RESEARCH ARTICLE

Risk Factors of Postoperative Nosocomial Pneumonia in Stage I-IIIa Lung Cancer Patients

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Abstract

Background: To investigate the related risk factors of postoperative nosocomial pneumonia (POP) in patients withI-IIIa lung cancer. Methods: Medical records of 511 patients who underwent resection for lung cancer between January 2012 to December 2012 were retrospectively reviewed. Risk factors of postoperative pneumonia were identified and evaluated by univariate and multivariate analyses. Results: The incidence of postoperative pneumonia in these lung cancer patients was 2.9% (15 cases). Compared with 496 patients who had no pneumonia infection after operation, older age (>60), histopathological type of squamous cell carcinoma and longer surgery time (>3h) were significant risk factors by univariate analysis. Other potential risk factors such as alcohol consumption, history of smoking, hypersensitivity, hypertension, diabetes mellitus and so on were not showed such significance in this study. Further, the multivariate analysis revealed that old age (>60 years) (OR 5.813, *p*=0.018) and histopathological type of squamous cell carcinoma (OR 5.831, *p*<0.001) were also statistically significant independent risk factors for postoperative pneumonia. Conclusions: This study demonstrated that being old aged (>60 years) and having squamous cell carcinoma histopathological type might be important factors in determining the risk of postoperative pneumonia in lung cancer patients after surgery.

Keywords: Risk factor - postoperative pneumonia - lung cancer

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Introduction

For several decades, lung carcinoma has been the most commonly diagnosed malignancy and the leading cause of cancer-related mortality. It accounts for 12% of all cancers diagnosed worldwide with an estimated 1.6 million new cases per annum (Abidoye et al., 2007; Ferlay et al., 2010). Generally, surgical resection is the best therapeutic option for lung cancer patients and is the primary treatment strategy for patients in the initial stages. however, one problem is that this treatment is subject to complications (D'journo et al., 2011). The general incidence of postoperative complications after thoracic surgery is approximately 30%, making it the most frequent and the most common causes of mortality after lung resection (Stephan et al., 2000; Kyriazi and Theodoulou, 2013). Moreover, patients undergoing lung cancer resection are at special risk for postoperative respiratory infections, with an incidence ranging from 2 to 20%. Mortality among these patients remains high, ranging from 22 to 67%, especially with the presence of postoperative pneumonia (POP) (Belda et al., 2005; Sogaard et al., 2013). Postoperative pneumonia is especially severe after thoracic surgery and is associated with high mortality, making it a life-threatening complication of lung resection (Gupta et al., 2013).

Clinical studies have identified several risk factors for postoperative pneumonia following pulmonary survey the most frequent risk factors were as follows: male sex (Alifano, Regnard 2010), age (Shiono et al., 2013), smoking history (Seok et al., 2013), coexistent chronic bronchitis or chronic obstructive pulmonary disease (COPD) (Sekine et al., 2013), poor nutritional status (Jagoe et al., 2001), alcohol consumption (Eliasen, et al., 2013), preoperative deterioration of lung function (Shiono et al., 2007), frequent extrathoracic comorbidities (Ferdinand and Shennib, 1998), prolonged duration of surgery and surgical stress, extent of the resection, tumor location and postoperative mechanical ventilation.

The exact incidence of POP after lung resection is paradoxically poorly known and the risk factors and causative pathogens have been rarely investigated. The objective of this study is to determine the main cause and the risk factors of postoperative pneumonia in 15 hospitalized lung cancer patients (I-IIIa) enrolled between January 2012 to December 2012 in a third-level university hospital.

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Materials and Methods

Tumor staging was assigned by the TNM classification criteria issued by the International Union Against Cancer (UIAC) in 2007. All the data concerning pathogenic bacteria detection, drug sensitivity of antibacterials, routine blood test and C-reactive protein results were based on the original records of hospital clinical laboratory department.

General data

Data concerning lung cancer patients who had undergone lung cancer surgery in our hospital between January 2012 to December 2012 were collected. Cancer staging was determined as I-IIIa by means of TNM classification with definite pathologic diagnosis, including 338 male patients and 173 female patients. The median age of these patients was 60 (26-79), of which 511 cases has underwent pulmonary resections for lung cancer. In detail, 218 after pneumonectomy, 237 after lobectomy, and 56 after wedge resection.

Pulmonary infection diagnosis criteria

We developed the pulmonary infection diagnosis criteria according to the standards published by the The pulmonary infection Symposium in 1990, in detail, POP was defined by the presence of a new or progressive infiltrate on chest radiography or computed tomography during the patient's hospitalization, together with any of the following: new onset purulent sputum, change in character of chronic sputum, fever ≥38°C, a new rise in C-reactive protein value or WBC count, positive blood cultures, or isolation of pathogen from sputum, transtracheal aspirate or bronchial washing.

Data ananlysis on risk facors that may be related to pulmonary infection

We colletced data on patient age (≥60or<60), smoking status, alcohol use, hypersensitivity, diabetes mellitus, hypersensitivity, tumor location, histopathological type, time period when surgery took place (≥3h or<3h), and preoperative chemotherapy.

Overall data was screened using the Chi square test to find risk factors with statistical significanc. Factors screened out were then evaluated using non-conditional logistic multivariate regression model.

The data were analyzed using version 15.0 of the SPSS software package. Chi square test was performed in univariate analyses whereas logistic regression was used in multivariate analyses. Statistical significance was assigned with p values of <0.05.

Results

Table1 summarizes the characteristics of our study population. The number of patients participated in the study was 511, with a median age of 60 (26-79), and 338 patients (66.2%) were males. Among them, 328 patients (63.0%)were ever-smokers and 216 patients (41.5%) had drinking history. Pathological stage I was diagnosed in 46.8% of patients. Pathological investigation revealed 288 adenocarcinomas (56.4%), 204 squamous cell carcinomas (39.9.3%), one large cell carcinoma, (0.2%) three small cell carcinomas (0.6%) and 15 other cell types (3.0%). Fifteen patients (2.9%) were satisfied with the criteria of pulmonary infection.There were no perioperative or postoperative deaths during the study period. Postoperative pneumonia developed in 15 patients (2.9%).

Among patients more than 60 years old, the incidence of postoperative pneumonia was 12 (4.3%) in the noneumonia group and 267 (95.7%) in the pneumonia group. 12 males and 3 females were diagnosed with pneumonia after surgery, and 11 (3.35%)patients had a smoking history. Besides, for patients with hypersensitivity, hypertension and diabetes mellitus, incidence of postoperative pneumonia were 3 (7.14%), 3 (2.6%), 2 (5%), respectively. histopathological type

Table 1. Baseline Characteristics of Patients who Underwent Lung Cancer Surgery

Variable	Value
Patients (n)	511
Age, median (range) (yr)	60 (26-79)
Sex, No. (%)	
Male	338 (66.2)
Female	173 (33.8)
Pulmonary infection	15 (2.9)
Pathology, No. (%)	
adenocarcinoma	288 (56.4)
Squamous cell carcinoma	204 (39.9)
Large cell carcinoma	1 (0.2)
Small cell carcinoma	3 (0.6)
Others	15 (2.9)
Pathological stage, No. (%)	
IA	88 (17.2)
IB	151 (29.6)
IIA	103 (20.2)
IIB	35 (6.8)
IIIA	134 (26.2)

Table 2. Univariate Analysis of Risk Factors for Postoperative Pneumonia in Lung Cancer Patients

Variable	Pneumonia group (n, %)	No Pneumonia group (n, %)	p value
Old age (>60 years)	12	267	0.037
Male	12	326	0.252
Cigarette smoking	11	317	0.398
Alcohol use	6	210	0.907
hypersensitivity	3	39	0.062
hypertension	3	112	0.886
diabetes mellitus	2	38	0.404
Surgical side			0.268
right	11	299	
left	4	207	
Tumor loacation			0.421
central	1	69	
peripheral	14	427	
histopathological type			0.032
Squamous cell carcinoma	10	194	
No squamous cell carcinoma	5	302	
Preoperative Chemotherapy	1	147	0.06
Procedure time (>3h)	5	36	<0.001

Table 3. Multivariate Analysis of Risk Factors for Pneumonia After Surgery in Lung Cancer Patients

Factors	Odds ratio	95%CI		*P*
		Lower	Upper	
Old age (>60 years)	5.813	1.351	25.012	0.018
Squamous cell carcinoma	5.831	2.293	14.83	<0.001
Procedure time (>3h)	1.132	0.346	3.71	0.837

OR Odds ratio, CI confidence interval

were also taken into consideration: 5 (1.7%) patients in the pneumonia group had preoperative adenocarcinoma, while the number of squamous cell carcinoma patients was 10 (3.3%). 1 (0.7%) patient in the pneumonia group received preoperative chemotherapy, and duration time of surgery were longer than 3h for 5 (12.5%) patients. (Table 2)

Of all the variables studied, those that showed statistically significant differences ($p<0.05$) between the pneumonia group and the non-pneumonia group in the univariate analysis were age, histopathological type (adenocarcinoma or squamous cell carcinoma) and procedure time.. The following factors appeared in the multivariate analysis as statistically significant independent risk factors for postoperative pneumonia, with a high predictive capacity: old age ($p=0.037$), histopathological type ($p=0.032$) and procedure time ($p<0.001$). (Table 2) Multivariate analysis revealed that presence of preoperative pneumonia was an independent factor associated with age factors (OR 5.813, $p=0.018$) and pathological type of squamous cell carcinoma (OR 5.831, $p<0.001$) (Table 2).

Discussion

In patients undergoing surgical resection for lung cancer, postoperative pulmonary complications are common and related with high mortality, among which nosocomial pneumonia is the most important risk factor for morbidity (Wada et al., 1998; Ogawa et al., 2013). The incidence of postoperative pneumonia in our study (2.9%) is lower than the previously reported rates of 5 to 20% (Arozullah et al., 2001; Belda et al., 2005) the disparities may be explained by different definitions and diagnostic tests of pneumonia among studies.

In our investigation, the major predictors for postoperative pneumonia are old age, carcinoma histopathological type and operating time. Old age has been associated with postoperative pulmonary complications in many studies. Old patients often have comorbidities because of their impaired physical conditions, leading to higher rate of postoperative complications after lung cancer surgery compared with young patients. Rivera et al. evaluated postoperative mortality in patients with Stage I or II non-small-cell lung cancer, showing a higher mortality in the more elderly patients >70 years (Rivera et al., 2011). Other investigators found that lung cancer patients of advanced age, in particular those 75 years and older, are a high-risk group for postoperative pneumonia and empyema (Shiono et al., 2007). It should be noted that in our study, the age limitation was decreased to older than 60.

Another factor identified by us that led to higher risk of postoperative was histopathological type of lung cancer. In our retrospective study, patients with squamous cell carcinoma were more likely to suffer pneumonia than adenocarcinoma patients, which was in accordance with the result reported by Seok in 2012 (Seok et al., 2012).

Lung cancer includes various histologic types; squamous cell carcinoma and adenocarcinoma are the most common. There are several differences in the clinical behavior of the histo-logical types. As squamous cell carcinomas are much more commonly endobronchial lesions protruding into and obstructing large central bronchi, which might profit to create an environment predisposing to post-obstructive pneumonia, while adenocarcinomas are much more commonly peripheral. Nevertheless, few studied have considered the effect of histopathological type on incidence of postoperative pneumonia, and the conclusion still need more evidence to prove.

Finally, the last risk factor identified was the procedure period, as previously reported, longer operations usually caused a higher risk of postoperative pneumonia (Schussler et al., 2006; Alifano and Regnard, 2010). Aokiet et al. demonstrated an association between surgery time and subsequent complications (Aoki et al., 2000). Shiono et al. suggested that surgery duration should be limited to the shortest possible time and also highlighted the importance of meticulous and skillful surgical technique (Shiono et al., 2013). Therefore, we suggest that surgery duration should be limited to the shortest possible time. A meticulous and skillful surgical technique is of the utmost importance, therefore a stapling technique or a new device may be useful in reducing surgery time and blood loss.

For other factors itemized in Table 2, such as sex, cigarette smoking, alcohol use, diabetes mellitus, hypertension and preoperative chemotherapy, all these variables seemed to have no relation with occurrence of postoperative pneumonia, which was consistent with previous reports.

As single-institution experiences are not adequate to make universal conclusions, this is the major limitation of our study. Furthermore, it was a retrospective study with a small sample size. A retrospective study of 44 cases on clinical characteristics of patients with bronchioloalveolar carcinoma carried out by Nigar Dirican faced the same problem (Dirican et al., 2013). More, even a strong statistical association does not necessarily indicate a cause-and-effect relation. Thus, to remedy these limitations, a prospective randomized controlled trial is needed.

To summarize, the importance of knowing the risk factors for pneumonia is potential for preventing this important complication. Our investigation can only help to identify aforementioned factors associated with postoperative pneumonia, and larger studies are needed to determine statistically significant variables that can guide future research. However, we should be aware that even a strong statistical association does not necessarily indicate a cause-and-effect relation. In conclusion, according to our research, patients older than 60, diagnosed with squamous cell carcinoma disease and prolonged surgery durations indicated an increased risk of postoperative pneumonia.

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