Original Article

Effect of exercise on the quality of life in cancer patients: a meta-analysis of different intervention

MICHELE ANDRADE DE BRITO¹, JOSÉ RAIMUNDO FERNANDES², ESTEBAN AEDO-MUÑOZ³,
DIEGO IGNACIO VANENZUELA PÉREZ⁴, ANDREIA CRISTIANE CARRENHO QUEIROZ⁵, PEDRO
HENRIQUE BERBERT DE CARVALHO⁶, CIRO JOSÉ BRITO⁷, BIANCA MIARKA⁸

^{1,2,3,5,6,7,8}Laboratory of Physiological and Motor Analysis in Health and Performance of the Physical Education
Department, Physical Education Department, Federal University of Juiz de Fora, BRAZIL

^{2,3}Physical Activity, Sport and Health Sciences Laboratory, Universidad de Santiago de Chile, CHILE

³Physical Education Department, Universidad Metropolitana de Ciencias de la Educación, CHILE

⁴Escuela de Kinesiología, Facultad de Salud, Universidad Santo Tomás Santiago, CHILE

⁸Laboratory of Psychophysiology and Performance in Combats & Sports, School of Physical Education and
Sports, Federal University of Rio de Janeiro, BRAZIL

Published online: September 30, 2020

(Accepted for publication: September 22, 2020)

DOI:10.7752/jpes.2020.05360

Abstract:

Cancer is considered a devastating disease and its treatment act directly on the individual's lifestyle, however, practicing exercises to the point of generating beneficial changes in the quality of life is still divergent. Therefore, the objective of this study was to evaluate whether there is a benefit of physical exercise on the Quality of Life of the patient. Electronic databases (i.e. Pubmed/Medline, ISI Web of Knowledge, Scopus, The Cochrane Library, and Lilacs) forward-citation searches and manual searches of reference lists were used to locate relevant studies up to June 2018. The terms used were "Physical Exercise", "cancer" and "EORTC QLQ C-30". Randomized clinical trials in humans with a 10-year cohort and exercise as a form of intervention and improvement in Quality of Life were included in the meta-analysis. The meta-analysis was based on 20 studies, scoring a maximum of 11 points in the PEDRo scale. Where they evaluated the effects of physical exercise on QOL. The present meta-analysis included studies with a diagnosis of breast cancer, esophageal, lung, gynecological, and other unspecified. The main modalities practiced were aerobic exercise, cardiovascular training, resistance training, strength training, gymnastics, 6 min walk, and Pilates. In meta-analysis indicated that comparisons between the intervention and control group had differences in the quality of life of patients during the interventions and after the time of exercise intervention. Our results also demonstrated a large heterogeneity between the effects of physical activities in the EQTC QLQ C-30 results would be most likely due to differences in the type of exercise and the respective periods carried out. Future studies are necessary in order to conclude a causal relationship between the type of exercise and the time of intervention in cancer patients.

Key-words: Neoplasms; Health-Related Quality of Life; Psychology; Cognitive Functions; Physical Fitness

Introduction

Currently, cancer is considered the second largest cause of death in the world, and its treatment directly influences the individual's lifestyle. (Machado & Sawada, 2008), the diagnosis of neoplasia causes a strong impact on the life of their patients (Carvalho, 2002).

Several aspects such as early diagnosis and the means of rehabilitation, physical, social, and psychological, are important in encouraging the fight against this disease. The inclusion of physical exercise in the daily lifestyle of an individual is known to promote many health benefits, the same is true for people with cancer. According to Oreinstein and Friedenreich (2002), physical exercise also has a beneficial effect on the diagnosis and the later stages of treatment (Friedenreich & Orenstein, 2002). Physical exercise improves well-being and can aid in the side effects of the treatment, its physiological and psychological effects, these changes can affect directly the life of the patient, (Macedo et al., 2003).

One of the symptoms present in the different stages of cancer is fatigue, which is characterized by excessive discomfort and physical exhaustion, (Gutstein, 2001). Fatigue is understood as a state of fatigue, weakness, exhaustion, or demotivation, which may be chronic or acute (Da Silva & Gonçalves, 2008). According to Mota and Pimenta (2002), fatigue affects more than 75% of patients, especially after the first cycle of chemotherapy, during periods of palliative care, or in more advanced stages (de Faria Mota & de Mattos Pimenta, 2002). Physical activity has been shown to be an important tool in the control of fatigue with a direct effect on the patient's well-being and quality of life (Battaglini et al., 2006). The exercises contribute to both the maintenance of muscle strength and to a minimal reduction of muscle strength, especially in hospitalized individuals (The Whoqol Group, 1998).

Quality of Life (QL) is a difficult term to define because it includes a potential variety of conditions that affect: the individual's perception, feelings, and behaviors related to their daily functioning, including their health condition, and medical interventions. The World Health Organization defines Quality of Life as "the individual's perception of their position in life in the context of the culture and value system in which they live and in relation to their goals, expectations, standards, and concerns" (Group, 1993; Makluf, 2005). QOL is an important tool for assessing treatment outcomes from the perspective of the patient. The systematic review analyzes the impact of physical exercise on cancer patients in relation to their quality of life. We know that both the disease and its treatment produce morbidities that gradually compromise the patients' lives (Velloso, Barra, & Dias, 2011), therefore, the evaluation is necessary because it is an important indicator of the influence of the side effects of the treatment on the individual. Assessing the quality of life of the cancer patient is an important resource for evaluating treatment outcomes from the perspective of the patient.

Methods

We performed a systematic review of the literature of published studies to evaluate the association between physical exercise and quality of life of cancer patients measured by the EORTC QLQ-C30 questionnaire. The meta-analysis required two moments, one qualitative and the other quantitative. In the qualitative phase, a bibliographic search of articles indexed in the databases Pubmed/Medline, ISI Web of Knowledge, Scopus, The Cochrane Library, and Lilacs from their inception up to June 2018. The articles were located from the search descriptors, selected the words "physical exercise", "pilates", "endurance", "conditioning training", "strength training", "workout", "resistance training" and "cancer" or "neoplasm" and "quality of life" or "EORTC QLQ C30". The inclusion criteria of the studies were: human studies, complete articles in English, with a 10-year cohort, randomized clinical trial, with quantitative data that could be statistically analyzed.

To evaluate the Quality of Life, the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire c-30 (EORTC QLQ-C30) version 3.0 (Berzon, 1998) was used, which consists of 30 items (five functional scales, three scales of symptoms, overall health status, symptoms such as dyspnea, loss of appetite, sleep disorder, constipation and diarrhea, and the financial impact of the disease and treatment). Scores vary from 0 to 100, and in function scales, the higher the score the better the Quality of Life, and on the scale of symptoms, the higher the score the worse the Quality of Life. The state of global health was used. (Makluf, 2005). Therefore, exclusion criteria were: studies in which they did not investigate the relationship between physical exercise, and quality of life of cancer patients, who did not use the EORTC QLQ - C30 quality of life questionnaire and that the statistical data were different from the mean and standard deviation pattern. The evaluated characteristics of the studies were the following: intervention strategy, inclusion and exclusion criteria, population characterization, EORTC QLQ C-30, and type of physical exercise. It was evaluated whether after the intervention with physical exercise there was a change in the quality of life of the patient. Figure 1 shows the flowchart of the present research (Liberati et al., 2009).

Figure 1.: Prisma Flow Diagram

The present study searched 93 identified articles, but only 35 were included from reading the titles. Of these, 10 were duplicates, one was excluded because they did not present EORTC QLQ C-30 data and four because they did not present the required data of mean and standard deviation. The methodological quality of the 20 included articles was evaluated through the PEDro Scale (table 1), which evaluates the methodological quality and statistical description of randomized controlled studies, contains 11 criteria, forming a total score ranging from 0 to 10, where the higher the score, the better the methodological quality and statistical description of the study (Shiwa et al., 2011). In this scale, the following criteria are evaluated: 1) eligibility specified; 2) random distribution by groups; 3) secret allocation; 4) similarity in prognostic indicators; 5) blinding of subjects; 6) blinding of therapists; 7) blindness of the evaluators; 8) analysis in more than 85% of subjects; 9) intention-to-treat analysis; 10) statistical analysis and 11) measures of precision and variability. This instrument is validated, having 11 items with questions related to quality, where each item can be answered with yes "Y" or no "N". In case of a "Y" answer, a point is assigned to the item. The maximum possible score is 11 and the higher, the better the study quality, the score will only be awarded when a criterion is satisfied. Afterward, the sum of the criteria 1 to 11 was generated. An inter-checklist agreement was performed and possible disagreements were resolved by consensus (Shea et al., 2009).

CRITERIA	DO, 2015	SCHMIDT, 2017	YUN, 2017	VULPEN, 2017	2018	2013	2016	2015	2014	2013	2012	2017	2016	2014	2013	2010	2009
1. eligibility criteria were specified	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
2. subjects were randomly allocated to groups	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
3. allocation was concealed	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
4. the groups were similar at baseline regarding the most important prognostic indicators	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
5. there was blinding of all subjects	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
6. there was blinding of all therapists who administered the therapy	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
7. there was blinding of all assessors who measured at least one key outcome	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
8. measures of at least one key outcome were obtained from more than 85% of the subjects initially allocated to groups	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
9. all subjects for whom outcome measures were available received the treatment or control condition as allocated.	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
10. the results of between-group statistical comparisons are reported for at least one key outcome	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
11. the study provides both point measures and measures of variability for at least one key outcome	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
TOTAL	7	7	7	7	7	7	7	7	7	7	7	7	7	7	7	7	7

All studies 20 studies scored a maximum of 11 points in the PEDRo scale (table 1). Where they evaluated the effects of physical exercise on QOL. The studies were statistically significant for an increase in QoL associated with exercise. They were published between 2009 and 2018. The main modalities practiced were: aerobic exercise, cardiovascular training, resistance training, strength training, gymnastics, 6 min walk, and pilates. The present meta-analysis included studies with a diagnosis of breast cancer, esophageal, lung, gynecological, and other unspecified.

After that, in the quantitative phase, the extraction of numerical data from the included studies described on average, standard deviation, and sample number was performed, the most frequent situation consisted of combining data that were presented in subgroups. Five meta-analyses were carried out to investigate the proposed goal. The effect size was observed using Hedges'g, with the following rule of thumb for interpreting results: Small effect < 0.2; Medium Effect < 0.5, and Large Effect < 0.8. We used the statistical package Comprehensive Meta-Analysis 2.0, a program developed to perform meta-analyses.

Results

Table 2 describes the EORCT Questionnaire QLQ C-30 of groups with two different measures of life quality (before, during, and after exercise intervention during the treatment) and demonstrates respective effect sizes. Table 2: Descriptive analysis of the EORCT Questionnaire QLQ C-30 of control and intervention groups in different moments (before, during or after the intervention) and respective effect size (G).

Study	Moment	TP	Cancer Type	Sex	Intervention Group		Control Group		diff in M	SE	G	SE	diff in M	SE
					N	M±SD	N	M±SD						
Adamsen (2009)	after	6	various	F-M	118	67.2±20.3	117	63.9±21.1	0.16	0.13	0.16	0.13	3.32	2.70
Adamsen (2009)	before	0	various	F-M	135	63.3±22.4	134	60.2±22.4	0.14	0.12	0.14	0.12	3.10	2.73
Banzer (2014)	after	16	various	F-M	33	73.7±14.7	33	56.5±15.7	1.13	0.27	1.12	0.26	17.20	3.74
Banzer (2014)	before	0	various	M	35	66.9±21.0	35	62.1±19.1	0.24	0.24	0.24	0.24	4.80	4.80
Banzer (2014)	during	8	various	F-M	33	67.7±17.0	33	55.2±19.8	0.68	0.25	0.67	0.25	12.50	4.54
Broderick (2013)	after	48	mama	F	24	70.5±23.7	24	69.1±17.1	0.07	0.29	0.07	0.28	1.40	5.97
Broderick (2013)	before	6	mama	F	24	69.1±17.1	24	69.1±17.1	0.00	0.29	0.00	0.28	0.00	4.94
Broderick (2013)	during	24	mama	F	24	69.8±19.8	24	69.1±17.1	0.04	0.29	0.04	0.28	0.70	5.34
Do (2015)	after	8	mama	F	32	87.3±13.7	30	82.4±19.9	0.29	0.26	0.29	0.25	4.90	4.32
Do (2015)	before	0	mama	F	32	58.0±18.6	30	61.7±16.2	-0.21	0.26	-0.21	0.25	-3.70	4.44
Do (2015)	during(a)	2	mama	F	32	77.5±11.5	30	65.3±14.0	0.96	0.27	0.94	0.27	12.20	3.25
Do (2015)	during(b)	4	mama	F	32	80.2±15.5	30	58.0±18.5	1.31	0.28	1.29	0.28	22.20	4.32
Do (2015)	during(c)	6	mama	F	32	85.5±13.7	30	75.8±19.3	0.58	0.26	0.58	0.26	9.70	4.23
Eygor (2010)	after	*	mama	F	27	77.0±21.8	15	63.8±23.8	0.59	0.33	0.58	0.32	13.24	7.25
Eygor (2010)	before	0	mama	F	27	70.1±20.6	15	62.6±29.3	0.31	0.32	0.31	0.32	7.52	7.72
Henke (2013)	after	*	lung	F-M	18	57.8±17.3	11	44.2±29.5	0.60	0.39	0.58	0.38	13.58	8.66
Henke (2013)	before	0	lung	F-M	18	52.0±21.8	11	50.6±28.2	0.06	0.38	0.06	0.37	1.44	9.33
Leesen (2017)	after	*	various	F-M	93	82.4±17.3	93	66.8±21.8	0.79	0.15	0.79	0.15	15.60	2.89
Leesen (2017)	before	*	various	F-M	93	66.8±21.8	93	66.8±21.8	0.00	0.15	0.00	0.15	0.00	3.20
Leesen (2017)	during(a)	0	various	F-M	93	74.7±18.5	93	21.8±21.8	0.39	0.15	0.39	0.15	7.90	2.97
Leesen (2017)	during(b)	*	various	F-M	93	83.3±16.2	93	66.8±21.8	0.86	0.15	0.86	0.15	16.50	2.82
Ligibel (2016)	after	16	mama	F	32	73.2±17.5	43	70.5±21.5	0.14	0.23	0.13	0.23	2.70	4.65
Ligibel (2016)	before	0	mama	F	32	67.2±19.4	43	71.5±20.2	-0.22	0.23	-0.21	0.23	-4.30	4.64
Ochalek (2017)	during	*	mama	F	23	67.3±17.3	22	65.5±23.0	0.09	0.30	0.09	0.29	1.80	6.05
Schimidt (2012)	after	*	mama	F	15	76.0±12.9	18	77.0±15.3	-0.07	0.35	-0.07	0.34	-1.00	4.99
Schimidt (2012)	before	0	mama	F	15	59.0±16.6	18	67.0±17.2	-0.47	0.35	-0.46	0.35	-8.00	5.93
Schimidt (2012)	during	*	mama	F	15	67.0±19.2	18	75.0±18.0	-0.42	0.35	-0.41	0.35	-8.00	6.60
Schimidt (2015)	after	12	mama	F	45	61.7±1.3	32	54.9±22.9	0.46	0.23	0.46	0.23	6.80	3.41
Schimidt (2015)	before	0	mama	F	45	61.5±17.5	32	59.4±16.6	0.12	0.23	0.12	0.23	2.10	3.96
Schimidt (2015)a	after	12	mama	F	41	68.1±33.8	26	30.9±15.2	1.32	0.28	1.30	0.27	37.13	7.07
Schimidt (2015)a	before	0	mama	F	41	61.5±38.0	26	31.1±19.8	0.94	0.26	0.93	0.26	30.36	8.08
Schmidt (2013)	during	*	various	F-M	50	64.0±18.0	36	66.0±17.0	-0.11	0.22	-0.11	0.22	-2.00	3.85
Schmidt (2016)	during	*	various	F-M	37	52.5±19.6	42	50.3±19.5	0.11	0.23	0.11	0.22	2.20	4.41
Shobeiri (2016)	after	40	mama	F	26	47.75±15.75	27	52.9±14.5	-0.34	0.28	-0.33	0.27	-5.13	4.16
Shobeiri (2016)	before	0	mama	F	26	48.76±25.0	27	81.8±16.3	-1.57	0.31	-1.55	0.31	-33.03	5.77
Vermaete(2013)	after	14	lymphoma	F-M	25	63.0±20.0	25	71.0±18.0	-0.42	0.29	-0.41	0.28	-8.00	5.38
Vermaete(2013)	before	0	lymphoma	F-M	25	71.0±18.0	25	71.0±18.0	0.00	0.28	0.00	0.28	0.00	5.09
Vermaete(2013)	during	9	lymphoma	F-M	25	67.0±20.0	25	71.0±18.0	-0.21	0.28	-0.21	0.28	-4.00	5.38
Villaron (2018)	after	8	various	F-M	21	88.24±13.6	22	83.64±12.7	0.35	0.31	0.35	0.30	4.60	4.00
Villaron (2018)	before	0	various	F-M	21	88.33±13.4	22	75.5±18.9	0.78	0.32	0.77	0.31	12.85	5.02
Vulpen (2017)	during	12	esophagus	F-M	51	15.1±17.7	51	6.1±17.1	0.52	0.20	0.51	0.20	9.00	3.45
Yang (2012)	after	4	reproductive system	F	12	64.6±16.5	12	62.8±16.3	0.11	0.41	0.11	0.39	1.80	6.70
Yang (2012)	before	0	reproductive system	F	12	62.8±14.9	12	69.6±20.8	-0.38	0.41	-0.36	0.40	-6.80	7.39
Yun (2017)	after	12	post-various	F-M	134	67.7±18.7	72	65.7±17.5	0.11	0.15	0.11	0.15	2.00	2.67
Yun (2017)	before	48	post-various	F-M	134	70.1±17.1	72	65.3±17.9	0.28	0.15	0.28	0.15	4.80	2.54
Yun (2017)	during	0	post-various	F-M	134	64.5±19.9	72	63.4±18.7	0.06	0.15	0.06	0.15	1.10	2.85

Note: TP – training period/weeks; F – female; M- male; N – number of participants; M – mean; SD – standard deviation; diff – difference; SE - standard error; G – effect size by Hedges' g.

Table 2 demonstrated a large effect of Do (2015) during two moments of training intervention during cancer of mama, after 2 weeks, and 4 weeks of training on quality of life. Leesen (2017) verified the large effect of training intervention during various types of cancer treatments during and after the training period. Figure 2 shows the meta-analysis of life quality in cancer patients of different intervention moments (before, during, and before). Figure 2 shows the meta-analysis of the EORCT Questionnaire QLQ C-30 of control and intervention groups in different moments (before, during, or after the intervention) in the cancer patients.

Table 3 demonstrates the mixed-effects analysis with effect size and 95% confidence interval, heterogeneity, and variance of each moment (before, after, and during interventions).

Table 3: The Mixed Effects Analysis between the studies of EORCT Questionnaire QLQ C-30 of control and intervention groups in different moments (before, during, or after the intervention) in the cancer patients.

Groups		Effect size and 95% confidence interval					Test of null (2-Tail)		Heterogeneity				Tau-squared			
Group	Number Studies	Point estimate	Standard error	Variance	Lower limit	Upper limit	Z-value	P-value	Q-value	df (Q)	P-value	I-squared	Tau Squared	Standard Error	Variance	Tau
Fixed effect analysis																
after	13	0.320	0.062	0.004	0.199	0.441	5.201	0.000	33.707	12	0.001	64.399	0.094	0.067	0.004	0.307
after	3	0.418	0.155	0.024	0.114	0.722	2.693	0.007	18.404	2	0.000	89.133	0.593	0.667	0.444	0.770
before	16	0.076	0.056	0.003	-0.034	0.186	1.356	0.175	53.248	15	0.000	71.830	0.134	0.079	0.006	0.367
during	9	0.124	0.076	0.006	-0.026	0.274	1.624	0.104	13.886	8	0.085	42.388	0.040	0.049	0.002	0.201
during(a)	2	0.523	0.130	0.017	0.269	0.777	4.032	0.000	3.397	1	0.065	70.560	0.112	0.225	0.051	0.335
during(b)	2	0.962	0.134	0.018	0.698	1.225	7.156	0.000	1.950	1	0.163	48.708	0.048	0.140	0.020	0.220
during(c)	1	0.583	0.259	0.067	0.074	1.091	2.246	0.025	0.000	0	1.000	0.000	0.000	0.000	0.000	0.000
Total within									124.592	39	0.000					
Total between									48.879	6	0.000					
Overall	46	0.260	0.033	0.001	0.195	0.324	7.900	0.000	173.472	45	0.000	74.059	0.144	0.047	0.002	0.379
Mixed effects analysis																
after	13	0.317	0.112	0.013	0.098	0.537	2.832	0.005								
after	3	0.422	0.471	0.222	-0.502	1.345	0.895	0.371								
before	16	0.027	0.113	0.013	-0.195	0.249	0.234	0.815								
during	9	0.115	0.105	0.011	-0.091	0.321	1.095	0.273								
during(a)	2	0.629	0.279	0.078	0.082	1.175	2.255	0.024								
during(b)	2	1.020	0.214	0.046	0.601	1.440	4.766	0.000								
during(c)	1	0.583	0.259	0.067	0.074	1.091	2.246	0.025								
Total between									22.440	6	0.001					
Overall	46	0.260	0.058	0.003	0.148	0.373	4.526	0.000								

After, Figure 3 displays the meta-analysis of life quality in cancer patients of different interventions by weeks.

Figure 3: A descriptive meta-analysis of the EORCT Questionnaire QLQ C-30 of control and intervention groups with different periods of training during the treatment of cancer patients.

After, table 4 demonstrates the mixed-effects analysis with effect size and 95% confidence interval, heterogeneity, and variance of different training periods.

Table 4: The Mixed Effects Analysis between the studies of the EORCT Questionnaire QLQ C-30 of control and intervention groups comparing studies with different training periods in the cancer patients.

Groups		Effect size and 95% confidence interval					Test of null (2-Tail)		Heterogeneity				Tau-squared			
Group	Number Studies	Point estimate	Standard error	Variance	Lower limit	Upper limit	Z-value	P-value	Q-value	df (Q)	P-value	I-squared	Tau Squared	Standard Error	Variance	Tau
Fixed effect analysis																
0 weeks	1	0.138	0.122	0.015	-0.101	0.378	1.134	0.257	0.000	0	1.000	0.000	0.000	0.000	0.000	0.000
0 weeks	15	0.079	0.059	0.003	-0.037	0.195	1.335	0.182	55.584	14	0.000	74.817	0.152	0.093	0.009	0.403
12 weeks	3	0.395	0.113	0.013	0.173	0.617	3.493	0.000	15.107	2	0.001	86.761	0.300	0.358	0.128	0.547
14 weeks	1	-0.420	0.286	0.082	-0.981	0.140	-1.470	0.141	0.000	0	1.000	0.000	0.000	0.000	0.000	0.000
14 weeks	2	0.571	0.175	0.031	0.227	0.915	3.256	0.001	7.930	1	0.005	87.389	0.433	0.700	0.491	0.658
24 weeks	1	0.038	0.289	0.083	-0.528	0.604	0.131	0.896	0.000	0	1.000	0.000	0.000	0.000	0.000	0.000
24 weeks	1	0.955	0.269	0.072	0.430	1.481	3.962	0.000	0.000	0	1.000	0.000	0.000	0.000	0.000	0.000
40 weeks	1	-0.339	0.277	0.077	-0.882	0.203	-1.226	0.220	0.000	0	1.000	0.000	0.000	0.000	0.000	0.000
40 weeks	2	0.233	0.131	0.017	-0.023	0.490	1.784	0.074	0.414	1	0.520	0.000	0.000	0.074	0.006	0.000
40 weeks	2	0.923	0.231	0.053	0.471	1.376	3.998	0.000	5.822	1	0.016	82.824	0.591	1.010	1.019	0.769
6 weeks	1	0.160	0.131	0.017	-0.096	0.416	1.227	0.220	0.000	0	1.000	0.000	0.000	0.000	0.000	0.000
6 weeks	2	0.322	0.193	0.037	-0.056	0.701	1.671	0.095	2.295	1	0.133	55.645	0.095	0.240	0.058	0.307
8 weeks	3	0.451	0.155	0.024	0.146	0.755	2.903	0.004	1.310	2	0.519	0.000	0.000	0.073	0.005	0.000
8 weeks	1	-0.210	0.284	0.080	-0.766	0.346	-0.741	0.459	0.000	0	1.000	0.000	0.000	0.000	0.000	0.000
not found	9	0.454	0.077	0.006	0.304	0.605	5.915	0.000	31.180	8	0.000	74.342	0.165	0.124	0.015	0.406
Total within									119.511	30	0.000					
Total between									53.860	15	0.000					
Overall	46	0.260	0.033	0.001	0.195	0.324	7.900	0.000	173.472	45	0.000	74.059	0.144	0.047	0.002	0.379
Mixed effects analysis																
0 weeks	1	0.138	0.122	0.015	-0.101	0.378	1.134	0.257								
0 weeks	15	0.028	0.125	0.016	-0.217	0.273	0.221	0.825								
12 weeks	1	0.517	0.201	0.041	0.123	0.912	2.569	0.010								
12 weeks	3	0.599	0.341	0.116	-0.070	1.267	1.756	0.079								
14 weeks	1	-0.420	0.286	0.082	-0.981	0.140	-1.470	0.141								
14 weeks	2	0.625	0.498	0.248	-0.350	1.601	1.257	0.209								

Discussion

Physical activity has been recommended as an effective adjunctive treatment to reduce the disruptions caused by cancer and its treatments (Schmitz et al., 2010). Numerous reviews are available reporting on the effects of exercise on psychological or emotional, physical, and social health for people who have or had cancer (Sabiston & Brunet, 2012; Schmitz et al., 2010). The present study aimed to establish the effects of exercise in cancer patients of interventions moments and therefore aimed to get a pooled estimate of effect size using Hedge's g , presenting relative weight and standardized mean difference. The present meta-analysis could be useful as well to get a more precise estimate of the time to increase the quality of life in cancer patients and the practical effects of time by weeks of randomized studies. The heterogeneity of tables 3 and 4 are the key issue of the present meta-analysis. Our results of the moment divided by before, after, and during were heterogeneous; therefore, we can assume that the same phenomenon has been measured in a sufficiently similar way and part of the exercise effects on patients with cancer. Present results assumed the original normality of the studies and the random-effects model observed exercise intervention and respective periods, following a normal distribution, and that individual studies were random draws from our model distributions (table 2).

For numerous diagnosed with cancer, people mean living with cancer as a chronic disorder, while for survivors, there are inconvenient long-term and persistent negative effects of the tumor or its treatments. The goal of physical activity in cancer is to provide the possibility for people to live as healthy a life as possible, one devoid of extra chronic disease, and one in which late negative effects are minimized (Smith et al., 2013). For instance, the health-related physical fitness parameter measurements of cardiopulmonary fitness, muscular strength, flexibility, and balance exhibited statistically significant improvements from the preintervention to the postintervention assessments. Smith et al. (2013) indicated that the 6-minute walk was lately validated against VO2 peak testing in 50 people who had cancer and found to be reliable ($r = .93$) (Smith et al., 2013). Preceding reports indicated that strength measurements of weight lifted during the chest and leg presses increased in a time-dependent and age-dependent manner; that is, in general, strength was gained between pre and post measurements, but younger survivors improved more dramatically than older survivors throughout the program. This is consistent with the age-dependent response of the physiologic milieu of the neuromuscular system in younger adults (Musanti, Chao, & Collins, 2019).

This research has argued that, while the observed exercise period may well have a normal distribution, is being expected that the larger part of the heterogeneity would be most likely due to differences in the type of exercise and the respective periods carried out and we can observe significant differences in the mixed-effects analysis by 13 studies before the intervention and studies with longer interventions presented as subgroups during divides by three moments "a", "b" and "c". The qualities, effects of present models (tables 3 and 4) were developed to take differences explicitly into account by studies treatments and their respective periods of a study quality score. The aim was to get better exercise intervention and the respective period based on available studies. At first, the present authors intended to produce heterogeneous results by treatments and respective periods, aiming to look for covariates that may explain the treatment or periods heterogeneities, and stratify studies into more homogeneous subgroups (weeks of interventions) accordingly. When observed week results of those subgroups, the present meta-analysis assumed that the studies have been measuring the same effects, however, chronological studies presented more factors interfered in their heterogeneity, increasing the varying quality (tables 3 and 4). Therefore, the quality effects model with the relative effects of each study, with respective periods (figures 2 and 3) is, in our opinion, clearly the best choice to verify their impacts.

To the authors' knowledge, it is the first time that a meta-analysis verified the efficiency of the period that exercise can increase with effects the quality of life. Present results demonstrated that the exercise intervention time which had the lower consistency of effect size was on Shobeiri et al. (2016), with 40 weeks of endurance exercise in patients with cancer of mama, while Schimidt et al. (2015a) demonstrated the best effect size with 12 weeks of resistance training. Despite this important result, when observed the mixed-effects analysis, we can verify a similar point estimated between studies with 12 weeks, but a significant impact just of Schimidt et al. (2015a) study on the effect size of the practical exercise application. Yuri et al. (2017) and Schimidt et al. (2014) with 12 weeks demonstrated lower effect size than Schimidt et al. (2015a) and Wefel, Kesler, Noll, & Schagen (2015).

In the meta-analysis model (table 3) we can verify that overall meta-analysis rejected the null hypothesis and a heterogeneity test indicated that comparisons between the intervention and control group had differences in the quality of life of patients during the interventions and after the time of exercise intervention. Intervention and control groups had similar results in the EORCT Questionnaire QLQ C-30. L-square showed that a higher precision within effect sizes and 95%IC presented by the studies in figure 2. Tau squared demonstrated a high variance between the studies probably because there have different types of exercise and durations (i.e. week comparisons) and Tau demonstrated a high standard deviation of the normal curve of the studies' effects.

Regarding the exercise moment by weeks, mixed-effects analysis verified impacts in studies with more than 6 weeks of exercise intervention and an overall difference between weeks used – with more effect size in

the quality of life of patients in interventions between 4 and 16 weeks. Probably, the longer duration studies in the training are also associated with groups with a long time of treatment of cancer that is associated with comorbidities like depression, anxiety, and cognitive (Wefel, Kesler, Noll, & Schagen, 2015). Moreover, physical debilities are associated with the time of cancer treatment (Miranda, 2019; Napoleão, 2018). The lack of similar protocols is a limitation, as all studies presented different interventions and respective times. Most of the studies demonstrated between 6 and 16 weeks, three researchers realized between 24 and 48 weeks of intervention with exercise. This time spent on the interventions presented greater heterogeneity and, consequently, in practical implications - most research had shown moderate to strong effect sizes of exercise on the quality of life of patients with cancer. Tau squared demonstrated a high variance between the time of treatments, which had theoretical implications because protocols are dissimilar, this limitation of control and manipulation increases bias, reducing the chances to determine the best interventions to improve the quality of life in people with cancer.

Conclusion

The present meta-analysis demonstrated the effects of exercise on quality of life in cancer patients and therefore aimed to get a pooled estimate of effect size using Hedge's g , presenting relative weight and standardized mean difference. The results could be useful as well to get a more precise estimate of the time to increase the quality of life in cancer patients and the practical effects of time by weeks of randomized studies. The meta-analysis indicated a higher difference between them. Our results of the moment divided by before, after, and during were heterogeneous; therefore, we can assume that the same phenomenon has been measured in a sufficiently similar way and part of the exercise effects on patients with cancer. Present results assumed the original normality of the studies and the random-effects model observed exercise intervention and respective periods, following a normal distribution, and that individual studies were random draws from our model distributions. Future studies are necessary in order to conclude a causal relationship between the type of exercise and the time of intervention in cancer patients.

Conflicts of interest - The authors certify that they have no affiliations with or involvement in any organization or entity with any financial interest, or non-financial interest in the subject matter or materials discussed in this manuscript.

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