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BASIC STUDY

CANCER SURVIVORS AND AEROBIC EXERCISE: THE POSSIBLE EASIEST SOLUTION TO IMPROVE QUALITY OF LIFE BUT WHICH IS THE MOST EFFECTIVE INTENSITY?

SURVIVANTS DU CANCER ET EXERCICE AÉROBIE : LA SOLUTION LA PLUS SIMPLE POUR AMÉLIORER LA QUALITÉ DE VIE, MAIS QUELLE EST L'INTENSITÉ LA PLUS EFFICACE ?

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KEYWORDS : NEOPLASM ; AEROBIC ; QUALITYOFLIFE ; TRAININGINTENSITY ; SYSTEMATICREVIEW

MOTS CLÉS : NÉOPLASME ; AÉROBIE ;QUALITÉ DE VIE ; INTENSITÉ DE L'ENTRAÎNEMENT ;

SUMMARY

Objective. — Nowadays, the number of cancer survivors continues to grow. Physical activity is effective in increasing their quality of life. There is a paucity of systematic reviews focusing only on the effects of aerobic exercise on cancer survivor's quality of life and there is little; information about the most effective exercise intensity. The aim of this review is to investigate the effects of supervised aerobic training on the quality of life in cancer survivors. Additionally, the effect size of different training intensities will be presented. The hypothesis is that aerobic exercise will increase the quality of life and the most effective exercise intensity will be light to moderate.

Data source. — Literature search was performed using Medline/Ovid, APA PsycInfo and Scopus on the 6th February 2020. This study was subsequently updated to include studies published between the second week of February 2020 (6th February) and the third week of June 2021 (22 June 2021). Two authors independently screened the papers based on the titles and abstract, and when appropriate based on the full text. The Preferred Reporting Items for Systematic Reviews (PRISMA) statement was followed.

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Study selection. — Inclusion criteria were: adult cancer survivors, supervised (by professionals) aerobic exercise only, validated questionnaires to assess quality of life. The articles had to be written in English or French.

Results. — 10 papers were included. All studies, with the exception one, found significant improvements in quality of life. There was no correlation between the improvements and the exercise intensity.

Conclusion. — The present review demonstrated the effectiveness of aerobic exercise in improving quality of life in cancer survivors. Influence of exercise intensity is yet to be found.

RÉSUMÉ

Objectif. — De nos jours, le nombre de survivants du cancer continue de croître. L'activité physique est efficace pour améliorer leur qualité de vie. Il y a peu de revues systématiques portant uniquement sur les effets de l'exercice aérobie sur la qualité de vie des survivants du cancer et il y a peu d'information sur l'intensité de l'exercice la plus efficace. L'objectif de cette étude est d'étudier les effets de l'entraînement aérobie supervisée sur la qualité de vie des survivants du cancer. De plus, les effets des différentes intensités d'entraînement y seront présentées. L'hypothèse est que l'exercice aérobie augmentera la qualité de vie et que l'intensité d'exercice la plus efficace sera léger à modéré.

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Matériels et méthodes. —Une recherche documentaire a été effectuée avec Medline/Ovid, APA PsycInfo et Scopus le 6 février 2020. Cette étude a ensuite été mise à jour pour inclure des études publiées entre la deuxième semaine de février 2020 (6 février) et la troisième de juin 2021 (22 juin 2021). Deux auteurs ont indépendamment examiné les articles en fonction des titres et des résumés, et le cas échéant en fonction du texte intégral. La checklist sur les rapports privilégiés pour les examens systématiques (PRISMA) a été suivi.

Sélection des études. —Les critères d'inclusion étaient les suivants: survivants adultes du cancer, exercice aérobique supervisé (par des professionnels), questionnaires validés pour évaluer la qualité de vie. Les articles devaient être rédigés en anglais ou en français.

Résultats. —Dix articles ont été inclus. Toutes les études, à l'exception d'une, ont permis de constater des améliorations importantes de la qualité de vie. Il n'y avait aucune corrélation entre les améliorations et l'intensité de l'exercice.

Conclusion. — La présente revue a démontré l'efficacité de l'exercice aérobie pour améliorer la qualité de vie des survivants du cancer. L'influence de l'intensité de l'exercice reste à trouver.

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1. Abbreviations

BMI : body mass index

CLMIT group : low-intensity group

EORTC QOL-C30 FACT-G : Functional Assessment of Cancer Therapy-General

FACT-B : Functional Assessment of Cancer Therapy-Breast cancer

HRR : heart rate reserve

HRmax : Maximum heart rate

RPE : Rating Scale of Perceived. Exertion

LVHIIT group : high-intensity exercise group

MCS : mental component score

PCS : physical component score

PEDro scale : Physiotherapy Evidence Database Scale

PRISMA : The Preferred Reporting Items for Systematic Reviews

SF36 : The Short Form (36) Health Survey

VO2max : maximum oxygen consumption

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2. Introduction

Cancer is the second leading cause of death globally with an estimated 9.6 million deaths in 2018 [1]. Nevertheless, within the last few decades, early detection, and improved treatments of cancer significantly improved survival of oncological patients. According to the 'Cancer treatment and survivorship statistics, 2016' the number of cancer survivors just in America were 15.5 million in 2016 and it is expected to be more than 20 million by 2026 [2].

Cancer treatment (chemotherapy, radiation,...) leads to many undesired side effects such as pulmonary disease, cardiac dysfunction or failure, decreased cardio-pulmonary abilities, neurological deficits, liver injury, fatigue, and endocrine disorders [3]. Toxicities from the drugs and therapies lead to all of these consequences, and these side effects tend to persist over time [3]. This, in turn, negatively affects the daily functioning of cancer survivors. In addition, cancer is strongly linked with aging with almost half of survivors older than 70 year [2]. The effects of age, combined with the side effects of cancer itself, as well as its treatment, increase the burden of cancer [4] and lead patients to a more sedentary lifestyle [5]. This, the effects of age as well as the consequences of toxicities from the drugs and therapies tend to alter the quality of life of cancer survivors [6].

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According to the World Health Organization (WHO), quality of life is defined as "an individual's perception of their position in life in the context of the culture and value systems in which they live and in relation to their goals, expectations, standards and concerns. It is a broad ranging concept affected in a complex way by the person's physical health, psychological state, personal beliefs, social relationships and their relationship to salient features of their environment" [7].

The WHO recommends that adults (18 years of age and older) perform at least 150 minutes of moderate physical activity per week or at least 75 minutes of sustained activity [8]. Regular physical activity is associated with a lower risk of developing specific cancers such as colon, breast cancer or lung cancer [9,10]. Moreover, it is well-established that physical activity can improve health related quality of life [3,4,11]. In particular, combining resistance and aerobic training programs in cancer survivors has been demonstrated to be effective in improving cancer patients and/or cancer survivor's quality of life [12]. In addition, supervised training sessions seem to be more effective than unsupervised or home-based training programs in this population [4]. Even though it is well-established that the most effective improvements in quality of life in cancer survivors are obtained combining resistance and aerobic training, the psychological perspective must be taken into consideration. It must face the fact that this type of intervention requires a huge behavioural change and it is hard to be implemented in real life. Previous studies have shown that few cancer survivors are actually engaged in physical activity

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due to several institutional, community and internal barriers that they have to face [13—16]. Aerobic exercise is defined as a type of physical activity primarily dependent on the aerobic energy generating process [17]. This specific type of exercise, rather than resistance or other types of training, is readily accessible, requiring no specialist knowledge or equipment [18]. For all these reasons, it might be easier, for a cancer survivor, to engage in aerobic exercise training alone.

Several studies were conducted on this topic as far as breast cancer survivors concern. The effect of aerobic exercise alone on quality of life has been demonstrated to be effective in enhancing the quality of life. Moreover, different intensities were found to have different effects: moderate intensity was demonstrated to be the most effective in improving fatigue [19,20], anxiety and depressive symptoms [4]. All these aspects are deeply related to the quality of life. Another recent review has been conducted in this field: Marinari et al. suggested that light to moderate aerobic physical activity would be the most effective in reducing the risk, primary, secondary and tertiary, of breast cancer. According to the authors, this intensity leads to oxidative stress, inducing the decrease in body fat which is associated with a decrease of some important risk factors for breast cancer such as the levels of sexual hormones, hormones regulating metabolism, and the rate of inflammation cells [21]. In addition, physical activity decreases the insulino-resistance and therefore it reduces the blood sugar that could promote the proliferation of cancer cells [21]. According to these evidences, it might be hypothesized that light to

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moderate intensity is the most effective in improving quality of life in breast cancer survivors and also in other types of cancer survivors.

In addition, there are reviews focusing on the effect of only resistance training on quality of life of this growing population [22,23] but there are only two reviews [12,24] focused only on aerobic exercise on breast cancer survivors.

The present review will enrich the work of Bekhet et al. (2019) [24] and Sweggers [12], and will answer the following question: which aerobic exercise intensity is most effective in improving quality of life of all types of cancer survivors? The hypothesis is that light to moderate intensity will be the most effective exercise intensity and not only in breast cancer survivors but also for all types of cancer survivors. The results of the present study will provide important information that can be applied to clinical and public health practice.

3. Material and method

The Preferred Reporting Items for Systematic Reviews (PRISMA) statement has been rigorously followed (Appendix 1).

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3.1. IDENTIFICATION AND SELECTION OF STUDIES

3.1.1. SEARCH STRATEGY

A comprehensive literature search was conducted the 7th February/2020, through three electronic databases: Medline/Ovid, APA PsycInfo and Scopus. This study was subsequently updated to include studies published between the second week of February 2020 (7th February) and the third week of June 2021 (22 June).

The terms used for the search strategy can be found in the supplementary Appendix 2.

3.1.2. STUDY SELECTION

Excel was used to import the results of the search. Two authors (C.L. and A.M.) manually identified and deleted the duplicate references. The titles and abstracts were independently screened by the same authors. Subsequently, the full text of the remaining articles was examined independently by the two reviewers. For each step, if there were discrepancies, a discussion to either include or exclude the article helped make the decision. If the issue remained unresolved, a third evaluator (D.M.) had the final decision. The selection of articles was based on predetermined inclusion and exclusion criteria (Table 1).

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The "after treatment" element, identified as one of the inclusion criteria, aims to specify that patients must have completed all cancer treatments (chemotherapy, hormone therapy, radiotherapy, immunotherapy).

As far as the inclusion criteria of the population, subjects over 80 years old because they could present associated pathologies as cognitive disorders (not mentioned in the article) and they could not reach a certain intensity.

Articles that included interventions longer than 6 months were excluded because the review focused on the short- and medium-term effects of aerobic exercise on quality of life and not on long-term effects.

Even though aerobic exercise does not require any specialized knowledge or equipment [18], the authors decided to exclude studies that included unsupervised training because to reduce the risk of bias, since during a homebased training it is impossible to verify whether the person performed the exercise correctly.

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Table 1 *Inclusion and exclusion criteria.*

	Inclusion criteria	Exclusion criteria
Study design	Interventional studies	Non interventional studies
Population	Cancer survivors between 18—80 years after their treatments	Animals Patients who are still undergoing cancer treatments. Patients who reported impairments of the cardiovascular, pulmonary, or musculoskeletal systems and/or cognitive impairments, neurodegenerative diseases (SNP/SNC), amputation and/or chronic illnesses children or beyond 80 years people
Intervention	The intervention was supervised by health professionals[a] and consisted exclusively of aerobic training, lasting from 6 weeks to 6 months	The intervention combined with other type of exercise such as resistance training or flexibility exercises or combined with psychological interventions, lasting beyond 6 months or less than 6 weeks
Outcomes	Quality of life through a validated questionnaire	Outcomes about other subject of quality of life outcomes with non-validated questionnaire. outcomes about just one item of quality of life
Language	Only French and English	Other language of English or French

[a] Health professional meant: a professional who has a link with health and physical activity (for example: a physiotherapist, a sports educator, ...).

3.2. ASSESSMENT OF CHARACTERISTICS OF STUDIES AND DATA ANALYSIS

3.2.1. DATA ITEM OF INTEREST AND SYNTHESIS OF RESULTS

Key data from the selected articles were extracted by the same two authors including information pertaining to the authors and years of publication, mean age of participants, BMI, type of cancer, time since last treatment, sample size, duration and frequency of the intervention, training equipment, intervention protocol, training intensity, instruments used to measure the outcomes.

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The study characteristics were presented in Table 2. The quality of studies assessment was presented in Table 3, findings in Tables 4 and 5. Limitations are presented in the discussion section. Any discrepancies between data extracted were discussed and consensus was achieved so that the included articles were identified.

In addition, included articles were divided in different groups based on the studied exercise intensity (Table 6). Moreover, studies used different variables to categorize the intensity of aerobic exercise (VO2 max (maximum oxygen consumption), HRR (heart rate reserve), HRmax (Maximum heart rate), RPE (Rating Scale of Perceived. Exertion)). The different exercise intensity thresholds were determined through scientific sources about VO2 max, HRR, HR max, RPE. According to the study of Borg (1982), intensity expressed from 9 to 11 RPE was considered low, RPE from 12 to 14 was considered moderate intensity while an intensity scored as 14 or more RPE was considered high [25]. According to the study of Gaber et al. (2011) [26] an exercise intensity <30% HHR is classified as very low intensity, from 30 to 39%HRR is considered light intensity, moderate intensity range from 40 to 59% HRR while vigorous intensity range from 60 to 89%HRR. Regarding the HR max, <57% HR max is considered as very light intensity, light intensity is defined as an intensity from 57 to 63% HR max, moderate intensity range from 64 to 76 and vigorous intensity range from 77 to 95%HR max [26]. Based on the guide for promotion and prescription

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of physical activity of the "Haute Autorité de santé" [27], < 50% VO2 max. was considered as low intensity, moderate intensity range from 50 to 75%VO max while > 75 VO2 max was considered as high intensity. In the discussion section the limitations of each article were analyzed. The principal summary measures are the differences between the score at validated quality of life questionnaire before and after the aerobic exercise training. We decided to investigate the effect of aerobic exercise on quality of life before exploring exercise intensities. For all missing data, the authors of included articles were solicited.

3.2.2. SUMMARY OF QUALITY OF LIFE QUESTIONNAIRES USED

The principal summary measure is the quality of life and it was assessed by the included articles through five different validated questionnaires. The questionnaires are presented and briefly described in the following list: The SF-36, is a 36-item scale that assess 8 health domains: (1) physical functioning, (2) role-physical, (3) bodily pain, (4) general health, (5) vitality, (6) social functioning, (7) role-emotional, and (8) mental health. Then, by adding the prespecified weighted contributions of each of the eight health domains scores, it is possible to calculate the mental component score (MCS) and the physical component score (PCS) [28]. The FACT-G is a 27-item scale, assessing 4 categories including (1) physical well-being, (2) social/family well-being, (3) emotional well-being, (4) functional well-being [29]. Another questionnaire is the FACT-B which is

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a 37 item scale representing 5 subscales: (1) physical well-being, (2) social/family wellbeing, (3) emotional well-being, (4) functional well-being, (5) breast cancer-related well-being (a 5-point scale from 0 (not at all), 2 (somewhat) to 4 (very much) [29]. The EORTC QOL-C 30 is a 30-item questionnaire, assessing 5 functional scales including (1) physical, (2) role, (3) cognitive, (4) emotional, and (5) social functioning. 3 symptom scales were used (1) fatigue, (2) pain, (3) nausea, and (4) vomiting, and 6 symptoms reported by cancer patients (1) dyspnea, (2) loss of appetite, (3) insomnia, (4) constipation, (5) diarrhea, and (6) financial difficulties. For each parameter the score ranged from 0 to 100 [30]. The last questionnaire of the list is the Quality of life Index for cancer patients. It is an index that includes 14 groups of questions divided into general physical condition, normal human activities, and personal attitudes related to general quality of life. Each parameter can be score from 0 (which corresponds to the worst) to100 (corresponding to the best) [31]. Difference in means of quality of life questionnaires before and after aerobic exercise were taken into consideration. When it was not possible to extract this information from the included articles, mean and standard deviation after aerobic exercise were compared with mean and standard deviation of a control group.

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3.2.3. Study quality

The assessment of methodological quality was performed independently by two reviewers. The quality assessment of the included articles was conducted using the PEDro scale (Physiotherapy Evidence Database Scale) [32]. The quality score was based on eleven items. One of these items was not included in the total score (items 1). The maximum score was 10, which represented the highest methodological quality. Studies were considered to be of excellent quality if they had a score of 10 or 9, they were considered to be good quality if they had a score between 8 and 6, a fair quality if they had 4 or 5 and poor quality if they had between 3 and 0 [33]. The two authors compared their results about the quality assessment of each study. All discrepancies were discussed and resolved. Quality assessment results are summarized in Table 3.

3.2.4. Statistical analysis

For the results of the quality of life questionnaire, a Pvalue of 0.05 was classified as statistically significant. The effect size was assessed for each outcome by calculating the Cohen's D to indicate the standardized difference between outcomes reported by the different studies (6). The effect sizes were considered as very small when D Cohen was between 0.01 and 0.2. A D Cohen ranging from 0.5 and 0.8 was considered as medium while from 0.8 to 1.2 was considered as large. The

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effect size was defined as very large when D Cohen was between 1.2 and 2. The Spearman's rank-order correlations were calculated using the R software (version 2.4-1).

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Table 2. *Study characteristics.*

Authors/year	Participants Age Mean ± SD	BMI at baseline Mean ± SD (Kg/m^2)	Type of cancer	Time from the last surgery and/or treatment before the intervention	Sample size	Duration and frequency of intervention	Training equipment	Training intensity	Intervention protocol	Instrument to measure outcome
Ray et al., 2018 [33]	Mean age 55.8 ± N/A and 58.3 ± 8.5	White Americans 32.4 ± 4.6 Afro-Americans 33.0 ± 4.2	Colorectal cancer	Mean time after last treatment 3.1 ± 2.5 months from last treatment	7 participants	2 per week 12 weeks	Cycle ergometers	Week 1–4 50/60% Vo2Peak Week 5–8 60/70% VO_2 Peak Week 9–12 70/80% VO_2 Peak	Week 1–4 5′ warm up, 20/25′, 5′ cool down Week 5–8 5′ warm up, 25/35′, 5′ cool down Week 9–12 5′ warm up, 35/45′, 5′ cool down	SF-36 + FACT-C (cancer colorectal)
Adams et al., 2018 [42]	43.7 ± 10.8	N/A	Testicular cancer	Completed treatment	62 participants	3 per week 12 weeks	On uphill treadmill walking or running	From 75% VO_2 Peak to 95% VO_2 Peak	5′ warm up, 4′ × 4 intervals/3′ active recovery, 5′ cool down	SF-36

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Authors/year	Participants Age Mean ± SD	BMI at baseline Mean ± SD (Kg/m^2)	Type of cancer	Time from the last surgery and/or treatment before the intervention	Sample size	Duration and frequency of intervention	Training equipment	Training intensity	Intervention protocol	Instrument to measure outcome
Toohey et al., 2018 [34]	51.48 ± 12.45	26.43 ± 4.08	All types of cancer were included	Participants within the first 24 months of diagnosis. In the post-treatment phase of the PEACE organizational model, once the acute effects of medical treatments had dissipated	57 participants	3 per week 12 weeks	Stationary bike	LVHIIT: 85% HRmax CLMIT:55% HRmax	LVHIIT group: 5′ warm up, 30′ × 7 intervals/1′ passive recovery, 5′ cool down CLMIT group:5′ warm up, 20′ cycling, 5′ cool down	FACT-G

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Authors/year	Participants Age Mean ± SD	BMI at baseline Mean ± SD (Kg/m^2)	Type of cancer	Time from the last surgery and/or treatment before the intervention	Sample size	Duration and frequency of intervention	Training equipment	Training intensity	Intervention protocol	Instrument to measure outcome
Di Blasio et al., 2016 [35]	56.17 ± 3.67	26.82 ± 4.23	Breast cancer patients	8–12 month from surgery post-treatment	23 breast cancer + 23 healthy	3 time per week 12 weeks	No equipment (because Nordic Walking)	Week 1–4 10–11 RPE Week 5–8 12–13 RPE Week 9–12 13–14 RPE	Week 1–4 15′ warm up, 45′ Nordic walking, 10′ cool down Week 5–8 15′ warm up, 45′ Nordic walking, 10′ cool down Week 9–12 15′ warm up, 45′ Nordic walking, 10′ cool down	SF-36

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Authors/year	Participants Age Mean ± SD	BMI at baseline Mean ± SD (Kg/m^2)	Type of cancer	Time from the last surgery and/or treatment before the intervention	Sample size	Duration and frequency of intervention	Training equipment	Training intensity	Intervention protocol	Instrument to measure outcome
De Jesus et al., 2017 [41]	53.1 ± 8.43	N/A	Breast cancer	After 4 months of the completion of therapy	17 females	3 per week 16 weeks	Cycle ergometers/treadmill/stepper	Week 1–4 50% VO_2 max Week 5–8 60% VO_2 max Week 9–16 70% VO_2 max	Week 1–3 15′ aerobic exercise Week 4 20′ aerobic exercise Week 5 25′ aerobic exercise Week 6 30′ aerobic exercise Week 7 35′ aerobic exercise Week 8 40′ aerobic exercise Week 9–16 45′ aerobic exercise	FACT-B

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Authors/year	Participants Age Mean ± SD	BMI at baseline Mean ± SD (Kg/m^2)	Type of cancer	Time from the last surgery and/or treatment before the intervention	Sample size	Duration and frequency of intervention	Training equipment	Training intensity	Intervention protocol	Instrument to measure outcome
Kellie Toohey et al., 2016 [40]	51.6 ± 13.01	N/A	Colon, cervical, melanoma, ovarian, breast, and a diagnosis breast and uterine, and breast and liver cancer	In post-treatment phase of the physical activity across the cancer experience (PEACE) organizational model, once the acute effects of medical treatments had dissipated	16 females' participants	3 per week 12 weeks	Stationary bike	LVHIIT group: 85% HRmax CLMIT group:55% HRmax	LVHIIT group: 5′ warm up, 30′ × 7 intervals/1′ passive recovery, 5′ cool down CLMIT group:5′ warm up, 20′ cycling, 5′ cool down	FACT-G
Vardar Yagli et al., 2015 [36]	47.38 ± 7.57	Aerobic exercise group = 29.27 ± 5.92 Yoga and aerobic exercise group = 29.16 ± 5.74	Unilateral breast cancer	Completed at least 3 years prior participated in the study	40 participants	3 per week 6 weeks	Treadmill	60/70% HRmax–90% HRmax	5′ warm up, 20′ aerobic exercise, 5′/10′ cool down	EORTC QOL-C30

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Authors/year	Participants Age Mean ± SD	BMI at baseline Mean ± SD (Kg/m^2)	Type of cancer	Time from the last surgery and/or treatment before the intervention	Sample size	Duration and frequency of intervention	Training equipment	Training intensity	Intervention protocol	Instrument to measure outcome
Murtezani et al., 2014 [37]	53 ± 11	25.9 ± 2.8	Breast cancer survivors	Completed treatment Mean time since surgery was approximately 19 months	62 females' participants	3 per week 10 weeks	Treadmill/stationary bike/stair-climbing machine	From 50% to 75% HRmax	5′ warm up, 15′ aerobic exercise (increased by 2, 2 min a week, such that it was 35 min during week 10) divided equally among the three exercise modalities, 5′ cool down	FACT-B

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Authors/year	Participants Age Mean ± SD	BMI at baseline Mean ± SD (Kg/m^2)	Type of cancer	Time from the last surgery and/or treatment before the intervention	Sample size	Duration and frequency of intervention	Training equipment	Training intensity	Intervention protocol	Instrument to measure outcome
Burnham and Anthony Wilcox, 2002 [38]	Low intensity group: 54.2 ± 8.1 Moderate intensity group:50.7 ± 8.2	Control group: 23.8 Low intensity group: 31.4 Moderate intensity group: 24.1	Breast, colon, or lung cancer	At least 2 months post-cancer treatment	18 participants	3 time per week 10 weeks	Treadmill/stationary bike/stair-climbing machine	25–60% HRR (LI = from 25–30% HRR to approximately 40% HRR; HI = from 40–50% HRR to 60% HRR)	14′. It was divided equally among the three exercise modalities: 4′ and 40′ on the treadmill, stair-climber, and stationary bicycle in a rotational order (increased by 2 min a week, such that it was 32 min during week 10)	Quality of life index for cancer patient

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Courneya et al., 2003 [39]	Mean 59 ± 5	29.2 ± 6.6 Exercise group: 29.4 ± 7.4	Breast cancer	Completed treatment	52 participants	3 time per week 15 weeks				

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Table 3. *Studies quality score.*

Authors/year	Items 1 (optional)	Items 2	Items 3	Items 4	Items 5	Items 6	Items 7	Items 8	Items 9	Items 10	Items 11	Total (/10)
Ray et al., 2018 [33]	Yes	?	?	No	No	No	?	No	Yes	Yes	Yes	3
Adams et al., 2018 [42]	Yes	Yes	No	Yes	No	No	?	Yes	Yes	Yes	Yes	6
Toohey et al., 2018 [34]	Yes	Yes	Yes	Yes	?	?	?	No	?	Yes	Yes	5
Di Blasio et al., 2016 [35]	Yes	Yes	?	No	No	No	?	Yes	Yes	Yes	Yes	5
De Jesus et al., 2017 [41]	Yes	No	No	Yes	No	No	No	Yes	Yes	Yes	Yes	5
Toohey et al., 2016 [40]	Yes	Yes	?	Yes	?	?	?	Yes	Yes	Yes	Yes	6
Vardar Yagli et al., 2015 [36]	Yes	Yes	Yes	Yes	No	No	?	No	No	Yes	Yes	5
Ardiana Murtezani et al., 2014 [37]	Yes	Yes	?	Yes	?	?	Yes	No	No	Yes	Yes	5
Courneya et al., 2003 [39]	Yes	Yes	Yes	Yes	No	No	Yes	Yes	Yes	Yes	Yes	8
Burnham and Wilcox, 2002 [38]	Yes	Yes	?	Yes	?	?	?	Yes	No	Yes	Yes	5

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Table 4. *Results of quality of life questionnaires: group A.*

Authors/year	Before intervention (mean ± SD)	After intervention (mean ± SD)	*P*-value (pre-/post-test)
Ray et al., 2018 [33]	SF36 Physical component 48.3 ± 9.8 Mental component 53.4 ± 5.0 FACT-C 108.9 ± 23.1	SF36 Physical component 51.7 ± 7.2 Mental component 54.8 ± 3.9 FACT-C 113.6 ± 15.7	SF36 Physical component *P* = 0.040* Mental component *P* = 0.444 FACT-C *P* = 0.407
Di Blasio et al., 2016 [35]	SF36 Physical component Physical activity 79.35 ± 14.87 Physical activity limitation 65.04 ± 40.91 Physical pain 65.70 ± 26.91 Physical health 210.08 ± 74.62 Mental component: N/A	SF36 Physical component Physical activity 83.70 ± 10.35 Physical activity limitation 80.43 ± 23.78 Physical pain 71.69 ± 22.50 Physical health 235.82 ± 47.54 Mental component: N/A	SF36 Physical component Physical activity *P* = 0.02* Physical activity limitation *P* = 0.04* Physical pain *P* = 0.01* Physical health *P* = 0.01* Mental component: N/A
De Jesus et al., 2017 [41]	FACT-B Physical well-being 18.5 ± 6.1 Functional well-being 15.7 ± 6.3 Social/family well-being 21.3 ± 6.1 Emotional well-being 17.4 ± 5.2 Total well-being 72.8 ± 18.3	FACT-B Physical well-being 22.3 ± 4.9 Functional well-being 19.4 ± 6.1 Social/family well-being 18 ± 6.5 Emotional well-being 18 ± 4.3 Total well-being 77.6 ± 17.4	FACT-B Physical well-being *P* ≤ 0.01* Functional well-being *P* ≤ 0.01* Social/family well-being *P* ≤ 0.01* (attention for this variable improvement is done for the control group) Emotional well-being *P* = 0.40 Total well-being *P* = 0.02*
Toohey et al., 2016 [40]	FACT-G CLMIT group: 81.25 ± 9.45 LVHIITgroup: 77.63 ± 13.59	FACT-G CLMIT group: 85.88 ± 7.38 LVHIIT group: 89.50 ± 6.82	FACT-G CLMIT group: *P* = 0.04* LVHIIT group: *P* = 0.01*
Vardar Yagli et al., 2015 [36]	EORTC QOL-C30 Global QOL 50.00 ± 18.81 Physical functioning 62.85 ± 18.56	EORTC QOL-C30 Global QOL 66.26 ± 17.96 Physical functioning 80.95 ± 18.77	EORTC QOL-C30 Global QOL *P* ≤ 0.05** Physical functioning *P* ≥ 0.05

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Authors/year	Before intervention (mean ± SD)	After intervention (mean ± SD)	*P*-value (pre-/post-test)
	Cognitive functioning 68.25 ± 82.25 Emotional functioning 78.57 ± 19.82 Social functioning 65.87 ± 24.98 Role functioning 90.47 ± 13.51	Cognitive functioning 81.74 ± 21.66 Emotional functioning 86.90 ± 13.83 Social functioning 76.19 ± 21.45 Role functioning 93.65 ± 13.41	Cognitive functioning $P \geq 0.05$ Emotional functioning $P \leq 0.05$** Social functioning $P \leq 0.05$** Role functioning $P \leq 0.05$**

SD: Standard deviation, **: statistically significant after aerobic intervention; N/A: No details of the result was present in the article.

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Table 5. *Results of quality of life questionnaire: group B.*

Authors/year	Before intervention (mean ± SD) (exercise group)	After intervention (mean ± SD) (control group)	Before intervention (mean ± SD) (exercise group)	After intervention (mean ± SD) (control group)	P-valeur (pre-/post-, control/exercise)
Murtezani et al., 2014 [37]	FACT-B Primary outcome 99.8 ± 11.4 FACT-G: 77.4 ± 9 Physical well-being: 18.2 ± 7.1 Functional well-being: 22.5 ± 2.7 Social/family well-being: 19.8 ± 2.8 Emotional well-being: 17.4 ± 2.7 Breast cancer subscale: 22.4 ± 5	FACT-B Primary outcome 102 ± 10.6 FACT-G: 79.6 ± 8.5 Physical well-being: mean ± SD = 20.8 ± 4.8 Functional well-being: 22.1 ± 2.5 Social/family well-being: 18.9 ± -3.1 Emotional well-being: 17.7 ± 3.6 Breast cancer subscale: 22.9 ± 5.74	FACT-B Primary outcome 113.2 ± 9.7 FACT-G: 86.5 ± 7.3 Physical well-being: 22.6 ± 4.4 Functional well-being: 24.2 ± 2.8 Social/family well-being: 20.2 ± 2.8 Emotional well-being: 19.5 ± 3.3 Breast cancer subscale: 26.6 ± 5.6	FACT-B Primary outcome 101.2 ± 9.5 FACT-G: 79.4 ± 7.5 Physical well-being: 19.4 ± 4.4 Functional well-being: 23 ± 2.5 Social/family well-being: 18.3 ± 3.5 Emotional well-being: 18.3 ± 3.5 Breast cancer subscale: 22.1 ± 5.5	FACT-B Primary outcome P = 0.003** FACT-G P = 0.008** Physical well-being: P = 0.141 Functional well-being: P = 0.010** Social/family well-being: P = 0.761 Emotional well-being: P = 0.035** Breast cancer subscale: P = 0.063
Courneya et al., 2003 [39]	FACT-B Primary outcome 110.5 ± 19 FACT-G: 85.5 ± 12.4 Physical well-being: 23.3 ± 3.6 Functional well-being: 22.5 ± 4.3 Social/family well-being: 20.5 ± 3.7 Emotional well-being: 19.2 ± 3.9 Breast cancer subscale: 25 ± 7.6	FACT-B Primary outcome 115.5 ± 12.4 FACT-G: 88.8 ± 9 Physical well-being: 25.4 ± 2.6 Functional well-being: 22.8 ± 3.8 Social/family well-being: 21.1 ± 3.3 Emotional well-being: 19.4 ± 2.8 Breast cancer subscale: 26.7 ± 4.6	FACT-B Primary outcome 119.6 ± 16.9 FACT-G: 91.3 ± 11 Physical well-being: 25.3 ± 2.5 Functional well-being: 23.4 ± 4 Social/family well-being: 21.1 ± 3.5 Emotional well-being: 21.5 ± 3.4 Breast cancer subscale: 28.4 ± 6.7	FACT-B Primary outcome 115.8 ± 14.9 FACT-G: 89.3 ± 10.9 Physical well-being: 25.3 ± 2.8 Functional well-being: 23.1 ± 4 Social/family well-being: 20.7 ± 3.6 Emotional well-being: 20.3 ± 3 Breast cancer subscale: 26.4 ± 5.1	FACT-B Primary outcome P = 0.001** FACT-G: P = 0.016** Physical well-being: P = 0.001** Functional well-being: P = 0.468 Social/family well-being: P = 0.180 Emotional well-being: P = 0.090 Breast cancer subscale: P = 0.001**

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Authors/year	Before intervention (mean ± SD) (exercise group)	After intervention (mean ± SD) (control group)	Before intervention (mean ± SD) (exercise group)	After intervention (mean ± SD) (control group)	P-valeur (pre-/post-, control/exercise)
Adams et al., 2018 [42]	SF36 Mental Component: 48 ± 9.4 Physical Component: 51 ± 7.3 Physical functioning 52.6 ± 6.9 Role- physical 50.0 ± 10.9 Bodily pain 50.7 ± 7.0 General health 48.5 ± 7.5 Vitality 51.2 ± 8.1 Social functioning 43.0 ± 7.6 Role emotional 49.5 ± 9.0 Mental health 50.9 ± 9.1	SF36 Mental Component: 50 ± 6.7 Physical Component: 53.4 ± 5.9 Physical functioning 54.1 ± 4.1 Role- physical 53.9 ± 5.3 Bodily pain 53.5 ± 8.4 General health 51.0 ± 8.1 Vitality 52.9 ± 9.6 Social functioning 44.2 ± 5.0 Role emotional 52.0 ± 6.7 Mental health 53.7 ± 6.4	SF36 Mental Component: 50.4 ± 6.3 Physical Component: 53.6 ± 5.2 Physical functioning 54.4 ± 4.4 Role- physical 53.4 ± 7.2 Bodily pain 52.5 ± 7.3 General health 52.2 ± 6.8 Vitality 55.0 ± 7.8 Social functioning 45.0 ± 5.1 Role emotional 51.4 ± 6.5 Mental health 53.4 ± 5.2	SF36 Mental Component: 47.3 ± 9.3 Physical Component: 54.1 ± 7 Physical functioning 54.8 ± 3.7 Role- physical 53.7 ± 6.0 Bodily pain 52.8 ± 7.9 General health 50.9 ± 8.3 Vitality 50.8 ± 8.9 Social functioning 42.6 ± 7.4 Role emotional 51.1 ± 7.7 Mental health 51.0 ± 8.3	SF36 Mental Component: P = 0.034** Physical Component: P = 0.34 Physical functioning: P = 0.77 Role-physical: P = 0.048** Bodily pain: P = 0.41 General health: P = 0.016** Vitality: P = 0.001** Social functioning: P = 0.011** General health: P = 0.016** Role-physical: P = 0.048** Mental health: P = 0.054
Toohey et al., 2018 [34]	FACT-G LVHIIT group: N/A CLMIT group: N/A	FACT-G LVHIIT group: N/A CLMIT group: N/A	FACT-G LVHIIT group: N/A CLMIT group: N/A	FACT-G LVHIIT group: N/A CLMIT group: N/A	FACT-G LVHIIT group: significantly improved the QQL score compared with CLMIT group and control group Physical well-being: LVHIIT and CLMIT significantly improved compared with control group (P = 0.02)** Functional well-being: LVHIIT significantly improved compared with CLMIT and control group (P = 0.02)** Social/family well-being: no statistically significant differences among the groups (P = 0.057) Emotional well-being: LVHIIT

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Authors/year	Before intervention (mean ± SD) (exercise group)	After intervention (mean ± SD) (control group)	Before intervention (mean ± SD) (exercise group)	After intervention (mean ± SD) (control group)	P-valeur (pre-/post-, control/exercise)
					group significantly improved compared with CLMIT group and control group (P ≤ 0.01)**
Burnham and Wilcox, 2002 [38]	Quality of life Index for cancer patients: mean ± SD = 85.7 ± 13.7	Quality of life Index for cancer patients: mean ± SD = 88.5 ± 8.3	Quality of life Index for cancer patients: mean ± SD = 95.1 ± 4.4	Quality of life Index for cancer patients: mean ± SD = 86.6 ± 6.2	The analysis revealed a significant increase in quality of life when compared with control group (P ≤ 0

SD: Standard deviation; **: statistically significant compared to control group.

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Table 6. Effect size and intensity.

Authors/Years	*D* Cohen
Vigorous intensity	
Adams et al., 2018 [42]	SF36 Physical Component Score = 0.41. (Small) Mental Component Score = 0.30. (small)* Vitality = 0.48. (small)* Social functioning = 0.31 (small)* General Health = 0.52. (medium)* Role-physique = 0.24 (small)* Mental health = 0.34 (small)
Toohey et al., 2018 [34]: LVHIIT group	FACT-G Physical well-being = 0.89 (large)* Functional well-being = 0.96 (large)* Emotional well-being = 1.04 (large)* Social well-being = 0.35 (small)
Toohey et al., 2016 [40] LVHIIT group	FACT-G = 1.10 (large)*
Moderate to vigorous intensity	
Ray et al., 2018 [33]	SF36 Physical component = 0.40 (small)* Mental component = 0.31 (small) FACT-C = 0.24 (small)
Vardar Yağlı et al., 2015 [36]	EORTC QOL-C30 Global score = 0.88 (large)* Physical functioning = 0.97 (large) Cognitive functioning = 0.22 (small) Emotional functioning = 0.49 (small)* Social functioning = 0.44 (small)* Role functioning = 0.24 (small)*
Courneya et al., 2003 [39]	FACT-B (primary outcomes) = 0.51 (medium)* FACT-B FACT-G = 0.49 (small)* Physical well-being = 0.65 (medium)* Functional well-being = 0.22 (small) Social well-being = 0.17 (very small) Emotional well-being = 0.63 (medium) Breast cancer subscale = 0.47 (small)*
Low to moderate intensity	

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Authors/Years	*D* Cohen
Murtezani et al., 2014 [37]	FACT-B (primary outcome) = 1.27 (very large)* FACT-G = 1.11 (large)* Physical well-being = 0.74 (medium) Functional well-being = 0.62 (medium)* Social/family well-being = 0.14 (small) Emotional well-being = 0.70 (medium)* Breast cancer subscale = 0.79 (medium)
De Jesus et al., 2017 [41]	FACT-B Physical well-being = 0.69 (medium)* Social/family well-being = 0.52 (medium)* Emotional well-being = 0.13 (small) Functional well-being = 0.60 (medium)* Total well-being = 0.27 (small)*
Di Blasio et al., 2016 [35]	SF36 Physical component Physical activity = 0.33 (small)* Physical activity limitation = 0.46 (small)* Physical pain = 0.24(small)* Physical health = 0.41 (small)* Mental component = N/A
Burnham and Wilcox, 2002 [38]	Quality of life Index for cancer patients = 0.92 (large)*
Low intensity (no study in this intensity)	
Toohey et al., 2018 [34] CLMIT group	FACT-G Physical well-being = 0.61 (medium)* Functional well-being = 0.64 (medium) Emotional well-being = 0.15 (small) Social well-being = 0.20 (small)
Toohey et al., 2016 [40] CLMIT group	FACT-G = 0.55 (medium)*

*: D Cohen of statistically significant results.

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4. Results

4.1. FLOW OF STUDIES THROUGH THE REVIEW

The search retrieved a total of 3288 papers. After duplicates removal the number of likely relevant articles was 2962. After screening by title and abstract, a total of 2731 articles were excluded because they did not meet the inclusion criteria. The remaining 231 studies were included, and the full papers were obtained. After screening the full papers independently and after a discussion between authors to resolve discrepancies in the selection process took place, 221 articles because they did not meet the inclusion and exclusion criteria. A total of 10 papers were included in the review according to the predetermined inclusion criteria.

4.2. CHARACTERISTICS OF STUDIES

Characteristics of the 10 included articles were summarized in Table 2. Out of those studies, there were 353 participants (any group combined: control, yoga, aerobic) and of these only 215 participants received aerobic training exclusively (high, low intensity, etc.).

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4.2.1. PATIENTS CHARACTERISTICS

The mean of age of the participants was 52.87 ± 4.38 years ranging from 44 to 59 years. Most of the included articles [34—40] calculated the mean BMI (Body Mass Index) of participants at the baseline, which averaged from 26.4 to 33.8Kg/m2. Three studies [41—43] did not mention the BMI.

Five studies [36—38,40,42] only included breast cancer patients, another study include only testicular cancer patients, another one [34] focused just on colorectal cancer patients. The remaining included articles investigated multiple types of cancer patients [35,39,41] (breast, cervical, liver, esophageal, colon, lung,...).

4.2.2. QUESTIONNAIRE OF QUALITY OF LIFE

Out of the 10 studies, 2 used the SF36 questionnaire to assess the quality of life [36,43], 1 used the EORTC QOL-C30 [37], 2 the FACT-G [35,41], 3 the FACT-B [37,39,41] (two of which contained the questionnaire FACT-G [38,40], 1 Quality of life index for cancer patients [39] and one used a combination of the SF36 and FACT-C [34]).

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4.2.3. Training characteristics

The duration of training averaged between 6 and 16 weeks. The mean duration of intervention was 11.7 ± 2.8 weeks. The training frequency was 3 times per week for all of the included articles [35—38,40—43] with the exception of the Ray et al.'s study (2018) [34] where participants trained twice per week. In the study of Burnham and Wilcox (2002) [39] the frequency was not specified.

The majority of the included articles [34,35,37,40—42] used just one training equipment, either treadmill, stationary bike, or cycle ergometers. One study [36] used no equipment (Nordic walking) while the study of Burnham TR and Wilcox A [39] used cycle ergometers, treadmill and stepper for the training intervention. Two of the included articles [35,41] included two intervention groups: lowintensity group (CLMIT group) and high-intensity exercise group (LVHIIT group).

4.2.4. Training intensity

Exercise intensities varied among the included articles. These intensities are represented in the Table 6. Moreover, studies used different variables to categorize the intensity of aerobic exercise (VO2 max, HRR, HRmax, RPE). For the studies using VO2 max to

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characterize the intensity [34,40,42,43] the mean intensity was 70.63 ± 10.87% VO2 max, and varied between 50% VO2 max to 95% VO2 max. The studies who used the HRmax [35,37,38,41] had a mean of intensity of 68.96 ± 4.58%, and varied between 50% to 90% of HR max. Only one study used the RPE [36]. The mean of this study's intensity was 12 ± 1.58 RPE. The last study used the HRR to categorize the intensity [39] with a mean intensity of 42.5 ± 24.75% HRR.

4.3. EFFECT OF INTERVENTION

4.3.1. QUALITY OF LIFE

Before investigating the impact of different intensities on quality of life, the effect of aerobic exercise was explored. To do so, mean and standard deviation before and after intervention were taken into consideration. In some of the included studies it was not possible to extract data: some authors just presented and compared the results after aerobic exercise with the results of a control group [35,38—40,43]. Therefore, included articles were divided in two groups: group A [34,36,37,41,42], studies comparing baseline to after aerobic exercise intervention, and group B [35,38—40,43], studies comparing the aerobic exercise group with a control group. Consequently, results were summarized in

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two different tables: in Table 4, the results of the studies in group A [34,36,37,41,42] are presented. Table 5 summarized the results of group B studies [35,38—40,43].

Regarding the group A, two studies [34,36], used the SF36 to measure the quality of life. In these articles, the physical component was significantly enhanced following intervention while there were no significant improvements for the mental component. In one of the studies [34] the self-reported scales of FACT-C were used to detect changes in quality of life and it reported no significant improvements ($P = 0.407$). Another included article [42] that used the FACT-B questionnaire, in the physical ($P \leq 0.01$), social/family ($P \leq 0.01$), functional ($P \leq 0.01$) and total wellbeing ($P = 0.02$) found significant improvements following intervention. Toohey et al. (2016) [41] assessed the quality of life using the FACT-G [41]. There were significant improvements ($P = 0.04$ and 0.01) for both intervention groups. Yagli et al. (2015) used the EORTC QOL-C30 (Global QOL) [37] and it demonstrated a significant improvement when comparing before and after treatment in the aerobic exercise group.

As far as the group B is concerned, two articles used the FACT-B questionnaire [38,40]. For these two studies the FACT-B primary results and FACT-G improved significantly in favor of the aerobic exercise group. Particularly, in the study of Murtezani et al. (2014)

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[38], the FACT-G (P = 0.008), the functional (P = 0.010) and emotional well-being (P = 0.035), and the primary outcomes of FACT-B were improved in the aerobic exercise group. Courneya et al. (2003) [40] found significant improvements in aerobic exercise, demonstrated by the FACT-B primary outcome, FACT-G, physical well-being and the Breast cancer subscale.

Another study in the group B [35] used a quality of life questionnaire, the FACT-G. In this study there were three experimental groups: two aerobic exercise groups (CLMIT and LVHIIT) and a control group. The analysis revealed a significant enhancement of the quality of life in the LVHIIT group when compared with the CLMIT group and the control group. Specifically, in both exercise groups (LVHIIT and CLMIT) the physical well-being significantly increased when compared with the control. On the contrary, just the LVHIIT group significantly improved the functional and emotional well-being scores compared to the CLMIT and the control group. Adams et al. (2018) [43] used the SF36 to assess the quality of life. Significant improvements were observed for half of the items. Specifically, the mental component (P = 0.034), role-physical (P = 0.048), general health (P = 0.016), vitality (P = 0.001) and social functioning (P = 0.011) were significantly improved in the exercise group when compared with the control. The last study of group B [39] used the

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Quality of life Index for cancer patients and demonstrated a significant improvement in the exercise group when compared with the control (P ≤ 0.001).

4.3.2. STUDY QUALITY ASSESSMENT

The overall quality of the studies was poor (Table 3). The average score for articles analyzed was 5.3/10 (±1.25), the minimum score was 3 and the maximal score was 8. Items 5-6 and 7 were for the majority of items not met or, the information was missing. Despite this, due to the low number of articles founded, studies with poor quality were included.

4.3.3. EXERCISE INTENSITY AND EFFECT SIZE

For each study, Cohen's D was calculated (Table 6). A detailed description of thresholds for interpretation of the effect size was given in the method section. The average effect size was 0.80 ± 0.30 and ranged from 0,13 to 1.27. Overall, two articles [34,36] had small effect sizes, 3 [40,42,43] had an effect size that varied between small and medium, three [35,37,38] had an effect size varied to between small and large. In the study of Courneya et al. [40] the effect size varied between medium and very small while in the study of Murtezani et al. [38] it varied between very large, medium and small. For studies who

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include vigorous intensity, three items had a small effect size and four had a large one. For moderate to vigorous intensity eleven items had small or very small effect size, three a medium and two a large effect size. For low to moderate intensity, eleven items had small or very small effect size, seven had a medium effect size and three a large or very large effect size. And for low intensity two items studies had small effect size and three a medium effect size. The Spearman's rank-order correlation between the quality of studies and effect size ($R = 0.18$, $P = 0.60$), was calculated. It was not possible to calculate the correlation between the effect size and the exercise intensity due to the differences in the questionnaires and the small number of included articles. Because of the diversity of the questionnaires and the lack of studies in each intensity class, no further analysis could be carried out.

5. Discussion

The present review summarizes the current knowledge of the effect of a supervised aerobic training on quality of life of cancer survivors. In addition, it is one of the first studies analyzing the effect of varying aerobic exercise intensities on quality of life.

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Pooled results include 10 interventional studies that included solely aerobic training in their intervention. According to what was hypothesized, all of the studies [35—43] found significant improvements in almost all the items assessed by quality of life questionnaires with the only exception one study [34] (Tables 4 and 5). On the contrary, regarding the influence of exercise intensity, the results are not in line with the hypothesis. No significant trend was identified (Table 6). It is important to highlight that this study [34] was found to have the highest risk of bias. Thus, the general conclusion does not change dramatically based on the study quality assessment (Table 3). In general, the included articles did not have a good quality with more than a half of the studies scored 5 [35—39,42] and one [34] scored 3.

The three studies using the FACT-B [38,40,42], presented all subscales results. In two of these articles [38,42], the exercise intensity was low to moderate (between 1.6 to 6 Mets) [44]. Despite the fact that the exercise intensity was similar in these studies, in one [42] the majority of subscales presented a significant improvement after aerobic exercise while in another [38] just four of the seven subscales were significantly enhanced after the intervention. In the third study using FACT-B questionnaire [40] the exercise intensity was moderate to vigorous (between 3 to > 6 Mets) [44] and it showed significant

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improvements in more than a half of the assessed categories. These findings suggest that there is no relationship between improvement in quality of life and exercise intensity.

In the three studies using SF-36 [34,36,43], there was a significant improvement of physical component for two studies [34,36], using a protocol with a moderate to vigorous intensity and low to moderate intensity respectively. On the contrary, the mental component did not significantly improve. The opposite results were found in the study of Adams et al. (2018) [43] with a significant improvement only for the mental component following vigorous exercise. Again, the exercise intensity does not appear to influence the results.

The two studies that used the FACT-G questionnaire [35,41] found significant improvements after exercise intervention in both the low and vigorous intensity groups. Improvements after intervention were found in the study using the EORTC-QOL-C30 questionnaire [37] with a moderate to vigorous intensity, and the study using the Quality of life Index for cancer patients to assess the quality of life [39]. In the aforementioned study participants trained at a low to moderate intensity.

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To summarize, according to all these results, exercise intensity does not significantly influence the impact of aerobic exercise in improving quality of life of cancer survivors. Nevertheless, this could be explained by the psychological benefits that aerobic exercise intervention itself, not matter the intensity, can give to cancer survivors. Indeed, according to Casla et al. [45], group-based physical activities offer the opportunity to meet other people who have experienced the same disease, which allows participants to motivate them to continue their training and develop important social connections.

Three out of the five studies showing the emotional well-being results [35,37,38,40,42] demonstrate that this health-related domain was significantly influenced by aerobic exercise [35,37,38]. The remaining two showed a non-significant influence of aerobic exercise on the emotional well-being [40,42]. These controversial results might be explained by the fact that emotional well-being is influenced by several factors such as social support, self-blame and coping strategies [46] Therefore, an intervention including just exercise might not be significantly effective in improving emotional well-being.

Some of the studies that analyzed the results of social functioning and social well-being [37,42] showed a significant improvement in these components. In a study by Taylor et al. [47] they suggested that physical activity could have a positive effect on these social

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components. In the studies that analyzed functional well-being, in most cases [35,38,42], there were significant improvements.

5.1. LIMITATIONS

When interpreting the results of the present review, several limitations must be kept in mind. The major limitations concern the risk of bias of included articles. As mentioned before, most of the included articles have insufficient quality. Nevertheless, it should be noted that the included studies confronted undeniable difficulties that negatively impacted the study quality: the intervention protocol itself made the assessors and therapists blinding impossible. In addition, patients might have some knowledge in the field of exercise training. Therefore, it might be difficult for them as well to be blinded about the exercise training they are performing for the intervention.

Another relevant limitation is the different protocols used in the included studies. For instance, in three studies, participants performed an High Intensity Interval Training (HIIT) [35,41,43]. Two of them [35,41] used exactly the same protocol with 7 intervals of 30 seconds interspersed with 1 minute of passive recovery while the third [43] used a completely different protocol that consists of 4 intervals of 4 minutes interspersed with

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3 minutes of active recovery. On the contrary, in nine of the ten included articles [34—42], participants performed continuous aerobic exercise training and even in this case, the protocol differed regarding the duration and frequency of training and the training equipment.

The search strategy posed some limitations: grey literature was not analyzed, and the systematic literature review was based on the results of just three databases. Increasing the number of databases could have made this review more exhaustive. Nevertheless, according to the new version of AMSTAR 2, 2 database minimum is sufficient to the search strategy [48]. Another important limitation concerns the sample size. Half of the included articles [34,36,39,41,42] had a small sample size, with a number of participants ranging from 7 to 23, while the remaining five [35,37,38,40,43] articles had a larger sample size, between 40 and 62 participants. An additional limitation relates to the quality of life questionnaires used and how authors reported their result. For instance, two of the questionnaires used (EORTC QOLC30 and FACT-G) are cancer-specific questionnaires. Their results may be more accurate or different from no cancerspecific questionnaires. Besides, these differences did not allow a comparison between the effect sizes. Besides, some authors presented the results of each subscales assessed by the

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questionnaire [37,38,40,42,43] while other studies just presented a global score or partially presented the subscales results [34—36,39,41].

5.2. IMPLICATIONS

All these limitations might have negatively impacted the results of the present review especially with regards to the differences among exercise intensities. Nevertheless, the results of the present review contribute to provide important information that can be used in health care exercise prescription. Firstly, exercise frequency was 2 or 3 times per week and almost all included articles found a significant improvement in quality of life. Secondly, this review underlines the need to provide an exercise intensity guideline to optimize the effects of aerobic exercise on quality of life in cancer survivors. Future studies should include more participants and focus on a single quality-of-life questionnaire to allow for an assessment of optimal training intensity.

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6. Conclusion

The present systematic review demonstrated the effectiveness of aerobic exercise in improving quality of life of cancer survivors. However, an influence of exercise intensity is yet to be found. Findings might be affected by the several limitations of the present review. Therefore, future research with high quality and large sample size are needed to investigate more in depth on the different impact of different aerobic exercise intensities on quality of life of cancer survivors. Additionally, there are important questions that remain to be answered such as what the best frequency is (1, 2 or 3 times per week) and volume of aerobic exercise to optimize its effect on quality of life of cancer survivors.

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DISCLOSURE OF INTEREST

The authors declare that they have no competing interest.

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SUPPLEMENTARY DATA

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