VATS anatomic resections for lung cancer: insights from the Italian VATS Group

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**Background:** The VATS Group and the National Register for VATS Lobectomy were set up in 2013. Both quality and quantity of collected data within the database are two fundamental tools for scientific and statistical purposes, similar to other important databases, such as the European Society of Thoracic Surgeons (ESTS) Database, the Society of Thoracic Surgeons General Thoracic Surgery Database (STS GTSD) and the Danish Lung Cancer Registry (DLCR).

**Methods:** Four thousand seven hundred and four VATS lobectomy patients have recruited to date. Several parameters were recorded, such as preoperative clinical condition, surgical treatment as far as technical details, postoperative course and follow-up.

**Results:** The Eastern Cooperative Oncology Group (ECOG) performance status was 0.27. Uniportal approach was used in 332 patients, three-portal approach in 3,825 and bi-portal approach in 547. Lymphadenectomy was performed in 4,704 patients; a sampling nodal dissection in 1,180 patients and a radical nodal dissection in 3,524 cases. Conversion rate was in 9.99% of cases. Adenocarcinoma is the most common histologic type (53.34%), followed by squamous carcinoma (15.53%).

**Conclusions:** The structure of the Italian Registry of VATS Lobectomy makes it a valid source to draw on for statistical studies for scientific purposes.

**Keywords:** VATS lobectomy; registry; data quality; VATS Group

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**Introduction**

The VATS Group and the Italian Register of VATS Lobectomy started in 2013, becoming immediately an established reality, whose purpose is to gather experiences from different accredited centers according to risk assessment, benefits, related costs and promoting the diffusion of minimally invasive techniques (1). An accessible database is now considered a key-point for carrying out any type of analysis aiming to clinical strategies planning, quality assessment, cost estimation and results comparison (2). Several scientific societies have long since adopted the use of such databases. The European Association of Cardiac Thoracic Surgery-European Society of Thoracic Surgeons (EACTS/ESTS) Working Group have instituted the ESTS database since 2001 (3), according to a blind data insertion strategy (patients, operators and countries) in order to minimize related selection bias and through simple consultation tables for rapid acquisition of scientific and statistical information (2,4). ESTS also collaborates with the Society of Thoracic Surgeons General Thoracic Surgery Database (STS GTSD), which is considered to be the most important and major database for Thoracic Surgery worldwide. A comparative study was carried out between ESTS and STS GTSD, about different pulmonary resections and post-intervention clinical outcomes of patients (2), resulting in a large number of patients [78,212] who underwent lung resections between 2010 and 2013. Specifically, 47,539 patients were inserted in the STS database, while the remaining 30,673 in the ESTS one, allowing an exhaustive comparison between minimally invasive and standard approaches according to morbidity, mortality rates and postoperative hospital stay (5). Even the Danish Lung Cancer Registry (DLCR), set up by the Danish Lung Cancer Group (DLCG), has its primary purpose in the evaluation of surgical and clinical management of lung cancer patients for both national and international cohort studies. At the time of DLCG foundation, in 1991, several published studies suggested that the overall survival in patients with lung cancer in Denmark was lower compared to morbidity and mortality 5-year International survival standards. Hence the common need for setting up a National Registry with, initially, 90 accredited centres, in order to detect and evaluate the different methods of clinical management in lung cancer patients, by monitoring the better treatment strategy and the possibilities of reducing the occurrence frequency of the disease, not only attributable to a strong anti-smoking campaign (6). Thanks to the presence of DLCR, Licht et al. have carried out a study related to the different evidence of nodal upstaging in patients with stage I NSCLC, undergoing VATS lobectomy and...
lobectomy via thoracotomy. One thousand five hundred and thirteen were recruited in the period from 1 January 2007 to 31 December 2011; 717 (47%) were treated with VATS lobectomy, while 796 (53%) underwent thoracotomy. The number of removed nodes in the two different approaches, was not statistically significant (5 nodes in VATS vs. 4 nodes in thoracotomy; P=0.37); the nodal upstaging, on the contrary, was observed in 281 patients, with greater frequency after lymphadenectomy via thoracotomy 24.6 % vs. 11.9%; (P=0.001). The 30-day mortality turned out to be 2% with greater frequency after thoracotomy (2.9% vs. 1.1%; P=0.02); a better medium and long-term survival, was also observed in patients who underwent VATS lobectomy (P=0.01) (7). With the same purposes of study and programming methodologies, the VATS Group proposes to analyze protocols and results, through the data collected in the VATS Lobectomy National Register.

Methods

The VATS Lobectomy National Register, incorporated within the VATS Group, was created in 2013, thanks to the collaboration of the various accredited centers and started to recruit patients from 1 January 2014. The official language is English (8). The VATS Group consists of 54 accredited centers, scattered all over the national territory. It can be stated that patients who are regularly inserted in the database are derived from about 90% of the Thoracic Surgery Departments in Italy. Four thousand seven hundred and four VATS lobectomy patients have been recruited to date, with an average of about 3.5 new patients per day (1). A number of parameters and variables are recorded, similarly to the other established national databases, in order to guarantee a wider insight of data: (I) upon admission: each patient is assigned an ID number in sequential order, according to the registration date, the numerical code of the center, the alphanumeric code identifying the patient, the gender, and the age of the patient; (II) oncological history: for each patient, an anamnestic evaluation of the presence or absence of previous neoplastic diseases, eventual localization and previous treatment (surgery, chemotherapy); (III) Charlson comorbidity index: represents the main and most widely used evaluation index for comorbidities possibly present in the patient being examined. Depending on comorbidities, each patient is assigned a score from 0 to 6, where 6 corresponds to the maximum degree of morbidity (9); (IV) risk stratification: evaluated using the Eastern Cooperative Oncology Group (ECOG) performance status, represented a criteria plot for disease progression monitoring, according to patient’s daily life repercussion (10); (V) pulmonary function evaluation: a cornerstone for preoperative patients’ assessment is a careful preoperative pulmonary function test by means of spirometry and hemogasanalysis. In such cases, additional complementary examinations are required, such as cardiac stress tests and pulmonary scintigraphy; (VI) thorax computed tomography (CT) scan and fluorine18 fluorodeoxyglucose positron emission tomography (¹⁸F-FDG-PET/CT): an accurate diagnostic study is a key examination in patients with lung cancer, as it allows to define the T parameter (tumor lesion), identify any lymphadenopathy (N parameter) and likely secondary lesions (M parameter). Concurrent ¹⁸F-FDG-PET/CT can be performed. Regarding CT framework, the size of the lesion, the its location in the lung location and relative lobe, any lymphadenopathy and metastases are reported, resulting in clinical lung cancer TNM staging process; (VII) regarding the PET examination, the same parameters are recorded in addition to standardized nuclide-avidity, in the SUVmax cut-off of 2.5 as prediction of malignancy (11); (VIII) preoperative diagnosis: the presence or absence of histologic data [fiberoptic bronchoscopy, endobronchial ultrasound/trans-bronchial needle aspiration (EBUS-TBNA), endoscopic ultrasound/fine needle aspiration (EUS-FNA), mediastinoscopy] is also reported; (IX) surgery data: after the preoperative evaluation process, surgical data are included according to number of ports, technique (i.e., vascular stapling, bronchial stapling, fissure completion) and chest drainage management; (X) final pathology report: in this section, definitive diagnosis reports are given according to lesions’ histology, number of harvested lymph nodes and lymphatic stations involved; (XI) postoperative complications: data related to morbidity and mortality rates; (XII) chemotherapy and radiotherapy: information regarding adjuvant therapies are reported; (XIII) discharge: this section includes data on the patient’s clinical condition after surgery, i.e., postoperative pain, any leakage from pleural drainage, and above all, an estimate of the quality of life in the patient’s healthcare status through the EuroQol 5 Dimension (EQ-5D) index (12); (XIV) follow-up: the last section contains information about long-term results and quality of life assessment at distance according to EQ-5D.

Results

Analyzing the large amount of data, it has been observed
that the majority of patients included in the Registry are male, i.e., 2,806 vs. 1,898 (56.99% vs. 40.34%); the average age of patients at the time of surgery was 67.2±12.1 years. Patients with negative oncologic history were 3,018 (64.16%) while 1,686 patients (35.84%) have a previous positive oncologic history. One thousand four hundred and forty-seven of 1,686 were treated with surgery for previous neoplasia, 527 were being treated with chemotherapy and 359 with radiotherapy. Charlson comorbidity index, used for the calculation of the ongoing comorbidities, has a mean value of 4.41 for patients in our database. ECOG performance status, used for risk stratification, has a mean grade of 0.27. A meticulous preoperative assessment of pulmonary function is performed to each patient, through spirometry and blood gas-analysis; among spirometric parameters, FEV1 mean value was 2.35% while DLCO/VA was 65.05%. Moreover, a Tiffeneau index mean value of 75.28 was obtained by using the collected data. All patients underwent CT scan brain-thorax-abdomen. Right lung turned out to be more involved in the neoplastic process with 3,071 vs. 1,633 cases. We observed 318 lymphadenopathies and 42 of these were metastatic. 

\[18^F\text{-FDG-PET/CT}\] carried out in 3,700 patients with the evaluation of SUVmax, and its mean value was 5.38. One thousand nine hundred and forty-two patients underwent surgery with preoperative histologic and/or cytologic diagnosis by: (I) fiber optic bronchoscopy in 445; (II) fine needle aspiration biopsy (FNAB) in 1,453; (III) mediastinoscopy in 4; (IV) EBUS-TBNA in 37; (V) EUS-FNA in 3. One hundred and thirteen patients needed neoadjuvant therapy. Regarding surgical procedure, the uniportal approach was used in 332 patients, threeportal approach in 3,825 and biportal approach in 547. Lymphadenectomy was performed in 4,704 patients: a sampling nodal dissection in 1,180 patients and a radical nodal dissection in 3,524 cases. Four hundred and four patients presented nodal metastasis not captured during preoperative diagnostic procedures, i.e., CT/PET scan, with 5.57% upstaging of N1 and 4.55% upstaging of N2. Six hundred and fourteen patients were treated with adjuvant therapy. Conversion rate was in 9.99% of cases (470 patients) due to different causes: (I) 66 adhesions; (II) 29 advanced staging; (III) 44 anatomical anomalies; (IV) 119 bleedings; (V) 90 calcified lymph nodes on pulmonary artery; (VI) 1 chest wall invasion-T3 tumour; (VII) 20 difficult localization of tumor lesion; (VIII) 60 incomplete or difficult fissures; (IX) 8 time limit; (X) 19 tumor crossing fissures; (XI) 3 wrong position of incision; (XII) 11 not specified. The final histologic analysis suggested that adenocarcinoma is the most common histotype (2,509 patients, 53.34%), follow by squamous carcinoma (730 patients, 15.53%). No intraoperative deaths were recorded, while 30-days mortality rate was 0.17%. Postoperative morbidity accounts for 497 patients (10.6%); persistent air leakage was the most common (187 patients) followed by pneumonia and pleural effusion (150 patients), persistent pleural effusion (103 patients), blood transfusion (32 patients), hemothorax (12 patients), ARDS (8 patients), bronchopleural fistula (3 patients) and myocardial ischemia (2 patients). The mean postoperative hospital stay was 5 days (6.48±3.77 days). In 293 patients, during follow-up, a disease relapse was observed over time. All the information was evaluated by data quality control, according to two systems: data completeness and data reliability, summed up by the Aggregate Data Quality score (ADQ) (13). Each of the accredited centers in the database is thus assigned a final ADQ, which accredits the structure.

**Discussion**

The existence of a National Database from which scientific information can be drawn, requires a systematic data collection. The extensive data collection ensures data as a tool for surgeon performance evaluation. Brunelli et al. (14) carried out a study, from June 2007 to August 2015, in order to develop a risk stratification, concerning 30-day mortality and cardiopulmonary morbidity, in patients who underwent lung resection. They observed 47,960 patients included in ESTS database and noticed that the majority were males [32,557] with average age of 62.55 years, similar to our results. During preoperative study two indexes are evaluated, aimed at defining comorbidities and how their possible have impact on surgical treatment: Charlson comorbidity index, and the index for risk stratification, i.e., ECOG Performance status. These indexes are used internationally for the same purpose. Suh et al. (15) used CCI and EOCG as evaluation tools, contextualized in association with other functional parameters, to identify the risk associated with different treatment methods in lung cancer patients. They observed 617 patients, 149 of whom received only palliative therapy, with CCI of 7.3±e.3.7 and an EOCG of 3–4 in 36% of cases. The remaining 468 patients had a CCI of 5.1±e.3.9 and an EOCG of 0 in 40% of cases. In our database the average value of CCI is 4.41, while 0.27 in the EOCG. Data collection relating to functional values, allowed to conduct studies regarding the possibilities to perform a VATS lobectomy in patients with FEV1 and DLCO <40%,
threshold value below which the postoperative morbidity and mortality risk has always been considered elevated. Burt et al. (16) studied a cohort of 13,376 patients with FEV1 of 81.7%±20.4% and DLCO of 73.0%±21.7%, 6,802 of whom underwent resection via thoracotomy and 6,574 via thoracoscopic approach. Patients treated with thoracotomy presented several cardio-pulmonary complications in 13.1% of cases, unlike patients treated with VATS lobectomy who experienced cardio-pulmonary complications only in 7.5%. Postoperative mortality was 2.1% in open surgery and 0.8% in VATS lobectomy. Preoperative study with 18F-FDG-PET/CT allows us to obtain an indication about the possible malignancy of the lesion relating to SUVmax value. Regarding the importance of PET/CT in the characterization of the lesions, we have conducted a retrospective study during the period from January 2014 to May 2016 (17) by recruiting patients with solitary pulmonary nodule (SPN) through the National Registry of VATS Lobectomy. Two thousand and six patients were observed and we found that PET/CT has a central role in the characterization of these lesions. SUVmax value resulted of 3.25±4.01 in case of adenocarcinoma and of 6.51±6.26 in case of squamous carcinoma; no malignant lesion had a SUVmax <2.5. In our evaluation, in patients submitted to VATS lobectomy SUVmax average value is 5.38. Lymphadenectomy represents another important aspect treated in our database, subject of study by several authors. In particular, the number of lymph nodes to be removed is a matter of significant interest, in order to accomplish lymphadenectomy. Liang et al. (18) conducted a study on this topic, currently still debated. Authors observed the correlation between the number of harvested lymph nodes and nodal downstaging in the setting of a proper NSCLC staging and their effects on long-term survival. Data for carrying out this study were taken from the Chinese multi-institution registry (n=5,706) and the US SEER database (n=38,806). There was a significant difference between the number of lymph nodes removed in the first group of patients (15 harvested lymph nodes) and those of the second (7 harvested lymph nodes). The study concluded that the correct number of lymph nodes should be removed in cN0 non-small cell lung cancer is 16. Bertani et al. (19) studied different procedures for lymphadenectomy as a complete dissection (CD) of hilar and mediastinal lymph nodes and a systematic sampling (SS) of predeterminate node stations. They wanted to correlate the two dissection techniques with the nodal upstaging. It has been observed that nodal upstaging N0–1 was 5.9% in patients submitted to CD and 6.4% in patients submitted to SS (P=0.627); upstaging N0–1 was 5.9% (CD) vs. 4.2% (SS) (P=0.086) and, upstaging N1–2 only in 19 patients who underwent CD. In our experience, adenocarcinoma and squamous carcinoma were the most common histotype. Soder et al. (20) reported their experience related to 117 VATS pulmonary resections from 2010 to 2015. Adenocarcinoma was 62.4%, followed by squamous carcinoma in 7.7%. The conversion rate in VATS lobectomy was 9.19% in our experience. It appears that the general reduction of conversion percentage seems to be related, in particular, to the number of performed VATS. Specifically, 50 annual procedures, at least, is taken as baseline for the end of the learning curve. In this study, a surgical conversion rate of 3.4% for a total amount of 4 patients was observed. In order to be statistically significant, it is critical to assess the quality of data before undertaking any project of study. The Italian Registry of VATS Lobectomy, like ESTS database, for this reason, uses a couple of quality indicators, i.e., completeness and reliability, both used for the evaluation of a third indicator (ADQ) able to state the quality of any item in the database, with a single value (2,13).

Conclusions

The presence of a National Register is an important tool for quality assessment and procedure standardization. The Italian VATS Group and the National VATS Lobectomy Register can be a valuable source for scientific purposes thanks to the large amount of data and collaboration with worldwide established database, such as ESTS one. From data collection analysis deriving from the National Register and from comparison with present data in other international registries, we are able to claim that there is a marked overlap regarding patient preoperative evaluation, managing procedures and intraoperative and postoperative treatment. This ensures the chance for the surgeon to confront different realities, validate or disprove his work, obtaining useful practical and statistical information in order to improve the results.

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Footnote

Conflicts of Interest: The authors have no conflicts of interest
to declare.

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