

# Effects of exercise on respiratory muscle function and functional capacity in patients with cancer. Systematic review

## Abstract

The objective of this review was to assess the effectiveness of therapeutic exercise interventions in respiratory muscle function and functional capacity in patients suffering from cancer. A systematic review was conducted from November to December 2022 in the following databases: MEDLINE (through its search engine PubMed), PEDro, EMBASE, LILACS, CINAHL, and Google Scholar. Results were reported according to the PRISMA guidelines, and the protocol was previously registered (PROSPERO: CRD42022379018). Two independent reviewers extracted data from the included studies. 12 randomized controlled trials, including 679 patients, were included in this systematic review. 11 assessed the effects of therapeutic exercise on respiratory muscle function, and 6 assessed the effects on functional capacity. The current evidence is limited, and studies offer heterogeneous results. Further studies should be developed implementing structured exercise protocols, and the effects of exercise on different cancer types should also be assessed. However, this review offers a first insight into the potential effectiveness of therapeutic exercise in respiratory muscle function impairment and functional capacity loss.

**Keywords:** Cancer, Exercise, Muscle strength, Respiratory function test, Systematic review

## Introduction

Currently, cancer constitutes one of the main causes of morbidity and mortality worldwide, as estimated by the *International Agency for Research in Cancer* 18,1 million cases to be diagnosed since the year 2020, and this number to be increased to 28 million cases in the following two decades.<sup>[1]</sup>

The management of this condition is handled through different therapeutic approaches, including surgery, immunotherapy, chemotherapy, radiotherapy, guided therapy, photodynamic therapy, hyperthermia, hormone therapy, and stem cell therapy.<sup>[2-4]</sup> Also, the therapeutic choice will depend on the individual clinical presentation and the stage at which the cancer is, even combining different treatments to ensure maximal efficacy. The main purpose of an oncologic treatment plan is to cure cancer, and when this is not possible, the goal is to reduce cancer down to a subclinical stage and ensure the patient's quality of life as much as possible.<sup>[3, 5]</sup>

Up to 50% of patients diagnosed with

cancer are expected to have a survival rate of ten or more years, and this rate is expected to increase as new effective treatments are developed. However, the longer these patients survive, the higher probability they have to develop associated comorbidities, such as cardiovascular or psychological problems. One of the underdiagnosed issues involves complications with the respiratory system, where a high risk to develop respiratory infections and exacerbations of preexisting conditions is predicted. Undertaking the high prevalence of respiratory complications in the general population, the heightened risk to develop respiratory comorbidities in patients suffering from cancer might have a significant impact on their morbidity and mortality.<sup>[6]</sup>

To manage these complications, one of the therapeutic available resources used both in the pre and post-surgical stages is a therapeutic exercise. However, there is an existing heterogeneity in the components included in these programs, and unfortunately, the evidence is insufficient and should be furtherly developed. Understanding the potential cost-effectiveness that these programs might

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have, interventional programs based on robust scientific evidence must be developed.<sup>[7]</sup>

Studies have shown the efficacy of resistance and aerobic exercise interventions in these patients regarding both psychological and physical factors. Physical functioning, health-related quality of life, and fatigue improve in these patients when implementing therapeutic exercise,<sup>[8]</sup> however, effects on the impairment of respiratory function are yet to be assessed. Analyzing these effects through the assessment of respiratory muscle function could enable a better understanding of how therapeutic exercise programs could be applied to effectively manage respiratory complications.

Therefore, the objective of this systematic review is to assess the effects of therapeutic exercise interventions on respiratory muscle function through its maximal respiratory pressures in patients suffering from cancer. Additionally, a secondary objective was the assessment of other factors that are related to respiratory functioning, such as functional capacity.

## Materials and Methods

This systematic review adhered to the guidelines established by the PRISMA (Preferred Reporting Items for Systematic

Reviews and Meta-Analyses) statement,<sup>[9]</sup> and the search protocol was previously registered in an international registry of systematic reviews (PROSPERO: CRD42022379018). To conduct this systematic review, the following databases were accessed: MEDLINE (through its search engine PubMed), PEDro, EMBASE, LILACS, CINAHL, and Google Scholar. Additionally, external sources were also consulted.

### Search strategy

The search was conducted between November and December of 2022. The PICO elements were used to formulate the search string. The population included adult (>18 years) patients diagnosed with cancer, the intervention included therapeutic exercise in any of its modalities, either aerobic, resistance, or combined, the control group was usual care, and the included outcomes were respiratory muscle strength assessed through the maximal inspiratory pressure (MIP) and maximal expiratory pressure (MEP), and functional capacity assessed through the 6-Minute Walk Test (6MWT).

A search was conducted using the MeSH (Medical Subject Headings) terms “respiratory muscle”, “cancer”, and “exercise”, all combined with the Boolean operator “AND”. (Table 1) presents a summary of the search strategy applied for each of the accessed databases.

**Table 1. Search strategy for the accessed databases**

Database	Search string	Filters
PubMed	“Respiratory muscle” AND “cancer” AND “exercise”	Randomized control trial 2012 – 2022 >18 years.
Pedro	“Respiratory muscle” “cancer” “exercise”	Clinical trial 2012 – 2022 >18 years
EMBASE	“Respiratory muscle” AND “cancer” AND “exercise”	2012 – 2022 Randomized controlled trials. >18 year
LILACS	“Respiratory muscle” AND “cancer” AND “exercise”	Randomized clinical trial
CINAHL	“Respiratory muscle” AND “cancer” AND “exercise”	
Google Scholar	“Respiratory muscle” AND “cancer” AND “exercise”	

### Study selection

Two independent reviewers conducted the study selection by screening the titles and abstracts of the studies that the search yielded. If necessary, the full text of the study was accessed, and further discrepancies were solved by consensus. Studies were included if they were (1) randomized controlled trials, (2) published in the last ten years, (3) included adult (>18 years) patients diagnosed with any type of cancer, (4) implemented a therapeutic exercise intervention centered in improving respiratory muscle strength, and (5) assessed at least one of the outcomes included in the review, either respiratory muscle strength through the MIP and MEP, or functional capacity through the 6MWT. Studies not meeting

either of the aforementioned criteria were excluded.

### Data extraction

Two independent reviewers registered data and tabulated results in a spreadsheet according to the PICO elements to facilitate the analysis. The analysis was structured around the main objective, type of therapeutic exercise, and type of cancer. Data was extracted through a protocol that ensured the extraction of the most relevant data for each study. Study design, duration, sample characteristics, intervention, assessed outcomes, and results were extracted from every study included in the review.

## Outcomes

### Respiratory muscle strength

Respiratory muscle strength is commonly assessed by using a non-invasive pressure gauge to register maximal respiratory pressures generate at the oral cavity.<sup>[10]</sup> Maximal respiratory pressures include the MIP and the MEP.

### Functional capacity

Functional capacity is usually assessed through the 6MWT, a simple and practical test where the patient is asked to walk the maximum distance possible in a 30,48 meter (100 feet) corridor for a total of six minutes.<sup>[11]</sup> This test assesses all of the systems that are involved in exercise and activities of daily living, as it is considered a submaximal effort test.

### Risk of bias assessment

The risk of bias was assessed using the PEDro scale, a valid measure of the methodological quality of clinical trials.<sup>[12]</sup> The PEDro scale assesses 11 items, including selection criteria, random allocation, blinding, follow-up, and intention to treat analysis. Items are given a value of 1 if they are present in the clinical trial or 0 if they are not, and an overall score is obtained. The lower the scores the higher risk of bias a study has, and authors report that total PEDro scores of 0-3 are considered “poor”, 4-5 “fair”, 6-8 “good”, and 9-10 “excellent”.<sup>[13]</sup>

## Results and Discussion

The systematic search yielded a total of 301 studies. 13 of them were duplicates, 256 were excluded after reading the title and abstract, and 20 studies were also excluded for not being related to the research objective. 12 studies were finally included in this review. A flow diagram illustrating the study selection process is shown in (Figure 1).

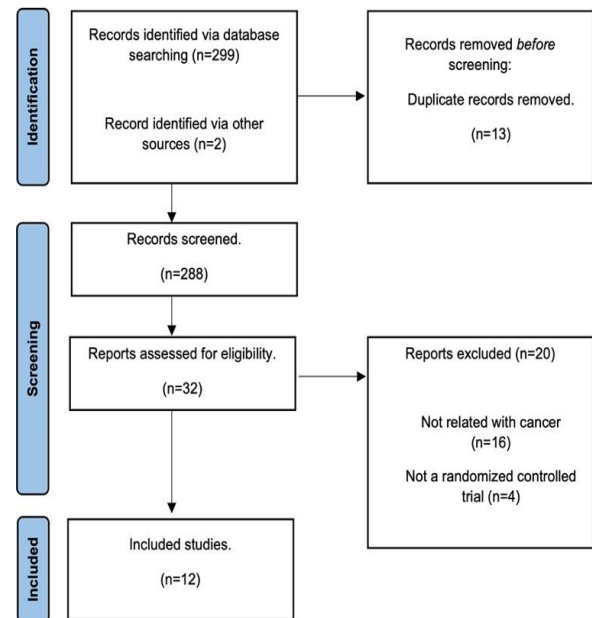


Figure 1. PRISMA Flow Diagram

### Study characteristics

A total sample of 679 patients was included in this review. The patient’s age range was between 36 and 69 years. 418 patients were male and 261 were female. 5 studies involved patients suffering from lung cancer,<sup>[14-18]</sup> 3 esophageal cancer,<sup>[19-21]</sup> 2 breast cancer,<sup>[22, 23]</sup> and 2 studies involved patients with any type of cancer.<sup>[24, 25]</sup> Every study was reported in English, except for a study in Portuguese.<sup>[25]</sup> Six studies performed their analysis during a presurgical phase, and the remaining six at a postsurgical phase. Characteristics of every included study are summarized in (Table 2).

Table 2. Description of the included study characteristics

Author/s & Year	Method	Sample	Intervention	Outcomes	Results
Brocki et al. 2016	2 groups 2 weeks  RCT	Mean age: 70 (SD=8) Gender: 57,5% male			
		Inclusion: -Patients included in a pulmonary resection surgery -High risk to develop complications  Exclusion: -Physical or psychological impairment -Unable to understand Danish -Previous ipsilateral pulmonary resection -Tumor activity in a different system -Major surgery within the last year.  Age range: 36-69 years. All female	Respiratory muscle training n=34  Control group n=34	-Respiratory muscle function (MIP and MEP)	-No significant difference between groups in MIP or MEP
Dahhak et al. 2022	2 groups 12 weeks  Pilot RCT	Inclusion: -Breast cancer -Reduced MIP -Dyspnea  Exclusion: -Presence of chronic cardiovascular or respiratory diseases	Therapeutic exercise + IMT n=10  Therapeutic exercise n=10	-Respiratory muscle strength (MIP and MEP)  -Functional capacity (6MWT)	-MIP increased significantly in the intervention group (from -74 ± 11 to -93 ± 19 cmH <sub>2</sub> O). MEP increased non-significantly in the intervention group (from 139 ± 25 to 144 ± 28 cmH <sub>2</sub> O)

-6MWT improved significantly (from  $557 \pm 87$  to  $584 \pm 71$  meters)

		Mean age: $43.6 \pm 15.2$ years and $46.6 \pm 13.2$ years. Gender: 84.1% female			
<b>de Almeida <i>et al.</i> 2020</b>	2 groups 5 weeks RCT	Inclusion: -Hospitalized patients -Age: >18/<65  Exclusion: -Smokers, alcoholics -Previous cardiovascular disease -Physically active -Patients with metastasis	Conventional physical rehabilitation + IMT n=15	-Respiratory muscle strength (MIP and MEP)	-MIP improved significantly in the intervention group (from $86.4 \pm 34.9$ to $103.1 \pm 44.6$ cmH <sub>2</sub> O). MEP showed no difference.
<b>Guinan <i>et al.</i> 2019</b>	2 groups 3 weeks RCT	n=60 Mean age: $64.13 \pm 7.8$ Inclusion: -Esophageal carcinoma -Cognitive capacity to perform IMT -Programmed esophagectomy -Able to understand English -Adult >18 years	Presurgical inspiratory muscle stretching group n=28  Control group n=32	-Respiratory muscle strength (MIP)  -Functional capacity (6MWT)	-MIP reduced significantly in the intervention group ( $-37.6$ (95% CI $-27.2$ – $-47.9$ ) cmH <sub>2</sub> O) and the control group ( $-31.5$ , (95% CI $-19.9$ – $-43.1$ ) cmH <sub>2</sub> O) after surgery.  -6MWT reduced significantly in the intervention group ( $194.6$ (95% CI $107.8$ – $281.4$ ) meters) and the control group ( $134.7$ (95% CI $102.1$ – $167.4$ ) meters) after surgery.
<b>Laurent <i>et al.</i> 2020</b>	2 groups 3 weeks RCT	Mean age: $63 \pm 8$ years. Gender: female: male 18:8 ratio Inclusion: -Adult patient planned for NSCLC resection surgery -Written informed consent  Exclusion: -Tracheotomy -Myasthenia gravis -Unstable coronary artery disease -Unable to perform resistance testing	Usual thoracic physiotherapy + RMET n=14	-Respiratory muscle strength (MIP and MEP)	-No differences were found in both MIP and MEP
<b>Liu <i>et al.</i> 2021</b>	2 groups 6 weeks RCT	Mean age: $64.2$ years (SD=5,9) Inclusion: -Lung cancer -Willing to participate in the study  Exclusion: -Unstable pH -Hemodynamical instability -Severe cardiopathy or limb weakness	Inspiratory muscle training and aerobic exercise n=26  Control group n=28	-Respiratory muscle strength (MIP and MEP)  -Functional capacity (6MWT)	-MIP improved significantly in the intervention group at week 6 (from $71.6 \pm 34.9$ to $94.3 \pm 32.8$ cmH <sub>2</sub> O). MEP improved significantly at week 12 (from $76.1 \pm 20.2$ to $98.6 \pm 35.3$ cmH <sub>2</sub> O)  -6MWT improved significantly at week 2 (from $359.8 \pm 50.7$ to $412.57 \pm 74.2$ meters)
<b>Messaggi-Sartor <i>et al.</i> 2019</b>	2 groups 8 weeks Pilot RCT	Mean age: $64,6$ years (SD=8,5) Inclusion: -Age <80 years -Lung cancer resection -Diagnosis NSCLC stage I or II  Exclusion: -Adjuvant treatment -Postsurgical complications, unable to perform the test -History of thoracic surgery	Aerobic training + IEMT n=16  Control group n=21	-Respiratory muscle strength (MIP and MEP)	-MIP showed a non-significant improvement in the intervention group (Mean difference 13.0% of predicted value). MEP showed a non-significant improvement in the intervention group (Mean difference 9.5% of the predicted value).

<b>Morano et al. 2013</b>	2 groups 4 weeks Pilot RCT	<p>Mean age: 67 years.</p> <p>Inclusion: -Lung resection -Previous lung disease -Obstructive airways disease or interstitial disease with functional impairment</p>	<p>Respiratory muscle resistance training group n=12</p> <p>Lung expansion group n=9</p>	<p>Respiratory muscle strength (MIP and MEP)</p> <p>-Functional capacity (6MWT)</p>	<p>-MIP improved significantly in the respiratory muscle resistance training group (from <math>90 \pm 45.9</math> to <math>117.5 \pm 36.5</math> cmH<sub>2</sub>O). MEP improved significantly in the respiratory muscle strength group (from <math>79.7 \pm 17.1</math> to <math>92.9 \pm 21.4</math> cmH<sub>2</sub>O)</p> <p>-6MWT improved significantly in the respiratory muscle strength group (from <math>425.5 \pm 85.3</math> to <math>475 \pm 86.5</math> meters)</p>
<b>Pimpão et al. 2021</b>	3 groups Pilot RCT	<p>Age range: 40-69 years</p> <p>Inclusion: -Patients diagnosed with cancer and referred to surgery -Age: 20-70 years -Not participating in another study</p> <p>Exclusion: -Patients with unstable hemodynamics -Previous resection surgery -Not physically fit</p>	<p>Kinesio-therapy group n=10</p> <p>IMT group n=10</p> <p>Control group n=10</p>	<p>-Respiratory muscle strength (MIP and MEP)</p> <p>-Functional capacity (6MWT)</p>	<p>-MIP improved significantly in the Kinesiotherapy group (from <math>60.5 \pm 16.4</math> to <math>80 \pm 16.3</math> cmH<sub>2</sub>O). MEP improved non-significantly (from <math>64 \pm 19.6</math> to <math>72.5 \pm 23.2</math> cmH<sub>2</sub>O).</p> <p>-MIP improved significantly in the IMT group (from <math>44 \pm 22.7</math> to <math>72 \pm 19.3</math> cmH<sub>2</sub>O). MEP improved significantly in the IMT group (from <math>55 \pm 18.4</math> to <math>74 \pm 16.4</math> cmH<sub>2</sub>O).</p> <p>-6MWT improved non-significantly in the Kinesiotherapy group (from <math>408 \pm 77.7</math> to <math>405 \pm 51.4</math> meters)</p> <p>-6MWT improved non-significantly in the IMT group (from <math>432 \pm 47.3</math> to <math>452 \pm 34.3</math> meters)</p>
<b>Valkenet et al. 2018</b>	2 groups 3 weeks RCT	<p>Mean age: 63.1 years (SD=7.5) Gender: female: male 68:27</p> <p>Inclusion: -Patients with esophageal cancer referred to surgery -Scheduled esophagectomy -Ability to perform IMT programs</p> <p>Exclusion: -Language barriers -Participation in another study -Underage &lt;18 years</p>	<p>Usual care +IMT n=120</p> <p>Usual care n=121</p>	<p>-Respiratory muscle strength (MIP)</p>	<p>-MIP improved significantly in the intervention group (from <math>76.2 \pm 26.4</math> to <math>89.0 \pm 29.4</math> cmH<sub>2</sub>O) and in the control group (from <math>74.0 \pm 30.2</math> to <math>80.0 \pm 30.1</math> cmH<sub>2</sub>O).</p>
<b>van Adrichem et al. 2014</b>	2 groups 3 weeks Pilot RCT	<p>n=39</p> <p>Inclusion: -Esophageal cancer referred to surgery -Age range 18-65 years -Ability to perform a spirometry</p> <p>Exclusion: -Neuromuscular impairment -Unstable asthma -History of spontaneous pneumothorax -Cognitive impairment</p>	<p>IMT-HI group n=20</p> <p>IMT-E group n=19</p>	<p>-Respiratory muscle strength (MIP)</p>	<p>-MIP improved significantly in the IMT-HI group (from <math>93.5</math> (69.0–120.5) to <math>104.5</math> (95.5–136.3) cmH<sub>2</sub>O) and in the IMT-E group (from <math>84.0</math> (67.0–94.0) to <math>113.0</math> (86.0–126.0) cmH<sub>2</sub>O).</p>

		Mean age: 49 years. All female		
<b>Vardar -</b> 2 groups		Inclusion:	Aerobic exercise + Yoga group n=24	-6MWT improved significantly in the Aerobic exercise + Yoga group (from 509.16 ± 40.97 to 603.01 ± 48.82 meters) and in the Aerobic exercise group (from 93.85 ± 29.56 meters).
<b>Yağlı et al. 2015</b>	6 weeks RCT	-Age 20-60 years -Diagnosed unilateral breast cancer -Finalized oncological treatment at least three years ago	Aerobic exercise group n=28	-Functional capacity (6MWT)
		Exclusion: -Systemic diseases and metastasis -Pharmacological treatment that impairs exercise -Diabetes type I and II		

6MWT: 6 Minute Walk Test; ET: Resistance Time; IEMT: Inspiratory and Expiratory Muscle Training; IMT: Inspiratory Muscle Training; IMT-HI: High Intensity Inspiratory Muscle Training; IMT-E: Resistance Inspiratory Muscle Training; MEP: Maximal Expiratory Pressure; MIP: Maximal Inspiratory Pressure; NSCLC: Non-Small Cell Lung Cancer; RCT: Randomized Controlled Trial; RMET: Respiratory Muscle Exercise Training; SD: Standard Deviation.

### Exercise modalities

Every study implemented respiratory muscle training-centered exercises using external devices, except for a study that implemented aerobic exercise combined with Yoga,<sup>[23]</sup> an indirect training of the respiratory muscles. Another study focused specifically on resistance training exercises for respiratory muscles.<sup>[15]</sup> Six studies combined specific respiratory muscle training exercises with other exercise modalities, such as aerobic exercise,<sup>[16-18, 22]</sup> or high-intensity training.<sup>[17, 21]</sup> The duration of the intervention ranged from two weeks<sup>[14]</sup> to three months,<sup>[22]</sup> with most of the interventions lasting around a period of four weeks.

### Outcome measures

Regarding respiratory muscle function, 8 studies assessed both MIP and MEP,<sup>[14-18, 22, 24, 25]</sup> and 3 studies assessed MIP alone.<sup>[19-21]</sup> Regarding functional capacity, 6 studies assessed the 6MWT.<sup>[16, 18, 19, 22, 23, 25]</sup> Studies assessing respiratory muscle function showed results as the mean difference in centimeters of water (cmH<sub>2</sub>O), except Messagi-Sartor *et al.*<sup>[17]</sup> who presented the mean difference of predicted value as a

percentage. Every study assessing functional capacity showed changes in meters in the 6MWT. Every study presented its results either with the standard deviation or the 95% confidence intervals.

3 studies found a significant improvement in MIP and MEP,<sup>[16, 18, 25]</sup> 4 studies found a significant improvement only in MIP,<sup>[20-22, 24]</sup> 3 studies found non-significant improvements in MIP,<sup>[14, 15, 17]</sup> 6 studies found non-significant improvements in MEP,<sup>[14, 15, 17, 22, 24, 25]</sup> and 1 study reported a worsening of MIP after surgery.<sup>[19]</sup> 4 studies showed significant improvements in the 6MWT,<sup>[16, 18, 22, 23]</sup> 1 found non-significant improvements,<sup>[25]</sup> and 1 found a worsening in 6MWT.<sup>[19]</sup>

### Risk of bias assessment

Results of the risk of bias assessment for the included studies are shown in **Table 3**. The overall risk of bias was good to excellent. 1 study showed “excellent” scores,<sup>[22]</sup> 9 studies showed “good” scores,<sup>[14-18, 20, 21, 24, 25]</sup> and only 2 studies showed scores considered to be “fair”.<sup>[19, 23]</sup>

**Table 3. Results of the risk of bias assessment through the PEDro scale**

Study	Number of Items											Total
	1	2	3	4	5	6	7	8	9	10	11	
Brocki <i>et al.</i> 2016	●	●	●	●			●	●	●	●	●	8/10
Dahhak <i>et al.</i> 2022	●	●	●	●	●		●	●	●	●	●	9/10
de Almeida <i>et al.</i> 2020		●	●	●				●	●	●	●	7/10
Guinan <i>et al.</i> 2019	●	●		●						●	●	4/10
Laurent <i>et al.</i> 2020		●	●	●				●	●	●	●	7/10
Liu <i>et al.</i> 2021	●	●	●	●			●	●		●	●	7/10
Messagi-Sartor <i>et al.</i> 2019	●	●	●	●			●			●	●	6/10
Morano <i>et al.</i> 2013	●	●	●	●			●		●	●	●	7/10
Pimpão <i>et al.</i> 2021	●	●	●	●			●	●	●	●	●	8/10
Valkenet <i>et al.</i> 2018	●	●	●	●			●	●	●	●	●	8/10
van Adrichem <i>et al.</i> 2014	●	●		●			●	●		●	●	6/10
Vardar-Yağlı <i>et al.</i> 2015	●	●	●	●						●	●	5/10

Survival rates of over ten years in patients suffering from cancer are increasing as therapeutic options develop. One of the common impairments found in these patients is related to

the respiratory system, and this is closely linked with muscle function loss. Despite therapeutic exercise being proposed as an effective therapy to overcome these impairments, protocol

components of these programs are heterogeneous, and the understanding of the real effects of therapeutic exercise on respiratory muscle function is not fully developed. Therefore, this systematic review aimed at assessing the effectiveness of therapeutic exercise in respiratory muscle function and functional capacity in patients suffering from cancer.

Considerable levels of heterogeneity were found both in the therapeutic exercise interventions used and the types of cancer, so it is challenging to obtain accurate conclusions. Despite 5 of the included studies (42%) dealing with patients suffering lung cancer,<sup>[14-18]</sup> a type of cancer that could be *a priori* linked with considerable respiratory afflictions, a further analysis assessing the effects of therapeutic exercise in different types of cancer could be an interesting approach, to determine if the effectiveness varies depending on the type of cancer suffered.

Studies implementing interventions of at least 4 weeks showed significant improvements in MIP and MEP.<sup>[16, 18, 22, 24]</sup> Studies not showing significant improvements implemented relatively short interventions, such as the studies conducted by Brocki *et al.*<sup>[14]</sup> (2 weeks) or Laurent *et al.*<sup>[15]</sup> (3 weeks). Conversely, the study with the longest intervention, conducted by Dahhak *et al.*<sup>[22]</sup> (12 weeks) showed significant improvements in every outcome. This aligns with evidence that establishes that to observe an improvement in muscle function, the intervention must be sustained for a minimum period of 4 weeks.<sup>[26]</sup> However, the study conducted by Messagi-Sartor *et al.*<sup>[17]</sup> implemented a relatively long intervention (8 weeks), yet were unable to evidence significant improvements, and this might be due to the limited sample (16 participants in the intervention group) they used, that might've been unable to reach statistical significance. Contrary to that, Valkenet *et al.*<sup>[20]</sup> used a larger sample (120 participants in the intervention group) and were able to reach statistical significance after only 3 weeks of intervention. This evidences that results should be interpreted with caution, as both time and sample size seem to be relevant when reaching statistical significance.

Studies assessing functional capacity showed significant improvements in 6MWT,<sup>[16, 18, 22, 23]</sup> except for the studies conducted by Guinan *et al.*<sup>[19]</sup> and Pimpão *et al.*<sup>[25]</sup> Firstly, Guinan *et al.* presented a study that is embedded within another included study in this review,<sup>[20]</sup> and they assessed their outcomes before and after a surgical esophagectomy. Even though significant improvements were found in the other study, advocating for the benefits of exercise prehabilitation, Guinan *et al.* evidenced that despite implementing a therapeutic exercise intervention before surgery (which they called “preoperative inspiratory muscle training to prevent postoperative pulmonary complications in patients undergoing esophageal resection”, or PREPARE) this intervention is insufficient to prevent muscle function loss, and they allude to an insufficient training period and differences between baseline characteristics of their sample groups to discuss these results. Additionally, reasons for the non-significant improvements in 6MWT results for Pimpão *et al.* could be aligned with the latter explanation of insufficient sample size (10 participants per group).

## Limitations

This study presents several limitations. As the authors wanted to review the latest published evidence, retrieved studies were limited to the last ten years, potentially omitting the inclusion of studies that might've influenced the interpretation of results. Also, further analyses involving different types of cancer should be conducted, as different types of cancer require different forms and intensities of exercise. Finally, any type of cancer and at any stage of treatment was considered for this review, and this could influence the generalizability of results.

However, this study also presents several strengths. Six different databases were accessed to retrieve studies, and no language restrictions were applied. Also, the review protocol was previously registered in the international registry PROSPERO. All of these elements ensure that this systematic review is not incurring several biases, assuring methodological quality as best as possible. The methodological quality of the included studies was also assured by the risk of bias assessment, as 83% of the included studies showed “good” to “excellent” scores on the PEDro scale.

## Conclusion

Studies assessing the effectiveness of therapeutic exercise on respiratory muscle function and functional capacity in patients suffering from cancer are limited and remain controversial. Further research is needed to gain a more thorough understanding of the effects of different types of exercise on different types of cancer, as therapeutic exercise has the potential to overcome the adjuvant impairments that might be present in these populations.

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## Conflict of interest

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## Ethics statement

None.

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