

# Effects of non-Pharmacological Approaches on Physical Symptoms of Individuals with Advanced Cancer: Systematic Review

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*Efeitos de Abordagens não Farmacológicas nos Sintomas Físicos de Indivíduos com Câncer Avançado: Revisão Sistemática*  
*Efectos de los Enfoques no Farmacológicos sobre los Síntomas Físicos de las Personas con Câncer Avanzado: Revisión Sistemática*

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## ABSTRACT

**Introduction:** Cancer is a public health problem, which, in advanced stages, can cause physical, psychosocial and spiritual discomfort. Thus, physiotherapeutic approaches and Complementary Integrative Practices (CIPS) appear as important tools for the control and improvement of physical symptoms of these individuals. **Objective:** To describe the effects of non-pharmacological approaches, involving physiotherapy techniques and CIPs on the physical symptoms of individuals with advanced cancer. **Method:** Systematic review of the literature with randomized controlled trials addressing the effects of physiotherapy approaches or CIPS on the physical symptoms of individuals diagnosed with advanced cancer. The PubMed, LILACS, PEDro, Cochrane, SciELO databases were selected, and the last search occurred in April 2021. PEDro scale was applied to evaluate the methodological quality of the studies. **Results:** Both approaches can have positive effects on physical symptoms, such as fatigue and pain, in the population investigated as demonstrated in the twenty-two studies included. **Conclusion:** Physical therapy and CIPS have positive effects on physical symptoms in individuals diagnosed with advanced cancer. However, there are few studies with sufficient methodological quality to confirm their effectiveness in the outcomes for this population.

**Key words:** neoplasm/therapy; palliative care; physical therapy modalities; complementary therapies.

## RESUMO

**Introdução:** O câncer é um problema de saúde pública que, em estágios avançados, pode ocasionar desconfortos físicos, psicossociais e espirituais. Assim, abordagens fisioterapêuticas e as Práticas Integrativas e Complementares em Saúde (PICS) surgem como ferramentas importantes para o controle e melhora de sintomas físicos nesses indivíduos. **Objetivo:** Descrever os efeitos de abordagens não farmacológicas, envolvendo técnicas fisioterapêuticas e PICS nos sintomas físicos de indivíduos com câncer avançado. **Método:** Revisão sistemática da literatura composta por ensaios clínicos randomizados que abordassem os efeitos de abordagens fisioterapêuticas ou PICS nos sintomas físicos de indivíduos diagnosticados com câncer avançado. Foram selecionadas as bases de dados PubMed, LILACS, PEDro, Cochrane, SciELO, e a última busca ocorreu em abril de 2021. A avaliação da qualidade metodológica dos estudos foi realizada por meio da escala PEDro. **Resultados:** Vinte e dois estudos foram incluídos, e demonstraram que ambas as abordagens têm efeitos positivos para os sintomas físicos, como fadiga e dor, na população estudada. **Conclusão:** A fisioterapia e as PICS têm efeitos positivos nos sintomas físicos em indivíduos com diagnóstico de câncer avançado. No entanto, existem poucos estudos com qualidade metodológica suficiente para confirmar a eficácia das duas abordagens nos desfechos estudados para essa população.

**Palavras-chave:** neoplasias/terapia; cuidados paliativos; modalidades de fisioterapia; terapias complementares.

## RESUMEN

**Introducción:** El cáncer es un problema de salud pública que, en etapas avanzadas, puede causar malestar físico, psicosocial y espiritual. Así, los enfoques fisioterapéuticos y las Prácticas Integradoras y Complementarias en Salud (PICS) aparecen como herramientas importantes para el control y mejoría de los síntomas físicos en estos individuos. **Objetivo:** Describir los efectos de los enfoques no farmacológicos, que incluyen técnicas de fisioterapia e PICS, sobre los síntomas físicos de las personas con cáncer avanzado. **Método:** Revisión sistemática de la literatura, que incluyó ensayos controlados aleatorios que abordaron los efectos de los enfoques de fisioterapia o PICS en los síntomas físicos de las personas diagnosticadas con cáncer avanzado. Se seleccionaron las bases de datos PubMed, LILACS, PEDro, Cochrane, SciELO y la última búsqueda se realizó en abril de 2021. La evaluación de calidad metodológica de los estudios se realizó mediante la escala PEDro. **Resultados:** Se incluyeron veintidós estudios que demostraron que ambos enfoques pueden tener efectos positivos sobre los síntomas físicos, como la fatiga y el dolor, en la población estudiada. **Conclusión:** La fisioterapia y las PICS tienen efectos positivos sobre los síntomas físicos en personas diagnosticadas con cáncer avanzado. Sin embargo, existen pocos estudios con suficiente calidad metodológica para confirmar la efectividad de ambos en los desenlaces estudiados para esta población.

**Palabras clave:** neoplasias/terapia; cuidados paliativos; modalidades de fisioterapia; terapias complementarias.

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## INTRODUCTION

Cancer is a health public problem and its diagnosis mainly at advanced stages with no perspective of cure brings great suffering both to the patient and its family<sup>1,2</sup>. Physical, psychosocial and spiritual discomforts that patients with cancer live occur simultaneously with other problems and this endless fight diminishes the quality-of-life<sup>3</sup>. At more advanced stages or in patients in palliative care, fatigue is more intense which should be the focus of healthcare professionals<sup>3</sup>.

Typically, patients with advanced cancer need readmissions due to physical symptoms as pain, fever, dyspnea and fatigue, the latter, one of the most prevalent symptoms in these patients, most of all with metastases, prolonging for days or years at any time in the course of the oncologic treatment<sup>4-6</sup>.

The etiology of these symptoms is multifactorial, and a vicious cycle ensues where patients usually lose muscle mass, reduce the levels of physical activity, resulting in generalized weakness and debilitating symptoms<sup>5</sup>. Thus, a significant reduction of the functional and psychosocial ability can occur causing limitations in performing daily physical and working activities with impact in their quality-of-life<sup>3,7</sup>.

The required transformation of the current caring model determined by a predominantly hospital-centered, fragmented curative and biologicism pattern is challenging if full attention to health is considered<sup>3,8</sup>. The integrality perspective is grounded in the holistic vision of the man which is based in a psychosocial model comprehending diverse skills in multiprofessional teams, including non-pharmacological approaches<sup>3,8</sup>.

The physiotherapy practice is included in this scenario, improving the muscle strength, aerobic capacity, production of energy, mood and emotional symptoms change, preventing functional decay and improving the quality-of-life and functionality<sup>6,9,10</sup>. In addition, the Integrative and Complementary Health Practices (PICS) may help to involve all the dimensions, beliefs and spirituality of the individual, offering an array of options as art therapy, Yoga, meditation, music therapy, chiropractic, osteopathy, Reiki, aromatherapy, bioenergetics among others, as a complement of physiotherapy treatment and eventually improving the physical symptoms of the individual with advanced cancer<sup>3,8</sup>.

The objective of this study is to describe the effects of non-pharmacological approaches involving physiotherapeutic practices and PICS in the physical symptoms of individuals with advanced cancer.

## METHOD

Systematic review of the literature registered at the International Prospective Register of Systematic Reviews

(PROSPERO), ID CRD42021243694 to identify studies addressing physiotherapy approach or PICS for physical symptoms of individuals with advanced cancer.

The identification of eligible studies followed the strategy PICOS: Population – individuals with advanced cancer of both sexes and any age range; Intervention – physiotherapy approach or PICS; Comparison – other approaches, usual care or no intervention; Outcome – physical symptoms evaluated with scales and/or tests validated; Study Design – randomized clinical trials (RCT).

The review was planned and conducted according to Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA)<sup>11</sup>, consisting in 27 items which ensures that the authors produce a complete and consistent report of systematic analyzes and meta-analysis.

Inclusion criteria were: RCT published in Portuguese, English and Spanish between January 2010 and February 2021, involving individuals with advanced cancer who underwent physiotherapy, and their physical symptoms were investigated. Duplicate articles, studies primarily investigating effects of another health area, clinical trial protocols, feasibility studies with statistical results of the outcomes evaluated, thesis, dissertations and abstracts were excluded. Original articles published were searched at the databases PubMed via Medical Literature Analysis and Retrieval System (MEDLINE), Latin American and Caribbean Literature on Health Sciences (LILACS), Physiotherapy Evidence Database (PEDro), Cochrane Library, and Scientific Electronic Library Online (SciELO), further to clinical trials with results related to published protocols, the last search occurred in April 2021. The search strategy utilized in the databases PubMed, LILACS, Cochrane Library and SciELO was: ((((((((((“physiotherapy”) OR (“physical therapy”) OR (“exercise”) OR (“exercise therapy”) OR (“integrative medicine”) OR (“integrative oncology”) OR (“complementary therapies”) AND (“advanced cancer”) OR (“advanced cancer patients”) OR (“neoplasm”) AND (“fatigue”) OR (“physical symptoms”). At PEDro database, only the expression AND was utilized for individual combinations of descriptors as shown in Chart 1. For all databases, last ten-years filter was applied and the filter clinical trial at the database Cochrane Library.

To avoid loss of articles, the search strategy at PubMed was included (((“integrative medicine”[MeSH Terms] OR “complementary therapies”[MeSH Terms] OR Integrative Oncology[MeSH Terms] OR “integrative medicine” OR “holistic”[TIAB] OR “alternative therap\*” OR “alternative medicine” OR “medicine alternative”)) AND ((“physical therapy modalities”[MeSH Terms] OR “Exercise Therapy”[Mesh] OR “physical therapy”[TIAB] OR physiotherap\*)) AND (advanced cancer patients).

Initially, two reviewers read titles and abstracts to find which were compatible with the theme proposed

Chart 1. PEDro search strategy

DESCRIPTORS AND COMBINATIONS	
1	- "Complementary therapy" "advanced cancer" "fatigue"
2	- "Complementary therapy" "advanced cancer" "physical symptoms"
3	- "Physiotherapy" "advanced cancer patients"
4	- "Exercise" "advanced cancer" "fatigue"
5	- "Exercise" "advanced cancer" "physical symptoms"
6	- "Physiotherapy" "advanced cancer" "fatigue"
7	- "Physiotherapy" "advanced cancer" "physical symptoms"
8	- "integrative medicine" "advanced cancer" "physical symptom"
9	- "integrative medicine" "advanced cancer" "fatigue"
10	- "integrative oncology" "advanced cancer" "physical symptom"

in the review; after this, they read the articles in full and selected those to be included in the study. Discrepancies were resolved upon consensus between the two reviewers and a third reviewer.

The purpose of the 11-items PEDro scale is to help the methodological evaluation of the RCT selected, in addition to the statistical description to verify if the studies present sufficient information to make their results interpretable. The first item of this scale is related to the external validity, not being used to calculate the score and a score range from zero to ten<sup>12</sup>. Two reviewers applied this scale and if discrepancies were found, a consensus was reached among them and a third reviewer.

Two independent reviewers extracted the descriptive data and the outcomes in accordance with standard forms adapted from the Cochrane handbook<sup>13</sup>. The general aspects of the studies, of the population evaluated (mean age, gender and diagnosis), of the intervention applied (sample size, protocols utilized, frequency, duration of each session, supervision), outcomes evaluated, assessment of clinical results and results presented were considered. Values of *p* or mean differences to analyze the clinical or significant improvement were analyzed. Discrepancies were resolved by consensus between the reviewers and the results were summarized in tables.

## RESULTS

After exclusion of repeated articles, 8,568 were screened, among them, 44 were selected for full reading review, of which 22 were included (Figure 1), with 1,717 participants randomized to join the studies. The

methodological quality of the studies was evaluated with PEDro scale and reached a mean of 5.3 points (Table 1).

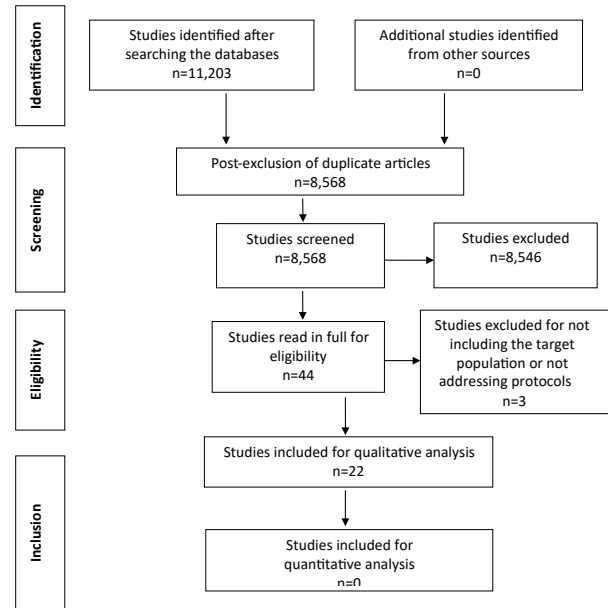


Figure 1. PRISMA flowchart with number of studies identified, included and excluded in the systematic review

The main characteristics of the articles included are shown in Table 2, all the studies were randomized clinical trials – RCT, but ten were crossovers and pilots<sup>14-23</sup>. Together, they encompass adult and older populations. The samples range from 20 to 286 participants.

The diagnoses of the participants were mainly: lung, gastrointestinal, prostate and breast stages III and IV cancer. The prevalent metastasis site was bone tissue, mainly at the spine.

Among the physical symptoms presented in patients with advanced diagnosis were fatigue and pain evaluated with several instruments. The other outcomes and respective evaluation instruments are listed in Table 2.

The studies which applied physiotherapy interventions<sup>15,17,19,21,22,24-32</sup> adopted the following approaches: resistance exercise, aerobic/cardiovascular, electrotherapy and manual therapy. The studies of PICS<sup>14,16,18,20,23,33-35</sup> involved acupressure, yoga (integrative mindful), reflexology aromatherapy massage and medical Qigong. The frequency ranged from one to five times a week with sessions lasting between 20 minutes and two hours for five to 12 days of intervention (Table 3).

Only one study selected<sup>25</sup> revealed that the physiotherapy intervention did not present clinical or statistically significant improvement in any of the outcomes evaluated. All the other studies showed improvement after intervention in at least one physical symptom evaluated (Table 2).

Table 1. Evaluation of the methodological quality by PEDro scale

Author/year	1	2	3	4	5	6	7	8	9	10	11	Total
Cheung et al., 2020	X	X	X	X			X	X	X	X	X	8/10
Cheville et al., 2013	X	X	X	X					X	X	X	6/10
Dhillon et al., 2017	X	X		X					X	X	X	5/10
Galvão et al., 2018	X	X	X	X				X		X	X	6/10
Jensen et al., 2014	X	X		X						X	X	4/10
Lai et al., 2011	X	X							X	X	X	4/10
López-Sendín et al., 2012	X	X		X			X		X	X	X	6/10
Lim et al., 2011	X	X	X	X				X	X			5/10
Litterini et al., 2013	X	X		X					X	X	X	5/10
Maddocks et al., 2013	X	X		X						X	X	4/10
Nakano et al., 2020	X	X		X				X	X	X	X	6/10
Oldervoll et al., 2011	X	X		X						X	X	4/10
Porter et al., 2019	X	X	X	X			X		X	X	X	7/10
Rief et al., 2014	X	X	X	X						X	X	5/10
Pyszora et al., 2017	X	X		X				X		X	X	5/10
Schuler et al., 2016	X	X		X						X	X	4/10
Scott et al., 2018	X	X		X					X	X		4/10
Sikorskii et al., 2020	X	X		X					X	X	X	5/10
Toth et al., 2013		X		X					X	X	X	5/10
Vadiraja et al., 2017	X	X	X	X						X	X	5/10
Vanderbyl et al., 2017	X	X		X			X			X	X	5/10
Wyatt et al., 2012	X	X	X	X			X	X	X	X	X	8/10

**Captions:** 1 = Eligibility criteria and origin of the participants; 2 = Random distribution; 3 = Allocation was concealed; 4 = Baseline comparability; 5 = Blinded participants; 6 = Blinded therapists; 7 = Blinded assessors; 8 = Proper follow-up; 9 = Analysis of the intent-to-treat; 10 = Groups comparisons; 11 = Point estimates and variability.

(\*) Item 1 not included in total points.

Among the eight studies applying PICS, those of integrative yoga<sup>34</sup>, aroma therapy massage<sup>16</sup> and reflexology<sup>33,35</sup> presented statistically significant improvement greater in the intervention group for the outcomes fatigue, physical domain of the McGill Quality of Life for Hong Kong Chinese, pain, severity of dyspnea and physical functioning. However, in an intragroup analysis, the studies applying medical Qigong<sup>23</sup> and aroma therapy massage<sup>16</sup> presented post-intervention statistically improvement in functioning capacity and constipation, respectively.

## DISCUSSION

This systematic review showed that physiotherapy or PICS have positive effects on physical symptoms of individuals diagnosed with advanced cancer. The studies selected suggest that PICS should be incorporated as complementary therapy in rehabilitation for this population.

Physiotherapy in oncology plays an important role in prevention and rehabilitation including individuals in palliative treatment, of oncologic-treatment related adverse effects and attempt to restore the functional-kinetic integrity of organs and systems, counting with an array of techniques to reach this goal<sup>36</sup>. Overall, the studies investigated utilizing therapeutic interventions brought significant improvement of physical symptoms as functional mobility (with balance and gait speed), functioning capacity, muscle strength, pain, daily life activities and, mainly, fatigue, the outcome mostly evaluated.

Other studies which analyzed the application of physiotherapy<sup>37-41</sup>, with electrotherapy, resistance or aerobic exercises have also indicated positive effects on physical symptoms, corroborating the present findings.

One study alone did not find significant improvement in any outcome. Possibly, its low methodological quality explains this conclusion, as other studies which have also specifically addressed individuals diagnosed with lung

Table 2. General characteristics of the studies selected

Author/year	Design	Objective	Characteristics of the Population	Outcomes and evaluation	Main results
Cheung et al., 2020	RCT (pilot)	To evaluate the feasibility and potential effects of patient-centered self-administered acupressure for alleviating fatigue and co-occurring symptoms among Chinese advanced cancer patients receiving treatment.	N=30 (26 reevaluated) Mean age: 58.93-61.8 years Gender: 24F Advanced stage cancer (IIIB or IV)	Fatigue (Chinese BFI), quality-of-life – items of physical questions and functioning well-being (FACT-G)	Clinical improvement in fatigue in the intervention group after 4 weeks (mean difference -0.58, 95% CI, -2.81 to 1.65), but without statistically significant difference. Only the intervention group presented clinical improvement of pain (MD = -0.35, 95% CI -1.89 to 1.19) without reaching statistic relevance
Chevillat et al., 2013	RCT	To estimate the effect of a rapid easy strength training (REST) and walking based in pedometer of patients debilitated with stage IV lung and colorectal cancer	N=66 (56 reevaluated) Mean age: 63.8-65.5 years Gender: 35M Metastatic lung and colorectal cancer (stage IV)	Self-reported mobility (AM-PAC CAT, AM-PAC Mobility Activities Short Forms; quality-of-life—items of physical questions and functioning well-being (FACT-G); Fatigue (FACT-F); Pain: NVS	Statistically significant improvement in SF mobility and fatigue in intra-group analysis ( $p=0.01$ and $p=0.02$ ) and inter-group ( $p=0.002$ and $p=0.03$ ) respectively
Dhillon et al., 2017	RCT	Assess whether a 2-month physical activity intervention improves fatigue and quality-of-life for people with advanced lung cancer	N=111 (90 reevaluated) Mean age: 64 years Gender: 61M Lung cancer (stages III and IV)	Fatigue (FACT-F), dyspnea (SBQ), function, activity and physical ability (6MWT, SFT, palm grip strength, Actigraphy GT1M accelerometers; AAQ, e Sedentary Behavior Questionnaire)	No relevant clinical or statistical improvement in any outcome
Galvão et al., 2018	RCT	Examine the efficacy and safety of a multimodal modular exercise program in patients with prostate cancer and bone metastasis	N=57 (49 reevaluated) Mean age: 70 (SD 8.4) years Bone metastasis	Physical functioning (SF-36, TUG-T; 6MWT –fast and slow; 400MWT); muscle strength (1RM); balance (SOT); lean and fat mass (dual-X-rays absorciometry); fatigue (FACIT-F)	After 3 months, there was statistically significant intergroup difference in physical functioning ( $p=0.028$ ) and muscle strength of extensors of LL ( $p=0.033$ ). There was no relevant improvement of other outcomes
Jensen et al., 2014	RCT (pilot)	Investigate the feasibility of two different physical training programs in patients with advanced gastrointestinal cancer in palliative chemotherapy	N=21 Mean age: 55 (SD 13.1) years Gender: 11F Advanced gastrointestinal cancer	Quality-of-life – physical functioning, fatigue, pain, dyspnea (EORTC-QLQ-C30 version 3), muscular strength (1RM), cardiorespiratory fitness (WHO Bicycle Modified Protocol); daily life activity (SenseWear) wrist-band; level of daily activity (Freiburg Questionnaire of Physical Activity)	Statistically significant improvement in group RET for LL muscles, posterior thoracic, biceps and knee flexors ( $p<0.05$ ); volume of daily physical activity improved in the group AET ( $p=0.034$ ); metabolic rate improved for both groups ( $p<0.03$ ); statistically significant improvement of fatigue for both groups ( $p=0.003$ ); health status and global function had better results in the group AET

to be continued

Table 2. continuation

Author/ year	Design	Objective	Characteristics of the Population	Outcomes and evaluation	Main results
Lai et al., 2011	RCT (pilot)	Verify the effect of aroma massage on constipation of patients with advanced cancer	N=45 (32 reevaluated) Gender: 24M Any advanced stage cancer	Constipation (CAS) and quality-of-life (MQOL-HK)	Improvement of constipation in group of aroma massage and massage, being statistically significant for the latter ( $p=0.0002$ ); great improvement in intra and intergroup analysis in aroma massage for physical domain of MQOL-HK
López- Sendín et al., 2012	RCT (pilot)	Determine the effects of physiotherapy, including massage and exercise, in pain and mood of patients with terminal advanced cancer	N=24 Mean age: 54 (SD=8) years Gender: 18M Any stage III and IV cancer	Pain (BPI and MPAC); symptoms of physical stress (MSAS)	Greater improvement in IG for BPI worst pain ( $p=0.036$ ), BPI pain right now ( $p=0.027$ ), BPI index ( $p<0.001$ ) and MPAC pain differences ( $p=0.04$ ). IG with significant improvement in intragroup analysis and MSAS physical
Lim et al., 2011	RCT (pilot)	Document the changes of symptoms after acupuncture and determine feasibility of randomized acupuncture study in incurable advanced cancer	N=18 Mean age: 55 years Gender: 15F Any advanced stage cancer	Change of symptoms like pain, tiredness, loss of appetite, nausea and shortness of breath (ESAS)	After 6 weeks, the group acupuncture presented clinical improvement of shortness of breath, tiredness and dizziness (reduction of 1.0-2.75 points); the group of support therapy had clinical improvement of nausea, dizziness, pain, tiredness and loss of appetite (reduction of 1.25-2.5 points)
Litterini et al., 2013	RCT	Compare the effects of resistance and cardiovascular training in functional mobility of individuals with advanced cancer	N=66 (52 follow-up) Mean age: 62.35 years Gender: 36F Any advanced stage cancer	Functional mobility – combination of balance, gait speed and strength of LL (SPPB); fatigue and pain (VAS 100-mm)	Intragroup analysis for both groups presented significant improvement of SPPB (total, balance and chair stands scores), fatigue. Great improvement in cardiovascular group in SPPB total score ( $p=0.45$ )
Maddocks et al., 2013	RCT	Determine the acceptability of NMES of the quadriceps in patients with non-small cells lung cancer in palliative chemotherapy	N=49 (15 reevaluated) Mean age: 60 years Gender: 28M Stage IV non-small cells lung cancer	Muscle strength of quadriceps (manual dynamometer); body composition (dual-X-rays absorciometry), fatigue (MFI-20); quality-of-life – physical functioning (EORTC-QLQ-C30 and LC-13)	Statistically significant improvement of fatigue ( $p=0.03$ ) favoring the group of electrical stimulation. No relevant change in peak force, muscle mass or aspects of physical activity
Nakano et al., 2020	RCT (crossover)	Evaluate the effects of TENS in pain and other physical symptoms in patients with advanced cancer in palliative care	N=20 Mean age: 70 (SD=6.3) years Gender: 17M Any advanced stage cancer	Pain (questionnaires involving NVS), physical symptoms (EORTC-QLQ- C15-PAL)	Group TENS presented statistically significant improvement for loss of appetite ( $p=0.02$ ) and in intra and intergroup analysis immediately post treatment and nausea/vomit ( $p<0.05$ )

to be continued



Table 2. continuation

Author/ year	Design	Objective	Characteristics of the Population	Outcomes and evaluation	Main results
Oldervoll et al., 2011	RCT	Examine the efficacy and safety of a multimodal modular exercise program in patients with prostate cancer and bone metastasis	N=231 (163 reevaluated) Mean age: 62 years Gender: 144F Any incurable advanced stage cancer	Fatigue (FQ); physical performance (OST, palm grip strength, shuttle walk test, SWT)	Compared to UCG, PAG presented statistically significant and clinical improvement in SWT ( $p=0.001$ ), OST ( $p=0.05$ ), palm grip strength ( $p=0.05$ ) and shuttle walk test ( $p=0.04$ ). There was also more weight gain in PAG
Porter et al., 2019	RCT (pilot)	Examine the acceptability of a yoga program for patients with metastatic breast cancer	N=63 (55 evaluated) Mean age: 57.3 (SD=11.5) years Metastatic breast cancer	Pain (Client Satisfaction Questionnaire-8); fatigue (BFI); functioning capacity (6MWT)	Women in yoga had discreet improvement of fatigue and walked longer distances post-treatment and after 6 months of follow-up
Rief et al., 2014	RCT (pilot)	Compare the effects of resistance training versus passive physiotherapy, fatigue, emotional stress during radiotherapy in patients with spine bone metastasis	N=60 Mean age: 61.3-64.1 years Gender: 33F Bone metastasis (sacral, lumbar or thoracic)	Fatigue (EORTC QLQ FA13)	After 6 months, patients of the intervention group presented statistically significant improvement of fatigue ( $p=0.013$ ) and interference in daily life ( $p=0.006$ )
Pyszora et al., 2017	RCT	Evaluate the effect of a physiotherapy program on cancer related fatigue and other symptoms in patients diagnosed with advanced cancer	N=60 (58 reevaluated) Mean age: 69.3-72.4 years Gender: 39F Any advanced stage cancer	Fatigue (BFI); intensity of other disease symptoms (ESAS)	The intervention group had statistically improvement of fatigue (BFI and ESAS), as well as pain, well-being and appetite ( $p<0.01$ )
Schuler et al., 2016	RCT	Test the impact of a structured individual sports program on fatigue in patients with advanced cancer	N=70 (40 follow-up) Mean age: 52.38 years Gender: 41M Any advanced stage cancer	Fatigue (MFI); functioning capacity – endurance (6MWT); physical activity (IPAQ)	Statistically significant improvement of severity of fatigue in evaluation and follow-up in the group of exercise plus physiotherapy near home ( $p=0.017$ and $p=0.006$ , respectively)
Scott et al., 2018	RCT	Determine acceptability and safety of aerobic training in metastatic breast cancer	N=65 Mean: 54 (SD=11) years Metastatic breast cancer	Dose of exercises (MME); cardiorespiratory fitness – VO <sub>2</sub> peak (PET-CT limited due to symptoms in supervised treadmill by 12 lead ECG); functioning capacity (6MWT, 30 seconds OST, TUG-T); physical functioning (SF-36); fatigue (FACT-F); pain (BPI)	Improvement of VO <sub>2</sub> peak, OST and TUG-T in the aerobic group and SF-36 ( $p<0.04$ ). Significant difference in favor of intervention group only in SF-36 ( $p=0.03$ )
Sikorskii et al., 2020	RCT	Examine symptom responses resulting from a home-based reflexology intervention delivered by a friend/family caregivers to women with advanced breast cancer	N=209 Mean age GI: 58.95 (SD=11.32) years Gender: 209F Stages III and IV breast cancer	Severity of symptoms such as pain, fatigue, shortness of breath, appetite reduction, dry mouth, nausea, vomit, numbness/tingling (MDASI)	Reflexology was helpful in decreasing patient-reported pain ( $p=0.03$ ), without significant differences for other symptoms despite clinical improvement for fatigue

to be continued

Table 2. continuation

Author/ year	Design	Objective	Characteristics of the Population	Outcomes and evaluation	Main results
Toth et al., 2013	RCT (pilot)	Determine the feasibility and effects of providing therapeutic massage at home for patients with metastatic cancer	N=39 Mean age: 55.1 (SD=11) years Gender: 32F Metastatic cancer	Pain (BPI and Pain Severity Subscale); daily life activity (Katz Scale)	Great improvement in the massage group for physical well-being ( $p=0.005$ ). Pain was reduced more than the no-touch intervention group ( $p=0.04$ ), but lost statistical significance after baseline adjustment
Vadiraja et al., 2017	RCT	Evaluate the effects of integrated yoga versus stress supportive therapy and fatigue of patients with advanced breast cancer	N=91 (75 reevaluated) Mean age: 50.54 years Gender: 91M Advanced breast cancer	Fatigue (FSI)	Severity, frequency, interference and daily variation of fatigue improved significantly than CG ( $p<0.001$ )
Vanderbyl et al., 2017	RCT (crossover)	Compare the impact of medical Qigong and physical exercise and identify if either one is better to improve functional capacity and reduce symptoms	N=36 (24 reevaluated) Mean age: 60 years Gender: 14M Gastrointestinal cancer or non-small cell lung cancer (stages III and IV)	Functional capacity (SFA – 6MWT + walking speed + OST + reach test); quality-of-life – physical function (FACT-G)	Greater improvement of the exercise group for well-being ( $p=0.03$ ), weakness ( $p=0.01$ ) and 6MWT ( $p=0.002$ ). Qigong group despite not better in exercise, improved significantly the 6MWT ( $p=0.02$ )
Wyatt et al., 2012	RCT	Evaluate safety and efficacy of reflexology	N=286 Mean age: 55.3 years Gender: 286F Stage III and IV recurrent and metastatic breast cancer	Physical functioning (SF-36), quality-of-life – physical, emotional, social, functional, aspects and others related to breast cancer (FACT-B), fatigue (BFI), pain (BPI-SF)	Reflexology group significantly improved the severity of dyspnea compared to CG ( $p<0.01$ ) and LFM group ( $p=0.02$ ) and in physical functioning compared to CG ( $p=0.04$ ); LFM group presented reduction of severity significantly greater compared to CG ( $p<0.01$ )

**Captions:** RCT = randomized clinical trial; BFI = Brief Fatigue Inventory; FACT-G = Functional Assessment of Cancer Therapy-General; MD = mean difference; CI = confidence interval; REST = rapid, easy, strength training; AM-PAC = Activity Measure for Post-Acute Care; CAT = Computer Adaptive Test; FACT-F = Functional Assessment of Cancer Therapy-Fatigue; NVS = numerical verbal scale of pain; SBQ = Shortness of Breath Questionnaire; 6MWT = six-minutes-walk test; SFT = Seniors Fitness Test; AAQ = Active Australia questionnaire; SD = Standard Deviation; SF-36 = 36 items Short-Form; TUG-T = Time Up and Go Test; 400MWT = 400-meters walk test; IRM = one repetition maximum; SOT = Sensory Organization Test; FACIT-F = Functional Assessment of Chronic Illness Therapy-Fatigue; LL = lower limbs; EORTC-QLQ-C30 = European Organization for Research and Treatment of Cancer Quality of Life Questionnaire; WHO = World Health Organization; RET = Resistance Exercise Training; AET = Aerobic Exercise Training; CAS = Constipation Assessment Scale; MQOL-HK = McGill Quality of Life for Hong Kong Chinese; BPI = Brief Pain Inventory; MPAC = Memorial Pain Assessment Card; MSAS = Memorial Symptom Assessment Scale; IG = intervention group; ESAS = Edmonton Symptom Assessment System; SPPB = Short Physical Performance Battery; VAS = visual analogue scale; mm = millimeter; NMES = neuromuscular electrical stimulation; MFI = Multidimensional Fatigue Inventory; LC-13 = Lung Cancer Module; TENS = Transcutaneous Electrical Nerve Stimulation; EORTC-QLQ-C15-PAL = European Organization for Research and Treatment of Cancer Quality of Life Questionnaire-Core 15-Palliative Care; FQ = Fatigue Questionnaire; OST = orthostatic sitting training; SWT = Shuttle Walk Test; UCG = usual care group; PAG = physical activity group; EORTC QLQ FA13 = European Organization for Research and Treatment of Cancer Quality of Life Questionnaire for Fatigue; IPAQ = International Physical Activity Questionnaire Short Form; MME = multiple metabolic equivalents; VO<sub>2</sub>peak = peak oxygen uptake; PET-CT = positron emission tomography computed; MDASI = The M.D. Anderson Symptom Inventory; FSI = Fatigue Symptom Inventory; CG = control group; SFA = Simmonds Functional Assessment; FACT-B = Functional Assessment of Cancer Therapy – Breast; BPI-SF = Brief Pain Inventory – Short Form; LFM = Lay Foot Manipulation.

**Value of  $p<0.05$ :** statistically relevant.

cancer presented statistically significant improvement in fatigue and mobility.

PICS applied in the selected studies encompassed yoga, acupressure, acupuncture, reflexology, aroma therapy massage and medical Qigong. Yoga and Qigong are included in practices of mind-body and target the interactions among brain, mind, body and behavior intended to use the mind as influencer of the physical

functioning and promote health. Both incorporate movements and positions, breathing techniques and meditation with the objective of creating harmony and reestablish the balance between mind and body. Consequently, have positive impact on emotional disorders (depression, anxiety), pain, physical fitness, sleep disorders and quality-of-life. In addition, according to the traditional Chinese medicine, cancer develops from



Table 3. Interventions of the studies selected – physiotherapy approaches and PICS

Author/year	Type	Session	Frequency	Duration	Supervision	Comparison Group
Cheville et al., 2013	Protocol REST + pedometer-based walking	1 <sup>st</sup> day: 90 minutes of instructive session; REST: enough time to do 10 (may reach 15) repetitions per exercise; Pedometer: 1 km in 20 minutes	REST: twice a week Walking: four times a week	8 weeks	Physiotherapists	Usual care
Dhillon et al., 2017	Individual physical activity program (emphasis in aerobic exercise – guidelines for resistance exercises) and behavioral support	Nearly 1 hour; PA: 30 to 45 minutes; BS: 15 to 30 minutes	Once a week	8 weeks	Consultant of physical activity	Usual care
Galvão et al., 2018	Physical exercise program (aerobic, resistance and flexibility exercises)	1 hour	Three times a week	3 months	Physiotherapist	Usual care
Jensen et al., 2014	Resistance and aerobic exercise programs	45 minutes	Twice a week	12 weeks	Not informed	–
López-Sendín et al., 2012	Manual therapy and exercises (ex.: PNF)	30 minutes	Three times a week	2 weeks	Physiotherapist	Contact/simple manual touch
Litterini et al., 2013	Resistance <i>versus</i> cardiovascular exercise	30-60 minutes	Twice a week	10 weeks	Physiotherapists	–
Maddocks et al., 2013	Neuromuscular electrical stimulation of quadriceps (Fr: 50 Hz; Ws: 350 ms, increasing cycle in 11%-18%-25% and steady hereinafter; amplitude: 0-120 mA)	30 minutes	At least three-times a week, possibly daily	8-11 weeks (3-4 cycles of chemotherapy)	Not informed	Usual care
Nakano et al., 2020	TENS (high-frequency: 100 Hz, except for constipation: 10 Hz)	30 minutes	Daily	5 days of intervention and 5 days of usual care	Investigator physician	–
Oldervoll et al., 2011	Physical exercise program (warming, circuit, stretching and relaxation)	50-60 minutes	Twice a week	8 weeks	Physiotherapists	Usual care
Rief et al., 2014	Resistance training	30 minutes	Five times a week (days of radiotherapy sessions)	2 weeks	Physiotherapists	Respiratory exercises
Pyszora et al. (2017)	Physiotherapy program	30 minutes	Three times a week	2 weeks	Physiotherapist	Previous pharmacological treatments or not provoking fatigue

to be continued

Table 3. continuation

Author/year	Type	Session	Frequency	Duration	Supervision	Comparison Group
Schuler et al., 2016	Additional structured and individual exercise program to one of the physiotherapy groups near home	20-30 minutes	Three times a week – aerobic Twice a week – resistance	12 weeks	Physiotherapist	Usual care
Scott et al., 2018	Aerobic training with intensity variation (55%, 65%, 75%-80% of VO <sub>2</sub> peak)	55% = 20 minutes	3x a week	12 weeks	Physiologist of the exercise	Stretching
Toth et al., 2013	65% = until 30 minutes 75%-80% = 30-45 minutes	Three times a week	12 weeks	Physiologist of the exercise	Stretching	No touch and usual care
Cheung et al., 2020	Acupressure	1 <sup>st</sup> week: 2 hours; 2 <sup>nd</sup> to 4 <sup>th</sup> week: 30 minutes of application n+ 1 hour of follow-up visit	1 <sup>st</sup> week: 2 training sessions; 2 <sup>nd</sup> to 4 <sup>th</sup> week: 1 follow-up visit a week + 30 minutes of application of acupressure per day	4 weeks	Senior student of chine traditional medicine and Nursing student	Usual care + talks about health not related to symptoms control in the third week
Lai et al., 2011	Aromatherapy massage and simple abdominal massage	15-20 minutes	Five times a week	5 consecutive days	Trained nurses to apply techniques of basic abdominal massage	No intervention
Lim et al., 2011	Electroacupuncture	20 minutes	Once a week	4 weeks	Certified physiotherapist in acupuncture, certified radiation oncologist and physician acupuncturist	Palliative care with nurse professional
Porter et al., 2019	Mindful yoga	120 minutes	Once a week	8 weeks	Certified yoga instructors	Social support group
Sikorskii et al., 2020	Reflexology	30 minutes	At least once a week	4 weeks	Caretaker (friend/ family member) previously coached by reflexologist	Usual care
Vadiraja et al., 2017	Integrative yoga program	1 hour	3-times a week	3 months	Licensed yoga instructor	Supportive Educational Therapy
Vanderbyl et al., 2017	Medical Qigong and standard physical activity	Qigong = 45 minutes Exercise: until reaching 60%-70% of Maximum HR or 2-4 MME	2-times a week	6 weeks each	Physiotherapist	Usual care
Wyatt et al., 2012	Reflexology or superficial feet manipulation	30 minutes	4 times a week	4 weeks	Licensed reflexologist	Usual care

**Captions:** REST = rapid, easy, strength training I; PA= physical activity; BS = behavioral support; PNF = Proprioceptive Neuromuscular Facilitation; Fr = frequency; Hz = Hertz; Ws = wrist size; mA = milliampere; TENS = Transcutaneous Electrical Nerve Stimulation; HR = heart rate; MME = multiple metabolic equivalent; ms = microsecond; VO<sub>2</sub>peak = peak oxygen uptake.

a disorder of external pathogens, diet, environments and emotions, leading to positive impacts in managing nausea/vomits, pain, heat flashes and fatigue<sup>42</sup>.

Aroma therapy massage and reflexology are non-invasive, low-cost complementary therapies which promote conviviality, confidence and safety in the patient-professional relationship through touch. Oils and aromatic herbs and volatile herbs are gradually absorbed by the skin during the aroma therapy, causing therapeutic results as sedation, analgesia, antispasmodic and antipyretic effects, positive for pain, anxiety, mental condition, fatigue, gastrointestinal conditions and sleep quality of the patients<sup>43</sup>. Reflexology promotes hemodynamic effects which increases the parasympathetic response and reduce the sympathetic stimulation, increasing blood circulation in the organs and production of energy, which favors muscle relaxation and homeostasis, further to promoting endorphin liberation in the organism and improving pain, muscle pressure, anxiety and fatigue<sup>44</sup>.

Cancer-related physical symptoms and their treatments are typically associated with emotional issues, mainly stress and depression, therefore, a therapeutic plan involving therapies with consequences on physical and emotional outcomes may be more effective for this population. Similar to this study, others<sup>45-48</sup> concluded that PICS are safe methods (when applied with supervision of skilled professionals) that can be beneficial to physical symptoms of oncologic patients, including in advanced stages, mainly for cancer-related fatigue and pain. However, there are still scarce studies utilizing each PICS in patients with advanced cancer, most of all with good methodological quality.

The limitations of this review are the methods of evaluation and heterogeneous subitems evaluated, possibly for being individuals diagnosed with different types of cancer, further to small number of studies that used each PIC since different types were utilized in the studies selected. In addition, the difference of frequency and duration of the treatment may have interfered in the results since those that did not present significant results in the approaches had low frequency or duration compared to other with similar therapeutic methods. The methodological quality of the studies is another topic to be remarked because the majority was of low quality based in the scale PEDro, none of them blinded reviewers or participants and few blinded the reviewers or promoted proper follow-up of the participants.

## CONCLUSION

Physiotherapy and PICS have positive effects in individuals with diagnosis of advanced cancer, reducing

the intensity of physical symptoms. However, few studies so far have sufficient methodological quality to substantiate their efficacy on the outcomes investigated for this population. New RCT investigating their effects, mainly PICS with therapeutic finality are necessary.

## CONTRIBUTIONS

All the authors contributed substantially to the study conception/design, acquisition, analysis and/or interpretation of the data, wording and/or critical review and final approval of the version published.

## DECLARATION OF CONFLICT OF INTERESTS

There is no conflict of interests to declare.

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