Predicting Lung Cancer Resection Morbidity and Mortality: the Eurolung models

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Honorary Clinical Associate Professor
St. James’s University Hospital, Leeds, UK
• Outcomes (i.e. morbidity and mortality) are still the most widely used quality indicators in thoracic surgery

• Outcomes need risk-adjustment, accounting for different case-mix and prevalence of risk factors to prevent risk-averse behaviours and misleading information
27 units from 14 Countries prospectively submitted data (2001-2003)

The ESOS model for in-hospital mortality was derived from 1694 patients with lung tumors (33 deaths) and validated on other 1128 patients showing satisfactory precision.

\[ \ln \frac{R}{1-R} = -5.8858 + 0.0501 \times \text{age} - 0.0218 \times \text{ppoFEV1} \]
Multicentric analysis of performance after major lung resections by using the European Society Objective Score (ESOS)

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\(^b\) Thoracic Surgery Service, Salamanca University Hospital, Spain
\(^c\) Department of Thoracic and Vascular Surgery, University Hospital Antwerp, Belgium

Comparison between observed and predicted in-hospital mortality rates within each unit

<table>
<thead>
<tr>
<th>Unit</th>
<th>Observed mortality rate</th>
<th>Predicted mortality rate</th>
<th>p-value</th>
<th>95% CI of differences</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>2.3% (6 cases)</td>
<td>1.6% (1.5–1.7)</td>
<td>0.8</td>
<td>−0.02 to 0.034</td>
</tr>
<tr>
<td>B</td>
<td>2.6% (7 cases)</td>
<td>2% (1.9–2.1)</td>
<td>0.8</td>
<td>−0.02 to 0.037</td>
</tr>
<tr>
<td>C</td>
<td>4.1% (7 cases)</td>
<td>2% (1.9–2.2)</td>
<td>0.3</td>
<td>−0.06 to 0.02</td>
</tr>
</tbody>
</table>

Predicted mortality rates are reported with 95% confidence limits.

<table>
<thead>
<tr>
<th></th>
<th>Unit A</th>
<th>Unit B</th>
<th>Unit C</th>
</tr>
</thead>
<tbody>
<tr>
<td>RAM</td>
<td>3.9%</td>
<td>3.3%</td>
<td>5.6%</td>
</tr>
</tbody>
</table>

Risk-Adjusted Mortality rate: the mortality rate a unit would have if its case-mix were similar to the average case-mix in the study (Tu JV et al. J Am Coll Cardiol 1997)
ESTS database
Features of European Society of Thoracic Surgeons Database

• Online
• Free to all ESTS members
• All thoracic surgery operations are included
• Multiple outcome and process indicators
• Standardized risk factors and outcomes
• Possibility to export data for internal usage
Report from the European Society of Thoracic Surgeons Database 2017: patterns of care and perioperative outcomes of surgery for malignant lung neoplasm

Michele Salati\textsuperscript{a,*}, Alessandro Brunelli\textsuperscript{b}, Herbert Decaluwe\textsuperscript{c}, Zalan Szanto\textsuperscript{d}, Marcel Dahan\textsuperscript{e}, Gonzalo Varela\textsuperscript{f} and Pierre-Emmanuel Falcoz\textsuperscript{g}, on behalf of the ESTS DB Committee

<table>
<thead>
<tr>
<th></th>
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<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>N OF PROCEDURES</td>
<td>3433</td>
<td>13018</td>
<td>25441</td>
<td>37929</td>
<td>46759</td>
<td>56959</td>
<td>67373</td>
<td>82608</td>
<td>100043</td>
</tr>
</tbody>
</table>

CUMULATIVE N OF PROCEDURES

0 275000 550000 825000 110000

VATS as a proportion of lobectomy

<table>
<thead>
<tr>
<th></th>
<th>No</th>
<th>Yes</th>
<th>Yes (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2007-2011</td>
<td>19610</td>
<td>1103</td>
<td>5.3%</td>
</tr>
<tr>
<td>2012-2016</td>
<td>19331</td>
<td>9058</td>
<td>31.9%</td>
</tr>
<tr>
<td>Total</td>
<td>38941</td>
<td>10161</td>
<td>20.7%</td>
</tr>
</tbody>
</table>

Cumulative non-adjusted 30-day mortality

<table>
<thead>
<tr>
<th>Cumulative non-adjusted 30-day mortality</th>
<th>Alive</th>
<th>Died</th>
<th>Died Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>2007-2012</td>
<td>22730</td>
<td>922</td>
<td>3.9</td>
</tr>
<tr>
<td>2013-2017</td>
<td>36817</td>
<td>646</td>
<td>1.7</td>
</tr>
<tr>
<td>Total</td>
<td>59547</td>
<td>1568</td>
<td>2.6</td>
</tr>
</tbody>
</table>
Rationale for developing Eurolung

To develop updated models of 30 day mortality and cardiopulmonary morbidity from a modern population of patients collected in the ESTS database.
Patients

47,960 patients submitted to anatomic lung resections from July 2007 through August 2015.

Observational analysis on the ESTS database

Exclusion criteria: non-anatomical resections, incomplete outcome data
Outcome variables

30-days or in-hospital

Cardiopulmonary morbidity
(one or more of the following complications: RF, ATE, Emb, Pulm Edema, Pneumonia, CF, MI, ARRH, Stroke, AKF)

Mortality

Selected risk factors

• Sex
• Age
• Body Mass Index
• Coronary artery disease
• Cerebrovascular disease
• Chronic Kidney disease
• Diabetes
• ppoFEV1%
• Type of resection (lobectomy vs. pneumonectomy)
• Type of surgical approach (VATS vs. open)
• Extended resection (i.e. + chest wall, SVC, diaphragm, sleeve etc.)
• Neoadjuvant chemotherapy

# Definition of variables

The Society of Thoracic Surgeons and The European Society of Thoracic Surgeons General Thoracic Surgery Databases: Joint Standardization of Variable Definitions and Terminology

Felix G. Fernandez, MD, Pierre E. Falcoz, MD, PhD, Benjamin D. Kozower, MD, MPH, Michele Salati, MD, Cameron D. Wright, MD, and Alessandro Brunelli, MD

<table>
<thead>
<tr>
<th>Variable</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 Date of birth</td>
<td>Patient’s date of birth using 4-digit format for year (dd/mm/yyyy)</td>
</tr>
<tr>
<td>2 Age</td>
<td>Patient’s age in years, at time of operation; this should be calculated from the date of birth and the date of operation</td>
</tr>
<tr>
<td>3 Gender</td>
<td>Patient’s gender at birth as either male or female</td>
</tr>
<tr>
<td>4 Height, m</td>
<td>Height of the patient in meters at the time of operation</td>
</tr>
<tr>
<td>5 Weight, kg</td>
<td>Weight of the patient in kilograms at the time of operation</td>
</tr>
<tr>
<td>6 Current treatment for hypertension</td>
<td>Patient has a diagnosis of hypertension, documented by current pharmacologic therapy, diet, and/or exercise to control hypertension</td>
</tr>
<tr>
<td>7 Current treatment for cardiac failure</td>
<td>Patient is currently using pharmacologic therapy to treat congestive heart failure; heart failure is defined as physician documentation or report of any of the following clinical symptoms of heart failure described as unusual dyspnea on light exertion, recurrent dyspnea occurring in the supine position, fluid retention; or the description of rales, jugular venous distention, pulmonary edema on physical examination, or pulmonary edema on chest roentgenogram; a low ejection fraction without clinical evidence of heart failure does not qualify as heart failure</td>
</tr>
<tr>
<td>8 Coronary artery disease</td>
<td>Patient has a history of coronary artery disease (CAD) as evidenced by one of the following: 1. Currently receiving medical treatment for CAD 2. History of myocardial infarction 3. Prior CV intervention including, but not limited to, CABG, PCI, or both</td>
</tr>
<tr>
<td>9 Any previous cardiac surgical procedures</td>
<td>Patient has undergone any prior cardiac surgical procedure that required a general anesthetic and an incision into the mediastinum or chest</td>
</tr>
<tr>
<td>10 Neoadjuvant chemotherapy</td>
<td>Patient received preoperative chemotherapy (or chemoradiotherapy) for the current thoracic malignancy; do not report treatment for prior cancers</td>
</tr>
<tr>
<td>11 Neoadjuvant radiotherapy</td>
<td>Patient received preoperative radiotherapy (or chemoradiotherapy) for the current thoracic malignancy; do not report treatment for prior cancers</td>
</tr>
</tbody>
</table>
Models building process

Univariable screening of variables

Variables with $p<0.05$ at univariable analysis selected for stepwise logistic regression analyses

Internal validation by bootstrap technique
Analysis of morbidity

Major cardiopulmonary complications: 8,805 patients (18.4%)

Significant variables after logistic regression:

- Age
- ppoFEV1
- CAD
- CVD
- CKD
- Thoracotomy
- Extended resections

All predictors with $p<0.0001$ and bootstrap frequency $>95\%$
Regression equation for morbidity EuroLung1

Logit = -2.465 + 0.497Xsex male + 0.026Xage + 0.231XCAD + 0.371XCVD + 0.152XCKD – 0.015XppoFEV1 + 0.514X extended resections + 0.497X thoracotomy

Hosmer Lemeshow goodness of fit statistics p=0.4, c-index 0.68
Analysis of mortality

In-hospital or 30 day mortality in 1,295 patients (2.7%)

30 day mortality by type of resection

- Lobectomies: 2.3%
- Segmentectomies: 1.4%
- Pneumonectomies: 6.8%
Significant variables after logistic regression:

- Age
- Sex male
- ppoFEV1
- CAD
- CVD
- BMI
- Thoracotomy
- Pneumonectomy
- Extended resections

All predictors with $p<0.005$ and bootstrap frequency $>80\%$
logit (mortality) = -5.82 + 0.903Xsex male + 0.044Xage + 0.264XCAD + 0.582XCVD - 0.064XBMI + 0.300Xextended resection + 0.929Xpneumonectomy + 0.894Xthoracotomy - 0.009XppoFEV1

Hosmer Lemeshow goodness of fit statistics p=0.2, c-index 0.74
# Aggregate Eurolung2

<table>
<thead>
<tr>
<th>Variables</th>
<th>Score (points)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ppoFEV1&lt;70%</td>
<td>1</td>
</tr>
<tr>
<td>CAD</td>
<td>1</td>
</tr>
<tr>
<td>Extended resections</td>
<td>1</td>
</tr>
<tr>
<td>Age&gt;65</td>
<td>2</td>
</tr>
<tr>
<td>CVD</td>
<td>2</td>
</tr>
<tr>
<td>Sex male</td>
<td>3</td>
</tr>
<tr>
<td>Thoracotomy</td>
<td>3</td>
</tr>
<tr>
<td>BMI&lt;18.5</td>
<td>3</td>
</tr>
<tr>
<td>Pneumonectomy</td>
<td>3</td>
</tr>
</tbody>
</table>
30 day mortality by aggregate Eurolung2

P<0.0001

<table>
<thead>
<tr>
<th>Range</th>
<th>Mortality Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-3</td>
<td>0.4</td>
</tr>
<tr>
<td>4-6</td>
<td>1.4</td>
</tr>
<tr>
<td>7-8</td>
<td>2.9</td>
</tr>
<tr>
<td>9-11</td>
<td>5.2</td>
</tr>
<tr>
<td>12-14</td>
<td>11.3</td>
</tr>
<tr>
<td>15-17</td>
<td>29.4</td>
</tr>
</tbody>
</table>

- 0.1% pts
- 3% pts
- 20% pts
Limitations

1. Retrospective analysis-selection bias, heterogeneity, lack of standardization
2. Missing variables (i.e. DLCO, VO2max)
3. Mortality period limited to 30 days
4. Representativeness of the database
5. Data quality- database is not formally audited
Clinical Applicability

Eurolung has been incorporated in the Composite Performance Score used for the European Institutional Accreditation.

Aggregate Eurolung represent a simple instrument of risk assessment. It can be used as information aid tool during preoperative counseling.

Eurolung may be used as inclusion criteria to enroll high-risk patients in efficacy trials of alternative surgical or non-surgical treatments (sublobar resections, SBRT etc.)
Risk-adjusted performance evaluation in three academic thoracic surgery units using the Eurolung risk models†

Cecilia Pompili, Yaron Shargall, Herbert Decaluwe, Johnny Moons, Madhu Chari and Alessandro Brunelli

Center 1: 721, center 2: 857, center 3: 433. Overall 65% by VATS

<table>
<thead>
<tr>
<th></th>
<th>CENTER 1</th>
<th>CENTER 2</th>
<th>CENTER 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Risk adjusted mortality</td>
<td>3.50%</td>
<td>0.92%</td>
<td>1.14%</td>
</tr>
</tbody>
</table>
PURPOSE OF ESTS INSTITUTIONAL ACCREDITATION

PROCESS aimed at standardizing and improving practice of European Thoracic Surgery units

ESTS Accreditation IS A QUALITY LABEL
ELIGIBILITY CRITERIA FOR ACCREDITATION

1. Participation to ESTS Database and contributing >150 anatomic lung resections in the last 3 years
2. Institution must reside in Europe
3. Head of unit or Clinical Audit lead must be an ESTS member
4. CPS > 0
5. Completeness of variables used to calculate CPS>70%
Preoperative care:
- % of pts having DLCO measured
- % of pts with CT enlarged or PET+ med nodes undergoing preop invasive mediastinal staging

Operative care:
- % of pts operated on for primary neoplastic disease submitted to systematic lymph node dissection

Postoperative care:
- Eurolung risk-adjusted cardiopulmonary morbidity rate
- Eurolung risk-adjusted mortality rate
The problem of record completeness

In 2017 only 25% of units had a completeness rate greater than 70% in the variables used to calculate the Eurolung2

Eurolung2 is not parsimonious: 9 variables

No allowance is made in the model for missing variables

Model may not be cost-effective
Ongoing Project: Development of a parsimonious version of Eurolung

**Rationale:**
- Improve utilization and user-friendliness
- Improve risk adjustment and quality monitoring

Larger sample size: 66,000 anatomic lung resections (+20,000)
Increased no. events (30 day mortality): 1583 (+300)

Parsimonious Eurolung: variables reduced from 9 to 6

AUC value 0.734 (AUC full model 0.736)
Lowess smoothing plots of the observed and predicted mortality, from both full model and parsimonious model.