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Combined Exercise is Best Exercise Modality to Improve Quality of life in Breast Cancer Survivors: A Systematic Review and Meta-Analysis

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- * Correspondence: fenghong0313@163.com; Tel.: +86-178-5717-8772 **Abstract:** A single paragraph of about 100 words to give a brief introduction to your work

Abstract: Globally, breast cancer is the most common cancer in women, posing a serious threat to women's health. We investigated the different types of exercise (aerobic exercise (AE), resistance exercise (RE), and combined aerobic and resistance exercise (CO)) to increase the quality of life (QoL) in breast cancer patients. Meta-analysis was used to estimate the effect sizes, and subgroup analyses were conducted based on types of exercise. The inclusion criteria were met by 28 studies (31 trials), comprising 2038 patients for exercise (n = 1039) and control (n = 999). Meta-analysis showed exercise intervention enhanced QoL (0.44; 95% CI: 0.26-0.62) in patients with breast cancer. Subgroup analysis revealed CO (0.97; 95% CI: 0.33-1.61) was better than AE (0.42; 95% CI: 0.17-0.67) and RE (0.13; 95% CI: -0.05-0.31) in increasing QoL in patients. In conclusion, exercise intervention has a positive impact on the QoL of breast cancer patients. The most appropriate type of exercise to improve QoL is probably CO.

Keywords: Breast Cancer; Quality of Life; Aerobic Exercise; Resistance Exercise; Exercise Rehabilitation

1. Introduction

Globally, breast cancer is the most common cancer in women, posing a serious threat to women's health. About 2.1 million new cases of breast cancers were diagnosed in 2018, accounting for one quarter of cancer cases in women[1]. Fortunately, owing largely to early detection and the development of medical technology, the survival rate of breast cancer patients after treatment is increasing[2]. However, the treatment of cancer produces a series of side effects (e.g., nausea, pain, insomnia, and limited limb movement), which seriously affect the quality of life (QoL) of cancer patients [3,4].

As a physical therapy, exercise has been included in the rehabilitation of breast cancer patients. Previous studies have shown that exercise intervention can change patients' body composition, enhance muscle strength, regulate mood, and increase QoL [5,6]. However, It is not clear which type of exercise is better for increasing the QoL of breast cancer patients. A meta-analysis of 25 RCTs found that a single type of exercise intervention, such as aerobic, yoga, or qigong, is more conducive to improving the QoL of breast cancer patients than combined aerobic resistance exercise [7]. An RCT on exercise and breast cancer patients reported that there was no difference between aerobic exercise (AE) and combined aerobic and resistance exercise (CO) in improving the QoL of breast cancer patients [8]. Another RCT indicted that resistance exercise (RE) and AE have the same effect on improving the QoL of breast cancer patients[9].

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Copyright: © 2021 by the authors. Submitted for possible open access publication under the terms and conditions of the Creative Commons Attribution (CC BY) license (http://creativecommons.org/licenses/by/4.0/). Therefore, the main purpose of this systematic review and meta analysis was to evaluate the efficacy of the different types of exercise intervention on the QoL of breast cancer patients.

2. Materials and Methods

2.1. Search strategy

The electronic databases we used to search for literature included PubMed, ScienceDirect, Google Scholar and Web of Science. We conducted the electronic search form database inception to November 2020. The search terms included "breast cancer" OR "breast tumor" OR "breast neoplasms" AND "sports" OR "physical activity" OR "exercise" OR "aerobic exercise" OR "resistance exercise" AND "quality of life" OR "QoL".

3. Results

3.1. Study Searching and Selection

Through a systematic search, a total of 1605 studies were identified. After removing duplicates, 764 studies remained. After reading titles and abstracts, 662 articles were excluded, and 102 potentially relevant studies remained. Finally, we checked the 102 full texts, removed 74 articles, and included 28 studies (31 trials) in our meta-analysis (Figure 1).



Figure 1. Flow chart of literature search.

3.2. Study Characteristics

The detailed characteristics of the 28 studies (31 trials) are presented in Table 1. A total of 2038 patients with breast cancer were included in these studies. The sample size included studies ranging from 16 to 242, and published between 2003 and 2016. The mean age of patients was between 26 and 78 years old.

Author	Year	Sample size	Mean age (years)	Type of exercise	Outcome measures
Cadmus et.al	2000	IG-H: 25; CG-H: 25	IG-H: 54.5±8.2; CG-H: 54.0±10.9	ND	FACT-B
	2009	IG-S: 37; CG-S: 37	IG-S: 56.5±9.5; CG-S: 55.1±7.7	INK	
Chandwani et.al	2010	IG: 27; CG: 29	IG: 51.39±7.97; CG: 40.2±9.96	AE	SF-36

Chen et.al	2013	IG: 49; CG: 47	IG: 45.3±6.3; CG: 44.7±9.7	AE	FACT-G
Courneya et.al	2003	IG: 24; CG: 28	IG: 59±5; CG: 58±6	AE	FACT-B
Courneya et.al	2007	IG-1: 78; IG-2: 82;	IG-1:30-75; IG-2:25-76;	IG-1: AE	
	2007	CG: 82	CG:26-78	IG-2: RE	TACT-A
Cramer et.al	2015	IG: 19; CG: 21	IG:48.3±4.8; CG:50.0±6.7	AE	FACT-B
Culos-Reed et.al	2005	IG: 18; CG: 18	All: 51.18±10.33	AE	C-30
Danhauer et.al	2009	IG: 13; CG: 14	IG: 54.3±9.6; CG: 57.2±10.2	AE	FACT-B
De Luca et.al	2016	IG: 10; CG: 10	IG: 50.2±9.7; CG: 46.0±2.8	Combined AE + RE	FACT-G
Galiano-Castill et.al	2016	IG: 39; CG: 37	IG: 47.4±9.6; CG: 49.2 ±7.9	Combined AE + RE	C-30
Hagstrom et.al	2016	IG: 19; CG: 15	IG:51.2±8.5; CG:52.7±9.4	RE	FACT-G
Haines et.al	2010	IG: 33; CG: 32	IG: 55.9±10.5; CG: 54.2±11.5	Combined AE + RE	C-30
Herrero et.al	2006	IG: 8; CG: 8	IG: 50±5; CG: 51±10	Combined AE + RE	C-30
Hornsby et.al	2014	IG: 10; CG: 10	IG:51±6; CG:46±11	AE	FACT-B
Lahart et.al	2016	IG: 37; CG: 33	IG: 52.4±10.3; CG: 54.7 ±8.3	AE	FACT-B
Littman et.al	2012	IG: 27; CG: 27	IG: 60.6±7.1; CG: 58.2±8.8	AE	FACT-G
Milne et.al	2008	IG: 29; CG: 29	IG:55.2±8.4; CG:55.1±8.0	Combined AE + RE	FACT-B
Moadel et.al	2007	IG: 84; CG: 44	IG: 55.11±10.07; CG: 54.23±9.81	AE	FACT-G
Murtezani et.al	2014	IG: 30; CG: 32	IG: 53±11; CG: 51±11	AE	FACT-B
Mutrie et.al	2007	IG: 82; CG: 92	IG: 51.3±10.3; CG: 51.8±8.7	Combined AE + RE	FACT-G
Reis et.al	2013	IG: 12; CG: 17	IG: 54±11.1; CG: 59±10.7	AE	FACT-G
Rogers et.al	2009	IG: 20; CG: 19	IG:52±15; CG:54±8	AE	FACT-B
Sandel et.al	2005	IG: 19; CG: 19	IG: 59.7±9.8; CG: 59.5±13.3	AE	FACT-B
Schmidt et.al	2015	IG: 45; CG: 32	IG: 53±11; CG: 51±11	RE	C-30
Shobeiri et.al	2016	IG: 27; CG: 26	IG: 43.5±8.6; CG: 42.7±9.6	AE	C-30
Steindorf et.al	2014	IG: 76; CG: 32	IG: 55.2±9.5; CG: 56.4±8.7	RE	C-30
Swisher et.al	2015	IG: 18; CG: 10	IG: 43-65; CG: 36-71	AE	FACT-B
Thorsten et.al	2015	IG-1: 21; IG-2: 21;	IG-1: 56±10.15; IG-2: 53±12.55;	IG-1: AE	C 20
		CG: 26	CG: 54 ±11.19	IG-2: RE	C-30

Note: IG: exercise intervention group; CG: control group; IG-H: home-based exercise intervention group; IG-S: supervised exercise intervention group; IG-1: aerobic exercise intervention group; IG-2: resistance exercise intervention group; AE: aerobic exercise; RE: resistance exercise; Combine AE + RE: combined aerobic and resistance exercise; NR: not reported; FACT-G: Functional Assessment of Cancer Therapy-General; FACT-B: Functional Assessment of Cancer Therapy-Breast; FACT-A: Functional Assessment of Cancer Therapy-Anemia; C-30: European Organization for Research and Treatment of Cancer Quality of Life Questionnaire; SF-36: Health Survey Short Form-36.

3.3. Effect of Exercise Intervention on QOL for Breast Cancer Survivors

Data from 28 articles (31 trials) were pooled for analysis. The result of meta-analysis showed that the change in QoL was extremely favourable for the exercise intervention group with heterogeneity Tau² = 0.18; Chi² = 114.13; degrees of freedom (df) = 30; I² = 74%, and the combined SMD (95% CI) was 0.44 (0.26–0.62). Due to the high heterogeneity, the random-effects model was used (Figure 2).

	Experimental		Control		Std. Mean Difference		Std. Mean Difference		
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% Cl
Cadmus-H et.al 2009	89.3	11.1	25	89.5	11.8	25	3.3%	-0.02 [-0.57, 0.54]	
Cadmus-S et.al	91.2	12.6	37	86.2	17.4	37	3.7%	0.33 [-0.13, 0.78]	
Chandwani et.al 2010	69.1	4	27	64.5	4.4	29	3.3%	1.08 [0.51, 1.64]	
Chen et.al 2013	76.6	16.4	49	80.8	15.7	47	3.9%	-0.26 [-0.66, 0.14]	
Courneya et.al 2003	119.6	16.9	24	115.8	14.9	28	3.3%	0.24 [-0.31, 0.78]	
Courneya-AE et.al 2007	144.7	25.2	78	139.9	28.2	82	4.2%	0.18 [-0.13, 0.49]	
Courneya-RE et.al 2007	140.9	24.8	82	139.9	28.2	82	4.2%	0.04 [-0.27, 0.34]	
Cramer et.al 2015	113.7	20.5	19	102.1	14.8	21	3.0%	0.64 [0.00, 1.28]	
Culos-Reed et.al 2005	78.24	20.24	18	62.5	15.46	18	2.8%	0.85 [0.17, 1.54]	
Danhauer et.al 2009	114.8	19.1	13	98.4	31.8	14	2.6%	0.60 [-0.17, 1.38]	10 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1
De Luca et.al 2016	87	12.3	10	65.9	14.7	10	1.9%	1.49 [0.47, 2.51]	the second se
Galiano-Castillo et.al 2016	72.86	19.93	39	57.21	21.71	37	3.6%	0.74 [0.28, 1.21]	
Hagstrom et.al 2016	95.98	8.66	19	91.63	9.81	15	2.8%	0.46 [-0.22, 1.15]	2
Haines et.al 2010	75.8	15.2	33	74	15.5	32	3.6%	0.12 [-0.37, 0.60]	2 To 1 1
Herrero et.al 2006	92	17.11	8	63	19.34	8	1.7%	1.50 [0.35, 2.65]	
Hornsby et.al 2014	80.2	16.7	10	85.9	6.2	10	2.2%	-0.43 [-1.32, 0.46]	the second se
Lahart et.al 2016	114.41	21.48	37	115.34	17.57	33	3.6%	-0.05 [-0.52, 0.42]	and the second second
Littman et.al 2012	90.3	11	27	87.7	15	27	3.4%	0.19 [-0.34, 0.73]	
Milne et.al 2008	110.5	10.3	29	82.6	14.3	29	2.9%	2.21 [1.55, 2.87]	10 THE 10 THE 10
Moadel et.al 2007	75.2	18.96	84	69.94	19.39	44	4.0%	0.27 [-0.09, 0.64]	1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1
Murtezani et.al 2014	113.2	9.7	30	101.2	9.5	32	3.3%	1.23 [0.69, 1.78]	100 million -
Mutrie et.al 2007	81	16.8	82	77.3	14.4	92	4.2%	0.24 [-0.06, 0.54]	
Reis et.al 2013	91.7	10.96	12	90.6	11.06	17	2.7%	0.10 [-0.64, 0.84]	and the second s
Rogers et.al 2009	114.4	16.2	20	118.7	14.4	19	3.0%	-0.27 [-0.91, 0.36]	and the second sec
Sandel et.al 2005	116.7	16.9	19	106.1	22.3	19	3.0%	0.52 [-0.12, 1.17]	
Schmidt et.al 2015	61.7	18.3	45	54.9	22.9	32	3.7%	0.33 [-0.13, 0.79]	
Shobeiri et.al 2016	81.79	16.34	27	52.88	14.51	26	3.0%	1.84 [1.19, 2.49]	
Steindorf et.al 2014	64	25	76	62	21	72	4.1%	0.09 [-0.24, 0.41]	
Swisher et.al 2015	119.6	14.6	18	104.6	30.6	10	2.5%	0.68 [-0.12, 1.47]	
Thorsten-AE et.al 2015	36.79	17.99	21	30.95	15.29	26	3.2%	0.35 [-0.23, 0.93]	
Thorsten-RE et.al 2015	31.29	15.88	21	30.95	15.29	26	3.2%	0.02 [-0.55, 0.60]	and the second
Total (95% CI)			1039			999	100.0%	0.44 [0.26, 0.62]	◆
Heterogeneity: Tau ² = 0.18; C	Chi² = 114	13, df=	30 (P ·	< 0.0000	1); l ² = 7	4%		_	
Test for overall effect: Z = 4.73 (P < 0.00001)								Favours control Favours experimental	

Figure 2. Meta-analyses of the impact of exercise on QoL.

3.4. Subgroup Analysis of Exercise Types

The subgroup analysis revealed that AE (SMD = 0.42; I² = 72%; 95% CI: 0.17–0.67, p = 0.0009) and CO (SMD = 0.97; I² = 87%; 95% CI: 0.33–1.61, p = 0.003) had a positive effect on QoL. However, as for RE, no significant difference was observed between the groups (SMD = 0.13; I² = 0%; 95% CI: -0.05–0.31, p = 0.17). The pooled SMD (95%) of CO (SMD = 0.97; 95% CI: 0.33–1.61) more than the pooled SMD (95%) of AE (SMD = 0.42; 95% CI: 0.17–0.67) (Figure 4).

	Experimental Control Std. Mean Difference					Std. Mean Difference	Std. Mean Difference		
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI
1.3.1 AE									
Chandwani et.al 2010	69.1	4	27	64.5	4.4	29	3.5%	1.08 [0.51, 1.64]	
Chen et.al 2013	76.6	16.4	49	80.8	15.7	47	4.1%	-0.26 [-0.66, 0.14]	
Courneya et.al 2003	119.6	16.9	24	115.8	14.9	28	3.6%	0.24 [-0.31, 0.78]	
Courneva-AE et.al 2007	144.7	25.2	78	139.9	28.2	82	4.4%	0.18 [-0.13, 0.49]	+
Cramer et.al 2015	113.7	20.5	19	102.1	14.8	21	3.3%	0.64 [0.00, 1.28]	
Culos-Reed et al 2005	78.24	20.24	18	62.5	15.46	18	3.1%	0.85 [0.17, 1.54]	
Danhauer et.al 2009	114.8	19.1	13	98.4	31.8	14	2.8%	0.60 (-0.17, 1.38)	
Hornsby et al 2014	80.2	16.7	10	85.9	6.2	10	2.4%	-0.43 [-1.32, 0.46]	
Lahart et al 2016	114.41	21.48	37	115.34	17.57	33	3.9%	-0.05 [-0.52, 0.42]	
Littman et al 2012	90.3	11	27	87.7	15	27	3.6%	0 19 [-0.34, 0.73]	
Moadel et al 2007	75.2	18.96	84	69.94	19.39	44	4 2%	0.27 [-0.09 0.64]	++
Murtezani et al 2014	113.2	9.7	30	101.2	9.5	32	3.6%	1 23 [0 69 1 78]	
Reis et al 2013	91.7	10.96	12	90.6	11.06	17	2 9%	0 10 -0 64 0 84	
Rogers et al 2009	114.4	16.2	20	1187	14.4	19	3 396	-0.27 [-0.91 0.36]	
Sandel et al 2005	116.7	16.9	10	106.1	22.3	19	3 296	0.52 - 0.12 1.17	+
Shoheiri et al 2005	91 79	16.34	27	52.88	14 51	26	3.2%	1 84 [1 19 2 49]	
Swicher et al 2015	110.6	14.6	10	104.6	20.6	10	2 7 96	0.69 L0 12 1 471	
Thereton AE at al 2015	26 70	17.00	21	20.06	16 20	26	2.7 10	0.00[-0.12, 1.47]	
Subtotal (95% CI)	30.75	17.55	533	30.93	15.28	502	61 /%	0.42 [0.17 0.67]	•
Hotorogonoitr Touis = 0.20: C	hiZ - 61 /	7 df -	17/0 -	0.000041	18 - 70	002	01.470	0.42 [0.11, 0.01]	•
Test for overall effect: 7 = 2.20, C	P = 0.0	000	17 (F S	0.00001,	(1 - 72)	. 20			
Testion overall ellect. Z = 3.51	(F = 0.0	003)							
132 DE									
Courses PE et al 2007	140.0	24.0	02	120.0	20.2	02	4 4 96	0.0410.27.0.241	
Liggetrom et al 2007	05.00	24.0	10	01.60	20.2	15	9.970	0.04 [-0.27, 0.34]	
Data sint at al 2010	90.90	0.00	19	91.05	3.01	10	3.170	0.40 [-0.22, 1.15]	
Oteinderfetel 2015	01.7	10.3	40	04.9	22.9	32	3.370	0.33 [-0.13, 0.79]	
Steindon et al 2014	04	47.00	70	20.02	45.00	12	4.470	0.09[-0.24, 0.41]	100 C
Subtotal (05% CI)	31.29	10.00	242	30.90	15.29	20	40.2%	0.02 [-0.55, 0.60]	L
Subtoral (95% CI) Z43 Z27 19.3% 0.13 [-0.05, 0.31]									
Heterogeneity: Tau*= 0.00; Chi*= 2.21, df= 4 (P = 0.70); P= 0%									
Test for overall effect. $Z = 1.38$	S (P = 0.1	0							
1.3.3 combined AE+RE									
De Luca et al 2016	87	123	10	65.9	147	10	21%	1 49 10 47 2 511	
Galiano-Castillo et al 2016	72.86	19.93	39	57 21	21.71	37	3.9%	0 74 10 28 1 211	
Haines et al 2010	75.8	15.2	33	74	15.5	32	3.8%	0.12 60.37 0.601	
Herrero et al 2006	92	1711		63	10.34		1.9%	1 50 (0 35 2 65)	
Milne et al 2008	110.5	10.3	20	87.6	14.3	20	3 796	2 21 [1 55 2 87]	
Mutrie et al 2007	01	16.9	020	77.2	14.0	02	4 596	0.24 1.0.06 0.541	<u>+</u>
Subtotal (95% CI)	01	10.0	201	11.5	14.4	208	10 3%	0.97 [0.33 1.61]	-
Subtraction (55.9 Cf) = 0.54 · Chi2 - 27.05 · df = 5 (0 × 0.00004)· (2 = 0.70)									
The fore a second seco									
Testion (verall elieur. 2 = 2.33 () = 0.003)									
Total (95% CI)			977			937	100.0%	0.46 [0.27, 0.66]	•
Heterogeneity: Tau ² = 0.20; C	hi ² = 112	.56, df=	28 (P	< 0.0000	1); l² = 7	5%			
Test for overall effect: Z = 4.67	' (P < 0.0	0001)							Favours control Favours experimental
Test for subaroup differences: Chi ² = 8.43. df = 2 (P = 0.01). I ² = 76.3%									

Figure 4. Subgroup analyses of exercise types.

4. Conclusions

In summary, our findings show that exercise intervention may increase self-reported QoL in breast cancer patients. The most appropriate type of exercise to improve QoL is probably CO.

Author Contributions: Conceptualization, W.Y., and Y.F.; methodology, W.Y., and F.H.; validation, W.Y., and Y.F.; formal analysis, F.H., and Y.F.; investigation, F.H., and W.Y.; resources, F.H., and W.Y.; data curation, F.H., and W.Y.; writing—original draft preparation, F.H. and W.Y.; writing—review and editing, Y.F.; visualization, F.H. and W.Y.; supervision, W.Y.; project administration, W.Y., and Y.F.; funding acquisition, W.Y.

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Conflicts of Interest: The authors declare no conflict of interest.

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