Cost-effectiveness comparisons of enhanced recovery after surgery (ERAS) *vs.* non-ERAS for esophageal cancer in China: a retrospective comparative cohort study

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Background: Esophageal cancer is a malignant tumor that seriously endangers human health. Compared with surgery alone, enhanced recovery after surgery (ERAS) has been widely used in clinical practice because it can improve perioperative care, minimize complications, and accelerate the recovery of esophageal cancer patients. However, there is a lack of data supporting the cost-effectiveness of ERAS.

Methods: This retrospective cohort study included 968 esophageal cancer patients according to the pre-determined inclusion and exclusion criteria. Based on the Chinese expert consensus and guidelines, we improved the ERAS protocols consisting of 17 core measures. Subjects receiving >60% of the ERAS optimization measures were classified as the ERAS group, while those receiving <60% were classified as the pre-ERAS group. The demographic information, clinical and cost data of these patients were collected from the medical records. Based on the data distribution, the clinical effects and costs between the two groups were examined using the independent-sample *t*-test, the rank sum test, or the chi-square test. The effect of cost-effectiveness ratio calculation was measured by the disease cure rate obtained from the discharge report.

Results: A total of 374 and 594 patients were included in the ERAS and pre-ERAS groups, respectively, and there were no significant differences in gender, American Society of Anesthesiologists (ASA) grade, tumor location, tumor stage, and other basic conditions between the two groups. The intraoperative blood loss, hospital stays, postoperative rehabilitation time, postoperative complications, and the number of secondary admissions within 30 days postoperatively of the ERAS group were lower than those of the pre-ERAS group (P<0.05). Compared with the pre-ERAS group, participants in the ERAS group had lower direct medical cost, direct non-medical cost, and indirect cost (P<0.05). Moreover, the cost-effectiveness ratio of the ERAS group (118,439.0 Yuan) was lower than that of the pre-ERAS group (143,369.0 Yuan) with respect to the cure rate.

Conclusions: The study demonstrated that compared with pre-ERAS, the application of ERAS in esophageal cancer patients may accelerate postoperative rehabilitation, reduce the length of hospital stays and postoperative complications, and have better cost-effectiveness, highlighting the potential of ERAS to improve the quality of medical care.

Keywords: Esophageal cancer; enhanced recovery after surgery (ERAS); cost-effectiveness; retrospective cohort study; China

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Introduction

Esophageal cancer is a malignant tumor that seriously endangers human health worldwide. According to GLOBOCAN data statistics, there were 324,000 new cases and 301,000 deaths in China in 2020, accounting for about half of the global cases and deaths (1). The overall cure rate of esophageal cancer is relatively worse compared with other types of cancer, with a 5-year survival rate of only about 30% (2), illustrating the major public health burden caused by esophageal cancer owing to its high incidence and low cure rate. Surgery is one of the main treatment modalities for esophageal cancer, but traditional surgery is often accompanied by more complications and may lead to postoperative death (3,4). Given the current situation, we must strive to reduce complications and promote early recovery. Enhanced recovery after surgery (ERAS), which is a promising strategy to solve these problems, aims to improve perioperative care, minimize complications, and accelerate recovery (5).

The concept of ERAS was first proposed by Henrik Kehlet in 1997 (6). The ERAS program, also known as fast-track surgery (FTS), is a patient-centered, surgeon-led system combining anesthesia, nutrition, psychology, and nursing (7). Its purpose is to minimize surgical stress, accelerate postoperative recovery, and reduce surgery-related complications during the perioperative period. Following many years of practice, ERAS has gradually become widely used in colorectal surgery, gastrectomy, and liver surgery (8-10). In 2019, the ERAS Society issued guidelines for enhanced recovery after esophagectomy, recommending the application of ERAS to improve the effect of esophagectomy (11). Recent studies have shown that compared with conventional surgery alone, ERAS can reduce the length of hospital stays and complications in patients undergoing esophageal cancer surgery (12,13).

In addition to meeting the basic needs, treatment effects, and prognosis of patients with esophageal cancer, treatment costs are also an important aspect that patients pay attention to in the treatment process. Whether it can be widely used in clinical practice in the future depends on its cost-effectiveness evaluation results. Therefore, there is a need to evaluate the health economics of ERAS by analyzing its clinical effect combined with the associated medical costs. Some studies indicated that the application of ERAS to hepatectomy, gynecologic surgery, colorectal surgery, and pancreatic surgery could reduce the economic burden of patients (14-16). However, there are very few studies have focused on the cost-effectiveness of ERAS in esophageal cancer surgery, so the evidence is limited (16). Therefore, this retrospective cohort study was performed to investigate the cost-effectiveness of ERAS applied in patients undergoing esophageal cancer surgery. We present the following article in accordance with the CHEERS reporting checklist (available at https://atm.amegroups.com/article/view/10.21037/atm-22-4169/rc).

Methods

Study population

This retrospective cohort study included 968 patients who were diagnosed with primary thoracic esophageal squamous cell carcinoma and underwent radical resection of esophageal cancer at the Department of Thoracic Surgery, Henan Cancer Hospital from January 2019 to December 2020. The inclusion criteria were as follows: (I) subjects aged between 18 and 80 years old and without a history of preoperative chemotherapy; (II) tumor sites in the upper, middle, and lower thoracic region; (III) cases involving preoperative organ function evaluation and anesthesia interview; and (IV) cases involving a diagnosis of grade I–III primary thoracic esophageal squamous cell carcinoma according to the American Society of Anesthesiologists (ASA) classification. Meanwhile, patients with a previous history of cervicothoracic abdominal surgery were excluded. This study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was reviewed and approved by the Medical Ethics Committee of Henan Cancer Hospital (No. 2021-KY-0107-004), and individual consent for this retrospective analysis was waived.

Grouping criterion

Based on the "non-tube no fasting" technology for esophageal cancer, we improved the ERAS protocols consisting of 17 core measures according to the "Chinese expert consensus and path management guide for accelerated rehabilitation surgery (2018 Edition)" and the "Guidelines for Perioperative Care in Esophagectomy: Enhanced Recovery after Surgery Society Recommendations" (17,18). The ERAS protocol mainly included psychological management, nutrition management, surgical management, anesthesia management, medication management, respiratory management, fluid management, tube management, pain management, and rehabilitation management in the perioperative period.

Subjects receiving >60% of the ERAS optimization measures for esophageal cancer from January 2019 to December 2020 were classified as the ERAS group, while those receiving <60% were classified as the pre-ERAS group. The optimization measures were as follows: (I) multiple forms of education and information about the specific measures to alleviate psychological stress and anxiety; (II) preoperative nutritional assessment and effective intervention; (III) food and bland liquid diet given 6 and 2 h before surgery, respectively; (IV) no preoperative mechanical bowel preparation; (V) anesthesia depth monitoring; (VI) preoperative utilization of anesthetics and prophylactic analgesia; (VII) antimicrobial prophylaxis at 30 min preoperatively; (VIII) airway management and lung protective ventilation strategy; (IX) temperature monitoring and thermal insulation; (X) goal-directed restrictive volume therapy strategy; (XI) unconventional placement of nasogastric tube; (XII) postoperative nutritional support and early oral feeding; (XIII) unusual placement of chest and abdominal drainage tubes; (XIV) postoperative multimodal analgesia; (XV) prevention of postoperative nausea and vomiting; (XVI) early removal of urinary catheter; and (XVII) ambulation on the first postoperative day.

Data collection

Data were collected from the medical records of patients, including their general conditions, clinical indicators, and costs. The general conditions included the patients' demographic characteristics, tumor locations, ASA grades, pathological stages, surgical methods, and main intraoperative monitoring indicators (surgical anesthesia time, operation time, blood loss, etc.). Clinical information covered a variety of indicators such as complications, the total length of hospital stay, postoperative hospital stays, secondary surgery within 30 days, and secondary hospitalization. The effect of cost-effectiveness ratio calculation was measured by the disease cure rate obtained from the discharge report. And the standard of cure is complete resection of the tumor. In addition, the cost data were calculated from the patients' perspectives. The cost included direct medical and non-medical cost and indirect cost. Direct medical costs included preoperative cost, intraoperative cost, and postoperative cost. Direct non-medical cost included catering and accommodation costs for the patients and their families, cost for caregivers, and cost of nutrition and health products, which was obtained by multiplying average daily cost and the hospital stays. Indirect cost mainly included lost wages, which were obtained by multiplying the average daily salary per capita and the loss of working time (19). We analyzed the lost wages based on the average annual income of urban non-private sector employees in Henan Province in 2020 (i.e., 70,239 Yuan), and obtained estimates of the other types of costs, including the per capita cost for the loss of working hours (264 Yuan per day), the cost of nursing workers (260 Yuan per day), the catering fee (60 Yuan per day), the accommodation fee (50 Yuan per day), and the cost of nutrition and health products (50 Yuan per day).

Statistical analysis

The measurement data were expressed as the mean ± standard deviation (SD) or median (P25, P75), and the counting data were expressed as a frequency. Variables that were not available were analyzed according to the missing data, which were not specially handled during statistical analysis. For measurement data, the *t*-test was used for comparisons between groups for variables conforming to a normal distribution, and the rank-sum test was used for inter-group comparisons for non-normally distributed data. The χ^2 test was used for inter-group comparisons of counting data. All analyses were performed using SAS software (Version 9.4; SAS Institute Inc., Cary, NC, USA), and a two-tailed P<0.05 was considered statistically significant.

Results

Basic information of the included patients

A total of 374 and 594 patients were included in the

Table 1 Comparison of the baseline data between the two groups

Characteristics	ERAS group (n=374)	Pre-ERAS group (n=594)	P value
Gender			0.543
Male	255	416	
Female	119	178	
Age (years)	65.1±7.7	64.0±8.1	0.037
BMI (kg/m^2)	23.5 (21.4, 25.7)	23.0 (21.0, 25.4)	0.035
History of diabetes	37	43	0.146
ASA grade			0.634
≤ II	330	530	
≥ III	44	64	
Tumor site*			0.172
Upper	39	92	
Mid	167	283	
Lower segment	108	167	
Tumor stage*			0.795
I	57	83	
II	193	319	
III	122	191	
Surgical method			<0.001
Open	64	256	
Minimally invasive	310	338	

Data are presented as mean ± standard deviation, median (P25, P75) or number. *, some data are missing. ERAS, enhanced recovery after surgery; BMI, body mass index; ASA, American Society of Anesthesiologists.

ERAS and pre-ERAS groups, respectively. There were no significant differences in the general characteristics between the two groups (P>0.05), except for age, body mass index (BMI), and operation mode (*Table 1*).

Clinical index

For the intraoperative indicators, laparoscopic surgery was performed in 338 (56.90%) cases in the pre-ERAS group and 310 (82.89%) cases in the ERAS group. The number of minimally invasive surgeries in the ERAS group was significantly higher than that in the pre-ERAS group (P<0.01). The intraoperative blood loss in the ERAS group (176.3±244.4 mL) was lower than that in the pre-ERAS group (221.4±272.5 mL, P=0.008). Moreover, there was no significant difference in the operation and anesthesia times between the two groups (P>0.05).

Also, the mean hospital stays (20.7±5.5 *vs.* 27.9±10.7 days) and postoperative hospital stays (10.9±4.7 *vs.* 18.0±9.8 days) of the ERAS group patients were markedly reduced compared to those of the pre-ERAS group patients (P<0.001). The P value for "secondary admission within 30 days postoperatively" is <0.05. Postoperative complications occurred less frequently in the ERAS group (P<0.001). Specifically, a total of 33 patients in the pre-ERAS group had postoperative complications, including 26 cases of anastomotic leakage and seven cases of other diseases, while there was only one patient who experienced postoperative complications in the ERAS group (hiatal hernia of the esophagus) (*Table 2*).

Health economics analysis

Direct medical cost of patients

The total direct medical cost of the ERAS group was 77,953.0 Yuan, less than the 95,338.6 Yuan of the pre-ERAS group (P<0.001). The preoperative cost was higher in the ERAS group (10,989.2 Yuan) than in the pre-ERAS group (9,909.8 Yuan), while the intraoperative and postoperative cost were higher in the pre-ERAS group than in the ERAS group (P<0.001) (*Table 3*).

Direct non-medical cost and indirect cost of patients

Most previous studies only focused on the direct costs of ERAS, while ignoring the direct non-medical cost and the indirect cost (20-23). In this study, we analyzed multiple types of costs and found that the direct non-medical costs (including the catering and accommodation costs, cost for caregivers, and cost of nutrition and health products) of the ERAS group was 8,400.0 Yuan, lower than that of the 10,500.0 Yuan of the pre-ERAS group (P<0.001). Also, the indirect cost (mainly included the lost wages) was 5,280.0 Yuan in the ERAS group, lower than that of 6,600.0 Yuan in the pre-ERAS group, owing to the shorter length of hospital stays among ERAS group patients (P<0.001) (*Table 3*).

The total cost included the direct medical cost, the direct non-medical cost and the in direct cost. So, the total cost of the ERAS group was 92,382.4 Yuan, much lower than the 113,261.5 Yuan of the pre-ERAS group (P<0.001) (*Table 3*).

Table 2 Comparison of the clinical observation indicators between the two groups

Indicators	ERAS group (n=374)	Pre-ERAS group (n=594)	P value
Operation time (min)	281.6±59.7	275.9±85.0	0.217
Anesthesia time (min)	301.7±56.7	295.9±84.3	0.198
Intraoperative blood loss (mL)	176.3±244.4	221.4±272.5	0.008
Hospital stays (days)	20.7±5.5	27.9±10.7	<0.001
Postoperative rehabilitation time (days)	10.9±4.7	18.0±9.8	<0.001
Postoperative complications (cases)	1	33	<0.001
Secondary admission within 30 days postoperatively (cases)	86	102	0.026
Reoperation within 30 days after operation (cases)	13	34	0.113

Data are presented as mean ± standard deviation or number. ERAS, enhanced recovery after surgery.

Table 3 Comparison of the direct and indirect costs between the two groups

Cost items	ERAS group (n=374)	Pre-ERAS group (n=594)	P value
Direct medical cost (RMB)	77,953.0 (68,934.1, 88,064.6)	95,338.6 (84,950.9, 109,124.1)	<0.001
Preoperative cost	10,989.2 (8,615.3, 14,987.6)	9,909.8 (7,997.8, 12,201.8)	<0.001
Intraoperative cost	37,961.5 (34,097.3, 47,669.2)	49,005.9 (42,314.2, 56,410.2)	<0.001
Postoperative cost	24,242.0 (19,996.5, 30,051.2)	35,227.3 (28,741.9, 44,527.0)	<0.001
Direct non-medical cost (RMB)	8,400.0 (7,140.0, 10,080.0)	10,500.0 (8,820.0, 13,020.0)	<0.001
Catering and accommodation cost	2,200.0 (1,870.0, 2,640.0)	2,750.0 (2,310.0, 3,410.0)	<0.001
Cost for caregivers	5,200.0 (4,420.0, 6,240.0)	6,500.0 (5,460.0, 8,060.0)	<0.001
Cost of nutrition and health products	1,000.0 (850.0, 1,200.0)	1,250.0 (1,050.0, 1,550.0)	<0.001
Indirect cost (cost for loss of working time, RMB)	5,280.0 (4,488.0, 6,336.0)	6,600.0 (5,544.0, 8,184.0)	<0.001
Total cost (RMB)	92,382.4 (81,656.4, 103,530.9)	113,261.5 (101,665.3, 128,382.6)	<0.001

Data are presented as median (P25, P75). ERAS, enhanced recovery after surgery.

Table 4 Comparison of the cure rates between the two groups

Groups	Number of patients treated	Number of cures	Cure rate (%)
Pre-ERAS group	594	467	78.6
ERAS group	374	290	77.5

Cure rate = number of cured patients/numbers of discharged patients. ERAS, enhanced recovery after surgery.

Cost-effectiveness analysis

The cure rates in the pre-ERAS and ERAS groups were 78.6% and 77.5%, respectively (*Table 4*). Compared with the pre-ERAS group, the ERAS group had a slightly lower effect, but importantly, the ERAS group also had a substantially lower average cost. As expected, the cost-effectiveness ratio of 118,439.0 Yuan in the ERAS group was lower than that of 143,369.0 Yuan in the pre-ERAS group (*Table 5*).

Discussion

At present, surgery is the preferred treatment for early- and intermediate-stage esophageal cancer and has always played a key role in esophageal cancer cure (24). ERAS for esophageal cancer is a novel comprehensive treatment strategy that reduces the occurrence of postoperative complications and can be considered safe and feasible. Based on the retrospective cohort analysis conducted in this study, we verified that the application of ERAS in esophageal cancer surgery could shorten the hospital stays

Table 5 Comparison of the cost-effectiveness between the two groups

Groups	Cost (RMB)	Effectiveness	Cost/effectiveness	Advantage program
Pre-ERAS group	113,261.5	0.79	143,369.0	
ERAS group	92,382.4	0.78	118,439.0	√

ERAS, enhanced recovery after surgery.

of patients and highlighted the positive role of ERAS in the early postoperative rehabilitation and reduction of medical costs.

In our study, owing to the optimized comprehensive ERAS measures, the ERAS group exhibited shorter hospital stays and postoperative recovery times, as well as significantly fewer postoperative complications than the pre-ERAS group. Tang *et al.* reported that the postoperative hospital stays in the "no tube and no ban" group with esophageal cancer was 10 days (6–90 days), which was shorter than the 14 days (10–42 days) in the traditional treatment group (P<0.05) (25). In addition, Wang *et al.* found that compared with the traditional group, the "no tube and no ban" group had markedly shorter postoperative hospital stays (8.1±3.6 *vs.* 11.9±3.4 days, P<0.001) and total hospital stays (18.9±4.7 *vs.* 22.3±4.1 days, P=0.001) (26). It has also been reported that following the implementation of ERAS, patients with esophageal cancer could be discharged on the 8th postoperative day (27). Additionally, a global systematic review showed that compared with traditional surgery, the ERAS diagnosis and treatment model could shorten the length of hospital stays and accelerate rehabilitation in patients undergoing esophageal, colorectal, liver, and lung resection (28).

Furthermore, the results of this study showed that the proportion of secondary admission within 30 days postoperatively was markedly reduced in the ERAS group; however, there was no significant difference in the proportions of 30-day postoperative secondary operation between the two groups, indicating that the implementation of ERAS for esophageal cancer will not increase the risk of secondary admission and secondary operation. These results highlighted the safety and feasibility of ERAS, which is consistent with the findings of previous studies (28,29). In addition, we found that the proportion of minimally invasive surgery in the ERAS group was higher than that in the pre-ERAS group. Patients had less physical trauma, reduced scarring, and faster recovery due to the application of minimally invasive techniques, which might explain why the ERAS diagnosis and treatment model promoted the rehabilitation of patients and improved their quality of life. Several studies have shown that compared with open surgery, thoraco-laparoscopy combined with minimally invasive surgery can shorten the length of hospital stays in patients with esophageal cancer (30,31).

In terms of the patients' treatment related costs, owing to the significantly shortened postoperative hospital stays, the total costs, including the direct medical cost, direct non-medical cost, and indirect cost, were all lower in the ERAS group than those in the pre-ERAS group, reducing the economic burden of medical treatment for patients. In this study, the shortened hospital stays and reduction of complications in the ERAS group also caused the diminution of the average total cost of esophageal cancer patients, which was consistent with the results of a previous meta-analysis (32). In addition, a systematic review showed that the application of ERAS for esophageal cancer could lead to a total cost saving of $1,472 per patient, and univariate sensitivity analysis showed that the ERAS diagnosis and treatment mode was more costly only at the extreme values of the ward, operation, and intensive care costs (16).

This study also found that although the total costs of the ERAS group patients were significantly lower than those in the pre-ERAS group. We observed that some specific cost categories, such as the preoperative cost, were higher in the ERAS group, which may be attributable to the higher cost of consumables in minimally invasive surgery. However, a guideline indicates that the key factor leading to the increased costs of esophageal cancer patients is not the medical minimally invasive surgery, but the postoperative complications (11). Through multiple linear stepwise regression analyses, some studies have shown that the major factor influencing the hospitalization cost of esophageal cancer patients was the length of stay (33-36). Therefore, on the premise of ensuring the treatment effect, reducing the length of hospital stays and postoperative complications is an effective means of controlling the hospitalization cost.

Our study has some limitations that should be noted. Firstly, although the sample size of this study was large, this retrospective cohort study inevitably had a selection bias, and there were some differences in the basic information of patients between the two groups. Secondly, the analysis of indirect costs was based on the average salary in Zhengzhou and not the specific city that each participant was residing in, which might have resulted in some errors. Third, the effect of cost-effectiveness ratio calculation was measured by the disease cure rate, which was subjective to a certain extent although doctors have a unified standard for cure. In future research, we will explore more suitable indicators for further analysis. Moreover, this study only collected data within 1 year. Additional studies covering a longer period are warranted to further verify the stability and accuracy of our results.

In conclusion, the ERAS model for esophageal cancer is an evidence-based approach for multidisciplinary and multimodal optimization of the perioperative process. This study showed that the implementation of ERAS in esophagectomy could accelerate postoperative rehabilitation, reduce the length of hospital stays, postoperative complications, as well as direct and indirect costs, which is an effective means of improving the quality of healthcare.

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Footnote

Reporting Checklist: The authors have completed the CHEERS reporting checklist. Available at https://atm.amegroups.com/article/view/10.21037/atm-22-4169/rc

Data Sharing Statement: Available at https://atm.amegroups.com/article/view/10.21037/atm-22-4169/dss

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://atm.amegroups.com/article/view/10.21037/atm-22-4169/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. This study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was reviewed and approved by the Medical Ethics Committee of Henan Cancer Hospital (No. 2021-KY-0107-004), and individual consent for this retrospective analysis was waived.

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