Editorial

The (un)lucky seven—how can we mitigate risk factors for postoperative pneumonia after lung resections?

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In a recent issue of *Translational Lung Cancer Research*, Bian and colleagues reported on a prospective observational study describing seven predictors for postoperative pneumonia after thoracoscopic lung cancer surgery (1). Postoperative pneumonia, which occurred in 10% (196 of 1,927) of cases, is of great clinical importance since it is a significant contributor to early mortality. Timely identification of independent risk factors for pneumonia may facilitate risk stratification and improve perioperative management of patients at risk for pneumonia to minimize severe clinical outcomes (2).

Epidemiology and definitions

Postoperative pneumonia is, next to prolonged air leakage, one of the most common postoperative pulmonary complications in patients undergoing minimally invasive lung cancer surgery (2,3). Postoperative pneumonia has a significant impact on 30-day mortality, and even more so, on 90-day mortality, prolonged hospital stay, and increased healthcare costs (4-6).

The incidence of postoperative pneumonia varies considerably in the literature, ranging from 2% to even 50% (2-5). This wide variation could be related to the heterogeneity of definitions applied throughout studies. The established definition by the National Institute for Health and Care Excellence of the United Kingdom (NICE), which is used in many other European countries, defines pneumonia as any symptom of a lower respiratory tract infection, combined with a chest radiograph showing shadowing that cannot be explained otherwise (7,8). In contrast, Bian and colleagues applied a more restrictive definition (1). In short, in their published cohort, patients required at least two chest radiographs showing infiltrative abnormalities, consolidations, or cavitation, along with at least two symptoms of a lower respiratory tract infection (i.e., purulent sputum, dyspnea, cough, increased respiratory rate, gas exchange deteriorating, or increased oxygen demand) and at least one symptom of infection in general (i.e., fever, elevated white blood cell counts, or

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altered mental state in elderly patients) in order to qualify for their definition of pneumonia. This is in line with the definition that was established by the United States Centers for Disease Control and Prevention (9). Other literature-derived definitions were less strict and included, amongst others, infiltrative abnormalities on a single X-ray in combination with an elevation of leukocyte count and fever (5), or a combination of infiltrative abnormalities on imaging along with at least one of the following symptoms: coughing, fever, hypothermia, lung consolidation on physical examination, elevated C-reactive protein (CRP), or pathogen isolation from blood or sputum cultures (10). These examples highlight the diversity of definitions used to describe the same disease. Since definitions of pneumonia vary, it is challenging to meaningfully measure, report, and investigate complication rates. It is therefore essential to reach agreement on unambiguous definitions of postoperative pneumonia. We advocate a simple and easy to use definition of postoperative pneumonia like new onset fever without other explanation, in combination with at least one symptom of a lower respiratory tract infection (i.e., purulent sputum, dyspnea, cough, increased respiratory rate, gas exchange deteriorating, or increased oxygen demand), and elevated leukocyte count or CRP, and at least one X-ray with infiltrative abnormalities within 30 postoperative days.

Risk factors and preventive measures

Bian and colleagues identified seven factors associated with an increased risk of postoperative pneumonia, including older age, higher body mass index (BMI), high smoking index, poor physical function, diabetes, respiratory disease, and nervous system disease (1). Other studies described other predictors for postoperative pneumonia encompassing neoadjuvant therapy, open surgery, and prolonged surgical duration (3-5). While certain factors (e.g., age and preexisting medical conditions) cannot be mitigated, precautionary measures can be undertaken to minimize the risk of postoperative pneumonia. Preoperative measures within the enhanced recovery after thoracic surgery (ERAS) guidelines especially, should be implemented in clinical practice, such as smoking cessation, optimizing nutritional status, weight management, and prehabilitation programs including early preoperative pulmonary physiotherapy and postoperative incentive spirometry, which have proven to reduce the risk of postoperative pulmonary complications (11-15). Aside from preventive measures to minimize the risk of postoperative pneumonia, thoracic surgeons should optimize their clinical practices by implementing ERAS guidelines that have not been discussed in this manuscript, including but not limited to adequate pain control, venous thromboembolism prophylaxis, early chest tube removal, and early ambulation, to optimize patient clinical outcomes even further (11). In total, the ERAS protocol consists of 45 evidence-base elements, that do not only prevent postoperative pneumonia, but have a proven positive effect on many more postoperative parameters like length of hospital stay and complications in general (11). However, detailed descriptions of these 45 elements, and strategies to implement them are limited (16), hampering global implementation. Therefore, more implementation-related publications concerning the ERAS guidelines are welcome, and opportunities to highlight their importance should be taken.

In addition to the ERAS guidelines, perioperative anesthesiologic strategies like intraoperative lung protective ventilation, goal-directed hemodynamics, and perioperative crystalloid fluids (less than 6 mL/kg) can likewise be used to reduce the risk of postoperative pulmonary complications (17).

Clinical significance

Bian and colleagues provided various risk factors to predict postoperative pneumonia and developed a scoring system, using a point scale axis, that predicts the patient-specific risk for pneumonia with a sensitivity of 80% and specificity of 74%. Even though these results are promising, the question arises whether such a risk stratification is useful in standard clinical practice. So far, several risk calculators for postoperative pneumonia in thoracic surgery and postoperative complications have existed for decades (18-20). However, their standard use in clinical practice is limited, except for the well-known American Society of Anesthesiologists (ASA) classification (21).

Most of these risk scoring systems incorporate identical factors in line with those found by Bian and colleagues, including age, BMI, smoking status, and other systemic comorbidities. These scoring systems could facilitate improved anticipation through prehabilitation and enhance awareness and subsequent early recognition and treatment of postoperative pneumonia. However, success rates of weight-loss programs and smoking cessation therapies are questionable to say the least. Successful 1-year smoking cessation rates of patients in cessation therapy programs for example, are only as high as 5% to 20% (22,23).

Nevertheless, endeavors to improve these smoking cessation numbers should be undertaken, since smoking cessation has a significant positive impact on the incidence of postoperative pulmonary complications after thoracic surgery with comparable outcomes to never-smokers (24). Considering this, in combination with the fact that there is a risk of multicollinearity between smoking-index and respiratory system disease, which are both classified in their risk scoring system, Bian and colleagues could have opted to include smoking status in the form of never-smoker, ex-smoker, and current smoker, since this might be of more added value than smoking-index alone. As for weight loss programs, a comparable percentage applies, with a success rate of around 20% when successful weight loss is defined as losing at least 10% of body weight (25). As such, pneumonia risk scoring systems presumably mostly aid in awareness and early recognition of postoperative pneumonia rather than prevention. Additionally, before it can be used in a clinical setting, future studies should be conducted for external validation of this risk classification model and compare its performance with other available scoring systems. Whereas the risk factors described by Bian and colleagues have already been described in the past in other studies, the publication of their scoring tool hopefully raised a renewed awareness concerning postoperative pneumonia. Whereas risk scoring tools like the one described by Bian and colleagues mostly aid in improving awareness, implementation of and adherence to the ERAS guidelines will actually positively impact postoperative outcomes in patients undergoing surgery for lung cancer. As such, this might even be more important than the awareness that is created by Bian and colleagues on postoperative pneumonia.

Conclusions

Postoperative pneumonia is one of the most common pulmonary complications following lung cancer surgery causing prolonged hospitalization duration, higher costs, and most importantly, an increased risk of postoperative mortality. An adequate risk scoring system for pneumonia could be useful for early recognition and treatment, and patient-tailored precautionary measures to minimize serious postoperative complications as a result of postoperative pneumonia, bearing in mind that some of these preventive measures may have limited feasibility and/or a low success rate. Hence, adequate implementation of the ERAS guidelines is of substantial importance not only to prevent postoperative pneumonia, but also to capitalize on their other proven benefits. Lastly, to provide more conclusive evidence regarding significant risk factors for pneumonia, a more unified definition should be used to adequately assess prevention and treatment strategies to optimize lung cancer care worldwide.

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