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# Risk factors for surgical complications after anatomic lung resections in the era of VATS and ERAS

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**Abstract**

**Background:** The aim of this study was to identify risk factors for surgical complications after anatomic lung resections in the era of video-assisted thoracic surgery (VATS) and enhanced recovery after surgery (ERAS).

**Methods:** A retrospective analysis of all consecutive adult patients who underwent elective anatomic lung resections between January and December 2020 at our institution was performed.

**Results:** Eighty patients (40 VATS, 40 thoracotomy) were included. The 30-day mortality rate was 1.3%. The overall rate of major postoperative complications was 18.8%. Most major complications occurred in patients who underwent open surgery (complication rate 32.5%, share of total complications 86.7%). Major morbidity after VATS resection was rare (complication rate 2.5%, share of total complications 13.3%). In univariable analysis, thoracotomy ($p = 0.003$), impaired preoperative lung function ($p = 0.003$), complex surgery ($p = 0.004$) and sleeve resection ($p = 0.037$) were associated with adverse outcomes. In multivariable analysis, thoracotomy ($p = 0.044$) and impaired preoperative lung function ($p = 0.028$) were the only independent risk factors for major postoperative morbidity.

**Conclusion:** Thoracotomy was associated with a 10-fold increased risk for postoperative complications compared with minimally invasive surgery and was an independent risk factor for surgical complications. In the era of VATS and ERAS, the fact that thoracotomy is performed may be a reliable parameter to identify patients at risk for postoperative complications.

**KEYWORDS**
enhanced recovery after surgery, postoperative complications, thoracic surgery, thoracotomy, VATS

## INTRODUCTION

Thoracic surgery has become an independent surgical specialty in most countries during the last decades. In order to improve the quality of care in this new surgical domain and to reduce the perioperative morbidity and mortality, a continuous evaluation of clinical risk factors is required. Two major advances have marked the modernization of thoracic surgery. First, the switch from open surgery to minimally invasive surgery, especially for anatomic lung resections and second, the introduction of structured clinical pathways based on the enhanced recovery after surgery (ERAS) guidelines in perioperative patient treatment.

Complications following anatomic lung resections have previously been described, mostly for open lobectomy. Little is known about complications after minimally invasive procedures or other types of resections, especially segmentectomies. Nevertheless, anatomic lung resections by VATS are commonly performed and have become an accepted alternative for early-stage lung cancer as it is associated with less postoperative pain and better quality of life.[1–3]

[†]Christian Galata and Ioannis Karampinis contributed equally to this study.

The first thoracic ERAS guideline was published 3 years ago.[4] The proposed changes have certainly led to significant changes in the way that many institutions function in the perioperative setting.[5] The aim of ERAS protocols is to decrease pulmonary and cardiac complications after thoracotomy.[6,7] They also appear to be beneficial in the elderly and after VATS lobectomy.[8] However, a recently published retrospective analysis of 1654 thoracic surgery patients identified several risk factors for delayed discharge under guidance of ERAS protocols.[9]

The aim of this study was to identify and assess risk factors for major surgical complications in patients undergoing elective anatomic lung resections following a structured, ERAS based pathway at a single center with a particular focus on minimally invasive surgery.

# METHODS

## Ethics approval

Ethics board approval was obtained from the ethics commission of the state chamber of physicians in Rhineland-Palatinate, Mainz, Germany (No. 2021-15 979). The review board waived the need for patient consent in this retrospective analysis. The study was performed according to the 1975 Declaration of Helsinki and its later amendments.

## Study design

This was a single-center retrospective cohort study.

## Patients

An ERAS based perioperative treatment protocol was implemented in our department in January 2020. The medical records of all consecutive adult patients undergoing elective anatomic lung resections were identified. Data required for assessing surgical complications were extracted accordingly.

## Postoperative outcomes

Mortality was assessed using the 30-day mortality. The Clavien-Dindo (CD) classification and its adaption for thoracic surgery, the thoracic morbidity and mortality (TM&M) classification system were used to grade surgical complications.[10,11] Major surgical complications were defined as complications ≥ grade 3. Postoperative bronchoscopy was considered an intervention according to the CD/TM&M classification in case of an unplanned intervention; planned bronchoscopies, such as routine anastomosis control after sleeve resection, were excluded. The eighth edition of the Union for International Cancer Control/American Joint Committee on Cancer (UICC/AJCC) staging system for non-small cell lung cancer (NSCLC) was used to determine tumor stage in all cases of NSCLC.

## ERAS-based clinical pathway

In November 2019, the Division of Thoracic Surgery at our institution was newly established. As of January 2020, all adult patients undergoing elective lung surgery were treated along a standardized protocol based on the recommendations of the ERAS Society and the European Society of Thoracic Surgeons (ESTS) for enhanced recovery after lung surgery.[4] Its 22 key features are summarized in Figure 1. Briefly, other components of this pathway were as follows.

### Preoperative phase

Preoperative assessment was performed on an outpatient basis. Inpatient admission for surgery took place one day

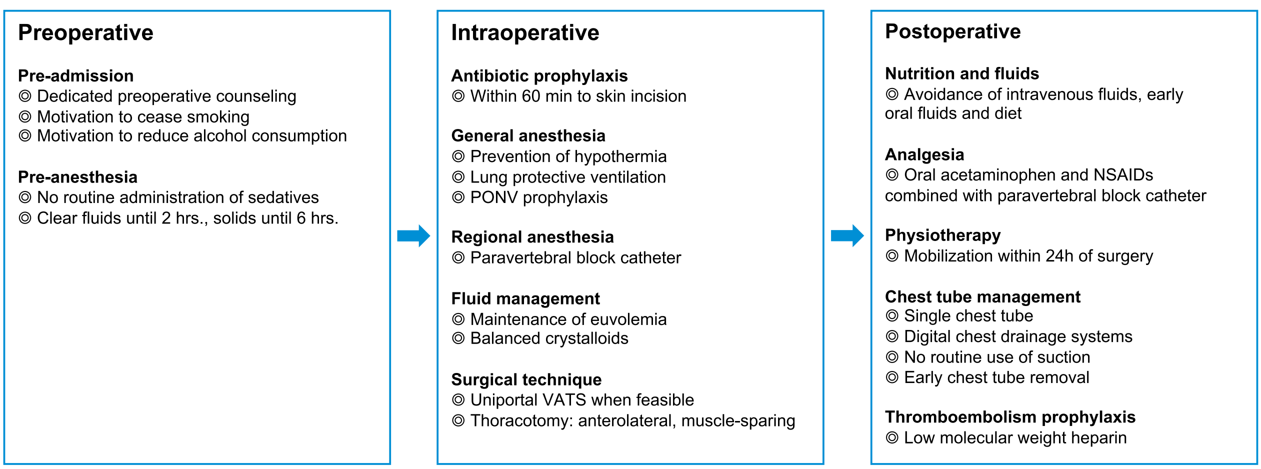


**FIGURE 1** Summary of the ERAS based clinical pathway. ERAS,enhanced recovery after surgery; NSAID, nonsteroidal anti-inflammatory drug; PONV, postoperative nausea and vomiting; VATS, video-assisted thoracoscopic surgery

before surgery or on the same day of surgery, as convenient for the patient.

## Perioperative phase

The standard for anatomic lung resection was uniportal VATS in all cases where technically feasible. Procedures that were not suitable for VATS for technical reasons underwent open surgery. Systematic nodal dissection in open and VATS procedures was performed according to the ESTS guidelines for intraoperative lymph node staging.[12] General anesthesia was combined with regional anesthesia. For this purpose, a paravertebral block catheter (PVBC) was placed intraoperatively by the surgeon under direct vision at the same intercostal space with the incision. After placement of the PVBC, a bolus of 15–20 ml ropivacaine solution (0.375%) was given; continuous infusion of ropivacaine (0.375%) was maintained at rates of 8–10 ml/h throughout the procedure and the postoperative period. A single, small-size, soft chest tube (18 French) was used together with a digital chest drainage system on gravity mode (−8 $cmH_2O$).

## Postoperative phase

If present, the urinary catheter was removed within 24 h after surgery. Analgesia followed a multidisciplinary pain management protocol combining the PVBC with oral analgesics to avoid parenteral medication and to reduce the use of opiates. Oral analgesics used were ibuprofen, acetaminophen and metamizole. If the administration of opiates was necessary (pain intensity on the numeric rating scale >3 at rest or >5 during exercise), oral oxycodone was given. The chest tube was removed when the digital chest drainage system showed no air leak for 24 h, regardless of the amount of serous fluid drained. The PVBC was removed together with the chest drain. All patients without the need for therapeutic anticoagulation received thromboembolism prophylaxis using low molecular weight heparin. All patients were visited twice a day by at least one consultant surgeon, from the day of surgery until the day of discharge, including weekends and holidays.

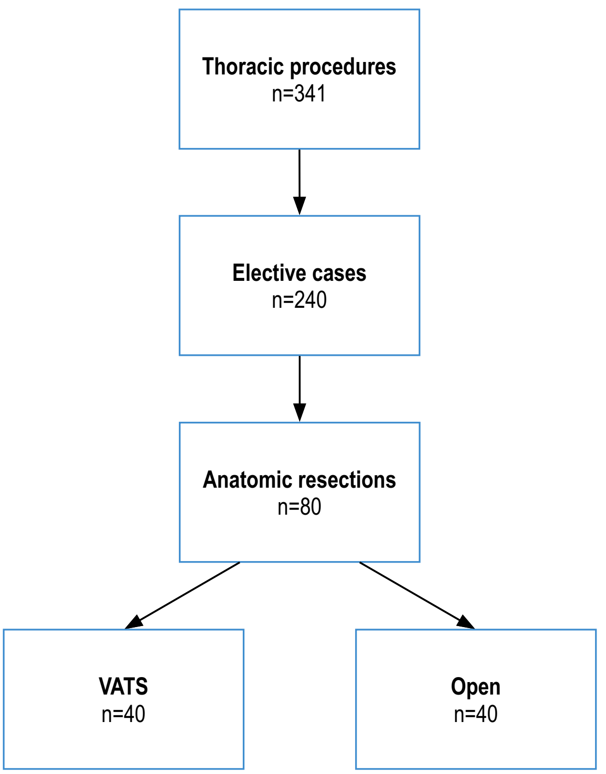


**FIGURE 2** Flowchart of the study population

## Follow-up

Routine follow-up was done in our thoracic surgery outpatient clinic within 1 month after surgery.

## Statistical analysis

The median, together with the interquartile range (IQR) is presented for quantitative variables. Qualitative variables are quoted as absolute numbers and relative frequencies. The Mann–Whitney U test was used to compare continuous variables that were not normally distributed. For binary variables, Fisher's exact test was used. The Cochran-Armitage test for trend was used to assess the association between a binary variable and an ordinal variable with >2 categories. All statistical tests for the comparison of two groups were two-tailed. A test result was considered statistically significant if $p < 0.05$. For the binary outcome "occurrence of major postoperative complications", a multiple logistic regression analysis was done. In this multiple analysis, the

**TABLE 1** Patient characteristics

| Variable | *n* / % / median | % / IQR |
|---|---|---|
| Female (*n*) | 34 | 42.5 |
| Age (years) | 67 | 56–74 |
| COPD (*n*) | 29 | 36.3 |
| Smoker (current) | 24 | 30.0 |
| BMI (kg/$m^2$) | 26 | 23–29 |
| FEV1 (% Ref) | 81 | 72–92 |
| DLCO (% Ref) | 75 | 64–91 |
| ASA | | |
| 2 | 15 | 18.8 |
| 3 | 59 | 73.8 |
| 4 | 6 | 7.5 |
| Anticoagulation | 30 | 37.5 |

Abbreviations: ASA, American Society of Anesthesiologists; BMI, body mass index; DLCO, diffusing capacity of the lungs for carbon monoxide; FEV1, forced expiratory pressure in 1 second; IQR, interquartile range.

backward stepwise selection based on the probability of the Wald statistic was used and a significance level of $\alpha = 0.05$ was chosen to detect several parameters that might influence the outcome. Odds ratios are presented together with their 95% confidence intervals (CI). Parameters were entered in the multiple analysis when they were statistically significant in the univariable analyses. A receiver operating characteristic (ROC) analysis was performed to determine an optimal cutoff value for the variable "preoperative forced expiratory pressure in 1 second" (FEV1) that separates patients with major complications from patients without major complications. All statistical tests were performed using IBM SPSS Statistics (version 26, IBM Corp.).

**TABLE 2** Data on surgery

| Variable | n / % / median | % / IQR |
|---|---|---|
| Type of surgery | | |
| Open | 40 | 50.0 |
| VATS | 40 | 50.0 |
| Procedures | | |
| Segmentectomy | 21 | 26.3 |
| RUL | 21 | 26.3 |
| RML | 6 | 7.5 |
| RLL | 5 | 6.3 |
| LUL | 9 | 11.3 |
| LLL | 13 | 16.3 |
| Bilobectomy | 3 | 3.8 |
| Pneumonectomy | 2 | 2.5 |
| Complex surgery | 22 | 27.5 |
| Sleeve resection | 8 | 10.0 |
| Thoracic wall / diaphragm | 8 | 10.0 |
| Angioplasty | 10 | 12.5 |
| Intrapericardial / pericardial resection | 9 | 11.3 |
| Histology | | |
| Benign | 5 | 6.3 |
| Metastasis | 14 | 17.5 |
| Primary lung malignancy | 61 | 76.3 |
| Type of primary lung malignancy | | |
| Adenocarcinoma | 34 | 55.7 |
| Squamous cell carcinoma | 17 | 27.9 |
| Small cell lung cancer | 2 | 3.3 |
| Carcinoid | 5 | 8.2 |
| Other | 3 | 4.9 |
| UICC Stage (NSCLC) | | |
| IA1 | 4 | 7.8 |
| IA2 | 12 | 23.5 |
| IA3 | 4 | 7.8 |
| IB | 8 | 15.7 |
| IIA | 3 | 5.9 |
| IIB | 5 | 9.8 |
| IIIA | 9 | 17.6 |
| IIIB | 2 | 3.9 |
| IVA | 4 | 7.8 |

Abbreviations: IQR, interquartile range; LLL, left lower lobectomy; LUL, left upper lobectomy; NSCLC, non-small cell lung cancer; RLL, right lower lobectomy; RML, right middle lobectomy; RUL, right upper lobectomy; UICC, union for international cancer control; VATS, video-assisted thoracoscopic surgery.

# RESULTS

## Patient characteristics

Between January and December 2020, a total of 341 surgical procedures were performed. Elective anatomic lung resections were performed in 80 adults. A flowchart of the study population is shown in Figure 2. Clinical characteristics of these patients are shown in Table 1. The majority of the patients were male and categorized as American Society of Anesthesiologists (ASA) physical status class 3, with a median age of 67 years. One-third of the patients were active smokers at the time of surgery, and more than one-third (36.3%) were on medical treatment for chronic obstructive pulmonary disease (COPD).

**TABLE 3** Postoperative outcomes

| Variable | n / % / median | % / IQR |
|---|---|---|
| Mortality (30 day) | 1 | 1.3 |
| Major complications | 15 | 18.8 |
| Reoperation | 4 | 5.0 |
| Unplanned bronchoscopy | 9 | 11.3 |
| Lung abscess[a] | 1 | 1.3 |
| Empyema[a] | 1 | 1.3 |
| Hemothorax[a] | 2 | 2.5 |
| Endoluminal bleeding[a] | 1 | 1.3 |
| Pericardial effusion[a] | 1 | 1.3 |
| Pleural effusion[a] | 1 | 1.3 |
| Atelectasis[a] | 4 | 5.0 |
| Bronchial stenosis[a] | 2 | 2.5 |
| ARDS | 2 | 2.5 |
| Other events | | |
| Pneumonia | 6 | 7.5 |
| Air leak intervention | 5 | 6.3 |
| Bronchoscopy (all) | 13 | 16.3 |
| Chest tube duration (days) | 2 | 2–4 |
| Hospital stay (days) | 5 | 4–7 |
| Chest x-ray results | | |
| Pneumothorax | 40 | 51.3 |
| Dystelectasis | 29 | 37.2 |
| Pleural effusion | 59 | 75.6 |
| Surgical emphysema | 27 | 34.6 |

Abbreviations: ARDS, acute respiratory distress syndrome; IQR, Interquartile range.
[a]Requiring intervention.

## Surgical procedures

All operations in this study were performed by two thoracic surgeons (ER and DS). Data on surgery are presented in Table 2. 93.8% of the patients underwent anatomic lung resection for malignant disease; 76.3% had primary malignancy of the lung. Resection by VATS was performed in 50.0% of the cases, while the other 50.0% underwent open resection via thoracotomy. The most common procedure was lobectomy (67.7%). A quarter of the patients (26.3%) underwent segmentectomy, while the rates of bilobectomies (3.8%) and pneumonectomies (2.5%) were low. The overall rate of complex procedures, including sleeve resections, was 27.5%.

## Postoperative complications

Postoperative outcomes are shown in Table 3. During the study period, one case of 30-day mortality (1.3%) was observed. This patient was readmitted to the hospital with pneumonia 2 weeks after initial discharge after an uneventful lower bilobectomy and died due to pulmonary complications despite intensive care therapy. Overall, 15 patients developed major postoperative complications (18.8%). Four patients (5.0%) required reoperation, two for infectious complications (lung abscess, pleural empyema), one for hemothorax, and one for symptomatic pericardial effusion. All patients who underwent reoperation had initially undergone open surgery including complex surgery in three out of four cases. Nonroutine postoperative bronchoscopy was performed in nine patients ($n = 2$ to exclude bronchial stump failure, $n = 4$ for atelectasis, $n = 2$ for bronchial stenosis with subsequent stenting, and $n = 1$ for endoluminal bleeding). The overall rate of postoperative pneumonia was 7.5%; two patients with pneumonia required reintubation and intensive care therapy due to acute respiratory distress syndrome (ARDS). Two patients underwent postoperative interventions not under general anesthesia, one for hemothorax and one for pleural effusion. The vast majority of postoperative complications were observed after thoracotomy (complication rate 32.5%, share of total complications 86.7%) while major morbidity after VATS resection was particularly rare (complication rate 2.5%, share of total complications 13.3%).

**TABLE 4** Risk factors for major postoperative complications in univariable and multivariable analysis

| | Univariable | Multivariable | |
|---|---|---|---|
| Variable | *p*-value | *p*-value | Odds ratio (95% CI) |
| FEV1 | 0.003* | 0.028* | 0.952 (0.911–0.955) |
| Open surgery | 0.003* | 0.044* | 0.181 (0.034–0.953) |
| Complex surgery | 0.004* | 0.459 | |
| Sleeve resection | 0.037* | 0.649 | |
| DLCO | 0.073 | | |
| BMI | 0.358 | | |
| Age | 0.208 | | |
| Gender | 0.248 | | |
| ASA | 0.859 | | |
| COPD | 0.146 | | |
| Smoking | 0.131 | | |
| Anticoagulation | 0.236 | | |
| Surgeon | 0.843 | | |
| Thoracic wall / diaphragm resection | 0.640 | | |
| Angioplasty | 0.387 | | |
| Pericardial resection | 0,058 | | |
| Segmentectomy | 0.748 | | |
| Histology | 0.252 | | |
| M category (NSCLC) | 0.377 | | |
| N category (NSCLC) | 0.580 | | |
| T category (NSCLC) | 0.178 | | |
| UICC stage (NSCLC) | 0.340 | | |

Abbreviations: ASA, American Society of Anesthesiologists; CI, confidence interval; COPD, chronic obstructive pulmonary disease; DLCO, diffusing capacity of the lungs for carbon monoxide; FEV1, forced expiratory pressure in 1 second; NSCLC, non-small cell lung cancer; UICC, Union for International Cancer Control.
*Indicates statistical significance.

## Risk factors for major postoperative morbidity

In univariable analysis, open resection via thoracotomy ($p = 0.003$), impaired preoperative lung function as expressed by reduced values of preoperative FEV1 ($p = 0.003$), complex surgery ($p = 0.004$) and sleeve resection ($p = 0.037$) were associated with major postoperative complications. In multivariable analysis, thoracotomy ($p = 0.044$) and impaired preoperative lung function ($p = 0.028$) were the only independent risk factors for major postoperative morbidity (Table 4). To determine an optimal cutoff value for preoperative FEV1 with respect to the occurrence of adverse events, a ROC analysis was performed. The highest Youden's J was observed for an FEV1 < 76.1% of the reference value adjusted for age, height, gender and ethnicity, with a sensitivity of 76.7% and a specificity of 75.0%, respectively.

## Complications after VATS versus open resection

As patients operated with thoracotomy had a significantly higher risk for postoperative major complications compared to patients undergoing a VATS resection, differences between the two groups were investigated. Patients who underwent open surgery were more likely to have complex surgical procedures (52.5% vs. 2.5%, $p < 0.001$) and had higher T stages on final pathology workup across all tumor entities ($p < 0.001$) and within the NSCLC group ($p < 0.001$). In cases with NSCLC, UICC/AJCC stages were significantly higher ($p = 0.005$) in the thoracotomy group, while preoperative FEV1 ($p = 0.004$) was significantly lower (thoracotomy: median 76.7% Ref., IQR 68.5%–82.8% vs. VATS: 86.3% Ref., IQR 77.9%–97.7%). Furthermore, a significantly higher rate of pleural effusions was observed on postoperative chest x-ray in patients who had undergone open surgery (thoracotomy: 89.7% vs. VATS: 61.5%, $p = 0.007$). Hospital stay (thoracotomy: median 6 days, IQR 4.25–8 days vs. VATS: 4 days, IQR 4–5.75 days) as well as chest tube duration (thoracotomy: 3 days, IQR 2–5 days vs. VATS: 2 days, IQR 2–4 days) were significantly longer in the thoracotomy group ($p = 0.001$ and $p = 0.022$, respectively). All other parameters were not significantly different between both groups. A table showing detailed results of the comparisons between the VATS and thoracotomy group are shown in Table S1.

# DISCUSSION

In this study we present data on risk factors for major postoperative complications in 80 consecutive patients who underwent anatomic lung resection at a single European center between January and December 2020. There were two main findings in this study. First, in an ERAS based setting, anatomic VATS resection was associated with a very low rate of postoperative adverse events. Second, patients who still required open surgery had a more than 10-fold increased risk for major postoperative morbidity compared to VATS resection.

In this study, we used the CD/TM&M classifications to categorize the postoperative morbidity. Both classifications offer a standardized way of analyzing post-surgical outcomes.[13] Historically, studies in thoracic surgery have often reported adverse events in a categorical manner, according to the definitions proposed by the ESTS.[14] Some authors have even reported only distinct complication categories, for example, pneumonia, atrial fibrillation etc.[15] This way of reporting can make the assessment of the severity of the adverse events and thus the actual impact on the patient challenging. In outcome studies designed to identify clinical risk factors, it has proven useful to classify surgical complications in relation to the effort necessary to treat them, as it is achieved by the CD/TM&M classifications.

We investigated postoperative complications in the setting of a 22 elements ERAS based protocol. A recent prospective, historically controlled, propensity score matched study on enhanced recovery after VATS lobectomy found that treatment along an ERAS pathway was associated with decreased length of stay, without increase in complication or readmission rates.[16] The huge difference in complication rates (32.5% vs. 2.5%) between VATS resections and patients with thoracotomy in our study is striking. Remarkably, one of the two independent risk factors for postoperative adverse events was incision itself. This contradicts randomized, controlled data. The randomized controlled trial by Bendixen et al. comparing VATS and open lobectomies found comparable rates of grade 3 and 4 adverse events in both groups (24 vs. 25 of 103 patients, $p = 0.78$).[3] In a secondary analysis of data from the American college of surgeons oncology group Z0030 randomized clinical trial, the authors found that patients undergoing VATS lobectomy had shorter length of hospital stay, less atelectasis requiring bronchoscopy and shorter chest tube drainage; however, all other complication rates, including ARDS, respiratory failure and hemorrhage, were not significantly different.[17] The fact that we found significantly more complications after thoracotomy in our patient cohort is most likely an effect of non-randomized patient selection. Patients in the thoracotomy group had higher UICC/AJCC stages, more complex resections, and worse preoperative pulmonary function than patients in the VATS group. This is consistent with the literature. Especially for patients with poor preoperative lung function, higher complication rates after thoracotomy compared with VATS resection have been reported.

The overall rate of postoperative pneumonia in our study was 7.5%, which is rather low compared to other studies. The pneumonia rate after segmentectomy or lobectomy in the literature ranges from 12.5% to 14.9%.[18] In a large retrospective review of 12 970 patients in The Society of Thoracic Surgeons (STS) general thoracic database, poor lung function predicted respiratory complications regardless of surgical approach, but respiratory complications increased at a significantly greater rate in lobectomy patients with poor lung function after thoracotomy compared to VATS.[19] In a retrospective cohort study of lung resections with a ppoFEV1 < 40%, a postoperative pneumonia rate after VATS of 4.3% was detected, compared to 21.7% after thoracotomy ($p = 0.035$, $n = 70$).[20] In general, in thoracotomy patients, a preoperative FEV1 < 60% seems to be associated with a higher rate of pulmonary complications.[21] Some authors report a FEV1 below 80% of predicted value as significantly associated with the occurrence of complications.[18] The cutoff value for preoperative FEV1 of 76.1% calculated in this study is in line with ESTS guidelines that recommend further evaluation by exercise testing (peak $V_{O2}$) for patients with a preoperative FEV1 < 80%.[22]

Several scoring systems for the perioperative risk assessment for patients undergoing thoracic surgery have been proposed so far. What these systems have in common is that, although they are precise, they require a vast number of parameters and feature a high inherent complexity. For instance, the EuroLung1 and EuroLung2 models for predicting cardiopulmonary morbidity and 30-day mortality rates contain 8 and 9 variables, respectively. As a result, they often remain academic and are rarely used in clinical practice. In contrast, the risk factor "thoracotomy" may be a very general surrogate parameter for postoperative major morbidity that it is easy to identify. It could prove to be a valuable and easy-to-use predictor for complications in the era of VATS and ERAS.

This study was conducted under the conditions of the coronavirus disease 2019 (COVID-19) pandemic. Nevertheless, the implementation of the ERAS protocol was feasible, and the type of surgery or complication rate are not likely to have been influenced by the pandemic. However, it must be noted that the pandemic may have had an impact on the number of cases scheduled for elective surgery during the study period due to limitations in intensive care capacity.

There are some limitations to this study. Due to the retrospective nature of this study and the relatively small number of patients, there is an inherent risk for bias. There may be known or unknown confounders that were not assessed. Furthermore, as mentioned above, our department focuses on minimally invasive surgery and every patient is primarily a candidate for a VATS procedure. Only complex cases undergo open surgery. It is therefore expected that those patients are at higher risk for all well-known surgical complications. This effect would probably be eliminated in a randomized study. However, the everyday routine of a thoracic center is not a randomized study. The results of this study show that thoracotomy patients in a modern thoracic center are at risk. Thoracotomy is an easily identifiable parameter for the ward physicians, the nursing staff and the physiotherapists and clearly marks patients that require attention.

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## CONFLICT OF INTEREST

The authors report no conflict of interest.

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## SUPPORTING INFORMATION

Additional supporting information may be found in the online version of the article at the publisher's website.

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