Supportive Care in Cancer (2021) 29:4911–4919
https://doi.org/10.1007/s00520-021-06095-y

REVIEW ARTICLE

Physical exercise and quality of life in patients with prostate cancer: systematic review and meta-analysis

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Received: 18 June 2020 / Accepted: 18 February 2021 / Published online: 2 March 2021

Abstract

Background Prostate cancer leads to worse quality of life due to treatment and consequences of disease; benefits of physical exercise remain unclear on the improvement of quality of life in this population. The aim of this study is to evaluate the effectiveness of physical exercise in improving quality of life in patients with prostate cancer.

Methods A systematic review and meta-analysis was carried out. For the search of studies, we used electronics databases such as Cochrane Library, MEDLINE via PUBMED, Regional Health Portal, and EMBASE, without language restrictions or year of publication. The descriptors used were as follows: "prostatic neoplasms," "exercise," and "quality of life." The risk analysis of bias in the meta-analysis was based on the Cochrane Collaboration Tool. For statistical analysis, the fixed effects model was used. Randomized controlled trials were included, which had a sample of patients with stage I–IV prostate cancer and that the intervention was aerobic physical exercise (AE) or resistance physical exercise (RE) or combined AE and RE.

Results Five thousand six hundred nineteen studies were identified, but only 12 studies were selected. The quality of life of the patients was measured using instruments (SF 36, EORTC, AQoL-8D, IPSS and FACT-P), which served to divide the studies in groups where they presented the same instrument used. The analysis carried out shows that the quality of life of patients with prostate cancer submitted to aerobic training regimens had a protective effect in relation to the others.

Conclusion Most studies show an improvement in the quality of life of patients when they practice physical exercise, perceived by increasing the score of the instrument in question. However, methodological and heterogeneous differences between the studies increase the analysis bias.

Keywords Prostatic neoplasms · Exercise, Quality of life

Introduction

Prostate cancer is the first most common cancer among men in the occidental countries [1] and the second globally in men [2, 3]. Treatment for patients with this type of cancer consists of methods such as surgery, chemotherapy, radiation, and hormone therapy [2, 4, 5]. Just as there is such diversity, plurality in the harm is also present, such as urinary incontinence, intestinal symptoms, erectile dysfunction [6], pain, body fatigue, and changes in body composition [7]. It is clear that these

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symptoms or the set of these symptoms cause great physical and psychological repercussions in the medium to long term in the life of the patient reflecting on their quality of life [4, 8].

Thinking of mitigating such consequences, the practice of physical exercises is widely studied in clinical trials. It has been reported that physical exercise—specifically aerobic, resistance, flexibility, and pelvic floor exercises—for 15 months decreased significantly symptoms of the urinary system, in addition to improving physical conditioning and emotional and social functioning and improvement of intestinal symptoms [6]. Fatigue mitigation, increased muscle strength, and maintenance of body composition are also some of the long-term benefits from exercise, especially endurance, also improving the quality of life [9]. Not only resistance exercises, but also simpler exercises, such as walking, selected as an exercise, is considered safe and accessible, which potentially decreases fatigue and increases the quality of life of the cancer patient's prostate [10].

The range of benefits of physical exercise is perceived in several aspects of the prostate cancer patient's life. It is reported that the positive effects on quality of life come mainly not only from the practice itself, but from patient exercising this practice in a structured environment and also improving their own physical condition in general, reflecting on quality of life [8]. A randomized clinical trial points out this repercussion on quality of life as the improvement of functions due to symptoms emotions, improved social function, improved mental health, and better scores in 6 out of 8 dimensions that make up the SF-36 quality of life assessment tool [11].

Thus, we aim to carry out a systematic review with meta-analysis to assess the relationship of the different types of exercise modality (resistance exercise, aerobic exercise and combined exercise) and the improvement of quality of life of patients with prostate cancer. This evaluation becomes necessary to point out the most efficient modality for this specific population which needs evidence for the elaboration of protocols that establish the role of aerobic and resistance physical exercise and thereby improve the prognosis of this population.

Methods

Search strategy

This systematic review complies with the recommendations and criteria described in the preferred report items for systematic reviews and meta-analyses (PRISMA) and Cochrane Handbook [12]. The question was as follows: what is the influence of physical exercise on the quality of life of patients with prostate cancer? A high-sensitivity search was carried out on electronic data platforms: Cochrane Library, MEDLINE via PUBMED, Regional Health Portal (VHL), and EMBASE (Supplementary Material).

Eligibility criteria

The eligibility criteria was established by our PICO strategy: "is the practice of physical exercise affects the quality of life of patients with prostate cancer?". Randomized clinical trials that evaluated the quality of life of people diagnosed with prostate cancer (stages I, IIA, IIB, IIC, IIIA, IIIB, IIIC, IVA) who underwent physical exercise were included, and studies with people with metastatic cancer (IVB), other types of cancer, and incomplete information were excluded [13]. There was no time or language limitation.

Data extraction

The material obtained through the extensive analysis of the platforms was exported to a Mendeley® file and exposed behind the PRISMA 1 diagram (Fig. 3). The first two screenings (selection by title and abstract) were carried out by three independent researchers (CR, JR, and ML), who performed a selection of potential articles to be included in the final compilation. In cases where there were disagreements, a fourth independent researcher (KCC) resolved the discrepancies. Regarding data extraction, the three independent researchers (CR, JR, and ML) used a form which was intended to record the following: study data (authors, journal name, country and study scenario, year of publication) and methodological information (objective of the study, design, size of the total sample, aspect or variable of quality of life, exercise practice, and instruments used to evaluate them).

Quality of studies

The two authors of the research (JR and CA) independently assessed the risk of bias in the selected studies and reported them to specialists (KCC and ML), according to the Cochrane Collaboration Tool to assess the risk of bias [12]. Possible sources of bias in randomized studies include random sequence generation, allocation concealment, concealment of participants and staff, blinding evaluation of results, incomplete data, selective reporting, and other biases. Three scores, yes, no, and uncertain, can be attributed to each of the items mentioned above, which are referred to as high risk, low risk, and uncertain risk, respectively. For the randomized controlled study, we used the RevMan 5 software to plot the assessments.

Data analysis

The meta-analysis was performed using the fixed effects model for continuous data, and the effect measures were obtained by mean values, standard deviation, and *n* sample of the post-intervention for all the evaluated instruments. The data referring to the SF-36 Physical Functioning instrument was used; the statistical heterogeneity of the treatment effect between the studies was assessed using Cochran's Q test (p value = 0.99) and the inconsistency test (I^2 = 0), since the result was a negative value, being highly significant, indicating the absence of heterogeneity between studies. For the EORTC Physical Instrument, the statistical heterogeneity of the treatment effect between the studies was assessed using Cochran's Q test (p value = 0.96) and the highly significant inconsistency test (I^2 = 0), indicating the absence of heterogeneity between studies. The data referring to the EORTC Global Health Status Instrument was used; the statistical heterogeneity of the treatment effect between the studies was assessed using the Cochran Q test (p value = 0.91) and the inconsistency test (I^2 = 0), since the result was a negative value, being highly significant, indicating the absence of heterogeneity between studies.

Risk of bias in the included studies

Figure 1 shows the characteristics of the included studies and their risk of bias. Figure 2 shows the summary of Risk of Bias: judgments of the reviewer on each risk item of bias in the included studies.

According to the Cochrane Collaboration Tool to assess the risk of in Fig. 2, of the 12 studies, six were assessed as low risk of bias [11, 14–18], 4 as a moderate risk of bias [3, 19–21], one as a serious risk of bias [22], and one as critical risk of bias [23]

For the randomized controlled studies, the 7 risk factors for bias are as follows:

1. Allocation: The included study was considered to be of low risk for selection because the study used random sequence generation and allocation concealment such as that by Bourke et al. [14], which used a computer algorithm for this.
2. Concealment: The study included was considered to have a high risk of concealing the participants, since patients previously knew what therapy they would undergo, such as that by Cormie et al. [22], in which he made it unclear whether there was due concealment.

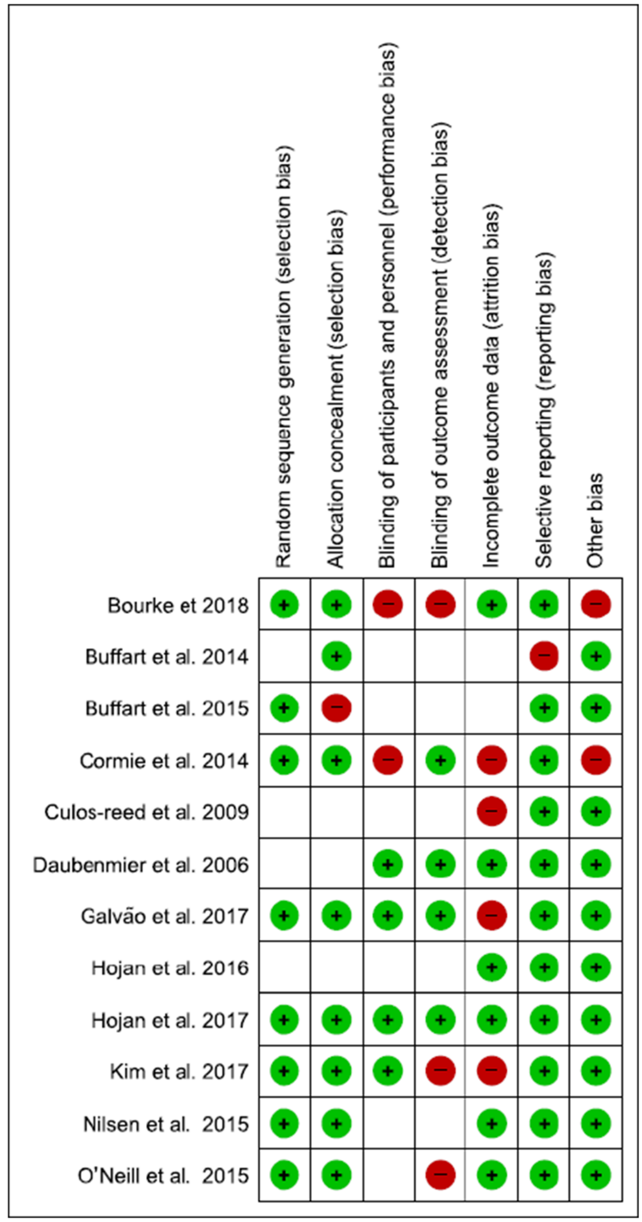

Fig. 2 Bias Risk Summary: judgments by the reviewer about each bias risk item in the included studies

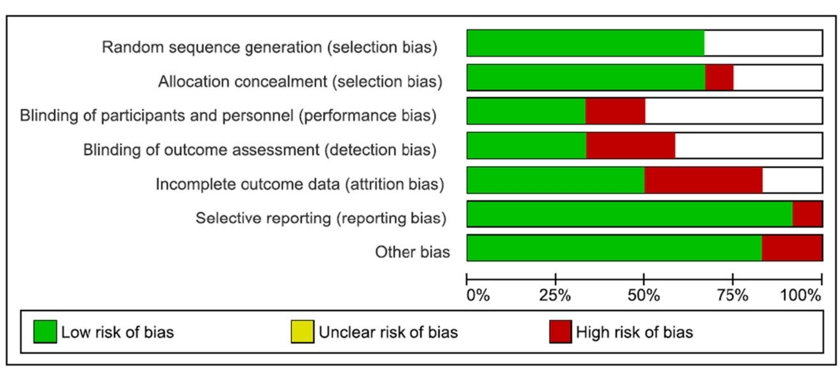

Fig. 1 "Bias Risk" graph: judgments by the reviewer about each bias risk item in the included studies being presented as a percentage

3. Incomplete data on the results: It is concluded that the study which considered high risk is the one that presented an imbalance in the number of patients within groups, the departure of many patients of the study, and if such effects had a strong impact on statistics, such as the study by Culos-Reed et al. [23], in which patients from the intervention and control groups were lost, so that the quantity has become uneven.
4. Selective reporting: A high-risk study was defined as one that the outcomes were not fully reported, incomplete, or that were not pre-specified, such as the study by Buffart et al. [3], who did not present a study protocol or its outcomes were fully discussed.
5. Other potential sources of bias: Study with other biases considered to be high risk that did not fit the other classifications, such as Cormie et al. [22], in which there were patients in the control group who did not respect their conditions and also performed physical exercises.

Results

Selection of studies

Five thousand six hundred nineteen studies were identified through four researches selected in databases data: 360 references from MEDLINE, 229 from EMBASE, 173 from Cochrane, and 4857 from Regional Portal from Virtual Health Library. After excluding 217 duplicates, a detailed analysis of 5402 titles and abstracts was done. Full text articles were retrieved for the remaining 52 records of which 41 were excluded, which did not meet the inclusion criteria for exclusion from this review as shown in the PRISMA diagram [12] (Fig. 3). Twelve studies were found eligible for inclusion in this revision for the qualitative synthesis and 8 for the meta-analysis.

Included studies

This review only contains randomized clinical trials, generating a sample of 1256 patients. Of the approved studies, 5 were located in the European Continent, 4 in Oceania, 1 in Asia, and 2 in the Americas. No studies from Africa, Oceania, or Antarctica were included. The years of publication varied from 2006 to 2018, and all studies were published in English. Table 1 shows the characteristics of the studies.

Meta-analysis

Exercise x quality of life by SF36 physical functioning

The meta-analysis (Table 2) demonstrated that the practice of both aerobic and resistance physical exercises promotes a significant increase (5%) of this parameter of quality of life of people with cancer (p value = 0.045), assessed by SF-36. So, according to the data shown in supplementary figure 1, it can be seen that the studies by Buffart et al. [3] and Daubenmier et al. [11] have a treatment effect that favors intervention (IT).

In this sense, in the meta-analysis (Table 2), there is a heterogeneity between the studies. In Buffart et al. [3] and Cormie et al. [22], there is the practice of combined exercise in both; however, it is worth noting that only one demonstrated protective effects on quality of life (Supplementary figure 1).

In a separate analysis, the trial by Cormie et al. [22] shows that participants in the IT group performed moderate to high intensity exercise (70 to 85% of maximum heart rate), being supervised for 60 min, and were encouraged to perform AE at home, without supervision, to complete the time of the proposed exercise protocol of 150 min per week, versus group control (CT), which received standard care. The pre-intervention score for the IT group was 53.2 (SD5.2) and group CT 53.8 (SD 4.2), a less promising score in the post-intervention (Table 1), favoring the CT group.

As for Buffart et al. [3], the IT group was submitted to AE which was based on cardiovascular exercises of 15 to 20 min, and RE programmed to be in series, with projections from 12 to 6 repetitions. However, AE and RE practices were fully supervised by professionals, versus CT group with standard care, without any additional support. The comparison of the result of the pre-intervention instrument (IT group 47.7 SD 7.1 and CT group 46.9 SD 10.2), with the post-intervention measurement (Table 2), demonstrates a positive effect for the improvement quality of life, favoring the IT group (Supplementary figure 1).

In addition, Daubenmier et al. [11] was favorable to the IT group; the study relied solely on AE with exercise practices 6 times a week, 30 min a day, for 52 weeks versus CT group that received usual care. In the pre-intervention measurement, the result of the instrument (IT group 52.9 SD 6.8 and CT group 53.2 SD 6.6) allows, compared to the post-intervention outcome (Table 1), affirming a favorable effect on the IT group (Supplementary figure 1).

The findings in the three studies of the present meta-analysis (Table 2) corroborate for the favoring the quality of life (Supplementary figure 1) of these patients who are submitted to practice combined exercise and AE alone, both supervised by professionals.

Exercise x quality of life by EORTC Global Health Status Instrument

The meta-analysis (Table 3) demonstrated that the practice of physical exercises promotes a significant increase (5%) in the quality of life of people with cancer (p value = 0.049) of

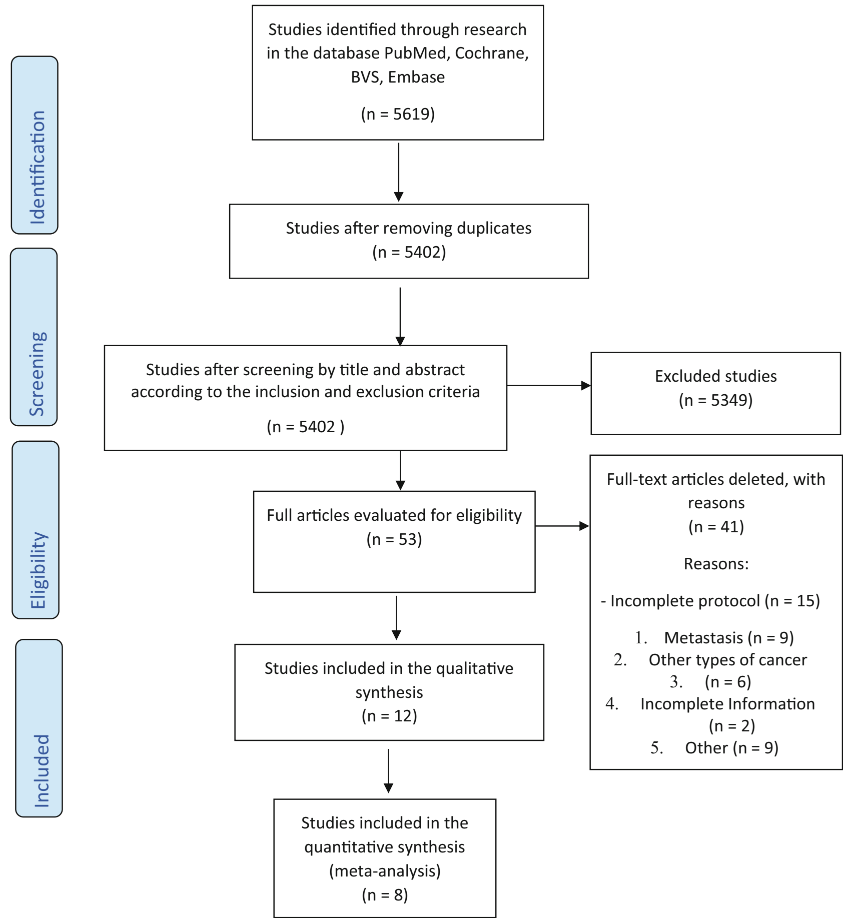

Fig. 3 PRISMA flow diagram of studies that investigated the influence of physical exercise on quality of life of people with prostate cancer

according to EORTC Physical Instrument (Supplementary figure 2).

In a specific analysis of this subgroup of the EORTC Global Health Status Instrument, in the study by Buffart et al. [20], it is clear that the physical exercise protocol favored the intervention; in this sense, the study used AE with cardiovascular exercises (20 to 30 min) and RE that was done in series designed to progress from 12 to 6 repetitions at most; in the first 6 months and from the 7th month to the 12th month, the patients received a program of domestic exercise of AE and RE and flexibility versus the CT group, which received the booklet modified with general guidelines for the 12 months of study. The present study revealed, from the measurement of the instrument in question, that the post-intervention result (Table 3) was higher than the pre-intervention (IT group 77.3 SD 13.6 and CT group 78.5 SD 15.9). It can be said that thus is a favorable effect of the intervention (Supplementary figure 2).

In the trial by Hojan et al. [17], the IT group (pre-intervention result of instrument 53.71 SD 18.2) was submitted to 30 min of AE and 15 min of RE, of moderate intensity (65% at 70% of maximum heart rate), 5 times a week for 22 weeks, versus CT group (pre-intervention result of instrument 54.16 SD 23.0), which received standard recommendations, obtaining a favorable result for the IT group (Supplementary figure 2). However, in Hojan et al. [18], the IT group (pre-intervention result of the instrument 53.7 SD 18.2) was submitted to combined AE and RE, which consisted of 5 sessions of 60 min per week, for 8 weeks (during radiotherapy) and for 10 months (after radiotherapy), 3 80-min sessions per week, while the CT group (result pre-intervention of the instrument 54.1 SD 23.0) only received standard recommendations. Those data suggest a long-term beneficial effect for patients requiring radiotherapy.

In Culos-Reed et al. [23], the IT group (pre-intervention result of the instrument 70.42 SD 17.39) had semi-supervised activities, with group and home activities. In the first week, personalized combined AE and RE programs were carried out by professionals and participants were advised to do it 3 to 5 times a week at moderate intensity. A weekly supervised group meeting was also held, lasting 1 h, using exercises similar to those at home, whereas the CT group (pre-intervention result of instrument 71.33 SD 18.65) was kept on a waiting list. The post-intervention results (Table 3), when compared with the post-intervention results, show a favoring of the IT group (Supplementary figure 2).

In Nilsen et al. [19], the IT group (pre-intervention result of the instrument76.5 SD 17.3) was submitted only under RE

Table 1 Characteristics of the included studies ($N = 12$)

First author	Country	Study duration	Control group	Type of intervention	Instrument used to measure the variable
Bourke et al. 2018	UK	52 weeks	Habitual care and active surveillance	Semi-supervised, 2x face-to-face, stationary cycles, oars, ergometer, or treadmill	EQ5D questionnaire
Buffart et al. 2014	Not informed	12 weeks	Habitual care and active surveillance	2 to 4 sets (upper/lower limb muscle strength)/15 to 20 min (cycling/walking/jogging)	SF36 general and SF36 physical functioning
Buffart et al. 2015	Australia and New Zealand	26 weeks	Modified booklet with general guidelines	2 to 4 sets (upper/lower limb muscle strength)/20 to 30 min (cycling/walking/jogging) = home(90 min) and supervised (60 min)	EORTC global health status and EORTC physical
Cormie et al. 2014	Australia	13 weeks	Habitual care and active surveillance	Upper/lower limb muscle strength/20 to 30 min (cycling/walking/jogging/rowing)	SF36 general and SF36 physical functioning
Culos-reed et al. 2009	Not informed	16 weeks	Habitual care and active surveillance	Home-based program, walking, stretching, and light resistance exercises (i.e., theraband) ,education	EORTC global health status
Daubenmier et al. 2006	USA	52 weeks	Habitual care and active surveillance	Home-based exercise, low-fat, vegan diet and stress management	SF36 physical functioning
Galvão et al. 2017	Australia	26 weeks	Habitual care and material for education	Monthly telephone-based, managing stress, physical activity; nutrition and diet; relationships; sex and intimacy, elastic exercise device	AQoL-8D all dimensions and IPSS
Hojan et al. 2016	Poland	22 weeks	Habitual care and active surveillance	30 min (brisk walking, running indoors or on a treadmill, cycling)/15 min 2X8 (biceps curl, triceps extension, leg extension, leg curl, abdominal crunch)	EORTC global health status and EORTC physical
Hojan et al. 2017	Poland	52 weeks	Habitual care and active surveillance	30 min (brisk walking, running indoors or on a treadmill, cycling)/25 min 2X8 (biceps curl, triceps extension, leg extension, leg curl, abdominal crunch)	EORTC global health status and EORTC physical
Kim et al. 2017	South Korea	26 weeks	Performed stretches	Home-based, weight-bearing exercise (150 min/w) and resistance (12 exercises-3Xw), 30-min educational session—DVD material	FACT-P physical well-being
Nilsen et al. 2015	Norway	16 weeks	Habitual care and active surveillance	9 RT exercises	EORTC global health status and EORTC physical
O’Neill et al. 2015	Ireland	26 weeks	Habitual care and active surveillance	Telephone-based, UK physical activity guidelines, dietary component	FACT-P physical well-being

Table 2 Meta-analysis for the influence of physical exercise on quality of life using the SF36 physical functioning instrument in people with prostate cancer

Study or subgroup	Post/intervention			Post/control			Relevance	Difference in means; fixed effect, 95% CI
	n	Mean	SD	*N*	Mean	SD		
Buffart et al. 2014	29	49.2	7.9	28	44.8	9.5	18.7	4.40 [− 0.12; 8.92]
Cormie et al. 2014	32	51.5	8.0	31	52.2	5.7	32.5	0.70 [− 4.14; 2.74]
Daubenmier et al. 2006	40	53.2	6.6	42	50.2	9.5	30.4	3.0 [− 0.55; 6.55]
Combined	101	51.3	0.78	101	49.1	2.19		1.84 [− 0,32; 4.00]

Heterogeneity: $Chi^2 = 0.012$, DF = 2, (p value = 0.99), $I^2 = 0$

Test for overall effect: $Z = 1.66$, (p value = 0.045)

regime, semi-supervised, 3 times a week, for 16 weeks (2 times of high intensity, interspersed with 1 time of medium intensity), composed of 1 to 3 sets of 9 resistance exercises, with a maximum of 6 to 10 repetitions versus CT group (pre-result intervention of the instrument 54.1 SD 23.0), which received standard care; the IT group was favored by the effect of the intervention (Supplementary figure 2).

The findings in the meta-analysis (Table 2) are in agreement with previous studies, demonstrating that combined AE and RE promotes a beneficial effect for patients with prostate cancer (Supplementary figure 2), measured by the EORTC Global Health Status Instrument.

Exercise x quality of life by EORTC Physical Instrument

The meta-analysis (supplementary table 1), punctually analyzing the physical domain, of the instrument EORTC Physical Instrument, has shown that physical exercise promotes a high significance (1%) of this quality of life parameter of people with cancer (p value = 0.004). Thus, and according to the data shown in supplementary figure 3, it can be seen that the studies present a treatment effect that favors the physical health of the IT group.

In a specific analysis of the studies, only Nilsen et al. [19] performed only RE, while the other 3 studies [17, 18, 20] performed combined AE and RE for the IT group. In this specific domain, the pre-intervention result of the IT group by Buffart et al. [20] was 90.5 (SD 12.7) and in the CT group 93.6 (SD 8.5); in Hojan et al. [17], the IT group obtained 79.7 (SD 18.9) and CT group 81.1 (SD 15.4); and in Hojan et al. [18], the IT group had 79.7 (SD 18.9) and the CT group 81.2 (SD 15.5).

The analysis of the three studies, comparing with the post-intervention result (Supplementary Table 1), allows to infer a protective effect on the physical health of patients with prostate cancer, who underwent the combined AE and RE (Supplementary figure 3).

Discussion

This systematic review with meta-analysis explored the influence of physical exercise on the quality of life of patients with prostate cancer, involving randomized clinical trials that differed regarding the exercise regime (aerobic, resistance, or combined) and the instrument used to measure quality of life (SF36 Physical Functioning, EORTC Physical Instrument, EORTC Global Health Status Instrument).

In the analysis carried out regarding meta-analysis 1, the performance of AE and combined exercise was effective in improving the quality of life of patients with prostate cancer, with no adverse effects arising from this type of practice being

Table 3 Meta-analysis for the influence of physical exercise on quality of life using the EORTC Global Health Status Instrument in people with prostate cancer

Study or subgroup	Post/intervention			Post/control			Relevance	Difference of means; fixed effect, 95% CI
	N	Mean	SD	*n*	Mean	SD		
Buffart et al. 2015	50	79.1	13.6	50	74.8	22.4	7.3	4.3 [− 2.96; 11.56]
Culos-Reed et al. 2009	40	73.1	15.9	25	69.0	15.1	6.3	4.1 [− 3.69; 11.89]
Hojan et al. 2016	27	55.4	19.9	28	55.1	17.7	3.9	0.3 [− 9.64;10.24]
Hojan et al. 2017	36	57.4	19.7	36	52.3	17.8	5.1	5.1 [− 3.57;13.77]
Nilsen et al. 2015	27	79.6	17.0	30	78.9	20.7	3.9	0.7 [− 9.20; 10.60]
Combined	180	68.92	2.66	169	66.0	2.85		3.28 [− 0.51; 7.07]

Heterogeneity: $Chi^2 = 0.59$, DF = 4, (p value = 0.96), $I^2 = 0$

Test for overall effect: $Z = 1.69$ (p value = 0.049) noticed. Only three studies have shown adverse effects involving research participants. In Hojan et al. [18], 3 participants in the IT group presented lesions in the extremities; as for Nilsen et al. [19], 3 patients left the search for pain in the posterior aspect of the leg, coast, and neck. Furthermore, in O´ Neill et al. [15], 3 patients experienced pain on the coast.

Physical exercise is associated with a significant reduction in the mortality rate in several types of cancer, reducing fatigue levels, improving quality of life and functional capacity [24]. In our study, physical exercise was also beneficial for patients with prostate cancer.

The recommendation of exercise guides for cancer patients in general varies between 30 and 75 min for more moderate activities and reaches up to 150 min for patients who perform more vigorous activities, preferably performed twice a week, so that the benefits are obtained the practice of physical exercise [25]. In our study, it was noticed that most of the articles lasted 30 min, being carried out at least twice a week and with the duration of the treatment program that varied widely, between 12 and 52 weeks.

In this study, exercise-based intervention allows benefits for the quality of life of patients with prostate cancer as a whole. For doctors working with patients with prostate cancer, this study recommends, combined with conventional treatment, the combined or aerobic exercise regime supervised by a suitably qualified professional, in order to increase the quality of life in patients with prostate cancer.

However, some limitations can be pointed out in this study, such as the heterogeneity of the sample of articles due to the non-standardization of time and the type of exercise performed in the different studies included in the analysis, as well as the protocol time applied in each of the studies that differed between them. Another limiting point is the method used to assess quality of life, in which several scales were used, but all are validated in the literature and are widely used to analyze the quality of life of cancer patients.

Conclusion

It can be concluded that the combined exercise and the aerobic exercise performed alone are effective modalities for improving the quality of life of patients with prostate cancer. In addition, it has a protective effect of combined aerobic exercise and resistance exercise for physical health of prostate cancer patients. However, the heterogeneity of the studies is a point that deserves attention; since the study's exercise protocols differ from one another, passive to sub-analysis, therefore, the results of this study must be interpreted with care. There were sub-analyses regarding the comorbidities and the type of treatment of the patients. The limitations regarding methodological characteristics of the study such as clarity about the supervision of the exercises are relevant. It is worth mentioning the need for trials randomized clinical trials with a more specific population of prostate cancer patients or, that is, with equal staging and stages, in addition studies that analyze the protective effect of physical exercise in patients undergoing androgen suppression therapy.

Supplementary Information The online version contains supplementary material available at https://doi.org/10.1007/s00520-021-06095-y.

Author contribution All authors were involved in the design of the study. KCC, MLS, and RSBR coordinated the study. KCC, MLS, JAR, CAMPR, and LBR performed the data analyses. LBR and RSBR drafted the manuscript. All authors critically revised the manuscript and read and approved the final manuscript.

Data Availability All data and materials were submitted for publication.

Code availability The analyses were performed with RevMan 5 (Cochrane Collaboration's).

Declarations

Ethics approval and consent to participate N/A

Consent for publication All authors consented to publish this paper.

Conflict of interest The authors declare no conflicts of interest.

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