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Retrospective Study

The role of enhanced recovery after surgery ⁵ in elderly patients with non-small cell lung cancer who underwent video-assisted thoracic surgery (VATS)

Enhanced recovery in NSCLC patients

Mei-Hua Sun, Liu-Sheng Wu, Ying-Yang Qiu, Jun Yan, Xiao-Qiang Li

Abstract

BACKGROUND

This study was designed to investigate the clinical outcomes of enhanced recovery after surgery (ERAS) in the perioperative period in elderly patients with non-small cell lung cancer (NSCLC).

AIM

The aim of this study was to investigate the potential enhancement of thoracoscopic surgery (VATS) in postoperative recovery in elderly patients with non-small cell lung cancer. With the increase in the elderly population, lung cancer is on the rise in elderly patients, and surgical treatment is still one of the main means of treatment. However, the physiological status and postoperative recovery of elderly patients are relatively fragile, so the impact of VATS on their postoperative recovery needs to be thoroughly understood. Through systematic studies, we aim to provide more targeted treatment recommendations for clinical treatment, optimize surgical options, and ultimately improve the surgical efficacy and quality of life of elderly patients with non-small cell lung cancer.

METHODS

We retrospectively analysed the clinical data of 85 elderly NSCLC patients who underwent ERAS (the ERAS group) and 327 elderly NSCLC patients who received routine care (the control group) after video-assisted thoracic surgery (VATS) at the Department of Thoracic Surgery of Peking University Shenzhen Hospital between May 2015 and April 2017. After propensity score matching of baseline data, we analysed the postoperative stay, total hospital expenses, postoperative 48-hour pain score, and postoperative complication rate for the 2 groups of patients who underwent lobectomy or sublobar resection.

RESULTS

After propensity score matching, ERAS significantly reduced the postoperative hospital stay (6.96 ± 4.16 d vs. 8.48 ± 4.18 d, $P = 0.001$) and total hospital expenses (48875.27 ± 18437.5 vs. 55497.64 ± 21168.63 Renminbi (RMB), $P = 0.014$) and improved the satisfaction score (79.8 ± 7.55 vs. 77.35 ± 7.72 , $P = 0.029$) relative to those for routine care. No significant between-group difference was observed in postoperative 48-hour pain score (4.68 ± 1.69 vs. 5.28 ± 2.1 , $p = 0.090$) or postoperative complication rate (21.2% vs. 27.1%, $P = 0.371$). Subgroup analysis showed that ERAS significantly reduced the postoperative hospital stay and total hospital expenses and increased the satisfaction score of patients who underwent lobectomy but not of patients who underwent sublobar resection.

CONCLUSION

ERAS effectively reduced the postoperative hospital stay and total hospital expenses and improved the satisfaction score in the perioperative period for elderly NSCLC patients who underwent lobectomy but not for patients who underwent sublobar resection.

Key Words: Enhanced recovery after surgery; Non-small cell lung cancer; Perioperative care; Propensity score matching

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Core Tip: This study was designed to investigate the clinical outcomes of enhanced recovery after surgery (ERAS) ⁴ in the perioperative period in elderly patients with non-small cell lung cancer (NSCLC). ERAS significantly reduced the postoperative hospital stay (6.96 ± 4.16 d vs. 8.48 ± 4.18 d, $P = 0.001$) and total hospital expenses (48875.27 ± 18437.5 vs. 55497.64 ± 21168.63 RMB, $P = 0.014$) and improved the satisfaction score (79.8 ± 7.55 vs. 77.35 ± 7.72 , $P = 0.029$) relative to those for routine care. ERAS effectively reduced the

postoperative hospital stay and total hospital expenses and improved the satisfaction score in the perioperative period for elderly NSCLC patients who underwent lobectomy but not for patients who underwent sublobar resection.

INTRODUCTION

Lung cancer ranks first in all malignant tumours with respect to morbidity and mortality¹. Surgery is the main treatment for early lung cancer², but the complication rate is approximately 30-50%, resulting in delayed recovery, poor long-term outcomes, and high medical costs³⁻⁵. Elderly patients with lung cancer often experience a slow recovery and high complication rates after thoracic surgery and thus are a high-risk group for surgical treatment⁶⁻⁸. To reduce the postoperative complication rate and accelerate postoperative recovery, many treatment strategies and perioperative management approaches have been incorporated into the surgical field, including infection control, nutritional support, improved fluid management, and comprehensive preoperative assessment. In 2001, Henrik Kehlet, a Danish gastrointestinal surgeon, first proposed the concept of enhanced recovery after surgery (ERAS)⁹. Empirical evidence has demonstrated that effective perioperative management that incorporates ERAS reduces the stress response to surgical trauma and complications and improves surgical safety and patient satisfaction. ERAS has been proven to effectively reduce common complications and general pain in patients. In recent years, the application of ERAS after thoracic surgery has reduced the perioperative complication rate, length of hospital stay, and hospital expenses¹⁰. However, evidence of the effectiveness of ERAS following video-assisted thoracic surgery (VATS) is still remains uncertain. In particular, no clinical studies have been conducted to investigate ERAS in elderly patients with lung cancer who underwent VATS.

¹ This study was designed to retrospectively analyse the clinical outcomes of ERAS in elderly patients with lung cancer who underwent VATS at Peking University Shenzhen Hospital over a 5-year period and to investigate the role of ERAS (after propensity score matching) in improving postoperative recovery.

MATERIALS AND METHODS

1.1 Clinical data

We retrospectively analysed the clinical data of 412 elderly patients with lung cancer who underwent VATS at the Department of Thoracic Surgery of Peking University Shenzhen Hospital between May 2015 and April 2017. Of these patients, 271 were men, and 141 were women; their mean age was 72.41 ± 4.7 years; and 85 patients underwent ERAS (the ERAS group), and 327 patients received routine care (the control group). Moreover, 187 patients underwent sublobar resection, and 225 patients underwent lobectomy; 330 patients were diagnosed with adenocarcinoma, and 82 patients were diagnosed with squamous cell carcinoma; and 235 patients were in TNM stage I, and 92 patients were in TNM stage II.

The inclusion criteria were as follows: 1) patients who underwent VATS and were pathologically confirmed to have non-small cell lung cancer (NSCLC) after surgery; 2) patients aged 65-80 years old; 3) patients with NSCLC in TNM stage I to II confirmed by postoperative pathology; and 4) patients with complete clinical data. The exclusion criteria were as follows: 1) patients with pneumonectomy or 2) patients with pathologically confirmed small cell lung cancer.

1.2 Methods

1.2.1 Perioperative management

The patients were divided into the control group and the ERAS group. The control group received routine care, and the ERAS group underwent ERAS (Table 1).

Preoperative management: All patients underwent a one-stop preoperative assessment by surgeons, anaesthesiologists, and nurses to facilitate optimal preoperative preparation and were closely monitored during and after the operation for any complications. The ERAS group was given a copy of an ERAS education brochure with detailed descriptions about daily goals and was asked to complete a

diary. Intraoperative management: all patients were given prophylactic antibiotics during the induction period. General anaesthesia was administered with double-lumen tracheal intubation and single-lung breathing. Intraoperative rehydration was achieved with intravenous infusion of balanced fluid, and hypertensive or antihypertensive drugs were given based on blood pressure monitoring during the operation. The indications and the feasibility for surgery were determined in accordance with the China Guidelines for the Diagnosis and Treatment of Primary Lung Cancer (2015). The scope of surgical resection was determined by the treating physician based on patient conditions. Effort was taken to make a small incision, and absorbable sutures were used to close the incision. At the end of surgery, a closed thoracic drainage tube was placed according to routine procedures. Postoperative management: Intravenous infusion was minimized, with adequate analgesia. Non-steroidal anti-inflammatory drugs (NSAIDs) and acetaminophen were used for pain management. Opioids were avoided whenever possible to prevent postoperative nausea and vomiting (PONV) and other opioid-related adverse reactions. Patients were encouraged to get out of bed as soon as possible. The catheter was removed at 12 h after operation (Table 2).

1.2.2. Criteria for discharge and follow-up

Discharge criteria were as follows: (1) removal of the closed thoracic drainage tube; physical mobility; (2) no difficulty breathing (no shortness of breath, wheezing or stridor; oxygen saturation > 94%); and (3) no serious complications; complications (if any) were under control.

1.2.3 Calculation of medical expenses

The hospital medical records were used to record and calculate the total medical expenses, including laboratory tests, physical examinations, medications, nursing, surgery, supplies, and postoperative rehabilitation.

1.2.4 Satisfaction

A homemade satisfaction questionnaire was used during the week after discharge to evaluate patient satisfaction. The contents included staff attitude, operating techniques, timeliness of nursing, overall hospital experience, and pain score. Quality of life was analysed, including physical performance, physical pain, mental state, and general health.

1.2.5 Statistical analysis

R language 3.5.3 was used for propensity score matching of pathological classification, TNM stage, and surgical approach at 1:1 between the ERAS group and the control group.

SPSS v25.0³ was used for statistical analysis. Measurement data are expressed as the mean value \pm standard deviation and analysed with the independent sample t-test or Mann-Whitney U test; count data are expressed as the frequency and were analysed with the chi-square test⁶ or Fisher's exact test. All tests were two-sided, and $p < 0.05$ was considered statistically significant.

RESULTS

2.1 Baseline data

Among the 412 elderly patients with lung cancer who underwent VATS, 327 patients were in the control group and 85 patients were in the ERAS group. No significant between-group differences were observed regarding age ($P = 0.220$), sex ($P = 0.982$), body mass index (BMI) ($P = 0.540$), or forced expiratory volume in the first second (FEV1) ($P = 0.615$)(Fig 1). Moreover, 330 patients had adenocarcinoma, and 82 patients had squamous cell carcinoma; 290 patients were in TNM stage I, and 122 patients were in stage II; 187 patients underwent sublobar resection, and 225 patients underwent lobectomy (Table 3). After matching, the control group and the ERAS group each included 85 patients.

No patient died during the perioperative period or required blood transfusion. At the end of surgery, the tracheal intubation was removed in the operating room, and the

patients were able to breathe spontaneously with normal blood gas analysis results. All patients were sent back to the general ward, and no patient required mechanical ventilation in the intensive care unit. Before discharge, any postoperative complications were alleviated and resolved with treatment.

2.2 Clinical outcome measures

ERAS significantly improved postoperative hospital stay (6.98 ± 4.3 vs. 8.92 ± 4.42 d, $P = 0.002$), total hospital expenses (52041.86 ± 19062.33 vs. 60760.79 ± 20511.58 , $P = 0.016$), and overall satisfaction (79.66 ± 7.5 vs. 76.26 ± 7.42 , $P = 0.013$) in the lobectomy subgroup (Table 4). Postoperative hospital stay also improved in the sublobar resection subgroup (6.94 ± 4.03 vs. 7.86 ± 3.78 d, $P = 0.09$), but the differences of total hospital expenses ($P = 0.247$) and overall satisfaction ($P = 0.621$) did not reach statistical significance. In the ERAS group ($n = 85$), 3 patients had atelectasis, 9 had pulmonary infection, 4 had atrial fibrillation, and 2 had arrhythmia; the postoperative complication rate was 21.2%. In the control group ($n = 85$), 4 patients had atelectasis, 12 had pulmonary infection, 4 had atrial fibrillation, and 3 had arrhythmia; the postoperative complication rate was 27.1%. The difference did not reach statistical significance. (Table 5).

DISCUSSION

ERAS is a multimodal perioperative protocol based on best medical evidence. In the 1990s, Kehlet *et al* first used it for patients undergoing colectomy to enhance postoperative recovery¹¹. It includes preoperative optimization, intraoperative stress management, and enhanced postoperative recovery, with the goal of accelerating the recovery and resumption of normal activities. It reduces the length of the hospital stay and hospital expenses without increasing the readmission rate. With the gratifying results and low surgical wound, VATS approach is recommended as the standard scheme by several international academic organizations, including the European Society of Thoracic Surgeon (ESTS), the American College of Chest Physicians (ACCP) and Minimally Invasive Cardiothoracic Surgery (MICS)¹². In thoracic surgeries, VATS is a main part of ERAS protocols in the relevant guidelines¹³. At present, class I evidence

of the effectiveness of ERAS after thoracic surgery is scarce, especially in elderly patients with lung cancer. This study showed that ERAS improved the clinical efficacy of VATS in elderly patients with lung cancer. At present, data on ERAS in patients undergoing thoracic surgery are limited. Cerfolio *et al* applied ERAS in patients undergoing open pneumonectomy, with a special focus on preoperative patient education, the use of epidural anaesthesia, active standardized removal of the catheter and drainage tube after surgery, early physical movement, and a daily plan for discharge within 4 days after surgery¹⁴. The intervention accelerated recovery without increasing the complication or mortality rate. A small randomized controlled study also showed that preoperative food intake (no fasting), conduction anaesthesia, early postoperative food intake, and early physical movement significantly reduced the incidence of postoperative pulmonary complications¹⁵. Salati *et al* performed propensity score matching and demonstrated that ERAS effectively reduced the length of the hospital stay. The study focused on preoperative patient education, standardized postoperative care, and active drainage tube management¹⁶. In recent years, thoracic surgery-specific ERAS has gradually improved. Madani described their ERAS procedures for open lobectomy, including standardized care, as well as preoperative, intraoperative, and postoperative management. The study showed that ERAS significantly reduced the length of the hospital stay and complications without increasing the readmission rate. However, their procedures were relatively conservative. Recent studies have shown that paraspinal block (instead of epidural analgesia) and a more aggressive closed thoracic drainage regimen may provide greater benefits to patients¹⁷⁻¹⁹. This study showed that ERAS significantly reduced postoperative hospital stay, total hospital expenses, and postoperative complications and improved satisfaction. Subgroup analysis per surgical approach (lobectomy *vs* sublobar resection) showed that ERAS did not significantly reduce postoperative hospital stay, total hospital expenses, and postoperative complications nor significantly improve satisfaction in the sublobar resection subgroup. The scope of sublobar resection was relatively small, with less impact on postoperative recovery, which may explain the

lack of a significant difference between patients with sublobar resection in the ERAS group and the control group. On the other hand, lobectomy involves a greater scope of resection and surgical trauma, and thus, ERAS was superior to routine care in postoperative recovery. These data provide a reference for the selection of an appropriate rehabilitation regime. For ERAS, clinicians must pay attention to the readmission rate. Some studies have shown that for patients with lung cancer, readmission is related to shorter survival¹⁹. However, it is not clear whether ERAS will increase the readmission rate of lung cancer patients²⁰. In this study, the 30-day readmission rate was 1.2% (only 1 patient in the ERAS group; $p > 0.05$), which was lower than those reported by other studies.

In recent years, a large body of evidence has demonstrated that VATS reduces complications and improves the prognosis of patients with lung cancer^{5,21}. At present, however, evidence of the effectiveness of ERAS following VATS is inadequate, especially evidence on the role of ERAS following VATS in elderly patients with lung cancer. This was the first study to investigate the role of ERAS in the perioperative period in elderly patients with lung cancer. We performed propensity score matching to optimize the control group and comprehensively analysed perioperative outcome measures, including postoperative hospital stay, total hospital expenses, postoperative 48-hour pain score, and satisfaction score. This study showed that for elderly patients with lung cancer, ERAS effectively improved postoperative recovery (including hospital stay and hospital expenses) and patient satisfaction and reduced the postoperative complication rates.

CONCLUSION

This is the first study to perform propensity score matching to demonstrate the effectiveness of ERAS for elderly patients with lung cancer. Further subgroup analysis showed that ERAS had significant effects in the lobectomy subgroup. In summary, ERAS may be used as an effective treatment for elderly patients with lung cancer, especially patients undergoing lobectomy.

ARTICLE HIGHLIGHTS

Research background

¹ Lung cancer is the leading cause of death worldwide, and non-small-cell lung cancer in the elderly accounts for a significant proportion. With the significant growth of the aging population, the need for surgical treatment of elderly patients has gradually become more prominent. Thoracoscopic surgery (VATS) has become an important choice ¹ for the treatment of senile non-small cell lung cancer due to its characteristics of less trauma and rapid recovery. However, current systematic studies on VATS in postoperative recovery in elderly patients are relatively limited. Therefore, an in-depth understanding of the influence of VATS on elderly patients and revealing its potential role in postoperative rehabilitation are of great significance for guiding the individualized treatment of elderly patients with NSCLC and improving surgical results.

Research motivation

² The aim of this study was to investigate the potential enhancement of thoracoscopic surgery (VATS) in postoperative recovery in elderly patients with non-small cell lung cancer.

Research objectives

This study was designed to investigate the clinical outcomes of enhanced recovery after surgery (ERAS) ⁴ in the perioperative period in elderly patients with non-small cell lung cancer (NSCLC).

Research methods

We retrospectively analysed the clinical data of 85 elderly NSCLC patients who underwent ERAS (the ERAS group) and 327 elderly NSCLC patients who received routine care (the control group) after video-assisted thoracic surgery (VATS) at the

Department of Thoracic Surgery of Peking University Shenzhen Hospital between May 2015 and April 2017. After propensity score matching of baseline data, we analysed the postoperative stay, total hospital expenses, postoperative 48-hour pain score, and postoperative complication rate for the 2 groups of patients who underwent lobectomy or sublobar resection.

Research results

After propensity score matching, ERAS significantly reduced the postoperative hospital stay (6.96 ± 4.16 d vs. 8.48 ± 4.18 d, $P = 0.001$) and total hospital expenses (48875.27 ± 18437.5 vs. 55497.64 ± 21168.63 Renminbi (RMB), $P = 0.014$) and improved the satisfaction score (79.8 ± 7.55 vs. 77.35 ± 7.72 , $P = 0.029$) relative to those for routine care. No significant between-group difference was observed in postoperative 48-hour pain score (4.68 ± 1.69 vs. 5.28 ± 2.1 , $p = 0.090$) or postoperative complication rate (21.2% vs. 27.1%, $P = 0.371$). Subgroup analysis showed that ERAS significantly reduced the postoperative hospital stay and total hospital expenses and increased the satisfaction score of patients who underwent lobectomy but not of patients who underwent sublobar resection.

Research conclusions

ERAS effectively reduced the postoperative hospital stay and total hospital expenses and improved the satisfaction score in the perioperative period for elderly NSCLC patients who underwent lobectomy but not for patients who underwent sublobar resection.

Research perspectives

We look forward to more large-sample, multicenter studies to validate the recovery benefits of VATS in elderly patients with non-small cell lung cancer and to further clarify the safety and effectiveness of the surgical technique. At the same time, combined with biological markers and imaging techniques, the specific mechanism of VATS on postoperative inflammatory response, immune function, and quality of life in

elderly patients was further studied. With the help of advanced technical means, the individual differences of elderly patients were finely delineated to provide a more accurate basis for personalized surgical treatment. In addition, the long-term efficacy and survival rate of VATS in elderly patients were evaluated through long-term follow-up to comprehensively understand the long-term impact of surgery. These future research directions will provide an in-depth and comprehensive understanding for further promoting the development of surgical treatment for elderly non-small cell lung cancer.

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