncol* 2020;31:387-94.
5. Kirkham AA, Jerzak KJ. Prevalence of Breast Cancer Survivors Among Canadian Women. *J Natl Compr Canc Netw* 2022;20:1005-11.
6. Santos TBD, Borges AKDM, Ferreira JD, et al. Prevalence and factors associated to advanced stage breast cancer diagnosis. *Cien Saude Colet* 2022;27:471-82.
7. Poort H, Peters MEWJ, van der Graaf WTA, et al. Cognitive behavioral therapy or graded exercise therapy compared with usual care for severe fatigue in patients with advanced cancer during treatment: a randomized controlled trial. *Ann Oncol* 2020;31:115-22.
8. Messaggi-Sartor M, Marco E, Martínez-Téllez E, et al. Combined aerobic exercise and high-intensity respiratory muscle training in patients surgically treated for non-small cell lung cancer: a pilot randomized clinical trial. *Eur J Phys Rehabil Med* 2019;55:113-22.
9. Adamsen L, Quist M, Andersen C, et al. Effect of a multimodal high intensity exercise intervention in cancer patients undergoing chemotherapy: randomised controlled trial. *BMJ* 2009;339:b3410.
10. Reis AD, Pereira PTVT, Diniz RR, et al. Effect of exercise on pain and functional capacity in breast cancer patients. *Health Qual Life Outcomes* 2018;16:58.
11. Odynets T, Briskin Y, Todorova V. Effects of Different Exercise Interventions on Quality of Life in Breast Cancer Patients: A Randomized Controlled Trial. *Integr Cancer Ther* 2019;18:1534735419880598.
12. Idorn M, Thor Straten P. Exercise and cancer: from "healthy" to "therapeutic"? *Cancer Immunol Immunother* 2017;66:667-71.
13. Rupnik E, Skerget M, Sever M, et al. Feasibility and safety of exercise training and nutritional support prior to haematopoietic stem cell transplantation in patients with haematologic malignancies. *BMC Cancer* 2020;20:1142.
14. Baguley BJ, Bolam KA, Wright ORL, et al. The Effect of Nutrition Therapy and Exercise on Cancer-Related Fatigue and Quality of Life in Men with Prostate Cancer: A Systematic Review. *Nutrients* 2017;9:1003.
15. Paulo TRS, Rossi FE, Viezel J, et al. The impact of an exercise program on quality of life in older breast cancer survivors undergoing aromatase inhibitor therapy: a randomized controlled trial. *Health Qual Life Outcomes* 2019;17:17.
16. Wu X, Gao S, Lian Y. Effects of continuous aerobic exercise on lung function and quality of life with asthma: a systematic review and meta-analysis. *J Thorac Dis* 2020;12:4781-95.
17. Nolte S, Liegl G, Petersen MA, et al. General population normative data for the EORTC QLQ-C30 health-related quality of life questionnaire based on 15,386 persons across 13 European countries, Canada and the United States. *Eur J Cancer* 2019;107:153-63.
18. Kaasa S, Bjordal K, Aaronson N, et al. The EORTC core quality of life questionnaire (QLQ-C30): validity and reliability when analysed with patients treated with palliative radiotherapy. *Eur J Cancer* 1995;31A:2260-3.
19. Aaronson NK, Ahmedzai S, Bergman B, et al. The European Organization for Research and Treatment of Cancer QLQ-C30: a quality-of-life instrument for use in international clinical trials in oncology. *J Natl Cancer Inst* 1993;85:365-76.
20. Moher D, Liberati A, Tetzlaff J, et al. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *PLoS Med* 2009;6:e1000097.
21. Pasyar N, Barshan Tashnizi N, Mansouri P, et al. Effect of yoga exercise on the quality of life and upper extremity volume among women with breast cancer related lymphedema: A pilot study. *Eur J Oncol Nurs* 2019;42:103-9.
22. Saarto T, Penttinen HM, Sievänen H, et al. Effectiveness of a 12-month exercise program on physical performance and quality of life of breast cancer survivors. *Anticancer Res* 2012;32:3875-84.
23. Schmidt ME, Wiskemann J, Armbrust P, et al. Effects of resistance exercise on fatigue and quality of life in breast cancer patients undergoing adjuvant chemotherapy: A randomized controlled trial. *Int J Cancer* 2015;137:471-80.
24. Moros MT, Ruidiaz M, Caballero A, et al. Effects of an exercise training program on the quality of life of women with breast cancer on chemotherapy. *Rev Med Chil* 2010;138:715-22.
25. Montagnese C, Porciello G, Vitale S, et al. Quality of Life in Women Diagnosed with Breast Cancer after a 12-Month Treatment of Lifestyle Modifications. *Nutrients* 2020;13:136.

26. Aydin M, Kose E, Odabas I, et al. The Effect of Exercise on Life Quality and Depression Levels of Breast Cancer Patients. *Asian Pac J Cancer Prev* 2021;22:725-32.
  27. Shobeiri F, Masoumi SZ, Nikraves A, et al. The Impact of Aerobic Exercise on Quality of Life in Women with Breast Cancer: A Randomized Controlled Trial. *J Res Health Sci* 2016;16:127-32.
  28. Zhu K, Wang L, Ji Q. Effects of aerobic exercise combined with resistance training on quality of life in postmenopausal breast cancer patients receiving aromatase inhibitor therapy. *Journal of Xinjiang Medical University* 2020;43:1078-83,1088.
  29. Thomas ET, Del Mar C, Glasziou P, et al. Prevalence of incidental breast cancer and precursor lesions in autopsy studies: a systematic review and meta-analysis. *BMC Cancer* 2017;17:808.
  30. Dieli-Conwright CM, Courneya KS, Demark-Wahnefried W, et al. Aerobic and resistance exercise improves physical fitness, bone health, and quality of life in overweight and obese breast cancer survivors: a randomized controlled trial. *Breast Cancer Res* 2018;20:124.
  31. Soriano-Maldonado A, Carrera-Ruiz Á, Díez-Fernández DM, et al. Effects of a 12-week resistance and aerobic exercise program on muscular strength and quality of life in breast cancer survivors: Study protocol for the EFICAN randomized controlled trial. *Medicine (Baltimore)* 2019;98:e17625.
  32. Stout NL, Baima J, Swisher AK, et al. A Systematic Review of Exercise Systematic Reviews in the Cancer Literature (2005-2017). *PM R* 2017;9:S347-84.
  33. Samuel SR, Maiya AG, Fernandes DJ, et al. Effectiveness of exercise-based rehabilitation on functional capacity and quality of life in head and neck cancer patients receiving chemo-radiotherapy. *Support Care Cancer* 2019;27:3913-20.
  34. Lipsett A, Barrett S, Haruna F, et al. The impact of exercise during adjuvant radiotherapy for breast cancer on fatigue and quality of life: A systematic review and meta-analysis. *Breast* 2017;32:144-55.
  35. Sweegers MG, Altenburg TM, Chinapaw MJ, et al. Which exercise prescriptions improve quality of life and physical function in patients with cancer during and following treatment? A systematic review and meta-analysis of randomised controlled trials. *Br J Sports Med* 2018;52:505-13.
  36. Bruce J, Mazuquin B, Canaway A, et al. Exercise versus usual care after non-reconstructive breast cancer surgery (UK PROSPER): multicentre randomised controlled trial and economic evaluation. *BMJ* 2021;375:e066542.
  37. Hasenoehrl T, Keilani M, Palma S, et al. Resistance exercise and breast cancer related lymphedema - a systematic review update. *Disabil Rehabil* 2020;42:26-35.
  38. Eyigor S, Karapolat H, Yesil H, et al. Effects of pilates exercises on functional capacity, flexibility, fatigue, depression and quality of life in female breast cancer patients: a randomized controlled study. *Eur J Phys Rehabil Med* 2010;46:481-7.
  39. Ficarra S, Thomas E, Bianco A, et al. Impact of exercise interventions on physical fitness in breast cancer patients and survivors: a systematic review. *Breast Cancer* 2022;29:402-18.
  40. Campbell KL, Zdravec K, Bland KA, et al. The Effect of Exercise on Cancer-Related Cognitive Impairment and Applications for Physical Therapy: Systematic Review of Randomized Controlled Trials. *Phys Ther* 2020;100:523-42.
  41. Toohey K, Pumpa K, McKune A, et al. The impact of high-intensity interval training exercise on breast cancer survivors: a pilot study to explore fitness, cardiac regulation and biomarkers of the stress systems. *BMC Cancer* 2020;20:787.
- (English Language Editor: J. Jones)

**Cite this article as:** Chen L, Peng P, Xu Z, Ding X. The effects of exercise on the quality of life of patients with breast cancer: a systematic review and meta-analysis based on the QLQ-C30 quality of life scale. *Gland Surg* 2023;12(5):633-650. doi: 10.21037/gs-23-126