



# What is the Role of Resistance Training in Supporting Patients with Head and Neck Cancer Receiving Radiotherapy Treatment? A Systematic Review

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## Abstract

**Purpose** The aim of this review was to collect data on physical exercise programs in patients with HNC and to analyze the compliance with the Frequency, Intensity, Time and Type (FITT) and progressive overload principles.

**Methods** The search strategy identified 1318 articles through February 2022. After deduplication, title and abstract review, and full-text review, 15 studies met all the inclusion criteria. The inclusion criteria were randomized controlled trials (RCTs) with interventions involving at least 10 patients, and the intervention protocol included, at least, programmed strength exercise.

**Results** Physical exercise programs were performed only during and after treatment, with durations varying from 6 to 12 weeks. Only 5 studies (33.3%) detailed all the characteristics concerning FITT and progressive overload principles. In addition, 10 trials measured the changes in body composition and physical function. In contrast, 6 studies included nutritional recommendations or follow-up.

**Conclusion** It has been proven that physical exercise programs may help people with head and neck cancer improve their body composition, strength, and quality of life. To examine the dose/response effects of physical activity more precisely, further information regarding FITT principles and the progression of the load undertaken in the treatments is required. Finally, it is necessary to investigate the optimal time to start a physical exercise program and its impact on survival.

**Keywords** Head and neck cancer · Physical exercise · FITT · Strength training · Aerobic training · Treatment

## Introduction

Head and Neck Cancers (HNC) are malignant tumors located in the lip, oral cavity, oropharynx, hypopharynx, larynx, nasopharynx, and salivary glands. It is estimated that HNCs are responsible for more than 450,000 deaths annually [57].

Radiotherapy is one of the main treatments for these tumors and is sometimes combined with surgery and/or chemotherapy [37]. The most frequent side effects are mucositis and dysphagia, leading to malnutrition and cachexia [29], with consequent loss of physical function, strength, and quality of life, and increased fatigue [28].

Multicomponent exercise programs (a combination of strength and aerobic exercises) aim to improve the adverse effects of treatment, increase lean mass, and regulate anabolic hormones [8, 34, 35, 52, 63]. Additionally, improved adherence, treatment adherence, and quality of life have been documented in patients with advanced cancer [2, 19, 60].

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However, the success of different interventions is conditioned by factors such as frequency, intensity, duration, and type of exercise, that is, the Frequency, Intensity, Time and Type (FITT) principle [7, 16]. For positive adaptations caused by physical training, it is necessary to comply with the principle of training progression, according to which the load (volume  $\times$  intensity) of exercise is increased in a controlled manner as the intervention program progresses (Gil-Rey et al. [7, 18]).

Although, the ideal exercise program for these patients (aerobic vs. strength, duration, and intensity) and the optimal timing (during or after cancer treatment) are unknown. Evidence of the benefit of physical exercise programs is more limited in patients with head and neck cancer than in those with other cancers, such as breast cancer [25].

Thus, the present systematic review aimed to collect randomized clinical trials (RCTs) in which physical exercise is used as supportive therapy in patients with HNC, and to analyze compliance with the FITT principle and the principle of training progression in different interventions.

## Methods

### Search Strategy and Selection Criteria

The PRISMA methodology was used in this review [43]. The PubMed/MEDLINE, CINAHL, and Embase databases were searched for articles published up to February 2, 2022. The search strategy was adapted to the characteristics of each of the databases as follows within PubMed: “Head and Neck Neoplasms” [Mesh] AND (“exercise” [Mesh] OR “resistance training” [Mesh]) (Supplementary Table 1).

Inclusion criteria were determined using the PICO tool [43] and included publications that included at least 10 participants diagnosed with head and neck cancer (P), (I) the intervention protocol included programmed strength training, but may additionally include aerobic exercise or other types of exercise performed before, during, or after cancer treatment; (C) patients were distributed in different intervention and/or control groups; and (O) they reported at least results concerning the impact of physical exercise on body composition, physical function, and/or quality of life of patients. The following exclusion criteria were applied: study protocols, systematic reviews and meta-analyses, case reports, interventions without physical exercise, and interventions focused on the improvement of a single organ (e.g., dysphagia). Only original articles written in English were selected. In addition, two researchers (E.M. and G.A.) independently reviewed the list of articles found in order to select

eligible articles at each stage of the search. If any doubts were found regarding a particular study, they were evaluated and resolved in consensus with all researchers.

The information was extracted (with the help of a professional librarian) by two researchers and the resulting disparities were determined by consensus of the whole team. The final results of the search and selection of articles are presented in the PRISMA diagram (Fig. 1) and Table 2.

### Data Extraction

The following demographic data and characteristics of the participants and the intervention were extracted from each study: study title, lead author, year of publication, study design, total sample, intervention and control group samples, disease stage, treatment, timing of treatment, and nutritional support. On the other hand, the following variables concerning the training programme were analyzed: duration of the intervention (weeks), frequency (weekly sessions), number of supervised sessions per week, volume (strength training: sets and repetitions; aerobic training: time) and intensity of strength and aerobic exercise, specifications of the training performed (aerobic, strength: elastic bands, free weights, guided machines), and results obtained (see Table 3).

### Assessment of Risk of Bias

The risk of bias was determined using the PEDro scale, which scores studies on a scale from 0 to 10 [36]. The score was determined using the PEDro database (<https://www.pedro.org.au>). If any of the studies were not scored within the database, they were scored according to the PEDro criteria of the researchers (see Table 1).

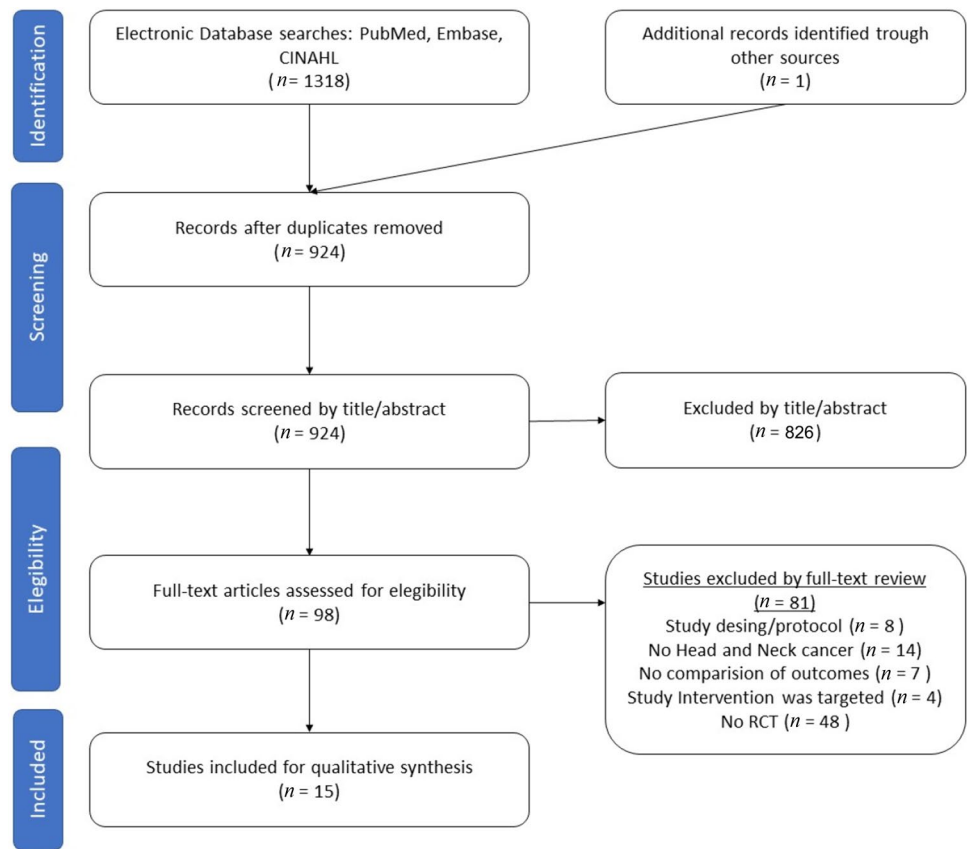
### Assessment of the Quality of the Exercise Programs

The training programs were analyzed according to the FITT parameters that they met [16]. Additionally, the progression of the loads used in the different programs was analyzed to determine whether they complied with the aforementioned principle of load progression [1] (see Table 3).

## Results

A total of 1318 results were obtained by searching the indicated databases, one article was manually included and 386 duplicates were eliminated. Subsequently, 924 articles were reviewed following the PRISMA methodology. The abstracts and full texts of 98 articles were analyzed, and 15 studies met the PICO inclusion and exclusion criteria determined in the previous section (see Fig. 1).

**Fig. 1** Study selection based on inclusion and exclusion criteria



**Table 1** Risk of bias assessment

Study	1	2	3	4	5	6	7	8	9	10	11	Score (/10)
[9]	x	x		x			x		x	x	x	6
[20]	x	x	x	x				x		x	x	6
[21]	x	x	x	x			x	x	x	x	x	8
[32]	x	x		x				x		x	x	5
[33]		x	x	x					x	x	x	6
[34]	x	x		x			x	x		x	x	6
[35]	x	x		x			x	x		x	x	6
[40]	x	x	x	x			x	x	x	x	x	8
[49]	x	x	x	x				x	x	x	x	7
[50]	x	x		x				x		x	x	5
[51]	x	x	x	x				x		x	x	6
[52]	x	x		x						x	x	4
[56]	x	x		x				x	x	x	x	6
[62]	x	x		x				x		x	x	5
[63]		x		x			x	x		x	x	6

x Criteria fulfilled

The basic characteristics of the included studies are presented in Table 2. In total, within the 15 studies, data were collected from 910 participants diagnosed with HNC from 7 countries, with stages I to IVb. Participants received radiotherapeutic treatment (RTx), except in two studies, where they only received chemotherapy (CTx),

and some received CTx and surgery (S) as adjuvant treatment.

The risk of bias of the studies, as determined using the PEDro scale, is listed in Table 1.

In reference to the timing of the physical exercise intervention, 10 programs were performed during RTx, CTx, or

**Table 2** Characteristics of the included studies (alphabetically organized)

Study	Country/area	Study design	Type of intervention	Sample	HNC stage	Cancer treatment (of the total <i>n</i> )
[9]	Canada	RCT	RT	60	I, II, III, IV	RTx ( <i>n</i> = 15); RTx + CTx ( <i>n</i> = 45)
[20]	Germany	RCT	RT	20	I, II, III, IV	RTx ( <i>n</i> = 7); RTx + CTx ( <i>n</i> = 13)
[21]	Denmark	RCT	RT	235	I, II, III, IVa, IVb	RTx ( <i>n</i> = 90); RTx + CTx ( <i>n</i> = 126); S ( <i>n</i> = 19)
[32]	Canada	RCT	RT	22	I, II, III, IV	S before RTx ( <i>n</i> = 15); RTx + CTx ( <i>n</i> = 18)
[33]	Taiwan, China	RCT	RT, AT & flexibility	57	I, II, III, IV	CTx ( <i>n</i> = 57)
[34]	Denmark	RCT	RT	41	I, II, III	RTx ( <i>n</i> = 20); RTx + CTx ( <i>n</i> = 21)
[35]	Denmark	RCT	RT	30	I, II, III, IV	RTx ( <i>n</i> = 10); RTx + CTx ( <i>n</i> = 20); additional S ( <i>n</i> = 2)
[40]	Canada	RCT	RT & ROM	52	I, II, III, IV	RTx (44); S ( <i>n</i> = 52); CTx ( <i>n</i> = 14)
[49]	US	RCT	RT	15	I, II, III, IV	RTx ( <i>n</i> = 11); RTx + CTx ( <i>n</i> = 7); additional S ( <i>n</i> = 7)
[50]	India	RCT	RT & AT	48	–	RTx + CTx ( <i>n</i> = 48)
[51]	India	RCT	RT & AT	148	III, IVa, IVb	RTx + CTx ( <i>n</i> = 148)
[52]	Norway	RCT	RT	41	–	RTx ( <i>n</i> = 24); RTx + CTx ( <i>n</i> = 17)
[56]	Taiwan, China	RCT	RT & AT	37	II, III, IV	RTx ( <i>n</i> = 11); CTx ( <i>n</i> = 16); additional S ( <i>n</i> = 37)
[62]	Taiwan, China	RCT	RT & AT	84	–	CTx ( <i>n</i> = 84)
[63]	US	RCT	RT & AT	20	II, III, IV	RTx + CTx ( <i>n</i> = 20)

HNC Head and neck cancer, RCT randomized controlled trial, RTx radiotherapy, CTx chemotherapy, S surgery, RT resistance training, AT aerobic training, US United States

RTx + CTx treatment [9, 21, 32–35, 49, 50, 62, 63], 2 programs were performed after the end of antineoplastic treatment [40, 56], and finally, 3 interventions were performed during and after treatment [20, 51, 52] (see Table 3).

Regarding physical exercise programs, eight programs performed only strength exercise [9, 20, 21, 32, 34, 35, 49, 52], five combined strength training and aerobic training [50, 51, 56, 62, 63], one added flexibility training [33], and one study performed strength and range of motion (ROM) training [40] (see Table 2).

The duration of the interventions ranged from 6 [21, 50] to 12 weeks [9, 32, 34, 35, 40, 49, 56], with exercises ranging from 1 [49] to 5 days a week [50, 51, 56]. The supervision of physical exercise varied from no supervised sessions [50] to interventions in which 100% of the sessions were carried out together with a professional [20, 21, 32, 33, 52].

The results of the analysis of the FITT principle and progression of the exercise load of the program are shown in Table 3. Out of the 15 physical exercise programs studied, only five (33.3%) detailed all the parameters mentioned [9, 20, 21, 33, 56], while six (40.0%) did not include one of the five parameters measured [32, 40, 49, 50, 62, 63], and four (26.7%) studies did not detail more than one of the parameters studied [34, 35, 51, 52].

On the other hand, four trials provided nutritional support for the participants [8, 21, 34, 52], while two had follow-up and nutritional advice [49, 63]. The remaining 10 studies did not indicate whether nutritional support or advice was provided during the process [20, 32, 33, 35, 40, 50, 51, 56, 62].

Regarding outcome measures, 10 trials measured changes in body composition, measured by bioimpedance, DEXA, or cross-sectional area tomography (CSAT) [9, 20, 32–35, 49, 52, 62, 63], participants' general and/or specific quality of life was recorded in 10 of the 15 studies using self-reported questionnaires [21, 32, 33, 35, 40, 49–51, 56, 63], and functional capacity was determined by the 6MWT in 7 studies [9, 20, 50, 51, 56, 62, 63], while 10 trials measured changes in participants' strength, with different combinations of tests [9, 20, 21, 32–35, 40, 49, 63].

## Discussion

Multi-component physical exercise programs, combining strength and aerobic exercises, have been shown to be effective in improving physical function and body composition in patients with head and neck cancer, as well as quality of life and tolerance to treatment. However, it is

**Table 3** Characteristics of the intervention programs with FITT criteria applied (alphabetically organized)

Study	Duration (weeks)	Intervention type	Timing related to treatment	Frequency per week	Intensity	Time (sets; repetitions)	Type	Progression	Supervision (%)	Nutrition intervention	Physical measurements	Results
[9]	12	RT	During	4	8–10RM	2–3; 8	Free-weight, elastic bands	Applied at 4, 6 and 9 weeks, advancing to 3×8(8)	50	Yes	Body composition (DEXA); handgrip; 30 s sit to stand; 6MWT; Sit and reach	Body composition ↓ 6MWT = Handgrip =
[20]	7	RT	During and post	3	7 (RPE 10)	3; 8–12	Machine based	If RPE < 7 weight increased	100	NR	Body composition (BIA); handgrip; 6MWT	Lean body mass ↑ Muscle strength ↓
[21]	6	RT	During	2	70%–85% IRM	2–3; 5–8	Machine based	Week 1–3 2×8, 70% IRM Week 4–6 3×5, 80% IRM	100	Yes	30 s sit to stand	30 s sit to stand ↑
[32]	12	RT+EO	During	3	NR	2; 8	Free-weight	If proper execution and safe weight up	100	NR	Body composition (CSAT); CPET; 30 s chair stand test	Muscle cross sectional area ↑* CPET ↑*
[33]	8	RT+AT+flexibility	During	3	RT moderate to hard (RPE) AE 60%–70% HR <sub>Max</sub>	RT 2; 8–12 AT 30'	Free-weight, elastic bands	Intensity up when patients will and be able to	100	NR	Body composition (BIA); 30 s arm curl test; 30 s chair stand test; TUG; back scratch test; sit and reach; 3 min step test	Skeletal muscle percentage ↑* Muscle strength ↑*
[34]	12	RT	During	2–3	NR	2–3; 8–15	NR	NR	26.6	NR	Body composition (DEXA); isokinetic dynamometry, 10 m maximal gait speed, 30 s chair rise, maximal stair climbing, 30 s maximal arm curl	Body lean mass ↑* Muscle strength ↑* Functional performance ↑

Table 3 (continued)

Study	Duration (weeks)	Intervention type	Timing related to treatment	Frequency per week	Intensity	Time (sets; repetitions)	Type	Progression	Supervision (%)	Nutrition intervention	Physical measurements	Results
[35]	12	RT	During	2–3	NR	2–3; 10	NR	NR	26.6	Yes	Body composition (DEXA); isokinetic dynamometry, 10 m maximal gait speed, 30 s chair rise, maximal stair climbing, 30 s maximal arm curl	Body lean mass ↑* Muscle strength ↑* Functional performance ↑*
[34]	12	RT + ROM	Post	2–3	25%–70% IRM 13 (RPE 20)	2; 10–15	NR	The resistance weight was increased by 1 kg to 2.5 kg once the participant was able to complete 2 sets of 15 repetitions with proper form	66.6	NR	IRM seated row, chest press (bilateral & unilateral); shoulder goniometry	Muscle strength ↑* ROM ↑*
[49]	12	RT	During	1	NR	2; 10	Elastic bands	Light resistance bands for the first 2 weeks, with the difficulty of the resistance bands gradually advanced every 2 weeks, based on whether the participant could easily do 2 additional repetitions after completing the prescribed 10 repetitions	50	Counseling	Body composition (BIA); back and leg dynamometry; handgrip; 8-foot walk time, 5 chair rise-and-sits	Lean body mass ↑ Handgrip ↑ 5 chair rise-and-sits ↑
[50]	6	RT + AT	During	5	3–5 (RPE 10)	RT 2–3; 8–10 AT 15–20'	NR	Progression was made from active to active-resisted exercises	0	NR	6MWT	6MWT ↑*
[51]	11	RT + AT	During and post	5	3–5 (RPE 10)	RT 2–3; 8–10 AT 15–20'	NR	NR	63.6	NR	6MWT	6MWT ↑*

Table 3 (continued)

Study	Duration (weeks)	Intervention type	Timing related to treatment	Frequency per week	Intensity	Time (sets; repetitions)	Type	Progression	Supervision (%)	Nutrition intervention	Physical measurements	Results
[52]	ENDUR 6 ENAF 3	RT	During and post	2–3	NR	3–4; 6–12	Machine based	NR	100	Yes	Body composition (CSAT)	Muscle mass =
[56]	12	RT + AE + flexibility	Post	5	RT 30%–60% IRM AT 12–13 (RPE 20)	RT 2; 10–15 AT 30'	Treadmill, machine based	Weight was gradually increased by 5% of 1 RM every week, up to 60% of 1 RM as tolerated AT maintained 12–13 (RPE 20)	40	NR	6MWT; shoulder ROM	6MWT ↑
[62]	8	RT + AT	During	3	RT 4–5 (RPE 10) AE 60%–70% HR <sub>Max</sub>	RT 3; 10 AT 30'	Elastic bands AE NR	NR	NR	NR	6MWT; body composition (BIA)	Muscle mass ↑* 6MWT ↑*
[63]	14	RT + AT	During	3	11–13 (RPE 20)	RT 3; 8–12 AT 30'	Free-weight	NR	50	Nutritional surveillance	Elbow flexion and knee extension isokinetic dynamometer; handgrip; 6MWT; Body composition (DEXA)	Lean body mass ↑ Handgrip = 6MWT ↑

RT Resistance training, RPE rating of perceived exertion, NR not reported, RM repetition maximum, EO eccentric overload, AT aerobic training, HR<sub>Max</sub> maximum heart rate, ROM range of movement, ENDUR exercise and nutrition during radiotherapy, ENAF exercise and nutrition after radiotherapy, Supervision % of supervised sessions with respect to total program sessions, DEXA dual energy X-ray absorptiometry, 6MWT 6 minute walking test, TUG timed up and go, CSAT cross sectional area tomography, CPET cardio pulmonary exercise testing, ↑ Improvement, ↓ Worsening, = no changes

\*P < 0.05

recommended that interventions comply with and detail some key aspects of the world of physical exercise, as detailed below:

This review collected 15 RCTs in which physical exercise was used as a supportive intervention in patients with head and neck cancer. Analysis of the FITT principle and progression of loads showed that only 33.3% of the studies met all the parameters. This is a remarkable detail in exercise programming because, as indicated by the ACSM, they are essential for the adaptations sought in the different types of variables to be produced [1, 16].

The frequency of training varied among the trials analyzed, from 1 day a week to 5. Thus, the current literature for cancer survivors recommends cardiovascular exercise three times a week, to which a minimum of two days of strength training is added [42]. Therefore, participation in a single weekly training session may be insufficient to acquire the beneficial adaptations caused by physical exercise.

On the other hand, in addition to the frequency of training, the intensity of training must also be taken into account. In the present review, five studies were found in which the intensity at which both strength and cardiovascular training exercises should be performed was not detailed [32, 34, 35, 49, 52]. This made it difficult to interpret the results. The recommendations for cancer patients state that the intensity of strength training should be at least 60% of 1RM, while cardiovascular exercises should be moderate. According to various exercise prescription guidelines, moderate intensity is defined as a score of 12–13 on the RPE scale, 64%–76% of maximum heart rate or 40%–59% of heart rate reserve [1, 17, 26, 42]. Therefore, detailing the intensity characteristics is considered an added value that brings quality and reproducibility to interventions.

However, with regard to the time or volume of the programs (represented in sets of each exercise), similarities were observed between all the interventions studied, generally between two and three sets. However, to determine the total training volume, it would be convenient to know the repetitions performed in each series (strength training) and the aerobic training time, as detailed in all interventions. Recommendations for cancer patients indicate that the optimal training program for general improvement is 2 to 3 sets with 8–15 repetitions, and for cardiovascular exercise, a minimum volume of 30 min per workout is recommended [5, 26, 42]. In the case of strength training, in two of the fifteen studies retrieved, the recommendations were not respected, performing fewer sets [9, 21], on the other hand, four of the six programs that included aerobic exercise complied with the minimum recommendation of 30 min [33, 56, 62, 63], while two did not exceed 20 min [50, 51] (see Table 3).

The main type of exercise is strength training in the programs studied, and six programs combine strength training with aerobic exercise [33, 50, 51, 56, 62, 63]. Physical exercise programs that only prescribe strength training have been shown to be beneficial in improving the strength levels and body composition of participants, however, they appear to be insufficient [5, 18, 26, 42]. Aerobic exercise in cancer patients has a positive association with reducing disease-related fatigue as well as increasing cardiorespiratory fitness [13, 53]. Therefore, there is a need to combine strength training with aerobic training, following the volume and intensity recommendations mentioned above [47].

Training programs produce adaptations to body systems; therefore, for the physical exercise stimulus to be optimal throughout the intervention, training loads must increase as the adaptations increase [7, 42, 47]. However, only nine programs reported this feature [9, 20, 21, 32, 33, 40, 49, 50, 56], just as intensity is vital when replicating or implementing the exercise program elsewhere.

In addition, exercise supervision is another important aspect to highlight to ensure adherence to the program and quality of exercise execution. It should be noted that oncology patients may have no previous experience in performing physical exercise and that they are generally a group of patients with a history of toxic habits and comorbidities. However, of the 15 physical exercise programs, only five were 100% supervised by professionals [20, 21, 32, 33, 52], and the level of supervision in the rest of the studies ranged between 26.6% and 66.6% (see Table 3). We consider that this fact may hinder the interpretation of the results in relation to the knowledge of the real adherence that patients had to the exercise program, as well as the quality of the execution (presumably better in the case of studies with a supervised program).

Supervised programs are more effective than unsupervised or self-conducted programs at home. This seems to be for two reasons: either because of the higher intensity of physical exercise when supervised, or because of other attributes such as motivation, attentiveness that are developed when training under professional guidance [3, 7].

Supervision may be even more relevant in certain patients who have difficulty performing certain exercises as a consequence of cancer treatment. In the case of patients with head and neck cancer, those undergoing up-front surgery before radiation therapy may have shoulder mobility dysfunction associated with neck lymph node dissection. This should be considered in the design of an exercise program to obtain the maximum possible benefit, considering individual limitations. Ideally, patients should be stratified according to previous yes/no surgery [3, 7]. However, having undergone surgery prior to the start of the physical exercise programme was not identified as a limiting factor in the investigations analysed.

Regarding the timing of interventions with respect to cancer treatment, interventions are found during and/or after treatment. Physical exercise interventions produce general improvements in patients with cancer, regardless of the time of application [54, 55]. However, there is no evidence of exercise programs initiated prior to the start of radiotherapy in patients with HNC.

Moreover, nutritional support is an aspect to be highlighted in patients diagnosed with head and neck cancer because weight loss is a frequently observed problem in this type of patient [14, 23]. In fact, up to 63% of the patients had a high state of malnutrition before starting treatment [10, 11, 23, 30]. In addition, weight loss as a consequence of (chemo-)radiotherapy is a common problem in patients with head and neck cancer [31]. During treatment, patients may develop side effects, among which dysphagia associated with mucositis is the most frequently observed. Acute toxicity causes pain and discomfort, leading to difficulties in eating. Therefore, during radiotherapy, the prevalence of malnutrition can be as high as 41%–88% of patients according to different authors [30, 46, 58].

Pretreatment weight loss has been shown to be a prognostic factor for overall survival (van den [59]). Furthermore, according to Langius et al. [31] critical weight loss during radiotherapy, defined as a body weight loss > 5% from the start of radiotherapy to week 8 or > 7.5% to week 12 according to the international consensus [61], is independently associated with a 1.7-fold risk of head and neck cancer-specific mortality. Although weight stabilization during radiotherapy may be difficult despite nutritional support, critical weight loss can be avoided [6]. Several studies in patients with HNC have shown that early and proactive nutritional intervention can be effective in stabilizing body weight during radiotherapy treatment and improving tolerance to cancer treatment [22, 48].

In this sense, both the European (ESPEN) [44] and American (ASPEN) [39] international guidelines recommend individualized early nutritional support during and after the end of (chemo-)radiotherapy treatment in patients with head and neck cancer. This nutritional approach involves dietary advice, oral supplementation, or feeding tubes depending on the patient's nutritional status.

The importance of nutritional support may be even more relevant in patients with head and neck cancer who participate in physical exercise programs because proper nutrition is essential for the effectiveness of the exercise program (maintaining the necessary caloric and protein intake to control weight and eventually facilitate muscle mass gain) [38]. In addition to enabling the beneficial effects of the exercise intervention, proper nutrition is also necessary to prevent catabolism, which could be brought on by exercise without adequate nourishment [12]. However, only 4 of the 15 studies in this review specified a nutritional approach for

patients [9, 21, 34, 52]. This may have influenced the results of the exercise program in terms of functional improvement and body composition.

However, it is estimated that up to 70% of weight loss can be attributed to loss of muscle mass, leading to a state of sarcopenia associated with decreased strength, functional capacity, and quality of life [24]. Additionally, sarcopenia has recently been associated with increased acute toxicity (dysphagia grade  $\geq 3$ ) during radiotherapy [27] and is an independent poor prognostic factor associated with decreased survival in patients undergoing radiotherapy with curative intent [4, 15, 45].

This clinical context supports the need to combine a supportive nutritional approach with physical exercise programs for such patients. Therefore, the need for body composition measurements as part of the diagnosis and follow-up of patients during cancer treatment is emphasised, especially if physical exercise programmes are established in order to be able to objectify the real impact (muscle mass gain) of exercise on patients' body composition. In the present review, only 10 out of 15 studies included measurements of body composition (mostly by bioimpedance or DEXA) [9, 20, 32–35, 49, 52, 62, 63]. Overall, patients stabilized or improved their body composition and, to a lesser extent, lean body mass [20, 32–35, 49, 62, 63]. Additionally, gains in strength and functional capacity were observed in 13 out of the 15 programs studied [20, 21, 32–35, 40, 49–51, 56, 62, 63].

Sequelae secondary to cancer treatment as well as loss of body weight may continue for several weeks after the end of radiotherapy treatment [30, 41]. This fact should be considered when establishing the timing of a physical exercise program. While an exercise program established during treatment may help mitigate the loss of muscle mass during cancer treatment, programme-initiated post-treatment may be critical in the recovery of sequelae. The optimal time to initiate a program is currently unknown, and in general, mid-term measurements during the follow-up of patients have shown similar results in body composition [9].

The availability of high-quality primary studies may have limited the present review as well as the search terms used, which could affect the analysis made. In addition, heterogeneity in study design and reported outcomes may make data synthesis difficult. Furthermore, the lack of uniform standards in the definition of exercise programs and outcomes of interest may complicate the comparison between studies. Finally, publication bias and the possibility that studies with negative results may not be published may have influenced the results.

Further research is needed on the timing of the physical exercise program during comprehensive treatment of patients. So far, the impact of exercise during and after treatment has been evaluated. Therefore, as a future line of

research, it is proposed to test the efficacy of a multicomponent physical exercise program (strength training and aerobic training), initiated before starting radiotherapy treatment as a prehabilitating exercise and to continue during cancer treatment. Thus, it would be possible to determine the best time to administer physical exercise and increase the level of evidence in this field of study.

Additionally, we consider necessary the association of nutritional support (to decrease sarcopenia and maximize muscle gain) of the patient and the association of measuring the impact on muscle composition and quality of life of the patients. Another endpoint to be considered in future studies is to evaluate the impact of exercise on progression-free survival or overall survival, as there is currently no evidence in this regard.

Likewise, it is appropriate to apply the FITT and progressive overload principle in future physical exercise programs to ensure an effective and reliable intervention that can be replicated by other professionals. We also enhance to further explore the role of the exercise program supervision (by a professional in the field) to optimize the results.

Currently, several trials are underway (NCT05432297, NCT04658706, NCT05594069, NCT04598087, and NCT05418842) that aim to study the application of the physical exercise program prior to starting cancer treatment, thus addressing the lack of information on this aspect in patients with head and neck cancer.

## Conclusion

In conclusion, some evidence suggests that physical exercise programs may have positive impact on body composition, strength, and quality of life in patients with head and neck cancer. However, it is crucial to exercise caution in drawing definitive conclusions because of the need for more precise information regarding FITT principles and load progression within these interventions. This additional detail is essential to conduct a more precise analysis of the dose–response effects of physical exercise in this population. By doing so, we can gain a clearer understanding of which type of exercise program (aerobic, strength, or combination) as well as the appropriate intensity, frequency and volume (number of sets and repetitions or times) would be the most beneficial for patients with head and neck cancer.

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**Data Availability** The dataset used and/or analysed during the current review is available from the corresponding author on reasonable request.

## Declarations

**Conflict of interest** The authors have no conflicts of interest to declare.

**Ethical Approval and Consent to Participate** Not applicable.

**Consent for Publication** Not applicable.

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## References

1. ACSM. ACSM's guidelines for exercise testing and prescription. 11th ed. Indianapolis: Wolters Kluwer; 2022.
2. Antoun S, Raynard B. Muscle protein anabolism in advanced cancer patients: response to protein and amino acids support, and to physical activity. *Ann Oncol*. 2018;29(S2):ii10–7. <https://doi.org/10.1093/annonc/mdx809>.
3. Baguley B, Bolam K, Wright O, Skinner T. The effect of nutrition therapy and exercise on cancer-related fatigue and quality of life in men with prostate cancer: a systematic review. *Nutrients*. 2017;9(9):1003. <https://doi.org/10.3390/nu9091003>.
4. Bardoscia L, Besutti G, Pellegrini M, Pagano M, Bonelli C, Bonelli E, Braglia L, Cozzi S, Roncali M, Iotti C, Pinto C, Pattacini P, Ciammella P. Impact of low skeletal muscle mass and quality on clinical outcomes in patients with head and neck cancer undergoing (chemo)radiation. *Front Nutr*. 2022;9:994499. <https://doi.org/10.3389/fnut.2022.994499>.
5. Brooke HL, Mazzoni A-S, Buffart LM, Berntsen S, Nordin K, Demmelmaier I. Patterns and determinants of adherence to resistance and endurance training during cancer treatment in the Phys-Can RCT. *BMC Sports Sci Med Rehabil*. 2022;14(1):155. <https://doi.org/10.1186/s13102-022-00548-5>.
6. Cacicedo J, Casquero F, Martinez-Indart L, del Hoyo O, de Iturriaga AG, Navarro A, Bilbao P. A prospective analysis of factors that influence weight loss in patients undergoing radiotherapy. *Chin J Cancer*. 2014;33(4):204–10. <https://doi.org/10.5732/cjc.013.10009>.
7. Campbell KL, Winters-Stone KM, Wiskemann J, May AM, Schwartz AL, Courneya KS, Zucker DS, Matthews CE, Ligibel

- JA, Gerber LH, Morris GS, Patel AV, Hue TF, Perna FM, Schmitz KH. Exercise guidelines for cancer survivors: consensus statement from international multidisciplinary roundtable. *Med Sci Sports Exerc.* 2019;51(11):2375–90. <https://doi.org/10.1249/MSS.0000000000002116>.
8. Capozzi LC, Boldt KR, Lau H, Shirt L, Bultz B, Culos-Reed SN. A clinic-supported group exercise program for head and neck cancer survivors: managing cancer and treatment side effects to improve quality of life. *Support Care Cancer.* 2015;23(4):1001–7. <https://doi.org/10.1007/s00520-014-2436-4>.
  9. Capozzi LC, McNeely ML, Lau HY, Reimer RA, Giese-Davis J, Fung TS, Culos-Reed SN. 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):1185–200. <https://doi.org/10.1002/cncr.29863>.
  10. Capuano G, Grosso A, Gentile PC, Battista M, Bianciardi F, Palma AD, Pavese I, Satta F, Tosti M, Palladino A, Coiro G, Palma MD. Influence of weight loss on outcomes in patients with head and neck cancer undergoing concomitant chemoradiotherapy. *Head Neck.* 2008;30(4):503–8. <https://doi.org/10.1002/hed.20737>.
  11. Capuano G, Gentile PC, Bianciardi F, Tosti M, Palladino A, Palma MD. Prevalence and influence of malnutrition on quality of life and performance status in patients with locally advanced head and neck cancer before treatment. *Support Care Cancer.* 2010;18(4):433–7. <https://doi.org/10.1007/s00520-009-0681-8>.
  12. Clemente-Suárez VJ, Redondo-Flórez L, Rubio-Zarapuz A, Martínez-Guardado I, Navarro-Jiménez E, Tornero-Aguilera JF. Nutritional and exercise interventions in cancer-related cachexia: an extensive narrative review. *Int J Environ Res Public Health.* 2022;19(8):4604. <https://doi.org/10.3390/ijerph19084604>.
  13. Cramp F, Byron-Daniel J. Exercise for the management of cancer-related fatigue in adults. *Cochrane Database Syst Rev.* 2012;11(11):CD006145. <https://doi.org/10.1002/14651858.CD006145.pub3>.
  14. Ehrsson YT, Hellström PM, Brismar K, Sharp L, Langius-Eklöf A, Laurell G. Explorative study on the predictive value of systematic inflammatory and metabolic markers on weight loss in head and neck cancer patients undergoing radiotherapy. *Support Care Cancer.* 2010;18(11):1385–91. <https://doi.org/10.1007/s00520-009-0758-4>.
  15. Findlay M, White K, Stapleton N, Bauer J. Is sarcopenia a predictor of prognosis for patients undergoing radiotherapy for head and neck cancer? A meta-analysis. *Clin Nutr.* 2021;40(4):1711–8. <https://doi.org/10.1016/j.clnu.2020.09.017>.
  16. Franchella J, Mezzano GA. Manual ACSM para la valoración y prescripción del ejercicio. 4th ed. Philadelphia, PA: Wolters Kluwer; 2021.
  17. Garber CE, Blissmer B, Deschenes MR, Franklin BA, Lamonte MJ, Lee IM, Nieman DC, Swain DP. American College of Sports Medicine. American College of Sports Medicine position stand. Quantity and quality of exercise for developing and maintaining cardiorespiratory, musculoskeletal, and neuromotor fitness in apparently healthy adults. *Med Sci Sports Exerc.* 2011;43(7):1334–59. <https://doi.org/10.1249/MSS.0b013e318213feb>.
  18. Gil-Rey E, Quevedo-Jerez K, Maldonado-Martin S, Herrero-Román F. Exercise intensity guidelines for cancer survivors: a comparison with reference values. *Int J Sports Med.* 2014;35(14):e1–9. <https://doi.org/10.1055/s-0034-1389972>.
  19. Gould DW, Lahart I, Carmichael AR, Koutedakis Y, Metsios GS. Cancer cachexia prevention via physical exercise: molecular mechanisms. *J Cachexia Sarcopenia Muscle.* 2013;4(2):111–24. <https://doi.org/10.1007/s13539-012-0096-0>.
  20. 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):215. <https://doi.org/10.1186/s13014-018-1157-0>.
  21. Hajdú SF, Wessel I, Dalton SO, Eskildsen SJ, Johansen C. Swallowing exercise during head and neck cancer treatment: results of a randomized trial. *Dysphagia.* 2022;37(4):749–62. <https://doi.org/10.1007/s00455-021-10320-5>.
  22. Isenring EA, Capra S, Bauer JD. Nutrition intervention is beneficial in oncology outpatients receiving radiotherapy to the gastrointestinal or head and neck area. *Br J Cancer.* 2004;91(3):447–52. <https://doi.org/10.1038/sj.bjc.6601962>.
  23. Jager-Wittenaar H, Dijkstra PU, Vissink A, van der Laan BFAM, Rob P van Oort, Jan L N Roodenburg. Critical weight loss in head and neck cancer—prevalence and risk factors at diagnosis: an explorative study. *Support Care Cancer.* 2007;15(9):1045–50. <https://doi.org/10.1007/s00520-006-0212-9>.
  24. Jager-Wittenaar H, Dijkstra PU, Vissink A, Langendijk JA, van der Laan BFAM, Pruijm J, Roodenburg JLN. Changes in nutritional status and dietary intake during and after head and neck cancer treatment. *Head Neck.* 2011;33(6):863–70. <https://doi.org/10.1002/hed.21546>.
  25. Joaquim A, Leão I, Antunes P, Capela A, Viamonte S, Alves AJ, Helguero LA, Macedo A. Impact of physical exercise programs in breast cancer survivors on health-related quality of life, physical fitness, and body composition: evidence from systematic reviews and meta-analyses. *Front Oncol.* 2022;12:955505. <https://doi.org/10.3389/fonc.2022.955505>.
  26. Jones LW, Douglas PS, Eves ND, Marcom PK, Kraus WE, Hurdon JE, Inman BA, Allen JD, Peppercorn J. Rationale and design of the exercise intensity trial (EXCITE): a randomized trial comparing the effects of moderate versus moderate to high-intensity aerobic training in women with operable breast cancer. *BMC Cancer.* 2010;10:531. <https://doi.org/10.1186/1471-2407-10-531>.
  27. Karavolia E, van Rijn-Dekker MI, van den Bosch L, van den Hoek JGM, Oldehinkel E, Meijer TWH, Halmos GB, Witjes MJH, Oosting SF, van der Hoorn A, Langendijk JA, Steenbakkers RJHM. Impact of sarcopenia on acute radiation-induced toxicity in head and neck cancer patients. *Radiat Oncol.* 2022;170:122–8. <https://doi.org/10.1016/j.radonc.2022.03.009>.
  28. Kilgour RD, Vigano A, Trutschnigg B, Hornby L, Lucar E, Bacon SL, Morais JA. Cancer-related fatigue: the impact of skeletal muscle mass and strength in patients with advanced cancer. *J Cachexia Sarcopenia Muscle.* 2010;1:177–85. <https://doi.org/10.1007/s13539-010-0016-0>.
  29. Kubrak C, Olson K, Jha N, Jensen L, McCargar L, Seikaly H, Harris J, Scrimger R, Parliament M, Baracos VE. Nutrition impact symptoms: Key determinants of reduced dietary intake, weight loss, and reduced functional capacity of patients with head and neck cancer before treatment. *Head Neck NA-NA.* 2010;32(3):290–300. <https://doi.org/10.1002/hed.21174>.
  30. Langius JAE, Doornaert P, Spreeuwenberg MD, Langendijk JA, Leemans CR, van Bokhorst-de van der Schueren MA. Radiotherapy on the neck nodes predicts severe weight loss in patients with early stage laryngeal cancer. *Radiat Oncol.* 2010;97(1):80–5. <https://doi.org/10.1016/j.radonc.2010.02.017>.
  31. Langius JAE, Bakker S, Rietveld DHF, Kruijenga HM, Langendijk JA, Weijs PJM, Leemans CR. Critical weight loss is a major prognostic indicator for disease-specific survival in patients with head and neck cancer receiving radiotherapy. *Br J Cancer.* 2013;109(5):1093–9. <https://doi.org/10.1038/bjc.2013.458>.
  32. Lavigne C, Twomey R, Lau H, Francis G, Culos-Reed SN, Millet GY. Feasibility of eccentric overloading and neuromuscular electrical stimulation to improve muscle strength and muscle mass after treatment for head and neck cancer. *J*

- Cancer Surviv. 2020;14(6):790–805. <https://doi.org/10.1007/s11764-020-00893-9>.
33. Lin KY, Cheng HC, Yen CJ, Hung CH, Huang YT, Yang HL, Cheng WT, Tsai KL. Effects of exercise in patients undergoing chemotherapy for head and neck cancer: a pilot randomized controlled trial. *Int J Environ Res Public Health*. 2021;18(3):1–14. <https://doi.org/10.3390/ijerph18031291>.
  34. Lonbro S, Dalgas U, Primdahl H, Overgaard J, Overgaard K. Feasibility and efficacy of progressive resistance training and dietary supplements in radiotherapy treated head and neck cancer patients—the DAHANCA 25A study. *Acta Oncol*. 2013a;52(2):310–8.
  35. Lønbro S, Dalgas U, Primdahl H, Johansen J, Nielsen JL, Aagaard P, Hermann AP, Overgaard J, Overgaard K. Progressive resistance training rebuilds lean body mass in head and neck cancer patients after radiotherapy - results from the randomized DAHANCA 25B trial. *Radiother Oncol*. 2013;108(2):314–9. <https://doi.org/10.1016/j.radonc.2013.07.002>.
  36. Maher CG, Sherrington C, Herbert RD, Moseley AM, Elkins M. Reliability of the PEDro scale for rating quality of randomized controlled trials. *Phys Ther*. 2003;83(8):713–21.
  37. Marur S, Forastiere AA. Head and neck squamous cell carcinoma: update on epidemiology, diagnosis, and treatment. *Mayo Clin Proc*. 2016;91(3):386–96. <https://doi.org/10.1016/j.mayocp.2015.12.017>.
  38. McCurdy B, Nejatnamini S, Debenham BJ, Álvarez-Camacho M, Kubrak C, Wismer WV, Mazurak VC. Meeting minimum ESPEN energy recommendations is not enough to maintain muscle mass in head and neck cancer patients. *Nutrients*. 2019;11(11):2743. <https://doi.org/10.3390/nu11112743>.
  39. McKeever L. New implementations for the ASPEN clinical guidelines and a call for protocol review on the nutrition guidelines for adult head and neck cancer. *J Parenter Enter Nutr*. 2021;45(7):1397–9. <https://doi.org/10.1002/jpen.2233>.
  40. McNeely ML, Parliament MB, Seikaly H, Jha N, Magee DJ, Haykowsky MJ, Courneya KS. Effect of exercise on upper extremity pain and dysfunction in head and neck cancer survivors: a randomized controlled trial. *Cancer*. 2008;113(1):214–22. <https://doi.org/10.1002/cncr.23536>.
  41. Mehanna H, West CML, Nutting C, Paleri V. Head and neck cancer—Part 2: treatment and prognostic factors. *BMJ*. 2010;341:c4690. <https://doi.org/10.1136/bmj.c4690>.
  42. Mishra SI, Scherer RW, Snyder C, Geigle PM, Berlanstein DR, Topaloglu O. Exercise interventions on health-related quality of life for people with cancer during active treatment. *Cochrane Database Syst Rev*. 2012;2012(8):CD008465. <https://doi.org/10.1002/14651858.CD008465.pub2>.
  43. Moher D, Shamseer L, Clarke M, Davina Gherzi, Alessandro Liberati, Mark Petticrew, Paul Shekelle, Lesley A Stewart; PRISMA-P Group. Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015 statement. *Syst Rev*. 2015;4(1):1. <https://doi.org/10.1186/2046-4053-4-1>.
  44. Muscaritoli M, Arends J, Bachmann P, Baracos V, Barthelemy N, Bertz H, Bozzetti F, Hütterer E, Isenring E, Kaasa S, Krznaric Z, Laird B, Larsson M, Laviano A, Mühlebach S, Oldervoll L, Ravasco P, Solheim TS, Strasser F, de van der Schueren M, Preiser JC, Bischoff SC. ESPEN practical guideline: clinical nutrition in cancer. *Clin Nutr*. 2021;40(5):2898–913. <https://doi.org/10.1016/j.clnu.2021.02.005>.
  45. Nagpal P, Pruthi DS, Pandey M, Yadav A, Singh H. Impact of sarcopenia in locally advanced head and neck cancer treated with chemoradiation: an Indian tertiary care hospital experience. *Oral Oncol*. 2021;121:105483. <https://doi.org/10.1016/j.oraloncology.2021.105483>.
  46. Nayel H, El-Ghoneimy E, El-Haddad S. Impact of nutritional supplementation on treatment delay and morbidity in patients with head and neck tumors treated with irradiation. *Nutrition*. 1992;8(1):13–8.
  47. Neil-Sztramko SE, Medysky ME, Campbell KL, Bland KA, Winters-Stone KM. Attention to the principles of exercise training in exercise studies on prostate cancer survivors: a systematic review. *BMC Cancer*. 2019;19(1):321. <https://doi.org/10.1186/s12885-019-5520-9>.
  48. Ravasco P, Monteiro-Grillo I, Camilo ME. Does nutrition influence quality of life in cancer patients undergoing radiotherapy? *Radiother Oncol*. 2003;67(2):213–20. [https://doi.org/10.1016/S0167-8140\(03\)00040-9](https://doi.org/10.1016/S0167-8140(03)00040-9).
  49. Rogers LQ, Anton PM, Fogleman A, Hopkins-Price P, Verhulst S, Rao K, Malone J, Robbs R, Courneya KS, Nanavati P, Mansfield S, Robbins KT. Pilot, randomized trial of resistance exercise during radiation therapy for head and neck cancer. *Head Neck*. 2013;35(8):1178–88. <https://doi.org/10.1002/hed.23118>.
  50. Samuel SR, Maiya GA, Samuel Babu A, Vidyasagar MS. Effect of exercise training on functional capacity & quality of life in head & neck cancer patients receiving chemoradiotherapy. *Indian J Med Res*. 2013;137(3):515–20.
  51. Samuel SR, Maiya AG, Fernandes DJ, Guddattu V, Saxena PUP, Kurian JR, Lin PJ, Mustian KM. Effectiveness of exercise-based rehabilitation on functional capacity and quality of life in head and neck cancer patients receiving chemo-radiotherapy. *Support Care Cancer*. 2019;27(10):3913–20. <https://doi.org/10.1007/s00520-019-04750-z>.
  52. Sandmæl JA, Bye A, Solheim TS, Stene GB, Thorsen L, Kaasa S, Lund JÅ, Oldervoll LM. Feasibility and preliminary effects of resistance training and nutritional supplements during versus after radiotherapy in patients with head and neck cancer: a pilot randomized trial. *Cancer*. 2017;123(22):4440–8. <https://doi.org/10.1002/cncr.30901>.
  53. Schmitz KH, Courneya KS, Matthews C, Demark-Wahnefried W, Galvão DA, Pinto BM, Irwin ML, Wolin KY, Segal RJ, Lucia A, Schneider CM, von Gruenigen VE, Schwartz AL, American College of Sports Medicine. American college of sports medicine roundtable on exercise guidelines for cancer survivors. *Med Sci Sports Exerc*. 2010;42(7):1409–26. <https://doi.org/10.1249/MSS.0b013e3181e0c112>.
  54. Scott JM, Lee J, Herndon JE, Michalski MG, Lee CP, O'Brien KA, Sasso JP, Yu AF, Rowed KA, Bromberg JF, Traina TA, Guicalp A, Sanford RA, Gajria D, Modi S, Comen EA, D'Andrea G, Blinder VS, Eves ND, Peppercorn JM, Moskowitz CS, Dang CT, Jones LW. Timing of exercise therapy when initiating adjuvant chemotherapy for breast cancer: a randomized trial. *Eur Heart J*. 2023. <https://doi.org/10.1093/eurheartj/ehad085>.
  55. Stout NL, Baima J, Swisher AK, Winters-Stone KM, Welsh J. A systematic review of exercise systematic reviews in the cancer literature (2005–2017). *PM&R*. 2017;9(S2):S347–84. <https://doi.org/10.1016/j.pmrj.2017.07.074>.
  56. Su TL, Chen AN, Leong CP, Huang YC, Chiang CW, Chen IH, Lee YY. The effect of home-based program and outpatient physical therapy in patients with head and neck cancer: a randomized, controlled trial. *Oral Oncol*. 2017;74:130–4. <https://doi.org/10.1016/j.oraloncology.2017.10.002>.
  57. Sung H, Ferlay J, Siegel RL, Laversanne M, Soerjomataram I, Jemal A, Bray F. Global cancer statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA Cancer J Clin*. 2021;71(3):209–49. <https://doi.org/10.3322/caac.21660>.
  58. Unsal D, Montes B, Akmansu M, Uner A, Oguz M, Pak Y. Evaluation of nutritional status in cancer patients receiving radiotherapy. *Am J Clin Oncol*. 2006;29(2):183–8. <https://doi.org/10.1097/O1.coc.0000198745.94757.ee>.
  59. van den Broek GB, Rasch CRN, Pameijer FA, Peter E, van den Brekel MWM, Tan IB, Schornagel JH, de Bois JA, Zijp LJ, Balm

- AJM. Pretreatment probability model for predicting outcome after intraarterial chemoradiation for advanced head and neck carcinoma. *Cancer*. 2004;101(8):1809–17. <https://doi.org/10.1002/cncr.20556>.
60. Virto N, Etayo-Urtasun P, Sánchez Isla JR, Arietanzibeaskoa MS. Effects of a 12-week exercise intervention on glycated hemoglobin (HbA1c) levels in cancer patients. *Retos: nuevas tendencias en educación física, deporte y recreación*. 2023;48:153–60.
  61. White JV, Guenter P, Jensen G, Malone A, Schofield M; Academy Malnutrition Work Group; A.S.P.E.N. Malnutrition Task Force; A.S.P.E.N. Board of Directors. Consensus statement: academy of nutrition and dietetics and American society for parenteral and enteral nutrition. *J Parenter Enteral Nutr*. 2012;36(3):275–83. <https://doi.org/10.1177/0148607112440285>.
  62. Yen CJ, Hung CH, Kao CL, Tsai WM, Chan SH, Cheng HC, Jheng WT, Lu YJ, Tsai KL. Multimodal exercise ameliorates exercise responses and body composition in head and neck cancer patients receiving chemotherapy. *Support Care Cancer*. 2019;27(12):4687–95. <https://doi.org/10.1007/s00520-019-04786-1>.
  63. Zhao SG, Alexander NB, Djuric Z, Zhou J, Tao Y, Schipper M, Feng FY, Eisbruch A, Worden FP, Strath SJ, Jolly S. Maintaining physical activity during head and neck cancer treatment: results of a pilot controlled trial. *Head Neck*. 2016;38(S1):E1086–96. <https://doi.org/10.1002/hed.24162>.