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Original Article

Incidence and risk factors of postoperative pulmonary complications after thoracic surgery for early non-small cell lung cancer

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Abstract: Objective: To evaluate the prevalence and risk factors of postoperative pulmonary complications (PPCs) in non-small cell lung cancer (NSCLC) patients after thoracic surgery. Methods: A retrospective analysis of 453 patients who underwent thoracic surgery for NSCLC between January 1, 2010 and December 31, 2014 was performed. Risk factors for PPCs were identified using unconditional stepwise logistic regression analyses. Results: The total incidence of PPCs in NSCLC patients was 29.0% (102/453), including 42.2% (43/102) for pulmonary edema, 31.4% (32/106) for atelectasis, 66.7% (68/102) for pneumonia, 7.8% (8/102) for acute respiratory distress syndrome and 1.0% (1/102) presented with respiratory failure. For these NSCLC patients with advanced age, history of smoking and comorbidity such as chronic obstructive pulmonary disease; receiveing thoractomy, and intraoperative excessive transfusion of crystalloids and colloids, massive blood loss, oliguria and increased lactate level would be prone to higher incidence of PPCs. Conclusion: The incidence of PPCs after thoracic surgery in the early NSCLC patients remains at a high level, which was associated with preoperative parameters, management of fluid and type of surgery and postoperative analgesia.

Keywords: Thoracic surgery, postoperative pulmonary complications, non-small cell lung cancer, risk factors

Introduction

Thoracic surgery involves the surgical treatment of thoracic trauma, pulmonary and esophageal diseases. The volume of thoracic surgery has increased, subsequent to an increased incidence of trauma and cancer. Thoracic surgery tends to affect the cardiopulmonary function of patients, who are often elderly and have been accompanying age-related and degenerative diseases. The reported incidence of postoperative pulmonary complications (PPCs) after thoracic surgery ranges from 4.8% to 54.6% [1-3] and mortality from PPCs between 10% and 20% [4]. Hence, PPCs in patients after thoracic surgery have attracted considerable attention in clinics.

Most patients with lung cancer need thoracic surgery, and many of them experience worsening pulmonary function and metastasis, which favor the occurrence of PPCs. Treatment for lung cancer mostly included pneumonectomy, lobectomy, segmentectomy and wedge resection. And the purpose of surgery is to have adequate tumor resection and preserve normal lung tissues as much as possible [5]. Unfortunately, common early PPCs in these patients include pulmonary edema, atelectasis, pneumonia, acute respiratory distress syndrome (ARDS) and respiratory failure [5, 6]. These complications affect the postoperative recovery of patients, resulting in increased mortality, prolonged hospitalization and increased expenditure. Several studies have shown that race, age, sex, smoking status and preoperative pulmonary function are risk factors associated with PPCs [2, 7, 8]. However, very little comprehensive risk analysis for PPCs after thoracic surgery for early non-small cell lung cancer (NSCLC) has been conducted.

The objective of this study was to investigate the incidence of PPCs in patients who underwent thoracic surgery for early NSCLC and identify relevant predictive factors for PPCs. We hypothesized that specific perioperative management and conditions could be associated to the occurrence of PPCs.

Materials and methods

Patients

This study was approved by the institutional review board of the Affiliated Tumor Hospital of Guangxi Medical University and carried out in accordance with the Declaration of Helsinki.

The clinical data of included patients who had written informed consent during a 5-year period between 1 January 1, 2010, and 31 December 2014 at the Affiliated Tumor Hospital of Guangxi Medical University, was retrospectively collected. These patients meeting the following inclusion criteria: age between 18 and 75 years and underwent thoracic surgery for NSCLC at stage I or II. The exclusion criteria included history of cardiovascular, liver, kidney or hematopoietic decompensation and psychiatric disease; undergoing radiotherapy or (and) chemotherapy; those patients with tumor metastasis.

Anesthesia management

A targeted controlled infusion of propofol (target plasma concentration 2-3 μg/mL), sufentanil 0.4-0.6 μg/kg and cisatracurium 0.2-0.3 mg/kg was adopted for anesthesia induction. Once the patients lost consciousness, a double-lumen tracheal tube was inserted and the location examined by fiberoptic bronchoscope. Ventilator tidal volume was set at 8-10 mL/kg, respiratory rate was 15/min, inspiratory-to-expiratory ratio was 1:2, inspired oxygen concentration was 50%, pressure of end-tidal carbon dioxide was maintained at 30-35 mmHg, and one-lung ventilation was performed in the beginning with the operation. Anesthesia was maintained with targeted controlled infusion of propofol (target plasma concentration of 2-2.5 μg/mL), sufentanil (target plasma concentration of 4-6 μg /mL) and intermittent intravenous bolus of cisatracurium 0.1-0.2 mg/kg. Bispectral index was monitored and maintained at 40-60. During the operation, hemodynamic variables were maintained within 20% of baseline values and pulse oxygen saturation was maintained at ≥90%. The internal jugular vein and radial artery catheter were reserved to monitor central venous and mean arterial pressure and for blood gas analysis. Circulating hemoglobin level was maintained at approximately 8 g/dL by transfusion of packed red blood cells (PRBCs).

Postoperative recovery

After operation, patients were transported to the intensive care unit (ICU) for intermediate care and recovery from anesthesia. Routine fluid replacement was executed by 6-8 mL/kg/h of lactated Ringer's solution, and colloid used for maintaining of stable heart rate, central venous pressure of 8-12 mmHg, urine output of 1 mL/kg/h, and steady mean arterial pressure. Additionally, hemoglobin level was maintained greater than 8 g/dL by transfusion of PRBCs. All patients were provided postoperative patient-controlled analgesia (PCA) by intravenous or epidural analgesia during the first three days after operation. Patient-controlled epidural analgesia (PCEA) was accomplished through the inserted epidural catheter at T12-L1 or L1-L2 level if without contraindications. Epidural infusions were conventionally using 0.125% bupivacaine with 0.1 mg/mL morphine at 2 mL/h. Several patients were also received patient-controlled intravenous analgesia (PCIA) through 1 mg/mL morphine with bolus doses of 3-5 mL and lockout interval of 20 min.

Definition of PPCs

Previous studies have identified PPCs as pulmonary edema, atelectasis, pneumonia, ARDS and respiratory failure [5, 9]. Briefly, pulmonary edema was clinically diagnosed on relevant symptoms and signs, and by measuring pulmonary capillary wedge pressure and identifying typical radiographic changes. Pulmonary atelectasis was confirmed by its radiographic appearance. Postoperative pneumonia was diagnosed according to American Thoracic Society guidelines [10] and diagnosis of ARDS was based on the Berlin definition [11]. Furthermore, patients with PaO_2 < 8.0 kPa were defined as having type I respiratory failure, and those with PaO_2 < 8.0 kPa and $PaCO_2$ > 6.5 kPa as type II respiratory failure [12]. Postoperative parameters included the occurrence of PPCs (defined

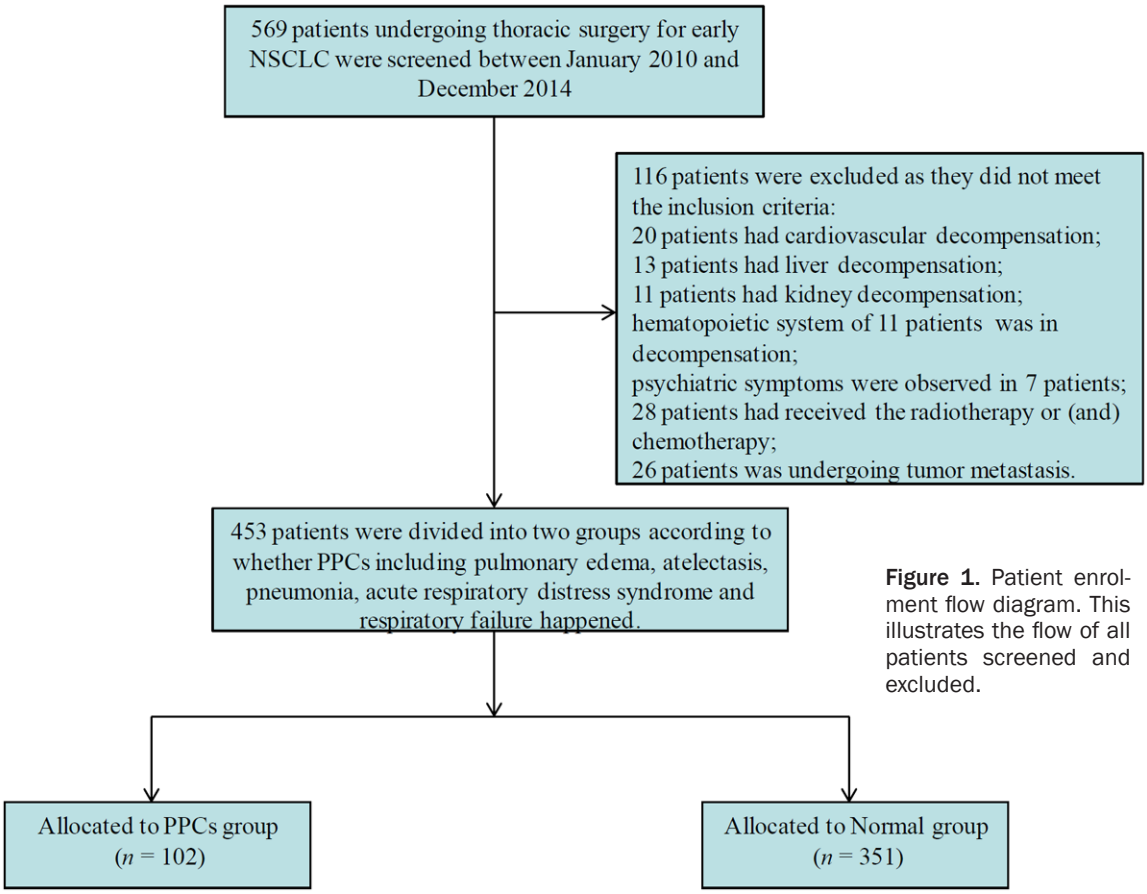

Figure 1. Patient enrolment flow diagram. This illustrates the flow of all patients screened and excluded.

as pulmonary edema, atelectasis, pneumonia, ARDS and/or respiratory failure), duration of mechanical ventilation, and duration of hospital and ICU stay.

Compared variables

Preoperative and intraoperative variables of patients who developed PPCs during their hospital stay were compared with those of their non-PPCs counterparts. Preoperative parameters included age, sex, body mass index (BMI), American Society of Anesthesiologists (ASA) classification, social history (smoking and alcohol status) and comorbidity (coronary heart disease [CHD], congestive heart failure [CHF], chronic obstructive pulmonary diseases [COPD], diabetes, and chronic kidney disease [CKD] and liver disease). Baseline laboratory results, including serum albumin, creatinine, lactate, hemoglobin and platelet level, were systematically collected. Intraoperative variables included type of surgery, method of operation, type of PCA, volume of blood transfusion and fluid infusions (crystalloids, colloids, fresh frozen plasma, PRBCs, platelets and cryoprecipitate), volume of urinary output and blood loss. Serum hemoglobin and lactate levels were recorded immediately after surgery.

Statistical analysis

SPSS 16.0 software (SPSS Inc., Chicago, IL, USA) was used for data analysis. Categorical data were recorded by the observed number of cases in each group and analyzed using the Chi-square (or Fisher's Exact test if required by sample size). Continuous data with a parametric distribution were described as mean ± SD and analyzed by Independent samples T-test, whereas non-parametric data were showed as median with interquartile range and analyzed by Mann-Whitney *U*-test. An unconditional logistic stepwise regression model was used to identify PPC risk factors and reported with odds' ratio (OR) with 95% confidence interval (CI). Spearman's correlation analysis was done to analyze the bivariate correlation of categorical variables and univariate comparisons with a *P* value less than 0.05 were included for multivariate analyses. The survival analysis was performed using the Mantel-Cox test. $P < 0.05$ were defined as statistical significance threshold.

Table 1. General characteristic of included patients and surgery

Clinical factors	Variables
Age (yr)	56 (43, 70)
Gender (M/F)	280/173 (61.8%/38.2%)
Height (cm)	165.7±12.5
Weight (kg)	63.8±10.9
Preoperative variables	
Smoking history (*n*; %)	300 (66.2%)
Alcohol abusing history (*n*; %)	208 (45.9%)
Hypertension (*n*; %)	238 (52.5%)
Coronary artery disease (*n*; %)	255 (56.3%)
Congestive heart failure (*n*; %)	13 (2.9%)
Chronic obstructive pulmonary disease (*n*; %)	164 (36.2%)
Diabetes (*n*; %)	91 (20.1%)
Chronic kidney diseases (*n*; %)	24 (5.3%)
Liver diseases (*n*; %)	110 (24.3%)
Lactate (mmol/L)	1.5±0.9
Hemoglobin (g/L)	137.7±20.5
Platelet (* 10^9/L)	218±82
Intraoperative variables	
Type of surgery (VATS/thoractomy)	388/65 (85.7%/14.3%)
Rane of surgery (lobectomy/segmentectory)	332/121 (73.3%/26.7%)
Duration of surgery (h)	5.6±0.9
Crystalloids (mL)	6045±1700
Colloids (mL)	3200±800
Fresh frozen plasma (mL)	800 (200, 4400)
Packed red blood cells (U)	4 (2, 18)
Fresh frozen plasma (mL)	600 (200, 2800)
Estimated blood loss (mL)	750 (300, 5200)
Urinary output (mL)	850±200
Postoperative variables	
Vasoconstrictors use in ICU (*n*; %)	208 (45.9%)
PCIA/PCEA (*n*; %)	338/115 (74.6%/25.4%)
ICU readmission (*n*; %)	58 (12.8)
Duration of ICU stay (day)	3±5
ICU ventilation (h)	27.3±19.4
Duration of hospitalization (day)	18.3±8.7
30-day surgical death (*n*; %)	5 (1.1%)

Continuous data are reported as means ± SD or medians (25% percentile, 75% percentile). Categorical data are given as counts (percentages). VATS = video-associated thoracoscopic surgery, ICU = intensive care unit, PCIA = patient controlled intravenous analgesia, PCEA = patient-controlled epidural analgesia.

Results

The baseline characteristics of included patients

Clinical data from a total of 453 consecutive adult patients undergoing elective thoracic surgery for were collected (**Figure 1**). The baseline characteristics of included patients and surgeries were shown by **Table 1**. There were 280 male patients (61.8%) and mean age was 56 years; mean height and weight was (165.7± 12.5) cm and (63.8±10.9) kg respectively. The majority of patients had video-associated thoracoscopic surgery (VATS) (85.7%; 388/453), with the remaining cases undergoing thoracotomy (14.3%; 65/453). Most of them (73.3%; 332/453) required total or partial lung resection and the rest of patients (26.7%; 121/453) underwent segmentectomy.

The incidence of PPCs and survival analysis

The overall incidence of PPCs (29.0%; 102/453 pts) appears in **Table 2**. Of these, 42 patients (41.2%) occurred with pulmonary edema, 32 (31.4%) with atelectasis, 19 (18.6%) with pneumonia, 8 (7.8%) with ARDS, and 1 (1.0%) with respiratory failure. Patients who received VATS showed fewer incidences of pulmonary atelectasis, pneumonia, ARDS and respiratory failure than those with thoractomy (both $P < 0.05$). The incidences of these PPCs between those who received lobectomy or segmentectomy were similar (both $P > 0.05$). In addition, patients undergoing PCIA showed higher incidence of pulmonary edema, atelectasis and pneumonia after thoracic surgery (both $P < 0.05$). Five patients out of 453 died during hospitalization (overall hospital mortality rate of 1.1%), including four cases from the PPCs group and one non-PPCs patient. Although only two patients died in PPCs group within 30 days of surgery, a significant difference in postoperative survival between the two

Table 2. Incidence of postoperative pulmonary complications

	Pulmonary edema	Pulmonary atelectasis	Pneumonia	ARDS	Respiratory failure
Overall incidence	42 (41.2%)	32 (31.4%)	19 (18.6%)	8 (7.8%)	1 (1.0%)
Type of surgery					
VATS (*n* = 388)	32 (8.2%)	23 (5.9%)	11 (2.8%)	4 (1.0%)	0 (0%)
Thoractomy (*n* = 65)	10 (15.4%)	9 (13.8%)	8 (12.3%)	4 (6.2%)	1 (1.5%)
P	0.066	0.021	0.000	0.004	0.014
Rane of operation					
Lobectomy (*n* = 332)	35 (10.5%)	20 (6.0%)	17 (5.4%)	8 (2.4%)	1 (0.3%)
Segmentectory (*n* = 121)	7 (5.8%)	12 (9.9%)	2 (0.8%)	0 (0%)	0 (0%)
P	0.122	0.152	0.103	0.081	0.733
PCA					
PCIA (*n* = 338)	37 (10.9%)	30 (8.9%)	18 (5.3%)	7 (2.1%)	1 (0.3%)
PCEA (*n* = 115)	5 (4.3%)	2 (1.9%)	1 (0.9%)	1 (0.9%)	0 (0%)
P	0.035	0.010	0.039	0.398	0.559

Note: These data are described as the number of cases (%). VATS = video-associated thoracoscopic surgery, PCA = patient-controlled analgesia, PCIA = patient-controlled intranasal analgesia, PCEA = patient-controlled epidural analgesia.

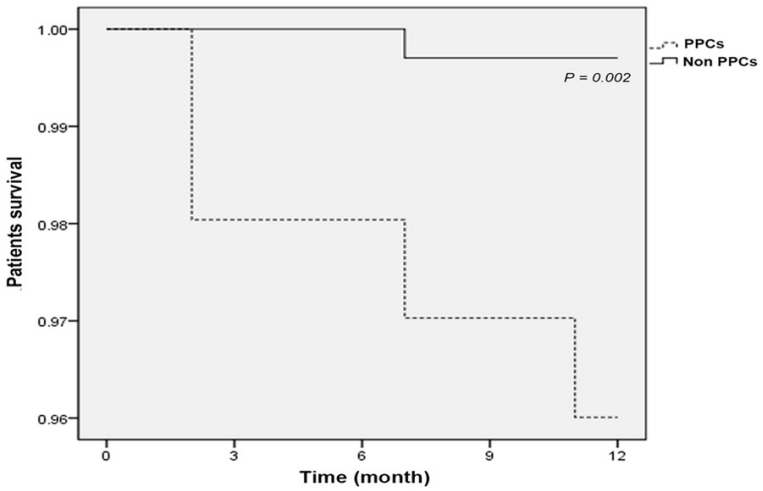

Figure 2. The survival curve between the PPC and non-PPC group after 1 year follow-up.

groups for 1-year survival was observed, at 96.01% (PPCs) vs. 99.71% (non-PPCs) (*P* = 0.002; **Figure 2**).

Univariate analysis for the risk factors of PPCs

As shown in **Table 3**, risk factors and predictors of PPCs from preoperative variables included age > 65 yr (56.9% vs. 43.3%; *P* = 0.016), higher ASA scores (83.3% vs. 29.1%; *P* < 0.001), higher BMI (70.6% vs. 51.7%; *P* = 0.001), history of smoking (90.2% vs. 59.3%; *P* < 0.001), history of COPD (70.6% vs. 26.2%; *P* < 0.001), history of diabetes (37.3% vs. 15.1%; *P* < 0.001), history of CKD (15.7% vs. 7.8%; *P* = 0.021) and liver disease (42.2% vs. 29.1%; *P* = 0.013). In addition, the serum albumin, hemoglobin and platelet levels of NSCLC patients in the PPCs group were decreased, whereas serum creatinine levels were elevated (both *P* < 0.05), compared with non-PPC patients. For intraoperative parameters (**Table 4**), those patients who underwent thoractomy and PCIA were associated with the occurrence of PPCs (both *P* < 0.05). Patients with PPCs also received excessive transfusion of crystalloids and colloids, massive blood loss, oliguria and accumulation of lactate (both *P* < 0.05) compared with non-PPC patients.

Multivariate analysis for the risk factors of PPCs

The risk factors predicating PPCs (**Table 5**) included advanced age (*P* = 0.008; OR = 12.299, 95% CI = 1.903-79.490), history of smoking (*P* = 0.004; OR = 5.367, 95% CI = 1.698-16.964), history of COPD (*P* = 0.001; OR = 3.027, 95% CI = 1.804-6.519), history of CKD (*P* < 0.001; OR = 6.585, 95% CI = 1.979-14.286), history of liver disease (*P* < 0.001; OR = 1.470, 95% CI = 1.030-5.318), massive blood

Table 3. Preoperative parameters

	Patients with PPCs (*n* = 102)	Patients without PPCs (*n* = 351)	*P* value	OR	95% CI
Age > 65 yr (*n*; %)	58 (56.9%)	152 (43.3%)	0.016	1.73	1.11-2.69
Male (*n*; %)	68 (71.6%)	212 (59.0%)	0.251	1.31	0.83-2.09
BMI ≥24 (*n*; %)	72 (70.6%)	182 (51.9%)	0.001	2.23	1.39-3.58
ASA scores ≥III (*n*; %)	85 (83.3%)	102 (29.1%)	0.000	12.21	6.91-21.57
Smoking history (*n*; %)	92 (90.2%)	208 (59.3%)	0.000	6.33	3.18-12.57
Alcohol abusing (*n*; %)	67 (65.7%)	141 (40.2%)	0.000	2.85	1.80-4.52
CHD (*n*; %)	52 (51.0%)	203 (57.8%)	0.219	0.76	0.49-1.18
CHF (*n*; %)	4 (3.9%)	9 (2.6%)	0.266	2.01	0.58-6.99
COPD (*n*; %)	72 (70.6%)	92 (26.2%)	0.000	6.76	4.15-11.01
Diabetes (*n*; %)	38 (37.3%)	53 (15.1%)	0.000	3.33	2.03-5.49
CKD (*n*; %)	10(9.8%)	14 (4.0%)	0.021	2.62	1.13-6.08
Liver diseases (*n*; %)	43 (42.2%)	67 (19.1%)	0.000	3.09	1.92-4.97
Albumin < 25 g/L (*n*; %)	27 (26.5%)	53 (15.1%)	0.008	2.02	1.19-3.43
Ccr < 30 mL/min (*n*; %)	15 (14.7%)	23 (6.6%)	0.009	2.46	1.23-4.91
Lactate > 2.4 mmol/L (*n*; %)	8 (7.8%)	10 (2.8%)	0.023	2.90	1.11-7.56
Hemoglobin < 90 g/L (*n*; %)	35 (34.3%)	83 (23.6%)	0.031	1.69	1.05-2.72
Platelet < 100 * 10^9/L (*n*; %)	29 (28.4%)	53 (15.1%)	0.002	2.23	1.33-3.76

Continuous data are reported as means ± SD or medians (25% percentile, 75% percentile). Categorical data are given as counts (percentages). PPC = postoperative pulmonary complication, OR = odds ratio, 95% CI = 95% confidence interval, BMI = body mass index, ASA = American Society of Anesthesiologists, CHD = coronary heart disease, CHF = congestive heart failure, COPD = chronic obstructive pulmonary diseases, CKD = chronic kidney disease, Ccr = creatinine clearance rate.

Table 4. Intraoperative variables

	Patients with PPCs (*n* = 102)	Patients without PPCs (*n* = 351)	*P* value	OR	95% CI
Surgery time > 4 h (*n*; %)	58 (56.9%)	185 (52.7%)	0.459	1.18	0.76-1.85
Type of surgery					
VATS (*n*; %)	70 (68.6%)	318 (90.6%)	0.000	0.23	0.13-0.39
Thoractomy (*n*; %)	32 (31.4%)	33 (9.4%)			
Rane of operation					
Lobectomy (*n*; %)	81 (79.4%)	251 (71.5%)	0.112	1.54	0.90-2.62
Segmentectory (*n*; %)	21 (20.6%)	100 (28.5%)			
PCA					
PCIA (*n*; %)	55 (53.9%)	283 (80.6%)	0.000	0.28	0.18-0.45
PCEA (*n*; %)	47 (46.1%)	68 (19.4%)			
Crystalloids > 6000 mL (*n*; %)	92 (90.2%)	196 (55.8%)	0.000	7.28	3.67-14.44
Colloids > 2000 mL (*n*; %)	85 (83.3%)	228 (65.0%)	0.000	2.70	1.53-4.75
FFP > 400 mL (*n*; %)	62 (60.8%)	201 (57.3%)	0.526	1.16	0.74-1.82
PRBCs > 4 U (*n*; %)	32 (31.4%)	85 (24.2%)	0.146	1.43	0.88-2.32
Platelets > 2 U (*n*; %)	28 (27.5%)	74 (21.1%)	0.175	1.42	0.86-2.35
Cryoprecipitate > 2 U (*n*; %)	28 (27.5%)	70 (19.9%)	0.105	1.52	0.91-2.52
Blood loss > 1600 mL (*n*; %)	52 (50.1%)	83 (23.6%)	0.000	3.36	2.12-5.32
Urinary output < 200 mL (*n*; %)	26 (25.5%)	58 (16.5%)	0.040	1.73	1.02-2.93
Hemoglobin < 80 g/L (*n*; %)	35 (34.3%)	90 (25.6%)	0.085	1.52	0.94-2.43
Lactate > 2.4 mmol/L (*n*; %)	38 (37.3%)	95 (27.1%)	0.047	1.60	1.01-2.55

Continuous data are reported as means ± SD or medians (25% percentile, 75% percentile). Categorical data are given as counts (percentages). PPC = postoperative pulmonary complication, OR = odds ratio, 95% CI = 95% confidence interval, VATS = video-associated thoracoscopic surgery, PCA = patient-controlled analgesia, PCIA = patient-controlled intranasal analgesia, PCEA = patient-controlled epidural analgesia, FFP = Fresh frozen plasma, PRBCs = packed red blood cells.

Table 5. Risk factors for PPCs by multivariate analysis

Variables	OR	95% CI	*P* value
Age (> 65 yr)	12.299	1.903-79.490	0.008
Type of surgery (VATS)	0.118	0.034-0.408	0.001
Type of cancer (NSCLC)	0.124	0.040-0.390	< 0.001
Type of analgesia (PCEA)	0.115	0.021-0.630	0.013
History of smoking	5.367	1.698-16.964	0.004
History of COPD (FEV1 ≤ 70%)	3.027	1.804-6.519	0.001
History of CKD (Ccr < 30 mL/min)	6.585	1.979-14.286	< 0.001
History of liver disease	1.470	1.030-5.318	< 0.001
Excessive crystalloids (< 6000 mL)	0.095	0.021-0.423	0.002
Excessive colloids (< 2000 mL)	0.054	0.011-0.027	< 0.001
Massive blood loss (> 1600 mL)	17.378	2.141-99.249	< 0.001
Oliguria (< 200 mL)	5.817	1.833-18.299	0.002
Accumulation of lactate (> 2.4 mmol/L)	1.852	1.022-3.458	0.015

OR = odds ratio, CI = confidence interval, VATS = video-associated thoracoscopic surgery, SCLC = small cell lung cancer, PCEA = patient-controlled epidural analgesia, COPD = chronic obstructive pulmonary disease, FEV1 = forced expiratory volume in 1 second, CKD = chronic kidney disease, Ccr = creatinine clearance rate.

loss ($P < 0.001$; OR = 17.378, 95% CI = 2.141-91.249), oliguria ($P = 0.002$; OR = 5.817, 95% CI = 1.833-18.299) and accumulation of lactate ($P = 0.015$; OR = 1.852, 95% CI = 1.022-3.458). There were some protective factors, including type of surgery (VATS) ($P = 0.001$; OR = 0.118, 95% CI = 0.034-0.408), cancer (SCLC) ($P < 0.001$; OR = 0.124, 95% CI = 0.040-0.390) and analgesia (PCEA) ($P = 0.013$; OR = 0.115, 95% CI = 0.021-0.630), limited crystalloids ($P = 0.002$; OR = 0.095, 95% CI = 0.021-0.423) and colloid's transfusion ($P < 0.001$; OR = 0.054, 95% CI = 0.011-0.027).

Discussion

In this retrospective study, the overall incidence of PPCs in patients with NSCLC at stage I or II after thoracic surgery was 29.0% ($n = 102$). Complications included pulmonary edema ($n = 42$), atelectasis ($n = 32$), pneumonia ($n = 19$), ARDS ($n = 8$) and respiratory failure ($n = 1$). The survival rate in PPC patients was evidently lower than in non-PPC patients. Previous studies reported PPCs following major surgery are not always clearly defined [2, 13, 14]. As an example, Petrar *et al.* reported a PPCs incidence of 44.8% in 105 patients who underwent major head and neck surgery. They included pulmonary edema, embolism, atelectasis, bronchospasm, pneumonia, pneumothorax and respiratory failure as PPCs [15]. This contrasts with our study, which investigated thoracic surgery and defined PPC differently.

Compared with previous studies [2, 13, 14], this study stood out in three aspects. First, all the related information of patients undergoing thoracic surgery for NSCLC at stage I or II in a tumor hospital was retrospectively included within this study. Although the number of included patients was small, the data from the single center in recent five years are of high quality; there are few missing outcomes and clinical materials were taken by professional coordinators to decrease various errors. In addition, all cases were identical and analyzed comprehensively. Second, the analyzed PPCs consisted of pulmonary edema, atelectasis, pneumonia, ARDS and respiratory failure. Third, a risk prediction analysis predicting PPCs after thoracic surgery was described from preoperative and intraoperative variables, and further analyzed by multivariate logistic regression.

In present study, age, history of smoking, comorbidities of COPD, CKD and liver disease, type of surgery and PCA, method of operation and the intraoperative blood loss, urinary volume, accumulation of lactate, transfusion of crystalloids and colloids were associated with PPCs. Similarly, Agostini et al. only reported age, BMI, ASA classification, smoking history and COPD as predictive risk factors for PPCs [2]. The risk of lung cancer rises with age, most patients undergoing lung cancer are over 50 years old and over one-third are older than 65 years [16]. Elder patients favored unsatisfactory physical status and high risk for major surgery. Although advanced age tends to with a higher incidence of coexisting comorbidities, itself is an independently powerful predictive risk factor. The impact of advanced age to PPCs may be different according to the methodology used to assess its contribution. We found a significantly higher contribution of advanced age for PPCs.

Smoking has been shown as a PPCs risk factor for major surgery other than thoracic. Of the various smoking-associated diseases, lung

cancer and COPD are mainly responsible for declined pulmonary functions of gas exchange, defense and immunity [17, 18]. Recent smoking cessation may have a higher postoperative complication prevalence than current smoking [19, 20], which may be related to sputum retention, delayed improvement of inflammation and reduction of irritable coughing. Lung cancer patients with continued smoking have obviously poorer quality of life, higher risk for subsequent cancers and reduced survival. In addition, lung cancer patients with COPD, CKD or liver disease comorbidity had a higher PPC incidence. COPD with declined pulmonary functions (ratio of the forced expiratory volume in one second [FEV1] and forced vital capacity [FVC] less than 80%), and chronic inflammation is positively related to PPCs [21]. The ability of the kidneys to excrete waste products is obviously decreased in CKD patients, indicating an imbalance of water, electrolytes and acid-base, accumulation of metabolite and perioperative medicines, and high risk of cardiac and cerebrovascular disease [22-24]. Similarly, in patients with liver disease, the breakdown and excretion of substances, waste products and medicines are impaired. The baseline physical status of patients with these comorbidities is inferior, increasing their tendency to develop PPCs.

In this study, contributions of type of surgery (VATS), options of surgery (lobectomy versus segmentectomy) and PCA (PCEA) for PPCs were also captured our attention. Compared with traditional thoractomy, VATS is advantageous for reduced infection and wound dehiscence resulting from faster recovery and greater chance for the wound to heal, and avoidance of muscle division and bone fractures to diminish duration and intensity of pain. A meta-analysis by Westeinde SCV reviewed that 47% (88/187) patients had ≥1 minor (7-57% in literature) and 10% (18/187) ≥1 major complication (2-26% in literature) following thoracotomy, but only 38% (6/16) had ≥1 minor complication and no major complications during VATS [25]. Various studies proved that VATS is associated with less postoperative pain and better quality of life than is the anterolateral thoracotomy for the first year after surgery [26, 27]. However, the contribution of lobectomy and segmentectomy for PPCs was similar as same as the outcomes of study by Lin Y [28]. Those who undergo segmentectomy resected less lung tissue and preserved more lung function compared with conventional lobectomy contributing to higher quality of life, but there are no significant differences reported at the rate of local tumor recurrence and total 5-year survival between these two surgical options [29, 30]). The skewed results that the similar contribution of lobectomy and segmentectomy for PPCs, in present and Lin Y' study, was brought because of retrospective study without standardized guidelines for the procedure selecting, and individual decision for which patients would undergo anatomic segmentectomy by surgeons. Furthermore, various studies proved that the application of PCEA through lumber or thoracic epidural catheter, in the early postoperative period, would decrease the risk of myocardial ischemia, atelectasis and pneumonia, and improve lung ventilation [31-33]. Our outcomes also favored this viewpoint and proved that PCEA is a protective factor for PPCs.

The intraoperative hematorrhea, oliguria, accumulation of lactate, transfusion of crystalloids and colloids were also identified as PPCs risk factors. During thoracic surgery, especially thoractomy, reducing the volume of intraoperative bleeding allows better visualization to provide more time for determing the scope of tumor involvement, better protection of the surrounding normal tissue owing to avoidance of tumor contamination and creation of more explicit tumor resection boundary, and better decrease in procedure duration and influence on homeostasis [34]. Less urine output intraoperatively is caused by two main reasons: unreseasonable fluid infusion and disorder of kidney function. Once transfusion of crystalloids and colloids is excessive, the excess fluid cannot excrete as indicators and risk factor for PPCs. Excessive transfusion of fluid increased the level of central venous pressure, and low central venous pressure was proved beneficial for preventing postoperative pulmonary complications [35].

Two limitations were identified in this retrospective study. First, the attending physician was in charge of the diagnosis of PPCs; thus, potential estimation bias for actual PPC incidence was unavoidable. Second, the analyzed cases from this study were taken from one university-affiliated tumor hospital rather than multiple centers, which is potentially unrepresentative of overall PPC incidence in thoracic surgery patients in China.

In conclusion, 29.0% of 453 patients who underwent thoracic surgery for NSCLC of early stage developed PPCs. The preoperative variables associated with PPCs included advanced age, history of smoking, comorbidity with COPD, CKD and liver disease. Type of surgery and postoperative analgesia, excessive transfusion of crystalloids and colloids, massive blood loss, oliguria and increased lactate level were identified as intraoperative parameters associated with PPCs. Further risk factor analysis would provide valuable information to assist in predicting and preventing complications in lung cancer patients undergoing thoracic surgery.

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Disclosure of conflict of interest

None.

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