Int Surg 2017;**102:**396–403
DOI: 10.9738/INTSURG-D-16-00193.1

The Role of an Array of Routine Clinical Variables to the Occurrence and Severity of Postoperative Pneumonia in Non–Small Cell Lung Cancer Patients

Qingwei Shen[1], Yutian LAI[2], Xiaoqu Li[1], Yanli Ji[2], Kun Zhou[2]

[1]*Department of Thoracic Surgery, General Hospital of CNPC Sichuan Administration, Chengdu 610041, People's Republic of China*

[2]*Department of Thoracic Surgery, West China Hospital, Sichuan University, Chengdu 610041, People's Republic of China*

Background and purpose: Data of an array of preoperative/intraoperative clinical variables may carry significant information for predicting the probability of postoperative pneumonia or chest infection in non–small cell lung cancer (NSCLC) patients. We aimed to investigate the association between those variables and the occurrence of postoperative pneumonia (POP) as well as the severity of POP, based on routine laboratory tests, basic characteristics, and perioperative variables during the in-hospital period.

Methods: A consecutive series of NSCLC patients undergoing lung cancer lobectomy at our department from January 2014 and December 2015 was used as the target patient group and stratified into 2 groups: pneumonia (POP) and non-pneumonia (N-POP), according to occurrence of pneumonia after lobectomy in 30 days. The POP was classified into 5 severity grades, based on the Clavien-Dindo complication classification system.

Results: Regarding binary logistic regression analysis for risk factors of POP, the following were found to be the independent risk factors of the occurrence of POP: postoperative predicted forced expiratory volume in 1 second [ppoFEV1%; odds ratio (OR): 0.996, 95% confidence interval (CI): 0.993–0.999; $P = 0.021$]; Charlson comorbidity index (CCI) score >3 (OR: 2.694, 95% CI: 1.462–4.965; $P = 0.001$); American Society of Anesthesiologists (ASA)score >3 (OR: 2.066, 95% CI: 1.060–4.029; $P = 0.033$); postoperative predicted diffusion capacity for carbon monoxide of the lung (ppoDlco%; OR: 0.458, 95% CI: 0.090–0.809; $P = 0.014$); and

Corresponding author: Qingwei Shen, No. 127 Tongji Road, Huayang Area, Chengdu, People's Republic of China.
Tel: +86-2885608042; Fax: +86-2885608042; E-mail:shemqw@hotmail.com

neutrophil-lymphocyte ratio (NLR; OR: 2.171, 95% CI: 1.721–2.737; $P < 0.001$). With regard to risk factors analysis of pneumonia severity via ordinal polytomous logistic regression, the following were the independent risk factors: early stage (OR: 0.626, 95% CI: 0.422–0.929, $P = 0.020$); CCI score >3 (OR: 1.914, 95% CI: 1.058–3.459, $P = 0.032$); ppoDlco% (OR: 0.638, 95% CI: 0.445–0.914, $P = 0.014$); and NLR (OR: 1.218, 95% CI: 1.031–1.436, $P = 0.020$).

Conclusion: Among an array of clinical variables in the hospital, major risk factors for POP following LC surgery were ppoFEV1%, ppoDlco%, NLR, ASA score >3, and CCI score>3; meanwhile, ppoDlco%, CCI score>3, NLR, and early tumor stage were the key predictors of POP severity.

Key words: Lung cancer – Surgery – Pneumonia – Risk factors

Lung cancer (LC) has become the leading cause of death in China, regardless of gender or region.[1] Surgery is still the cornerstone of management and treatment for LC patients, and currently is the only therapy offering a potential hope for cure, especially for patients diagnosed in the early stages. Postoperative pneumonia (POP) is one of the most common complications in LC patients after therapeutic surgical resection, as it potentially increases mortality risk and hospitalization expenses, prolongs length of stay in hospital, and significantly influences the sequential recovery and prognosis of patients; also, POP may be a marker of increased long-term mortality after LC surgery.[2–4]

To better prevent or predict pneumonia in surgical patients with LC, up-to-date data on POP risk factors are urgently necessary, as recent studies have revealed that the ratios of POP are quite different.[2–4] Furthermore, an effective assessment of risk of POP would allow physicians to set realistic expectations for postoperative therapies and care. Various genetic and molecular biomarkers show promise for being predictors of POP; however, the majority of them may not yet be available in routine practices, not to mention the high cost and need for specialized equipment and expertise. Therefore, analyzing the risk factors of POP in some routine variables that may carry significant importance is considered to be more feasible or practicable. Based on this, we performed a cohort study to examine patient-related risk factors for POP as well as severity of POP following therapeutic LC lobectomy in routine variables.

Materials and Methods

Patients selected

This study was a retrospective and single-center study of consecutive patients who underwent LC lobectomy at the Department of Thoracic Surgery of our hospital between January 2014 and December 2015. Subjects were selected from NSCLC-identified patients receiving surgery in our department. From a total of NSCLC-identified patients, we excluded patients with advanced stage or unknown stage cancer, secondary lung cancer, histology of cancers other than non–small cell lung cancer (NSCLC), or those with incomplete or loss of relevant data.

Ethics approval

The ethics committee gave its approval for the publication of this study with a waiver of informed consent. Clinical data were collected by well-trained coordinators using a hospital database. All operations were performed by an experienced surgical team.

POP diagnosis criteria and classification of POP severity

We defined an episode of POP as either a hospital discharge date, a new hospital admission date, a hospital outpatient clinic visit date, or an emergency department visit date with a primary or secondary diagnosis code of pneumonia occurring within 30 days after the date of surgery (index-admission with surgery included).

Pneumonia was defined as at least 3 of the following: leukocytosis >10,000/mm^3 or <3,000/mm^3, temperature >38.5°C, purulent sputum, persistent infiltrate on chest X-ray, or pathogenic microorganisms cultured from endotracheal aspirate.

Clavien-Dindo classification of surgical complications,[5] which has been validated in surgical areas, was used to stratify POP into 5 severity grades: grade I was defined as pneumonia meeting the diagnosis criteria without the need of pharmacolog-

Table 1 POP severity grades classified by Clavien-Dindo classification of surgical complications

Grade	Definition	Pneumonia
Grade I	Any deviation from the normal postoperative course without the need for pharmacologic treatment or surgical, endoscopic and radiologic interventions. Allowed therapeutic regimens are: drugs as antiemetics, antipyretics, analgesics, diuretics and electrolytes, and physiotherapy. This grade also includes wound infections opened at the bedside	Pneumonia meeting the diagnosis criteria without the need for pharmacologic treatment or surgical, endoscopic, and radiologic interventions
Grade II	Requiring pharmacologic treatment with drugs other than such allowed for grade I complications Blood transfusions and total parenteral nutrition are also included	Pneumonia treated with antibiotics on the ward
Grade III	Requiring surgical, endoscopic, or radiologic intervention	Pneumonia requiring Suction during bronchoscopy or other surgical interventions
Grade IIIa	Intervention not under general anesthesia	
Grade IIIb	Intervention under general anesthesia	
Grade IV	Life-threatening complication (including CNS complications)‡ requiring IC/ICU-management	Severe pneumonia requiring ICU-management, or
Grade IVa	single organ dysfunction (including dialysis)	With respiratory failure, organ dysfunction (s)
Grade IVb	multi organ dysfunction	
Grade V	Death of a patient	Severe pneumonia leading to death
Suffix "d"	If the patient suffers from a complication at the time of discharge, the suffix "d" (for "disability") is added to the respective grade of complication. This label indicates the need for a follow-up to fully evaluate the complication	

ic treatment or surgical, endoscopic, and radiologic interventions; grade II was defined as pneumonia needing treatment with antibiotics; grade III was defined as pneumonia requiring suction during bronchoscope; grade IV was defined as severe pneumonia requiring ICU-management, or with respiratory failure, organ dysfunction(s); and grade V was defined as pneumonia leading to death.

Definition of neutrophil-lymphocyte ratio (NLR)

Sampling of venous blood was taken within 3 days before the surgery, collected in an ethylenediaminetetraacetic acid–containing tube. The definition of NLR was: NLR = percentage of neutrophils for whole white blood cells (WBC)/percentage of lymphocytes for whole WBC.

Statistical analysis

All statistical analyses were carried out using statistical software (SPSS 21.0 software, SPSS Inc, Chicago, Illinois, USA). All statistical tests were two-sided. Numeric variables were expressed as mean ± SD. Discrete variables were compared using the χ^2 test or Fisher exact test. Multivariate analysis was performed using binary logistic regression analysis and ordinal polytomous logistic regression for risk factors analysis of POP as well as POP severity. All results were considered significant at $P < 0.05$.

Results

Population characteristics

Data from 1058 patients were included in this retrospective analysis. All of them were diagnosed as LC with the histology of NSCLC (mean age: 61.3 ± 10.0 years; range: 39–86 years); 55.5% (587/1058) of them were males and 21.3% (225/1058) were current-smokers; of them, 150 (14.2%) patients suffered from POP and divided into the POP group, compared with 908 (85.8%) in the N-POP group. Details of baseline characteristics were listed in Table 2. Patients in the POP group were older than in the N-POP group (64.5 ± 12.4 versus 58.8 ± 9.4, $P < 0.001$). Meanwhile, higher proportions of patients with American Society of Anesthesiologists (ASA) scores ≥3 (17.3%, 26/150 versus 8.0%, 73/908, $P < 0.001$); Charlson comorbidity index (CCI) scores ≥3 (22.0%, 33/150 versus 7.6%, 69/908; $P < 0.001$); body mass index (BMI) ≥30 (8.7%, 13/150 versus 2.9%, 26/908; $P < 0.001$) were also found (Table 2).

Clinical characteristics

Higher WBC count as well as NLR and longer operation time were identified in the POP group

Table 2 Baseline characteristics between the groups

	POP group	N-POP group	*P* value
Age, mean ± SD	64.5 ± 12.4	58.8 ± 9.4	<0.001
Gender, n (%)			
Men	83 (55.3)	504 (55.5)	0.968
Current smoking status	29 (19.3)	196 (21.6)	0.532
FEV1, L	2.5 ± 0.2	2.5 ± 0.2	0.678
PPoFEV1%	64.9 ± 18.7	69.4 ± 18.1	0.006
Dlco, mL/min/mm Hg	20.6 ± 5.2	22.0 ± 5.0	0.231
ppoDlco%	67.8 ± 24.3	72.7 ± 24.3	0.024
Comorbidities, n (%)			
Hypertension or/and coronary disease	10 (6.7)	70 (7.7)	0.413
COPD	13 (8.7)	52 (5.7)	0.165
Diabetes	18 (12.0)	73 (8.0)	0.109
ASA score ≥3, n (%)	26 (17.3)	73 (8.0)	<0.001
CCI score ≥3, n (%)	33 (22.0)	69 (7.6)	<0.001
BMI ≥30, n (%)	13 (8.7)	26 (2.9)	<0.001
Clinical stage, n (%)			0.258
Stage I	68 (45.3)	438 (48.2)	
Stage II	60 (40.0)	361 (39.8)	
Stage III	20 (13.3)	97 (10.7)	
Stage IV	2 (1.3)	12 (1.1)	
Pathologic type, n (%)			0.247
Adenocarcinoma	98 (65.3)	650 (71.6)	
Squamous cell carcinoma	47 (31.3)	226 (24.9)	
Other	5 (3.3)	32 (3.5)	

compared with the N-POP group (WBC: 7.4 ± 2.9 versus 5.9 ± 1.7 × 10^9; $P < 0.001$; NLR: 3.2 ± 1.2 versus 2.4 ± 0.9; $P < 0.001$; operation time: 124.2 ± 29.4 versus 118.8 ± 32.2 minutes; $P < 0.001$). Patients in the POP group had longer total hospital and postoperative stay length of stay than those in the N-POP group (total hospital stay: 22.0 ± 9.2 versus 15.9 ± 4.1 days; $P < 0.001$; postop stay: 13.2 ± 9.0 versus 7.8 ± 3.2 days; P<0.001). Also, the POP group's total in-hospital and postoperative expenses were higher than the N-POP group (in-hospital: ¥57,499.7 ± ¥19,019.4 versus ¥45,962.2 ± ¥8452.5; $P < 0.001$; postoperative: ¥12,389.8 ± ¥1466.9 versus ¥6012.0 ± ¥2563.7; $P < 0.001$), with no difference observed in preoperative expense between the groups (¥3108.5 ± ¥1106.2 versus ¥3126.1 ± ¥1235.4; $P = 0.276$; Table 3).

Risk factors of POP and POP severity

We performed multivariate analyses via binary logistic regression analysis and ordinal polytomous logistic regression for analyzing risk factors analysis of POP as well as POP severity.

Regarding the binary logistic regression analysis for risk factors of POP, variables analyzed included operation time; bleeding amount; CCI score >3; ASA score >3; postoperative predicted diffusion capacity for carbon monoxide of the lung (ppoDlco%); postoperative predicted forced expiratory volume in 1 second (ppoFEV1%); WBC count; NLR; albumin/globulin (A/G) ratio; platelet (PLT); surgical approaches [open/video-assisted thoracic surgery (VATS)]; chronic obstructive pulmonary disease (COPD); cardiovascular diseases; diabetes mellitus; early stage; gender; and age. The following

Table 3 Clinical characteristics between the groups

	POP group	N-POP group	*P* value
Preoperative variables			
WBC, 10^9/L	7.4 ± 2.9	5.9 ± 1.7	<0.001
HB, g/L	137.8 ± 14.2	136.6 ± 15.6	0.546
PLT, 10^9/L	183.9 ± 54.8	182.7 ± 55.1	0.103
NLR	3.2 ± 1.2	2.4 ± 0.9	<0.001
A/G ratio	1.8 ± 1.7	1.7 ± 0.3	0.463
Surgical approach, n (%)			0.269
VATS	92 (61.3)	599 (66.0)	
Open	58 (38.7)	253 (34.1)	
Intraoperative variables			
Amount of blood loss, mL	131.0 ± 45.3	128.7 ± 46.0	0.230
Operation time, min	124.2 ± 29.4	118.8 ± 32.2	<0.001
Average time of in-hospital stay, d	22.0 ± 9.2	15.9 ± 4.1	<0.001
Preoperative, d	8.4 ± 1.1	8.3 ± 2.0	0.230
Postoperative, d	13.2 ± 9.0	7.8 ± 3.2	<0.001
In-hospital cost, ¥			
Total	57,499.7 ± 19,019.4	45,962.2 ± 8,452.5	<0.001
Preoperative	3108.5 ± 1106.2	3126.1 ± 1235.4	0.276
Postoperative	12,389.8 ± 1,466.9	6012.0 ± 2563.7	<0.001

HB, hemoglobin.

Table 4 Multivariate analysis of POP risk factors

Variables*	OR	*P* value	95% CI
Ppo FEV1%	0.996	0.021	(0.993, 0.999)
CCI score >3	2.694	0.001	(1.462, 4.965)
ASA score >3	2.066	0.033	(1.060, 4.029)
PpoDlco%	0.458	0.014	(0.090, 0.809)
NLR	2.171	<0.001	(1.721, 2.737)

*Variables analyzed included operation time; bleeding amount; CCI score >3; ASA score >3; ppoDlco%; ppoFEV1%; WBC count; NLR; A/G; PLT; surgical approaches (open/VATS); COPD; cardiovascular diseases; diabetes mellitus; early stage; gender; and age.

Table 6 Ordinal polytomous logistic regression for risk factor analysis of POP severity

Variables	OR	*P* value	95% CI
Early stage	0.626	0.020	(0.422, 0.929)
CCI score >3	1.914	0.032	(1.058, 3.459)
PpoDlco	0.638	0.014	(0.445, 0.914)
NLR	1.218	0.020	(1.031, 1.436)

*Variables analyzed included operation time; bleeding amount; CCI score >3; ASA score >3; ppoDlco%; ppoFEV1%; WBC count; NLR; A/G; PLT; surgical approaches (open/VATS); COPD; cardiovascular diseases; diabetes mellitus; early stage; gender; and age.

were found to be the independent risk factors of the occurrence of POP: PpoFEV1% (OR: 0.996, 95% CI: 0.993–0.999; $P = 0.021$); CCI score >3 (OR: 2.694, 95% CI: 1.462–4.965; $P = 0.001$); ASA score >3 (OR: 2.066, 95% CI: 1.060–4.029; $P = 0.033$); ppoDlco% (OR: 0.458, 95% CI: 0.090–0.809; $P = 0.014$); and NLR (OR: 2.171, 95% CI: 1.721–2.737; $P < 0.001$; Table 4).

With regard to POP severity, 19 (12.7%, 19/150) patients were classified as grade I; 89 (59.3%, 89/150) as grade II; 33 (22.0%, 33/150) as grade III; 7 (4.7%, 7/150) as grade IV; and 2 (1.3%, 2/150) as grade V (Table 5). Ordinal polytomous logistic regression was used for risk factor analysis of pneumonia severity. We observed the following to be independent risk factors of POP severity: early stage (OR: 0.626, 95% CI: 0.422–0.929, $P = 0.020$); CCI score >3 (OR: 1.914, 95% CI: 1.058–3.459, $P = 0.032$); ppoDlco% (OR: 0.638, 95% CI: 0.445–0.914, $P = 0.014$) and [insert risk factor here] (OR: 1.218, 95% CI: 1.031–1.436, $P = 0.020$; Table 6).

Discussion

The aim of this study is to provide evidence for several important risk factors for POP and POP severity in LC patients undergoing LC surgery, and subsequently, better evaluate patients' physical status after surgery in order that appropriate and prophylactic measures—especially specific prophylactic measures including individualized antibiotic therapy—can be properly carried out. Unlike other studies in which the identified risk factors for POP following LC surgery are similar to those for community-acquired pneumonia in general populations,[6,7] this study includes some routine clinical variables such as pulmonary function tests, preoperative WBC count, and NLR, which are easy to collect. Meanwhile, we used a Clavien-Dindo classification system to assess the POP severity, and investigate the risk factors of POP severity, which may potentially provide an innovative aspect of POP analysis.

Table 5 Proportions of POP grades

Pneumonia grade	n (n/150)
Grade I	19 (12.7)
Grade II	89 (59.3)
Grade III	33 (22.0)
Grade IV	7 (4.7)
Grade V	2 (1.3)

The occurrence of POP prolongs the length of hospital stay, increases costs for health care systems, and may indicate the increased long-term mortality in patients after LC surgery. Finding out risk factors in POP after LC lobectomy, and formulating a feasible and scientific model to assess the risk of POP could help physicians develop suitable therapies or preventions. According to our study, patients in the POP group had higher in-hospital costs and longer in-hospital stays compared with patients in the N-POP group. This might validate the negative effects of POP in surgical LC patients.

A history of previous pneumonia is a clinically important predictor, which may be a cost-effective and easy screening tool to identify patients at high risk of POP. Meanwhile, many large-sample studies speculate that a history of community-acquired pneumonia increases the risk of subsequent new episodes of pneumonia, indicating that history of previous pneumonia may be significantly associated with the occurrence of POP after lobectomy.[6,8] Our results revealed that preoperative WBC count was higher in the POP group, which provided evidence for the possibility that history of previous pneumonia resulted in higher preoperative WBC counts, and sequentially the higher risk of incidence of POP.

Moreover, numerous studies have been performed to investigate postoperative-related factors including a large number of inflammation-based prognostic markers in the tumor microenvironment and peripheral blood of patients with NSCLC, though the basis of this is not altogether clear.[9,10] White cells subtypes, in particular neutrophils and lymphocytes, play an active role in the inflammation process. NLR, correlating neutrophil and lymphocyte, have been repeatedly reported and confirmed to be useful biomarkers to measure the inflammatory status of the immune system, as the active inflammatory status of the immune system is deemed to expedite the process of tumor invasion and metastasis.[11] Plenty of studies are focusing on the association between NLR and postoperative survival of cancer patients, and many of their results have shown a NLR as a predictor of postoperative survival of cancer patients.[11] Moreover, NLR may also potentially be a factor to indicate the incidence of postoperative pneumonia. Therefore, we conducted a retrospective study involving LC patients in our department, to assess the association of NLR with the incidence of postoperative pneumonia. The result shows that NLR is an independent factor for POP as well as POP severity, which provides evidence to us to predict the occurrence of POP, though further study is needed to confirm the conclusion.

FEV1 and DLCO are the most commonly used pulmonary function variables, considering the promising correlation with postoperative mortality, complications, and respiratory failure after LC surgery.[12–16] Moreover, FEV1% and DLCO% have been further refined to ppoFEV1% and ppoDLCO%, as ppo values are suggested to more accurately stratify postoperative risk by normalizing to the extent of resection. Several investigators have demonstrated stronger relationships between ppoFEV1% and ppoDLCO%, and postoperative risk after pulmonary resection compared with their parent FEV1% and DLCO% values.[17–20] According to our results, the ppoFEV1% and ppoDlco% can each be valuable for predicting the occurrence of POP as well as POP severity, confirming their correlation with POP, one of the most frequently occurring PPCs (postoperative pulmonary complications).

With the prolonged life expectance, the epidemiology shows an increasing rate of LC patients suffering from multicomorbidities such as pulmonary, cardiac, and vascular diseases, which make the affected patients more susceptible to PPCs compared with youngsters. The risk factor analysis shows that age is not a risk factor for POP, though some studies have reported the impact of age on postoperative complications.[21] Also, chronic pulmonary diseases including COPD, which is strongly associated with a history of smoking and decreased lung function, is shown to not be the independent risk factor for POP, though the relationship between comorbidities and postoperative complications has been confirmed by numerous researches.[22,23] Moreover, the CCI, which is used to measure comorbidities, is observed as one independent risk factor for both POP and POP severity. Although our study does not confirm smoking as a risk factor for postoperative complications, the impact of smoking on pulmonary function is significant, considering that pulmonary function is closely related to the occurrence and severity of postoperative complications. Many studies have repeatedly confirmed that the relatively low risk of POP in thoracoscopic surgery, compared with the approach of open surgery—though lacking the statistical significance in the result of surgical approaches between the two groups—leads the analysis to be opposite.[24,25]

A few limitations to this study are worth noting. First, it is only a retrospective research rather than a prospective randomized trial. Although we endeavored to develop proper inclusive/exclusive criteria to remove other factors that may confound the study, excluding some patients (e.g., patients whose missing data accounted for 30%, who once received antibiotic therapy or had pneumonia before the surgery) would reduce the generalizability of the study, and inevitably affect the results

Moreover, we evaluated the patients undergoing a surgical treatment by several surgeons in a single center, and the study only aims to find out the risk factors of POP or POP severity needing further study to confirm or promote the relevant conclusions. We should focus on and formulate a new, economical, and feasible model using routine variables to predict or assess the risk of POP (e.g., the next step for future studies is the creation of a clinical scoring system). Furthermore, the mechanism of the persistent elevation of the postoperative inflammatory response remains unclear. We only illustrate our clinical findings and present the conclusion. More studies and prospective researches should be performed to refine or confirm the relevant conclusions.

In conclusion, among an array of clinical variables in hospital, major risk factors for POP

following LC surgery were ppoFEV1%, ppoDlco%, NLR, ASA score >3, and CCI score >3; meanwhile, ppoDlco, CCI score >3, NLR, and early tumor stage were the positive predictors of POP severity.

Acknowledgments

Conflict of Interest Statement: The authors have no conflicts of interest to disclose.

Funding: This study was supported by Foundation of Science and Technology Support Plan, Department of Sichuan Petroleum Corporation (20130310-11-02).

Author Contributions: Qingwei Shen and Yutian Lai made substantial contributions to the concept and design of the work; Yutian Lai, Qingwei Shen, and Xiaoqu Li drafted the work and revised it critically for important intellectual content; Kun Zhou contributed to the acquisition, analysis, and interpretation of data for the work collected.

References

1. He Y, Li D, Song G, Li Y, Liang D, Jin J *et al*. lung cancer incidence and mortality in china, 2010. *Thorac Cancer* 2016;**7**(3): 323–332
2. Wang Z, Cai XJ, Shi L, Li FY, Lin NM. Risk factors of postoperative nosocomial pneumonia in stage I-IIIa lung cancer patients. *Asian Pac J Cancer Prev* 2014;**15**(7):3071–374
3. Pei G, Zhou S, Han Y, Liu Z, Xu S. Risk factors for postoperative complications after lung resection for non-small cell lung cancer in elderly patients at a single institution in China. *J Thorac Dis* 2014;**6**(9):1230–1238
4. Shiono S, Yoshida J, Nishimura M, Hagiwara M, Hishida T, Nitadori J *et al*. Risk factors of postoperative respiratory infections in lung cancer surgery. *J Thorac Oncol* 2007;**2**(1):34–38
5. Dindo D, Demartines N, Clavien PA. Classification of surgical complications: A new proposal with evaluation in a cohort of 6336 patients and results of a survey. *Ann Surg* 2004;**240**(2):05–213
6. Almirall J, Bolíbar I, Serra-Prat M, Roig J, Hospital I, Carandell E *et al*; Community-Acquired Pneumonia in Catalan Countries (PACAP) Study Group. New evidence of risk factors for community acquired pneumonia: a population-based study. *Eur Respir J* 2008;**31**(6):1274–1284
7. Kornum JB, Nrgaard M, Dethlefsen C, Due KM, Thomsen RW, Tjnneland A *et al*. Obesity and risk of subsequent hospitalization with pneumonia. *Eur Respir J* 2010;**36**(6):1330–1336
8. Schnoor M, Klante T, Beckmann M, Robra BP, Welte T, Raspe H *et al*. CAPNETZ Study Group, Risk factors for community-acquired pneumonia in German adults: the impact of children in the household. *Epidemiol Infect* 2007;**135**(8):1389–1397
9. Cousse LM, Werb Z. Inflammation and cancer. *Nature* 2002;19-26;**420** (6917):860–687
10. Kolb R, Liu GH, Janowski AM, Sutterwala FS, Zhang W. Inflammasomes in cancer: a double-edged sword. *Protein Cell* 2014;**5**(1):12–20
11. Guthrie GJ, Charles KA, Roxburgh CS, Horgan PG, McMillan DC, Clarke SJ. The systemic inflammation-based neutrophil-lymphocyte ratio: Experience in patients with cancer. *Crit Rev Oncol Hematol* 2013;**88**(1):218–230
12. Colice GL, Shafazand S, Griffin JP, Keenan R, Bolliger CT; American College of Chest Physicians. Physiologic evaluation of the patient with lung cancer being considered for resectional surgery: ACCP evidenced-based clinical practice guidelines (2nd edition). *Chest* 2007;**132**(suppl 3):161S–177S
13. Brunelli A, Kim AW, Berger KI, Addrizzo-Harris. Physiologic evaluation of the patient with lung cancer being considered for resectional surgery: diagnosis and management of lung cancer, 3rd ed: American College of Chest Physicians evidence-based clinical practice guidelines. *Chest* 2013; **143**(suppl 5):e166S–e90S
14. British Thoracic Society. Society of Cardiothoracic Surgeons of Great Britain and Ireland Working Party. BTS guidelines: guidelines on the selection of patients with lung cancer for surgery. *Thorax* 2001;**56**(2):89–108
15. Ferguson MK, Little L, Rizzo L, Popovich KJ, Glonek GF, Leff A *et al*. Diffusing capacity predicts morbidity and mortality after pulmonary resection. *J Thorac Cardiovasc Surg* 1988;**96**(6): 894–900
16. Markos J, Mullan BP, Hillman DR, Musk AW, Antico VF, Lovegrove FT *et al*. Preoperative assessment as a predictor of mortality and morbidity after lung resection. *Am Rev Respir Dis* 1989;**139**(4):902–910
17. Kearney DJ, Lee TH, Reilly JJ, DeCamp MM, Sugarbaker DJ. Assessment of operative risk in patients undergoing lung resection: importance of predicted pulmonary function. *Chest* 1994;**105**(3):753–759
18. Santini M, Fiorello A, Vicidomini G, Di Crescenzo VG, Laperuta P. Role of diffusing capacity in predicting complications after lung resection for cancer. *Thorac Cardiovasc Surg* 2007;**55**(6):391–394
19. Ferguson MK, Vigneswaran WT. Diffusing capacity predicts morbidity after lung resection in patients without obstructive lung disease. *Ann Thorac Surg* 2008;**85**(4):1158–1164
20. Cerfolio RJ, Bryant AS. Different diffusing capacity of the lung for carbon monoxide as predictors of respiratory morbidity. *Ann Thorac Surg* 2009;**88**(2):405–410
21. Ogawa F, Wang G, Matsui Y, Hara H, Iyoda A, Satoh Y. Risk factors for postoperative complications in the elderly with lung cancer. Asian *Cardiovasc Thorac Ann* 2013;**21**(3):313–318

22. Sekine Y, Yamada Y, Chiyo M, Iwata T, Nakajima T, Yasufuku K. Association of chronic obstructive pulmonary disease and tumor recurrence in patients with stage IA lung cancer after complete resection. *Ann Thorac Surg* 2007;**84**(3):946–950
23. Sekine Y, Behnia M, Fujisawa T. Impact of COPD on pulmonary complications and on long-term survival of patients undergoing surgery for NSCLC. *Lung Cancer* 2002; **37**(1):95–101
24. Simonsen DF, Sgaard M, Bozi I, Horsburgh CR, Thomsen RW. Risk factors for postoperative pneumonia after lung cancer surgery and impact of pneumonia on survival. *Respir Med* 2015;**109**(10):1340–1346
25. Whitson BA, Groth SS, Duval SJ, Swanson SJ, Maddaus MA. Surgery for early-stage non-small cell lung cancer: a systematic review of the video-assisted thoracoscopic surgery versus thoracotomy approaches to lobectomy. *Ann Thorac Surg* 2008; **86**(6):2008–2016