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The role of exercise-based prehabilitation in enhancing surgical outcomes for patients with digestive system cancers: a meta-analysis



Shasha Xu¹, Rong Yin¹, Haiou Zhu¹, Yin Gong¹, Jing Zhu¹, Changxian Li¹ and Qin Xu^{2*}

Abstract

Background Prehabilitation is a crucial component of tumor rehabilitation that attempts to improve patients' preoperative health, although its efficacy in treating patients with cancers of the digestive system is still up for debate.

Methods The records from PubMed (MEDLINE), Embase, Web of Science, Cochrane Library, EBSCO, Scopus, CNKI and Wan fang database up to November 2024 were systematically searched. The Cochrane Collaboration tool was employed for evaluating the risk of bias in each study, and the PRISMA 2020 checklist provided by the EQUATOR network was utilized.

Results Through quality analysis, 20 articles were included, involving 1719 patients. Although its effect on severe complications is still unknown, the prehabilitation significantly decreased overall postoperative complications when compared to standard care, with a risk ratio (RR) of 0.74 (95% CI: 0.65 to 0.84). Despite not shortening the postoperative hospital stay (MD: -0.13, 95% CI: -0.29 to 0.03), prehabilitation demonstrated notable improvements in the 6-minute walk distance (6MWD), with preoperative gains (MD: 25.87, 95% CI: 14.49 to 37.25) and sustained benefits at 4 weeks postoperatively (MD: 22.48, 95% CI: 7.85 to 37.12). However, no significant differences in 6MWD were observed at 6 or 8 weeks postoperatively. The average improvement in 6MWD from baseline to preoperative was 28.99 (95% CI: 10.89 to 47.08, P=0.002), and from 4 weeks postoperative to baseline, it was 25.95 (95% CI: 6.84 to 45.07, P=0.008), with no significant change at 8 weeks. The acceptance and completion rates of prehabilitation were commendably high at 61% (95% CI: 47–75%) and 90% (95% CI: 87–93%), respectively, alongside a relatively low dropout rate of 10% (95% CI: 7% to 13%).

Conclusions Prehabilitation reduces postoperative complications and improves short-term physical function in digestive surgery patients, with good patient acceptance; however, the long-term effects are unknown due to a lack of follow-up data.

Registration It was registered with the International Prospective Register of Systematic Reviews (PROSPERO) with the identification code CRD42022361100.

Keywords Prehabilitation, Digestive system cancer, Physical exercise, Functional capacity, Complications

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Introduction

Digestive system cancers are among the most common worldwide, with their incidence and mortality rates continuing to rise. In 2022 alone, these malignancies accounted for 4.9 million new cases and 3.3 million deaths, representing 24.6% of all cancer cases and 30% of cancer-related deaths globally [1, 2]. This escalation is attributed to lifestyle shifts, environmental complexities, and an aging population, underscoring a critical public health challenge [1, 2].

Surgery, a cornerstone in tumor treatment, has significantly improved patient survival rates and quality of life [3]. However, the trauma, stress, and potential complications that come with surgical procedures highlight the need for effective strategies to minimize these challenges [4, 5]. Empirical evidence highlights a strong correlation between suboptimal preoperative functional status and increased risks of postoperative mortality and complications [6]. Consequently, identifying effective methods to minimize surgical risks and enhance outcomes has become a critical focus in clinical research. In this context, prehabilitation, an innovative preoperative management approach, has gained increasing attention due to its perceived benefits.

Prehabilitation is a multidisciplinary intervention that aims to improve patients' functional capacity and physiological resilience before surgery. This comprehensive approach, also known as preoperative optimization, usually includes dietary advice, psychological counseling, and fitness training [7, 8]. Despite growing evidence supporting prehabilitation, its efficacy in the clinical management of digestive system tumor patients remains controversial. Mareschal et al.'s systematic review on prehabilitation for gastrointestinal tumor surgery lacked quantifiable outcomes, limiting practical application [9]. Wee et al.'s meta-analysis found no significant short-term benefits for colorectal cancer prehabilitation, possibly due to small sample size [10]. Inconsistent results on postoperative pulmonary complications were observed in an esophageal cancer prehabilitation meta-analysis, with differences between randomized controlled trials (RCTs) and observational studies [11]. Garoufalia et al. showed reduced hospital stay and improved preoperative function after rectal surgery rehabilitation [12]. On the other hand, prehabilitation had no discernible impact on hospital stay duration in colon cancer surgery, according to Zhou et al.'s meta-analysis of 17 RCTs [13].

This study aims to address the gaps and inconsistencies in existing research by systematically reviewing and analyzing the effects of exercise-based prehabilitation on patients undergoing surgery for digestive system tumors. The study will focus on critical outcome measures such as postoperative complication rates and length of hospital stay. By updating the evidence base and strictly adhering to RCTs, this research seeks to provide a more reliable foundation for clinical practice, inform preoperative management strategies, and ultimately improve surgical outcomes. Additionally, the study will examine the acceptance, completion, and dropout rates of RCTs, offering new insights and evidence to guide future research efforts.

Methods

The investigation was conducted following the protocols specified in the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) standards. The study has been registered on the Global Prospective Register of Systematic Reviews (PROSPERO).

Search strategy

To guarantee the accuracy of the entire search procedure, two authors (SX and HZ) who independently finished the systematic learning of database search conducted a systematic literature search. Searches were conducted in PubMed (MEDLINE), Embase, Web of Science, Cochrane Library, EBSCO, Scopus, CNKI and Wan fang from their inception through December 2021, with an updated search extending to November 2024. The search criteria, which included the following keywords: ("digestive system tumor" OR "Esophageal Neoplasms" OR "Stomach Neoplasms" OR "Colorectal Neoplasms" OR "Liver Neoplasms" OR "Gallbladder Neoplasms" OR "Biliary Tract Neoplasms" OR "Pancreatic Neoplasms") AND ("Preoperative Exercise" OR "Acute Exercise" OR "Resistance Training" OR "Strength Training" OR "Nutrition" OR "Psychosocial Intervention") AND (Preoperative Period), were derived from a combination of MeSH phrases and free text words. As shown in (Supplement Table 1), the search approach uses PubMed as an example.

Study selection

The search results for each database are downloaded and merged into Endnote 20, which is used to catalog the retrieved articles and exclude duplicates. According to inclusion criteria and placement criteria, two authors (YG, JZ) screened the literature independently, with the first screening focusing on the title and abstract, the second screening on the full text, and any differences reviewed by the third author (SX).

Eligibility criteria

Studies that met the predetermined inclusion criteria were included: (1) Patients scheduled for surgery due to digestive system cancers. (2) Patients aged 18 years or older. (3) Interventions: Based on exercise, combined with nutrition, psychological interventions, or other techniques. (4) Duration of intervention: preoperative intervention; greater than one week. (5) Control group: no preoperative exercise intervention or counselling advice etc. or ERAS etc. (6) Functional status, total complications, severe complications, length of stay (LOS), psychological status, study acceptance, completion, dropout rates, etc. are among the postoperative outcomes that studies are required to report. (7) The study is of the RCT type and is only available in Chinese and English. The following criteria were used to disqualify studies: (1) Studies for which attempts to contact the authors were unsuccessful in obtaining comprehensive data. Some studies, even after contacting the authors, could not give comprehensive data. (2) Study publications that are duplicates. (3) Commentaries, case reports, correspondence, and reviews.

Data extraction

EndNote 20 was used to catalog the articles obtained from the designated databases. Both authors (SX and CL) independently extracted the data, which included details like the author, year, country, tumor type, sample, age, gender, intervention time, interventions, outcomes, etc., and entered it into Excel in a standardized format. The authors engaged in a discourse to resolve their differences. If there was insufficient data available, the original study's authors were contacted to obtain the necessary information.

Quality assessment

Two authors (JZ and SX) independently assessed each included study's risk of bias (RoB 2) using the Cochrane Improved Risk of Bias Tool for Randomized Trials [14, 15]. The RoB Excel tool was used for the RoB 2 evaluation. Each study's potential for bias was assessed using an instrument that looked at five different potential sources of bias: bias resulting from the randomization process, bias resulting from a deviation from the intended intervention, prejudice resulting from incomplete outcomes information, bias resulting from measurement of results, and bias resulting from public outcome selection. Each included study was evaluated for all areas, and each domain was categorized as either "low risk of bias," "some concern," or "high risk of bias" [14]. The study's overall risk of bias was calculated by taking the highest RoB 2 across all domains. A third reviewer arbitrated disputes if necessary, following a discussion and arbitration process (YG).

Statistical analyses

The data was subjected to a meta-analysis with Stata 17. A value was considered statistically significant if the *p*-value was less than 0.05. To determine the presence of heterogeneity among the research, the Chi-Squared test was initially utilized. If the value of I^2 is less than or equal

to 50% and *p*-value is more than or equal to 0.1, then it is possible to consider numerous comparable studies as homogenous. A fixed-effects model was selected for the meta-analysis. In case of merely statistical heterogeneity with I^2 >50% and P < 0.1, a random-effects model might be chosen for the descriptive analysis of the data. Three levels of heterogeneity were evaluated: low ($I^2 \leq 50\%$), moderate (50–75%), and high ($I^2 > 75\%$). Mean differences are used to express continuous data, risk ratios to express binary data, and 95% confidence intervals (CI) are included. During the study, efforts were made to address missing data by contacting authors via phone or email. However, in cases where authors could not be reached or failed to provide the necessary information, those studies were excluded from the meta-analysis. The subgroup data were examined in terms of the type of intervention time, staff supervision of the activity, the intervention measures, and other factors. To assess publication bias, funnel plots and the Egger test were employed. Analyses of sensitivity were conducted to evaluate the robustness of the main outcomes.

Moreover, additional meta-analysis was done to determine the pooled differences and 95% confidence interval in acceptance rate, completion rate and dropout rate between the prehabilitation and control groups. The total number of respondents who provided consent was divided by the total number of individuals approached to participate in the experiment to get the overall acceptance rate. The completion rate was calculated by dividing the total number of trial participants who finished the study by the total number of trial admissions. Similarly, to determine the dropout rate, one had to divide the total number of those enrolled in each treatment arm who opted out of the study by the total number of research participants who agreed to participate [16]. The data was aggregated using random-effects models, and rates were estimated using the sample size of each study. Each rate is accompanied by a 95% confidence interval and a proportion.

Results

Study selection

Our extensive electronic search initially generated 4,143 results. Following deduplication, 2,730 entries were assessed based on titles and abstracts, with 405 publications being evaluated for eligibility in full text. Following rigorous screening, 20 papers met our inclusion criteria and were included in our review, as shown in Fig. 1.

Study characteristics

Table 1 shows the total number of individuals [17-36] included in the analysis, with 1,719 participants. Of these, 849 belonged to the control group, and 870 were in the experimental group. Sample sizes in studies varied from

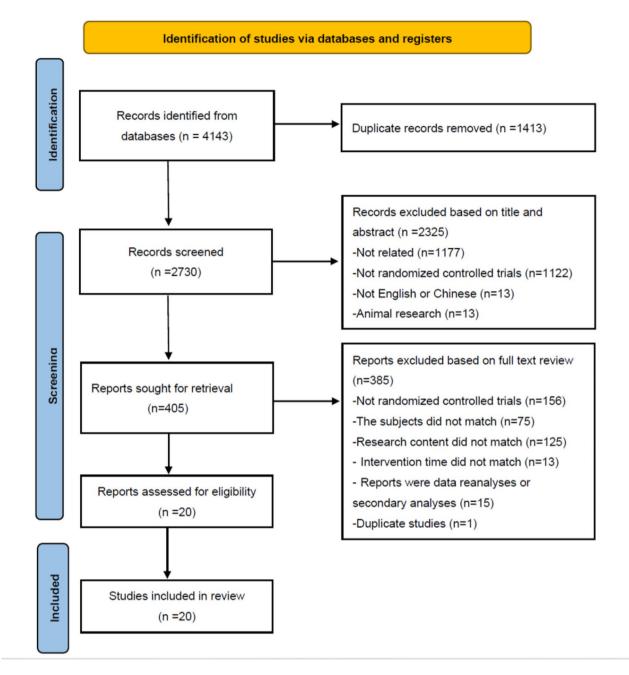


Fig. 1 The PRISMA flow chart

20 to 251 individuals, with a median of 86 participants per study. The average age of study participants varied between 58.3 and 79 years, with a median age of 68.2. The research was published from 2009 to 2024, while 2021 acting as the median publication year. Detailed prehabilitation interventions included in the study are presented in the supplement materials (Supplement Table 2).

Study quality

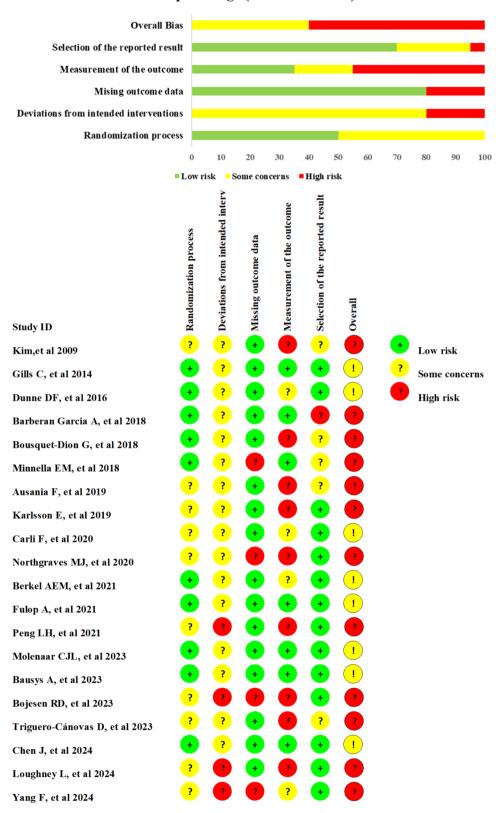
As shown in Fig. 2, an evaluation analysis of the studies involved found that 8 were of intermediate quality and 12 were of low quality. This rating emphasizes the overall methodological integrity of the works under examination.

Quantitative synthesis of outcomes Total postoperative complications

Nineteen studies [17–35], with 1672 participants, examined postoperative problems. One study [30] lacked a specified complication collection timeframe, while four studies reported within 90 days [18, 22, 27, 34] and fourteen within 30 days post-surgery [17, 19–21, 23–26, 28,

Study	Country	Tumor	Design	z	Mean	Age,	Male	Intervention Time	Measures of Intervention group	nterventi	on group		Supervi-	Measures E	Exercise	Primary outcome
		type			Age	mean(I/C)			Measures	Exercise	Nutrition	Psychology	sion of exercise	of control i group	intensity	measure
Yang F, et al. 2024 [17]	China	Colorectal cancer	RCT	50/45	61.9	60/64	34/24	13.2±4.8 days	Exercise prehabilitation	`	×	×	×	Standard L ERAS recom- menda- tions	Low intensity	Fried Frailty Phenotype (FP) score.
Loughney Ireland L, et al. 2024 [18]	Ireland	Oesopha- geal and gastric cancer	RCT	36/35	62.2	62.8/61.5	27/25	12.7±2.4weeks	Exercise prehabilitation	`	×	×	×	Usual Care P	Usual Care Moderate to high intensity	Moderate to Change in 6-minute high intensity walk test (6MWT) pre-surgery, Estimated VO2peak (ml/kg/min).
Chen J, et al. 2024 [19]	China	Gastric cancer	RCT	57/58	74	73/74	33/28	3 weeks	Triple prehabilitation	`	`	\$	`	Standard- ized ERAS recom- menda- tions	Moderate to high intensity	30-day postoperative complications.
Triguero- Cánovas D, et al. 2023 [20]	Spain	Colorectal cancer	RCT	23/21	67.7	68.1/67.2	16/13	30days	Triple prehabilitation	`	`	`	×	Standard care i	Moderate intensity	Change in physical condition (CPET,6MWT).
Bojesen RD, et al. 2023 [21]	Denmark	Colorectal cancer	RCT	16/20	79	80/78	11/6	4 weeks	Exercise + Nutrition	>	`	×	`	Standard H Care	High intensity	High intensity The recovery of patients within the first 3 postoperative day (QOR-15).
Bausys A, et al. 2023 [22]	Lithuania	Gastric cancer	RCT	61/61	62.5	61/64	35/42	4 weeks	Triple prehabilitation	`	`	`	×	Standard L Care r	Low to moderate intensity	postoperative complications within 90 days.
Molenaar CJL, et al. 2023 [23]	Netherlands, Canada, Spain, Italy, Denmark	Colorectal Cancer	RCT	123/128	69	69/71	62/76	4 weeks	Triple prehabilitation	`	`	`	`	Standard F Care	High intensity	High intensity 30-day postoperative complications (CCI).
Peng LH, et al. 2021 [24]	Chhina	Colorectal cancer	RCT	109/104	62.5	63/62	65/53	14.3±5.2days	Exercise prehabilitation	`	×	×	×	Standard- L ized r enhanced i recovery	Low to moderate intensity	Recovery of gastro- intestinal function (I- FEED scoring system).
Fulop A, et al. 2021 [25]	Hungary	Colorectal Cancer	RCT	27/77	70	70/70	37/39	4 weeks	Triple prehabilitation	`	`	`	`	Standard ERAS i protocol	Moderate intensity	Functional capacity (6MWD, Respiratory reserve), quality of Life (SF-36, HADS).
Berkel AEM, et al. 2021 [26]	Netherlands	Colorectal cancer	RCT	28/29	73.6	74/73	16/14	3 weeks	Exercise prehabilitation	`	×	×	`	Standard Care	Moderate to high intensity	The number of patients with one or more complications within 30 days of surgery.
North- graves MJ, et al. 2020 [27]	ň	Colorectal cancer	RCT	11/01	63.8	64.1 /63.5	4/7	≥ 2 weeks	Exercise prehabilitation	\$	×	×	`	Standard L care r i	Low to moderate intensity	Postoperative length of hospital stays and complications, preoperative physical functioning and health-related quality of life.

Study Country		Design	z	Mean	Age,	Male	Intervention Time	Measures of Intervention group	nterventi	on group		Supervi-		Exercise	Primary outcome
	type		(1/0)	Age	mean(I/C)	(1/C)		Measures	Exercise	Nutrition	Psychology	 sion of exercise 	of control group	intensity	measure
Carli F, et Canada al. 2020 [28]	da Colorectal cancer	al RCT	55/55	78	78/82	29/23	4 weeks	Triple prehabilitation	`	>	>	`	Rehabilita- tion	Moderate intensity	30-day Comprehen- sive Complication Index (CCI).
Karlsson E, Sweden et al. 2019 [29]	en Colorectal cancer	al RCT	10/11	76	83.5/74.0	4/4	2-3weeks	Exercise prehabilitation	>	×	×	`	Standard care	Moderate intensity	Process feasibility and scientific feasibility; functional ability (30 days).
Ausania F, Spain et al. 2019 [30]	Pancreatic cancer	ic RCT	18/22	65.9	66.1 /65.7	9/13	≥7 days	Exercise + Nutrition prehabilitation	`	\$	×	`	Standard care	High intensity	High intensity Postoperative complications.
Minnella Canada EM, et al. 2018 [31]	la Esopha- gogastric cancer	c RCT	26/25	67.6	67.3/68.0	18/20	4 weeks	Exercise + Nutrition prehabilitation	`	>	×	×	Usual Care Moderate intensity	Moderate intensity	Change in functional capacity(6MWD).
Bousquet- Canada Dion G, et al. 2018 [32]	da Colorectal cancer	al RCT	37/26	72.7	74/71	30/16	4 weeks	Triple prehabilitation	`	`	`	`	Rehabilita- tion	Moderate intensity	Functional exercise capacity (6MWD).
Barberan Spain Garcia A, et al. 2018 [33]		Gastrointes- RCT tinal tumors surgery	62/63	F	17/17	43/51	4 weeks	Exercise prehabilitation	`	×	×	`	Standard preopera- tive care	High intensity	High intensity Postoperative complications.
Dunne DF, UK et al. 2016 [34]	Colorec- tal liver metastasis	RCT	20/17	62	61 /62	13/13	4 weeks	Exercise prehabilitation	>	×	×	`	Standard preop- erative prepara- tion and advice	High intensity	High intensity. Oxygen uptake at the anaerobic threshold (AT).
Gills C, et Canada al. 2014 [35]	da Colorectal cancer	al RCT	38/39	65.8	65.7/66.0	21/27	4 weeks	Triple prehabilitation	>	`	`	×	Rehabilita- tion	Moderate intensity	Functional walking capacity measured by the 6-minute walk test (6MWT) 8 weeks after surgery.
Kim DJ, et Canada al. 2009 [36]	da Colorectal Cancer	al RCT	14/7	58.3	55 /65	9/4	4 weeks	Exercise prehabilitation	\$	×	×	×	The con- trol group received basic instruc- tions	Low to moderate intensity	Maximal Aerobic Capacity Indicators (Peak power output, VO2max).



As percentage (intention-to-treat)

Fig. 2 Results of article quality evaluation

29, 31–33, 35]. We documented postoperative complications for each study (Supplement Table 3). Figure 3(a) displays the distribution and results of direct comparisons of total postoperative complications. A meta-analysis demonstrated that prehabilitation may reduce total postoperative complications compared to traditional care. The Risk Ratio (RR) was 0.74 (95% CI: 0.65 to 0.84), indicating minimal heterogeneity (I^2 =34.2%). The Egger test (P=0.215) revealed no publication bias (Fig. 3.b), and sensitivity analysis confirmed the results' robustness (Supplement Fig. 1).

Subgroup analysis (Fig. 3.c) reveals that colorectal cancer patients with a mean age of <70 years old, interventions lasting less than 4 weeks, supervised training, high-intensity exercise, multimodal prehabilitation programs, and complications collected within 30 days have lower heterogeneity.

Postoperative severe complications

Thirteen studies reported severe complications, with eleven utilizing the Clavien-Dindo classification ≥ 3 for evaluation [18,21,22,25,26,28,30,31,32,34,35], and two employing a Comprehensive Complication Index exceeding 20 for determination [19,23].Prehabilitation potentially exhibits efficacy in mitigating severe complications (Comprehensive Complication Index > 20) when

compared to conventional care approaches, as evidenced by a relative risk of 0.53 (95% CI: 0.35 to 0.80) (Fig. 4.a). Eleven studies reported postoperative severe complications (Clavien-Dindo classification \geq 3) following surgery, with no statistically significant distinction between the two categories (Risk Ratio (RR): 0.94, 95% CI: 0.68 to 1.30) (Fig. 4.a). The Egger test result revealed that P = 0.00, with publication bias (Fig. 4.b). Before and after using the trim and fill method (Fig. 4.c), the combined results were not statistically significant, and the results remained consistent. Sensitivity analysis confirmed the results' robustness (Supplement Fig. 2).

Length of hospital stay

The results of 19 studies [17–35] including 1672 participants appear to show that there was no statistically significant difference in the length of hospital stay between the two groups (MD: -0.13, 95% CI: -0.29 to 0.03, P=0.109) with low heterogeneity (I^2 = 0.00%), as shown in Fig. 5.a. The Egger test showed no publication bias with P=0.262 (P>0.05) (Fig. 5.b). Using the leave-one-out method, each study was sequentially excluded, and all P-values remained above 0.05 (Fig. 5.c). Sensitivity analysis further demonstrated that all effect sizes crossed zero, indicating stable results (Supplement Fig. 3).

study a [™]	RR (95% CI)	% Weight	c le	vel	studies		Risk Ratio (95% Cl)	i2	subp
Yang F(2024) Loughney L(2024) Chen J (2024) Triguero-Cánovas D (2023)	0.70 (0.28, 1.72) 1.29 (0.79, 2.13) 0.62 (0.36, 1.08) 0.34 (0.10, 1.12) 0.77 (0.43, 1.38)	3.79 6.70 2.46	Re As Eu No	urope	3 12 4 p = 0.153)	L	0.68 (0.46, 1.00) 0.69 (0.59, 0.81) 0.92 (0.71, 1.18) 0.74 (0.65, 0.84)	0 50.7 0	.913 .022 .619
Bausys A (2023) Molenaar CJL (2023) Peng LH (2021) Fulop A (2021) Berkel AEM (2021)	0.40 (0.24, 0.66) 0.75 (0.54, 1.04) 0.74 (0.39, 1.41) 0.99 (0.54, 1.81) 0.59 (0.37, 0.96)	15.55 5.41 4.86	<7 ≥7 St	70 ýr ubtotal (I-squared = 0.0%, p	11 8 = 0.480)	1	0.71 (0.59, 0.84) 0.78 (0.64, 0.94) 0.74 (0.65, 0.84)	24.2 51.2	.213 .045
Northgraves MJ (2020) Carli F (2020) Karlsson E (2019) Ausania F (2019)	0.82 (0.24, 2.82) 1.00 (0.66, 1.51) - 3.30 (0.85, 12.75 0.61 (0.29, 1.30)	1.12 7.34 0 0.56 3.17	Co Th Su	ne Others ubtotal (I-squared = 72.9%, j	12 7 p = 0.055)	1	0.81 (0.69, 0.96) 0.63 (0.52, 0.77) 0.73 (0.64, 0.83)	1.1 59.1	.433 .023
Minnelia EM (2018) Bousquet-Dion G (2018) Barberan-Garcia A(2018) Dunne DF (2016) Gills C (2014)	0.81 (0.53, 1.23) 1.23 (0.61, 2.50) 0.50 (0.32, 0.75) 0.90 (0.42, 1.92) 0.72 (0.40, 1.31)	2.76 11.36 2.30	< ≥4 St	ubtotal (I-squared = 0.0%, p	7 12 = 0.788)	1	0.71 (0.55, 0.93) 0.74 (0.64, 0.86) 0.73 (0.64, 0.83)	0 47.8	.425 .033
Overall (I-squared = 34.2%, p = 0.073)	0.72 (0.65, 0.84)		Ye Na Su	o ubtotal (I-squared = 0.0%, p	12 7 = 0.375)		0.77 (0.66, 0.90) 0.68 (0.54, 0.85) 0.74 (0.65, 0.84)	26 53.1	.188 .046
b Funnel plot of postoperative complications,Pr	(Egger)=0.215	5	Lo Mi Hi	oderate intensity	1 10 8 = 0.715)		0.70 (0.28, 1.72) 0.78 (0.64, 0.95) 0.70 (0.59, 0.83) 0.73 (0.64, 0.83)	46.1 29.5	.054 .192
			Us		16 3 p = 0.073)	┣	0.70 (0.61, 0.80) 0.95 (0.70, 1.29) 0.74 (0.65, 0.83)	34.8 0	.084 .501
se(logRR)			E) M	easures of intervention group vercise prerehabilitation ultimodal prerehabilitation ubtotal (I-squared = 0.0%, p		1	0.75 (0.60, 0.93) 0.73 (0.62, 0.86) 0.74 (0.65, 0.84)	50.5 24.4	.049 .211
	· .	•	W W No		4 14 1 = 0.887)		0.69 (0.51, 0.93) 0.75 (0.65, 0.87) 0.74 (0.65, 0.84) 0.74 (0.67, 0.81)	73.3 19.6	.011 .24
∞ -1 0 1 RR 2		3	-		I .27 Intervention better	1 1.73 Control better	1		

Fig. 3 Forest plot (a), Funnel plot (b) and Subgroup analysis (c) of postoperative total complications

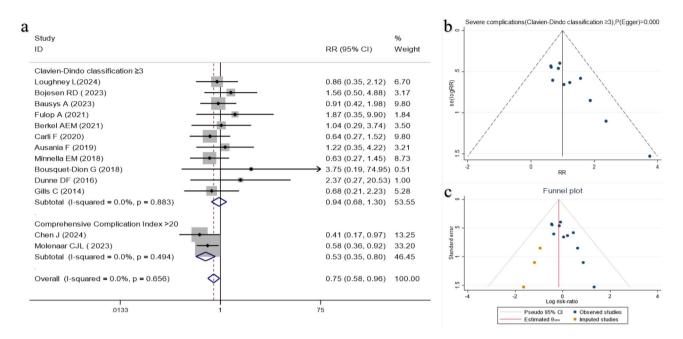


Fig. 4 Forest plot (a), Funnel plot (b) and Funnel plot (Trim and Fill Method) (c) of severe postoperative complications

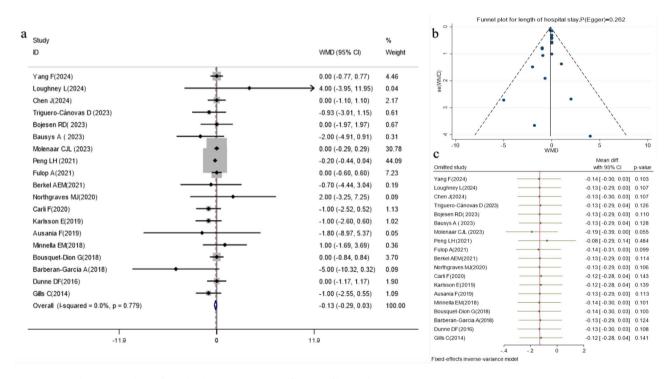


Fig. 5 Forest plot (a), Funnel plot (b) and Subgroup analysis (c) of length of hospital stay

Functional status: Six-Minute Walk Distance (6MWD)

Fourteen studies [17–19, 21–23, 25, 27–29, 31–33, 36], involving 1155 participants, provided data on the 6MWD before surgery (Fig. 6.a). Overall, prehabilitation was associated with a notable increase in pre-surgical 6MWD compared to standard care (MD: 25.87, 95% CI: 14.49 to 37.25) with low heterogeneity ($I^2 = 28.5\%$) (Fig. 6.a). The Egger test result revealed that P=0.752, with no

publication bias, and the sensitivity analysis results demonstrate stability (Supplement Fig. 4).

Seven studies [19, 23, 25, 28, 29, 31, 32] with 620 participants documented the six-minute walk distance (6MWD) at 4 weeks, two studies [18, 20] at 6 weeks, and three studies [23, 25, 32] at 8 weeks, providing a comprehensive overview of the temporal changes in 6MWD

	itudy		%
()	WMD (95% CI)	Weight
		40.00 / 07.50 /7.50	
	ang F(2021)	10.00 (-27.50, 47.50)	9.21
	oughney L(2024)	76.10 (7.54, 144.66)	2.76
	Chen J(2024)	37.00 (12.74, 61.26)	22.01
	lojesen RD(2023)	44.00 (-18.72, 106.72)	3.29
	lausys A(2023)	4.00 (-29.13, 37.13)	11.80
	Iolenaar CJL(2023)	17.00 (-13.43, 47.43)	13.99
	ulop A (2021)	73.00 (32.02, 113.98)	7.71
	korthgraves MJ(2020)	13.00 (-72.13, 98.13)	1.79
	arli F(2020)	30.30 (-17.68, 78.28)	5.63
	arlsson E(2019)	-28.00 (-154.88, 98.88)	0.80
	finnella EM(2018)	62.60 (13.42, 111.78)	5.35
	lousquet-Dion G(2018)	-1.00 (-53.01, 51.01)	4.79
	larberan-Garcia A(2017)	4.00 (-33.47, 41.47)	9.22
	im DJ(2009)	-37.00 (-125.72, 51.72)	1.65
	Overall (I-squared = 28.5%, p = 0.151)	25.87 (14.49, 37.25)	100.00
	-155 0 1	1 55	
	Study		%
	D	WMD (95% CI)	Weight
	3MWD 4 weeks after surgery		
	Chen J(2024)	21.50 (-0.62, 43.62)	30.13 15.75
	Molenaar CJL(2023)	22.00 (-8.60, 52.60) -15.00 (-55.60, 25.60)	15.75 8.94
	Carli F(2020)	50.30 (-3.68, 104.28)	5.06
	Karlsson E(2019)	→ 51.50 (-96.39, 199.39)	0.67
	Minnella EM(2018) Bousquet-Dion G(2018)	101.70 (41.30, 162.10) -3.00 (-62.02, 56.02)	4.04 4.23
	Subtotal (I-squared = 49.0%, p = 0.067)	22.48 (7.85, 37.12)	68.83
	6MWD 6 weeks after surgery		
	Loughney L(2024)	30.70 (-33.73, 95.13)	3.55
	Triguero-Cánovas D (2023)	58.20 (-22.95, 139.35)	
	Subtotal (I-squared = 0.0%, p = 0.603)	41.33 (-9.13, 91.79)	5.79
	SMWD 8 weeks after surgery		
	Molenaar, CJ.L(2023)	30.00 (-2.29, 62.29)	14.14
	Fulop A(2021)	-22.00 (-69.31, 25.31) -4.00 (-60.29, 52.29)	6.59 4.65
	Subtotal (I-squared = 42.3%, p = 0.177)	10.27 (-13.83, 34.37)	25.38
	Heterogeneity between groups: p = 0.492	20.48 (8.33, 32.62)	100.00
	Overall (I-squared = 35.0%, p = 0.110)	20.46 (6.33, 32.02)	100.00
	-199 0	1 199	
	Study ID	WMD (95% CI)	% Weight
	Preoperative change in 6MWD from baseline		
	Triguero-Cánovas D (2023)	96.10 (37.26, 154.94)	2.75
	Bojesen RD(2023)	-44.90 (-85.46, -4.34) 24.00 (13.28, 34.72)	4.46 9.30
	Northgraves MJ	61.00 (28.39, 93.61)	5.56
	Karlsson E	19.00 (-17.13, 55.13)	5.04
	Minnella EM Bousquet-Dion G	59.70 (31.17, 88.23) 11.00 (-8.03, 30.03)	6.21 7.91
	Gillis C (2014)	41.60 (20.08, 63.12)	7.91
	Kim DJ (2009)	4.00 (-46.63, 54.63)	3.40
	Subtotal (I-squared = 75.3%, p = 0.000)	28.99 (10.89, 47.08)	52.08
	Postoperative change in 6MWD at 4 weeks from baseline Molenaar, C.J.L(2023)	22.50 (9.85, 35.15)	9.01
	Fulop A	14.00 (4.16, 23.84)	9.42
	Minnella EM	- 97.20 (47.91, 146.49) 12.00 (27.16, 51.16)	3.52
	Bousquet-Dion G Subtotal (Lsquared = 72.9%, p = 0.011)	12.00 (-27.16, 51.16) 25.95 (6.84, 45.07)	4.63 26.58
	Postoperative change in 6MWD at 8 weeks from baseline		
	Fulop A	-3.00 (-14.09, 8.09)	9.24
	Bousquet-Dion G Gillis C (2014)	9.00 (-19.28, 37.28) 45.20 (14.46, 75.94)	6.26 5.85
	Subtotal (I-squared = 76.6%, p = 0.014)	14.35 (-13.08, 41.79)	21.35
	Overall (I-squared = 77.2%, p = 0.000)	25.29 (13.85, 36.74)	100.00
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Fig. 6 Forest plots of pre-surgical 6MWD (a), post-surgical 6MWD (b), and changes from baseline (c)

across different time points (Fig. 6.b). Compared to standard care, prehabilitation significantly improved 6MWD at 4 weeks after surgery (MD: 22.48, 95% CI: 7.85 to 37.12) with low heterogeneity ($I^2 = 49\%$). The Egger test showed that P = 0.527 (P > 0.05) without publication bias (Supplement Fig. 5). There was no statistically significant difference with 6MWD between the two groups at 6 weeks or 8 weeks after surgery.

Additionally, nine studies [20, 21, 25, 27, 29, 31, 32, 35, 36] showed 6MWD from baseline preoperatively improved by an average of 28.99 (95%CI:10.89 to 47.08, P=0.002), with high inconsistency ($I^2 = 75.3\%$). Four studies [23, 25, 31, 32] found 6MWD from baseline to 4 weeks postoperatively improved by 25.95 (95%CI:6.84 to 45.07, P=0.008), with moderate inconsistency ($I^2 = 72.9\%$). Three studies [25, 32, 35] looked at 8 weeks post-surgery, but there was no significant change in 6MWD (P=0.305) (Fig. 6.c). The Egger test indicated a *P*-value of 0.132 (P>0.05), suggesting no publication bias (see Supplement Fig. 6).

Acceptance rate, completion rate and dropout rate

Among the 4147 patients evaluated for digestive system cancer eligibility, 2228 were deemed ineligible and hence eliminated from the study. The study was completed by 1746 participants, with 884 in the intervention group and 862 in the control group. A total of 173 individuals discontinued the preoperative intervention due to various causes, such as modifications in surgery plans, withdrawals, lack of follow-up, mortality, inability to finish the intervention plan, and transition to palliative care only or neoadjuvant treatment without surgery. Across all included studies, the mean approval rate was 61%, completion was 90%, and dropout was 10%. Meta-analysis of all included studies comparing prehabilitation and control groups revealed significant differences in acceptance and success rates, but not in dropout rates (Fig. 7a, b, c): acceptance: 61%, 95% CI: 47-75%; completion: 90%, 95% CI: 87-93%; dropout: 10%, 95% CI: 7-13%).

Discussion

Our meta-analysis's objective is to evaluate RCT results on the impact of exercise-based prehabilitation in the context of digestive system cancer surgery, with a particular emphasis on key postoperative outcome variables. We found that prehabilitation reduces overall postoperative complications but does not affect severe complications or hospital stay. It improves preoperative and 4-week postoperative 6MWD but has no significant effect at 6 or 8 weeks postoperatively. The completion rates and dropout rates associated with the prehabilitation program show that pre-adaptation is feasible and accepted by a highly motivated cohort of patients willing to participate in the study. It is essential to identify effective strategies that support prehabilitation patients in completing the intervention and reduce the likelihood of dropout.

research demonstrates that prehabilitation The approaches are possibly effective in lowering postoperative problems in patients with digestive system malignancies, when compared to normal care. This observation aligns with the existing literature, which highlights the advantages of exercise-based prehabilitation strategies in enhancing surgical outcomes. For instance, studies conducted by researchers such as Bibo et al. [37] and Wang et al. [38] have demonstrated that patients undergoing prehabilitation experience a similar reduction in the incidence of postoperative complications. These outcomes suggest an agreement on the positive impact of prehabilitation across various surgical disciplines. The rationale behind the reduction of postoperative complications through prehabilitation can be attributed to several interconnected mechanisms. Pre-rehabilitation interventions, typically comprising physical exercise, nutritional optimization, and psychological support, collectively enhance patients' physiological and psychological readiness for surgery [39]. Engaging in physical activity enhances respiratory health, cardiovascular fitness, and muscle strength, which lowers the risk of pulmonary problems after surgery and speeds up recovery from it [40]. Nutritional support addresses preoperative malnutrition, a known risk factor for surgical complications, by ensuring patients are in an optimal nutritional state before undergoing surgery [41]. Psychological interventions help manage preoperative anxiety and stress, which have been linked to adverse surgical outcomes [42]. Together, these components of prehabilitation prepare the body and mind for the stresses of surgery, improve the immune response, and promote a faster return to baseline functional status postoperatively [43, 44]. By addressing these key areas, prehabilitation may alleviate the risk factors associated with postoperative complications, paving the way for a smoother recovery process for patients having digestive system cancers.

The meta-analysis reveals a significant reduction in overall postoperative complications with prehabilitation group (33% compared to 42%). Among the twelve included studies [17, 19, 20, 22, 23, 26, 28–31, 33, 35], detailed postoperative complication data were reported. Seven of these studies focused on complications following colorectal resection [17, 20, 23, 26, 28, 29, 35], while others covered esophagogastrectomy and pancreatic resection complications. Medical complications primarily involved cardiac and pulmonary issues, whereas surgical complications were mainly ileus, wound infection, and anastomotic leakage. However, the effect of prehabilitation on reducing severe complications was inconclusive. While it may be effective for severe complications

Study	%
ID	ES (95% CI) Weight
Yang F(2024)	- 0.81 (0.74, 0.88) 5.00
Loughney L(2024)	0.70 (0.61, 0.79) 4.96
Chen J(2024)	0.58 (0.51, 0.64) 5.01
Triguero-Cánovas D (2023)	- 0.91 (0.84, 0.98) 5.00
Bojesen RD (2023)	
Bausys A (2023)	
Molenaar, C.J.L(2023)	 0.22 (0.19, 0.24) 5.06
Peng LH (2021)	 0.96 (0.93, 0.98) 5.06
Fulop A (2021)	0.99 (0.97, 1.00)5.06
Berkel AEM (2021)	0.56 (0.48, 0.65) 4.97
Northgraves MJ (2020)	• 0.20 (0.13, 0.28) 4.99
Carli F (2020)	• 0.29 (0.24, 0.33) 5.04
Karlsson E (2019)	
Ausania F (2019)	 0.77 (0.67, 0.88) 4.92
Minnella EM (2018)	• 0.31 (0.25, 0.37) 5.02
Bousquet-Dion G (2018)	- 0.91 (0.85, 0.97) 5.02
Barberan-Garcia A (2018)	 0.69 (0.63, 0.75) 5.01
Dunne DF (2016)	
Gills C (2014)	
Kim DJ (2009)	1.00 (1.00, 1.00) 5.07
Overall (I-squared = 99.8%, p = 0.000)	0.61 (0.47, 0.75) 100.00
NOTE: Weighte are from random affects analysis	
NOTE: Weights are from random effects analysis	I
-1 0	1
Study	%
ID	ES (95% CI) Weight
Yang F(2024)	0.94 (0.89, 0.99) 6.04
Loughney L(2024)	0.82 (0.73, 0.91) 4.37
Chen J(2024)	• 0.91 (0.86, 0.96) 5.92
Triguero-Cánovas D (2023)	0.73 (0.62, 0.85) 3.62
Bojesen RD (2023)	
Bausys A (2023)	
Molenaar, C.J.L(2023)	 0.96 (0.94, 0.99) 6.73
Peng LH (2021)	 1.00 (1.00, 1.00) 6.98
Fulop A (2021)	◆ 0.95 (0.92, 0.98) 6.52
Berkel AEM (2021)	0.77 (0.67, 0.87) 4.16
Northgraves MJ (2020)	0.78 (0.61, 0.95) 2.25
Carli F (2020)	0.92 (0.87, 0.97) 5.91
Karlsson E (2019)	0.91 (0.80, 1.03) 3.52
Ausania F (2019)	0.83 (0.73, 0.94) 3.83
Minnella EM (2018)	0.91 (0.84, 0.98) 5.23
Bousquet-Dion G (2018)	0.91 (0.85, 0.97) 5.44
Barberan-Garcia A (2018)	0.76 (0.69, 0.83) 5.15
Dunne DF (2016)	0.92 (0.84, 1.01) 4.52
Gills C (2014)	• 0.94 (0.90, 0.99) 5.97
Kim DJ (2009)	
Overall (I-squared = 90.8%, p = 0.000)	0.90 (0.78, 1.03) 3.22
	¥ 0.80 (0.67, 0.83) 100.00
NOTE: Weights are from random effects analysis	i
-1.03 0	1.03
Study	% FC (05% CI)
ID	ES (95% CI) Weight
Yang F(2024)	0.06 (0.01, 0.11) 6.02
Loughney L(2024)	0.18 (0.09, 0.27) 4.35
Chen J(2024)	0.09(0.04, 0.14) 5.91
Triguero-Cánovas D (2023)	0.27 (0.15, 0.38) 3.61
Bojesen RD (2023)	0.10(0.01,0.19) 4.24
Bausys A (2023)	0.05 (0.01, 0.08) 6.35
Molenaar, C.J.L(2023)	0.04 (0.01, 0.06) 6.72
Peng LH (2021)	0.00 (-0.00, 0.00) 6.98
Fulop A (2021)	0.05 (0.02, 0.08) 6.51
Berkel AEM (2021)	• 0.23 (0.13, 0.33) 4.14
Northgraves MJ (2020) -	0.17 (0.02, 0.33) 2.50
Carli F (2020) -	0.08 (0.03, 0.13) 5.90
Karlsson E (2019)	0.09 (-0.03, 0.20) 3.51
Ausania F (2019)	0.17 (0.06, 0.27) 3.81
Minnella EM (2018)	0.09(0.02, 0.16) 5.21
Bousquet-Dion G (2018)	0.09(0.03, 0.15) 5.43
Barberan-Garcia A (2018)	0.24 (0.17, 0.31) 5.14
Dunne DF (2016)	0.24 (0.17, 0.31) 5.14
Gills C (2014)	0.06 (0.01, 0.16) 4.51
	0.10(-0.03, 0.22) 3.21
Kim DJ (2009)	
Kim DJ (2009) Overall (I-squared = 90.8%, p = 0.000)	0.10 (0.07, 0.13) 100.00

Fig. 7 Forest plot of pooled difference in acceptance rate (a), completion rate (b), dropout rate (c) in the study

(Comprehensive Complication Index > 20), its impact on severe complications (Clavien-Dindo grade \geq 3) was not significant. Given the clinical prevalence of the Clavien-Dindo classification for severe complications, further research is warranted to validate these findings. Severe complications might be more related to surgical technique, tumor characteristics, or patient-specific factors that prehabilitation cannot fully address [45–47]. Akagi et al. [48] found a 28.4% overall postoperative complication rate and a 5.2% rate of severe complications in elderly right hemicolectomy patients, risk factors included male gender, limited daily activities, hypertension, thrombocytopenia, low serum sodium, and elevated PT-INR. Van et al. 's review [49] found similar risk factors for severe complications during surgery for gastrointestinal tumors. By targeting these ameliorable factors, prehabilitation can reduce the likelihood of severe postoperative complications in patients with digestive system cancers. These findings raise a key question: if prehabilitation reduces complications, especially those linked to patient-specific factors, could it also shorten hospital stay?

However, we unexpectedly found that prehabilitation measures were not effective in reducing hospital length of stay in the meta-analysis. This discovery aligns with the findings of Lau et al.'s meta-analysis in the field of gastrointestinal diseases [50] but starkly contrasts with the conclusions drawn by Lambert et al. [51]. Our study suggests that prehabilitation may not possess the capability to diminish severe postoperative complications, nor significantly decrease hospital stay. This result hints at a potential close correlation between severe postoperative complications and the duration of hospitalization. There is a pressing need for additional research data to support the idea that prehabilitation actually reduces hospital stays. A large-scale observational study of 4,495,582 patients in the American College of Surgeons National Surgical Quality Improvement Program (ACS-NSQIP) registry [52] observed that preoperative characteristics (such as males, black patients, smokers, general surgery, etc.), preoperative comorbidities (including hypertension, obesity, and diabetes mellitus, among others), and postoperative complications were all associated with a longer median length of stay. In particular, postoperative complications were significantly correlated with an increase in postoperative length of stay. This finding indicates that while some risk factors contributing to prolonged hospitalization are immutable, other risk factors should be the focus of preoperative patient optimization strategies.

Additionally, the study demonstrates that prehabilitation, both prior to and following surgery, significantly increases 6-minute walk distance (6MWD) in patients with cancers of the digestive system. Faster recovery and better postoperative results were indicated by the prehabilitation group's increase of 25.87 m before surgery and 22.48 m four weeks after surgery. However, these benefits were not sustained at six and eight weeks postoperatively, highlighting the importance of timing and duration of prehabilitation. An analysis of nine studies reveals that five [20, 25, 27, 31, 35] employing a multimodal approach (combining exercise, nutrition, and psychological interventions) reported significant increases in 6MWD, while studies with less comprehensive interventions showed limited effects [53], indicating the superiority of multimodal methods in holistic rehabilitation [54]. Further research by Liu et al. [55] and Inoue et al. [56] supports that a higher preoperative 6MWD is associated with fewer postoperative complications, emphasizing its importance as a recovery predictor. Based on current research data, multimodal prehabilitation shows potential in improving 6MWD, but further studies are needed to validate its long-term effects and optimal implementation methods.

The prehabilitation program for patients with digestive system cancers, characterized by high completion and low dropout rates, underscores its acceptability and feasibility, highlighting its clinical significance. This success is attributed to its holistic, patient-centered approach, tailored to individual needs [57, 58], incorporating exercise, nutritional guidance, and psychological support [4, 59]. The multidisciplinary team, including surgeons, physiotherapists, dietitians, and psychologists, provides comprehensive support, enhancing patient adherence and minimizing dropouts [60]. Early integration of prehabilitation fosters trust between patients and healthcare providers, contributing to higher completion rates [61]. These findings demonstrate the effectiveness, practicality, and patient receptivity of prehabilitation, emphasizing patient readiness for proactive care and the importance of patient empowerment in the recovery process [62]. This suggests the potential for prehabilitation to become a standard preoperative care component, improving outcomes through comprehensive, multidisciplinary, patient-centered approaches.

The main advantage of our research is the incorporation of 20 RCTs involving 1719 individuals with digestive system malignancies, together with a thorough and methodical approach to meta-analysis. This enhances the reliability and applicability of our findings, offering a comprehensive understanding of prehabilitation's effects on surgical outcomes across different tumor types and intervention methods. However, our study is not devoid of limitations. Firstly, the included studies were dominated by colorectal tumors and may not be fully representative of patients with other digestive system cancers, limiting the general applicability of the conclusions. There are significant differences in intervention time and intervention measures, including the type, frequency, intensity, and duration of exercise, which makes it difficult to draw a uniform optimal prehabilitation strategy. Secondly, the predominance of medium and low-quality studies may temper the robustness of our conclusions. More high-quality literature is required to investigate the effects of prehabilitation. Finally, the absence of longterm follow-up data in many included studies restricts our comprehension of the enduring effects of prehabilitation on postoperative outcomes beyond the immediate recovery period.

Conclusion

According to this study, exercise-based prehabilitation interventions for patients with tumors of the digestive system improve 6-minute walk distance (6MWD) before surgery and four weeks after surgery, while also lowering overall postoperative complications. Furthermore, when compared to traditional care, the prehabilitation group's changes in 6MWD from baseline before surgery and from baseline to four weeks after surgery are more favorable. However, there may be no statistically significant differences in severe complications, length of stay, 6MWD at 6 weeks and 8 weeks postoperatively. Additionally, the acceptance, completion, and dropout rates of the RCTs in this study provide guidance for future clinical trials and research. To better demonstrate the clinical benefits of rehabilitation, future studies should comprehensively assess or selectively target specific surgeries, include high-risk patients, and offer personalized, supervised rehabilitation based on objective monitoring.

Supplementary Information

The online version contains supplementary material available at https://doi.or g/10.1186/s12876-025-03626-3.

Supplementary Material 1

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Author contributions

SX, RY and QX designed the study and supervised the entire project. SX and HZ participated in the literature search, YG, JZ, and SX were involved in literature screening and quality analysis, SX and CL were involved in data extraction, RY and SX provided statistical analysis and wrote the manuscript. All authors have checked to make sure that our submission conforms as applicable to the Journal's statistical quidelines.

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Data availability

The data supporting this study's findings are available in the supplementary material of this article.

Declarations

Ethics approval and consent to participate

Ethical approval and participation consent are irrelevant since this is a metaanalysis of randomized controlled trials, and we were in accordance with the 1975 Helsinki declaration and its later amendments.

Consent for publication

Not relevant. There are no human subjects in this study.

Competing interests

The authors declare no competing interests.

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