

Effectiveness of the Tailored, Early Comprehensive Rehabilitation Program (t-ECRP) Based on ERAS in Improving the Physical Function Recovery for Patients Following Minimally Invasive Esophagectomy: A Prospective Randomized Controlled Trial

Funa Yang (✉ yangfuna_403@126.com)

Henan Cancer Hospital <https://orcid.org/0000-0002-6797-1376>

Lijuan Li

Henan Cancer Hospital

Yanzhi Mi

Henan Cancer Hospital

Limin Zou

Henan Cancer Hospital

Xiaofei Chu

Henan Cancer Hospital

Aiying Sun

Henan Cancer Hospital

Haibo Sun

Henan Cancer Hospital

Xianben Liu

Henan Cancer Hospital

Xiaoxia Xu

Henan Cancer Hospital

Research Article

Keywords: Esophageal cancer, Minimally invasive esophagectomy, Bowel function, Physical function, Rehabilitation

Posted Date: June 22nd, 2021

DOI: <https://doi.org/10.21203/rs.3.rs-460781/v1>

License:  This work is licensed under a Creative Commons Attribution 4.0 International License.

[Read Full License](#)

Version of Record: A version of this preprint was published at Supportive Care in Cancer on February 22nd, 2022. See the published version at <https://doi.org/10.1007/s00520-022-06924-8>.

Abstract

Background

Perioperative rehabilitation management is essential to enhanced recovery after surgery (ERAS). Few reports, however, focused on quantitative, detailed early activity plans for patients after minimally invasive esophagectomy (MIE). The purpose of this research was to estimate the Tailored, Early Comprehensive Rehabilitation Program (t-ECRP) based on ERAS in the recovery of bowel function and physical function for patients undergoing MIE.

Methods

In this single-blind, 2-arm, parallel-group, randomized pilot clinical trial, patients were selected from June 2019 to February 2020 and assigned to the intervention group (IG) or the control group (CG) randomly. The participants in IG received a t-ECRP strategy during the perioperative period, and the CG received routine care. The recovery of bowel and physical function, readiness for hospital discharge (RHD) and postoperative hospital stay evaluated on the day of discharge.

Results

215 cases were enrolled and randomized to the IG (n=107) or CG (n=108). There was no significant difference between the two groups in terms of demographic and clinical characteristics and baseline physical function. After the t-ECRP intervention, the IG group presented a significantly shorter time to first flatus ($P < 0.001$) and to first bowel movement postoperative ($P = 0.024$), and a better physical function recovery ($P < 0.001$), compared with the CG group. The analysis also showed that participants in the IG have higher scores of RHD and shorter length of postoperative stay than the CG ($P < 0.05$).

Conclusions

The findings suggest that the t-ECRP can improve bowel and physical function recovery, ameliorate patients' RHD, and shorten postoperative hospital stay for patients undergoing MIE.

Trial registration

ClinicalTrials.gov (Identifier: NCT01998230)

Introduction

Esophageal cancer (EC) is the eighth most common cancer and the sixth most common cause of death overall on the global burden of cancer worldwide.[34] In China, the latest epidemiological survey showed that around 145,700 new cases and 188,100 deaths of EC occurred in 2015, which were higher than the average level of worldwide.[8] Surgery is still the standard treatment for resectable EC, which is comprised

of esophagectomy with radical lymphadenectomy. Esophagectomy is also a major and complex surgery with unacceptable morbidity and mortality rates. A global review of high-volume hospitals performing esophagectomy showed overall morbidity of 59% and 30-day mortality of 2.4%. [20]

Many new strategies and technologies attempted to reduce complications and promote fast recovery, such as minimally invasive esophagectomy (MIE) and the concept of enhanced recovery after surgery (ERAS). ERAS was described first in 1997 by Henrik Kehlet, which is a multimodal pathway integrating evidence-based protocols into clinical practice, and has been widely applied to reduce the surgical stress response, postoperative medical complications, hospital stay and improve recovery after major surgery. [2, 13, 19, 33] ERAS was initially applied in colorectal cancer, and have since been expanded to orthopedics, gynecologic, urology, colorectal by the enhanced recovery after surgery (ERAS) Society. [17, 23] In 2019, the guidelines for perioperative care in esophagectomy was published by ERAS Society, which provided standard norms for perioperative ERAS care protocol of EC. [19]

According to the concept of ERAS, prehabilitation includes a series of measures of increasing the initial physiological reserve and optimizing the organ function of patients before surgery, thereby fast recovery after surgery. The prehabilitation strategies recognized by experts currently include psychological counselling, nutritional supplementation, physical exercise and respiratory optimization. Studies showed that, as a critical part of "prehabilitation", physical exercise program involving both aerobic and strengthening activity, had been proposed to improve outcomes, like reducing depression, anxiety, fatigue, and improving the quality of life [4, 5]. Besides, respiratory optimization with deep spirometry, inspiratory muscle training, and breathing exercises also could decrease postoperative pulmonary complications. [6]

Early ambulation in the postoperative period should be encouraged under the guidance of ERAS, and the key determinant in evaluating the success of ERAS is whether patient can quickly recover to an acceptable level of functional activity after surgery. [19] However, results from longitudinal studies showed that patients after esophagectomy tended to have lower levels of physical activity compared with their preoperative levels. [14] It had been shown that activity capacity was associated with postoperative complications intently. [32] Long-term bed rest after surgery would increase the risk of complications, such as venous thromboembolism, muscle loss, insulin resistance, and pulmonary complications. [26, 31] Therefore, it seems particularly important to do the management of perioperative rehabilitation for patients with surgery.

Research indicated that postoperative mobilization should start on the day of surgery preferably whenever feasible, and increase the amount of activity gradually every day to achieve predetermined goals [10]. However, because patients with EC are often accompany by malnutrition, frailty, pain, drainage pipes and various restrictions of treatment measures, these factors make it more difficult for patients to rehabilitation early. Moreover, although some non-randomized studies concluded that early mobilization might hasten functional recovery after surgery, the evidence and studies on the timing and nature of

mobilization are lack at present.[19] Hence, the provision of a quantified activity target and structured exercise approach will be more conducive to the recovery of patients.

Overall, although perioperative rehabilitation management after esophagectomy is crucial, there are few studies focus on the formulation of early postoperative rehabilitation programs. An early, standardized, quantized, and comprehensive rehabilitation intervention program tailored to individual patients and based on ERAS, is thus warranted for patients after esophagectomy urgently. In this study, we hypothesized that, the Tailored, Early Comprehensive Rehabilitation Program (t-ECRP) based on ERAS, might improve bowel and physical function recovery for patients after MIE. This randomized controlled clinical trial had been conducted to evaluate the role of t-ECRP in improving recovery outcomes of EC patients after surgery, and thus could provide a reference for clinical work.

Materials And Methods

Study design and setting

The study was conducted at the Affiliated Cancer Hospital of Zhengzhou University, Zhengzhou, China. In this single-blind, 2-arm, parallel-group, randomized pilot clinical trial, patients with EC undergoing MIE were selected and divided into intervention group (IG) and control group (CG) randomly by lottery. Researchers involving in the formulation and implementation of intervention programs were informed about the allocated intervention. However, research assessors, data management staff and all patients were blinded to the intervention. Furthermore, research subjects would be placed into different wards in order to avoid mutual interference between patients. All participants in this study received and written informed consent from patients or their family prior to the trial. In addition, the principles of the Helsinki Declaration was respected. This study was approved by the Ethics Committee of the local Medical Ethics Committee(2014xjs4), and the protocol registered in the ClinicalTrials.gov (NCT01998230).

Study participants

The study performed between June 2019 and February 2020 at the Department of Thoracic Surgery of Henan Cancer hospital in China. All patients with MIE surgery recruited by the following conditions. Eligibility criteria: (a) histologically proven EC and selected for MIE, (b) age \leq 75 years, (c) volunteer to this research and (d)be informed consent. Exclusion criteria included (a) previous severe lung, brain and heart organic diseases, bone and joint disorders, (b) emergency surgery, (c) serious postoperative complications such as anastomotic leakage, (d) inability to perform language communication or text understanding.

t-ECRP procedures

Participants in the IG received the t-ECRP from admission to discharge. A t-ECRP team formed before intervention, including two thoracic surgeons, four nurses, one rehabilitation therapist and respiratory therapist. Comprehensive evaluation should conducted when patients admitted to the hospital, such as disease conditions, cardiopulmonary function, disease cognition, self-disease management ability, social

support, etc. Then a tailored ECRP practical target developed with the joint participation of patients and researcher team.

According to the treatment courses of participants during the perioperative period, the t-ECRP designed into three main stages based on the concept of ERAS: (1) pre-rehabilitation, which was defined as the duration from admission to the day before surgery; (2) the day of surgery; (3) fast-rehabilitation, which was defined as the duration from the first day after surgery to discharge. The content and procedure of t-ECRP protocol during each stage were as follows:

Stage I: In the pre-rehabilitation stage, participants were required to perform Steps climbing training (SCT) and Inspiratory muscle training (IMT) in the rehabilitation training room under the guidance of professionals. At program commencement, participants received one face-to-face instructional session. The SCT performed 3 to 5 times per day for ten minutes each time. During the SCT, the step height is 15cm, training speed should be controlled at 20 ~ 40 steps/minute, and individualized training intensity will be adjusted in time by rehabilitation therapist after the physical conditions evaluating. The IMT needs to carry out with a tapered flow resistive inspiratory loading handheld device, performed 6 to 8 times per day for ten minutes each time. 60% of maximal inspiratory pressure was commenced at the beginning of training, and the exercise intensity will be adjusted in time by the respiratory therapist according to participant-reported rate of perceived exertion.

Stage II: On the day of surgery, participants began to perform exercise on the bed after waking up from anesthesia. The whole exercise includes toe flexion and extension, ankle joint and knee joint movement, leg muscle isometric contraction, and hips lifting off the bed, for 2–3 times on the day of surgery led by nurse.

Stage III: In the part of fast-rehabilitation after surgery, participants were encouraged to get out of bed on POD 1 for 4–6 times following the “5-3-1 methods”: sitting on the bed for 5 minutes, standing on the bed for 3 minutes, and moving the legs and feet for 1 minute, under the help and guidance of nurses. Then participants started to walk on POD 2 after surgery in the ward corridor, and an individualized daily walking plan was tailored based on participant’s physical status, as well as the advice from the thoracic surgeon and rehabilitation therapist. For example, on POD 2–3, participants were recommended to walk 6 times per day with a target quantity of 500–1000 meters; 8 times walking per day with 1000–1500 meters target on POD 4–5, and more than 8 times per day with 2000 meters target from POD 6 to discharged. The trained nurses would motivate and promote patients to fulfill the daily walking plan, and the appropriate adjustment of the walking plan was made if necessary. Besides, the IMT needs to keep exercise same as preoperative by the supervised of respiratory therapist.

Throughout the intervention process, the guidance and supervision of medical staff were essential especially when patients begin to perform SCT and at the first time of get out of bed. Rehabilitation activities should stop immediately, when patients suffered from arrhythmia, chest tightness, suffocation and other discomforts, and the next rehabilitation plan would decide after the evaluation and treatment

by t-ECRP team. A recording table of perioperative rehabilitation activities had established, so that researchers could record the times and amount of patient's daily activities.

Control group

Patients in the CG received usual nursing measures after MIE, which included conventional postoperative feeding, pain management, safe and comfortable environment, wound care, diet guidance, medication care, psychological counseling, regular postoperative rehabilitation exercises etc. The pulmonary rehabilitation and physical exercise conducted by nurses according to the routine of postoperative care.

Outcome measures and study instruments

The primary endpoints were bowel function recovery (measured as the time to first flatus and bowel movement postoperative) and physical function (measured by the timed up and go test and frailty score) in both the groups. In the Timed up and go test (TUGT), time will be recorded for participants to rise from a chair, walk 3 meters, and turn around, walk back to the chair and sit down[28]. Take the TUGT test twice, and the average value used as the research result. The frailty score was developed by Fried and colleagues[11], whose criteria comprise five components: exhaustion, unintentional weight loss, slowness, weak muscle strength, and low physical activity. For the five frailty criteria, 1 score would be given if the criterion was met. The total scores ranges between 0 and 5, and participants would be classified as robustness states (0 score), pre-frailty (1 or 2 scores), or frailty (3 or more scores)[9].

The secondary endpoints were readiness for hospital discharge (RHD) and postoperative hospital stay in two groups. The RHD questionnaire was developed by Weiss et al in 2006[35] and has been translated and revised into Chinese version by Taiwanese scholars[16]. This scale consists 12 items and 3 dimensions, covering physical status, adaptive ability, and expected support. The score range of each item is from 0 to 10. The overall Cronbach's α coefficient of the scale was 0.89[16], confirming its validity.

Data collection procedure

At baseline, all patients underwent a preoperative assessment on the day of admission, including sociodemographic data, medical history and comorbidities, and physical function. Subsequently, the t-ECRP or usual care measures implemented until patient discharge. Then research outcomes measured again on the day of discharge, which usually was on the 7-9th day postoperative.

Sample size calculation

The sample size was calculated based on the primary outcome—the time to first flatus after surgery. Previously published results [24] showed that the mean values of time to first flatus in the IG and CG were 2.6 days and 3.4 days, and the standard deviation was 1.7 days. Group sample sizes of 72 and 72 achieve 80.08% power to reject the null hypothesis of equal means when the population mean difference is $\mu_1 - \mu_2 = 3.4 - 2.6 = 0.8$, with a standard deviation for both groups of 1.7 and with a significance level (alpha) of 0.05, using a two-sided two-sample equal-variance t-test by PASS 15.0 software. Allowing for 20% attrition, we increased the sample size to 180 patients (90 participants per group) at baseline.

Statistical analysis

Descriptive statistics can be used for demographic and clinical characteristics at baseline. Continuous variables were presented as Means \pm SD and compared using the unpaired *t* test. Categorical or ranked variables were presented as frequency (%), and analyzed with the χ^2 . *P* < 0.05 was considered statistically significant. The statistical analysis performed using SAS 9.4 (SAS Institute Inc., Kerry, USA).

Results

Participant demographics and clinical characteristics

327 potential participants were recruited, of whom 250 (76.45%) patients were included, and randomized into two groups randomly to receive the intervention of usual care or t-ECRP. During the research, 35 patients were excluded, and 215 patients were included in the final analyses (IG, *n* = 107; CG, *n* = 108). The detailed selection process of the participants was as shown in Fig. 1.

The mean (SD) age of IG was 63.09 (8.98) years, and 61.14 (10.02) years in CG. The mean (SD) operation times of IG and CG groups were 5.11 (0.63) hours and 4.97 (0.75) hours respectively. The majority of subjects were men (153/237, 71.16%), married (201/237, 93.49%), living with family (198/237, 92.09%), and middle location of tumor (115/237, 53.49%). Pathological staging was concentrated in stages I and II (170/237, 79.07%), and 20 (9.30%) participants experienced recurrent nerve paralysis, which was temporary. Demographic and clinical characteristics were similar between intervention and control groups, the analysis showed no statistically significant difference (Table 1).

Table 1
Demographic and clinical characteristics of patients with MIE in the two groups

Variable	Intervention Group(n = 107)	Control Group(n = 108)	Statistics	P Value
Age, y	63.098.98	61.1410.02	1.50 ^a	.135
Gender			1.56 ^b	.212
Male	72	81		
Female	35	27		
Marital status			1.34 ^b	0.512
Married	98	103		
Divorced	6	3		
Widowed	3	2		
Living situation				
Living alone	12	5	3.20 ^b	0.074
Living with family	95	103		
Occupational status			3.01 ^b	0.08
Employed	39	52		
Unemployed or Retired	68	56		
Operation time, h	5.110.63	4.970.75	1.90 ^a	0.058
Location of tumor			5.46 ^b	0.065
Upper	18	16		
Middle	64	51		
Lower	25	41		
Pathological stage*			7.46 ^b	0.059
0	3	2		

*According to the 8th edition TNM staging standard of esophageal cancer by the Union for International Cancer Control;

^a Independent t-test;

^b χ^2 test

Variable	Intervention Group(n = 107)	Control Group(n = 108)	Statistics	P Value
□	18	22		
□	30	46		
□	56	38		
Recurrent nerve paralysis			0.62 ^b	0.734
No	94	98		
Yes	11	9		
Uncertain	2	1		
*According to the 8th edition TNM staging standard of esophageal cancer by the Union for International Cancer Control;				
^a Independent t-test;				
^b χ^2 test				

Efficacy of effect of the t-ECRP

The primary outcomes about bowel function and physical function recovery were outlined in Tables 2 and 3 respectively. As shown in Table 2, the mean (SD) time to first flatus postoperative were 3.24 (1.11) days in IG and 4.19 (1.67) days in CG, the mean (SD) time to first bowel movement were 4.55 (2.34) days in IG and 5.38 (2.98) days in CG. Compared with the CG, the IG presented a significantly shorter time to first flatus ($P < 0.001$) and to first bowel movement ($P = 0.024$).

Table 2
The bowel function recovery of patients with MIE in the two groups

Variable	Intervention Group (n = 107)	Control Group (n = 108)	t Value	P Value
Time to first flatus (d)	3.241.11	4.191.67	-4.92	< .001
Time to first bowel movement (d)	4.552.34	5.382.98	-2.27	.024

Table 3
The physical function recovery of patients with MIE in the two groups

Variable	Pre-intervention		Post-intervention	
	Time of TUGT (s)	Frailty score	Time of TUGT (s)	Frailty score
Intervention Group (n = 107)	9.012.33	1.25.56	13.224.05	2.16.75
Control Group (n = 108)	8.871.89	1.38.48	16.135.42	3.221.10
<i>t</i> Value	.48	-1.83	-4.46	-8.26
<i>P</i> Value	.629	.069	< .001	< .001

The t-ECRP was even more effective than usual care in improving physical function recovery as measured by the TUGT (s) and Frailty score. As summarized in Table 3, before the intervention (the day of admission), no significant differences in baseline physical function between the two groups were observed ($P>0.05$). After the t-ECRP intervention (the day of discharge), the mean (SD) time of TUGT (s) was 13.22 (4.05) seconds in IG and 16.13 (5.42) seconds in CG, the mean (SD) score of Frailty was 2.16 (0.75) in the IG and 3.22 (1.10) in CG, which showed physical function recovery in IG was significantly better than CG ($P<0.001$).

After the t-ECRP intervention, except the dimension of expected support, the total scores of RHD ($P<0.001$), the dimension of physical status ($P<0.001$) and adaptive ability ($P= 0.001$) were significantly higher in IG than that in CG, as showed in Table 4. Likewise, compared with the CG, patients in the IG presented a significantly shorter in the time of postoperative stay (9.083.48d vs. 12.144.05, respectively, $t=-5.94$, $P< 0.001$).

Table 4
The RHD of patients with MIE in the two groups

Dimensions of RHD	Intervention Group (n = 107)	Control Group (n = 108)	<i>t</i> Value	<i>P</i> Value
Physical status	8.481.45	7.571.82	4.06	< .001
Adaptive ability	8.821.50	8.012.05	3.31	.001
Expected support	9.052.85	8.352.70	1.85	.066
Total	8.921.42	7.861.79	4.81	< .001

Discussion

Esophagectomy has identified as a particularly complex surgical procedure due to documented high levels of perioperative morbidity and mortality [30]. Advances in perioperative management concepts and medical technology had been proposed to reduce surgical risk and perioperative morbidity and mortality, thus improving surgical short- and long-term outcomes.[1, 25, 27] According to the components of ERAS guidelines, early and structured mobilization is an essential factor to accelerate recovery, and there is a strong relationship between physical activity and quality of life generally [12]. Ambulate early not only prevents complications associated with bed rest and maintain muscle function, but also empowers patients to play an active role in their rehabilitation from surgery.[19] Therefore, an early and tailored rehabilitation plan of each day perioperative should formulate by the involvement of thoracic surgeons, nurses, rehabilitation therapist and respiratory therapist for patients with MIE.

Cardiopulmonary fitness and physical functioning are key determinants of fitness for major thoracic surgery.[22] One strength of our study is preoperative rehabilitation, which was involved in t-ECRP intervention and included SCT and IMT. "Pre-rehabilitation before the operation can accelerate recovery after operation", this is the philosophy of our team in the implementation of ERAS. Previous research showed that preoperative moderate intensity activity was associated with a lower risk of postoperative complications following oesophagectomy and therefore may have therapeutic potential.[21] One scoping review [29] provided an overview of the available evidence of possible beneficial effects of preoperative exercise therapy in surgery, which showed that the preoperative exercise programs could increase in exercise capacity and physical fitness, preserve pulmonary function, reduce the incidence of postoperative complications, and decrease the length of hospital stay. Although, some studies [19] suggested that the preoperative rehabilitation program requires at least 4 weeks, there is limited data for esophagectomy about the general consensus or clear practical guidance currently regarding exercise methods and exercise time norms.

This randomized clinical trial provided evidence that t-ECRP, involving pre-rehabilitation and early postoperative activity, was effective in promoting recovery of bowel function and physical function in patients undergoing MIE. TUGT test is a common method to observe patient's balance motor function and daily activities, and is an important index to evaluate patient's prognosis.[18] Although the physical fitness of EC patients was affected to a certain extent due to the operation, analysis of this study showed that the time of TUGT in the IG (13.224.05) was significantly shorter than the CG (16.135.42) when discharged after the intervention of t-ECRP. The frailty scores was range from 1 to 4, there were significant statistical differences between the two groups. Something worth noting is that 32.09% of patients are in a frailty state (three or more scores) and 56.28% are in a pre-frailty state (one or two scores) after MIE, which should require adequate attention from medical staffs.

RHD is a self-perception of patients about whether they are ready to be discharged, it is related to medical satisfaction and safety after discharge closely. Studies [7, 15] have shown that the higher RHD, the stronger ability to cope with health challenges after discharge. In this study, the RHD of patients after MIE was at a medium level. Given that physical recovery is closely related to the patient's self-feeling and self-care ability in life when discharged from hospital, the improvement of RHD from patients was

hypothesized as a potential secondary benefit of this program. Furthermore, t-ECRP was beneficial to enhance the level of RHD as well as shorten the postoperative hospital stay. Surprisingly, in this trial, the findings showed that the postoperative hospital stay was approximately 3 days shorter in the t-ECRP group (9.083.48d) than usual care (12.144.05d). One systematic review from 26 studies showed that early enteral nutrition could promote intestinal function recovery and shorten the time of postoperative hospital stay for patients undergoing gastrointestinal surgery.[36] This reduced postoperative hospital stay was likely the result of the early flatus and bowel movement after surgery, which will shorten fasting time of patients, and achieve the purpose of early oral intake, nutrition improvement, and fast postoperative recovery.

Maximizing the patient's subjective initiative in disease management during the perioperative rehabilitation process is very important. Therefore, before the program is formulating, researchers need to explain the concept of ERAS and the significance of early activities to patients, and discuss pre- and post-operative rehabilitation types and target amount together. Moreover, positive encouragement should be given when the target is completed, and adjustment of rehabilitation plan would be conducted based on cause analysis of researcher and patient, when the goal is not completed.

In our study, some efforts also made to provide foundation and guarantee for the implementation of t-ECRP, such as adequate analgesia management and extubation as soon as possible. Previous data[3] showed that adequate pain management accelerates return of bowel function, increases patient mobility, decreases hospital stay, and optimizes patient outcome. Therefore, painlessness is the prerequisite for early postoperative activities. In our study, multimodal analgesia and individualized analgesia programs were used to control the patient's pain to less than 3 points (Visual analogue scoring). Besides, tubes on the patient's body can hinder postoperative activities, especially the urinary tube and gastric tube, so our team adheres to the concept of early extubation as soon as possible after evaluation by the research team to facilitate activities.[37]

Strengths and Limitations

The advantage of this study lies in the emphasis on the subjective initiative of the patients in rehabilitation and the establishment of professional multidisciplinary team to ensure patient safety. This study also had some notable limitations. First, due to the limited preoperative time, the time of preoperative rehabilitation in this study is relatively short (approximately 7–10 days), which may not be able to fully offer the possibility for improving fitness. Second, in this study research staff were aware of the interventions and randomization results. Despite all efforts to maintain blinding, we could not implement a double-blind method owing to the nature of the interventional research. Third, due to the limitations of research conditions, we could not evaluate patients' electrophysiological indicators to reflect the improvement of physical function, which is an important research field of rehabilitation medicine.

Conclusion

In conclusion, the current study showed that the t-ECRP, which was a nurse-led, three-staged procedure, was practical and feasible in accelerating bowel and physical function recovery for patients after MIE based on the context of ERAS. Besides, the t-ECRP can also improve patient's RHD and shorten the postoperative hospital stay, which may enhance patient's medical experience and hospital operation efficiency. Clinical nurses play a key role in patient's perioperative enhanced recovery, the results of this research motivate nurses to formulate quantitative, detailed and individualized early activity plans for patients combining with multidisciplinary collaboration.

Declarations

Funding: The study was supported by the Joint Co-construction Project of Science and Technology Tackling Plan of Henan Provincial Health Commission [LHGJ20200194]. This funding provided support to give medical agents, data analysis and editorial assistance with the writing of the manuscript, but had no role in study design and data collection.

Conflicts of interest/Competing interests: The authors have no conflicts of interest to declare.

Availability of data and material: This article is distributed under the terms of the Creative Commons Attribution 4.0 International License, which permits unrestricted use, distribution, and reproduction in any medium, provided you give appropriate credit to the original author(s) and the source, provide a link to the Creative Commons license, and indicate if changes were made.

Code availability: N/A

Authors' contributions: FN Yang, XX Xu and XB Liu contributed to concept, design supervision the research. All authors contributed, reviewed, and approved the final manuscript.

Ethics approval: This study was approved by the Ethics Committee of the local Medical Ethics Committee(2014xjs4), and the protocol registered in the ClinicalTrials.gov (NCT01998230).

Consent to participate: The authors would like to thank all the participants in this study. All participants in this study received and written informed consent from patients or their family prior to the trial.

Consent for publication: All authors in this study have no conflicts of interest and agree to publication.

References

1. (2015) The Impact of Enhanced Recovery Protocol Compliance on Elective Colorectal Cancer Resection: Results From an International Registry *Ann Surg* 261: 1153-1159
2. Bisch SP, Wells T, Gramlich L, Faris P, Wang X, Tran DT, Thanh NX, Glaze S, Chu P, Ghatage P, Nation J, Capstick V, Steed H, Sabourin J, Nelson G (2018) Enhanced Recovery After Surgery (ERAS) in gynecologic

oncology: System-wide implementation and audit leads to improved value and patient outcomes

Gynecologic oncology 151: 117-123

3. Capdevila X, Moulard S, Plasse C, Peshaud JL, Molinari N, Dadure C, Bringuier S (2017) Effectiveness of Epidural Analgesia, Continuous Surgical Site Analgesia, and Patient-Controlled Analgesic Morphine for Postoperative Pain Management and Hyperalgesia, Rehabilitation, and Health-Related Quality of Life After Open Nephrectomy: A Prospective, Randomized, Controlled Study *Anesthesia and analgesia* 124: 336-345

4. Carli F, Gillis C, Scheede-Bergdahl C (2017) Promoting a culture of prehabilitation for the surgical cancer patient *Acta oncologica (Stockholm, Sweden)* 56: 128-133

5. Carli F, Silver JK, Feldman LS, McKee A, Gilman S, Gillis C, Scheede-Bergdahl C, Gamsa A, Stout N, Hirsch B (2017) Surgical Prehabilitation in Patients with Cancer: State-of-the-Science and Recommendations for Future Research from a Panel of Subject Matter Experts *Physical medicine and rehabilitation clinics of North America* 28: 49-64

6. Cassidy MR, Rosenkranz P, McCabe K, Rosen JE, McAneny D (2013) I COUGH: reducing postoperative pulmonary complications with a multidisciplinary patient care program *JAMA surgery* 148: 740-745

7. Causey-Upton R, Howell DM, Kitzman PH, Custer MG, Dressler EV (2019) Factors Influencing Discharge Readiness After Total Knee Replacement *Orthopedic nursing* 38: 6-14

8. Chen R, Zheng RS, Zhang SW, Zeng HM, Wang SM, Sun KX, Gu XY, Wei WW, He J (2019) [Analysis of incidence and mortality of esophageal cancer in China, 2015] *Zhonghua yu fang yi xue za zhi [Chinese journal of preventive medicine]* 53: 1094-1097

9. Dong L, Qiao X, Tian X, Liu N, Jin Y, Si H, Wang C (2018) Cross-Cultural Adaptation and Validation of the FRAIL Scale in Chinese Community-Dwelling Older Adults *Journal of the American Medical Directors Association* 19: 12-17

10. Feldheiser A, Aziz O, Baldini G, Cox BP, Fearon KC, Feldman LS, Gan TJ, Kennedy RH, Ljungqvist O, Lobo DN, Miller T, Radtke FF, Ruiz Garces T, Schricker T, Scott MJ, Thacker JK, Ytrebø LM, Carli F (2016) Enhanced Recovery After Surgery (ERAS) for gastrointestinal surgery, part 2: consensus statement for anaesthesia practice *Acta anaesthesiologica Scandinavica* 60: 289-334

11. Hsieh TJ, Su SC, Chen CW, Kang YW, Hu MH, Hsu LL, Wu SY, Chen L, Chang HY, Chuang SY, Pan WH, Hsu CC (2019) Individualized home-based exercise and nutrition interventions improve frailty in older adults: a randomized controlled trial *The international journal of behavioral nutrition and physical activity* 16: 119

12. Ichijo Y, Takeda Y, Oguma Y, Kitagawa Y, Takeuchi H, Doorenbos AZ (2019) Physical Activity Among Postoperative Esophageal Cancer Patients *Cancer nursing* 42: 501-508

13. Ji HB, Zhu WT, Wei Q, Wang XX, Wang HB, Chen QP (2018) Impact of enhanced recovery after surgery programs on pancreatic surgery: A meta-analysis *World journal of gastroenterology* 24: 1666-1678
14. Komatsu H, Watanuki S, Koyama Y, Iino K, Kurihara M, Uesugi H, Yagasaki K, Daiko H (2018) Nurse Counseling for Physical Activity in Patients Undergoing Esophagectomy *Gastroenterology nursing : the official journal of the Society of Gastroenterology Nurses and Associates* 41: 233-239
15. Larsson C, Wågström U, Normann E, Thernström Blomqvist Y (2017) Parents experiences of discharge readiness from a Swedish neonatal intensive care unit *Nursing open* 4: 90-95
16. Lin YH, Kao CC, Huang AM, Chi MT, Chou FH (2014) [Psychometric testing of the chinese version of the readiness for hospital discharge scale] *Hu Li Za Zhi* 61: 56-65
17. Ljungqvist O, Scott M, Fearon KC (2017) Enhanced Recovery After Surgery: A Review *JAMA surgery* 152: 292-298
18. Long J, Cai T, Huang X, Zhou Y, Kuang J, Wu L (2020) Reference value for the TUGT in healthy older people: A systematic review and meta-analysis *Geriatric nursing (New York, NY)* 41: 325-330
19. Low DE, Allum W, De Manzoni G, Ferri L, Immanuel A, Kuppusamy M, Law S, Lindblad M, Maynard N, Neal J, Pramesh CS, Scott M, Mark Smithers B, Addor V, Ljungqvist O (2019) Guidelines for Perioperative Care in Esophagectomy: Enhanced Recovery After Surgery (ERAS®) Society Recommendations *World journal of surgery* 43: 299-330
20. Low DE, Kuppusamy MK, Alderson D, Ceconello I, Chang AC, Darling G, Davies A, D'Journo XB, Gisbertz SS, Griffin SM, Hardwick R, Hoelscher A, Hofstetter W, Jobe B, Kitagawa Y, Law S, Mariette C, Maynard N, Morse CR, Nafteux P, Pera M, Pramesh CS, Puig S, Reynolds JV, Schroeder W, Smithers M, Wijnhoven BPL (2019) Benchmarking Complications Associated with Esophagectomy *Ann Surg* 269: 291-298
21. Moran J, Guinan E, McCormick P, Larkin J, Mockler D, Hussey J, Moriarty J, Wilson F (2016) The ability of prehabilitation to influence postoperative outcome after intra-abdominal operation: A systematic review and meta-analysis *Surgery* 160: 1189-1201
22. Moran J, Wilson F, Guinan E, McCormick P, Hussey J, Moriarty J (2016) Role of cardiopulmonary exercise testing as a risk-assessment method in patients undergoing intra-abdominal surgery: a systematic review *British journal of anaesthesia* 116: 177-191
23. Nelson G, Bakkum-Gamez J, Kalogera E, Glaser G, Altman A, Meyer LA, Taylor JS, Iniesta M, Lasala J, Mena G, Scott M, Gillis C, Elias K, Wijk L, Huang J, Nygren J, Ljungqvist O, Ramirez PT, Dowdy SC (2019) Guidelines for perioperative care in gynecologic/oncology: Enhanced Recovery After Surgery (ERAS) Society recommendations-2019 update *International journal of gynecological cancer : official journal of the International Gynecological Cancer Society* 29: 651-668

24. Ohkura Y, Shindoh J, Ueno M, Iizuka T, Haruta S, Udagawa H (2018) A new postoperative pain management (intravenous acetaminophen: Acelio®) leads to enhanced recovery after esophagectomy: a propensity score-matched analysis *Surgery today* 48: 502-509
25. Pecorelli N, Hershorn O, Baldini G, Fiore JF, Jr., Stein BL, Liberman AS, Charlebois P, Carli F, Feldman LS (2017) Impact of adherence to care pathway interventions on recovery following bowel resection within an established enhanced recovery program *Surg Endosc* 31: 1760-1771
26. Pedrinolla A, Colosio AL, Magliozzi R, Danese E, Kirmizi E, Rossi S, Pogliaghi S, Calabrese M, Gelati M, Muti E, Cè E, Longo S, Esposito F, Lippi G, Schena F, Venturelli M (2020) The Vascular Side of Chronic Bed Rest: When a Therapeutic Approach Becomes Deleterious *Journal of clinical medicine* 9
27. Pfirmann D, Tug S, Brosteanu O, Mehdorn M, Busse M, Grimminger PP, Lordick F, Glatz T, Hoepfner J, Lang H, Simon P, Gockel I (2017) Internet-based perioperative exercise program in patients with Barrett's carcinoma scheduled for esophagectomy [iPEP - study] a prospective randomized-controlled trial *BMC Cancer* 17: 413
28. Podsiadlo D, Richardson S (1991) The Timed "Up & Go": A Test of Basic Functional Mobility for Frail Elderly Persons *Journal of the American Geriatrics Society* 39: 142-148
29. Pouwels S, Hageman D, Gommans LN, Willigendael EM, Nienhuijs SW, Scheltinga MR, Teijink JA (2016) Preoperative exercise therapy in surgical care: a scoping review *Journal of clinical anesthesia* 33: 476-490
30. Reynolds JV, Preston SR, O'Neill B, Baeksgaard L, Griffin SM, Mariette C, Cuffe S, Cunningham M, Crosby T, Parker I, Hofland K, Hanna G, Svendsen LB, Donohoe CL, Muldoon C, O'Toole D, Johnson C, Ravi N, Jones G, Corkhill AK, Illsley M, Mellor J, Lee K, Dib M, Marchesin V, Cunnane M, Scott K, Lawner P, Warren S, O'Reilly S, O'Dowd G, Leonard G, Hennessy B, Dermott RM (2017) ICORG 10-14: NEOadjuvant trial in Adenocarcinoma of the oEsophagus and oesophagoGastric junction International Study (Neo-AEGIS) *BMC Cancer* 17: 401
31. Sáez de Asteasu ML, Martínez-Velilla N, Zambom-Ferraresi F, Ramírez-Vélez R, García-Hermoso A, Cadore EL, Casas-Herrero Á, Galbete A, Izquierdo M (2020) Changes in muscle power after usual care or early structured exercise intervention in acutely hospitalized older adults *Journal of cachexia, sarcopenia and muscle*
32. Smith TB, Stonell C, Purkayastha S, Paraskevas P (2009) Cardiopulmonary exercise testing as a risk assessment method in non cardio-pulmonary surgery: a systematic review *Anaesthesia* 64: 883-893
33. Sun HB, Li Y, Liu XB, Zhang RX, Wang ZF, Lerut T, Liu CC, Fiorelli A, Chao YK, Molena D, Cerfolio RJ, Ozawa S, Chang AC (2018) Early Oral Feeding Following McKeown Minimally Invasive Esophagectomy: An Open-label, Randomized, Controlled, Noninferiority Trial *Ann Surg* 267: 435-442

34. Sung H, Ferlay J, Siegel RL, Laversanne M, Soerjomataram I, Jemal A, Bray F (2021) Global cancer statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries CA: a cancer journal for clinicians
35. Weiss ME, Piacentine LB, Lokken L, Ancona J, Archer J, Gresser S, Holmes SB, Toman S, Toy A, Vega-Stromberg T (2007) Perceived readiness for hospital discharge in adult medical-surgical patients Clinical nurse specialist CNS 21: 31-42
36. Yang F, Wei L, Huo X, Ding Y, Zhou X, Liu D (2018) Effects of early postoperative enteral nutrition versus usual care on serum albumin, prealbumin, transferrin, time to first flatus and postoperative hospital stay for patients with colorectal cancer: A systematic review and meta-analysis Contemp Nurse 54: 561-577
37. Zhang R, Li Y, Liu S, Liu X, Sun H, Wang Z, Zheng Y, Chen X, Liu Q, Zhu Z, Xu L (2018) FA01.03: USE OF 'NON-TUBE NO FASTING' ERAS PROTOCOL IN PATIENTS AFTER MIE WITH LI'S ANASTOMOSIS: OUTCOMES IN THE FIRST 113 PATIENTS PERFORMED BY A SURGEON AFTER TRAINING COURSE Diseases of the esophagus : official journal of the International Society for Diseases of the Esophagus 31: 1-2

Figures

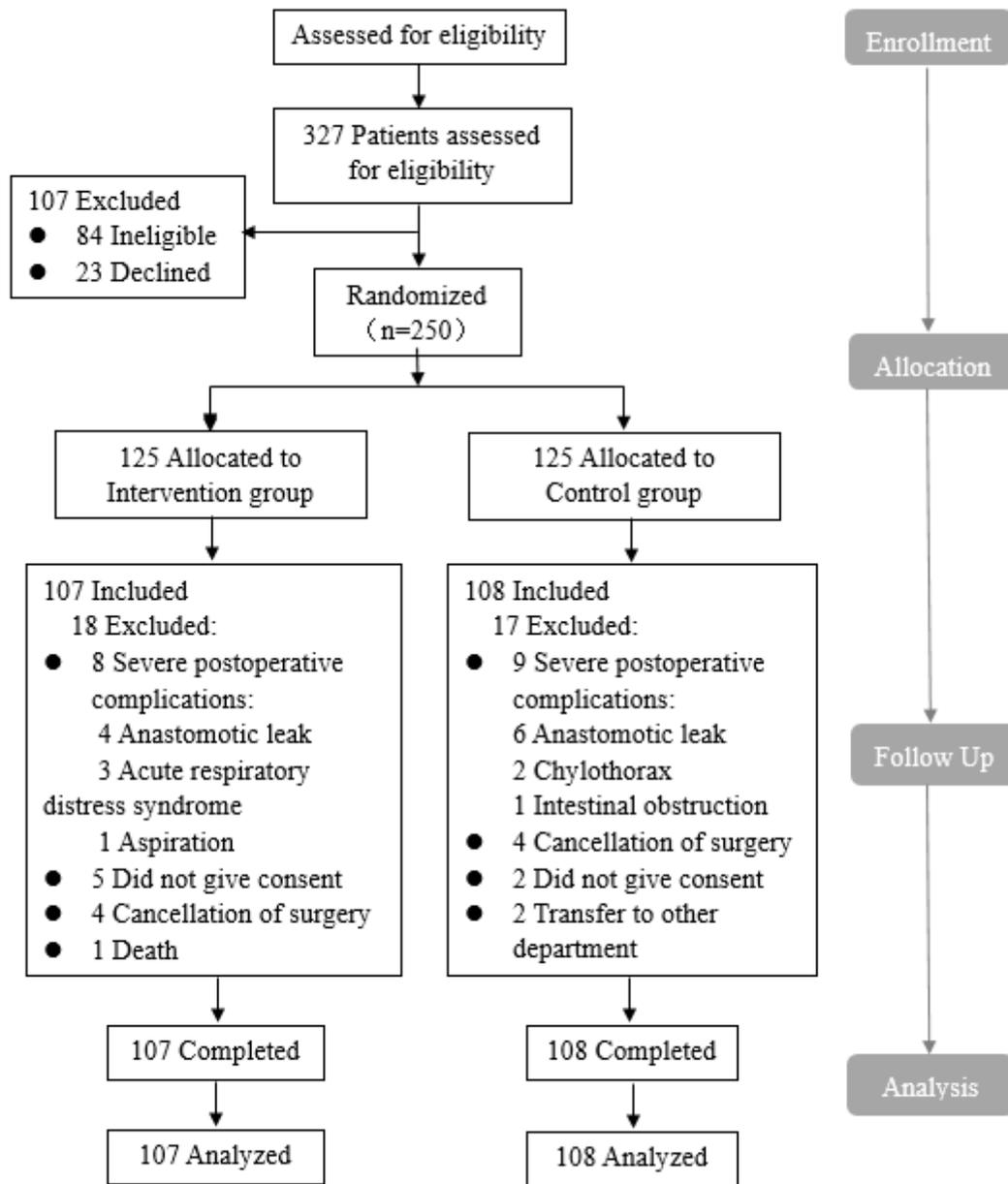


Figure 1

Consort diagram for the study