Propensity Score Analysis Comparing Videothoracoscopic Lobectomy With Thoracotomy: A French Nationwide Study

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Background. **Video-assisted thoracoscopic surgery (VATS) lobectomy has recently become the recommended approach for stage I non-small cell lung cancer. However, these guidelines are not based on any large randomized control trial. Our study used propensity scores and a sensitivity analysis to compare VATS lobectomy with open thoracotomy.**

Methods. **From 2005 to 2012, 24,811 patients (95.1%) were operated on by open thoracotomy and 1,278 (4.9%) by VATS. The end points were 30-day postoperative death, postoperative complications, hospital stay, overall survival, and disease-free survival. Two propensity scores analyses were performed: matching and inverse probability of treatment weighting, and one sensitivity analysis to unmask potential hidden bias. A subgroup analysis was performed to compare "high-risk" with "low-risk" patients. Results are reported by odds ratios or hazard ratios and their 95% confidence intervals.**

Results. **Postoperative death was not significantly reduced by VATS whatever the analysis. Concerning postoperative complications, VATS significantly decreased the occurrence of atelectasis and pneumopathy with both analysis methods, but there were no differences in the occurrence of other postoperative complications. VATS did not provide a benefit for high-risk patients. The VATS approach decreased the hospital length of stay from 2.4 days (95% confidence interval, –1.7 to –3 days) to –4.68 days (95% confidence interval, –8.5 to 0.9 days). Overall survival and disease-free survival were not influenced by the surgical approach. The sensitivity analysis showed potential biases.**

Conclusions. **The results must be interpreted carefully because of the differences observed according to the propensity scores method used. A multicenter randomized controlled trial is necessary to limit the biases.**

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Video-assisted thoracoscopic surgery (VATS) lobectomy for non-small cell lung cancer (NSCLC) has had a major effect on thoracic surgery. Recent meta-analyses on early-stage NSCLC highlighted the benefit of VATS regarding 5-year overall survival (OS), hospital length of stay (LOS), and a lower incidence of postoperative complications compared with open thoracotomy (OT) [1–8].

In 2013 the American College of Chest Physicians issued new guidelines for patients with clinical stage I NSCLC, suggesting that a minimally invasive approach, such as VATS, should be preferred to OT for anatomic pulmonary resection [9]. Nowadays, VATS lobectomy is considered superior to OT; however, it must be pointed out that no large randomized controlled trials (RCTs) have compared these approaches, and the American College of Chest Physicians guidelines are based only on retrospective observational studies from databases using propensity-matching analysis [10].

Propensity score (PS) matching, which is the most widely used technique in the literature, has several

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Abbreviations and Acronyms

ASA = American Society of Anesthesiologists
CI = confidence interval
DFS = disease-free survival
FEV = forced expiratory volume
FSTCS = French Society of Thoracic and Cardiovascular Surgery
IPTW = inverse probability of treatment weighting
LOS = length of stay
NSCLC = non-small cell lung cancer
OS = overall survival
OT = open thoracotomy
PS = propensity score
RCT = randomized controlled trial
VATS = video-assisted thoracoscopic surgery

limitations, including the exclusion of unmatched individuals from the analysis [11]. This may significantly affect the study's results, which thus apply only to the subset of patients that could be matched, and could lead to uncertain conclusions [12]. Moreover, most of the published studies that used matching did not assess the performance appraisal by a sensitivity analysis to look for hidden bias [13].

The combination of matching and inverse probability of treatment weighting (IPTW) tends to eliminate systematic differences between experimental and control participants to a greater degree than does stratification or covariate adjustment [11, 14]. To this extent, our study is the first to compare VATS lobectomy with OT using two PS methods and a sensitivity analysis. The aim of this study was to assess the effect of lobectomy by VATS compared with OT on outcomes and survival for NSCLC using data from the French national database Epithor by PS matching and IPTW combined with a sensitivity analysis.

Patients and Methods

The French Society of Thoracic and Cardiovascular Surgery (FSTCS) Institutional Review Board approved the prospective electronic database used for this study and the study itself, as previously described [15]. The FSTCS Institutional Review Board certified that this study respected the current regulations framing clinical research in France, referenced as CERC-SFCTCV-2015-1-12-11-1-34-PAPi.

Data Collection

Epithor, the FSTCS database, was created in 2002 as a voluntary and free initiative of general thoracic surgeons. At present, about 100 private and public institutions contribute daily to this database, which now includes more than 180,000 procedures recorded to date. Its technical characteristics have been previously described in detail [15, 16].

Patients

From January 2005 to December 2012, 26,089 patients underwent lobectomy for NSCLC and were entered into the French national database. Among these, 24,811 patients (95.1%) were operated on by OT and 1,278 (4.9%) by VATS. Baseline demographics included age, gender, smoking, American Society of Anesthesiologists (ASA) Physical Status Classification score, body mass index, medical history, and history of thoracic operations.

For subgroup analysis, patients were defined as high-risk or low-risk for lobectomy according to the criteria reported by the American College of Surgery Oncology Group trial [17].

The primary end point was postoperative complications, including cardiopulmonary morbidity, prolonged air leaks over 7 days, bronchopleural fistula, empyema and hemorrhage. Cardiopulmonary morbidity was reported as proposed by the European Society of Thoracic Surgery [18].

The secondary end points were postoperative death, OS, disease-free survival (DFS), and LOS. Postoperative death was defined as patients who died within the first 30 days after the operation and those who died later during the same hospitalization. OS was defined as the time from the date of the operation plus 30 days (to exclude in-hospital death) until death from any cause or the last consultation. DFS was defined as the length of time after treatment during which no disease was found. Follow-up time ranged from 1 month to 5 years; median follow-up time for the cohort was 2 years and was determined using censoring distribution.

Variables Used for PS Analysis

Variables used to estimate the PS were age, sex, ASA score, dyspnea score, forced expiratory volume, site of resection, side, pathologic stage, histology, year of operation, type of center, and hospital volume of activity.

The proportion of missing ASA scores and forced expiratory volume varied between 1.8% and 20%. We assumed that the missing data were missing at random. We applied a multiple imputation framework to compensate for missing prognostic factor data for the ASA score and forced expiratory volume. The number of imputations was 20. We created a dummy variable for missing data concerning the pathologic stage and histology. For each hospital, hospital volume of activity was calculated in the period from 2005 to 2012. Centers were ranked by the number of procedures performed per year. We created a categoric variable detailing five categories of hospital volume of activity.

Statistical Analysis

PS techniques were used to balance the distributions of measured potentially confounding covariates for patients treated by VATS or OT, as previously described [15]. Two statistical analyses were performed: matching and IPTW [19].

Finally, odds ratios were used for the dichotomous variables of postoperative death, atelectasis, pneumonia,

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