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Original Article

Risk factors for enhanced recovery after surgery failure in patients undergoing lung cancer resection with concomitant cardiovascular disease: A single-center retrospective study

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ABSTRACT

Objective: Enhanced recovery after surgery (ERAS) has been widely used in patients with lung cancer, and its effectiveness has been confirmed; however, some lung cancers with poor clinical outcomes lead to ERAS failure after radical resection. This study aimed to analyze risk factors associated with ERAS failure after radical resection in patients with lung cancer and concomitant cardiovascular disease.

Methods: In total, 198 patients who underwent ERAS following radical lung cancer surgery for concomitant cardiovascular disease between January 2022 and September 2023 were enrolled in this retrospective study. The patients were categorized into two groups based on the definition of ERAS failure: ERAS success group ($n = 152$) and ERAS failure group ($n = 46$). Univariate and multivariate analyses were performed to investigate the risk factors of ERAS failure.

Results: Univariate analysis showed that gender, tumor location, operation time, estimated blood loss (EBL), suction drainage, and total cholesterol were associated with ERAS failure. Multivariate analysis showed that operation time (odds ratio [OR] = 1.015; $P = 0.011$) and suction drainage (OR = 3.343; $P = 0.008$) were independent risk factors for ERAS failure.

Conclusions: Operation time and suction drainage were independent risk factors for ERAS failure after radical resection of combined cardiovascular lung cancer. Therefore, improving surgical efficiency and postoperative chest drain management are important for successful ERAS.

Introduction

In total, approximately 2,001,140 new cancer cases and 611,720 cancer deaths are predicted to occur in 2024, with lung and bronchus estimating approximately 234,580 new cases and 125,070 deaths in the United States; thus, lung cancer remains the leading cause of cancer deaths.[1] Lung cancer accounts for the highest incidence and mortality rate worldwide, and more than half (69%) of lung cancer patients have comorbidities, with cardiovascular disease (CVD) being a common comorbidity.[2,3] Studies have shown that patients with CVD, such as heart disease, vascular disease, and hypertension, have a 67% increased risk of developing lung cancer, and patients with lung cancer and comorbid CVD, such as coronary artery disease (CAD), hypertension, arrhythmias, and peripheral atherosclerosis, have a 30% increased risk of death compared to patients with lung cancer without comorbidities.[4,5] Lobectomy is the most important treatment for early stage lung cancer.[6] Postoperative complications, such as prolonged hospital stay, unplanned reoperation after surgery, and readmission or death, affects patients' quality of life, reduces hospital efficiency, and reduced their social and economic benefits.[7] Therefore, perioperative rehabilitation is particularly important.

In 1997, Kehlet proposed the concept of enhanced recovery after surgery (ERAS), which is the use of multidisciplinary teamwork to administer various rehabilitory means to minimize the traumatic stress of surgery on the patient's psychology and physiology, thus aiming to decrease the postoperative hospitalization time, reduce the incidence of postoperative complications and mortality, and improve patient satisfaction.[8,9] It was initially applied in colon surgery, then gradually widely used in > 20 subspecialties such as neurology, hepatobiliary surgery, thoracic surgery, gynecology.[10] Limited evidence exits regarding preoperative ERAS in lung cancer with CVD. Thus, existing guidelines for perioperative lung cancer management were used with path-specific modifications made based on clinical practice-derived logical theories.

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However, many concerns remain to be overcome owing to the large number of personnel and procedural changes involved during guideline implementation. For instance, patients with lung cancer who undergo percutaneous coronary intervention < 3 years before surgery routinely use antiplatelet drugs to prevent stent thrombosis; however, when undergoing lung cancer resection, the American College of Chest Physicians does not recommend routine heparinization for patients who are on dual antiplatelet therapy and require surgery. Heparinization may be an obstacle to pain control during epidural anesthesia and may lead to heparin-induced thrombocytopenia. Therefore, perioperative antithrombotic therapy is controversial.[11] As CVD affects the motor function of patients with lung cancer, patients with poor functional status (defined as the inability to walk four blocks or climb two flights of stairs) increase the incidence of perioperative complications.[12] Preoperative cardiac risk assessment by exercise capacity and functional status is required to predict the probability of a postoperative major adverse cardiac event (MACE) in patients undergoing noncardiac surgery.[13] Postoperative pain can increase vagal tone, leading to sinus bradycardia and even cardiac block, however best practices for perioperative pain management have not been fully elucidated.[14]

Although ERAS is widely used and known to be effective in the field of lung cancer, the presence of cardiovascular complications, such as CAD and arrhythmia, before the operation increases the risk of postoperative MACE and perioperative death in patients with lung cancer, thus affecting the ERAS outcome.[11,15] Myocardial infarction (MI) is believed to be an independent risk factor for perioperative stroke and is associated with an eight-fold increase in perioperative mortality.[16] Preoperative arrhythmias, such as atrial flutter or supraventricular tachycardia, may respond to vagal manipulation or nodular medication. Studies have shown an increased atrial fibrillation (AF) incidence post-noncardiac surgery. The peak incidence occurred 1–3 d post-surgery, ranging from 0.37% in large population studies of non-cardiothoracic surgery to 30% after major non-cardiothoracic surgery, such as pneumonectomy.[17–19] Mcfalls et al.[20] reported that coronary revascularization before elective macrovascular surgery did not improve long-term survival or reduce the incidence of early postoperative outcomes, including death, MI, and length of hospital stay in patients with stable CAD.

It has been reported that the number of patients with cancer complicated with CVD has increased from 5% to 43%, with the percentage of patients increasing to varying degrees in different regions.[21,22] Furthermore, CVD and lung cancer share many risk factors,[23] such as smoking, alcohol consumption, and obesity. These risk factors can induce inflammation,[24,25] which may cause lung cancer by secreting inflammatory mediators such as cytokines and growth factors, increasing reactive oxygen species production, and inducing DNA damage and chromosomal instability.[26] Oxidative stress and chronic inflammation worsens the prognosis of patients with stages I and II lung cancer with CAD.[27] Pleiotropy, such as DYRK1B mutations, also increases the risk of CAD and lung cancer.[28] Tobacco exposure is more common in patients with lung cancer and may contribute to CVD by reducing nitric oxide levels, inducing vascular dysfunction, and promoting oxidative stress.[29] However, few reports have elucidated the risk factors associated with comorbid CVD impact on the clinical deterioration of patients with lung cancer after using ERAS measures. This retrospective study aimed to analyze the risk factors associated with ERAS failure that may affect patients with lung cancer and comorbid CVD, with the aim to facilitate early recovery for future interventions in these variables at an early stage.

Methods

Patients and methods

In total, 198 patients who underwent the ERAS combined with CVD (Table 1) and lung cancer radical surgery between January 2022 and September 2023 were enrolled in our retrospective study. The exclusion criteria were preoperative radiotherapy, other tumors in combination, autoimmune disorders, severe blood disorders, severe endocrine system disorders, pregnancy or lactation, and emergency surgery.

Table 1
Cardiovascular comorbidities.

Cardiovascular comorbidities	Diagnose
Hypertension	SBP on both days is ≥ 140 mmHg and/or DBP on both days is ≥ 90 mmHg.[30] For patients with preexisting CVD or those considered a high cardiovascular risk the WHO guidelines for the pharmacological treatment of hypertension in adults, recommends blood pressure lowering treatment if SBP is ≥ 130–139 mmHg.[31]
Coronary artery disease	Angiographic: the severity of coronary stenosis (> 50%); electrocardiographic abnormalities: deviations in the ST segment, morphology of ST-segment changes (horizontal or downsloping versus upsloping), and deviation magnitude; provocative testing for inducible myocardial ischemia: ST elevation or depression during electrocardiographic monitoring; exercise or pharmacological stress testing: assessment of wall motion abnormalities on echocardiography and/or reversible perfusion defects by nuclear scintigraphy or magnetic resonance imaging.[32]
Atrial fibrillation	ECG: Irregularly irregular R–R intervals; absence of repeating P waves and irregular atrial activations; minimum duration of ECG tracing of 30 s is required (entire 12-lead ECG).[33]
Tachycardia	Atrial rates > 100 b.p.m. at rest. (ECG: narrow or wide QRS tachycardias or regular rhythms) or treated with catheter ablation therapy.[34]
Bradycardia	Atrial rates were < 50 b.p.m. at rest or after a pacemaker was placed.[35]
Premature ventricular complexes	12-lead ECG: precordial T-wave inversion beyond lead V_2 or right ventricular conduction delay pathological Q waves, an early precordial transition accompanied by a prominent S wave in V_6.[36]
Premature atrial contractions	An atrial complex with similar QRS morphology to the sinus beat and < 80% coupling interval to the preceding QRS, when compared to the mean R–R interval.[37]
Tetralogy of Fallot	Echocardiogram: right ventricular outflow tract obstruction, ventricular septal defect, overriding of the aorta, and right ventricle hypertrophy.[38]

b.p.m., beat per minute; DBP, diastolic blood pressure; ECG, electrocardiogram; SBP, systolic blood pressure; CVD, cardiovascular disease; WHO, World Health Organization.

Demographic characteristics and clinical data

Patient demographic characteristics and clinical data were obtained from electronic cases, and data analysis included: preoperative factors (gender, age, body mass index [BMI], tumor node metastasis [TNM] stage, comorbidities, blood pressure classification, American Society of Anesthesiologists [ASA] classification, New York Heart Association [NYHA] class, preoperative hemoglobin, troponin, myoglobin, albumin, globulin, albumin/globulin [A/G], total cholesterol, triglyceride, high-density lipoprotein [HDL], low density lipoprotein [LDL], lipoprotein α, carcinoembryonic antigen [CEA], heat shock protein 90 α, interleukin-1β [IL-1β], tumor necrosis factor-α [TNF-α], forceful lung capacity [FVC%], first second forceful expiratory volume [FEV_1], FEV_1/FVC, peak expiratory flow [PEF]), intraoperative indices (type of lobectomy, number of lymph nodes, surgical approach, operation time, estimated blood loss [EBL], intraoperative fluid, urinary catheter) and postoperative outcomes (C-reactive protein [CRP], procalcitonin [PCT], suction drainage, postoperative transfer to intensive care unit [ICU] or not, postoperative length of stay, complications, unplanned reoperation, unplanned readmission, death).

ERAS protocol

All patients underwent the same ERAS protocol (Table 2) and discharge criteria. The treatment plan was provided by the same medical team. The clinical data of the patients were collected by the same

Table 2
ERAS protocol for lung cancer with cardiovascular surgery.

Preoperative	Health education on postoperative drainage tube precautions and bed and lower limb exercises was provided to the patients using the teach-back method through video broadcasting and health brochures. Nutritional risk screening 2002 (NRS 2002) was used to assess the nutritional status of patients before surgery, and nutritional meals were provided by the nutristion department after consultation. Patients received 400 mL of a 12.5% carbohydrate drink 2 h before surgery without mechanical bowel preparation. Opioids and other analgesics were not routinely used, and antibiotics were used prophylactically.
Intraoperative	No nasogastric tube was routinely used. Remifentanil and sufentanil were used for general anesthesia combined with peripheral nerve block. The patient's body temperature was monitored during and until the operation, then the core body temperature was maintained at $\geq 36^{\circ}C$ facilitated by infusion heating devices.
Postoperative	After waking up, the patients received warm water and were instructed to eat the nutritional powder configured by the nutrition department. They gradually transitioned to a semi-liquid diet. The catheter was removed 24 h post-surgery. Sit up in bed on the 1st postoperative day and lowered limb ankle pumping and breathing exercises. Move out of bed on the 2nd postoperative day, and ambulation for at least 2 h daily depending on the patient's condition. Patients were instructed to follow up in the outpatient clinic on the 30th postoperative day.

ERAS, enhanced recovery after surgery; NRS, nutrition risk screening.

researchers to minimize data bias. The discharge criteria for patients are that they have returned to a normal diet, vital signs are stable and normal, there are no serious postoperative complications, no obvious pain, and no infection symptoms; the patients wounds are free of infection and healing is improved; chest drains, urinary catheter, and other drainage tubes need to be removed, and if they need to be carried for a prolonged duration, there should be no obvious adverse reactions and regular follow-up visits should be provided; and the patients and their families agree to be discharged from the hospital.

ERAS failure

ERAS failure was defined as a prolonged postoperative hospital stay (the average length of stay for patients with lung cancer in this study was 5 d), postoperative ICU stay > 24 h; unplanned postoperative reoperation and rehospitalization or death within 30 postoperative days. Fulfilling one of these conditions was considered an ERAS failure.[39] Postoperative complications were assessed according to the Clavien–Dindo classification complication grade:[40] grade I, not requiring surgical or radiologic intervention, for example, atrial fibrillation which can be treated with medications and pulmonary atelectasis requiring physiotherapy; grade II, requires other medications, transfusion, or parenteral nutrition; grade III, requires surgical, endoscopic, or radiologic treatment, for example, antibiotic treatment for pneumonia and urinary tract infection; grade IV, requiring IC/ICU treatment for life-threatening complications, for example, lung failure requiring intubation; and grade V, causes death. Patients with lung cancer and cardiovascular comorbidities who underwent 198 radical lung cancer operations with ERAS were categorized into an ERAS success group ($n = 152$) and ERAS failure group ($n = 46$).

Data analysis

Patient data were obtained from electronic medical records and entered into Excel spreadsheets (Microsoft Corp., Washington, Redmond). IBM SPSS Statistics version 25.0 (IBM Corp., Armonk, NY) was used for data analysis. Classification variables were described by frequency percentages, continuous variables following normal distribution were described by mean ± standard deviation, and non-normal distribution continuous variables were described by median and interquartile ranges (IQR). Univariate analysis of ERAS failure was performed using chi-square or Fisher's exact tests for categorical variables, and two independent sample *t*-tests or Mann–Whitney *U* tests for continuous variables. In multivariate analysis, binary logistic regression was used to determine independent risk factors ($P < 0.05$) for ERAS failure.

Ethical considerations

This study was conducted after obtaining approval from the Research Ethics Review Committee of Binzhou Medical University (IRB No. 2023-311). Because of the retrospective nature of our study, the data were obtained from available medical records and the identity and privacy of the subjects were not involved; therefore, informed consent was waived by our Institutional Review Board.

Results

Demographics and perioperative outcomes

Finally, we enrolled 198 patients with lung cancer and cardiovascular comorbidities (Fig. 1). Baseline and clinical characteristics of the patients are shown in Table 3. Thirty-one (15.7%) patients experienced postoperative complications, including a small pneumothorax ($n = 16$), chylothorax ($n = 4$), pleural effusion ($n = 3$), postoperative atrial fibrillation (POAF; $n = 3$), lower extremity arterial embolism ($n = 2$), pulmonary infection ($n = 2$), and pulmonary atelectasis ($n = 1$).

Of the 198 patients, 46 (23.2%) were defined as ERAS failure (Table 4), whereby the average length of hospital stay was 5 d, and 42 (21.2%) patients had a prolonged hospital stay. Three (1.5%) patients were admitted to the ICU for intraoperative oxygenation of < 80 in the 24 h postoperative period; six (3.0%) had an unplanned reoperation, including two patients undergoing angiography for venous filter implantation, two undergoing closed chest drainage for pneumothorax, one undergoing chest tube ligation for chylothorax, and one undergoing bronchoscopy for pulmonary atelectasis; three (1.5%) patients were unplanned readmitted post-surgery, reasons for readmission included chylothorax ($n = 1$), massive pleural effusion after going home ($n = 1$), poor healing of the postoperative incision ($n = 1$); and no patient died within 30 postoperative days.

Risk factors for ERAS failure

Univariate analysis ($P < 0.05$) showed that ERAS failure was associated with gender, tumor location, operation time, EBL, suction drainage, and total cholesterol (Table 5). Univariate significant factors were included in the binary logistic regression of multivariate analysis, which showed that operation time (odds ratio [OR] = 1.015; $P = 0.011$) and suction drainage (OR = 3.343; $P = 0.008$) were independent risk factors for ERAS failure (Table 6).

Discussion

CVD prevalence, predominantly hypertension, is increasing due to sociodemographic, environmental, poor health behaviors, and clinical factors.[41,42] CVD and lung cancer share common risk factors such as smoking, advanced age, and similar case-physiologic mechanisms such as inflammation and oxidative stress.[23,26] Previous studies have focused on demonstrating that ERAS application reduces postoperative pulmonary complications (PPCs) and mortality. However, analyzing factors affecting ERAS failure is rare and of little interest to patients with CVD. Herein, we assessed the possible predictive factors of lung cancer in patients with CVD.

This study's univariate analysis showed that ERAS failure was associated with gender, tumor location, operation time, EBL, suction

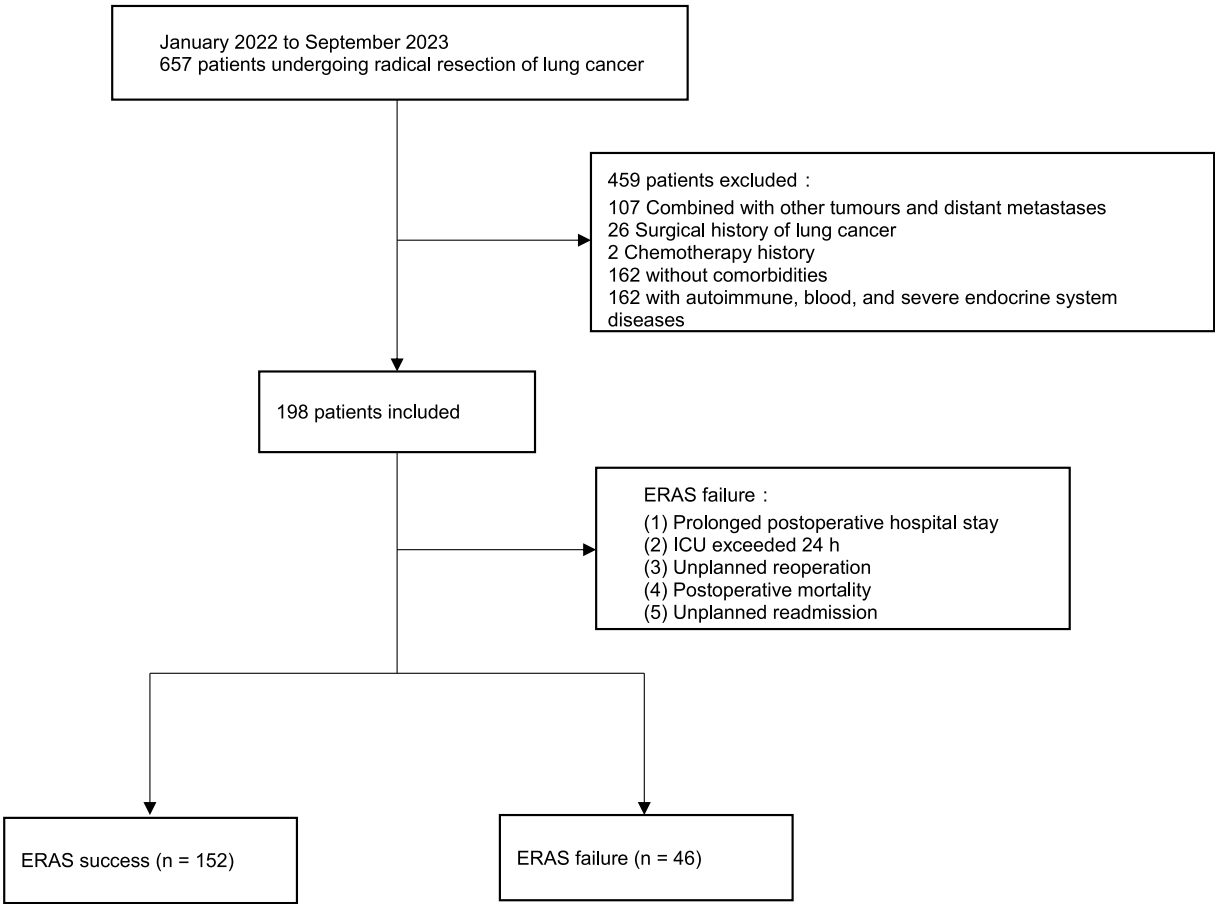

Fig. 1. Flow chart of patients enrolled and included. ERAS, enhanced recovery after surgery; ICU, intensive care unit.

drainage, and total cholesterol. A bilobectomy refers to the simultaneous resection of two unilateral lung lobectomies: upper and lower lobes of the left lung, upper and lower lobes of the right lung, upper and middle lobes of the right lung, and lower and middle lobes of the right lung. Except for gender, the other variables were related to the poor physical status of the patients, difficult surgical techniques, and slow postoperative recovery, which is consistent with clinical practice. Multivariate analysis showed that operation time (OR = 1.015; $P = 0.011$) and suction drainage (OR = 3.343; $P = 0.008$) were independent risk factors for ERAS failure. There were no meaningful cardiovascular-related indicators in the multifactorial results, and some studies showed no correlation between the cardiovascular comorbidities of lung cancer and PPCs, with no difference in postoperative outcomes and no significant difference in mortality and morbidity,[43] which is consistent with our findings.

Operation time was independent risk factors for ERAS failure

Lobectomy is the preferred surgical method for patients with lung cancer.[44] With the gradual development of minimally invasive surgery, video-assisted thoracoscopic and robotic-assisted thoracoscopic surgeries have been widely used in thoracic surgery, and minimally invasive techniques reduce postoperative complications and decrease hospitalization time compared with thoracotomy.[45] According to a meta-analysis by Aiolfi et al.,[46] the mean operative time for video-assisted thoracic surgery and robotic lobectomy for non-small cell lung cancer was 99–247 min, which is consistent with the mean operative time observed in the current study (118.4 min). Patients undergoing lung resection experience unique physiological changes, such as lung atelectasis/reinflation with one-lung ventilation (OLV), hypoperfusion/ischemia and reperfusion, and increased inflammatory mediators.[47] Surgical stress/trauma and mechanical ventilation at the onset of lung cancer surgery generates free radicals with a slight increase in malondialdehyde levels, and surgical trauma releases inflammatory cytokines and neutrophil chemotaxis, which produces large oxidants amounts. During surgery, the scavenging systems cannot confront the oxidant outburst of the trauma itself, causing oxidative stress.[48] The longer the duration of pulmonary atelectasis, the stronger the subsequent oxidative stress, affecting organ and tissue function. Free oxygen radicals are highly reactive species that interact with cytoarchitectural molecules, causing endothelial cell dysfunction. After free radicals are produced, OLV exerts a severe oxidative load on the organism a few minutes after pulmonary reventilation in atelectasis. During surgery, systemic pro-inflammatory and compensatory anti-inflammatory responses induce systemic inflammation (SI).[49] In SI, the innate immune system and response are activated. Primary immune cells capable of phagocytosis and antigen presentation (neutrophils, macrophages, natural killer cells, and dendritic cells) migrate to the surgically injured tissues. These primary immune cells recognize injury-associated molecular patterns in damaged tissues (e.g., surgical incisions and preparations), releasing pro-inflammatory and anti-inflammatory cytokines, such as IL-6, IL-8, IL-10, IL-1β, and TNF-α. IL-6, IL-8, and IL-10 levels, among others, may be elevated at skin closure after pneumonectomy, increasing the risk of postoperative complications.[50] Operative time increases the risk of intraoperative hypoxemia, delayed extubation, PPCs, prolonged air leaks, POAF, transfusions, and other adverse perioperative prognostications, and decreases the likelihood of early hospital discharge,[6,51] which is consistent with our findings.

The impact of operation time on nursing practice and research

Studies have shown that organizational change in hospitals is often associated with high failure rates.[52] To improve surgical efficiency,

Table 3
Characteristics of the patients ($N = 198$).

Variables	n/mean ± SD	%
Age (years)	64.9 ± 7.5	
Gender		
Male	86	43.4
Female	112	56.6
BMI (kg/m^2)	25.1 ± 3.5	
Type of lobectomy		
Left upper lobectomy	44	22.2
Left lower lobectomy	35	17.7
Right upper lobectomy	62	31.3
Right middle lobectomy	9	4.5
Right lower lobectomy	35	17.7
Bilobectomy	13	6.6
TNM stage		
I	186	93.9
II	3	1.5
III	9	4.5
ASA classification		
I	7	3.5
II	134	67.7
III	56	28.3
Comorbidities		
Hypertension	160	80.8
Coronary artery disease	56	28.3
Atrial fibrillation	5	2.5
Tachycardia	5	2.5
Bradycardia	4	2.0
Premature ventricular complexes	3	1.5
Premature atrial contractions	2	1.0
Tetralogy of Fallot	1	0.5
Surgical approach		
Thoracoscope	159	80.3
Da Vinci Robotic	39	19.7
Operation time (min)	118.4 ± 33.2	
EBL (mL)	21.5 ± 19.5	
Intraoperative fluid (mL)	1083.3 ± 388.4	
Complications grade		
I	9	
II	19	
III	3	
IV	0	
Total	31	15.7

ASA, American Society of Anesthesiologists; BMI, body mass index; Complications grade, Clavien–Dindo classification complication grade; EBL, estimated blood loss; *n*, frequency; SD, standard deviation; TNM, tumor node metastasis.

Table 4
Enhanced recovery program failure in 198 lung cancer with cardiovascular surgery.

Reasons	*n*	%
Prolonged postoperative hospital stay[a]	42	21.2
ICU exceeded 24 h[b]	3	1.5
Unplanned reoperation[c]	6	3.0
Postoperative mortality[d]	0	0.0
Unplanned readmission[e]	3	1.5
Total[f]	46	23.2

ICU, intensive care unit.
[a] More than 5 postoperative days.
[b] Postoperative stay in the ICU exceeded 24 h.
[c] Unplanned reoperation within 30 postoperative days.
[d] Postoperative mortality.
[e] Unplanned readmission within 30 postoperative days.
[f] Including one cases simultaneously indexed in two categories (a) and (b), five cases simultaneously indexed in two categories (a) and (c), two cases simultaneously indexed in two categories (a) and (e).

factors such as high levels of motivation, support, and competent execution, in addition to surgical technique, should be improved to enhance awareness, consistency, engagement, standardization, leadership, and mentoring among all involved surgical team members.[53] To

Table 5
Risk factors for ERAS failure (univariable analysis).

Variables	ERAS success ($n = 152$)	ERAS failure ($n = 46$)	$\chi^2/F/t/U$	*P*
Age (years, mean ± SD)	64.9 ± 7.2	65.2 ± 8.3	−0.265	0.792
Gender			4.177	0.041
Male	60 (39.5)	26 (56.5)		
Female	92 (60.5)	20 (43.5)		
BMI (kg/m^2, mean ± SD)	25.2 ± 3.5	24.8 ± 3.6	0.678	0.499
Type of lobectomy			12.059	0.027
Left upper lobectomy	35 (23.0)	9 (19.6)		
Left lower lobectomy	33 (21.7)	2 (4.3)		
Right upper lobectomy	45 (29.6)	17 (37.0)		
Right middle lobectomy	7 (4.6)	2 (4.3)		
Right lower lobectomy	25 (16.4)	10 (21.7)		
Bilobectomy	7 (4.6)	6 (13.0)		
TNM stage			0.109	0.741
0/1/2	146 (96.1)	43 (93.5)		
3/4	6 (3.9)	3 (6.5)		
Blood pressure classification			4.468	0.215
0	30 (19.7)	8 (17.4)		
1	14 (9.2)	8 (17.4)		
2	56 (36.8)	11 (23.9)		
3	52 (34.2)	19 (41.3)		
ASA classification			5.028	0.081
I	7 (4.6)	1 (2.2)		
II	108 (71.1)	26 (56.5)		
III	37 (24.3)	19 (41.3)		
Comorbidities				
Hypertension	122 (80.3)	38 (82.6)	0.125	0.723
Coronary artery disease	46 (30.3)	10 (21.7)	0.880	0.348
Atrial fibrillation	3 (2.0)	2 (4.3)	0.132	0.717
Tachycardia	4 (2.6)	1 (2.2)	0.000	1.000
Bradycardia	3 (2.0)	1 (2.2)	/	1.000
Premature ventricular complexes	3 (2.0)	0 (0.0)	/	1.000
Premature atrial contractions	2 (1.3)	0 (0.0)	/	1.000
Tetralogy of Fallot	0 (0.0)	1 (2.2)	/	0.232
Number of lymph nodes (IQR)	6 (3.3–6.0)	6 (6.0–6.0)	−1.049	0.294
Operation time (min, IQR)	110 (95.0–130.0)	127.5 (110.0–160.0)	−3.081	0.002
EBL (mL, IQR)	20 (20.0–20.0)	20 (20.0–20.0)	−2.401	0.016
Intraoperative fluid (mL, IQR)	1000 (800.0–1300.0)	1300 (950.0–1300.0)	−1.896	0.058
Surgical approach			0.673	0.412
Thoracoscope	124 (81.6)	35 (76.1)		
Da Vinci robotic	28 (18.4)	11 (23.9)		
NYHA			0.813	0.537
1	33 (21.7)	8 (17.4)		
2	116 (76.3)	37 (80.4)		
3	3 (2.0)	1 (2.2)		
4	0 (0.0)	0 (0.0)		
Suction drainage			11.101	0.010
Yes	20 (13.2)	16 (34.8)		
No	132 (86.8)	30 (65.2)		
Urinary catheter			0.770	0.380
Yes	146 (96.1)	46 (100.0)		
No	6 (3.9)	0 (0.0)		
Hemoglobin (g/L, IQR)	137 (128.0–146.0)	139 (125.5–147.5)	−0.109	0.913
Troponin (ng/mL, IQR)	25 (25.0–25.0)	25 (6.9–25.0)	−1.521	0.128
Myohemoglobin (ng/mL)			0.527	0.468
< 1	117 (77.0)	33 (71.7)		
≥ 1	35 (23.0)	13 (28.3)		
Albumin (g/L, mean ± SD)	41.0 ± 2.6	40.6 ± 3.6	−0.265	0.316
Globulin (g/L, mean ± SD)	26.7 ± 4.1	25.6 ± 2.8	1.536	0.126
A/G (mean ± SD)	1.6 ± 0.2	1.6 ± 0.2	−0.760	0.448
Total cholesterol (mmol/L, mean ± SD)	5.3 ± 1.2	4.9 ± 1.1	1.978	0.049
Triglyceride (mmol/L, IQR)	1.4 (1.0–1.9)	1.3 (0.9–1.7)	−1.599	0.110
HDL (mmol/L, IQR)	1.4 (1.1–1.6)	1.3 (1.0–1.6)	−1.257	0.209
LDL (mmol/L, IQR)	3.3 ± 1.0	3.0 ± 0.9	1.279	0.202
Lipoprotein α (mg/L, IQR)	123 (71.0–244.0)	138 (60.0–259.5)	−0.026	0.979
CEA (ng/L, IQR)	1.9 (1.1–2.7)	2.3 (1.3–4.0)	−1.849	0.065
HSP 90α (ng/L, IQR)	53.5 (39.1–75.6)	56.2 (38.9–79.2)	−0.357	0.721

(*continued on next page*)

Table 5 (*continued*)

Variables	ERAS success ($n = 152$)	ERAS failure ($n = 46$)	$\chi^2/F/t/U$	P
IL-1β (pg/L, IQR)	1.4 (0.9–1.9)	1.4 (0.9–1.7)	−0.480	0.631
TNF-α (ng/L, IQR)	1.6 (1.0–2.2)	1.4 (0.9–2.1)	−0.943	0.346
CRP (mg/L, IQR)	36.7 (23.0–59.5)	39.5 (25.1–75.5)	−0.347	0.729
PCT (ng/mL, IQR)	0.2 (0.1–0.5)	0.3 (0.1–0.8)	−0.623	0.533
FVC (%, IQR)	91 (84.0–100.0)	92 (84.0–98.5)	−0.281	0.779
FEV_1 (%, IQR)	93 (86.0–105.0)	93 (86.5–99.0)	−0.784	0.433
FEV_1/FVC (%, IQR)	103 (97.0–107.0)	100 (94.5–105.0)	−1.833	0.067
PEF (%, IQR)	101 (90.0–112.0)	90 (80.5–112.5)	−1.870	0.062

HSP 90α, heat shock protein 90 α; A/G, albumin/globulin; ASA, American Society of Anesthesiologists; BMI, body mass index; CEA, carcinoembryonic antigen; CRP, C-reactive protein; EBL, estimated blood loss; $FEV_{1,}$ first second forceful expiratory volume; FVC, forceful lung capacity; HDL, high-density lipoprotein; IL-1β, interleukin-1β; IQR, interquartile range; LDL, low density lipoprotein; NYHA, New York Heart Association; PCT, procalcitonin; PEF, peak expiratory flow; SD, standard deviation; TNF-α, tumor necrosis factor-α; TNM, tumor node metastasis. Univariate analysis: chi-square or Fisher's exact tests for categorical variables, and two independent sample *t*-tests or Mann–Whitney *U* tests for continuous variables.

Table 6
Independent risk factors for enhanced recovery program failure (multivariable analysis).

Variables	B	SE	OR	95% CI	*P*
Gender	−0.637	0.406	0.529	0.239–1.171	0.116
Type of lobectomy					
Left upper lobectomy (ref)					
Left lower lobectomy	−1.297	0.845	0.273	0.052–1.432	0.125
Right upper lobectomy	0.322	0.517	1.379	0.500–3.802	0.534
Right middle lobectomy	0.100	0.938	1.105	0.176–6.944	0.915
Right lower lobectomy	0.446	0.577	1.562	0.504–4.844	0.440
Bilobectomy	1.197	0.769	3.312	0.734–14.952	0.119
Operation time (min)	0.015	0.006	1.015	1.003–1.027	0.011
EBL (mL)	0.010	0.008	1.010	0.993–1.027	0.253
Suction drainage	1.207	0.453	3.343	1.376–8.124	0.008
Total cholesterol (mmol/L)	−0.257	0.187	0.774	0.536–1.117	0.171

CI, confidence interval; EBL, estimated blood loss; OR, odds ratio; SE, standard error.

reduce postoperative complications in patients, thoracic surgeons should be trained in the surgical process through virtual reality simulators, such as televised thoracoscopic surgery for lobectomy,[54] all surgeons should standardize the approach to minimally invasive lobectomy to reduce unnecessary delays.[55] The procedures complexity should be assessed preoperatively based on the patient's baseline, and the patient should be allocated appropriately based on the surgeon's experience and competence.[56] All steps during surgery or in a patient's care should be evaluated to reduce variation in how individual procedures are performed. Steps determined to be nonvalue-added should be eliminated, and value-added steps, such as the placement of a double-lumen endotracheal tube, should be performed more efficiently.[57] Multidisciplinary teams should collaborate to improve surgical procedures by improving the operating room admittance process, total quality management, plan-study-action, plan-operate-check-operate, statistical process, or quality management improvement approaches.[58]

Suction drainage was independent risk factors for ERAS failure

Residual pleural space is eliminated through chest drains after minimally invasive surgery in patients with lung cancer to promote lungs re-expansion and suction drainage maintenance, preventing postoperative complications such as pneumothorax or pleural effusion.[59] Pleural effusion drainage improves the patient's respiratory mechanical parameters, including end-expiratory cross-pulmonary pressure, respiratory compliance, respiratory resistance, and end-expiratory lung volume.[60] Drainage can increase lung volume or relieve bronchial compression, improve respiratory resistance, improve functional residual capacity, and improve diaphragmatic length-tension relationship in patients with spontaneous breathing, promoting lung function by enhancing contractile function and thereby reducing inspiratory force during tidal breathing.[61,62] Pulmonary collapse and oxygenation in poorly ventilated areas may be improved after pleural effusion drainage, improving ventilation-perfusion matching in these areas and reducing arteriovenous shunt.[63] Decreased Pmusc index (the difference between the plateau pressure of end-inspiratory occlusion and sum of end-expiratory positive pressure and pressure support), increased respiratory compliance, improved maximal inspiratory pressure,[64] and reduced PPCs. A large pleural effusion has adverse effects on cardiovascular hemodynamics. An increase in intrapleural pressure is observed in the pericardium and is accompanied by a pericardial tamponade-like effect, resulting in a linear increase in intrapericardial pressure and an increase in right ventricular diastolic pressure, which may reverse after pleural drainage.[65] Studies have found that removing a large amount of pleural effusion can reduce transmural pressure, increase preload, reduce pulmonary capillary wedge pressure, and increase left ventricular end-diastolic volume and ratio of early to late transmitral flow velocity, thereby improving cardiac function.[66]

The impact of suction drainage on nursing practice and research

However, there is no consensus on whether using non-suction or suction drainage routinely reduces the hospital stay duration and complications incidence.[67,68] Gocyk et al.[69] showed that non-suction was superior to suction drainage regarding volume, drainage duration, and persistent air leakage incidence, but it could increase asymptomatic residual airspace incidence. Zhou et al.[70] showed that compared with the non-suction group, the addition of external suction drainage to the chest catheter increased the duration of the median chest tube and persistent air leaks incidence, which is consistent with our results. A meta-analysis showed that external suctioning, compared with water-sealing alone, accelerates the expulsion of air and fluid to expand the remaining lung post-lobectomy, and the chest tube is relatively more stable to ensure drainage function, thus, it reduces the incidence of postoperative pneumothorax and other cardiorespiratory complications, however chest tube drainage duration increases.[68] Currently, there are no guidelines on when and how to use aspiration drainage for pleural effusion drainage after lung cancer surgery, and central negative pressure drainage may limit postoperative activity. Whether digital drainage devices and postoperative non-catheter drainage are universal and whether the timing and rate of drainage are beneficial to patients are unknown, Wang et al.[66] illustrated that cardiac preload, systolic function, and diastolic were significantly improved after massive pleural effusion (2000 mL) drainage. Razazi et al.[60] showed no improvement in hemodynamic variables in mechanically ventilated patients after clearing at least 1000 mL of pleural effusion. Draining a large quantity of pleural effusion (> 500 mL) improved oxygenation, increased end-expiratory lung volume, and decreased pulmonary arterial pressure. In practice, this threshold will guide clinicians. However, the risk/benefit ratio must be assessed in a clinical context whereby clinicians can judge whether due to diaphragmatic dyskinesia a patient can derive the expected benefit from pleural effusion drainage.

Limitations

First, several variables that were inaccessible or included in the case system may have influenced the postoperative ERAS outcomes, such as cardiovascular imaging findings and psychosocial factors. Although clinical ERAS is performed with preoperative health education focusing on exercise and postoperative encouragement to get out of bed early, the

time and frequency of patients leaving the bed for exercise are inaccessible, potentially affecting patients' postoperative hospitalization duration. The patients' preoperative smoking cessation results and smoking status are unavailable, which may be related to the PPCs of combined CVD. Second, the number of patients with comorbid CVD in various categories was low, and there was no severity rating for the CVD scale assessment. Considering the different characteristics and etiologies of different populations with comorbid CVDs (hypertension, CAD, arrhythmias), the analyzed studies may be heterogeneous, making result interpretation uncertain. Third, it is a retrospective single-center study, which limits generalizability. The sample size is limited and combined cardiovascular coverage type is incomplete. Further prospective, multicenter, and large-sample studies are needed, and the statistical results may still retain bias. Finally, ERAS failure is only a theoretical definition, and further research according to disease type, surgical methods, and different comorbidities is needed.

Future directions

The emergence of multimodal treatment options, accompanied by an aging population and a progressive increase in multimorbidity incidence, intensified the need for multidisciplinary cancer care, while increasing interdisciplinary care coordination challenges. Interdisciplinary teamwork, such as the clinical multi-team system, is a key but understudied aspect of cancer care. A successful scientific team must focus on key factors such as team selection, communication, leadership and mentoring, shared goals, team responsibility, authorship, and conflict management. These teamwork processes within and between teams provide a foundation for coordinated care. Valuable tools for reducing fragmented care and identifying key variables affecting care coordination to improve interprofessional team care will advance the science and practice of cancer care delivery.

Currently, there is limited medical evidence for preoperative ERAS in patients with lung cancer or comorbid CVD. Future research on ERAS evaluation and management should cover a spectrum ranging from randomized controlled trials to regional and national registry studies to focus on patient outcomes after surgery. This study did not study the long-term outcomes of postoperative CVD, and further refining the data through follow-up and long-term survival analyses to provide a more comprehensive and reliable clinical reference is suggested. The value of diagnostic imaging modalities for cardiovascular screening, such as coronary calcium scoring, computed tomography angiography, and cardiac magnetic resonance imaging in preoperative screening, remains uncertain and requires further study. Future development and validation of comprehensive preoperative risk scoring systems for patients with lung cancer and cardiovascular comorbidities are needed, including patient demographic characteristics, medical information on cardiac risk, social determinants, and data from non-invasive or invasive test results, or both, to comprehensively assess patient outcomes after surgery.

Conclusions

Operation time and suction drainage were independent risk factors for surgical ERAS failure in patients with combined cardiovascular lung cancer. Therefore, we suggest that the interdisciplinary teamwork of oncologists, cardiologists, and anesthesiologists and postoperative thoracic drainage tubes management should be emphasized for ERAS.

Ethics statement

This study was conducted after obtaining approval from the Research Ethics Review Committee of Binzhou Medical University (IRB No. 2023-311). Because of the retrospective nature of our study, the data were obtained from available medical records and the identity and privacy of the subjects were not involved; therefore, informed consent was waived by our Institutional Review Board.

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CRediT authoship contribution statement

Lili Sun: Resources, Collected the data, Data curation and analysis, Software, Writing – Original draft. **Yutong Lu:** Software, Data curation and analysis. **Yanfang Zhang:** Software, Data curation and analysis. **Chan Jin:** Software, Data curation and analysis. **Zhenwei Yuan:** Software, Data curation and analysis, Writing – Review & Editing, Supervision. **Renhua Xu:** Conceptualization, Methodology, Writing – Review & Editing, Supervision, Project administration, Funding acquisition. All authors had full access to all the data in the study, and the corresponding author had final responsibility for the decision to submit for publication. The corresponding authors attest that all listed authors meet authorship criteria and that no others meeting the criteria have been omitted.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data availability statement

The data that support the findings of this study are available from the corresponding author, Renhua Xu and Zhenwei Yuan, upon reasonable request.

Declaration of generative AI and AI-assisted technologies in the writing process

No AI tools/services were used during the preparation of this work.

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