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CARDIO-ONCOLOGY (EH YANG, SECTION EDITOR)

Prehabilitative Exercise for the Enhancement of Physical, Psychosocial, and Biological Outcomes Among Patients Diagnosed with Cancer

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Abstract

Purpose of Review This review summarizes the effects of prehabilitative exercise interventions on the physical, psychosocial, and biological outcomes among patients with cancer. Current gaps and future directions in prehabilitative exercise research will be addressed.

Recent Findings Prehabilitative exercise mitigates the detrimental impact of cancer surgery on physical fitness, noted by increases in maximal oxygen consumption and 6-min walk distance. Beneficial effects on psychosocial and biological outcomes remain inconclusive. Aerobic exercise interventions were often prescribed and included low-, moderate-, or high-intensity exercise. Resistance exercise interventions were often performed in conjunction with aerobic exercise.

Summary Prehabilitative exercise elicits robust improvements in physical fitness; however, effect on psychosocial and biological outcomes remains inconclusive. Exercise prescription parameters varied greatly by frequency, intensity, time, and type across multiple cancer diagnoses. Future investigations are needed to systematically dose exercise for a wider variety of outcome measures, with an overall goal to set forth pre-operative exercise guidelines.

Keywords Prehabilitative exercise · Cancer patients · Physical fitness · Psychosocial health · Cancer-related biomarkers

Introduction

Exercise oncology research has expanded in recent years to include prehabilitative exercise focusing largely on improving physical fitness prior to surgery in patients with cancer [1–3, 4•]. Prehabilitative exercise historically has been employed in the orthopedic patient population to improve or maintain muscular strength, endurance, and range of motion prior to surgery [5]. More recently, prehabilitative exercise research for patients with cancer has utilized physical, nutritional, and psychological interventions [6•] or varying combinations of the three [7], in order to address physical function and quality of life declines often associated with cancer treatment.

Decreased physical function as a result from major surgery can vary in severity dependent upon the success of surgery, associated complications, or length of hospital stay [8]. Patients experience larger decreases in physical functioning if surgical complications arise or length of hospital stay increases [9]. Declines often include decreased VO_2peak [10], lean body mass, muscle strength [11], and ability to perform activities of daily living [12]. Prehabilitative exercise-induced increases in aerobic capacity or muscular endurance and strength before surgery can result in a shorter hospital stay or fewer postoperative complications among patients with cancer [6•, 13]. For example, the rate of pneumonia, thromboembolism, and urinary tract infections are all

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reduced by improving mobility in the acute period following surgery [14]. Since physical measures such as baseline fitness level, body mass index, lean body mass, and body fat percentage are negatively affected throughout the course of cancer treatment and influence postoperative outcomes [15], prehabilitative exercise is a non-pharmacologic strategy that may positively impact postoperative outcomes through modulation of these physical measures.

With cancer treatment that includes but is not limited to chemotherapy, radiotherapy, hormone therapy, and tumor removal surgery, patients often report lower quality of life due to decreased independence, anxiety, fatigue, or other specific impairments [16]. Side effects of chemotherapy, preoperative stress, and the burden of a cancer diagnosis can profoundly affect psychological well-being [16, 17], and exercise interventions concurrent with cancer treatment or prior to surgery may potentially offset associated weakness, fatigue, and malaise [18]. In addition to physical and psychosocial benefits, prehabilitative exercise may also affect biological outcomes related to tumor biology, modulating biomarkers associated with tumor growth, immune function, or inflammation based on pre-clinical models [19]. Therefore, the purpose of this review is to summarize the effects of prehabilitative exercise interventions on the physical, psychosocial, and biological outcomes among patients with cancer (Fig. 1). The review will discuss current gaps in the prehabilitative exercise literature and future directions for relevant studies in patients diagnosed with cancer.

Physical Outcomes (Table 1)

Declines in physical function observed in patients with cancer result in profound increases in mortality rates [44, 45•]. While physical outcomes include a variety of measures such as muscular strength, flexibility, and body composition, cardiorespiratory fitness is the most widely studied measure to predict mortality in cancer patients [46]. Cardiorespiratory fitness, often assessed by maximal oxygen update (VO_2peak) or 6-min walk test (6MWT) distance, is an important element to measure during cancer survivorship because reduced VO_2peak or 6MWT distance strongly predicts an increase in cancer mortality [47, 48]. In fact, for each 1 metabolic equivalent (MET) increase in VO_2peak, there is a 5% reduction in risk for cancer mortality ($p = 0.01$) as observed in a cohort of 447 men with all cancer types [49]. VO_2peak is 17% lower prior to adjuvant therapy and 25% lower after adjuvant therapy in patients with cancer than age-matched individuals without a cancer history [50]. Therefore, patients with cancer may be able to exploit the prehabilitative period with exercise to improve cardiorespiratory fitness as there is a waiting period of approximately 7 to 52 days (median 21 days) from time of diagnosis until date of surgery [51, 52].

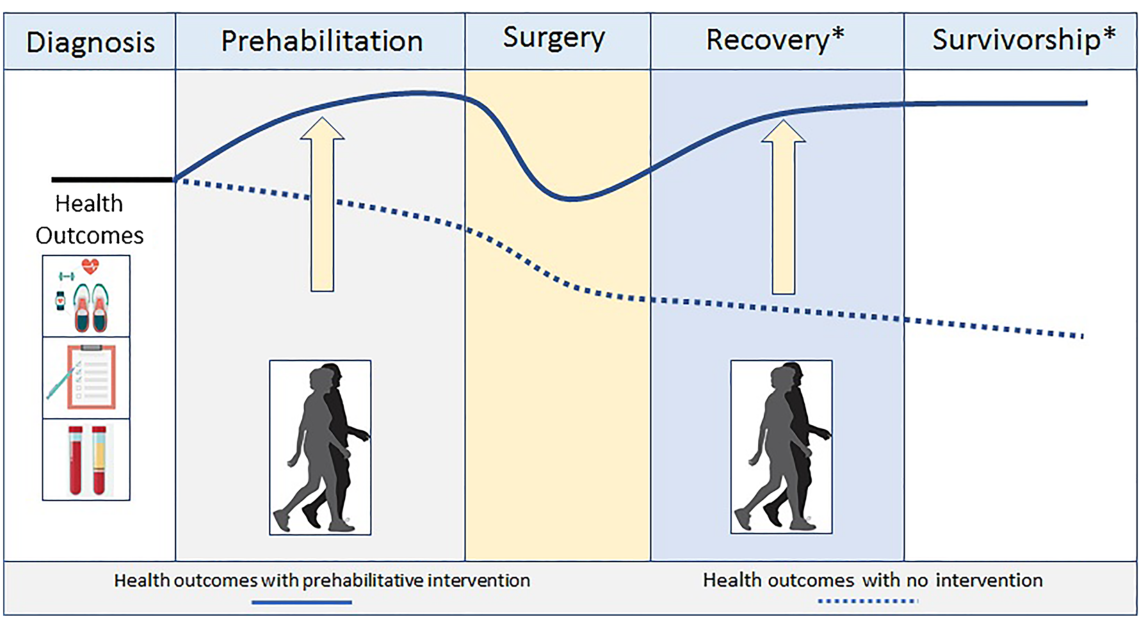

Fig. 1 Prehabilitative exercise can potentially improve physical outcomes, psychosocial outcomes, and cancer-related biomarkers, creating a better foundation for success and recovery after surgery. *Effects of prehabilitative exercise alone or in combination with rehabilitation exercise on improvements in post-surgical outcomes or long-term survivorship remain inconclusive

Table 1 Prehabilitative exercise interventions and physical function and psychosocial outcomes

Author, year, reference	Sample, Design	Outcome Variables/Measurements	Intervention	Additional intervention	Adherence	Results/Outcomes	Prehab Window
	PHYSICAL OUTCOMES						
Jones et al. 2007 [20•]	25 non-small cell lung cancer patients; prospective, single-arm design	Preoperative and postoperative markers; Exercise capacity: VO_{2peak} relative to body mass (ml/kg/min), VO_{2peak} percent predicted, 6-minute walk distance (6MWD), and pulmonary function (PFT)	Supervised aerobic exercise training Frequency: 5x week Intensity: Week 1: 60-65% Week 2-3: 60-65%, 4x wk with 5th session at ventilatory threshold Week 4-:60-65%, 3x wk, one threshold, one interval [30s at peak VO2 followed by 60s active recovery for 10-15 intervals] Time: Week 1: 20-30 min Week 2-3: 25-30 min, 4x wk with 5th session 20-25 min Week 4-: 20-30 min, 4x wk with 5th session 30s interval with 60s recovery, 10-15 intervals Type: Cycle ergometer	N/A	72%	Improvements* seen in: Mean peak oxygen consumption ($p=0.002$), % predicted VO_{2peak} ($p<.0.001$), VO_{2peak} (L/min) ($p<0.001$), & 6MWD ($p=0.003$) No improvements* in: FEV1, Forced Vital Capacity (FVC), Total lung capacity (TLC), Single breath D_{LCO}, Residual Volume ($p>0.05$)	4–6 weeks
Carli et al. 2010 [2]	133 colorectal cancer patients; prospective, two-arm randomized control trial	Preoperative and postoperative markers; Exercise capacity: 6-minute walk test (6MWT)	Unsupervised aerobic exercise training combined with either resistance or breathing exercise Frequency: Aerobic & breathing training, 7x week; Resistance training, 3x week Intensity: Aerobic training, 50% maximal heart rate at Week 1, increasing by 10% each week as tolerated; resistance training, body weight Time: Aerobic training, 20 minutes	N/A	16%	No improvements in: 6MWT for either group ($p>0.05$)	7-8 weeks

Table 1 (continued)

Author, year, reference	Sample, Design	Outcome Variables/Measurements	Intervention	Additional intervention	Adherence	Results/Outcomes	Prehab Window
			at Week 1, increasing up to 30 minutes as tolerated; resistance training, 10-15 minutes Type: Aerobic training, cycle ergometer, walking; Resistance training, body weight resistive exercise; Breathing training, deep breathing, diaphragmatic breathing, huffing, and coughing				
Dronkers et al. 2010 [1]	42 patients undergoing elective abdominal oncological surgery (type of cancer unspecified); prospective, two-arm randomized control trial	Preoperative and postoperative markers; Exercise capacity: Timed-Up-and-Go, chair rise time, maximal inspiratory pressure, hand grip strength	Supervised aerobic, resistance, and breathing training Frequency: 2x week Intensity: Aerobic training, 55–75% of maximal heart rate or between 11 and 13 on the Borg Scale; Resistance training, 60-80% of 1 repetition maximum; Breathing training, 10–60% of the maximal inspiratory pressure Time: 60 minutes Type: Aerobic training, walking or cycling; Resistance training, leg extensor exercise; Breathing training, breathing against resistance	N/A	98%	No improvements in: Timed-Up-and-Go, chair rise time, maximal inspiratory pressure, or hand grip strength ($p>0.05$) in either group	2-4 weeks
Benzo et al. 2011 [21]	19 patients with non-small cell lung cancer and moderate-severe chronic obstructive pulmonary disorder; prospective, two-arm randomized control trial	Post-operative markers; Exercise capacity: Shuttle walk test Surgical outcomes: Hospital length of stay and post-operative pulmonary complications	Supervised aerobic, resistance, and breathing training Frequency: 2-3x week Intensity: Aerobic training, intensity unspecified; Resistance training, chosen intensity of "high self-efficacy"	N/A	100%	Improvements seen in: decreased time of chest tube drainage, fewer prolonged chest tube placements for >7 days ($p=0.03$), hospital length of stay neared significance	1 week

Table 1 (continued)

Author, year, reference	Sample, Design	Outcome Variables/Measurements	Intervention	Additional intervention	Adherence	Results/Outcomes	Prehab Window
			and level of perceived exertion of at least "light"; Breathing training, level of perceived exertion of "somewhat hard" Time: 60 minutes Type: Aerobic training, treadmill, arm ergometer, or Nu-Step; Resistance training, TheraBand; Breathing training, breathing against resistance			(p=0.058) in the prehabilitation group No improvements in: Shuttle walk test (p>0.05) in the prehabilitation group or control group	
Li et al. 2013 [3]	87 patients with colorectal cancer; two-arm study with prospective recruitment of prehabilitation group and retrospective analysis of control group	Preoperative and postoperative markers; Exercise capacity: 6MWT, Community Healthy Activities Model Program for Seniors (CHAMPS) short-form questionnaire	Unsupervised (home-based) aerobic and resistance training Frequency: 3x week Intensity: Aerobic training, initially set at 50% of maximal heart rate, then progressing individually as tolerated; Resistance training, volitional fatigue Time: Aerobic training, 30 minutes; Resistance training, unspecified Type: Aerobic training, walking or cardio machine; Resistance training, calisthenics and elastic band exercises	Nutrition: protein supplement to achieve intake of 1.2 g/kg body weight of protein daily Anxiety reduction: Relaxation and breathing exercises with a psychologist and at home with a CD, unspecified dosage	45% exercised 3x/week, 70% exercised 2x/week	Improvements seen in: 6MWD (p<0.01), self-reported weekly physical activity energy expenditure (p<0.01) in the prehabilitation group	3-7 weeks
Stefanelli et al. 2013 [10]	40 patients with both non-small cell lung cancer and chronic obstructive pulmonary disorder; prospective, two-arm randomized control trial	Preoperative and postoperative markers; Exercise capacity and lung function: VO_2 peak, FEV1, FVC, FEV1/FVC ratio, diffusion of lung CO, and dyspnea	Supervised aerobic and breathing training Frequency: 5x week Intensity: Aerobic training, individualized workload according to baseline CPET starting at 70% of	N/A	Not reported	Improvements seen in: VO_2 peak prior to surgery (p<0.05) in the prehabilitation group No improvements in: Pulmonary function or dyspnea (p>0.05) in	3 weeks

Table 1 (continued)

Author, year, reference	Sample, Design	Outcome Variables/Measurements	Intervention	Additional intervention	Adherence	Results/Outcomes	Prehab Window
		measured by the modified BORG scale	maximum CPET wattage and increased by 10 watts as tolerated Time: 3 hours Type: Aerobic training, walking or using cardio machine; Breathing training, respiratory exercises on the bench, mattress pad and wall bars			the prehabilitation group or control group	
Gillis et al. 2014 [4•]	77 patients with colorectal cancer; prospective, two-arm randomized control trial	Preoperative and postoperative markers; Exercise capacity: 6MWT	Unsupervised (home-based) aerobic and resistance training Frequency: at least 3x week Intensity: Aerobic training, started at 40% of heart rate reserve, progressed when tolerated; Resistance training, 8-12 repetitions progressed in resistance when 15 repetitions of an exercise could be reached Time: Aerobic training, 20 min; Resistance training, 20 min of resistance training Type: Aerobic training, walking, jogging, swimming, or cycling; Resistance training, calisthenics and elastic band exercises	Nutrition: protein supplement to achieve intake of 1.2 g/kg body weight of protein daily Anxiety reduction: Relaxation and breathing exercises performed at home with a CD 2-3 times/wk.	78%	Improvements seen in: 6MWT at 8 weeks post-surgery: prehabilitation group, on average, were above baseline while rehabilitation group remained below baseline (p=0.01); a higher proportion of the prehabilitation group were either above or recovered to baseline walking capacity compared to rehabilitation group (p=0.049)	4 weeks
West et al. 2014	39 patients with rectal cancer; prospective, two-arm	Preoperative and postoperative markers;	Supervised aerobic interval training; all	N/A	96%	Improvements seen in: VO_2 at lactate threshold (p=0.0001) and VO_2	6 weeks

Table 1 (continued)

Author, year, reference	Sample, Design	Outcome Variables/Measurements	Intervention	Additional intervention	Adherence	Results/Outcomes	Prehab Window
	randomized control trial	Exercise capacity and lung function: VO_2, FEV1, FVC, FEV1/FVC, VE/VO_2, VE/VCO_2, and VO_2/heart rate	subjects exercised in pairs Frequency: 3x week Intensity: moderate-intensity intervals (80% of work rate at VO_2 at lactate threshold), 4x3-minutes, followed by high-intensity (50% of work rate difference between VO_2peak and VO_2 at lactate threshold), 4x 2-minute intervals for the first two sessions. For the rest of the sessions, the duration was increased to 40 min, 6×3 min intervals at moderate intensity and 6×2 min intervals at high intensity Time: 20-40 minutes Type: cycle ergometer			at peak (p=0.0005) in the prehabilitation group No improvements in: FEV1, FVC, FEV1/FVC, VE/VO_2, VE/VCO_2, and VO_2/heart rate in either group	
Chen et al. 2016	116 patients with colorectal cancer; prospective, two-arm randomized control trial	Preoperative and postoperative markers; Exercise capacity: 6MWT, CHAMPS short-form questionnaire	Unsupervised (home-based) aerobic and resistance training Frequency: 3x week Intensity: Aerobic training, 50% of age-predicted maximal heart rate; Resistance training Time: Aerobic training, 20 minutes; Resistance training, 20 minutes Type: Aerobic training, patient-chosen modality; Resistance training, TheraBand	Nutrition: protein supplement to achieve intake of 1.2 g/kg body weight of protein daily Anxiety reduction: Relaxation and breathing exercises with a psychologist and at home with a CD, unspecified dosage	Not reported	Improvements seen in: 6MWT (p=0.002) and self-reported weekly physical activity energy expenditure (p=0.001) in the prehab group compared to a rehab group	4 weeks
Jensen et al. 2016 [22]	107 patients with bladder cancer; prospective, two-arm	Preoperative and postoperative markers;	Unsupervised (home-based) aerobic and resistance training	N/A	66% participants were adhered to	Improvements seen in: leg extension power at the time of	2 weeks

Table 1 (continued)

Author, year, reference	Sample, Design	Outcome Variables/Measurements	Intervention	Additional intervention	Adherence	Results/Outcomes	Prehab Window
	randomized control trial	Exercise capacity: leg extension power on the dominant side	Frequency: 2x day, 7x week Intensity: Aerobic training, not specified; Resistance training, 10-15 repetitions Time: Aerobic training, 30 minutes; Resistance training, ~30 minutes Type: Aerobic training, step trainer; Resistance training, muscle strength and endurance exercise		more than 75% to the program	surgery ($p<0.002$) in the prehabilitation group	
Singh et al. 2016	16 patients with prostate cancer; prospective, single-arm design	Preoperative and postoperative markers; Exercise capacity: 1-repetition maximum (RM) for seated row, chest press, leg press, and leg extension. Usual and fast 6-meter walk, 6-meter backward walk, repeated chair rise, stair climb, and 400-meter walk. Total body lean mass, fat mass, and percentage fat Urinary incontinence: 24-hour pad test (postoperative only), International Consultation on Incontinence Modular Questionnaire (ICIQ)	Supervised aerobic and resistance training Frequency: 2x week Intensity: Aerobic training, 60% to 80% of estimated maximum heart rate; Resistance training, 2 to 4 sets per exercise at 6 to 12 repetition maximum intensity Time: 90 minutes per session, including 20 minutes of aerobic training Type: Aerobic training, walking, jogging, cycling, or rowing; Resistance training, chest press, seated row, latissimus pull-down, leg press, leg extension, leg curl, plank, reverse bridge on swiss ball, side plank exercises	N/A	50% of patients completed >80% of the 12 training sessions	Improvements seen in: muscle strength in all resistance exercises, fast 6-meter walk, repeated chair rise test, and 400-meter walk from baseline to surgery ($p<0.05$) No improvements in: muscle strength, total body lean mass, fat mass, percentage fat, usual or backward 6-meter walk, or urinary incontinence from baseline to post-surgery ($p>0.05$)	6 weeks
Karenovics et al. 2017 [23]	164 patients with non-small	Preoperative and postoperative markers;	Supervised aerobic training Frequency: 3x week	N/A	Mean 87%	Improvements seen in: VO_2peak ($p<0.01$) from	3-4 weeks

Table 1 (continued)

Author, year, reference	Sample, Design	Outcome Variables/Measurements	Intervention	Additional intervention	Adherence	Results/Outcomes	Prehab Window
	cell lung cancer; prospective, two-arm randomized control trial	Exercise capacity and lung function: VO_2, peak work rate (WR_{Peak}), FEV1, FVC, KCO	Intensity: 5-minute warm up at 50% WR_{Peak}, followed by two 10-minute series of 15-second sprint intervals, with 15 seconds of rest in between each interval at 100% WR_{Peak}, then 5 minutes of cool down at 30% WR_{Peak} Time: 30 minutes Type: cycle ergometer			baseline to pre-surgery in the prehabilitation group No improvements in: VO_2peak (-12.2%) in both groups from pre-surgery to 1-year follow-up. Baseline FEV1, FVC, KCO were maintained throughout ($p>0.05$) in both groups	
Minnella et al. 2017 [24•]	185 patients with colorectal cancer; pooled results from two prospective, two-arm randomized control trials and one prospective, single-arm trial	Preoperative and postoperative markers; Exercise capacity: 6MWT, CHAMPS short-form questionnaire	Unsupervised (home-based) aerobic, resistance, and flexibility training Frequency: Aerobic training, 3x week; Resistance and flexibility training, 2x week Intensity: Aerobic training, moderate continuous training defined by Borg scale; Resistance training, not specified Time: Aerobic training, 20-30 minutes; Resistance training, not specified Type: Aerobic training, not specified; Resistance training, targeted major muscle groups of lower body, upper body and core	Nutrition: Protein supplement to achieve 1.5g/kg/body weight of protein per day Anxiety reduction: Daily practice of relaxation and imagery techniques taught in a counselling session	70-98% from the 3 pooled studies	Improvements seen in: 6MWD ($p<0.001$) during preoperative period and less functional decline ($p=0.015$) 4-8 weeks following surgery in the prehabilitation group Results of CHAMPS short-form questionnaire not reported.	4 weeks prior to surgery until 8 weeks after surgery
Ngo-Huang et al. 2017 [25]	20 patients with resectable pancreatic cancer; prospective, single-arm design	Preoperative and postoperative markers; Exercise capacity: International Physical Activity Questionnaire	Unsupervised (home-based) aerobic and resistance training Frequency: Aerobic training, at least 3x week; Resistance	Nutrition: instructed to consume at least 20 g of protein within 1 hour after	80% achieved 120 minutes of total exercise per week	Improvements seen in: self-reported physical function 1 month after surgery associated with aerobic exercise ($p=0.02$), faster	Median 17 weeks (Range of 5-35 weeks)

Table 1 (continued)

Author, year, reference	Sample, Design	Outcome Variables/Measurements	Intervention	Additional intervention	Adherence	Results/Outcomes	Prehab Window
		(IPAQ) Short Form, 10-meter walk test, Dynamic Gait Index, 5-times sit-to-stand test	training, at least 2x week Intensity: Aerobic training, 12-13 on the Borg Scale; Resistance training, 3 sets of 8-12 repetitions; resistance increased when 3 sets of 12 could be completed without difficulty Time: Aerobic training, 20 minutes; Resistance training, 30 minutes Type: Aerobic training, walking; Resistance training, exercises involving the proximal upper body, shoulders, abdominals, back, and legs	resistance training		10-meter walk test associated with greater duration of exercise (p=0.03) No improvements in: dynamic gait index or 5-times sit-to-stand (p>0.05)	
Banerjee et al. 2018 [26]	60 patients with bladder cancer; prospective, two-arm randomized control trial	Preoperative and postoperative markers; Exercise capacity and lung function: VO_2peak, minute ventilation, anaerobic threshold, peak oxygen pulse, and power output	Supervised aerobic training Frequency: 2x week Intensity: warm-up at 50-watt resistance, followed by 6×5-minute intervals at a target perceived exertion of 13–15 on the Borg Scale, then a cool-down at 50-watt resistance Time: 30 minutes Type: cycle ergometer	N/A	90% (intervention), 83% (control)	Improvements seen in: v entilatory efficiency (p=0.002), peak values of oxygen pulse (p=0.001), and power output (p<0.001) in the prehabilitation group No improvements in: VO_2 peak (p=0.057) or anaerobic threshold (p=0.637) in either group	3-6 weeks
Barassi et al. 2018 [27]	32 patients with non-small cell lung cancer; prospective, two-arm randomized control trial	Preoperative and postoperative markers; Lung function: FVC, FEV1, FEV1/FVC, peak expiratory and inspiratory flow	Supervised yoga breathing vs standard breathing training Frequency: 30x day, 7x week Intensity: Yoga breathing, 3 sets of 10 yoga breaths; Standard	N/A	Not reported	Improvements seen in: FVC, FEV1, peak expiratory and inspiratory flow (p<0.0001) in the yoga breathing group	1 Week

Table 1 (continued)

Author, year, reference	Sample, Design	Outcome Variables/Measurements	Intervention	Additional intervention	Adherence	Results/Outcomes	Prehab Window
			breathing, 3 sets of 10 deep breaths Time: not specified Type: yoga breathing, inspiration, air retention and slow expiration; Standard breathing, deep breathing			Change in FEV1/FVC ratio not reported.	
Bousquet-Dion et al. 2018 [28]	80 patients with colorectal cancer; prospective, two-arm randomized control trial	Preoperative and postoperative markers; Exercise capacity: 6MWD, CHAMPS	Unsupervised (home-based) aerobic and resistance training, supervised 1x a week Frequency: 3-4x week Intensity: Aerobic training, 60–70% of maximal heart rate; Resistance training, 2 sets of 8-15 repetitions until volitional fatigue Time: Aerobic training, 30 minutes; Resistance training, ~30 minutes Type: Aerobic training, walking, cycling or jogging; Resistance training, eight exercises targeting major muscle groups using TheraBand	Nutrition: protein supplementation to achieve at least 1.2g/kg/body weight of protein intake daily Anxiety reduction: relaxation and breathing exercises with a psychologist and at home with a CD, unspecified dosage	98%	Improvements seen in: moderate and vigorous self-reported weekly physical activity energy expenditure (>3 METS) in the prehabilitation group pre-operatively (p=0.021) No improvements in: preoperative difference in 6MWD (p>0.05) between the prehab and rehab, and rehab only groups	4 weeks
Christensen et al. 2018	62 patients with gastro-esophageal junction adenocarcinoma; prospective, two-arm non-randomized control trial	Preoperative and postoperative markers; Exercise capacity: $Watt_{max}$, VO_2peak, one-repetition maximum, fat mass, bone mass, fat-free mass, and bone mineral density	Supervised aerobic and resistance training Frequency: 2x week Intensity: Aerobic training, high-intensity 4×4 minute intervals; Resistance training, 3 sets of 8–12 repetitions Time: 75 minutes	N/A	68.7%	Improvements seen in: $Watt_{max}$ (mean difference +12W), VO_2peak (mean difference +1.39 ml/min/kg), and muscle strength (mean difference +18%) in the prehabilitation group No improvements in: body	9-19 weeks

Table 1 (continued)

Author, year, reference	Sample, Design	Outcome Variables/Measurements	Intervention	Additional intervention	Adherence	Results/Outcomes	Prehab Window
			Type: Aerobic training, stationary bicycle; Resistance training, chest press, leg press, row, and knee extension			composition measures in either group	
Minnella et al. 2018 [29]	68 patients with esophagogastric cancer; prospective, two-arm randomized control trial	Preoperative and postoperative markers; Exercise capacity: 6MWT Postoperative outcomes: rate of complications, length of hospital stay, emergency department visits, or readmission rates	Unsupervised (home-based) aerobic and resistance training Frequency: Aerobic training, 3x week; Resistance training, 1x week Intensity: Aerobic training, moderate-intensity steady state reaching 12-13 on the Borg scale; Resistance training, 3 sets of 8-12 repetitions Time: Aerobic training, 30 minutes; Resistance training, 30 minutes Type: Aerobic training, walking, jogging, or cycling; Resistance training, TheraBand exercises	Nutrition: protein supplementation to ensure protein intake of 1.2 to 1.5 g/kg/body weight per day	63%	Improvements seen in: 6MWD immediately before and after surgery (p<0.001) in the prehabilitation group No improvements in: rate of complications, length of hospital stay, emergency department visits, or readmission rates	~5 weeks (range of 2-11 weeks)
Santa Mina et al. 2018 [30]	86 patients with prostate cancer; prospective, two-arm randomized control trial	Preoperative and postoperative markers; Exercise capacity: 6MWD, body fat percentage, grip strength, waist circumference	Unsupervised (home-based) aerobic, resistance, and pelvic floor training Frequency: 3-4x week Intensity: Aerobic and Resistance training, moderate-intensity; Pelvic floor training, intensity not specified Time: 60 minutes Type: Aerobic training, walking; Resistance training, TheraBand	N/A	Aerobic exercise: 69.2% Pelvic floor exercise: 36.8% (intervention) and 38.9% (control)	Improvements seen in: 6MWD at 4 weeks post-op (p=0.006), body fat percentage prior to surgery and at 4- and 12-weeks post-op (p=0.001-0.008), grip strength (p=0.022) and waist circumference (p=0.022) at 26 weeks post-op in the prehabilitation group	Mean 7 weeks

Table 1 (continued)

Author, year, reference	Sample, Design	Outcome Variables/Measurements	Intervention	Additional intervention	Adherence	Results/Outcomes	Prehab Window
			and stability ball; Pelvic floor exercises				
Valkenet et al. 2018 [31]	270 patients with esophageal cancer; prospective, two-arm randomized control trial	Preoperative and postoperative markers; Exercise capacity: mean maximal inspiratory muscle strength and endurance, FEV1, FVC	Unsupervised (home-based) breathing training Frequency: 2x day, 7x week Intensity: 30 breaths, starting at 60% of baseline maximum inspiratory pressure, maintaining a rate of perceived exertion >7/10 Time: not specified Type: inspiratory muscle exercises against a tapered flow resistive inspiratory loading device	N/A	67.5%	Improvements seen in: mean maximal inspiratory muscle strength and endurance in both groups but significantly larger in the prehabilitation group ($p<0.001$) No improvements in: FEV1 or FVC in either group ($p>0.05$)	At least 2 weeks
Alejo et al. 2019 [32]	12 patients with rectal adenocarcinoma; prospective, single-arm randomized control trial	Preoperative and postoperative markers; Exercise capacity: VO_2peak, 5-repetition sit to stand test	Six supervised, educational exercise sessions combining aerobic, resistance, and flexibility training Frequency: 1x week Intensity: Session 1: Informational; Session 2: aerobic exercise at 70-95% of HR max; Session 3: resistance exercise, 2 sets of 10-15 repetitions, rate of perceived exertion (RPE) 6-7/10; Session 4: flexibility exercises, 5 inhalations per exercise; Session 5: strength and joint mobility exercises at RPE 7; Session 6:	N/A	89%	No improvements in: VO_2peak or 5-repetition sit to stand time	6 weeks

Table 1 (continued)

Author, year, reference	Sample, Design	Outcome Variables/Measurements	Intervention	Additional intervention	Adherence	Results/Outcomes	Prehab Window
			combined aerobic (30 min intervals at >95% HR max), strength (see session 3, RPE 7-10), and flexibility (see session 4, 2 sets each) Time: 35 minutes increasing to 60 minutes Type: See Intensity for session details				
Boereboom et al. 2019 [33]	18 patients with colorectal cancer; prospective, single-arm trial	Preoperative and postoperative markers; Exercise capacity: VO_2peak, anaerobic threshold	Supervised high-intensity aerobic training Frequency: 3-4x week Intensity: 5 x 1-minute intervals at 100%-120% maximum CPET wattage Time: 18 minutes Type: cycle ergometer	N/A	100%	No improvements in: VO_2peak or anaerobic threshold ($p>0.05$)	2-3 weeks
Gillis et al. 2019 [34]	139 patients with colorectal cancer; prospective, two-arm randomized control trial	Preoperative and postoperative markers; Exercise capacity: lean body mass and body fat mass, 6MWT	Unsupervised (home-based) aerobic and resistance training Frequency: at least 3x week Intensity: Aerobic training, started at 40% of heart rate reserve, progressed when tolerated; Resistance training, 8-12 repetitions maximum progressed when 15 repetitions of an exercise could be reached Time: Aerobic training, 20 min; Resistance training, 20 min	Nutrition: protein supplement to achieve intake of 1.2 g/kg body weight of protein daily Anxiety reduction: Relaxation and breathing exercises performed at home with a CD 2-3 times/wk.	88.3% (preop – prehab group), 68.3% (postop – prehab group), 54.3% (postop-rehab group)	Improvements seen in: lean body mass and fat mass ($p<0.001$) and 6MWT ($p<0.002$) at 4 and 8 weeks after surgery in the prehabilitation group	4 weeks prior to surgery until 8 weeks after surgery

Table 1 (continued)

Author, year, reference	Sample, Design	Outcome Variables/Measurements	Intervention	Additional intervention	Adherence	Results/Outcomes	Prehab Window
			Type: Aerobic training, walking, jogging, swimming, or cycling at patient discretion; Resistance training, calisthenics and elastic band				
Gravier et al. 2019 [35]	50 patients with non-small cell lung cancer; retrospective, single-arm trial	Preoperative and postoperative markers; Exercise capacity: VE/VCO_2 slope, VO_2peak, maximal CPET power	Supervised combined aerobic, resistance, and inspiratory muscle training Frequency: 3-5x week Intensity: Aerobic training, starting at ventilatory threshold, increasing by 5-10 watts as tolerated; Resistance training, 60-70% of 1-repetition maximum, 3 sets of 12 repetitions; Inspiratory training, 30% of maximum inspiratory pressure Time: 90 minutes Type: Aerobic training, cycle ergometer or treadmill; Resistance training, quadriceps press, leg extension, upper limb pull-downs; Inspiratory muscle strengthening	N/A	Not reported	Improvements seen in: VO_2peak ($p<0.01$), and maximum power reached ($p<0.01$) No improvements in: VE/VCO_2 slope.	4-8 weeks
Minnella et al. 2019 [13]	70 patients with bladder cancer, prospective, two-arm randomized control trial	Preoperative and postoperative markers; Exercise capacity: 6MWT, CHAMPS short-form questionnaire Surgical outcomes: postoperative complications, readmission rates, length of hospital stay,	Unsupervised (home-based) aerobic and resistance training Frequency: 3x week Intensity: Aerobic training, moderate-intensity steady state reaching 12-13 on the Borg scale; Resistance training, 3 sets of 8-12 repetitions	Nutrition: Food-based intervention aimed at anindividualized caloric and macronutrient intake program, calculated with the	83.3%	Improvements seen in: 6MWD 4 weeks postoperative ($p=0.014$) in the prehabilitation group No improvements in: physical activity reported on the CHAMPS questionnaire, postoperative complications,	4 weeks

Table 1 (continued)

Author, year, reference	Sample, Design	Outcome Variables/Measurements	Intervention	Additional intervention	Adherence	Results/Outcomes	Prehab Window
		emergency department visits after discharge	Time: Aerobic training, 30 minutes; Resistance training, 30 minutes Type: Aerobic training, walking, jogging, or cycling; Resistance training, TheraBand exercises for 8 muscle groups	Harris-Benedict equation and a stress factor of 1.2. Protein supplement to achieve 1.5g/kg/body weight of protein per day Anxiety reduction: Daily practice of relaxation and imagery techniques taught in a counselling session		readmission rates, length of hospital stay, emergency department visits after discharge in either group	
Moug et al. 2019 [36]	48 patients with rectal cancer; prospective, two-arm randomized control trial	Preoperative and postoperative markers; Exercise capacity: 6MWD, 30 second sit-to-stand test	Unsupervised (home-based) aerobic training Frequency: 3-5x week Intensity: Weeks 1–2: extra 1500 steps at least 3 days a week. Weeks 3–4: extra 1500 steps at least 5 days a week. Weeks 5–6: extra 3000 steps at least 3 days a week. Weeks 7–8: extra 3000 steps at least 5 days a week. Weeks 9–17: maintenance of weeks 7–8 Time: about 15 minutes (weeks 1-4) to 30 minutes (weeks 5+) per day Type: walking	N/A	75%	No improvements in: 6MWD or 30 second sit-to-stand test of either group (p>0.05)	Minimum 13 weeks
Nakajima et al. 2019 [37]	76 patients with hepato-pancreato-biliary cancer; prospective recruitment of prehabilitation	Preoperative and postoperative markers; Exercise capacity: 6MWD, body composition measures including fat	Unsupervised (home-based) aerobic and resistance training Frequency: 3x week	Nutrition: Consumption of a leucine-rich essential amino acid supplement within 30	Not reported	Improvements seen in: 6MWD (p<0.001), fat mass (p<0.001 for males, p=0.009 for females), and muscle/fat ratio	4-5 weeks

Table 1 (continued)

Author, year, reference	Sample, Design	Outcome Variables/Measurements	Intervention	Additional intervention	Adherence	Results/Outcomes	Prehab Window
	group with retrospectively-matched controls, two-arm trial	mass, lean mass, and muscle/fat ratio	Intensity: Aerobic training, 3-4 on the modified Borg scale; Resistance training, 2 sets of 10 repetitions Time: Aerobic training, 30 minutes; Resistance training, 30 minutes Type: Aerobic training, walking; Resistance training, squats, calf raises, sit ups, bridges, and upper limb movements	minutes following exercise		(p<0.001 for males, p=0.028 for females) between the 1st and 2nd hospital stay in the prehabilitation group No improvements seen in: Lean mass in either males or females (p>0.05)	
	PSYCHOSOCIAL OUTCOMES						
Sueppel et al. 2001 [38]	16 patients with prostate cancer; prospective, two-arm randomized control trial	Preoperative and postoperative markers; Psychosocial health: American Urological Association (AUA) Symptom Index for benign prostate hyperplasia (BPH)	Unsupervised (home-based) pelvic floor training Frequency: 3x day, 7x week Intensity: using biofeedback from a rectal pressure probe, otherwise unspecified Time: 30 minutes per day Type: pelvic muscle contraction exercises	N/A	69%	Improvements seen in: quality of life (QOL) from the AUA Symptom Index for BPH at 6 weeks post-surgery (but no statistical analyses done) in the prehabilitation group	Several weeks prior to surgery
Burgio et al. 2006 [39]	125 patients with prostate cancer; prospective, two-arm randomized control trial	Preoperative and postoperative markers; Psychosocial health: Hopkins Symptom Checklist for incontinence, Short Form Health Survey-36 (SF-36)	Unsupervised (home-based) pelvic floor training Frequency: 3x day, 7x week Intensity: using biofeedback from a rectal pressure probe, otherwise unspecified Time: 30 minutes per day Type: pelvic muscle contraction exercises	N/A	90%	No improvements in: incontinence impact (p = 0.36), psychological distress (p = 0.69) or QOL (p = 0.31 to 0.89) for either group	1 week
Peddle et al. 2009 [40]	9 patients with lung cancer; prospective, single-arm	Preoperative and postoperative markers;	Supervised aerobic exercise training Frequency: 5x week	N/A	88%	No improvements in: QOL or fatigue from baseline	8-9 weeks

Table 1 (continued)

Author, year, reference	Sample, Design	Outcome Variables/Measurements	Intervention	Additional intervention	Adherence	Results/Outcomes	Prehab Window
	randomized control trial	Psychosocial health: Functional Assessment of Cancer Therapy – Lung (FACT-L)	Intensity: Week 1: 60-65% VO_2peak Week 2-3: 60-65% VO_2peak, 4x wk with 5th session at ventilatory threshold Week 4-:60-65% VO_2peak, 3x wk, one threshold, one interval [30s at VO_2peak followed by 60s active recovery for 10-15 intervals] Time: Week 1: 20 minutes Week 2-3: 25-30 min, 4x wk with 5th session 20-25 min Week 4-: 20-30 min, 4x wk with 5th session 30s interval with 60s recovery, 10-15 intervals Type: Cycle ergometer			to pre-surgery on the Functional Assessment of Cancer Therapy – Lung (FACT-L)	
Carli et al. 2010 [2]	133 colorectal cancer patients; prospective, two-arm randomized control trial	Preoperative and postoperative markers; Psychosocial health: Hospital Anxiety and Depression Scale (HADS)	As described in *Physical Outcomes*	N/A	16%	Improvements seen in: anxiety in the post-surgery timepoint in both groups ($p<0.001$), depression in the cycling group before surgery ($p=0.04$) No improvements in: anxiety before surgery in both groups ($p>0.05$)	7-8 weeks
Centemero et al. 2010 [41•]	118 patients with prostate cancer; prospective, two-arm randomized control trial	Preoperative and postoperative markers; Psychosocial health: International Continence Society (ICS) Male Short Form	Unsupervised (home-based) pelvic floor training, supervised 2 days per week	N/A	100%	Improvements seen in: ICS male SF mean score both 1 mo and 3 mo after surgery ($p = 0.002$) in the prehabilitation group	~4 weeks

Table 1 (continued)

Author, year, reference	Sample, Design	Outcome Variables/Measurements	Intervention	Additional intervention	Adherence	Results/Outcomes	Prehab Window
			Frequency: 2x week supervised, 5x week unsupervised Intensity: unspecified intensity of contraction Time: 30 minutes per day Type: pelvic muscle contraction exercises focusing on the superficial perineal				
Dronkers et al. 2010 [1]	42 patients undergoing elective abdominal oncological surgery (type of cancer unspecified); prospective, t wo-arm randomized control trial	Preoperative and postoperative markers; Psychosocial health: European Orangisation for Research and Treatment of Cancer (EORTC) Quality of Life Questionnaire (EORTC QLQ-C30 version 3), Abbreviated Fatigue Questionnaire	As described in *Physical Outcomes*	N/A	98%	No improvements in: QOL or fatigue ($p>0.05$) in both groups	2-4 weeks
Li et al. 2013 [3]	87 patients with colorectal cancer; two-arm study with prospective recruitment of prehabilitation group and retrospective analysis of control group	Preoperative and postoperative markers; Psychosocial health: SF-36, HADS	As described in *Physical Outcomes*	As described in *Physical Outcomes*	45% exercised 3x/wk, 70% exercised 2x/wk	No improvements in: SF-36 or HADS in both groups	4-5 weeks
Gillis et al. 2014 [4•]	77 patients with colorectal cancer; prospective, two-arm randomized control trial	Preoperative and postoperative markers; Psychosocial health: SF-36, HADS	As described in *Physical Outcomes*	As described in *Physical Outcomes*	78%	No improvements in: SF-36 or HADS in both groups	4 weeks
Jensen et al. 2014 [42•]	129 patients with bladder cancer; prospective, two-arm randomized control trial	Preoperative and postoperative markers; Psychosocial health: EORTC Core Quality of Life questionnaire (QLQ -C30)	Unsupervised (home-based) aerobic and resistance training Frequency: 2x day, 7x week Intensity: Aerobic training, not specified;	N/A	77%	Improvements seen in: single-item scales of constipation ($p=0.02$) and abdominal flatulence ($p=0.05$), and dyspnea ($p=0.05$) in the prehabilitation group, and significantly better	2 weeks

Table 1 (continued)

Author, year, reference	Sample, Design	Outcome Variables/Measurements	Intervention	Additional intervention	Adherence	Results/Outcomes	Prehab Window
			Resistance training, 10-15 repetitions Time: Aerobic training, 30 minutes; Resistance training, ~30 minutes Type: Aerobic training, step trainer; Resistance training, six muscle strength and endurance exercise			sleep (p=0.04) in the control group	
Sebio Garcia et al. 2017 [43]	40 patients with lung cancer; prospective, two-arm randomized control trial	Preoperative and postoperative markers; Psychosocial health: SF-36	Supervised aerobic and resistance training Frequency: 3-5x week Intensity: Aerobic training, four cycles of one minute at high intensity (80% of W_{peak}) plus four minutes of active rest (50% of W_{peak}); Resistance training, 15 repetitions of TheraBand exercises Time: Aerobic training, 30 minutes; Resistance training, 30 minutes Type: Aerobic training, cycle ergometer; Resistance training, TheraBand	N/A	55%	Improvements seen in: physical summary component (p=0.008) in the prehabilitation group	~7-8 weeks
Christensen et al. 2018	62 patients with gastro-oesophageal junction adenocarcinoma; prospective, two-arm non-randomized control trial	Preoperative and postoperative markers; Psychosocial health: Functional Assessment of Cancer Therapy – Esophageal (FACT-E) questionnaire	As described in *Physical Outcomes*	N/A	68.7%	Improvements seen in: physical wellbeing at the time of surgery (p<0.05)	9-19 weeks
Santa Mina et al. 2018 [30]	86 patients with prostate cancer; prospective, two-arm randomized control trial	Preoperative and postoperative markers; Psychosocial health: Functional Assessment of Cancer Therapy – Prostate (FACT-P) questionnaire,	As described in *Physical Outcomes*	N/A	Aerobic exercise: 69.2% Pelvic floor exercise: 36.8% (intervention) and 38.9% (control)	Improvements seen in: in anxiety before surgery (p=0.035) and 26 weeks after surgery (p=0.025) in the aerobic and resistance exercise group	7 weeks

Table 1 (continued)

Author, year, reference	Sample, Design	Outcome Variables/Measurements	Intervention	Additional intervention	Adherence	Results/Outcomes	Prehab Window
		Functional Assessment of Cancer Therapy – Fatigue (FACT-F) questionnaire, HADS				No improvements in: FACT-P or FACT-F in either group	
Valkenet et al. 2018 [31]	270 patients with esophageal cancer; prospective, two-arm randomized control trial	Preoperative and postoperative markers; Psychosocial health: Multidimensional Fatigue Inventory [MFI-20], EuroQol-5D [EQ-5D] and Short Form 12 [SF-12]	As described in *Physical Outcomes*	N/A	67.5%	No improvements in: fatigue, quality of life, and physical activity level measures at any time points in either group (p>0.05)	Minimum 2 weeks
Alejo et al. 2019 [32]	12 patients (3 male) with rectal adenocarcinoma; prospective, single-arm randomized control trial	Preoperative and postoperative markers; Psychosocial health: Health Related Quality of Life (HRQoL) questionnaire	As described in *Physical Outcomes*	N/A	89%	Improvements seen in: depression (p=0.017) and QoL domain "emotional function" (p=0.027) in the prehabilitation group	6 weeks
Moug et al. 2019 [36]	48 patients with rectal cancer; prospective, two-arm randomized control trial	Preoperative and postoperative markers; Psychosocial health: Becks Depression Inventory (BDI-II), Functional Assessment of Cancer Therapy – Colorectal (FACT-C), Positive and Negative Affect Schedule (PANAS), EORTC QLQ CR29 and C30	As described in *Physical Outcomes*	N/A	75%	No improvements in: psychological questionnaires at any time point (p>0.05) in either group	Minimum 13 weeks

VO_{2peak} peak oxygen consumption, *6MWD* 6-min walk distance, *PFT* pulmonary function, *Wk* week, *FEV1* forced expiratory volume in the first second, *FVC* forced vital capacity, *TLC* total lung capacity, D_{LCO} diffusing capacity of the lungs for carbon monoxide, *CHAMPS* Community Healthy Activities Model Program for Seniors, *g* gram, *kg* kilogram, *CPET* cardiopulmonary exercise test, VE/VO_2 ventilatory equivalents for oxygen, VCO_1 volume of carbon dioxide, *min.* minutes, *prehab* prehabilitation, *rehab* rehabilitation, *RM* repetition maximum, *ICIQ* International Consultation on Incontinence Modular Questionnaire, WR_{Peak} peak work rate, *KCO* carbon monoxide transfer coefficient, *IPAQ* international physical activity questionnaire, *MET* metabolic equivalent of task, *AUA* American urological association, *BPH* benign prostate hyperplasia, *QOL* quality of life, *SF-36* short-form health survey-36, *FACT-L* functional assessment of cancer therapy-lung, *HADS* hospital anxiety and depression scale, *ICS* international continence society, *EORTC* European organization for research and treatment of cancer, *QLQ* quality of life questionnaire, W_{peak} peak workload, *FACT-E* functional assessment of cancer therapy-esophageal, *FACT-P* functional assessment of cancer therapy-prostate, *FACT-F* functional assessment of cancer therapy-fatigue, *MFI-20* multidimensional fatigue inventory, *EQ-5D* EuroQol, *SF-12* Short-form-12, *HRQoL* health-related quality of life, *BDI-II* Becks depression inventory, *FACT-C* functional assessment of cancer therapy-colorectal, *PANAS* positive and negative affect schedule

*Improvement defined as significant change as reported by original author

Lung Cancer

Surgical resection is the most effective curative option in the treatment of lung cancer; however, patients with lung cancer often experience reduced cardiorespiratory fitness before lung resection, which is detrimental to overall survival rate [44]. The importance of cardiorespiratory fitness in this patient population is notable given that patients with lung cancer with high cardiorespiratory fitness levels (> 10 MET) at the time of diagnosis exhibit a longer survival time compared with those with low cardiorespiratory fitness (< 5 MET; 11.5 years vs 4.6 years, respectively) [44]. Table 2 lists examples of exercises by intensity or metabolic equivalent (MET) level.

It is evident that prehabilitative exercise incorporating aerobic training of moderate or high intensity improves cardiorespiratory fitness in lung cancer patients. Jones et al. (2007) reported that a preoperative exercise intervention on a cycle ergometer improved postoperative VO_2peak (+16%) and 6MWT distance (+15%) in 25 patients with lung cancer [20•, 43]. This finding is further supported by a recent study conducted by Gravier et al. (2019) in patients with lung cancer ($n = 50$) awaiting resection surgery, showing that VO_2peak significantly increased (+12%) in patients who performed aerobic + resistance training and inspiratory muscle training [35]. The authors found that patients who performed 15 sessions or greater of prehabilitative exercise had improved VO_2peak compared with those who completed less than 15 sessions [35]. Lastly, Stefanelli et al. (2013) found a 19% increase in VO_2peak using aerobic exercise in patients with lung cancer ($n = 40$). Duration of each session incorporated by Stefanelli et al. (2013) was 150 min longer than those executed by Jones et al. (2007) and Gravier et al. (2019); thus, this prescription may have resulted in greater improvements in VO_2peak out of the three studies [10]. High-intensity aerobic exercise utilized by Jones et al. (2007) and Stefanelli et al. (2013) resulted in greater improvements in VO_2peak than the moderate-intensity aerobic exercise used by Gravier et al. (2019). Therefore, duration and intensity of each training session may affect the amount of improvement seen in patients with lung cancer.

High-intensity interval training has recently gained notable attention in prehabilitative oncology care. In addition to the two aforementioned studies utilizing high-intensity training, Karenovics et al. (2017) reported a significant increase in VO_2peak (+18%), among patients with lung cancer ($n =$ 164) awaiting surgery who participated in an intervention comprised of sprint intervals on a cycle ergometer. VO_2peak significantly declined (− 6%) in the usual care group during the preoperative waiting period [53•]. At the 1-year follow-up, however, both groups experienced similar reductions in VO_2peak (−12%) compared with the preoperative VO_2peak [23], which indicates that the benefits of the exercise intervention may not persist long-term. In summary, studies to date have demonstrated the efficacy of exercise interventions to improve VO_2peak prior to surgery for lung cancer, ranging from an increase in VO_2peak of 12–19% in the exercise group and a decrease of 6–12% in the usual care group [10, 20•, 53•]. Cancer survivors experienced similar improvements in VO_2peak (+ 13%) following a 3-month period of aerobic exercise; however, the rehabilitation period for cancer survivors offers more freedom for longer interventions (from months to years) than prehabilitative interventions, which are often only for a few weeks [54].

In relation to physical function, other measures studied include shuttle walk test [21], pulmonary function [10, 20•], and postoperative outcomes [21], but no significant differences were found. Barassi et al. (2018) was the only study to date to report a change in pulmonary function among patients with lung cancer ($n = 32$); however, this was in the absence of exercise. The authors compared yoga-style breathing and deep breathing in the lung cancer population and found significant improvement in FVC (12%), FEV1 (18%), peak expiratory flow (14%), and peak inspiratory flow (10%) in the yoga breathing group [27]. Overall, prehabilitative exercise appears to mitigate the detrimental impact of surgery, particularly noted by an increase in cardiorespiratory fitness in patients with lung cancer. Both high- and moderate-intensity aerobic exercise improve cardiorespiratory fitness for this cancer type.

Table 2 Exercise intensity and examples of exercises by MET Level

Intensity of Exercise	MET Level	Examples
Light	< 3.0	Standing, light walking, washing dishes, laundry, cooking, cleaning, sweeping with light effort
Moderate	3.0–6.0	Bicycling 9–14.5kph, water aerobics, weight training, dancing, recreational swimming, gardening, yard work, moderate home repair or housework, fishing, hunting
Vigorous	> 6.0	Brisk walking (> 8kph), jogging, running, backpacking, circuit weight training, tennis, lap swimming, heavy gardening and housework, conditioning exercise

MET metabolic equivalent

Adapted from: Stefani et al (2017) *Clinical Implementation of Exercise Guidelines for Cancer Patients and Ainsworth et al (2011) 2011 Compendium of Physical Activities: A Second Update of Codes and MET Values*

Colorectal Cancer

Although colorectal cancer is commonly treated by surgical removal of the tumor, patients who undergo surgery often present with low VO_2peak (range, 16.7–18.6 mL/kg/min), and patients with higher VO_2peak experience a lower risk [odd ratio 0.76 (0.67–0.85); *P* 0.0001] of postsurgical complications [55]. Recent clinical trials among patients with colorectal cancer have demonstrated the benefits of prehabilitative exercise on cardiorespiratory fitness outcomes such as VO_2peak and 6MWT distance, often as a multi-modal prehabilitation program [3, 4•]. West et al. (2014) implemented a supervised aerobic interval training program in patients with rectal cancer ($n = 39$) and reported a significant improvement in VO_2peak and lactate threshold ($p < 0.001$) [56]. This study was supported by Li et al. (2013) which utilized an exercise intervention comprising of aerobic exercise and resistance band exercises combined with whey protein supplementation and an anxiety reduction program among patients with colorectal cancer ($n = 87$) [3]. Following the intervention, 6MWT distance significantly increased (+ 10%) in the exercise group [3]. Importantly, 81% (34 out of 42) of the prehabilitated patients returned to their baseline 6MWT distance 8 weeks post-surgery after an immediate post-surgical decline, compared with 40% (18 of 45) from the control group ($p = 0.01$).

Gillis et al. (2014) directly compared differences in 6MWT distance between patients in a prehabilitative setting or rehabilitative setting, participating in a home-based aerobic and resistance exercise program combined with whey protein supplementation and an anxiety reduction program among patients with colorectal cancer ($n = 77$). The prehabilitative group received the intervention for 4 weeks prior to surgery, and both groups received the intervention for 8 weeks following surgery. The 6MWT distance was significantly higher in the prehabilitation group (+ 6%) before surgery as well as 8 weeks after surgery (+ 5%) when compared with baseline levels, whereas the rehabilitation group deteriorated 3% before surgery and 5% 8 weeks after surgery [4•]. This finding was supported by a supervised multi-modal intervention (exercise, nutrition, and anxiety coping) study conducted by Minnella et al. (2017) which implemented a combined moderate-intensity aerobic and resistance training program defined by the Borg scale in patients with colorectal cancer ($n = 185$). The prehabilitative group participated in a 4-week intervention prior to surgery and continued the intervention for 8 weeks following surgery, while the rehabilitative group only received the intervention for 8 weeks post-surgery. The 6MWT distance was higher in the prehabilitative group immediately before surgery (+ 7% vs − 1%), and at 4 weeks (− 3% vs − 17%), and 8 weeks following surgery (+ 4% vs − 2%) compared with baseline and the rehabilitation group [24•]. Chen et al. (2016) also reported a beneficial effect on the 6MWT distance with a combined aerobic and resistance training in patients with colorectal cancer ($n = 116$) [57]. In contrast, five studies reported no change in the 6MWT [2, 28] distance or VO_2peak [26, 32, 33] with a combined aerobic and resistive training program. Within these studies that found no change, one included a high-intensity interval training intervention with an intensity of 100–120% maximum cardiopulmonary exercise test (CPET) wattage that found no significant changes in VO_2peak [33]. Lastly, aerobic exercise and body weight exercise sessions found a trend towards improved VO_2peak despite a low frequency and study duration, yet this was not significant [32].

Regarding lesser studied outcome measures, Dronkers et al. (2010) was the only study assessing changes in physical function measured by timed up and go in older (> 60 years old) patients ($n = 42$) undergoing elective abdominal oncological surgery. The timed up and go test is designed to assess mobility of a participant by measuring total time (seconds) taken from standing up from the chair, walk 3 m forward, walk back to the chair, and sit down. The intervention was comprised of aerobic exercise and resistance exercise; however, no significant change was reported [1].

Only one study thus far has examined changes in body composition in this patient population. Gillis et al. (2019) with the same intervention and design as we previously described by Gillis et al. (2014) reported a significant increase in lean body mass ($p < 0.001$) and a decrease in fat mass ($p < 0.001$) at 4- and 8-week post-surgery in an intervention utilizing both prehabilitative and continued rehabilitative exercise among 139 patients after surgery [34]. In summary, exercise interventions effectively improve VO_2peak and 6MWT distance among patients with colorectal cancer; however, the impact on functional measures and body composition is lacking conclusive evidence.

Esophageal and Gastric Cancer

Among patients diagnosed with esophageal and gastric cancers, declines in cardiorespiratory fitness may translate to poorer survival [8]. VO_2peak < 13.9 ml/kg/min is associated with reduced 1 year survival in the upper gastrointestinal cancer, and furthermore, VO_2peak < 12 ml/kg/min is associated with increased postoperative complications in lower gastrointestinal cancer compared with those with a VO_2peak > 12 ml/kg/min [58]. Thus, improving cardiorespiratory fitness is a critical outcome in these patients in the preoperative phase. Currently, three randomized controlled trials have utilized prehabilitative exercise in patients with esophageal and gastric cancer, but all three utilized different methodology to assess cardiorespiratory fitness [18, 29, 31]. Minnella et al. (2018) implemented a home-based aerobic exercise intervention and resistance training in patients with esophagogastric cancer ($n = 68$). The intervention was complimented with daily whey protein supplementation. Following the intervention, 6MWT distance was greater in the prehabilitative group (+ 10%) before surgery compared with the control group (+2%) [59]. Notably, the positive effect of prehabilitative exercise on the 6MWT distance was maintained immediately after surgery in the prehabilitative group, while the control group experienced further deterioration in the 6MWT distance (− 23%). While these changes in physical function are robust, the authors did not note any changes in rate of complications, length of hospital stay, emergency department visits, or readmission rates. Christensen et al. (2018) reported the effect of a high-intensity aerobic exercise program in patients with gastro-esophageal junction cancer ($n = 62$), though they did not specify the exact numerical intensity. The intervention found improvements in peak power and VO_2peak (+ 8% and + 6%, respectively) [18]. Valkenet et al. (2018) in patients with esophageal cancer ($n = 270$) utilized an inspiratory muscle training intervention and found significant improvements in inspiratory muscle strength (+ 17%) [31]. These results are promising, as all studies in patients with this cancer type demonstrated improvements in these outcome measures utilizing either a multimodal program, high-intensity aerobic training, or breathing training.

Prostate Cancer

Decreases in cardiorespiratory fitness and lean body mass are associated with androgen deprivation therapy use and longer hospital stays following prostatectomy, and exercise can improve these physical outcomes [60]. Currently, two studies have been conducted in patients with prostate cancer, examining walking ability and body composition. Santa Mina et al. (2018) reported an improvement in the 6MWT distance ($p = 0.006$) and decreased body fat percentage ($p = 0.001$) at 4 weeks postoperatively among patients with prostate cancer ($n = 86$); this difference was only significant for decreased body fat percentage preoperatively. The authors utilized an aerobic and resistive exercise program combined with pelvic floor exercises [30]. Singh et al. (2016) also used a combined aerobic and resistive exercise program among patients with prostate cancer ($n = 16$) and found significant improvements in multiple physical tests, including the 6-m fast walk (− 7%), 400-m walk test (− 5%), the repeated chair rise test (− 7%), and 1 repetition maximum muscle strength (+ 8% seated row; + 24% leg press) [11]. However, Singh et al. (2016) found no differences in any body composition measure throughout the intervention. Overall, among patients with prostate cancer, combined aerobic and resistance exercise improves 6MWT distance, muscle strength, and a variety of physical function tests, yet the effects on body composition remain inconclusive.

Bladder Cancer

Patients undergoing radial cystectomy for bladder cancer often experience debilitating side effects, functional decline, longer hospital stays, and increased complication rates from surgery at a higher rate than patients undergoing surgeries for other cancers [61]; thus, interventions to preserve physical function during cancer treatment are critical. Two studies have examined prehabilitative exercise and physical function changes prior to radical cystectomy [13, 22, 26]. Jensen et al. (2016) used a home-based aerobic step-trainer program with six strength and endurance exercises among 107 patients, and found a significant improvement in leg extensor power (+ 18%) assessed by leg extensor power rig at the time of surgery compared to baseline [22]. This was supported by Banerjee et al. (2018) which reported an increase in power output (+ 13%) from the CPET along with improvements in ventilatory efficiency (+12%) and O_2 pulse (+12%) after aerobic interval training among 60 patients [26]. This was consistent with the findings from studies of other cancer types in that changes in VO_2peak may take a longer adaptation period of 6 weeks or greater [32, 33, 62].

Minnella et al. (2019) found improvements in the 6MWT distance after a multimodal aerobic exercise, nutrition, and anxiety reduction program among 70 patients. However, the authors also included surgical outcomes as secondary measures and found no change in postoperative complications, readmission rates, length of hospital stay, or emergency department visits after discharge in either group. Overall, for patients undergoing radical cystectomy, muscle-specific outcomes, CPET values, and cardiorespiratory fitness measures all showed improvement following these exercise programs; however, potential improvements of exercise on surgical outcomes have yet to be supported.

Pancreatic Cancer

Patients with pancreatic cancer demonstrate impaired cardiorespiratory fitness and maximal isometric muscle contraction following resection compared with the matched healthy population [63]. Interestingly, one previous study demonstrated that patients who engaged in regular exercise a year before diagnosis experienced significantly increased VO_2peak and maximum isometric contraction of the knee extensors 12 weeks after surgery [63]. Thus, it is plausible that exercise in the preoperative period may be an efficient strategy to improve physical fitness. Currently, one study examined prehabilitative exercise in patients with resectable pancreatic cancer [25], and one study examined patients with hepato-pancreato-biliary cancer [37]. Ngo-Huang et al. (2017) utilized a combined aerobic and resistance exercise intervention in patients with pancreatic cancer ($n = 20$). The authors found a significant ($p = 0.01$) increase in patient reported MET-min/

week from pre-treatment to preoperative visit. However, no significant changes were found in physical function outcome measures within or between groups. Nakajima et al. (2019) studied patients with hepato-pancreato-biliary cancer ($n = 76$), of which 72% had biliary tract cancer and 20% had pancreatic cancer, and utilized an aerobic exercise intervention combined with resistance exercises. The authors found improvements in 6MWT distance (5%), absolute fat mass (− 5%), and muscle/fat ratio (5%), but did not see improvements in lean mass preoperatively. In summary, a combined aerobic and resistance exercise program may improve physical fitness and body composition.

Overall, prehabilitative exercise can effectively improve physical function among patients diagnosed with lung [10, 20•, 35], colorectal [2, 4•, 34], esophagogastric [18, 29, 31], prostate [11, 30], bladder [13, 22, 26], and pancreatic [25, 37] cancers. However, optimal exercise prescription including frequency, intensity, time, and type as well as type of intervention setting (i.e., home-based or clinic-based) have not been established. Current evidence commonly targets VO_2peak and 6MWT distance as physical fitness outcomes, while other measures such as frailty or gait speed should be assessed given their association with cancer morbidity [64, 65]. Future studies are warranted to identify the optimal prehabilitative exercise prescriptions to improve comprehensive physical function outcomes and to assess the short- and long-term benefits of the interventions on surgical outcomes and survival in patients including and beyond the aforementioned diagnoses.

Psychosocial Health Outcomes (Table 1)

Each cancer type presents unique symptoms that can have distinct effects on psychosocial health. Cancer diagnosis, treatment, and associated surgeries can also have a profound negative impact on a patient's quality of life (QOL). For example, patients with prostate and bladder cancer often experience urinary incontinence or changes in the urinary stream following their surgical treatment [39]. Patients with colorectal and esophageal cancer experience declines in physical function with additional gastrointestinal symptoms, resulting in psychosocial burden throughout the course of treatment [66, 67]. Increased psychosocial burden can also arise in circumstances surrounding anticipation and results of surgery, imaging, or treatment outcomes [16]. Both aerobic and resistance exercise have been linked to the promotion of positive mood, increased sense of physical well-being, improved self-esteem, mood states, and QOL [68], and have been demonstrated to improve anxiety and depression among patients with cancer in rehabilitative settings [69]. However, the current literature demonstrates conflicting results on the effect of prehabilitative exercise on anxiety, depression, and QOL.

Lung Cancer

Patients with lung cancer may experience fatigue, dyspnea, and coughing, affecting their ability to perform daily activities resulting in decreased independence and decreased ability to perform societal roles, thereby negatively impacting psychosocial health [70]. Sebio Garcia et al. (2017) assessed QOL, before and following an exercise intervention among 40 patients, using the Short Form Health Survey (SF-36), which captures role limitations, vitality, emotional well-being, and social functioning. The intervention included an aerobic and resistance exercise program using interval aerobic training on a cycle ergometer, followed by resistance band exercises among 40 patients with lung cancer. Post-intervention, improvements (45%) in the physical summary component of the SF-36 were observed [43]. However, Peddle et al. (2009) used aerobic exercise on a cycle ergometer prior to surgery which resulted in no change in QOL or fatigue from baseline to pre-surgery using the Trial Outcome Index (TOI) and the Lung Cancer Subscale (LCS) from the Functional Assessment of Cancer Therapy-Lung (FACT-L) questionnaire among nine patients with lung cancer [40]. Peddle et al. (2009) noted a significant decline in QOL and fatigue from the pre-surgery to post-surgery time points in both prehabilitative and control groups (− 5% change overall in the FACT-L), supporting the detrimental effect of lung resection surgery on psychosocial health. Overall, it is difficult to draw any specific conclusions as to the impact of prehabilitative exercise on psychosocial health among patients with lung cancer in part due to the small sample sizes, paucity of studies in this area, primary focus on QOL, and varied exercise prescription parameters.

Colorectal Cancer

Poor emotional health is common in patients with colorectal cancer, with the incidence of depression up to 57% and anxiety up to 47% [71]. Therefore, targeted interventions that improve psychosocial health are vital to consider during the prehabilitative period, yet few studies to date have addressed this focus area. Carli et al. (2010) compared an unsupervised, home-based cycling program and body weight training intervention to a self-paced walking plus breathing intervention among patients with colorectal cancer ($n = 133$). Both groups exhibited improvements in depression scores on the Hospital Anxiety and Depression Scale (HADS; 6% cycling/weight training group; 7% walking/breathing group). No change in anxiety in either group was noted [2]. Alejo et al. (2019) prescribed educational sessions of aerobic and resistance exercises among patients with colorectal cancer ($n = 12$) and found reduced scores for depression on the HADS (−19%) and the QOL domain "emotional function" (10%) on the Health Related Quality of Life (HRQoL) questionnaire [32].

Interestingly, the intervention by Carli et al. (2010) was performed daily for 52 days with a compliance rate of 16%, and the intervention by Alejo et al. (2019) was performed once a week for 6 weeks with a compliance rate of 100%, yet both studies found improvements in depression scores [2, 32]. In opposition, Li et al. (2013) conducted a multimodal aerobic and resistance exercise program previously described in a sample of 87 patients with colorectal cancer and did not find a significant change on the HRQoL as a secondary outcome measure [3]. Null findings were also the case in other studies on prehabilitative exercise in patients with colorectal cancer that implemented either a walking program [36] or a combined aerobic and resistance program [1, 4•]. In sum, the inconclusive findings and limited number of studies in this population can only provide modest evidence that prehabilitative exercise improves psychosocial health among patients with colorectal cancer.

Esophageal and Gastric Cancer

Patients diagnosed with esophageal or gastric cancer may experience a multitude of symptoms including difficulty swallowing, coughing or hoarseness, vomiting, and indigestion, which can lead to pain, fatigue, weight loss, and difficulty with socializing over meals [72], ultimately resulting in compromised psychosocial health [73]. Christensen et al. (2018) studied the effect of an aerobic and resistance exercise program, which included supervised exercise on a cycle ergometer followed by eight resistance exercises in patients with gastro-esophageal junction adenocarcinoma ($n = 62$). The exercise group experienced significantly greater improvements (12.6-point mean increase; baseline values were not reported) in the Functional Assessment of Cancer Therapy-Esophageal (FACT-E) as a secondary outcome measure at the time of surgery [18]. Valkenet et al. (2018) employed an unsupervised inspiratory muscle training intervention using a tapered flow resistive inspiratory loading device in patients with esophageal cancer ($n = 270$). No change in fatigue (using the Multidimensional Fatigue Inventory [MFI-20]) or QOL (using the EuroQol-5D [EQ-5D] and Short Form 12 [SF-12]) was observed as secondary outcome measures [31]. The intervention by Christensen et al. (2018) lasted up to 7–17 weeks longer, and also included aerobic and resistance exercise when compared with the inspiratory muscle training intervention by Valkenet et al. (2018), suggesting that type and duration of intervention impact exercise-induced benefits on psychosocial health. Ultimately, the impact of prehabilitative exercise on psychosocial health in patients with esophageal or gastric cancer is inconclusive, with only heterogenous studies to compare, and varied exercise prescription.

Prostate Cancer

Patients with prostate cancer often experience decreased QOL due to changes in urination or sexual function commonly associated with treatment [74]. Therefore, prehabilitative exercise studies have focused their interventions specifically on targeting symptomatic outcomes such as integration of pelvic floor exercises. Pelvic floor exercises with and without biofeedback produced mixed results on improvements in psychosocial health. Centemero et al. (2010) utilized a pelvic floor exercise intervention prior to surgery in patients with prostate cancer ($n = 118$). Post-intervention, significant improvements in the International Continence Society (ICS) Male Short Form, a QOL assessment more commonly used for benign prostate hyperplasia, was observed at 1 month (20% improvement over the control group) and 3 months (34% improvement over the control group) after surgery; baseline values were not reported [41•]. Sueppel et al. (2001) prescribed pelvic floor exercise combined with biofeedback prior to surgery among 16 patients and found an improvement in QOL (39%), using the American Urological Association Symptom Index for benign prostate hyperplasia, at 6 weeks postoperatively [38]. However, Sueppel et al. did not report if this improvement was statistically significant. Additional pelvic floor prehabilitation and prostate cancer studies did not find a significant change in QOL [39, 75]; this includes one study with a smaller sample size of 16 patients [75] and another study that employed an intervention lasting only 1 week [39].

Santa Mina et al. (2018) integrated a combined approach of both aerobic exercise and daily pelvic floor exercises and studied changes in anxiety and depression as secondary outcome measures in 86 patients. The authors found a significant reduction in anxiety as measured by the HADS in patients with prostate cancer immediately before surgery; HADS score was also significantly improved in the exercise group (1.59-point improvement compared with the control group) at 26 weeks following surgery [30].

On average, pelvic floor exercise programs were performed one to three times per day for one to 7 weeks prior to surgery; however, the studies that significantly improved psychosocial health included exercise performed for a longer duration (greater than 1 month) [30, 38, 41•] than studies with an intervention period less than 1 month [39]. Among this population, pelvic floor prehabilitative exercise interventions show promise in improving psychosocial health outcomes such as anxiety, depression, and QOL.

Bladder Cancer

Patients undergoing open, laparoscopic, or robotic-assisted radical cystectomy for bladder cancer experience complication rates as high as 59% with infection, cardiac, wound, or gastrointestinal complications appearing most commonly [61, 76], with notable side effects including changes in urinary or erectile function [61] that may impact psychosocial health. Despite this, investigations on the impact of prehabilitative exercise on psychosocial health among patients with bladder cancer are lacking. However, it is worth mentioning a study by Jensen et al. (2014) which examined the effect of prehabilitative exercise on disease-specific symptoms [42•] such as abdominal pain, flatulence, and constipation among 107 patients. Jensen et al. (2014) examined the effects of a home-based aerobic and resistance exercise intervention, which involved a step trainer and six strength and endurance exercises on QOL, assessed by the European Organization for Research and Treatment of Cancer (EORTC) Core QOL questionnaire (QLQ-C30) [42•]. The intervention group experienced a significant decrease in single-item scales of abdominal flatulence and constipation (12% improvement), and a 10% improvement in dyspnea from baseline to 4 months post-surgery [42•]. The control group experienced a significant yet unexpected improvement in insomnia (14%) on the EORTC QLQ-C30 during the study period [42•]. This single study on prehabilitative exercise in patients with bladder cancer found changes in single-item scales on the EORTC QLQ-C30, but currently no other studies have addressed this cancer type and conclusions cannot be drawn.

In summary, the results of the aforementioned studies examining psychosocial outcomes were mixed, whereby some interventions improved psychosocial health [30, 32, 38, 41•, 42•, 43, 77] and others did not [1, 4•, 31, 36, 39]. This indicates the need for more comparative studies addressing the different types and volumes of exercise and perhaps the selection of qualitative measures used in these studies. Interventions ranged from 1 to 19 weeks and varied greatly by frequency, intensity, time, and type of exercise (Table 1). Controlled differences in duration, type, or intensity of interventions have not yet been explored in a single study. Though some qualitative measures used by aforementioned studies have been validated in their respective cancers (i.e., FACT-E, FACT-BL, and LCS), others are more related to general medicine and health (i.e., SF-36, HRQoL, HADS) and may not capture the nuances of psychosocial health specific to patients with cancer. When interpreting these data, it is important to consider baseline psychosocial health, as patients diagnosed with certain cancers may have a relatively high self-reported baseline compared with the general population (i.e., colorectal cancer), and therefore these patients may not see or experience significant change due to a ceiling effect [67]. Additional factors to consider are the individual patient's physical limitations, mental outlook, motivation, and exercise preference during the course of the disease and treatment, which may affect how their psychosocial characteristics change with a prehabilitative intervention and subsequent follow-up assessments. Lastly, differing levels of motivation and human connection may contribute to changes in psychosocial health, especially when considering supervised vs. unsupervised exercise interventions. Overall, the benefit of prehabilitative exercise on psychosocial health immediately before surgery and in the months following surgery is inconclusive; however, no studies noted a decline in QOL in the intervention groups compared with the control groups.

Biological Outcomes (Table 3)

To date, few published studies have examined the effect of prehabilitative exercise on cancer-related biomarkers among patients with cancer, as work in this area remains bolstered by preclinical models. Cancer-related biomarkers such as the forkhead box P3 (FOXP3) gene [86], insulin receptor expression [87], interleukin-6, and tumor necrosis factor [88] have been linked to cancer pathogenesis via metabolic, inflammatory, and immune changes or dysregulations [89]. These biomarkers are often used to justify certain exercise interventions in humans [80•] as exercise has been shown to modulate systemic inflammation, upregulate immune pathways, or affect PI3K and other metabolic pathways in previous animal models [81–83]. Exercise initiated prior to cancer surgery may influence these biomarkers and subsequent tumor volumes [19], cellular proliferation [81, 83], systemic inflammation [19], and outcomes related to prognosis, survival, and mortality.

Clinical Trials

Presently, prehabilitative exercise studies among patients with cancer examined changes in Ki67 expression (breast cancer only) [80•], pro-inflammatory and immunological markers [78], tumor tissue and volume changes [56], and tumor gene expression [80•]. Ligibel et al. (2019) tested an aerobic and resistance training intervention consisting of supervised aerobic exercise, followed by strength training, on women diagnosed with breast cancer ($n = 49$). Additional exercise prescription consisted of home-based aerobic exercise to achieve a total of 220 min of exercise per week in a mean of 29.3 days prior to breast surgery. The primary outcome measure was Ki-67, while secondary outcome measures included metabolic, immune, and inflammatory biomarkers, tumor apoptosis, expression of insulin receptors, and tumor gene expression. The study demonstrated that the intervention, which increased exercise of the patients by 200 min per week from baseline, did

Table 3 Prehabilitative exercise interventions in humans and preclinical models with cancer-related biomarkers

Author, year, reference	Sample, design	Outcome variables/measurements	Intervention	Additional intervention	Adherence	Results/outcomes	Prehab window
	Human trials						
Jones et al. 2009 [78]	Twenty patients with non-small cell lung cancer; prospective, single-arm trial	Preoperative and postoperative cancer-related markers: intracellular adhesion molecule (ICAM)-1, macrophage inflammatory protein-1a, interleukin (IL)-6, IL-8, monocyte chemotactic protein-1, C-reactive protein, and tumor necrosis factor-a	Supervised aerobic exercise training Frequency: 5× week Intensity: week 1: 60–65% Week 2–3: 60–65%, 4× week. with 5th session at ventilatory threshold Week 4: 60–65%, 3× week, one threshold, one interval [30 s at peak VO2 followed by 60 s active recovery for 10–15 intervals] Time: week 1: 20–30 min Week 2–3: 25–30 min, 4× week. with 5th session 20–25 min Week 4: 20–30 min, 4× week. with 5th session 30 s interval with 60 s recovery, 10–15 intervals Type: cycle ergometer	N/A	78%	Improvements seen in reduction in ICAM-1 ($p = 0.04$) No improvements* in other inflammatory markers	4–6 weeks
Demark-Wahnefried et al. 2017 [79]	Forty patients with prostate cancer; prospective, two-arm randomized control trial	Preoperative and postoperative cancer-related markers: leptin, insulin, glucose, total testosterone, sex -hormone binding globulin (SHBG), prostate-specific antigen (PSA), tumor necrosis factor B (TNF-b), tumor VEGF, Ki67, and tumor gene expression	Supervised and unsupervised home-based aerobic exercise training Frequency: 2× week supervised, 5× week unsupervised Intensity: 60 to 80% of MHR as per tolerance, targeting 250 kcal of deficit per day Time: 10 min, increasing to 30 min as per tolerance Type: supervised ergometer and treadmill exercise, unsupervised aerobic exercise of any type	Nutrition: subtraction of 1000 kcal per day to promote an average weight loss of 1 kg per week	95%	Improvements* seen in testosterone ($p = 0.0418$), sex hormone-binding globulin ($p = 0.0023$), leptin ($p = 0.0355$), Ki67 expression ($p = 0.0061$), and upregulation in cathepsin L (CTSL), glycogen synthase kinase 3 beta (GSK3B), mediator complex subunit 12 (MED12), and laminin subunit gamma 2 (LAMC2) genes in the prehabilitation group No improvements* in plasma glucose, PSA, TNF-b, and VEGF in either group	Mean 7 weeks
Ligibel et al. 2019 [80•]	Forty-nine patients with breast cancer; prospective, two-arm randomized control trial	Preoperative and postoperative cancer-related markers: Ki-67 expression, serum metabolic and inflammatory biomarkers, tumor apoptosis (CC3), expression of insulin receptor (IR) and immune markers (CD8, CD4, FOXP3, CD56 and CD163) in breast tumor tissue, tumor gene expression	Supervised aerobic and resistance exercise training Frequency: 2× week Intensity: aerobic training, moderate-intensity; resistance training, not specified Time: aerobic training, 30–45 min; resistance training, 20 min. Type: aerobic training, participant's choice, monitored via pedometer; resistance training, resistance machines and free weights	Education: reading of prepare for surgery, heal faster, and listening to the audioguide 2× day (control group only)	> 95%	Improvements seen in reduction in leptin ($p = 0.008$), changes in gene expression, most notably cytokine–cytokine receptor interactions, and NK-mediated cytotoxicity ($p < 0.05$) in the prehabilitation group No improvements in: Ki-67, CC3, IR expression, or any other metabolic or immune markers in either group	1–10 weeks prior to surgery; mean 4 weeks
West et al. 2019 [56]	Thirty-five patients with rectal cancer; prospective, two-arm non--randomized control trial	Preoperative and postoperative cancer-related markers: MRI and histopathological outcomes measured by mrT-stage, ymrT-stage, ymrTRG, ypT-stage, ypTRG	Supervised aerobic interval training Frequency: 3× week Intensity: moderate-intensity intervals (80% of work rate at VO_2 at lactate threshold), 4 by 3 min, followed by high-intensity (50% of work rate difference between VO_2peak VO_2 at lactate threshold), 4 by 2-min intervals) for the first two sessions. Remainder of sessions, the duration was increased to 40 min (6 × 3 min intervals at moderate intensity and 6 × 2 min intervals at high intensity) Time: 20–40 min Type: cycle ergometer	N/A	98%	Improvements seen in greater histological tumor regression in the exercise group ($p = 0.02$) No improvements in the other MRI or histopathological outcomes in either group	6 weeks

Table 3 (continued)

Author, year, reference	Sample, design	Outcome variables/measurements	Intervention	Additional intervention	Adherence	Results/outcomes	Prehab window
	Animal trials						
Jiang et al. 2009 [81]	One hundred and thirty-five healthy female Sprague Dawley rats	Cancer-related markers following injection of carcinogen and after exercise: cyclin D1, hyper phosphorylated Rb, E2F-1, p21, p27, caspase 3 activity	Unsupervised wheel running intervention Frequency: 7× week Intensity: unspecified Time: unspecified Type: wheel running	Restricted feeding: restricted feeding to a body weight gain at the same rate as a paired control rat	100%	Changes** noted in cyclin D1, hyper phosphorylated Rb and E2F-1, were reduced, and p21 and p27 were elevated ($p = 0.0026$), and caspase 3 activity was increased ($p = 0.001$) in physical activity rats	Unspecified
Zhu et al. 2012 [82]	One hundred and twenty healthy female Sprague Dawley rats	Cancer-related markers following injection of carcinogen and after exercise: insulin-like growth factor-1 (IGF-1), IGF-binding protein 3 (IGFBP-3), insulin, glucose, C-reactive protein (CRP), serum amyloid protein (SAP), interleukin- 6 (IL-6), tumor necrosis factor (TNF-a), adiponectin, leptin, progesterone, and 17-b-estradiol	Unsupervised wheel running intervention Frequency: 7× week Intensity: 37 m/min, for a maximum of 3500 m/d (WR-HIGH group) or 1750 m/d (WR-LOW group) Time: unspecified Type: wheel running	Restricted feeding: restricted feeding to 85% of the control rats	100%	Changes** noted in reduced bioavailable IGF-1 ($p < 0.001$), insulin ($p < 0.001$), IL- 6 ($p = 0.002$), SAP ($p = 0.001$), TNF-a ($p = 0.001$), and leptin ($p = 0.001$) and increased IGFBP-3 ($p = 0.006$), and adiponectin($p = 0.019$) in the exercise/controlled feed rats No change in plasma-fasting glucose, C-reactive protein, estradiol, and progesterone ($p > 0.05$) in any rats	~5–6 weeks
Gueritat et al. 2014 [83]	Forty male Copenhagen rats with pre-established subcutaneous prostate tumors	Cancer-related markers before and after exercise: tumor growth speed, Ki67 expression, enzymatic antioxidant defenses in muscle, superoxide dismutase (SOD) expression in muscle, Thiobarbituric Acid Reactive Substances (TBARS) and 8-oxodGuo levels in tumors	Supervised treadmill intervention Frequency: 5× week Intensity: 22–25 m/min Time: 40–60 min Type: treadmill running	Nutrition: consumption of 750 µl pomegranate juice daily	100%	Changes noted in slowed tumor growth, decreased Ki67 staining, increased enzymatic antioxidant defenses in muscle, reduced TBARS and 8-oxodGuo levels ($p < 0.05$) in tumors of exercise rats No changes in tumor SOD activity, oxygen radical absorbance capacity ($p > 0.05$) in any rats	4 weeks
Isanejad et al. 2016 [84]	Sixty-four female BALB/c mice with pre-established breast tumors	Cancer-related markers before and after exercise: tumor volumes, serum E2, tumor VEGF level, microRNAs miR-21, miR-206, let-7, ERα HIF-α mRNA expression, PDCD-4 mRNA expression	Supervised treadmill intervention Frequency: 5× week Intensity: 16–18 m/min, 0% grade Time: 10–14 min Type: treadmill running	None	100%	Changes noted in decreased tumor volume, serum E2, tumor VEGF level, Ki67/CD31 protein expression, miR-206/let-7a overexpression, miR-21 down-expression, ERα HIF-α mRNA down-expression, PDCD-4 mRNA overexpression (all $p < 0.05$) in exercise rats	5 weeks
Figueira et al. 2018 [85]	Fifty healthy Sprague Dawley rats	Cancer-related markers following injection of carcinogen and after exercise: Ki67 expression, cell death of tumor tissue, collagen deposition in tumor tissues	Supervised treadmill intervention Frequency: 5× week Intensity: 20 m/min of speed (70% of VO2 max) Time: 60 min Type: Treadmill running	None	100%	Changes noted in lower Ki67 expression in tumors ($p = 0.002$), increased cell death in exercise rats ($p = 0.0186$); higher collagen deposition ($p = 0.0012$) in control rats	35 weeks

ICAM intracellular adhesion molecule, *IL* interleukin, *kcal* kilocalorie, *SHBG* sex hormone binding globulin, *PSA* prostate-specific antigen, *PDCD-4* programmed cell death protein 4, *TNF* tumor necrosis factor, *MHR* maximum heart rate, *CTSL* cathepsin, *E2* estradiol2, *GSK3B* glycogen synthase kinase 3 beta, *MED12* mediator complex subunit 12, *LAMC2* laminin subunit gamma 2, *let-7* lethal-7, *VEGF* vascular endothelial growth factor, *IR* insulin receptor, *CC3* cleaved caspase3, *CD8* cluster of differentiation 8, *CD4* cluster of differentiation 4, *CD56* cluster of differentiation 56, *CD163* cluster of differentiation 163, *Era* estrogen receptor alpha, *FOXP3* forkhead box protein P3, *NK* natural killer, *MRI* magnetic resonance imaging, *miR-21* microRNA 21, *miR-206* microRNA 206, *HIF-a* hypoxia-inducible factor alpha, *IGF-1* insulin-like growth factor, *IGFBP-3* IGF-binding protein 3, *CRP* C-reactive protein, *SAP* serum amyloid protein, *m* meter, *WR* work rate, *TBARS* thiobarbituric acid reactive substances

*Improvement defined as significant change as reported by original author

**Change defined as significant change as reported by original author not change Ki67 expression but significantly reduced leptin (− 12%) and upregulated cytokine–cytokine receptor interactions, NF-kB and chemokine signaling, and natural killer cell-mediated cell cytotoxicity [80•]. West et al. (2019) prescribed an aerobic interval training program on a cycle ergometer, administered to patients with rectal cancer ($n = 35$). The intervention led to significant increases in histological tumor regression postoperatively according to grade on magnetic resonance imaging (ymrTRG) compared with controls ($p = 0.02$) [56]. Lastly, Jones et al. (2009) reported a significant reduction in intracellular adhesion molecule (ICAM-1, 9.6% reduction) following aerobic exercise on a cycle ergometer in 20 patients with lung cancer ($n = 20$) [78].

Energetics may also play a role in tumor markers and pathogenesis, which was explored further by Demark-Wahnefried et al. (2017) in patients with prostate cancer ($n = 40$). The authors combined aerobic exercise with a nutritional intervention of 1250 kcal deficit per day and a target weight loss of 1 kg per week. Post-intervention, improvements were observed in testosterone (+15%), sex hormone-binding globulin (+25%), leptin (− 15%), Ki67 expression (+ 2.75%), upregulation in Cathepsin L (CTSL), glycogen synthase kinase 3 beta (GSK3B), mediator complex subunit 12 (MED12), and laminin subunit gamma 2 (LAMC2) genes in the prehabilitation group [79].

In summary, the limited number of studies that examined biological outcomes in patients with cancer provides promising insight regarding the benefits of exercise on cancer-related biomarkers, as well as a targeted energetics approach with exercise and caloric deficit. Additional studies are needed to examine the effect of specific exercise prescriptions on novel biomarkers that are specific to certain cancer types, and the subsequent impact on prognosis and recurrence.

Future Directions (Table 4)

Prehabilitative exercise recommendations for patients with cancer continue to evolve as new studies and trials explore novel outcomes or exercise interventions. Targeted or comparative exercise prescriptions, new or understudied outcome measures of interest, and challenges to prehabilitative exercise should be explored in this population to optimize participation and surgical outcomes. Prehabilitative exercise research is also scarce for other common cancers such as kidney, liver, lymph, blood, skin, head and neck, thyroid, leukemia, and lymphoma.

Studies thus far have prescribed prehabilitative exercise in the form of aerobic training [36], resistance training [4•], inspiratory muscle training [31], and/or pelvic floor exercise [39]. For aerobic exercise, high-intensity interval training [18], moderate-intensity steady-state training [42•], and low-intensity steady-state training [36] have been implemented in community and laboratory settings or in the form of home-based programs. All studies have either focused on one prehabilitative intervention in a single-group design [11, 20•] or a two-group design with a control group [10, 53•] or rehabilitation group [4•]. Direct comparisons of one type of intervention to another would be important to explore with the goal of determining the ideal prehabilitative exercise prescription in the cancer populations (i.e., comparing high-intensity training versus low-intensity training or aerobic exercises versus resistance exercise). Modifying and comparing the frequency, intensity, time, or type of intervention would offer greater insight in optimal exercise prescription in terms of total load or duration. For example, an intervention that incorporates 300 exercise min per week may be more efficacious than one that incorporates 150 exercise min per week; however, no studies have yet addressed this directly.

A wide range of physical outcome measures have been studied thus far in prehabilitative exercise studies in patients with cancer. VO_2peak and 6MWT distance are the two most common outcomes for physical function [2, 3, 4•, 10, 20•, 23, 24•, 32, 33, 57, 90], but some studies have examined muscle strength [11], timed up and go [1], chair rise time [1, 11], and lung function [26, 27]. Muscular strength and body composition are hugely important given the treatment-related complications associated with sarcopenia, including increased incidence of chemotherapy-induced toxicity and poor survival [91]. Other clinically relevant physical function outcome measures such as short physical performance battery and gait speed are understudied, yet they are highly predictive of complications and morbidity in cancer patients [45•, 92].

Only three studies in the present review have studied the effect of prehabilitative exercise on surgical outcomes including length of hospital stay, complications, and readmission rates with no significant findings [13, 21, 29]. Due to large patient and hospital burden, surgical outcomes, length of stay, and complication rates require further study to determine optimal prehabilitative exercise guidelines. Prehabilitative exercise may favorably affect each of these variables and therefore implementation of individualized prescriptive exercise is a vital component of future investigations.

Studies measuring changes in psychosocial health following a prehabilitative exercise intervention largely utilize general questionnaires such as the HADS [2, 4•, 30] and the HRQoL questionnaire [32], but specific cancer side effects should also be addressed in order to quantify change with the patient's entire presentation in mind. QOL studies of prostate and bladder cancer often employ questions related to incontinence, urgency, or pain during urination [41•], though studies of men with prostate cancer may also elect to use measures of QOL surrounding sexual function such as the EPIC-26 [93]. However, studies in this review only used outcome measures focused on urinary symptoms for prostate and

Table 4 Future directions for prehabilitative exercise interventions in patients diagnosed with cancer

Research area	Examples
Patient population	
Cancer diagnosis	Kidney cancer Liver cancer Skin cancer Head and neck cancer Thyroid cancer Hematologic cancers Genitourinary cancers Gastrointestinal cancers
Age	Pediatric patients Adolescent and young adult patients Geriatric patients
Outcomes	
Mortality	Long-term cardiovascular disease mortality Long-term cancer-specific mortality
Cancer treatment	Tolerability to cancer treatment Toxicity of cancer treatment
Physical outcomes	Cardiorespiratory fitness Muscular strength Body composition SPPB Gait speed
Surgical outcomes	Length of hospital stay Complication rates Readmission rates
Cancer-specific side effects	Quality of life/psychosocial health Sleep quality Dyspnea, wheezing, coughing (Lung) Chemotherapy-induced peripheral neuropathy Bowel function (gastric/colorectal) Cognitive function Lymphedema
Biomarkers	microRNAs cell-free DNA Circulating Tumor DNA CTCs
Compliance/barriers	Supervised vs unsupervised Distress Fatigue Anxiety Social economic status Pre-diagnosis physical activity level Difficulty with healthcare system
Long term follow-up	6 months 1 year 2 year 5 year
Exercise intervention	
Exercise intervention comparison	Aerobic vs resistance vs combined aerobic + resistance High intensity vs low vs moderate intensity
Modification of prescription	Frequency Intensity Time Type
Exercise prescription comparison	Frequency vs time Frequency vs intensity Frequency vs type Intensity vs time

SPPB short physical performance battery, *CTC* circulating tumor cells

bladder cancer [38, 41•], which may not capture the full scope of side effects in these cancer types. Psychosocial measures used in lung cancer focused on patient-reported physical function and fatigue [40, 43], but none examined dyspnea, wheezing, or coughing, all which are common symptoms in lung cancer patients and are directly tied in to patient well-being [70]. Finally, in regard to esophagogastric or colorectal cancer patients, an area for future studies to consider is bowel function and abdominal discomfort, which can change either positively or negatively with mobilization and exercise. Overall, examining cancer-specific psychosocial outcomes can help identify specific exercise prescriptions that will maximize benefits for patients and their most common and relevant side effects.

Lastly, given the paucity of research in prehabilitative exercise and cancer-related biomarkers, much remains to be explored in that realm. Not only do we require more research in the previously mentioned metabolic, inflammatory, immunologic, and tumor biomarkers, since they all play a critical role in cell proliferation and cancer pathogenesis, but we also require study into novel biomarkers such as microRNAs [94], cell-free DNA, circulating tumor DNA, and circulating tumor cells given these markers can characterize prognosis of both primary and metastatic cancers [95, 96]. These biomarkers are potentially useful targets for prehabilitative exercise in all cancer types.

The prehabilitative phase is a particularly complicated intervention period due to the timing in relation to when a patient is informed of a diagnosis and preparing for treatment strategies. Therefore, considerations to address compliance are necessary for future investigations. Patients may be more compliant with supervised programs compared with unsupervised programs, or in cases, with integrated social support [97]; however, no study has directly looked at factors affecting compliance to prehabilitative exercise programs. Distress from the diagnosis, fatigue from chemotherapy or radiation therapy, pre-surgical anxiety, socioeconomic status, prior activity level, or difficulty in navigating and interacting with the healthcare system, may contribute [98]. However, at this moment, no study to date has examined compliance to prehabilitation interventions in groups with different levels of social support. If a particular intervention has been shown to be particularly effective, the next step is modifying unique barriers to participation for improved outcomes.

Importantly, most studies in this review did not follow patients beyond 8 weeks post-surgery; therefore, sustained improvements induced by exercise are largely unknown. Sustained improvements are particularly important to study given that improved cardiorespiratory function is linked to decreases in all-cause mortality as seen in cancer survivors [99–101], though it is unclear if any patients sustained their exercise habits or functional gains in the months or years following these interventions. Overall, the future of research in prehabilitative exercise has considerable potential to expand to a wider range of cancer types, exercise interventions, outcome measures, and follow-up durations.

Ongoing Exercise Trials

A number of ongoing clinical trials show promise in expanding the literature in prehabilitative exercise and biological outcomes among patients with cancer. The exercise-induced changes in colorectal cancer tissues (EDICT) trial [102] seeks to examine the effect of a 2-week aerobic interval training intervention on insulin receptor signaling, DNA fragmentation, and insulin receptor gene expression in patients with colorectal cancer [102]. Among older adult patients with hematologic malignancies, an ongoing trial is examining the effects of a 4-month pre-transplant walking program performed 30 min two times per week combined with strengthening/balance retraining exercises for 30 min performed three times per week on cyclin-dependent kinase inhibitor 2A (p16) [103], which is essential for regulation of the cell cycle [104]. Lastly, an intervention is underway which is studying the effects of yoga practice three times per week for 6 weeks on pro-inflammatory biomarkers and natural killer cell and regulatory T cell levels among patients with prostate cancer prior to undergoing radical prostatectomy [105]. Based on the limited number of previous and ongoing trials in this area, there is immense opportunity and need to explore a variety of biomarkers and the different prehabilitative exercises that influence them among a broad spectrum of cancer types.

Preclinical Studies

Several preclinical studies have examined the effect of exercise on markers of tumor proliferation among rodents. However, only a few studies have involved pre-established tumors [83, 84], and no study to date included a surgical procedure to address the tumor(s). Gueritat et al. (2014) studied rats with pre-established prostate tumors who underwent treadmill running (22–25 m/min) for 40–60 min 5 days per week for 5 weeks. Post-exercise, Ki67 staining decreased in prostate tumor tissues (~ 75%) and increased enzymatic antioxidant defenses in the soleus muscle (approximately 20%) [83]. Similarly, Isanejad et al. (2016) examined rats with pre-established breast tumors performing treadmill running at 16–18 m/min for 10–14 min, 5 days per week for 5 weeks and found a decrease in tumor volume (~ 65%), tumor vascular endothelial growth factor level (~40%), and Ki67/CD31 protein expression (~ 50%) [84].

Studies by Jiang et al. (2009), Zhu et al. (2012), and Figueira et al. (2018) investigated healthy rats following injection of a carcinogen to examine the effects of physical activity on tumor growth [81, 82, 85]. Jiang et al. (2009) used a wheel running program with a pellet dispenser to enforce daily running for 40 days, combined with restricted feeding to restrict body weight gain, and found a significant reduction in cell proliferation associated proteins, though exact data was not reported [81]. Zhu et al. (2012) used a similar wheel running program to that of Jiang et al. for 40 days at high (3500 m per day) or low (1750 m per day) work load combined with restricted feeding and found reduced bioavailable insulin-like growth factor-1 (high 27%; low 25%), insulin (high 40%; low 24%), tumor necrosis factor (high 15%; low 14%), and leptin (high 48%; low 48%) in both groups of exercise rats following the intervention with no significant changes between groups [82]. Lastly, Figueira and colleagues (2018) implemented a supervised treadmill running program for 60 min per day, 5 days per week at 20 m per minute of running speed (approximately 70% of VO_2max) for 35 weeks. Post-exercise, there was a decrease in immunopositive cells per μm^2 of Ki67 (39% difference between exercised and control rats) and increased cell death per μm^2 in established infiltrative lesions (50% difference between exercised and control rats) [85]. Of note, Zhu et al. (2012) and Jiang et al. (2009) incorporated intervention groups with a restricted feeding regime in combination with exercise [81, 82], and this nutritional component may account for a portion of the significant findings from these studies, especially in reduced cell proliferation and insulin-like growth factor-1 (IGF-1). Results from these preclinical studies are promising and highlight the work necessary to determine effects of aerobic or resistance exercise on pre-established tumors, with or without a restricted nutritional component.

Conclusions

A growing body of evidence has emerged in recent years highlighting the benefits of prehabilitative exercise for a multitude of cancer types. Cardiorespiratory fitness measures, in particular, show a robust and positive response to prehabilitative exercise with outcomes measured including VO_2peak and 6MWT distance, with no reports of detrimental effects of prehabilitative exercise among patients diagnosed with lung, colorectal, or esophagogastric cancer when compared with control groups [3, 4•, 10, 11, 18, 20•, 23, 24•, 29, 30, 34, 37, 42•, 57, 90]. The preoperative waiting period, which in most cases is anywhere from 2 to 6 weeks, can therefore provide a window of opportunity for patients to improve cardiorespiratory fitness measures that often show a significant decline following cancer surgery [13, 34]. This decline from baseline in terms of cardiorespiratory fitness and body composition could be lessened with prehabilitative exercise and would be more effective in preventing overall decline than rehabilitation alone [34].

The effect of prehabilitative exercise on psychosocial health measures is inconclusive. Few studies reported a decrease in anxiety and depression [2, 32] and an improvement in symptoms specific to prostate cancer [38, 41•] and bladder cancer [42•] following the prehabilitative intervention, while other studies reported no significant change in QOL, anxiety, or depression [1, 36]. Different factors may account for this inconsistency such as varying baseline psychosocial health status, disease course, symptoms, treatment, individual coping strategies, resilience, amount of social support, and exercise prescription variations. Of importance, exercise did not decrease psychosocial health in any intervention groups studied (lung, prostate, colorectal, bladder, esophageal, or gastric cancers).

Lastly, prehabilitative exercise and cancer-related biomarkers are an up-and-coming area of research, with some preliminary knowledge emerging in patients with breast [80•], lung [78], prostate [79], and colorectal cancer [56]. Studies on animal models of breast and prostate cancer have explored exercise interventions after an injection of carcinogen, but most of the studies began the exercise intervention immediately, rather than after confirmed tumor establishment [81, 82, 85]. In these animal studies, the “prehabilitation window” is unclear given that no treatment or surgery was performed after the interventions. Nonetheless, this area presents an opportunity for further exploration given the potential impact exercise has on cancer recurrence [106•].

Regarding exercise prescription, most of the exercise interventions in the aforementioned studies were comprised of sessions of 30–60 min, 2–5 sessions per week, and incorporated both aerobic and resistance exercise [1, 3, 4•, 10, 11, 13, 18, 24•, 25, 28, 29, 32, 34, 35, 37, 42•, 57]. A multi-modal approach was occasionally used, as exercise prescriptions were supplemented by nutritional guidance and anxiety reduction techniques [3, 4•, 24•]. Compliance ranged from 16 to 100% but the vast majority reported rates > 70%, even for unsupervised home programs (Tables 2 and 3) [2, 3, 4•, 13, 24•, 28, 30, 34]. Supervised programs had a compliance range of 68.7 [18] to 100% [90], and unsupervised programs had a compliance range of 16 [2] to 98% [28].

Based on the current evidence, prehabilitative exercise can improve VO_2peak and 6MWT distance; however, exercise has an inconclusive effect on other physical function measures, psychosocial health, and cancer-related biomarkers due to small sample size, few studies, and examination of only a handful of cancer types. Aerobic exercise prescription was most common in all cancer types, usually in conjunction with resistance exercise or a multi-modal program. Aerobic exercise programs were performed 15–30 min per session, with high-intensity interval interventions performed 3–4 days per week, and lower-intensity programs performed 3–7 days per week. Resistance training interventions utilizing weight machines or resistance bands were all performed in conjunction with aerobic exercise and similarly lasted 15–30 min for 2–3 days per week. Prehabilitative exercise has the potential to become a widely accessible intervention for cancer patients. In doing so, patients can be provided with exercise intervention before, during, and after cancer treatment to maximize individual wellness and projected outcomes.

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Compliance with Ethical Standards

Conflict of Interest Kyuwan Lee, Judy Zhou, Mary K. Norris, Christina Chow, and Christina M. Dieli-Conwright declare they have no conflict of interest.

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