



## Review

## Nonpharmacological Management of Cancer-Related Cachexia: A Systematic Review

Cloconi Constantina<sup>a,b,\*</sup>, Economou Mary<sup>b</sup>, Orphanos George<sup>a</sup>, Ferentinos Konstantinos<sup>a</sup>, Kouta Christiana<sup>b,†</sup>, Middleton Nicos<sup>b</sup>, Charalambous Andreas<sup>b</sup>

<sup>a</sup> Radiation Oncology Department, German Oncology Center, Limassol, Cyprus

<sup>b</sup> Nursing Department, Cyprus University of Technology, Limassol, Cyprus

## ARTICLE INFO

## Key Words:

Cachexia  
Cancer  
Education  
Prevention  
Management  
Treatment  
Nutrition

## ABSTRACT

**Objectives:** Cancer-related cachexia affects approximately 50% to 80% of cancer patients and contributes significantly to cancer-related mortality, accounting for 20% of deaths. This multifactorial syndrome is characterized by systemic inflammation, anorexia, and elevated energy expenditure, leading to severe weight loss and muscle wasting. Understanding the underlying mechanisms is critical for developing effective interventions. While progress has been made over the past decade, most therapeutic approaches have centered on pharmacological agents or nutritional supplements. This systematic review seeks to address a critical gap by examining interventional studies that focus on nonpharmacological, nonsupplement, and nonparenteral strategies for managing cancer-related cachexia.

**Methods:** A systematic review followed the guidelines provided by PRISMA 2020. The review was conducted to identify clinical trials on the nonpharmacological, nonsupplement, and nonparenteral management of cancer-related cachexia. The literature search encompassed PubMed, CINAHL, and Scopus, targeting studies published between 2014 and 2024. Inclusion criteria required studies to be written in English, involve human participants aged 18 years or older, and focus on individuals diagnosed with active solid tumors. Studies involving participants with hematological malignancies were excluded due to the unique dietary requirements associated with these conditions.

**Results:** The search identified 2,949 articles, of which 10 met the eligibility criteria. The nonpharmacological interventions examined included acupuncture, nutritional advice, education and support, informational booklets, behavior change support, and exercise. Significant heterogeneity was observed in both the types of interventions and the sample sizes across the studies. Most participants were outpatients. Commonly, assessed outcomes included body weight, body mass index, quality of life (QoL), and muscular strength. This variation highlights the need for more standardized approaches to better evaluate the impact of such interventions.

**Conclusions:** Exercise interventions improved lean mass, QoL, and fatigue. Complementary interventions like acupuncture have demonstrated promising benefits in managing cancer-related cachexia. These include improved appetite, enhanced Karnofsky Performance Status (indicating better functional ability), and reduced weight loss. While some studies suggest nutritional interventions may positively impact weight or dietary habits, the evidence remains inconclusive. This highlights the importance of initiating interventions early in the course of care, just after the diagnosis and the start of treatment to maximize potential benefits. Additionally, actively involving patients in their care is crucial, as this can enhance adherence, personalize strategies, and address individual needs more effectively.

**Implications for Nursing Practice:** The assessment and nonpharmacological management of cancer-related cachexia play a vital role in enhancing the QoL for cancer patients. Individualized nutritional interventions, educational programs, exercise routines, and tailored lifestyle advice have shown the potential to positively impact food intake, body composition, fatigue levels, and overall patient satisfaction during anticancer treatments. These approaches not only address the physical challenges of cachexia but also support the psychological and emotional well-being of patients, contributing to a more comprehensive and patient-centered care strategy.

© 2025 Elsevier Inc. All rights are reserved, including those for text and data mining, AI training, and similar technologies.

\* Address correspondence to: Constantina Cloconi, Radiation Oncology Department, German Oncology Center, 1, Nikis Avenue 4108, Agios Athanasios, Limassol, Cyprus.  
E-mail address: [tina\\_cl92@hotmail.com](mailto:tina_cl92@hotmail.com) (C. Constantina).

† Colleague Prof Christiana Kouta passed away (25.03.2023).

## Layperson Summary

### What we investigated and why

Cancer-related cachexia is a condition that affects 50% to 80% of people with cancer. It causes significant weight loss, muscle loss, and fatigue, often alongside inflammation, loss of appetite, and increased energy use by the body. These changes can lower quality of life and make cancer treatment harder. This review aimed to retrieve studies that explored nonpharmacological and nonsupplement interventions, such as lifestyle or supportive strategies, to see how they help.

### How we did our research

A literature search was conducted to identify these non-pharmacological interventions. 10 studies out of 2,949 were found. These studies focused on interventions that didn't involve medicines, supplements, or intravenous feeding. The interventions included acupuncture, nutritional support, educational booklets, and exercise.

### What we have found

The studies varied in the types of interventions used and the number of participants, making it difficult to compare results directly. However, some promising insights were:

- Exercise programs improved muscle mass, reduced fatigue, and improved quality of life.
- Acupuncture improved appetite, performance levels, and body weight.
- Nutritional support showed some potential benefits for improving diet and weight, though the results were inconsistent.

### What it means

Nonpharmacological interventions like exercise, acupuncture, and nutritional support can play a key role in managing cancer-related cachexia. There's still a need for more research to fully understand how to use these strategies to improve their quality of life and overall well-being during cancer treatment.

Cachexia originates from the Greek words *kakos* (meaning "poor") and *hexis* (meaning "condition"), reflecting a state of severe tissue wasting and poor physical condition associated with various diseases.<sup>1</sup> In the context of cancer, cancer-related cachexia specifically refers to this syndrome as it occurs in patients with cancer. Cancer-related cachexia affects approximately 50%–80% of cancer patients and contributes significantly to cancer-related mortality, accounting for 20% of deaths.<sup>2–4</sup> It is characterized by progressive loss of skeletal muscle and fat tissue, driven by complex metabolic alterations. Some studies describe cancer-related cachexia as the terminal phase of cancer or even refer to it metaphorically as "self-cannibalism," highlighting the devastating and self-destructive nature of the condition.<sup>5</sup>

Cancer-related cachexia is also referred to as cachexia syndrome or cancer-induced anorexia-cachexia syndrome. Fearon et al (2011) define it as a multifactorial syndrome marked by the progressive loss of skeletal muscle mass, with or without accompanying.<sup>1</sup> This tissue loss is not fully reversible through nutritional support alone. The pathophysiology of cancer-related cachexia is driven by a combination of negative protein and energy balance, reduced food intake, and dysregulated metabolism, highlighting its complex and systemic.<sup>1</sup>

Cachexia is associated with a decline in quality of life (QoL), diminished response to chemotherapy, poor surgical outcomes, and

overall negative clinical outcomes in cancer patients.<sup>6</sup> The prevalence of this syndrome varies by tumor type, with certain primary cancers inducing more severe cachexia.<sup>7,8</sup> Annually, over eight million deaths (accounting for half of all global cancer-related mortality) are linked to diseases frequently associated with cachexia.<sup>9</sup> Furthermore, nearly one-third of cancer deaths are attributed to muscle wasting and the resulting physiological impairment.<sup>7</sup> More than one in three cancer patients aged 65 years or older are malnourished before the initiation of chemotherapy.<sup>10</sup>

Numerous studies have explored potential solutions for managing cancer-related cachexia. However, the majority of these studies have primarily focused on pharmaceutical interventions, investigating specific medications aimed at slowing the progression of cachexia. Additionally, many studies have centered on patients receiving parenteral nutrition, either as a standalone intervention or in combination with patient education and nutritional supplementation. While these approaches have shown some promise, there is still a significant need for further research into nonpharmacological and non-supplement-based strategies to manage cachexia more effectively and holistically, addressing the complex and multifaceted nature of the condition.<sup>11–16</sup> Furthermore, these approaches have been aimed at later stage of cachexia.

There is still a need for more comprehensive methods that include earlier, noninvasive measures including oral nutritional support, behavioral/lifestyle interventions, and multimodal therapies. The nonpharmacological interventions could potentially reduce the onset of cancer-related cachexia and improve overall patient outcomes; nevertheless, they are underexplored compared to pharmacological and parenteral nutrition.

A similar scoping review was previously conducted to identify nonpharmacological interventions for cancer-related cachexia; however, it included studies that involved the use of feeding tubes and supplements.<sup>17</sup> In this review, our objective was to identify studies examining nonpharmacological interventions for patients, explicitly excluding those involving the use of nutritional supplements. A key inclusion criterion was that the patients in these studies were orally fed, as opposed to receiving nutrition via tube feeding.

## Materials and Methods

### Data Sources and Search Strategy

This systematic review followed the guidelines provided by PRISMA 2020 and was done by two reviewers.<sup>18</sup> Ethical approval was not required. Reviewers searched PubMed (Medline), Cinahl, and Scopus from 2014 to September 2024. A combination of medical subject headings (MeSH) and keywords contain "cancer," "neoplasm," "oncology," "tumour," "malignancy," "carcinoma," "cachexia," "education," "training," "program," "teaching," "instruction," "strategies," "management," "treatment," "intervention," "therapy," "prevention." Only clinical trials in English Language, written in the last 10 years accepted. We did not do additional searches, but instead reviewed the references of the listed papers for more relevant articles.

### Study Selection

The PICO(S) framework (Population, Intervention, Comparison, Outcomes, Study Design) guided the search strategy and defined inclusion criteria (reported in Table 1).

The inclusion criteria were as follows: (1) prospective studies investigating the management of cancer-related cachexia, (2) studies published in English, (3) studies involving patients aged 18 years or older with solid tumors, (4) studies that excluded the use of medications or supplements, and (5) studies that involved only oral feeding, without the use of feeding tubes.

**TABLE 1**  
PICOS Criteria for Inclusion and Exclusion of Studies

	Inclusion criteria	Exclusion criteria
Population	In vivo human models over 18 y old, diagnosed with solid tumors. Oral feeding only.	In vitro studies, bibliographic reviews, and meta-analyses. Feeding tubes.
Intervention	Nonpharmacological, nonsupplement, nonparenteral.	Inclusion of supplements, medicines, or a combination.
Comparators	Control group or placebo group.	No control group.
Outcome	Effects in weight, energy or protein intake, cachexia stage, body composition, or quality of life.	Any other measurements.
Study Design	Experimental studies.	Bibliographic/systematic reviews and meta-analyses, clinical studies, theses, dissertations, book chapters.

We excluded: (1) articles published before January 2014, (2) in vitro studies, (3) reviews or meta-analyses, (4) animal studies, (5) letters, conference abstracts, or any other nonpeer-reviewed publications, (6) studies involving the use of medications or supplements, (7) studies including participants with hematologic cancers, and (8) studies published in languages other than English.

### Data Extraction and Analysis

The two reviewers (CC and ME) objectively screened the titles and abstracts of the obtained articles. The entire text was examined as needed depending on the predetermined qualifying criteria. The potentially relevant studies based on the eligibility criteria were chosen. Disagreements among reviewers over research inclusion were settled by a third reviewer (AC). Once many studies were excluded through titles or duplicates, abstracts were independently filtered by two reviewers (Health Care Professionals, a dietitian, and an oncology nurse) and irrelevant papers were removed. 10 studies were included according to inclusion criteria and after discussion. Data were managed on the Rayyan program. The systematic review did not investigate the effectiveness of nonpharmacological therapies. To facilitate reading and identifying relevant papers, we have included a summary table (Table 2).

### Results

The search retrieved 2,949 studies, which were reduced to 140 after adding filters. After the screening by title and abstracts another 90 studies were excluded. A total of 27 were discarded after removing duplicates and 13 more were discarded after the further screening of 23 studies. Ten studies were included in the review. Fig. describes the research inclusion procedure in full.

All 10 studies included in this systematic review, were published during the period 2015 to 2023. Of the 10 studies included in the review, two studies featured a single group of participants with pre- and postmeasurements.<sup>19,20</sup> Most of the studies were clinical trials ( $N=9$ ), with only one being across-sectional analytical study.<sup>21–28</sup> Heterogeneity in the intervention process was observed across the studies. The interventions varied widely and included acupuncture ( $N=2$ ), nutritional advice/education/support ( $N=3$ ), behavior change support and informational booklet ( $N=1$ ), and exercise programs ( $N=4$ ). The most common clinical measurements were body mass index (BMI), body composition (eg, fat mass, muscle mass, weight), hand grip strength, Karnofsky Performance Status, and blood biomarkers such as C-reactive protein and albumin. Assessment tools such as the visual analog scale, PG-SGA score, 24-hour dietary record, Depression Scale (CES-D), EORTC QLQ-30, Centre for Epidemiological Studies Depression Scale, Multidimensional Fatigue Inventory Scale, Zarit Burden Scale, and Functional Assessment Questionnaire were used.

### The Study Population

The results of the systematic review showed heterogeneous and small samples of a range 7 to 468 patients. Two studies referred to

gastrointestinal cancer, while another two targeted head and neck cancer. The remaining studies primarily involved patients with advanced cancer such as pancreatic cancer, breast cancer etc. The inclusion and exclusion criteria to enroll the participants were also quite different. There was significant variation between studies in terms of the timing of interventions. Most interventions were administered either before or during cancer treatments, such as radiotherapy and chemotherapy, while one study implemented the intervention after surgery. Most of the participants were outpatients.

Two studies used acupuncture as their primary intervention<sup>19,20</sup> while the other two focused on exercise/training programs.<sup>25,26</sup> Two other trials included exercise, psychoeducational activities, and lifestyle interventions.<sup>22,28</sup> The remaining trials used a range of interventions, including nutritional support and education, counseling, lifestyle interventions, nutrition guides/booklets, and prepared meals.<sup>21,23,24,27</sup>

In six out of 10 studies, BMI was used as a measurement.<sup>19–22,26,28</sup> Five studies assessed weight as an outcome,<sup>21–25</sup> while two studies included blood analyses, such as C-reactive protein and albumin levels.<sup>25,27</sup> Nutritional intake was measured in three studies,<sup>21,23,25</sup> and only one study utilized an X-ray absorptiometry scan.<sup>22</sup>

One study reported a statistically significant improvement in participants' levels of malnutrition.<sup>21</sup> Another study demonstrated a significant increase in energy and protein intake, as well as weight gain, in the intervention group.<sup>24</sup> Improved mobility following a training program was observed in the intervention group compared to the control group in another study.<sup>26</sup>

In most studies, although improvements were observed in indicators such as BMI, functional scores, dietary status, blood biomarkers, and QoL, these results were not statistically significant when compared to the control groups.<sup>22,23,25,27</sup>

### Evidence Quality Assessment of Included Studies

The quality assessment of the included studies is summarized in Tables 3 to 5. The studies were independently assessed by two reviewers. Randomized clinical trials were evaluated using the Cochrane Risk of Bias Tool 2 tool, while nonrandomized clinical trials were assessed with the Newcastle–Ottawa Scale 16. Among the studies, six were randomized controlled trials, four were nonrandomized controlled trials, and one was a cross-sectional study. Seven of the studies included a comparative control group, while three studies incorporated both pre- and postintervention measurements. Direct comparisons between studies were challenging due to variations in intervention durations, outcome measures, and follow-up periods. However, all the included studies consistently reported body weight as one of their primary outcomes.

### Discussion

This systematic review examines the effects of nonpharmacological interventions on management of cancer-related cachexia. Although there was significant heterogeneity in the types of

**TABLE 2**  
Characteristics of Included Studies

Study	Study design	Population	Measurements	Groups	Instruments	Results
Yoon et al <sup>19</sup>	Prospective feasibility pilot study (pre and post)	7 gastrointestinal cancer patients	–Body mass index –Bioelectrical impedance analysis	One group—intervention: acupuncture	–Karnofsky Performance Status scale –Simplifies Nutritional Appetite Questionnaire (SNACKS) –Visual analog scale (VAS)	Postintervention results: –Improvement in appetite and SNACKS scores –Increased 7% of Karnofsky Performance Status score –Reduction of weight by 1.3%
Zaid et al <sup>21</sup>	Randomized controlled trial	42 colorectal cancer patients receiving chemotherapy	–Height –Weight –Body mass index –Dietary intake	<u>Control group:</u> received standard nutritional advice (focused on symptom management) <u>Intervention group:</u> received intensive nutritional support and life-style advice and a booklet containing information on nutrition and cancer	–Patient-Generated Subjective Global Assessment (PG-SGA) –24 h dietary record	–High prevalence of malnutrition –More participants in the intervention group were assessed as being well-nourished than malnourished (statistically significant at wk 8) –Energy and protein intake did not differ significantly –Intervention group increased protein and energy intake for 4 wk then were like that consumed to the baseline –Control group decreased their protein and energy intake, increased only at wk 16 –Intervention group had a small effect on lean body mass, BMI and percentage body fat, but not significantly –Effect size by 12-wk for total grip strength (sit to stand, sit and reach scores) indicated a moderate effect in the intervention group, but not significant because of the sample size –Significant declines in both groups QOL scores were present, but return to baseline by 24 wk –Depression symptoms increased for both groups over 12 wk but returned to baseline levels by 24 wk –Small to moderate effect at the intervention group on nutrition status –No significant differences between two groups for functional score
Capozzi et al <sup>22</sup>	Exploratory randomized controlled exercise trial	60 head and neck cancer patients	–X-ray absorptiometry scan –Body mass index –Lean body mass –Body fat percentage –Muscle strength	<u>Control group:</u> 12-wk delayed life-style intervention <u>Intervention group:</u> 12-wk immediate lifestyle intervention (1. physician referral and clinic support, 2. health education, 3. behavior change support, 4. an individualized exercise program, 5. a group-based exercise setting to capitalize on social support)	–Godin's Leisure Time Exercise Questionnaire –FACT-anemia –FACT-head/neck symptom index-22 –Centre for Epidemiological Studies Depression Scale (CES-D) –PG-SGA	–Significant declines in both groups QOL scores were present, but return to baseline by 24 wk –Depression symptoms increased for both groups over 12 wk but returned to baseline levels by 24 wk –Small to moderate effect at the intervention group on nutrition status –No significant differences between two groups for functional score
Leedo et al <sup>23</sup>	Randomized controlled trial	40 lung cancer patients	–Hand grip strength –Body weight –Dietary intake	<u>Control group:</u> habitual diet <u>Intervention group:</u> offered energy and protein-rich main meals and snacks, delivered 3 times per wk	–EORTC QLQ-30 –Centre for Epidemiological Studies Depression Scale (CES-D) –Digital Hand Dynamometer	–No significant difference between the participant's demographics –Energy and protein intake increased (significantly) in the intervention group –Patients in the control group lost weight during the hospitalization/patients in the intervention group gain weight (statistically significant) –Improvement in patients' satisfaction in the intervention group (significant increase in the overall satisfaction)
Sathiaraj et al <sup>24</sup>	Cross-sectional analytical study	160 cancer patients	–Body weight –Nutritional intake	<u>Control group:</u> traditional foodservice model <u>Intervention group:</u> patient-centered foodservice model	–NutritionDay Questionnaires –24 h dietary record –Nutritive Value of Indian Foods –Patient satisfaction survey	–Intervention group: reduction of FM by 30%/increase of lean mass by 1% (nonsign) –Control group: reduction by 20%/decrease of lean mass by 1% (nonsign) –Not significant difference in the increase of
Grote et al <sup>25</sup>	Randomized controlled pilot feasibility trial	20 head and neck cancer cachectic patients	–Weight –Muscle strength –Blood test (CRP, hemoglobin, interleukin-6)	<u>Control group:</u> usual care <u>Intervention group:</u> received training, 3 times weekly for 30 min (3 exercises for major muscle groups)	–Multidimensional Fatigue Inventory (MFI) SCALE –FAACT (Anorexia/Cachexia) –Six-Minute Walk Test (6MWT) –Hand-held dynamometry	

(continued on next page)

TABLE 2 (Continued)

Study	Study design	Population	Measurements	Groups	Instruments	Results
				with 8-12 repetition max for 3 sets each)		reduced activity in the two groups (Intervention: 11% Control: 8%) —Not significant difference in the reduction of motivation (Intervention: 7% control: 14%) —Improvement in QoL and fatigue (general, mental, physical) —BMI was relatively constant after eight sessions of acupuncture ( $20.25 \pm 3.1$ ; $P > .00$ ) BIA measurement, FFM decrease only 0.4% ( $P > .05$ ) and FM increases by 0.4% ( $P > .05$ ) —Compared to the control group, the resistance training group showed significant improvement in mobility. —Muscle strength was also significantly improved in the resistance training group than in the control group —No difference was found between the NEC and usual care groups in nutrition status and blood biomarkers at baseline —After radiotherapy, patients in the NEC group had lower PG-SGA scores (5.6 vs 6.9; MD = -1.3, $P < .001$ ) and lower malnutrition rate (56.0% vs 70.5%; OR = 0.5; $P = .004$ ) compared with the usual care group —Six dyads showed compliance greater than 50% for both components of the bimodal intervention —QoL decreased over time, and the caregiver burden diminished between enrollment and 4 wk after the enrolment
Yuliatun et al <sup>20</sup>	Exploratory and experimental study (pre and post)	7 breast cancer patients	—Body mass index —Fat mass —Fat-free mass	One group—intervention: eight acupuncture sessions before chemotherapy and radiotherapy procedure	—FAACT (anorexia/cachexia)	
Kamel et al <sup>26</sup>	Single-blind RCT	40 pancreatic cancer patients	—Body mass index —Body weight —Fat mass —400 m walk	<u>Control group</u> : standard care (no exercise) <u>Intervention group</u> : resistance training	—Six-Minute Walk Test (6MWT)	
Zhang et al <sup>27</sup>	Cluster-randomized clinical trial	468 adult cancer patients during radiotherapy	—Nutrition-related blood biomarkers	<u>Control group</u> : usual care <u>Intervention group</u> : nutrition education and counseling (NEC) program	—PG-SGA	
Buonaccorso et al <sup>28</sup>	Prospective mixed-method pilot study	—24 patients with advanced cancer and their caregivers	—Karnofsky Performance Status (KPS) —Body mass index—Weight	<u>Intervention group</u> included psycho-educational activities, exercise sessions, and standard care (a specialized PC visit)	—FAACT (anorexia/cachexia) —Zarit Burden Scale —Hand-grip —Sit to stand	

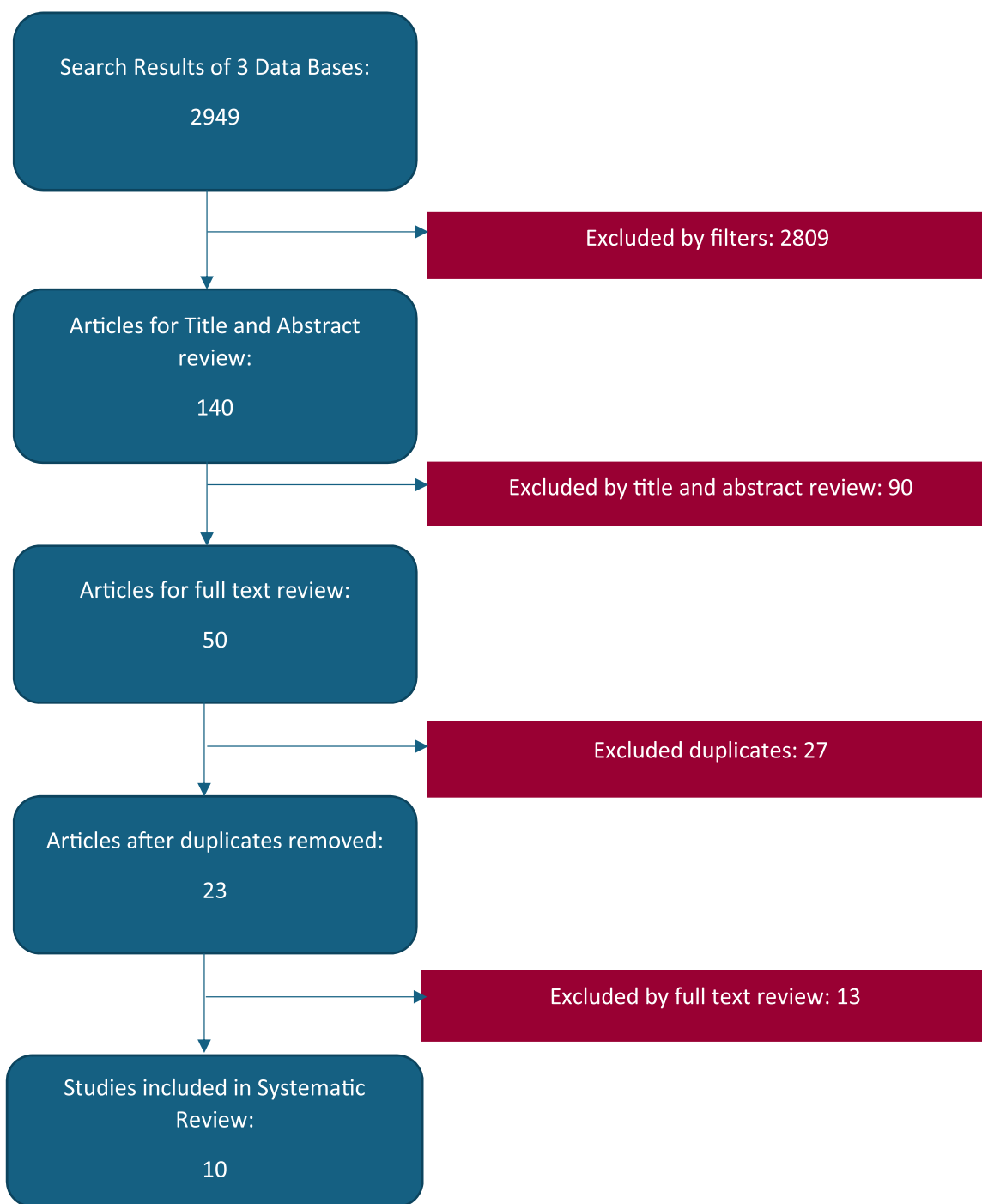


FIG. Systematic review process.

TABLE 3

Evidence Quality Assessment of RCTs according to Cochrane Risk of Bias Tool 2 (RoB2) Tool

References	Design	Randomization process	Deviations from intended interventions	Missing outcome data	Measurement of the outcome	Selection of the reported results	Overall bias
Zaid et al <sup>21</sup>	RCT	Low risk	Some concerns	Low risk	Low risk	Some concerns	Some concerns
Capozzi et al <sup>22</sup>	RCT	Low risk	Some concerns	Low risk	Low risk	Some concerns	Some concerns
Leedo et al <sup>23</sup>	RCT	Low risk	Some concerns	Low risk	High risk	Some concerns	High risk
Grote et al <sup>25</sup>	RCT	Low risk	Some concerns	Low risk	High risk	Some concerns	High risk
Kamel et al <sup>26</sup>	RCT	Low risk	Some concerns	Low risk	Low risk	Some concerns	Some concerns
Zhang et al <sup>27</sup>	RCT	Low risk	Low risk	Low risk	Some concerns	Some concerns	Some concerns



**TABLE 4**  
Evidence Quality Assessment of NRCTs According to Newcastle–Ottawa Scale16

References	Design	Definition adequate	Representativeness of the exposed cohort	Selection of Controls	Demonstration of outcome	Assessment of outcome	Follow-up long enough for outcomes to occur	Adequacy of follow
Yoon et al <sup>19</sup>	NRCT	✓		✓		✓		✓
Yuliatun et al <sup>20</sup>	NRCT	✓	✓	✓		✓		✓
Buonaccorso et al <sup>28</sup>	NRCT	✓	✓	✓		✓		

**TABLE 5**  
Evidence Quality Assessment of NRCTs According to Newcastle–Ottawa Scale16

Reference	Design	Definition adequate	Representativeness of the exposed cohort	Selection of Controls	Definition of controls	Comparability	Ascertainment of exposure	Same method of ascertainment	Nonresponse rate
Sathiaraj et al <sup>24</sup>	Cross sectional	✓	✓				✓	✓	

interventions analyzed, all studies indicated a negative association between these interventions and the progression of cancer cachexia. However, it should be noted that not all results achieved statistical significance.

### Nutrition Support

Patients with cancer often fail to meet their protein requirements, consuming levels even lower than those recommended for healthy individuals.<sup>29</sup> However, two studies examining the effects of nutritional support on functional scores reported an increase in protein intake among participants.<sup>21,24</sup> The malnutrition status dropped from 72.7% at baseline to 27.3% 8 weeks after the individualized diet and lifestyle counseling intervention.<sup>21</sup> In addition, studies have indicated significant increase in body weight among patients in the intervention group receiving nutritional support when compared to those in the control group. This outcome is based on the implementation of patient-centered foodservice model intervention.<sup>24</sup> Furthermore, enhanced energy and protein consumption was strongly correlated with significant improvements in QoL, functional scores, handgrip strength, symptom management, and performance metrics.<sup>23</sup> Higher patient satisfaction ratings were reported by Sathiaraj et al,<sup>24</sup> after a Patient-Centered Foodservice Model intervention, reflecting improvements in various aspects of food service, including food quality and flavor, timeliness of delivery, diet education, and overall satisfaction. In contrast to another study with nutritional education and counseling, no significant differences were observed in nutritional status between the intervention and control group.<sup>27</sup>

### Exercise/Resistance Training

A study by Capozzi<sup>22</sup> evaluated the effects of a progressive resistance-training intervention during treatment and found no significant impact on the primary outcome of body composition, despite a notable increase in weekly physical activity among participants in the intervention group. However, small-to-medium improvements were observed in some secondary outcomes, including fitness, QoL, and nutritional status. Similarly, Grote et al<sup>25</sup> explored the timing of initiating a lifestyle intervention combined with progressive resistance training and found it had a small-to-medium positive impact on QoL and nutritional status, outperforming resistance training alone, which showed no significant changes.

### Acupuncture

A study by Yoon et al<sup>19</sup> found that appetite improved after acupuncture intervention compared to baseline. Despite this

improvement in appetite, overall weight decreased by an average of 1.3% from baseline over 8 weeks. However, the performance status of participants, as measured by the Karnofsky Performance Status scale, remained stable throughout the study. In another study by Yuliatun et al,<sup>20</sup> BMI was relatively constant after eight acupuncture sessions.

### Exercise/Training

Progressive resistance training has shown promise in managing aspects of cancer-related cachexia, particularly in functional and quality-of-life outcomes. In one study, the resistance training group demonstrated significant improvements in mobility and chair rise performance compared to the control group. Another study found that, while changes from baseline were not statistically significant, the intervention group exhibited trends toward better general fatigue management and improved QoL at follow-up, 4 weeks after the intervention.<sup>25,26</sup> These findings highlight the potential of resistance training to enhance physical function and alleviate fatigue-related symptoms, even in the context of cancer-related cachexia.

### Strengths and Limitations

This study offers several strengths, including its comprehensive synthesis of research on nonpharmacological interventions for patients who are still able to feed orally, prior to the necessity of tube feeding. This approach highlights two critical insights: first, the importance of managing cancer cachexia at its early stages, before patients lose the ability to feed by mouth; and second, the value of integrating multiple interventions—such as exercise, nutrition support, and acupuncture—into a combined strategy for more effective management of cancer-related cachexia, rather than relying on these methods in isolation. The primary sources of bias identified in the included trials were related to missing outcome data and inconsistencies in outcome measurement across studies. Another significant limitation was the small sample sizes, with seven out of 10 studies including fewer than 50 participants, thereby reducing the generalizability of the findings to the broader population. Furthermore, the interventions were often conducted over relatively short durations, typically lasting only a few weeks, which may not have been sufficient to achieve or observe the desired outcomes. The limited number of studies retrieved—only 10—also poses a constraint, as does the variability in study designs and heterogeneity in intervention exposures and their effects. These limitations collectively highlight the need for more robust and comprehensive research in this area.

## Conclusions

This review proposes that altering the trajectory of cancer-related cachexia by improving lean body mass, functional capacity, and overall body composition, including body weight, may contribute to better prognoses and improved treatment outcomes for cancer patients. Targeted interventions aimed at mitigating the impact of cachexia could enhance patients' physical resilience, response to therapy, and QoL.

Specifically, exercise interventions have been shown to improve lean body mass, and QoL, and reduce fatigue in patients. Complementary therapies, such as acupuncture, have demonstrated benefits in enhancing appetite, increasing Karnofsky Performance Status, and preventing weight loss. However, inconsistencies in the findings exist, with only a few studies indicating that nutritional interventions can positively affect weight or dietary habits. To maximize the benefits, interventions should be implemented early in the treatment process, with patients actively involved in their care.

However, healthcare professionals need education on this topic. More than 90% of nurses participating in a survey of nurses' knowledge in relation to the Anorexia-Cachexia Syndrome in Cancer Patients in two European Countries reported not using a tool to assess their patients' nutritional status at the time of diagnosis.<sup>30</sup>

A multimodal approach, which combines exercise, complementary therapies, and nutrition, appears to offer the most comprehensive benefits. However, further clinical trials with larger patient populations are needed to achieve more statistically significant results. This holistic strategy could enhance patient's outcomes, but robust evidence is still required to fully establish its efficacy. Finally, involving caregivers in future interventions for managing cancer-related cachexia could significantly enhance the effectiveness of nutritional strategies. Caregivers often play a pivotal role in a patient's nutritional care, as they may be responsible for meal preparation, grocery shopping, and guiding patients in making appropriate dietary choices during treatment. Their active participation (in nutritional education) could ensure better adherence to nutritional interventions and support the overall management of cancer-related cachexia.

## Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this article.

## CRediT authorship contribution statement

**Cloconi Constantina:** Data curation, Methodology, Writing – original draft. **Economou Mary:** Writing – review & editing, Methodology. **Orphanos George:** Supervision. **Ferentinos Konstantinos:** Supervision. **Kouta Christiana:** Supervision. **Middleton Nicos:** Supervision. **Charalambous Andreas:** Writing – review & editing, Supervision.

## Funding

The authors did not receive financial support from any organization for the submitted work.

## References

1. Fearon KS, Rome I, Baracos VE, et al. Definition and classification of cancer cachexia: an international consensus. *Lancet Oncol*. 2011;12:489–495. <https://doi.org/10.1016/S1470>.

2. Yue M, Qin Z, Hu L, Ji H. Understanding cachexia and its impact on lung cancer and beyond. *Chin Med J Pulm Crit Care Med*. 2024;2:95–105. <https://doi.org/10.1016/j.pccm.2024.02.003>.
3. Ni J, Zhang L. Cancer cachexia: definition, staging, and emerging treatments. *Cancer Manag Res*. 2020;12:5597–5605. <https://doi.org/10.2147/CMAR.S261585>.
4. Marican CR, Tiucă OM, Marican A, Cotoi OS. Cancer cachexia: new insights and future directions. *Cancers (Basel)*. 2023;15(23):1–22. <https://doi.org/10.3390/cancers15235590>.
5. Burckart K, Beca S, Urban RJ, Sheffield-Moore M. Pathogenesis of muscle wasting in cancer cachexia: targeted anabolic and anticatabolic therapies. *Curr Opin Clin Nutr Metab Care*. 2010;13(4):410–416. <https://doi.org/10.1097/MCO.0b013e328339fdd2>.
6. Arthur ST, Van Doren BA, Roy D, Noone JM, Zacherle E, Blanchette CM. Cachexia among US cancer patients. *J Med Econ*. 2016;19(9):874–880. <https://doi.org/10.1080/13696998.2016.1181640>.
7. Hasselgren PO, Fischer JE. Muscle cachexia: current concepts of intracellular mechanisms and molecular regulation. *Ann Surg*. 2001;233(1):9–17. <https://doi.org/10.1097/0000658-200101000-00003>. PMID: 11141219; PMCID: PMC1421177.
8. Dewys WD, Begg C, Lavin PT, Band PR, Bennett JM, Bertino JR, Cohen MH, Douglass Jr HO, Engstrom PF, Ezdinli EZ, Horton J, Johnson GJ, Moertel CG, Oken MM, Perlia C, Rosenbaum C, Silverstein MN, Skeel RT, Sponzo RW, Tormey DC. Prognostic effect of weight loss prior to chemotherapy in cancer patients. Eastern Cooperative Oncology Group. *Am J Med*. 1980;69(4):491–497. [https://doi.org/10.1016/s0149-2918\(05\)80001-3](https://doi.org/10.1016/s0149-2918(05)80001-3). PMID: 7424938.
9. Baracos VE, Martin L, Korc M, Guttridge DC, Fearon KCH. Cancer-associated cachexia. *Nat Rev Dis Primers*. 2018;4:17105. <https://doi.org/10.1038/nrdp.2017.105>. PMID: 29345251.
10. Caillet P, Liuu E, Raynaud Simon A, et al. Association between cachexia, chemotherapy and outcomes in older cancer patients: a systematic review. *Clin Nutr*. 2017;36(6):1473–1482. <https://doi.org/10.1016/j.clnu.2016.12.003>.
11. Nunthanawach P, Wichansawakun S, Luangjinda C, Hudthagol C. Effectiveness of web applications on improving nutritional status of patients with colorectal cancer. *Nutrients*. 2024;16(3):1–11. <https://doi.org/10.3390/nu16030408>.
12. Bagheri A, Asoudeh F, Rezaei S, Babaei M, Esmailzadeh A. The effect of mediterranean diet on body composition, inflammatory factors, and nutritional status in patients with cachexia induced by colorectal cancer: a randomized clinical trial. *Integr Cancer Ther*. 2023;22:1–11. <https://doi.org/10.1177/15347354231195322>.
13. Wen HS, Li X, Cao YZ, et al. Clinical studies on the treatment of cancer cachexia with megestrol acetate plus thalidomide. *Chemotherapy*. 2013;58(6):461–467. <https://doi.org/10.1159/000346446>.
14. Takayama K, Katakami N, Yokoyama T, et al. Anamorelin (ONO-7643) in Japanese patients with non-small cell lung cancer and cachexia: results of a randomized phase 2 trial. *Support Care Cancer*. 2016;24(8):3495–3505. <https://doi.org/10.1007/s00520-016-3144-z>.
15. Pascoe J, Jackson A, Gaskell C, et al. Beta-hydroxy beta-methylbutyrate/arginine/glutamine (HMB/Arg/Gln) supplementation to improve the management of cachexia in patients with advanced lung cancer: an open-label, multicentre, randomised, controlled phase II trial (NOURISH). *BMC Cancer*. 2021;21(1):1–11. <https://doi.org/10.1186/s12885-021-08519-8>.
16. Mantovani G, Macciò A, Madeddu C, et al. A phase II study with antioxidants, both in the diet and supplemented, pharmacological support, progestagen, and anti-cyclooxygenase-2 showing efficacy and safety in patients with cancer-related anorexia/cachexia and oxidative stress. *Cancer Epidemiol Biomark Prev*. 2006;15(5):1030–1034. <https://doi.org/10.1158/1055-9965.EPI-05-0538>.
17. Bertocchi E, Frigo F, Buonaccorso L, Venturelli F, Bassi MC, Tanzi S. Cancer cachexia: A scoping review on non-pharmacological interventions. *Asia Pac J Oncol Nurs*. 2024;11(5):100438. <https://doi.org/10.1016/j.apjon.2024.100438>. PMID: 38774537; PMCID: PMC11107192.
18. Page MJ, McKenzie JE, Bossuyt PM, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. *The BMJ*. 2021;372:1–9. <https://doi.org/10.1136/bmj.n71>.
19. Yoon SL, Grundmann O, Williams JJ, Carriere G. Novel intervention with acupuncture for anorexia and cachexia in patients with gastrointestinal tract cancers: a feasibility study. *Oncol Nurs Forum*. 2015;42(2):E102–E109. <https://doi.org/10.1188/15.ONF.E102-E109>. PMID: 25806891.
20. Yuliatun L, Rahayu P, Poeranto S, Ahsan, Handayani D, Budianto MB. Acupuncture prevent progression of cachexia in breast cancer in outpatients of Dr. Saiful Anwar General Hospital Malang East Java Indonesia. *Journal of Global Pharma Technology*. 2019;11(4):174–181.
21. Improving the Nutritional Status of Patients with Colorectal Cancer Undergoing Chemotherapy through Intensive Individualised Diet and Lifestyle Counselling. *Malaysian Journal of Nutrition*. January 2016;1(22):65–79.
22. Capozzi LC, McNeely ML, Lau HY, et al. Patient-reported outcomes, body composition, and nutrition status in patients with head and neck cancer: results from an exploratory randomized controlled exercise trial. *Cancer*. 2016;122(8):1185–1200. <https://doi.org/10.1002/cncr.29863>.
23. Leedo E, Gade J, Granov S, et al. The effect of a home delivery meal service of energy- and protein-rich meals on quality of life in malnourished outpatients suffering from lung cancer: a randomized controlled trial. *Nutr Cancer*. 2017;69(3):444–453. <https://doi.org/10.1080/01635581.2017.1283421>.
24. Sathiaraj E, Priya K, Chakraborty S, Rajagopal R. Patient-centered foodservice model improves body weight, nutritional intake and patient satisfaction in patients undergoing cancer treatment. *Nutr Cancer*. 2019;71(3):418–423. <https://doi.org/10.1080/01635581.2018.1506490>.
25. Grote M, Maihöfer C, Weigl M, Davies-Knorr P, Belka C. Progressive resistance training in cachectic head and neck cancer patients undergoing radiotherapy: a



- randomized controlled pilot feasibility trial. *Radiat Oncol*. 2018;13(1):1–10. <https://doi.org/10.1186/s13014-018-1157-0>.
26. Kamel FAH, Basha MA, Alsharidah AS, Salama AB. Resistance training impact on mobility, muscle strength and lean mass in pancreatic cancer cachexia: a randomized controlled trial. *Clin Rehabil*. 2020;34(11):1391–1399. <https://doi.org/10.1177/0269215520941912>.
27. Zhang Z, Zhu Y, Zhang L, et al. Nutritional education and counseling program for adult cancer patients during radiotherapy: a cluster-randomized clinical trial. *Support Care Cancer*. 2022;30(4):3279–3289. <https://doi.org/10.1007/s00520-021-06704-w>.
28. Buonaccorso L, Fugazzaro S, Autelitano C, et al. Psycho-educational and rehabilitative intervention to manage cancer cachexia (PRICC) for advanced patients and their caregivers: lessons learned from a single-arm feasibility trial. *Cancers (Basel)*. 2023;15(7):1–20. <https://doi.org/10.3390/cancers15072063>.
29. Ravasco P. Nutrition in cancer patients. *J Clin Med*. 2019;8(8):1–13. <https://doi.org/10.3390/jcm8081211>.
30. Socratous G, Cloconi C, Tsatsou I, Charalambous A. Nurses' knowledge in relation to the anorexia–cachexia syndrome in cancer patients: a cross-national comparison in two European countries. *SAGE Open Nurs*. 2021;7:1–13. <https://doi.org/10.1177/23779608211035208>.