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Original Article

Prehabilitation for Patients with Cancer Undergoing Radiation Therapy: a Scoping Review

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Abstract

Aims: Prehabilitation is a process of identifying and assessing factors that could compromise the physical and psychological health of patients undergoing cancer treatment and implementing an intervention to combat such concerns. The use of prehabilitation in cancer surgery has yielded positive outcomes in rectal, lung and abdominal cancers. Prehabilitation strategies have potential to improve the management of patients receiving radiation therapy or chemoradiation. The aim of the present study was to map the evidence of the assessment and evaluation of prehabilitation for radiation therapy patients.

Materials and methods: A database search using EMBASE and PubMed was conducted. The PRISMA guidelines were adhered to. Keywords included prehabilitation, radiation therapy/radiotherapy, chemoradiotherapy/chemoradiation, intervention and exercise. Types of prehabilitation strategy, their purposes and impact, according to cancer site, were analysed.

Results: Prehabilitation is most commonly evaluated in head and neck cancer, whereby unimodal, physical interventions manage dysphagia. Prehabilitation for lung cancer demonstrated its ability to widen treatment options for patients. Physical prehabilitation is administered to combat adverse effects of neoadjuvant chemoradiation therapy in patients with rectal cancer.

Conclusion: Prehabilitation is adaptive and tailored to specific patient and site needs; thus it is applied across a wide range of cancer sites. More interventions by which radiation therapy is the definitive treatment modality and larger sample sizes within these studies are warranted to increase prehabilitation utilisation for patients undergoing radiation therapy.

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Key words: Cancer; head and neck; outcomes; prehabilitation; radiation

Introduction

Cancer prehabilitation adopts the principles of rehabilitation but is implemented between diagnosis until and during the start of primary treatment [1]. There are two chief categories of prehabilitation: unimodal and multimodal. Unimodal interventions target a single aspect of patient care. Multimodal prehabilitation consists of various interventions. Multimodal prehabilitation has been regarded as more advantageous than unimodal prehabilitation [2]. The three primary domains included in prehabilitation programmes are physical activity, dietary advice and psychological support. Interventions focus on physical health and fitness, nutrition, psychosocial well-being, smoking cessation and education [3–6]. The levels of prehabilitation are defined as universal, targeted or specialist. Universal interventions involve adopting healthy lifestyle habits, whereas targeted interventions are patient-tailored. Specialist interventions require input from multidisciplinary teams to focus on specific aspects of care [6].

In general, prehabilitation has a role for all cancer sites and for cancer surgery; it is well-established. Lau and Chamberlain's [7] meta-analysis confirmed that prehabilitation improves exercise capacity before and after gastrointestinal cancer surgery. The preoperative period has been described as 'teachable', whereby patients are motivated and amenable to interventions [8]. Prehabilitation reduced postoperative hospital length of stay by 3 or more days in patients who underwent abdominal cancer surgery [9].

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In the context of radiation therapy, prehabilitation could also prove to be beneficial. There is a link between exercising during radiation therapy and counteracting side-effects [10]. A 12-week resistance training programme found significant improvements in general cancer-related fatigue ($P = 0.044$) for 155 breast cancer patients [11], a side-effect that affects up to 65% of patients undergoing radiation therapy [10]. Moreover, a systematic review found that exercise during radiation therapy significantly improved physical function in 16 of 16 studies (100%) [12]. Psychosocial interventions, such as relationship building, needs assessment and patient education sessions led by radiation therapists, are effective in mitigating patient anxiety [13].

The current evidence of cancer prehabilitation is 'highly variable' [6]. Current trials are heterogenous in terms of patient populations and the types of intervention that are tested. Gaps are also present regarding treatment modalities, with surgery dominating the existing evidence [6]. Macmillan Cancer Support recommends that future research should be directed towards prehabilitation for non-surgical therapies [6]. The benefits of prehabilitation for cancer patients include improved post-treatment recovery, fewer treatment-related complications and enhanced pre-treatment functional capacity [14]. This scoping literature review examines how prehabilitation is being investigated as an intervention prior to radiation therapy or chemoradiation. The review identifies patients with head and neck cancer as the cohort most likely to be offered prehabilitation, but extends the analysis to patients with other cancers. The analysis seeks to report on the type, purpose and potential benefit of each tested programme.

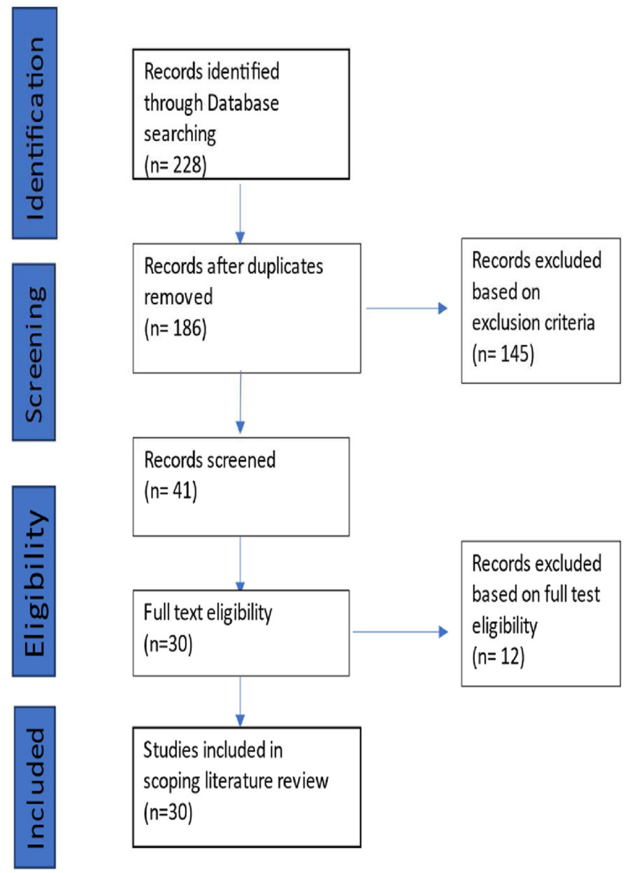

Fig 1. PRISMA flow chart illustrating the number of records included and excluded at various screening and reviewing steps, leading to the final list of records for data extraction and reporting.

Methodology

Search Strategy for the Identification of Studies

The Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) guidelines were adhered to during the research for this scoping literature review. Data were collected by comprehensive database searching (EMBASE and PubMed). Searching concluded on 5 October 2022. Keywords and phrases included: (prehabilitation AND radiation therapy OR radiotherapy), (prehabilitation AND chemoradiotherapy OR chemoradiation), (intervention AND prior to radiation therapy OR prior to radiotherapy) and (exercise AND before radiation therapy OR before radiotherapy). Reference lists of identified articles were also scrutinised (Figure 1). Records from the year range 2011–2022 were collected. Records in the English language only were included.

Type of Study

Randomised and non-randomised controlled trials, trial protocols, retrospective cohort studies and qualitative studies were included. Feasibility studies were included to analyse methodologies and protocols. Systematic and literature reviews were not included. Conference abstracts, abstract-only texts and supplements were excluded.

Type of Participant

Only human studies were included. All cancer sites were included. All patients regardless of nationality, age and gender were included.

Type of Intervention

Studies where prehabilitation was implemented prior to radiation therapy or chemoradiation were analysed. Studies that focused on rehabilitation rather than prehabilitation were excluded. Additionally, studies that focused on cancer surgery only or chemotherapy only were excluded. Unimodal and multimodal prehabilitation interventions were included.

Type of Outcome

Identified outcomes included quality of life, feasibility, physical activity/fitness, dysphagia outcomes, functional capacity, adherence, psychosocial outcomes, patient-reported outcome measures and percentage benefits.

Description of Studies

In total, 228 records were yielded from the search, with 30 studies meeting the inclusion criteria. The chosen studies consisted of 10 randomised controlled trials, 10 pilot/feasibility studies, four retrospective cohort studies, three qualitative studies, two non-randomised controlled trials and one trial protocol. In total, eight cancer sites were identified. Head and neck, gynaecological, lung, oesophageal, glioma, prostate, breast and rectal cancer were represented. Additionally, four studies involved patients of various cancer sites. In terms of interventions, 20 studies involved unimodal/physical prehabilitation and 10 studies were non-physical. Six of these 10 records were multimodal prehabilitation studies. Across the 30 studies, there were 5011 participants (Figure 2).

Prehabilitation Strategies in Head and Neck Cancers

The most common anatomical site where prehabilitation strategies were identified was the head and neck, with eight of 30 studies [15–22]. One study investigated prehabilitation for glioma patients [23]. In total, 3374 patients were recruited across these nine studies. Loewen *et al.* [24] discussed that prehabilitation for this site exists as either ‘pre-treatment prehabilitation’ or ‘treatment-concurrent prehabilitation’. Most participants performed prehabilitative strategies during their treatment and, thus, this strategy is defined as the latter.

Prehabilitation was employed by one centre to assess the risk of and to prevent radiation-induced lymphoedema, a toxicity that affects up to 50% of head and neck cancer patients [15,25]. Baseline assessments at the time of diagnosis were carried out for all patients to assess swelling and the risk of other side-effects, such as trismus and loss of motion [15]. Assessment consisted of functional testing, clinician- and patient-reported outcome measurement tests [15]. The intervention involved lymphoedema educational sessions and a home programme encompassing self-care management and exercises [15]. The detection rate of lymphoedema increased from 27 to 48% ($P = 0.0002$) due to this programme’s impact [15].

Radiation-induced dysphagia negatively impacts quality of life [24]. Prophylactic swallowing exercises to hinder radiation dysphagia were considered in five of eight studies [16,17,19,21,22]. Delays in referring patients to swallowing rehabilitation has justified a need for prehabilitation in this setting [16]. These studies utilised unimodal, physical prehabilitation. Although, all studies had a similar purpose, the assessment, exercise type and duration of the interventions varied between programmes (Table 1).

Baseline assessment was similar across all studies, but the exercise interventions and outcomes varied. Baseline assessment was conducted no more than 2 weeks prior to radiation therapy in all studies [16,17,19,21,22]. A videofluoroscopic swallowing study is considered the gold standard assessment for dysphagia [22]. Exercises such as The Effortful Swallow, Mendelssohn manoeuvre and tongue resistance exercises are customary across swallowing prehabilitation [17,21]. The most prevalent exercise schedule is 10 repetitions of exercises, three times a day, daily [17,19]. It is proposed that the ‘three times a day’ logic is convenient for patients to incorporate their exercises with mealtimes [17]. The primary outcomes of the studies were swallowing function [17,21], Swallowing Performance Status [19] or changes in dysphagia severity [16]. Quality of life was

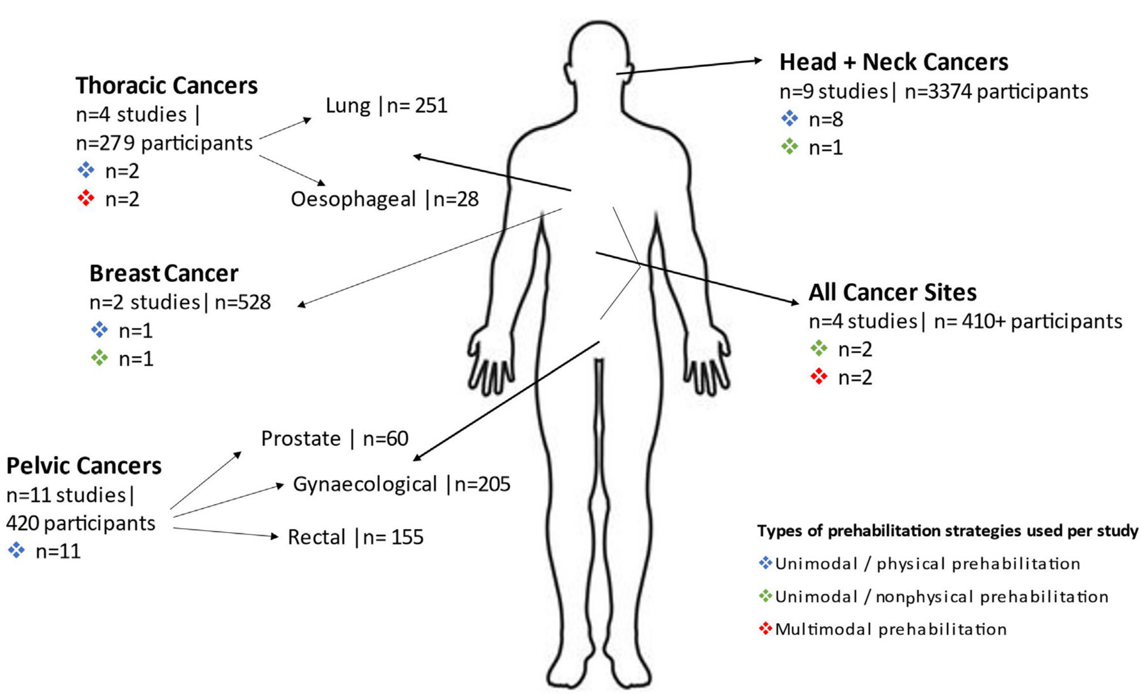

Fig 2. The breakdown of studies based on their sites, including the number of participants per site and the types of prehabilitation used.

Table 1
Summary of studies involving swallowing prehabilitation in head and neck cancer for radiation dysphagia, a type of unimodal, physical prehabilitation

Reference	No. patients	Baseline assessment	Timepoints for assessment	Duration of intervention	Types of exercise	Intensity/ frequency	Measurement tests/endpoints
Carmignani *et al.*, 2018 [21]	12	M.D Anderson Dysphagia Inventory and Dysphagia Handicap Index	3 timepoints	2 weeks pre-RT	Home swallowing exercises	10 repetitions, twice a day	Swallowing outcomes assessed by M.D Anderson Dysphagia Inventory and Dysphagia Handicap Index
Guillen-Sola *et al.*, 2019 [16]	52	VFSS	5 timepoints. Baseline, immediately after CRT, 3, 6 and 12 months post-CRT	2 weeks pre-CRT to 12 weeks post-CRT (21 weeks)	IEMT + standard swallowing therapy	3 sets of 5 repetitions. 3 times a day, 5 days a week	Primary outcome: change in dysphagia severity Observed by VFSS and assessed with Penetration-Aspiration scale
Kotz *et al.*, 2012 [17]	26	FOIS PSS-H&N	6 timepoints. Baseline, immediately after CRT, 3, 6, 9 and 12 months post-CRT	Duration of chemoradiation	5 intervention swallowing exercises + swallowing therapy	3 sets of 10 repetitions, 3 times a day Weekly swallowing therapy	Swallowing function
Martino *et al.*, 2021 [22]	952	VFSS	Pre-RT, 3 and 12 months post-RT	Pre-RT + 6 week duration of RT	Swallowing therapy sessions every 2 weeks + swallowing exercises	Daily, during mealtimes + outside of mealtimes	Duration of feeding tube dependency 1-year post-RT
Mortensen *et al.*, 2015 [19]	44	Modified barium swallow examination	9 timepoints. From baseline to 11 months post-RT	Pre-RT to 8 months post-RT	Swallowing exercises + resistance exercises	10 repetitions, 3 times a day, 7 days a week	Impact of swallowing exercises on dysphagia outcomes as per swallowing performance status scale

CRT, chemoradiation; FOIS, functional oral intake scale; IEMT, inspiratory and expiratory muscle training; PSS-H&N, performance status scale for head and neck cancer patients; RT, radiation therapy; VFSS, video-fluoroscopic swallowing study.

assessed as an outcome using the EORTC QLQ-C30 questionnaire and its subdivision, HN35, for head and neck cancer [16,19,21]. The PRO-ACTIVE trial is an ongoing, international, randomised clinical trial involving 952 patients assigned to standard reactive swallowing therapy or proactive swallowing prehabilitation [22]. The results of this trial will assist in decision-making regarding dysphagia treatment for patients receiving radiation therapy [22].

A pilot trial perceived dyadic yoga and other relaxation techniques beneficial and feasible for glioma patients undergoing at least 20 fractions of radiation therapy [23]. The assessment consisted of patient-reported outcome measures. Cancer-related symptoms, depressive symptoms, fatigue and quality of life were assessed [23]. Due to the burden of a glioma diagnosis on family and friends, this intervention was also offered to the caregivers of the patients. The intervention resulted in a large effect decrease in caregivers' depressive symptoms [23].

Prehabilitation is utilised most commonly for the prevention and management of radiation dysphagia for head and neck cancer. Additionally, prehabilitation has shown benefit in preventing lymphoedema. Prehabilitation also relieves cancer-related symptoms associated with gliomas.

Prehabilitation Strategies in Thoracic Cancers

In the thoracic region, prehabilitation strategies were identified in lung and oesophageal cancers across four of 30 studies. Lung cancer was the focus for two of six studies [26,27]. One study examined oesophageal cancer alone [2] and one other included both lung and oesophageal cancer patients [28].

Toxicities such as pneumonitis and radiation fibrosis [29] manifest during and after radiation therapy for lung cancer [30]. There is a role for interventions at all stages of treatment, including the pre-treatment phase [30]. Multimodal prehabilitation consisting of exercise, dietary advice, smoking cessation and psychological support are offered [30]. Optimising pulmonary fitness and cardiac health is prioritised [30]. Radiation therapists are trained with providing education to patients regarding smoking cessation prior to lung radiation therapy as well as monitoring their progress during their treatment [14].

Two hundred and sixteen patients with lung cancer underwent pulmonary prehabilitation assessment and intervention prior to surgery, radical radiation therapy or systemic therapy [27]. Twenty-six patients received radiation therapy. The purpose of prehabilitation in this study was to improve dyspnoea, performance status and pulmonary function [27]. Assessment included measuring World Health Organization (WHO) performance status scale, Medical Research Council (MRC) dyspnoea score, 6-min walking test and levels of frailty [27]. The 2–4-week multimodal intervention programme involved respiratory muscle and cardiovascular exercise, education and smoking cessation [27]. Prehabilitation increased the rate of operable patients from 41.2 to 75.8% ($P = 0.00001$) as well as improved all aforementioned outcomes for patients who received radiation therapy [27]. Improving radiation therapy options (e.g. radical versus palliative versus stereotactic ablative radiotherapy (SABR) with prehabilitation is an area for future research.

Two examples of unimodal, physical prehabilitation were identified [26,28]. Aerobic interval training five times a week during chemoradiation for 15 patients with lung cancer was deemed feasible and well-tolerated [26]. The volume of oxygen uptake, a surrogate for aerobic capacity, was measured together with the 6-min walking test to record functional capacity at baseline assessment and after 7 weeks of the intervention [26]. Patients receiving thoracic radiation therapy and their caregivers participated in a dyadic yoga programme, similar to that trialled for glioma patients [28]. This pilot trial showed feasibility and benefit of dyadic yoga for this cohort of patients [23].

Despite, over half of lung patients requiring non-surgical treatments, there are few programmes that focus on non-surgical candidates. Standardised prehabilitation programmes for all lung patients regardless of treatment modality are warranted [31].

Prehabilitation Strategies in Breast Cancers

Postigo-Martin *et al.* [32] presented a trial that used physical prehabilitation for breast cancer, whereas Halkett *et al.* [33] examined the use of psychological methods. Postoperative rehabilitative exercise to the axilla prior to radiation therapy enhances the range of motion and improves tolerance to treatment for patients with breast cancer [34]. This form of radiation therapy prehabilitation is commonly observed in clinical practice. Evidence suggests that aerobic exercise is an effective intervention to mitigate cardiotoxicity in breast cancer patients [35]. Patients undergoing radiation therapy to their breast are at risk of pericarditis, coronary artery disease and arrythmias [36].

The aim of the *ATOPE* therapeutic exercise programme [32] is to highlight the benefit of introducing exercise in the prehabilitative phase to diminish cardiotoxicity associated with breast radiation therapy. *ATOPE* is a patient-tailored unimodal, physical programme. Patients with breast cancer are randomised to undergo 12–18 sessions of a variety of exercise training. The primary outcome is cardiotoxicity and secondary outcomes include cardiorespiratory fitness and patient-reported quality of life [32]. Cardiac function and cardiopulmonary exercise tests are carried out at four assessment timepoints. Notably, baseline assessment is immediately after diagnosis [32].

In contrast to exercise interventions, psychological interventions have been analysed for patients with breast cancer. RT Prepare [33], a radiation therapist-led psychoeducational programme, yielded significantly less psychological distress ($P = 0.001$) and levels of anxiety ($P = 0.003$) in the intervention group. In total, 408 patients were randomised to the intervention group ($n = 190$) or usual care ($n = 218$). Baseline assessment involved surveying patients prior to their computed tomography planning appointment. Patients were also assessed before their first fraction and 6–7 weeks later, within a week of finishing therapy [33]. Interventions consisted of two patient and radiation therapist meetings prior to planning and treatment delivery. Psychosocial needs of patients were assessed and patients were educated about the radiation therapy process and taught anxiety reduction strategies [33]. Psychological distress measured by the Hospital Anxiety and Depression scale was the primary outcome [33]. Apart from showing significant benefits in the psychosocial health of breast cancer patients, RT Prepare [33] demonstrated the role that radiation therapists can play in psychological prehabilitation. Radiation therapists are equipped with communication skills that can relieve patient concerns prior to radiation therapy [13,33].

Prehabilitation Strategies in Pelvic Cancers

Across the pelvic region, four of 11 studies reviewed gynaecological cancers and one of 11 was based on prostate cancer; rectal cancer was the dominant site, being the focus of six of 11 studies. In total, 420 patients participated in these studies inclusively. These sites are similar in terms of treatment technique and side-effects and thus are categorised together. For patients with gynaecological cancers undergoing radiation therapy there is an emphasis on minimising gastrointestinal and genitourinary toxicity and preserving psychosexual wellbeing [37]. Four of four studies consisted of patients with cervical cancer [38–41]. Patients with endometrial cancer were included in three of four studies [38–40]. Patients with vulvar cancer [39] and patients with vaginal cancer [40] were involved in one study each. Prehabilitation goals vary among each patient group due to their different patient needs. For example, prehabilitation aids weight loss in patients with cervical and endometrial cancer [42].

Up to 14% of gynaecological patients treated with radiation therapy are at risk of radiation-related insufficiency fractures to their pelvic bone [43,44]. Radbone [38] is a UK trial currently investigating the feasibility and potential effectiveness of a musculoskeletal health package combined with a Prehab4Cancer [18] prehabilitation programme to prevent radiation-related bone damage. Forty patients randomised to the intervention group will undergo a musculoskeletal health assessment, fracture risk assessment and a 3-month prehabilitation exercise regimen [38]. Pelvic magnetic resonance imaging, patient-reported outcome measures and blood testing at 6, 12 and 18 month post-radiation therapy will be performed to assess the efficiency of the programme in managing radiation-related insufficiency fractures [38].

Two unimodal, physical prehabilitation approaches utilised pelvic floor muscle exercises to preserve pelvic floor muscle strength and function and to prevent incontinence [39,41]. Araya-Castro *et al.* [39] also introduced using vaginal dilators before radiation therapy to maintain sexual function. Similarly, a study targeting patients with prostate cancer determined that pelvic floor muscle exercises are a useful method to prevent urinary incontinence [45]. The non-prehabilitation control group experienced significantly more leakage ($P < 0.05$) than the prehabilitation group [45]. In the pilot study of pre-rehabilitation of the pelvic floor before radiation therapy for cervical cancer, 49 participants attended an educational session to learn pelvic floor muscle exercises and were instructed to perform the exercises at home 1 month prior to and until the completion of radiation therapy [41]. Follow-up of this intervention included 28 of 49 (57%) participants. The primary outcome was pelvic floor strength assessed by bidigital vaginal examination at 1 month before radiation therapy or baseline and at follow-up, which was 1-month post-radiation therapy [41]. This study displayed feasibility, but no significant results were observed. The short duration of follow-up and non-adherence of patients to complete the follow-up assessments limited this study [41]. Another unimodal, physical strategy was tested to improve patient positioning for radiation therapy by minimising inter-fraction sacral slope variability [40]. Sacral slope angles, a surrogate for variable patient positioning, was the main endpoint, measured at baseline using a digital reconstructed radiograph from the planning computed tomography scan [40]. The variation in sacral slope angles was measured daily using verification imaging over the course of treatment [40]. A significant decrease in sacral slope angle was demonstrated due to the exercise programme. The exercise prescription consisting of extension and external rotation of the hip was completed by eight participants [40]. This limitation indicates the requirement for larger trials to probe the effectiveness of prehabilitation to improve patient positioning for radiation therapy. Rectal cancer was the primary site in six studies and, in total, 155 patients were recruited [46–51]. The value of prehabilitation in rectal cancer treatment has been shown [52]. Trépanier *et al.* [53] reported 5-year disease-free survival of 73.4% with prehabilitation versus 50.9% with the omission of prehabilitation prior to colorectal cancer surgery. Declining functional capacity caused by chemoradiation is reduced by exercise prehabilitation [53]. There is a trend in the provision of prehabilitation for rectal cancer whereby prehabilitation is prescribed to mitigate the negative effects of neoadjuvant chemoradiation therapy (NACRT) [48,54]. Structured responsive exercise training programmes have been shown to recover fitness and mitochondrial content following NACRT-induced damage [48,54]. However, this form of prehabilitation is prior to surgery, implemented during or immediately post-chemoradiation.

All six studies were unimodal, physical programmes with five of six studies applying a structured responsive exercise training strategy (Table 2). An important component of this form of exercise prehabilitation is baseline testing measured by cardiopulmonary exercise testing (CPET). CPET influences decision-making to derive patient-personalised exercise prescriptions, as well as monitoring patient progress during the intervention [55]. CPET measures the volume of oxygen uptake and gives an indication of pulmonary and cardiovascular function [55]. The volume of oxygen uptake at peak exercise and lactate threshold are the primary endpoints in three rectal cancer studies [47–49]. There are various timepoints for CPET assessment during these programmes, which include baseline, week 0, 3 and 6 of the exercise intervention and during the follow-up

Table 2
Summary of structured responsive exercise training programmes in rectal and lung cancers, a type of unimodal, physical prehabilitation

Reference	Cancer site	No. patients	Baseline assessment	Timepoints for assessment	Duration of programme	Type of exercise	Intensity/ frequency	Measurement tests/endpoints
Alejo *et al.*, 2019 [49]	Rectal cancer	12	One-mile walk test to determine baseline fitness	Baseline (before NACRT) Immediately before surgery	5 weeks	• Aerobic, resistance and flexibility exercises	• 6 total sessions • 35–60 min	• Fitness: VO2 peak measured by 1-mile walk and sit to stand test • Physical activity: accelerometery assessment
Egegaard *et al.*, 2019 [26]	Non-small cell lung cancer	15	Measuring endpoints listed at their baseline level	Baseline (before RT) After 7 weeks (completion of RT)	7 weeks	• Ergometer cycling • Aerobic interval training	• Daily (Monday–Friday) • 20-min sessions	• Aerobic capacity (VO2peak) • Functional capacity (6MWT) • Lung function
Goldsmith *et al.*, 2021 [27]	Lung cancer	216	Measuring endpoints listed at their baseline level	Baseline 30 days, 90 days and 1 year post-treatment	2–4 weeks	• Respiratory muscle training • Cardiovascular • Exercises via ergometer cycling or walking	• 2 sessions per week • 70-min sessions • Daily breathing exercises at home × 3 times a day	• WHO performance status • MRC dyspnoea score • Activity level • Frailty • 6MWT
Heldens *et al.*, 2016 [50]	Rectal cancer	13	6MWT to measure functional capacity Submaximal multiple repetition test to measure muscle strength	Baseline After 5 weeks of training (post-NACRT) After 10 weeks of training 8 weeks post-surgery	Individualised (started week 1 of CRT and ended at surgery)	• Endurance exercises via treadmill + cycle ergometer • Resistance exercises	• 2 sessions per week • 45–60 min	• Functional exercise capacity (6 MWT) • Muscle strength (X-RM)
Loughney *et al.*, 2021 [47]	Rectal cancer	33	CPET HRQoL questionnaires	Measured pre-NACRT, baseline (post-NACRT), weeks 3, 6 and 9	9 weeks	• Ergometer cycling • Aerobic interval training	• 3 sessions a week • 30–40 min sessions	• CPET • HRQoL questionnaires • Changes in VO2 at anaerobic threshold

Table 2 (*continued*)

Reference	Cancer site	No. patients	Baseline assessment	Timepoints for assessment	Duration of programme	Type of exercise	Intensity/ frequency	Measurement tests/endpoints
Singh *et al.*, 2018 [46]	Rectal cancer	10	X-RM test Physical performance tests	Pre-exercise Post-exercise (after 10 weeks)	10 weeks	• Resistance exercises using resistance training machine equipment • Aerobic interval training via walking/jogging on treadmill or cycling/rowing on ergometer	• 2 sessions a week • 1-h sessions • Additional 2 × 15-min sessions a week	• Dynamic muscle strength (X-RM test) • Physical performance (6-MWD test +400 m walk) • HRQoL (EORTC QLQ-C30)
West *et al.*, 2015 [48]	Rectal cancer	39	CPET	Measured at baseline (pre-NACRT), weeks 0 (post-NACRT), 3, 6, 9 and 14.	6 weeks	• Ergometer cycling • Aerobic interval training	• 3 sessions a week • 40-min sessions	VO2 at lactate threshold and VO2 at peak measured by CPET

6MWT, 6-min walking test; CPET, cardiopulmonary exercise testing; HRQoL, health-related quality of life; NACRT, neoadjuvant chemoradiation therapy; RT, radiation therapy; VO2, volume of oxygen uptake; X-RM, submaximal muscle repetition.

period, typically at week 9 [47,48]. The interventions are implemented during 5 weeks of NACRT and are usually aerobic interval training using a cycling ergometer or treadmill [46–48,50]. Correspondingly, such exercise training strategies are used for lung cancer prehabilitation (Table 2) [26,27].

Prehabilitation Strategies for All Cancer Sites

Four studies applied prehabilitation strategies across a multitude of cancers [56–59]. Two of four studies were unimodal, psychoeducational interventions [56,59], with the remaining two studies classified as multimodal prehabilitation [57,58]. These data are limited as most studies are prospective projects with no outcome data yet.

CAN-FIT aimed to educate patients about cancer-related fatigue and teach fatigue management strategies prior to radiation therapy [59]. Most patients recruited had breast or prostate cancer. Patients were randomised to four arms. Patients in two of four arms received the intervention in the pre-radiation stage [59]. There were three assessment timepoints. Ax1 occurred pre-radiation therapy, Ax2 at post-radiation therapy and Ax3 was conducted at the 6-week follow-up. The primary outcome was patient fatigue evaluated by the Multidimensional Fatigue Inventory [59]. The pre-radiation therapy intervention was a 1-h education session 1 week prior to treatment. CAN-FIT did not significantly influence the primary outcome, thus the authors questioned if education only is sufficient to manage treatment adverse effects [59].

The two multimodal programmes included are not specific to radiation therapy alone but are offered to patients receiving radiation therapy. Multimodal prehabilitation has a role for all cancer patients, regardless of their treatment modality, in improving patient knowledge, forming positive health habits and alleviating the adverse effects of both cancer and its treatment [24,58].

Prehab4Cancer, implemented in the Greater Manchester region, is the first widespread, multimodal prehabilitation service in the UK [58]. Prehab4Cancer is an evolution of the Enhanced Recovery After Surgery+ programme, which improved surgical care for patients of Greater Manchester [60]. Patients enrolled are offered a combination of cardiovascular and resistance exercise training, psychological assessment, interventions, smoking cessation, nutritional support and medication management [58]. There are four assessment timepoints: at initial referral, pre-treatment, post-treatment and on completion of the rehabilitation component, 12 weeks after treatment [58]. The pre-treatment intervention is 3–6 weeks. From 2019 to 2020, this service had over 600 referrals and the figure is growing [58].

Geriatric patients are susceptible to increased mortality and morbidity after medical and surgical cancer procedures [57,61]. PROADAPT is an on-going trial regarding multimodal prehabilitation for geriatric patients only [57]. Patients must be over 70 years old or 60 years with a comorbidity or disability. Therefore, a geriatric assessment is a vital element. This programme aims to transition patients from hospital to home through education, nutrition and physical activity. Patients enrolled engage in endurance and strength exercise training two to three times a week, together with a nutritional plan and patient/caregiver education sessions [57].

Giles and Cummins [62] explained that prehabilitation can appear as an extra burden to the patient during diagnosis. Additional staff and multidisciplinary co-operation are required for successful implementation [62,63]. Finance and socioeconomic disparities impede the routine use of prehabilitation services [62,63].

Conclusion

Prehabilitation programmes originally designed for cancer surgery, such as Prehab4Cancer [58], being applied in a radiation therapy setting shows the evolution of this tool in practice. An attraction of prehabilitation is that it can be tailored for any patient. Therefore, there is a prehabilitation programme suitable for all patients, regardless of their treatment modalities.

Although, several studies applied prehabilitation prior to primary radiation therapy, many studies applied prehabilitation where radiation therapy was used multimodally with surgery or chemotherapy. Future studies where prehabilitation directly influences the outcomes of radiation therapy only would be worthwhile for the development of this resource.

The head and neck is the most dominant cancer site of prehabilitation use. The rationale for prehabilitation in this site is in an effort to lessen chronic damage from radiation adverse effects. Such toxicities include mucositis, xerostomia, lymphoedema, trismus, osteoradionecrosis and dysphagia. Prophylactic swallowing exercises are a common intervention identified for this site. It is assumed that prehabilitation is advantageous over rehabilitation in improving quality of life and dysphagia severity [16].

A unique hallmark of prehabilitation is that it exists as unimodal or multimodal interventions. Some cohorts, such as patients with lung cancer, benefit from multimodal more than unimodal prehabilitation, as it incorporates several aspects of cancer care, such as exercise, nutrition, psychological health and smoking cessation. Additionally, as prehabilitation is conventionally implemented promptly after diagnosis, it can influence the treatment options for patients. For example, initial inoperable patients became suitable for lung cancer surgery after undergoing 2–4 weeks of prehabilitation [27].

The main obstacles to the routine implementation of prehabilitation in the foreseeable future is the heterogeneity, together with the relatively small patient samples within the current literature. Standardisation of measurement testing and endpoints across programmes, larger patient samples and more randomised controlled trials can assist in deepening the understanding of the value that prehabilitation holds for patients undergoing radiation therapy.

There is a lack of data for prehabilitation in radiation therapy. However, prehabilitation can be modified according to cancer site and the specific patient needs of the site. Prehabilitation that is personalised and implemented in a timely manner between diagnosis and treatment has the potential to improve outcomes and treatment experiences.

Conflicts of interest

The authors declare no conflicts of interest.

Author contributions

EH conducted the search and analysis of the literature. Both authors contributed to the preparation of the manuscript.

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