Systematic Review and Meta-Analysis

Medicine

OPEN

Aerobic exercise combined with resistance exercise training improves cardiopulmonary function and blood lipid of patients with breast cancer

A systematic review and meta-analysis

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Abstract

Background: To compare the therapy effects following the aerobic exercise combined with resistance exercise training (AET + RET) and common care treatment for patients with breast cancer.

Methods: Articles about the effects of AET + RET on the breast cancer patients in 4 online databases were searched. The differences of cardiopulmonary function, blood pressure, blood lipid, and body mass index between the AET + RET treatment and the usual care treatment were compared.

Results: Totally, 8 articles were involved into the meta-analysis. The qualities of the 8 articles were medium. The combination results showed that AET + RET increased the VO_2peak (weighted mean difference (WMD) = 2.93 mL/kg/min; 95% CI: 0.38, 5.49; $P = .02$) and VO_2max (WMD = 6.98 mL/kg/min; 95% CI: 2.04, 15.92; $P = .01$), demonstrating its improving effects in cardiopulmonary function. Moreover, the AET + RET decreased the TG (WMD = –57.95 mg/dL; 95% CI: –112.25, –3.64; $P = .04$), demonstrating its improving effects in blood lipid. While or the HRpeak, RERpeak, systolic blood pressure, diastolic blood pressure, high-density lipoprotein cholesterol, and body mass index, there are no significant differences between the AET + RET and usual care treatment ($P < .05$).

Conclusion: Our results demonstrated that AET + RET can significantly improve the cardiopulmonary function and blood lipid for breast cancer patients.

Abbreviations: AET = aerobic exercise training, BMI = body mass index, CI = confidence interval, DBP = diastolic blood pressure, HDL-C = high-density lipoprotein cholesterol, HRpeak = peak heart rate, LDL-C = low-density lipoprotein cholesterol, RCT = randomized controlled trials, RERpeak = peak respiratory exchange ratio, RET = resistance exercise training, SBP = systolic blood pressure, TC = total cholesterol, TG = triglycerides, UC = usual care, WMD = weighted mean difference.

Keywords: blood lipid, blood pressure, BMI, breast cancer, cardiopulmonary function, exercise method

1. Introduction

Breast cancer is considered the most common cancer in women, and its incidence is rapidly increasing.[1] Recently, the effective treatments for breast cancer have received great achievement and improved patients' survival rate and prognosis.[2] The usual treatments for breast cancer include surgery, chemotherapy, radiotherapy, and hormonotherapy. Nevertheless, the side effects after treatment still bothered many women like obesity, cardiovascular disorder, abnormal blood pressure, and so on.[3] Physical activity has been considered a solution to limit adverse outcomes and improve breast cancer patients' quality.[4]

Physically exercise has been reported to be an effective intervention to improve the patients' quality of life, condition the vascular function effect, and enhance physical functioning in breast cancer patients.[5] A meta-analysis suggests that exercise training can effectively reduce chemotherapy-related

This study was supported by Social Science Fund of Jiangsu Province (No. 21TYB013).

The authors declare that they have no conflict of interest.

The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

Ethical approval is not applicable because this is a meta-analysis.

Supplemental Digital Content is available for this article.

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How to cite this article: Kong L, Gao R. Aerobic exercise combined with resistance exercise training improves cardiopulmonary function and blood lipid of patients with breast cancer: A systematic review and meta-analysis. Medicine 2022;101:51(e32391).

Received: 1 November 2022 / Received in final form: 1 December 2022 / Accepted: 2 December 2022

http://dx.doi.org/10.1097/MD.0000000000032391

side effects in breast cancer patients who have completed treatment.[6] Recently, resistance exercise training (RET) and aerobic exercise training (AET) have been demonstrated to be beneficial in decreasing vascular stiffness.[7] The important role of exercise training has been emphasized in patients with breast cancer, while randomized controlled trials (RCTs) have shown significant variation in results between AET combined with RET treatment and usual treatment in the peak oxygen uptake (VO_2peak),[8–10] maximal oxygen consumption (VO_2max),[11,12] and blood pressure.[11,13] For example, the VO_2peak change of the training groups in Mijwel et al[9] was significantly higher than in the Herrero et al (2006)[14](about 3.0 vs about 3.9 mL kg^{-1} min^{-1}). The various results might be in terms of the intervention time, intensity, and mean. It is necessary for us to find a new perspective to investigate and arrive at a standard conclusion regarding exercise training in breast cancer management.

Meta-analysis will provide a systematic and comprehensive recognition to investigate the general effects of AET combined with RET and the usual care (UC) treatment. Moreover, meta-analysis is well-known for its advantages in eliminating some differences between studies.[15] In this study, we aimed to evaluate the effect of AET combined with RET on the cardiopulmonary system, blood lipid, blood pressure, body mass index (BMI) and other indicators of breast cancer patients through searching and re-analyzing the previous RCT studies.

2. Materials and Methods

All procedures were performed following the guideline in Preferred Reporting Items for Systematic Reviews and Meta-Analyses.[16]

2.1. Search strategy

Following the pre-established retrieval strategy, a systematic search for articles was conducted in PubMed, EMBASE, The Cochrane Library, and Web of Science. The search terms included "breast neoplasms," "breast cancer," "aerobic exercise," "aerobic training," "resistance training," and "strength training." Database-specific controlled, and free-text terms were combined for searching, and keywords of the same and different categories were combined with "OR" and "AND," respectively. Moreover, the retrieval strategies were adjusted in accordance with the characteristics of the databases (see Tables S1–S4, Supplemental Digital Content, http://links.lww.com/MD/I181, which shows the retrieval strategies of each database). Each database was searched from inception to December 1, 2021. Manual retrieval of the paper version of the literature was carried out for screening the relevant reviews and included references to obtain more articles for our meta-analysis.

2.2. References selection

Inclusion criteria for the meta-analysis included: adults patients (≥ 18 years old) with pathologically diagnosed breast cancer who had completed primary therapy, such as surgery, radiotherapy, bundled therapy, or chemotherapy; the experimental group treated with AET + RET and the control group treated with UC without exercise intervention; RCT studies; one or more of the following outcomes were reported: VO_2peak, VO_2max, peak heart rate (HRpeak), peak respiratory exchange ratio (RERpeak), BMI, systolic blood pressure (SBP), diastolic blood pressure (DBP), high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), triglycerides (TG), and total cholesterol (TC).

Exclusion criteria were nonoriginal articles like reviews, conference abstracts and comments; studies that did not report post-intervention measurements (mean ± SD) or could not be obtained from other parameters in the articles; for repeated articles or the same data used in multiple articles, the one with the most complete research information was chosen.

2.3. Data extraction and quality assessment

Two investigators independently screened the references following the above protocol. After determining the articles chosen for the meta-analysis, data extraction was accomplished independently according to the pre-designed table. The information in the table includes: the name of the first author, publication year, countries in which the studies were conducted, the basic characteristics of candidates (sample size, age, and breast cancer stage), intervention program, intervention program, and study outcomes. The Cochrane Collaboration's tool for assessing risk was utilized to estimate the methodological quality of all chosen studies.[17] A consensus was reached in case of disagreement in literature data extraction and quality evaluation after discussion with the third author.

2.4. Statistical analysis

Weighted mean difference (WMD) and 95% confidence interval (CI) were performed to evaluate the differences between the AET + RET and UC groups. The heterogeneity among studies was determined by the Cochran's Q test and I^2 statistics. $P < .05$ or $I^2 > 50\%$ was determined as significant heterogeneity, and random-effects models were conducted for meta-analysis; $P \geq .05$ and $I^2 \leq 50\%$ were determined as nonsignificant heterogeneity, and fixed-effect models were adopted for meta-analysis. Moreover, sensitivity analyses removing one research at a time were conducted to explore the stabilities of the combined results. Egger's tests were conducted to understand whether significant publication bias existed among studies,[18] and $P < .05$ was determined as a significant publication bias. All the above statistical analyses were performed using RevMan 5.3 and Stata12.0 software.

3. Results

3.1. Articles retrieval

The results of articles retrieval are in Fig. 1. A total of 1594 articles were screened. An initial 897 articles were selected after removing the 697 duplicates. The 897 articles were further screened to 15 through reading the title and abstract. Of the 15 articles, 4 were repeated studies[19–22]; 2 laced the available data[23,24]; and 1 control group was not UC.[25] The manual search failed to find studies that could be included in the meta-analysis. Finally, 8 articles were chosen for the following meta-analysis.[1,8–14]

3.2. Characteristics of the chosen articles

The basic information of the 8 chosen articles is contained in Table 1. All participants did not perform exercises such as running, cycling, swimming, or resistance training with a fixed frequency in daily life. The publication dates of the articles were from 2006 to 2021, and the sample contained in these studies was from 14 to 134. A total of 470 samples were concluded in the meta-analysis, with 252 controls (UC) and 218 experiments (AET + RET). There were no significant differences in age and menopausal status between the UC and AET + RET groups. As for the stage of the breast cancer, patients in 6 articles were in stages I to III,[1,8–11,13] 1 was in stages I and II,[14] and 1 was in stage IV.[12] The intervention time of 8 studies was from 8 to 16 weeks. In addition, 2 studies reported the outcomes of the measurements after 6–12 months of follow-up.[8,9]

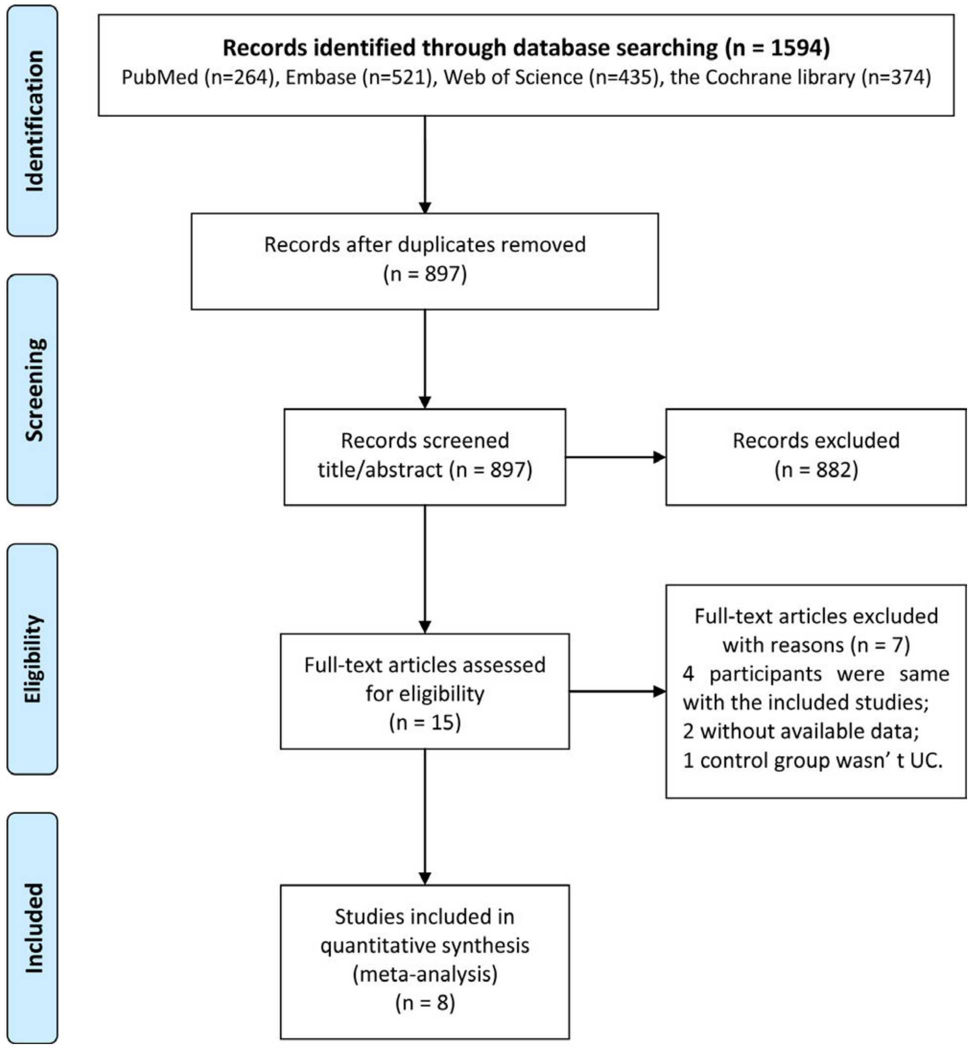

Figure 1. The process and results of literature retrieval.

3.3. Quality assessment

The methodological quality evaluation results for the chosen studies are shown in Supplementary Figs. S1A and S1B (see Fig. S1, Supplemental Digital Content, http://links.lww.com/MD/I182, which shows the methodological quality evaluation of the included studies). Due to the characteristics of the intervention measures, the included studies could not achieve blindness of researchers and participants. Some studies[8,9,11,12] did not implement or clearly describe whether blind outcome measurements were implemented, respectively. Two studies did not report specific methods of random grouping[10,14] or grouping concealment.[10,11] Therefore, the bias mainly focuses on allocation concealment, performance, and detection biases. Overall, the bias degree of the included studies was uncertain, and the methodological quality was moderate.

3.4. Meta-analysis for the cardiorespiratory parameters

The differences in VO_2peak, VO_2max, HRpeak, and RERpeak between the AET + RET and UC groups are shown in Fig. 2. Four articles[8–10,14] reported the differences in VO_2peak between the AET + RET and UC groups. The heterogeneity test was $I^2 = 69\%$, $P = .02$, indicating that the 4 studies maintained significant statistical heterogeneity. Further random-effects model implied that VO_2peak in AET + RET group was significantly higher than that in the UC groups (WMD = 2.93 mL/kg/min; 95% CI: 0.38, 5.49; $P = .02$; Fig. 2A). Three studies[1,11,12] reported the results of VO_2max, and these studies were also significantly heterogeneous ($I^2 = 94\%$, $P < .00001$). The combined results in the random-effects model suggested that the VO_2max in the AET + RET group was significantly higher than that in the UC group (WMD = 6.98 mL/kg/min; 95% CI: 2.04, 15.92; $P = .01$; Fig. 2B). Two studies[8,14] reported the results of HRpeak and RERpeak. The 2 indexes maintained no obvious heterogeneity ($I^2 < 50\%$, $P > .05$). The combined results in the fixed-effects models showed no significant differences between the AET + RET and UC groups ($P < .01$; Fig. 2C and 2D). In addition, 2 studies[8,9] reported the differences in VO_2peak after follow-up. The results in the 2 studies showed significant heterogeneity ($I^2 = 59\%$, $P = .12$). The combined results in the random-effects model showed that no significant differences occurred between the AET + RET and UC groups ($P = .05$; see Supplemental Fig. S2, Supplemental Digital Content, http://links.lww.com/MD/I183, which shows forest plots comparing the differences in following-up VO_2peak between AET + RET and UC groups).

3.5. Meta-analysis for the blood pressure and blood lipid

The differences in the SBP and DBP between the AET + RET and UC groups are shown in Fig. 3. The studies involving the 2

Table 1

Characteristics of the 8 included studies.

Study	Cancer Stage	N	Age, years	Menopause status #	Intervention	Exercise session duration, frequency	Duration	Outcomes
Chung, WP 2021 (China)	I–III	16 13	52.4 ± 8.9 50.3 ± 7.7	6/10 5/8	AET + RET UC	40 min, 50–75% HRmax (AET); 2–3 sets of 10–20 repetitions, 15 min (RET); 2–3 sessions/week	12 weeks	VO_2peak, HRpeak, RERpeak
Dieli-Conwright, CM 2018 (USA)	I–III	50 50	52.8 ± 10.6 53.6 ± 10.1	23/27 22/28	AET + RET UC	30 min at 65-80% HR maximum; 3–4 sessions/week (AET); 3 sets of 10 repetitions, 2 sessions/week (RET)	16 weeks	SBP, DBP, HDL-C, TG, BMI
Dieli-Conwright, CM 2021 (USA)	I–III	29 a 19 a 27 b 22 b	46.9 ± 10.2 55.6 ± 10.5 46.7 ± 10.0 55.9 ± 10.3	15/14 7/12 14/13 9/13	AET + RET UC	30 min at 65–80% HR maximum; 3–4 sessions/week (AET); 3 sets of 10 repetitions, 2 sessions/week (RET)	16 weeks	VO_2max
Herrero, F 2006 (Spain)	I–II	8 8	50.0 ± 5.0 51.0 ± 10.0	0/8 0/8	AET + RET UC	3/week, 90 min, 70-80% HRmax (AET); 1–3 sets of 8–20 repetitions (RET)	8 weeks	VO_2peak, HRpeak, RERpeak
Jones, LM 2020 (New Zealand)	I–III	26 25	55.8 ± 7.2 55.9 ± 7.1	3/23 5/20	AET + RET UC	Twice weekly, 60 min/session (AET); 10–12 repetitions with 30s between sets (RET)	12 weeks	BMI, VO_2max, SBP, DBP
Mijwel, S 2019 (Sweden)	I–III	74 60	52.7 ± 10.3 52.6 ± 10.2	36/38 33/37	AET + RET UC	Twice weekly, 60 min cycle ergometer (AET); 2–3 sets of 8–12 repetitions (RET)	16 weeks	VO_2peak, BMI
Nuri, R 2012 (Iran)	I–III	14 15	58.3 ± 6.3	NR NR	AET + RET UC	Twice weekly, 25–45 min brisk walk (AET); 60 min, 10–14 repetitions per set, 3 sets/session (RET)	15 weeks	VO_2peak, BMI, SBP, TG, HDL-C
Yee, J 2019 (Australia)	IV	8 6	60.1 ± 12.7 65.0 ± 6.9	2/6 0/6	AET + RET UC	Twice weekly, 10–15 minute brisk walk (AET); 30–40 min, 2 sets of 10–12 repetitions (RET)	8 weeks	VO_2max

#, number of premenopause/postmenopause; a, Hispanic breast cancer survivors; b, non-Hispanic breast cancer survivors.
AET = aerobic exercise training, BMI = body mass index, DBP = diastolic blood pressure, HDL-C = high density lipoprotein cholesterol, HRpeak = peak heart rate, RERpeak = peak respiratory exchange ratio, RET = resistance exercise training, SBP = systolic blood pressure, TG = triglycerides, UC = usual care, VO2max = maximal oxygen consumption, VO2peak = peak oxygen uptake.

indexes exhibited significant heterogeneity ($I^2 > 50\%$, $P < .05$). The combined results for SBP ($P = .18$; Fig. 3A) and DBP ($P = .12$; Fig. 3B) in the random-effects model showed no significant differences between the AET + RET and UC groups.

Two studies[10,13] reported the differences in HDL-C and TG (Fig. 4). The 2 indexes were all significantly heterogeneous ($I^2 > 50\%$, $P < .05$). The combined results for the 2 indexes in the random-effects models showed a difference. There were no significant HDL-C differences between the AET + RET and UC groups ($P = .16$; Fig. 4A). A significant difference was showed in the TG between the AET + RET and UC groups, and AET + RET group showed lower TG compared to the UC group (WMD = -57.95 mg/dL; 95% CI: −112.25, −3.64; $P = .04$; Fig. 4B).

In addition, only 1 article[13] reported the results of TC, and no article focused on the LDL-C. Therefore, we did not perform a meta-analysis for the 2 indexes.

3.6. Meta-analysis for the BMI

Two studies[8,9] stated the results of BMI and the differences in BMI between AET + RET and UC groups are shown in Fig. 5. The 2 studies involved showed no significant heterogeneity ($I^2 = 12\%$, $P = .33$). Further fixed-effects model showed no significant differences in BMI between the 2 groups (WMD = −0.90 kg/m^2; 95% CI: −1.86, 0.07; $P = .07$).

3.7. Sensitivity analyses and publication bias analyses

Sensitivity analyses and publication bias tests were performed for outcomes combined with more than 2 articles (VO_2peak, VO_2max, SBP, and BMI; Table 2). Sensitivity analyses showed that the results of VO_2peak, VO_2max, SBP, and BMI were not stable. Nevertheless, Egger's test showed that the 4 indexes maintained no significant publication bias ($P > .05$).

4. Discussion

Breast cancer is considered the most common cancer in women.[1] Physical activity has been considered an approach to limit adverse outcomes and improve breast cancer patients' quality.[4] Considering the inconsistent results in different RCT studies, we conducted a meta-analysis to investigate the important role of AET + RET treatment in patients with breast cancer. In our results, AET + RET treatment intervention significantly increased the VO_2peak and VO_2max and decreased the TG. However, for the HRpeak, RERpeak, SBP, DBP, HDCL-C, and BMI, there are no significant differences between the AET + RET and UC treatments.

AET + RET increased the cardiorespiratory function of patients with breast cancer compared to the UC groups, expressed as higher VO_2max and VO_2peak. VO_2peak is an independent predictor of mortality and cardiovascular prognosis, and low VO_2peak is related to cardiotoxicity, cancer-associated mortality, and low quality of life.[26] High-intensity exercise impacts the VO_2peak response in patients with breast cancer.[27] We confirmed that the AET + RET treatment increased the VO_2peak than the UC treatment, demonstrating a better cardiorespiratory function. The results were consistent with the previous RCT studies[8,9] and meta-analysis.[26,27] Moreover, in the study conducted by Jones et al,[11] VO_2peak increased by 16% following the exercise training, which is in line with our results. While in the estimation of HRpeak and RERpeak, there were no significant changes in the training groups, and the results were consistent with the original RCT.[8,14]

We further compared the blood pressure and blood lipid function in the AET + RET and UC groups. Lowering blood pressure is related to a lower risk of cardiovascular disease in breast cancer patients.[28] The SBP and DBP included in our analysis showed no significant differences between the 2 groups of breast cancer patients. The results were inconsistent with the previous meta-analysis, which showed that exercise decreased the SBP and DBP in breast cancer and, therefore, improved patients' BP.[27]

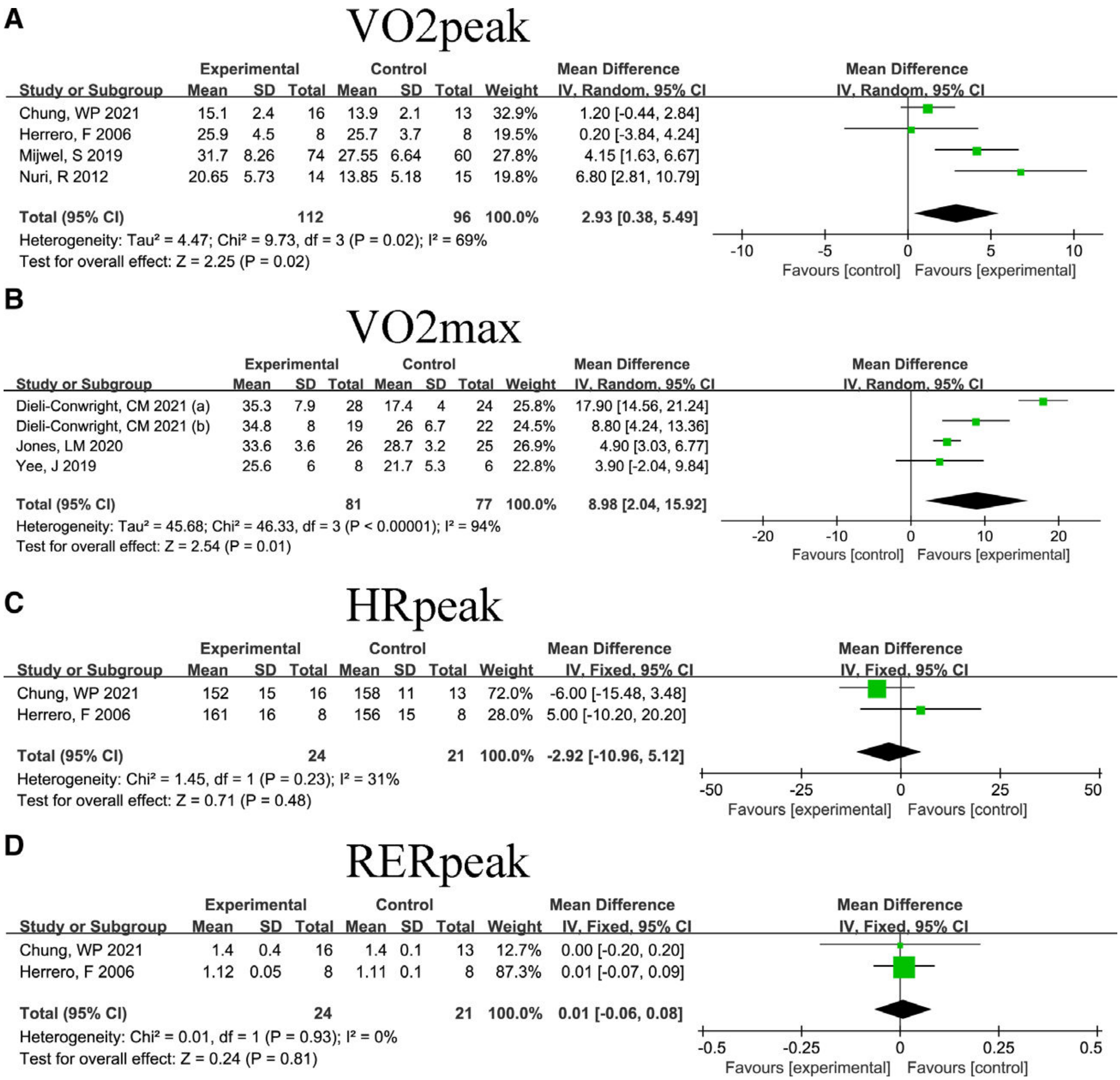

Figure 2. Forest plots comparing the differences in cardiorespiratory parameters between aerobic exercise training combined with resistance exercise training (AET + RET) and unral care (UC) groups. (A) The results of peak oxygen uptake (VO_2peak); (B) The results of maximal oxygen consumption (VO_2max); (C) The results of peak heart rate (HRpeak); (D) The results of peak respiratory exchange ratio (RERpeak). Experimental group represent the AET + RET group, and the control group represent the UC group (the same below).

The inconsistency in the results might be from the high heterogeneity of the original included articles and the diverse intervention methods. Furthermore, we also investigated the blood lipid between the AET + RET and UC groups, and the results showed that the level of TG in the AET + RET group was significantly lower. A previous study suggests that blood lipid-like HDCL-C and TG are risk factors.[29] Once the body absorbs a large amount of fat, it will induce cell damage and affect cancer progression.[30] In all, we confirmed that the AET + RET could improve the blood lipid in breast cancer patients.

The exploration of the role of exercise training on BMI showed diverse results for a long time. High BMI is well-known to induce stress in the cardiovascular system and increase the risk of mortality.[31] A meta-analysis conducted in 2018[32] showed no significant BMI change between the exercise training and the control groups, which is in line with our results. While in a recent meta-analysis,[27] a reduced BMI was reported in the exercise intervention.

One of the advantages of this study is that all included articles were RCTs, with the priority of small research design heterogeneity and relatively ideal bias degree. Furthermore, while the included studies contain various intervention methods, we only focused on the role of AET + RET in the therapy of patients with breast cancer. Thus, the extrapolation of the combined results would show effectiveness. Egger test suggested no significant publication bias in the combined results. Nevertheless, several limitations still exist. Firstly, the large heterogeneity of outcomes in most studies may come from differences in intervention time, specific exercise method, tumor stage, etc. However, due to the small number of studies, it is not sufficient to evaluate the influence of these factors on heterogeneity and combined results through quantitative methods such as subgroup analysis and meta-regression. Secondly, due to the small number of included studies and small sample size, the sensitivity analysis showed that the combined results were unstable, indicating that more high-quality and large-sample RCTs would be further conducted

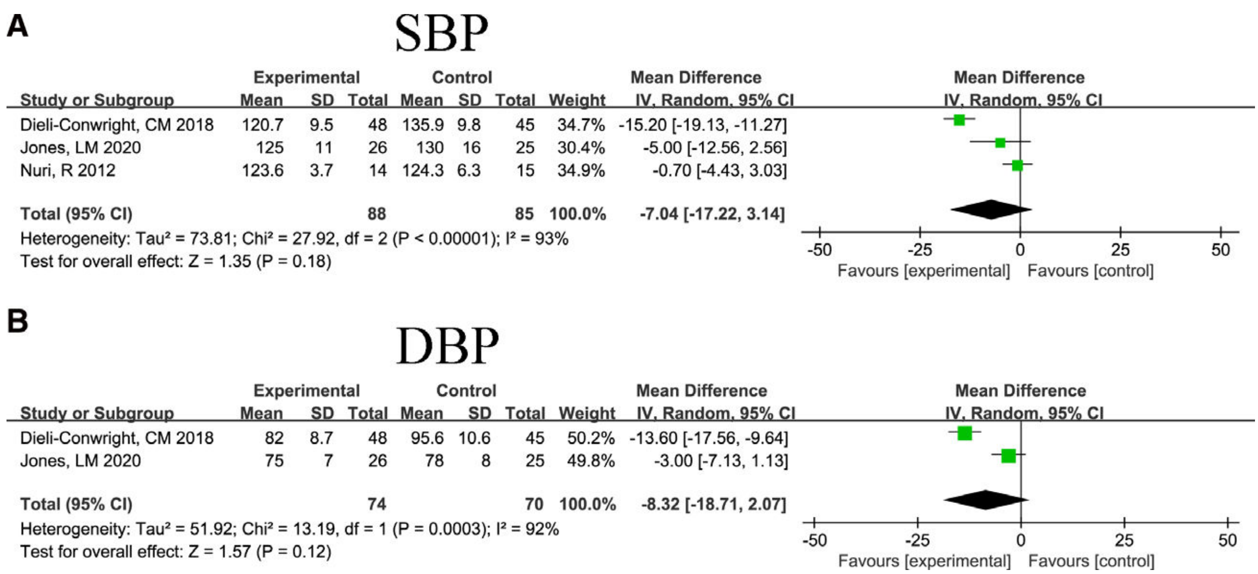

Figure 3. Forest plots comparing the differences in blood pressure between AET + RET and UC groups. (A) The results of systolic blood pressure (SBP); (B) The results of diastolic blood pressure (DBP).

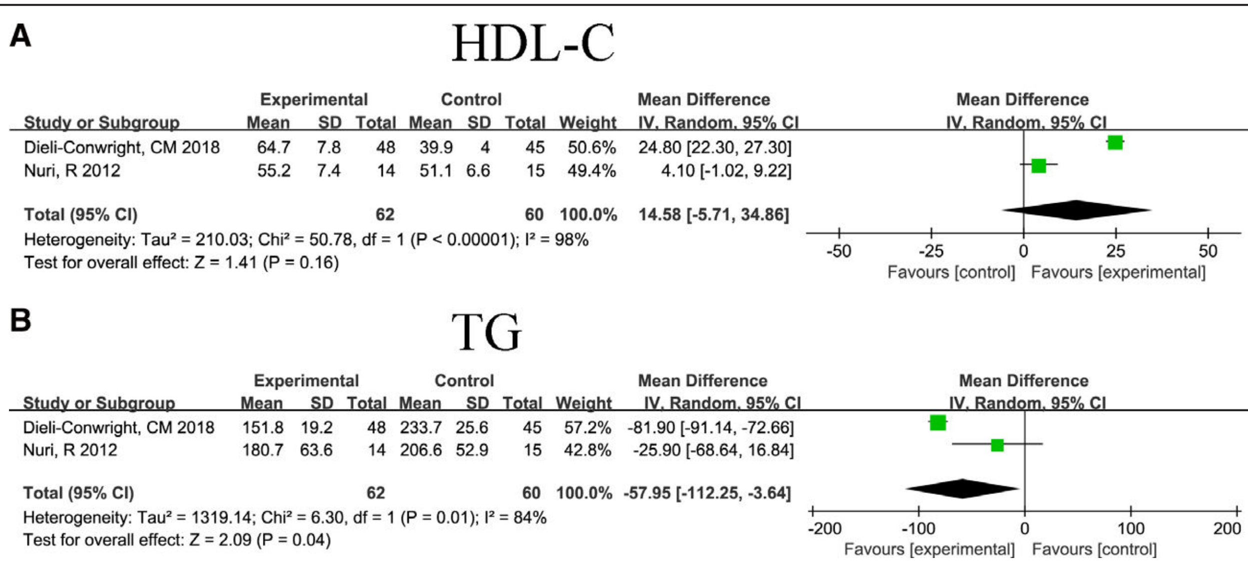

Figure 4. Forest plots comparing the differences in serum lipids between AET + RET and UC groups. (A) The results of high-density lipoprotein cholesterol (HDL-C); (B) The results of triglycerides (TG).

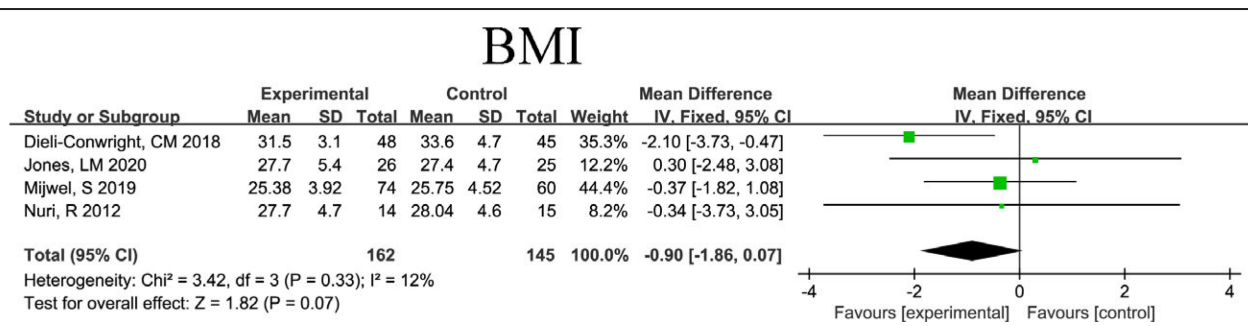

Figure 5. Forest plots comparing the differences in body mass index (BMI) between AET + RET and UC groups.

to verify the stability of the combined results. Thirdly, although there was only one indicator(VO$_2$peak) and only 2 studies[8,9] were included, the long-term effects of AET + RET were not significantly different from those of UC.

Table 2

Outcomes of the sensitivity analysis and test of publication bias.

		Sensitivity analysis		Egger' s test
Outcomes	**No. of studies**	**WMDs (95% CI)**	**Robust**	***P* value**
VO_2peak	4	2.00 (–0.20, 4.21) to 3.78 (5.11, 7.04)	No	.494
VO_2max	4	9.00 (–0.32, 18.33) to 10.49 (1.98, 19.00)	No	.655
SBP	3	–10.63 (–20.57, -0.69) to –1.54 (–4.89, 1.80)	No	.973
BMI	4	–1.31 (–2.61, –0.02) to –0.24 (–1.44, 0.96)	No	.639

BMI = body mass index; SBP = systolic blood pressure; WMD = weighted mean difference.

5. Conclusions

AET combined with RET could significantly increase VO_2peak and VO_2max and decrease TG for breast cancer patients. However, due to the limitations of this meta-analysis (few included studies and poor stability of combined results), more high-quality and large-sample RCTs for verification are recommended. Therefore, breast cancer patients should regularly participate in moderate AET and RET, to improve their cardiopulmonary function and blood lipid.

Author contributions

All authors read and approved the final manuscript.
Conception and design of the research: RG.
Acquisition of data: LFK.
Analysis and interpretation of data: LYK.
Statistical analysis: RG.
Drafting the manuscript: LFK.
Revision of the manuscript for important intellectual content: RG.

References

[1] Dieli-Conwright CM, Fox FS, Tripathy D, et al. Hispanic ethnicity as a moderator of the effects of aerobic and resistance exercise on physical fitness and quality-of-life in breast cancer survivors. J Cancer Surviv. 2021;15:127–39.
[2] Rugo HS. Achieving improved survival outcomes in advanced breast cancer. Mass Medical Soc. 2019;381:371–2.
[3] Gernaat S, Ho P, Rijnberg N, et al. Risk of death from cardiovascular disease following breast cancer: a systematic review. Breast Cancer Res Treat. 2017;164:537–55.
[4] Anthony FY, Jones LW. Breast cancer treatment-associated cardiovascular toxicity and effects of exercise countermeasures. Cardio-Oncol. 2016;2:1–9.
[5] McNeely ML, Campbell KL, Rowe BH, et al. Effects of exercise on breast cancer patients and survivors: a systematic review and meta-analysis. CMAJ. 2006;175:34–41.
[6] Meneses-Echávez JF, González-Jiménez E, Ramírez-Vélez R. Effects of supervised exercise on cancer-related fatigue in breast cancer survivors: a systematic review and meta-analysis. BMC cancer. 2015;15:1–13.
[7] Figueroa A, Park SY, Seo DY, et al. Combined resistance and endurance exercise training improves arterial stiffness, blood pressure, and muscle strength in postmenopausal women. Menopause. 2011;18:980–4.
[8] Chung WP, Yang HL, Hsu YT, et al. Real-time exercise reduces impaired cardiac function in breast cancer patients undergoing chemotherapy: a randomized controlled trial. Ann Phys Rehabil Med. 2021;65:101485.
[9] Mijwel S, Jervaeus A, Bolam KA, et al. High-intensity exercise during chemotherapy induces beneficial effects 12 months into breast cancer survivorship. J Cancer Surviv. 2019;13:244–56.
[10] Nuri R, Kordi MR, Moghaddasi M, et al. Effect of combination exercise training on metabolic syndrome parameters in postmenopausal women with breast cancer. J Cancer Res Ther. 2012;8:238–42.
[11] Jones LM, Stoner L, Baldi JCv Circuit resistance training and cardiovascular health in breast cancer survivors. Eur J Cancer Care (Engl). 2020;29:e13231.
[12] Yee J, Davis GM, Hackett D, et al. Physical activity for symptom management in women with metastatic breast cancer: a randomized feasibility trial on physical activity and breast metastases. J Pain Symptom Manage. 2019;58:929–39.
[13] Dieli-Conwright CM, Courneya KS, Demark-Wahnefried W, et al. Effects of aerobic and resistance exercise on metabolic syndrome, sarcopenic obesity, and circulating biomarkers in overweight or obese survivors of breast cancer: a randomized controlled trial. J Clin Oncol. 2018;36:875–83.
[14] Herrero F, San Juan AF, Fleck SJ, et al. Combined aerobic and resistance training in breast cancer survivors: a randomized, controlled pilot trial. Int J Sports Med. 2006;27:573–80.
[15] Lee YH. An overview of meta-analysis for clinicians. Korean J Intern Med. 2018;33:277–83.
[16] Liberati A, Altman DG, Tetzlaff J, et al. The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate health care interventions: explanation and elaboration. Epidemiol Biostat Public Health. 2009;6:e1–e34.
[17] Higgins JP, Green S. Cochrane handbook for systematic reviews of interventions. vol 5. New Jersey: Wiley Online Library; 2008.
[18] Egger M, Davey Smith G, Schneider M, et al. Bias in meta-analysis detected by a simple, graphical test. research Support, U.S. Gov't, Non-P.H.S. BMJ (Clinical Research ed). 1997;315:629–34.
[19] Dieli-Conwright CM, Courneya KS, Demark-Wahnefried W, et al. Aerobic and resistance exercise improve patient-reported sleep quality and is associated with cardiometabolic biomarkers in Hispanic and non-Hispanic breast cancer survivors who are overweight or obese: results from a secondary analysis. Sleep. 2021;44:1–10.
[20] Dieli-Conwright CM, Sweeney FC, Courneya KS, et al. Hispanic ethnicity as a moderator of the effects of aerobic and resistance exercise in survivors of breast cancer. Cancer. 2019;125:910–20.
[21] Lee K, Sami N, Tripathy D, et al. Aerobic and resistance exercise improves Reynolds risk score in overweight or obese breast cancer survivors. Cardiooncology. 2020;6:27.
[22] Lee K, Tripathy D, Demark-Wahnefried W, et al. Effect of aerobic and resistance exercise intervention on cardiovascular disease risk in women with early-stage breast cancer: a randomized clinical trial. JAMA Oncol. 2019;5:710–4.
[23] Carayol M, Ninot G, Senesse P, et al. Short- and long-term impact of adapted physical activity and diet counseling during adjuvant breast cancer therapy: the "APAD1" randomized controlled trial. BMC Cancer. 2019;19:737.
[24] Hiraoui M, Al-Haddabi B, Gmada N, et al. Effects of combined supervised intermittent aerobic, muscle strength and home-based walking training programs on cardiorespiratory responses in women with breast cancer. Bull Cancer. 2019;106:527–37.
[25] de Paulo TRS, Winters-Stone KM, Viezel J, et al. Effects of resistance plus aerobic training on body composition and metabolic markers in older breast cancer survivors undergoing aromatase inhibitor therapy. Exp Gerontol. 2018;111:210–7.
[26] Maginador G, Lixandrão ME, Bortolozo HI, et al. Aerobic exercise-induced changes in cardiorespiratory fitness in breast cancer patients receiving chemotherapy: a systematic review and meta-analysis. Cancers. 2020;12:2240.
[27] Wang S, Yang T, Qiang W, et al. Effectiveness of physical exercise on the cardiovascular system in breast cancer patients: a systematic review and meta-analysis of randomized controlled trials. Complement Ther Clin Pract. 2021;44:101426.
[28] Hegde SM, Solomon SD. Influence of physical activity on hypertension and cardiac structure and function. Curr Hypertens Rep. 2015;17:1–8.
[29] Li X, Tang H, Wang J, et al. The effect of preoperative serum triglycerides and high-density lipoprotein-cholesterol levels on the prognosis of breast cancer. The Breast. 2017;32:1–6.

[30] Guo R, Chen Y, Borgard H, et al. The function and mechanism of lipid molecules and their roles in the diagnosis and prognosis of breast cancer. Molecules. 2020;25:4864.
[31] Petrofsky JS, Alshammari F, Bains GS, et al. What is more damaging to vascular endothelial function: diabetes, age, high BMI, or all of the above? Med Sci Monitor: Int Med J Exp Clin Res. 2013;19:257.
[32] Singh B, Spence RR, Steele ML, et al. A systematic review and meta-analysis of the safety, feasibility, and effect of exercise in women with stage II+ breast cancer. Arch Phys Med Rehabil. 2018;99:2621–36.