Pneumonia After Thoracic Surgery

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14.1 Introduction

The developments in the field of thoracic surgery and perioperative anesthetic management have extended its patient population; those who were previously inoperable are now undergoing surgery.

Preoperative evaluations by a multidisciplinary team that includes thoracic surgeons, chest physicians, intensive care physicians, and anesthesiologists have benefited patients in terms of reduced postoperative morbidity and mortality.

The causes of postoperative complications can be divided into three categories: infectious, surgery related, and cardiovascular. The most frequent and severe complications after thoracic surgery are respiratory complications. Some are surgery related such as hemorrhage, bronchopleural fistula, and atelectasis. Other respiratory complications are pneumonia, acute lung injury, and acute respiratory distress syndrome (ARDS). Hypoventilation and ineffective cough caused by several mechanisms such as inappropriate pain management increase the risk of postoperative pneumonia. There are also cardiovascular complications including arrhythmias, pulmonary thromboembolism, and cardiac failure.

The incidence of pneumonia after thoracic surgery is approximately 5.3–22 % [1, 2]. Factors that influence the incidence of pneumonia include patient population, type of surgery, antibiotic prophylaxis, and diagnostic criteria for pneumonia. The incidence of pneumonia is higher when using clinical criteria compared with objective criteria.

The mortality rate of postoperative pneumonia is approximately 17 %; after thoracic surgery the rate rises to 19–40 % [1, 3]. Due to the high risk for mortality in this patient population, risk prediction is also crucial for surgical decision-making and informed patient consent. Pneumonia after thoracic surgery causes longer stays in intensive care units (ICU) and hospitals, which in turn increases the costs.

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Table 14.1 Risk factors for postoperative pneumonia after thoracic surgery

Age ≥ 75
Male
Smoking history
$FEV_1 < 70\%$
Induction therapy
Pathologic stages III–IV
Duration of operation > 3 h
COPD
Histopathologic type (squamous cell carcinoma)

FEV1 forced expiratory volume in one second, *COPD* chronic obstructive pulmonary disease

14.2 Risk Factors

During the perioperative period, many risk factors play a role in the development of postoperative pneumonia. With the exception of abdominal surgery, the risk of pneumonia after thoracic surgery is 38 times greater than other type of surgery [4]. Deterioration in pulmonary function after abdominal and thoracic surgery has previously been evidenced through pulmonary function tests, imaging methods, and physiologic measurements [5, 6].

The risk factors for postoperative pneumonia after thoracic surgery can be separated into three phases as the preoperative, intraoperative, and postoperative periods.

Risk factors related with postoperative pneumonia in thoracic surgery are listed in Table 14.1 [7, 8].

Arozullah et al. used a combination of risk factors to create a risk index for predicting pneumonia after noncardiac surgery [9]. The authors developed the risk index from the data obtained from preoperative patient-specific and operation-specific risk factors. They found that abdominal aortic aneurysm repair and thoracic surgery had the highest risk for postoperative pneumonia. The risk index may be useful for high-risk patients; therefore giving these patient groups more attention in the perioperative period and taking preventive measures may reduce the incidence of pneumonia.

Predictors of postoperative pneumonia are explained in some other chapters of this book; there we are going to focus on approach during postoperative period.

14.3 The Postoperative Period

Secretions cause atelectasis and pneumonia during the postoperative period, especially in patients with a smoking history, pain, and inefficient cough. Secretion retention in airways may cause obstruction of broncopulmonary units and atelectasis, and this is even more pronounced in smokers and in patients with chronic lung disease. The diagnosis of sputum retention can be clinical and it is characterized by

respiratory distress with rapid, shallow, and bubbly breaths. There was a strong association between sputum retention and postoperative pneumonia in patients with chronic obstructive pulmonary disease (COPD), smoking history, and poor analgesia [10]. There is a great importance for physiotherapy in this situation. At least two daily visits should be performed; some patients need more. Another noteworthy point is the hydration of patients for secretion mobilization. Oxygen therapy via a facemask inevitably dries secretions when non-humidified oxygen is used. This causes mucociliary dysfunction and a decreased ability to clear secretions, so humidified oxygen should be used. Sometimes mucolytic agents can be helpful. Chest physiotherapy is a therapeutic modality that should be kept in mind. Postural drainage, percussion, and vibration are applied to the affected lung opening and promote coughing during which physicians should provide adequate analgesia. Despite these interventions, tracheal suctioning can be used in patients who cannot remove secretions. Before suctioning, high oxygen fraction should be used in patients at risk for hypoxemia.

Fiberoptic bronchoscopy may be used for clearance of secretions which has the advantage of direct visualization of the tracheobronchial tree and the ability to take sputum samples for culture when a clinically infection is suspected. Sedation is required for this procedure in nonintubated patients; noninvasive ventilation may be used during the intervention to avoid hypoxemia.

14.4 Pulmonary Rehabilitation

Many comorbid conditions accompany lung cancer surgery. Approximately 50% of patients with lung cancer also have COPD [11]. Patients with COPD may have ineffective cough, increased secretions, and impaired gas exchange after lung resections, especially hypercapnia secondary to hypoventilation. Some patients may need reintubation and mechanical ventilation. Pulmonary rehabilitation includes breathing exercise, cough training, and self-management education; psychosocial support has been shown to decrease complications [12, 13]. Preoperative assessment of these patients for targeting reduces postoperative complications and improves survival. Pneumonia is the most significant postoperative complication that increases morbidity and mortality. These interventions may help reduce the incidence, severity, and risks of pneumonia. Smoking cessation and pharmacological therapies such as bronchodilators, mucolytics, and antibiotics if necessary are useful for patients preparing for lung resection and also those with chronic lung disease.

Pulmonary rehabilitation programs can be preoperatively and postoperatively conducted at certain time periods. These programs include breathing and coughing techniques, inspiratory muscle strength, home-based aerobic exercise, and incentive spirometry [14–16]. Spruit et al. showed that patients with poor functional status after lung cancer treatment improved their exercise capacity using a pulmonary rehabilitation program with a 6-min walk [17]. However, after patients are diagnosed as having lung cancer, they often feel that surgery must be planned as soon as possible and thus may refuse a pulmonary rehabilitation program.

14.5 Analgesia

The thoracic analgesia is crucial to keep the patient comfortable for reducing postoperative pulmonary complications after surgery. Surgical incision, intercostal nerve injury, and inflammation are major causes of pain after thoracic surgery. Thoracic epidural analgesia is still considered the gold standard for pain relief after thoracotomies, but recently some evidence showed that a paravertebral block had a similar analgesic effect with fewer adverse effects than thoracic epidural analgesia [18]. For reduced complications after thoracic surgery, patients should be able to breathe deeply, cough, and remove secretions and should be mobilized early. Postoperative ineffective pain relief associates with worsened pulmonary complications. Belda reported that a higher postoperative pain score was an independent predictor of postoperative respiratory infections [19]. Recently, multimodal analgesia has been preferred for post thoracotomy pain. In this regimen, regional blocks are combined with opioids, nonsteroidal anti-inflammatory drugs, acetaminophen, selective cyclooxygenase −2 inhibitors, and α2 agonists. Multimodal analgesia is more effective and has fewer adverse effects. When the age and comorbid conditions of these patients are considered, more attention must be paid to the drugs used for analgesia in this population.

14.6 Does Bronchial Colonization-Airway Colonization Play a Role in Postoperative Pneumonia After Thoracic Surgery?

In normal conditions, the lower respiratory tract is sterile. Most patients who undergo surgery have a history of smoking with subsequent impairment of mucociliary function and accumulation of secretions in the lung; therefore these patients have facilitating factors for the development of infection.

The source of pathogenic microorganisms responsible for pneumonia in this patient population is not yet clear. Preoperative colonization, colonization during intubation or mechanical ventilation, and aspiration during the perioperative period can cause pneumonia after thoracic surgery [20]. The incidence of airway colonization in patients with lung cancer varied between 10 and 83 % [1, 19, 21]. Taking samples using different methods (bronchoalveolar lavage (BAL), protected specimen brush (PSB), endotracheal aspiration (ETA), spontaneous sputum) and at different times (preoperative, perioperative, or postoperative period) may account for this wide range.

Some studies have been shown that healthy, nonsmoking patients have no airway colonization [22, 23]. Healthy smokers and patients with COPD had bacterial colonization at 29 % and 66 %, respectively [24, 25]. Monso showed that 25 % of 40 stable patients with COPD had airway colonization; the most commonly isolated microorganisms were *Haemophilus influenzae* and *Streptococcus pneumonia* [26].

Patients who undergo thoracic surgery have similar colonization patterns to patients with COPD. Although the relationship between airway colonization and

ventilator-associated pneumonia has been proven, bronchial colonization and pneumonia in patients after lung cancer surgery are unclear. Several studies investigated this issue. Hirakata et al. investigated the airway colonization patterns in patients with primary lung cancer and nonmalignant lung disease and healthy volunteers [27]. The rate of bacterial colonization was significantly higher in patients with lung cancer (51.9 %) than in those with nonmalignant lung disease (37.3 %) and healthy volunteers (37.8 %), and the Gram-negative colonization was higher in this cancer group than in other patient populations. The pathogenesis of airway colonization in patients with lung cancer is not clear, but centrally located tumors and high body mass index were found to be risk factors for colonization [28]. Smoking and poor pulmonary functions also add risk for colonization in patients with COPD. Furthermore, sampling methods that evaluate the incidence of airway colonization are imperative in this patient population.

Which time period is important to the development of pneumonia with respect to colonization? Sok et al. performed a study to verify the origin of microorganisms that caused pulmonary infections after lung cancer surgery [29]. They obtained samples of sputum 3 days before surgery, during surgery, and 3 days after surgery. The microorganisms that caused infections were isolated as preoperative 18 %, intraoperative 13 %, and postoperative 63 %. They found that the microorganisms which caused pneumonia were the same with microorganisms which were isolated in sputum at the 3rd postoperative day. The authors concluded that the colonization of the airway usually occurs during the postoperative period; the oral cavity and pharynx were the source of pathogens.

Cabello et al. investigated distal airway colonization in patients with pulmonary carcinoma and obtained samples from proximal to the endobronchial lesion using a PSB [22]. They used $\geq 10^2$ cfu/mL as a cutoff value for colonization and found that 42 % of patients had bronchial colonization. Sixteen of 25 isolated microorganisms were non-potential pathogenic microorganism, and the most isolated potential pathogen microorganism was *H. influenza*. Similarly, Ionas et al. found 41 % bronchial colonization in patients with resectable lung cancer [28].

Rather than the colonization of the airway, the similarity of microorganisms that colonize the airway and cause pneumonia is a more relevant issue. The correlation between these pathogens is controversial. Ionas reported that there was no relationship between postoperative infectious pulmonary complications and bronchial colonization [28]. Sok demonstrated that postoperative infective complications were caused by Gram-negative bacteria, whereas most of the positive cultures obtained preoperatively were Gram positive [29]. The change in the pattern suggests that the colonization of microorganisms in the early postoperative period may be caused by the aspiration of gastric contents and frequent interventions to the airway in the operating room and ICU. In contrast to these studies, some authors reported a good correlation between microorganisms isolated from patients who developed postoperative pneumonia with the same agents identified preoperatively [1, 19, 21, 30]. Appropriate prophylactic antibiotics and optimal duration of prophylaxis are the most imperative considerations for the prevention of postoperative pneumonia in patients who are colonized with potentially pathogenic microorganisms (PPMs) preoperatively.

The most common preoperatively isolated microorganisms from the airway are *H. influenzae*, *S. pneumonia*, and *Staphylococcus aureus*. Although approximately 50 % of postoperative pulmonary pathogens are not documented, some of the isolated pathogens have been different in various studies. In pneumonia developed during late postoperative period, resistant strains of gram-negative bacteria should be considered as potential pathogens. In the early postoperative period (first week), *H. influenzae* and *S. pneumonia* are the most common pathogens, but more resistant microorganisms such as *Pseudomonas aeruginosa*, *Acinetobacter baumannii*, and *Klebsiella pneumonia* cause pneumonia in the late postoperative period. Cytomegalovirus (CMV) infection in patients with hematologic malignancies, patients who are human immunodeficiency virus positive, and lung transplant recipients is common, but the incidence of CMV infection in other types of cancer patients is not well known. A study performed in a surgical ICU showed that the incidence of CMV infections was around 35.6 % [31]. The essential thing here is to suspect a CMV and make the correct diagnosis, especially in patients under treatment with steroids. Preemptive antiviral therapy is administered in selected patient populations but not in thoracic surgery. Antiviral therapy should be considered for patients with severe pneumonia, ARDS, and resistant to classical antibacterial therapy in postoperative period especially for patients who underwent induction therapy. The widespread use of antibiotics also affects the type of microorganisms that colonize.

14.7 Antibiotic Prophylaxis

Antibiotic prophylaxis should be used for thoracic surgery because of the clean contaminated nature of these operations. The relationship between airway colonization during the perioperative period and postoperative pneumonia after thoracic surgery enhances the significance of antibiotic prophylaxis in this field. Despite the routine use of antibiotic prophylaxis, the incidence of postoperative pneumonia is also high (24 %) [1, 2]. In several studies the onset of postoperative pneumonia developed in the first week.

Which type of prophylactic antibiotics is recommended in this type of surgery? First- and second-generation cephalosporins such as cefazolin, cefamandole, cefuroxime, and cefepime are the most frequently used agents for prophylaxis in pulmonary resections in many countries. These agents are highly successful in preventing surgical wound infections but their effectiveness in pneumonia should be questioned [32]. In a study that investigated the efficacy of prophylaxis, it was shown that the microorganisms that caused pneumonia were not sensitive to prophylactic antibiotics [32].

Most of the microorganisms responsible for postoperative pneumonia are Gram negative and are resistant to first- and second-generation cephalosporins.

Preoperative microbiologic examination of the tracheobronchial tree may be helpful to select effective antibiotic prophylaxis. Several studies investigated the effect of different prophylactic agents on postoperative pneumonia (1, 33). Schussler compared cefamandole (3 g/24 h) with amoxicillin-clavulanate (6 g/24 h) and found

a significant decrease in the incidence of postoperative pneumonia in the second group and concluded that antibiotic prophylaxis may decrease the rate of pneumonia after surgery. Another study compared cefuroxime and cefepime and found that cefuroxime was more effective than cefepime as a prophylactic agent [33]. Most of the microorganisms responsible for postoperative pneumonia are Gram-negative bacteria, and 50 % of them are *Enterobacteriaceae* spp., which are resistant to these antibiotics [32].

The dose and duration of antibiotics used for prophylaxis are another major challenge. The first dose is usually administered after the induction of anesthesia. Some protocols only use a single dose, whereas other protocols use antibiotics for 24 or 48 h for prophylaxis [34].

Skin and oropharyngeal flora can be the source of microorganisms that cause postoperative pneumonia after thoracic surgery. Therefore antibiotic prophylaxis should be considered before surgery and in cases of pneumonia microorganisms from the skin, and oropharyngeal flora must be covered.

Microorganisms that colonize the bronchial tree are usually responsible for postoperative pneumonia. In addition to antibiotic prophylaxis, surveillance results and antibiotic sensitivity patterns should be considered.

Using classical criteria for diagnosis of pneumonia after lung resection is more difficult than other types of surgery because fever, hypoxemia, and abnormal chest X-ray findings are commonly seen after lung resections.

14.8 Diagnosis

The actual incidence of postoperative pneumonia after thoracic surgery is unknown. There is no gold standard for the diagnosis of postoperative pneumonia so the incidence of pneumonia varies in the literature. Many centers use only clinical criteria, whereas others use invasive diagnostic techniques. Fever > 38 °C, leukocytosis (white blood cell count ≥12000cells/μL) or leukopenia (white blood cell count ≤4000 cells/μL), purulent secretion, and new or progressive consolidation on chest X-ray are parameters used when pneumonia is suspected (Fig. 14.1). In addition to these criteria, dyspnea, worsening oxygenation, and changes in the amount or character of sputum support the diagnosis of pneumonia. Radiologic signs of pneumonia may be difficult to differentiate pneumonia from pulmonary embolism or atelectasis, especially in the immediate postoperative period. Chest X-rays are taken in the ICU with portable machines, which also add difficulty resulting in suboptimal quality images. The evaluation of chest X-rays is more difficult in patients who undergo lung surgery, and for these reasons, chest X-rays are only used to support the diagnosis; therefore thorax CT may be useful for definitive diagnosis in this situation (Figs. 14.2 and 14.3).

Endotracheal aspiration cultures are mostly used for the diagnosis of pneumonia. This is an inexpensive, easy, and quick method when compared with bronchoscopic cultures. However, its accuracy is questionable in many respects; distinguishing between infection and colonization is very difficult. If ETA samples are quantitatively analyzed, the accuracy of the results is close to bronchoscopic results.

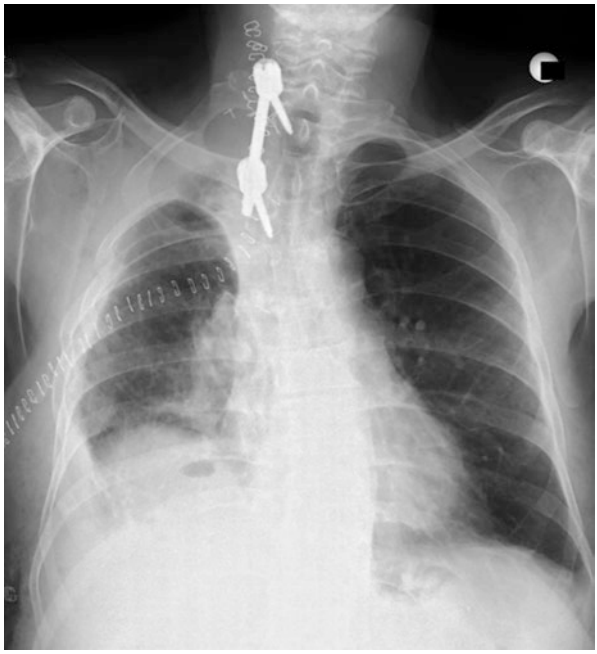

Fig. 14.1 Chest X-ray showing pneumonia after the right pulmonary resection

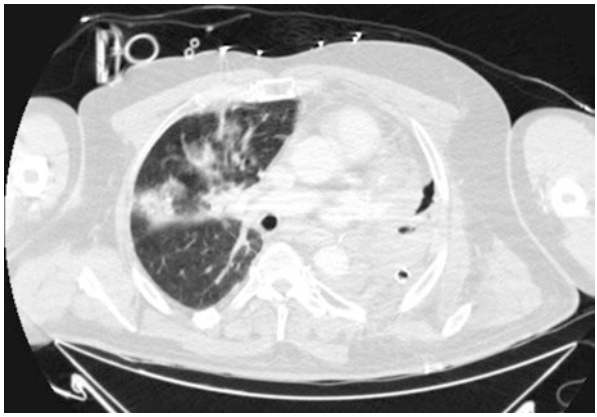

Fig. 14.2 CT image of right pneumonia after the left pneumonectomy

Differential diagnosis in this period is quite difficult. Sputum samples should be obtained if patients can cough effectively. For patients being treated in the ICU and being mechanically ventilated, fiberoptic bronchoscopy is very convenient. Bronchoscopic sampling should especially be performed in patients who fail to respond to antibiotic treatment. Bronchoscopic sampling is appropriate for rare microorganisms such as viral, fungal, and atypical etiologic agents in patients who had induction therapy before surgery. Microorganisms isolated from airways during the perioperative period may help to initiate empiric antibiotic treatment.

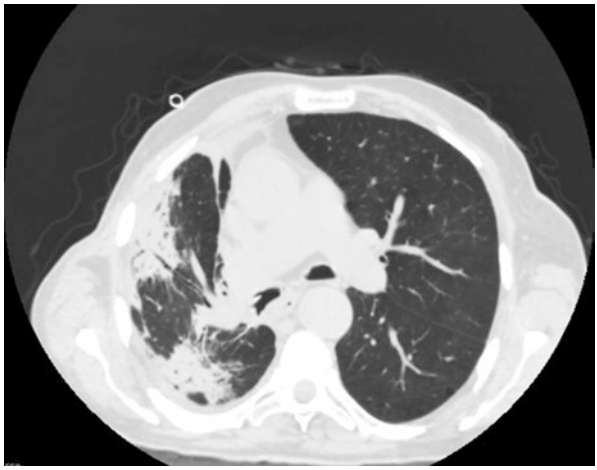

Fig. 14.3 CT image of right pneumonia after the right pulmonary resection

14.9 Treatment

The empirical antibiotic treatment should be started based on patient factors, local infection, and susceptibility patterns. If patients have no risk factors for multidrug-resistant microorganisms (MDR) such as neoadjuvant therapy, longer entubation time, and steroid therapy aminopenicillin (sulbactam/ampicillin or amoxicillin/clavulanic acid), third-generation cephalosporin (cefotaxime) or narrow-spectrum carbapenem (ertapenem) can be used. If patients have risk factors for MDR, antipseudomonal cephalosporin (cefepime, ceftazidime), or antipseudomonal carbapenem (meropenem, imipenem), β-lactam/β-lactamase inhibitor (piperacillin/tazobactam) + antipseudomonal fluoroquinolone (ciprofloxacin) or aminoglycoside (amikacin, gentamicin) can be used, and if MRSA is suspected, vancomycin or linezolid should be used. Antibiotic therapy is arranged according to culture results and patient clinical status. In recent years there has been an increased incidence of resistance to *Acinetobacter* spp., which should be taken into account because this bacteria is only susceptible to colimycin.

References

1. Schussler O, Alifano M, Dermine H et al (2006) Postoperative pneumonia after major lung resection. Am J Respir Crit Care Med 173:1161–1169
2. Bernard A, Ferrand L, Hagry O, Benoit L, Cheynel N, Favre JP (2000) Identification of prognostic factor determining risk groups for lung resection. Ann Thorac Surg 70:1161–1167
3. Nagasaki F, Flehinger BJ, Martini N (1982) Complications of surgery in the treatment of carcinoma of the lung. Chest 82:25–29
4. Torres A (2006) Respiratory infections after lung cancer resection. Expert Rev Anti Infect Ther 4(5):717–720
5. Hedenstierna G, Rothen HU (2000) Atelectasis formation during anesthesia:causes and measures to prevent it. J Clin Monit Comput 16(5–6):329–335

6. Hedenstierna G, Edmark L (2005) The effects of anesthesia and muscle paralysis on the respiratory system. Intensive Care Med 31(10):1327–1335
7. Shiono S, Yoshida J, Nishimura M et al (2007) Risk factors of postoperative respiratory infections in lung cancer surgery. J Thorac Oncol 2:34–38
8. Wang Z, Cai XJ, Shi L, Li FY, Lin NM (2014) Risk factors of postoperative nosocomial pneumonia in stage I-IIIa cancer patients. Asian Pac J Cancer Prev 15:3071–3074
9. Arozullah AM, Khuri SF, Henderson WG, Daley J (2001) Development and validation of a multifactorial risk index for predicting postoperative pneumonia after major noncardiac surgery. Ann Intern Med 135:847–857
10. Bonde P, McManus K, McAnespie M, McGuigan J (2002) Lung surgery: identifying the subgroup at risk for sputum retention. Eur J Cardiothorac Surg 22(1):18–22
11. Loganathan RS, Stover DE, Shi W, Venkatraman E (2006) Prevalence of COPD in women compared to men around the time of diagnosis of primary lung cancer. Chest 129:1305–1312
12. Nici L, Donner C, Wouters E, ATS/ERS Pulmonary Rehabilitation Writing Committee et al (2006) American Thoracic Society/European Respiratory Society statement on pulmonary rehabilitation. Am J Respir Crit Care Med 173:1390–1413
13. Ries AL, Bauldoff GS, Carlin BW et al (2007) Pulmonary rehabilitation: joint ACCP/AACVPR evidence-based clinical practice guidelines. Chest 131(5 Suppl):4S–42S
14. Bobbio A, Chetta A, Ampollini L et al (2008) Preoperative pulmonary rehabilitation in patients undergoing lung resection for non-small cell lung cancer. Eur J Cardiothorac Surg 33:95–98
15. Weiner P, Man A, Weiner M et al (1997) The effect of incentive spirometry and inspiratory muscle training on pulmonary function after lung resection. J Thorac Cardiovasc Surg 113:552–557
16. Wilson DJ (1997) Pulmonary rehabilitation exercise program for high-risk thoracic surgical patients. Chest Surg Clin N Am 7:697–706
17. Spruit MA, Janssen PP, Willemsen SC, Hochstenbag MM, Wouters EF (2006) Exercise capacity before and after an 8-week multidisciplinary inpatient rehabilitation program in lung cancer patients: a pilot study. Lung Cancer 52:257–260
18. Grider JS, Mullet TW, Saha SP, Harned ME, Sloan PA (2012) A randomized, double-blind trial comparing continuous thoracic epidural bupivacaine with and without opioid in contrast to a continuous paravertebral infusion of bupivacaine for post-thoracotomy pain. J Cardiothorac Vasc Anesth 26(1):83–89
19. Belda J, Cavalcanti M, Ferrer M et al (2005) Bronchial colonization and postoperative respiratory infections in patients undergoing lung cancer surgery. Chest 128:1571–1579
20. Morran GG, McNaught W, McArdle CS (1995) The relationship between intraoperative contamination of the lower respiratory tract and post- operative chest infection. J Hosp Infect 30:31–37
21. Yamada Y, Sekine J, Suzuki H et al (2010) Trends of bacterial colonization and the risk of postoperative pneumonia in lung cancer patients with chronic obstructive lung disease. Eur J Cardiothorac Surg 37:752–757
22. Cabello H, Torres A, Celis R et al (1997) Bacterial colonization of distal airways in healthy subjects and chronic lung disease: a bronchoscopic study. Eur Respir J 10:1137–1144
23. Kirkpatrick MB, Bass JB (1989) Quantitative bacterial cultures of bronchoalveolar lavage fluids and protected specimens from normal subjects. Am Rev Respir Dis 139:546–548
24. Soler N, Ewig S, Torres A, Filella X, Gonzalez J, Zaubet A (1999) Airway inflammation and bronchial microbial patterns in patients with stable chronic obstructive pulmonary disease. Eur Respir J 14:1015–1022
25. Riise GC, Larsson S, Larsson P, Jeansson S, Andersson BA (1994) The intrabronchial microbial flora in chronic bronchitis patients: a target for N-acetylcysteine therapy? Eur Respir J 7:94–101
26. Monsó E, Ruiz J, Rosell A et al (1995) Bacterial infection in chronic obstructive pulmonary disease. A study of stable and exacerbated outpatients using the protected specimen brush. Am J Respir Crit Care Med 152:1316–1320

27. Hirakata Y, Katoh T, Tsukagoshi M, Hayashi M, Sugiyama Y, Kitamura S (1997) Bacterial colonization of the upper respiratory tract of patients with primary lung cancer and nonmalignant lung disease. Chemotherapy 43:400–405
28. Ioanas M, Angrill J, Baldo X et al (2002) Bronchial bacterial colonization in patients with resectable lung carcinoma. Eur Respir J 19:326–332
29. Sok M, Dragas AZ, Erzˇen J, Jerman J (2002) Sources of pathogens causing pleuropulmonary infections after lung cancer resection. Eur J Cardiothorac Surg 22:23–29
30. Wansbrough-Jones MH, Nelson A, New L, Wilson A, Wright N, Pepper JR (1991) Bronchoalveolar lavage in the prediction of post-thoracotomy chest infection. Eur J Cardiothorac Surg 5:433–434
31. Heininger A, Jahn G, Engel C, Notheisen T, Unertl K, Hamprecht K (2001) Human cytomegalovirus infections in nonimmunosuppressed critically ill patients. Crit Care Med 29(3):541–547
32. Radu DM, Jauréguy F, Seguin AM et al (2007) Postoperative pneumonia after major pulmonary resections: an unsolved problem in thoracic surgery. Ann Thorac Surg 84:1669–1674
33. Turna A, Kutlu CA, Ozalp T, Karamustafaoglu A, Mulazimoğlu L, Bedirhan MA (2003) Antibiotic prophylaxis in elective thoracic surgery: cefuroxime versus cefepime. Thorac Cardiovasc Surg 51:84–88
34. Olak J, Jeyasingham K, Forrester-Wood C, Hutter J, al- Zeerah M, Brown E (1991) Randomized trial of one-dose versus six-dose cefazolin prophylaxis in elective general thoracic surgery. Ann Thorac Surg 51:956–958