Report from the European Society of Thoracic Surgeons prospective thymic database 2017: A powerful resource for a collaborative global effort to manage thymic tumours

Report from the European Society of Thoracic Surgeons (ESTS) Database 2017. ~~Preliminary~~ Rresults of the ESTS prospective thymic database: a powerful resource for the collaborative global effort in the management of thymic tumors.

Enrico Ruffini[1], Francesco Guerrera[1], Alessandro Brunelli[2], Stefano Passani[3], Danilo Pellicano[3], Pascal Thomas[4], Dirk Van Raemdonck[5], Gaetano Rocco[6], Federico Venuta[7], Walter Weder[8], Frank Detterbeck[9], Pierre-Emmanuel Falcoz[10]

[1]Department of Thoracic Surgery, University of Torino, Torino, Italy

[2]Department of Thoracic Surgery, St. James's University Hospital, Leeds, United Kingdom

[3]KData Clinical, Rome, Italy

[4]Department of Thoracic Surgery, Aix-Marseille University, Marseille, France

[5] Thoracic Surgery, University Hospitals Leuven, Leuven, Belgium

[6]Thoracic Surgery, ~~National Cancer Institute~~Memorial Sloan Kettering Cancer Center, ~~Pascale Foundation, Naples, Italy~~New York, USA

[7]Thoracic Surgery, University of Rome "Sapienza", Policlinico Umberto I, Rome, Italy

[8]Thoracic Surgery, University Hospital, Zurich, Switzerland

[9]Thoracic Surgery, Yale University, New Haven, CT, USA

[10]Department of Thoracic Surgery, University Hospital, Strasbourg, France

Word count: 5082

Corresponding author:

Enrico Ruffini

Department of Thoracic Surgery

14, Corso Dogliotti, 10126 Torino, Italy

email: enrico.ruffini@unito.it

Phone No.: +390110915380; Fax No.: +390110915365

VISUAL ABSTRACT

KEY QUESTION: The ESTS prospective thymic database was queried for analysis and for comparison with the ESTS retrospective thymic database.

KEY FINDINGS: An increased use of minimally-invasive techniques and a wider use of perioperative chemotherapy was observed.

TAKE-HOME MESSAGE: The ESTS prospective thymic database is a powerful tool open to any ESTS Institution for the global effort in the management of thymic tumors.

ABSTRACT

OBJECTIVES: We queried the European Society of Thoracic Surgeons (ESTS) prospective thymic database for descriptive analysis and for comparison with the ESTS retrospective thymic database (1990-2010). *METHODS*: Data were retrieved (1/2007-11/2017) about 1122 patients from 75 ESTS Institutions. *RESULTS*: There were 484(65%) thymomas, 207(28%) thymic carcinoma and 49(7%) neuroendocrine thymic tumors (NETT). Staging (Masaoka) included 483(67%) Stage I and II, 100(14%) Stage III, and 70(10%) Stage IV tumors. The new IASLC/ITMIG TNM classification was available in 224 patients, including 177(85%) Stage I-II, 37(16%) Stage IIIA, 10(4%) Stage IIIB. Chemotherapy as induction and adjuvant treatment was used in 14% and 15% of the patients. Radiotherapy was almost exclusively employed postoperatively (24%). A minimally-invasive surgical approach (VATS/RATS) was used in 276(33%) patients. Overall recurrence rate was 10.8%(N=38). As compared to the ESTS retrospective database, an increased prevalence of thymic carcinomas (from 9% to 28%) and NETT (from 2% to 7%), an increased use of minimally-invasive techniques (from 6% to 34%), and a wider use of chemotherapy as induction (from 9% to 15%) and adjuvant (from 2% to 16%) treatment was observed in the prospective database. The introduction of a set of variables considered essential for the data use ("minimum dataset") resulted in an increased average completeness rate. *CONCLUSIONS*: The reported data from the ESTS prospective thymic database confirm the recent trends in the management of thymic tumors. The ESTS prospective thymic database represents a powerful resource open to all ESTS members for the global effort in the management of these rare tumors.

Abstract word count: 250

Keywords: Database, Thymus neoplasms, ESTS

INTRODUCTION

The European Society of Thoracic Surgeons (ESTS) is the largest pure thoracic surgery society worldwide and its aim is to gather the experience of thoracic surgeons from different continents in the different fields of thoracic surgery. Among the major initiatives of the Society, there is the ESTS Registry, established in 2001 to collect the procedures for lung cancer among ESTS members. After an initial limited number of procedures from few participating centres, the project has gained an increasing and steady push forward and the number of procedures and contributors have increased over the recent years. The 2017 registry report included more than 110,000 lung cancer patients from 240 participating units, and 145 institutions contributed with more than 100 procedures.

The ESTS registry was recently implemented by adding some satellite databases collating data of patients with other thoracic malignancies.

Among the ESTS satellite databases, the thymic registry was established in 2013 with the intent to reunite the experience of as many ESTS institutions as possible with an interest in thymic tumors. The thymic registry was the natural implementation of the initial ESTS retrospective thymic database, established in 2010, that was managed by the ESTS thymic working group and which collated data from 1990 to 2010. The unprecedented collection of data from the retrospective database represented a major contribution to the development of the 8th TNM staging system of thymic tumors (**1**), together with thymic databases from the International Thymic Malignancies Interest Group (ITMIG) and the Japanese Association for Research on the Thymus (JART) and under the coordination of the International Association for the Study of Lung Cancer (IASLC). After the success of the retrospective database, it was decided to launch the prospective thymic database project as satellite database of the ESTS Registry platform with the intent to provide an up-to-date, online platform collecting claims and EMR (electronic medical record) data of patients with thymic malignancies from ESTS institutions. The prospective ESTS thymic registry is under the direct supervision of the ESTS Database Committee, and it is managed, audited and periodically maintained by KData Clinical, the official platform of the ESTS Registry.

In the present paper the preliminary results of the ESTS prospective thymic registry are presented, compared and discussed with the current available literature on thymic neoplasms and with the ESTS thymic retrospective database to highlight the trends in the presentation and management of thymic tumors in the ESTS community over the last decades.

MATERIALS AND METHODS

We downloaded from the ESTS registry satellite thymic database all the cases from the prospective dataset. The collection of data started in 2010 and data from 2007 were retrieved until November 2017. The retrieved data (forming the "ESTS_Data Base_Thymus" for the present study) underwent a process of data cleaning before the analysis. The rate of completeness and reliability rates of the core variables (**2**) were evaluated. The completeness and reliability measurements were obtained following a standardized methodology (**3**). All the variables of interest were collected and analysed, and the completeness of the data for each variable for a preset number of variables considered "essential" was recorded. These variables constituted the "minimum dataset", which was defined as the minimum set of variables considered essential for the use of the patient record. The list of the variables of the minimum dataset is shown in ***Table 1***. The minimum dataset as well as information about cTNM and pTNM including N descriptor according to the ITMIG/IASLC nodal map were introduced and implemented into the ESTS thymic Registry in 2016.

RESULTS

From January 2007 to November 2017 a total of 1122 patients were registered in the ESTS thymic prospective database. The accrual rate increased steadily through the years, with an annual accrual of more than 160 cases in the last 3 years. A total of 75 Institutions contributed to the database, including 62 from Europe, 5 from Asia (4 from Turkey and 1 from Thailand), 7 from South America (Brazil) and 1 from Africa (Morocco) (~~**Appendix 1**~~**Supplemental file 1**). The distribution of the European centres by country is shown in ***Table 2***. The mean number of patients/Institution was 15 (range 5-83).

Table 3 summarizes the patient characteristics of the patient population.

Demographics and preoperative characteristics.

Mean age at diagnosis was 54 years; 414 patients (37%) were older than 50 at diagnosis. There was an equal distribution between genders (50,2% male, 49.8% female). One third of the patients (N=216, 32%) had Myasthenia Gravis at diagnosis. History of previous malignancy was recorded in 82 cases (15%), mostly breast (N=13) and colon (N=10) cancer. A preoperative cyto/histologic diagnosis was ~~deemed unnecessary~~performed in ~~79~~21% of the cases (N=~~434~~115).

Histology and staging.

The majority of patients had thymoma (N=484, 65%); 207 (28%) had thymic carcinoma and 49 (7%) had neuroendocrine thymic tumors (NETT). In the thymoma group, 58% (N=253) had low-risk tumors (A, AB, B1) while 183 (42%) had high-risk tumors (B2-B3). More than half of the patients (N=399) presented with large tumors (> 5 cm). The most frequently involved structures at surgery where the perithymic fat/mediastinal pleura (N=199, 30%), pericardium (N=50, 8%), lung (N=53, 8%), and brachiocephalic vessels/superior vena cava (N=59, 9%). The clinical (pretreatment) and pathologic (post-surgical) Masaoka stage was recorded. At surgery, 34% (N=248) of the patients were at Stage I, 33% (N=235) at Stage II, 14% (N=100) at Stage III, and 10% (N=70) at Stage IV. In 24% of the cases, a clinical Stage I was not confirmed pathologically. Clinical Stage II was rarely

recorded (N=93, 17%), while pathological Stage II (Stage IIa/IIb) was much more frequently reported (N=234, 33%). There was a good concordance between clinical and pathological Stage III (N=77-14,1% vs. N=100-14.0%), Stage IVA (N=37-6.8% vs. N=45-6.3%) and Stage IVB (N=13-2.4% vs. N=25-3.5%).

Information about the IASLC/ITMIG TNM classification (8th edition) was available in 224 patients, both clinically and pathologically. More discordance was observed between cTNM and pTNM as compared to cMasaoka and pMasaoka (Table 3): percentages in cTNM and pTNM for the different T categories were as follows: T1: 70% and 56%; T2: 15% and 22%; T3: 10% and 16%; T4: 4% and 4.4%. As for the N determinant, a very low frequency of N+ disease was reported (3%, N=7). The frequency of M disease was 7% (N=17).

Surgical information

A complete resection was achieved in 89% of the cases (N=710). The most frequent extent of resection included a complete thymectomy + thymomectomy (thymothymomectomy) in 90% of the cases (N=682), while in 56 cases (7%) only thymomectomy was performed, leaving the thymus behind. Of these there were 32 Stage I-II patients, which represents 6.6% of the entire Stage I-II population (N=483). The most frequent reported surgical approach was full-length ~~total~~ sternotomy (N=389), which was performed in almost half of the patients (48%). Minimally-invasive techniques were employed in 33% (N=276) of the patients, including VATS (N=167, 20%) and Robotic (N=109, 13%). Extended approaches (sterno-thoracotomy, hemi or clamshell) were reported in 5% of the patients (N=41). The most frequently resected structures included the pericardium (N=110, 18%), the mediastinal pleura (N=93, 15%), the phrenic nerve (N=48, 8%). Resection of the great venous vessels was not infrequent (brachiocephalic veins – 24 cases, superior vena cava – 9 cases). As for the associated lung resection for pulmonary involvement (N=112), the most frequent procedure was a wedge resection, which was performed in 98 cases. Anatomic resections were performed in 14 cases (segmentectomy, 1 case, lobectomy in 9 cases and pneumonectomy in 4 cases). Very rarely were other mediastinal/thoracic structures resected. Pleural procedures for

pleural involvement included resection of pleural implants (N=14), diaphragm (N=8) and extrapleural pneumonectomy (EPP, N=3).

Perioperative treatments and outcome.

As for perioperative treatments, radiotherapy and chemotherapy were used as an adjunct to surgery in different settings. Radiotherapy was used more often in an adjuvant (postoperative) setting in 164 patients (25%), while chemotherapy was evenly employed in the preoperative setting as an induction treatment (N=69) and in the postoperative (adjuvant) setting (N=71) in 15% and 16% of the patients, respectively.

The vast majority of patients were discharged alive from the hospital (N=939, 99%). ~~Only 5~~Five patients died in hospital, and an additional 4 patients died at 30 days.

Overall, we had information about recurrence status in 451 patients. Of these, 49 patients experienced a recurrence (10.8% recurrence rate). Eleven patients presented more than one recurrence episode.

Data completeness.

Figure 1 shows the completeness rate of the fields of the minimum dataset, which include the datafields which are considered essential for the use of the record for the analysis. The median completeness rate was 63.3%, ranging from 39.8% (chemotherapy) to 90% (WHO histology).

DISCUSSION

The present manuscript presents the preliminary results of the ESTS prospective thymic database as of November 2017. It provides an overview of the clinical presentation, histology, staging and management of thymic tumors among 75 ESTS Institutions.

Clinical presentation and preoperative assessment.

In the present registry thymic tumors occurred with almost equal frequency in males and females, and in one-third of the cases they were associated with Myasthenia Gravis. This is in line with the current literature (**4, 5, 6**).

An increased rate of extrathymic neoplasms in patients with thymic tumors was reported by Filosso and associates (**7**). In our database, the overall rate of extrathymic tumors was 15%, of whom breast and colon were the most frequent primaries.

The need of a preoperative cyto-histologic diagnosis was long required in the past. With the advancements of radiologic imaging (last generation CT and MRI), a preoperative cyto-histologic diagnosis of a suspected thymic tumors progressively lost its importance and is currently limited to the infrequent occurrence of an equivocal radiologic imaging or in the presence of a non resectable tumor to institute an induction treatment. This tendency had already been confirmed in a survey among the ESTS members and in the retrospective ESTS database (**8**) and it is further evident in the present report where 79% of the patients did not have a preoperative cyto/histologic confirmation.

WHO histology and staging

The prevalence of the three different types of thymic tumors (thymoma, thymic carcinoma and neuroendocrine thymic tumors, NETT) in the present database was 65%, 28% and 7% respectively. The prevalences of thymic carcinoma and NETT are higher than the figures commonly reported in the literature. Most of the largest series in the literature report a prevalence of thymic carcinoma around 15-20% (**9, 10, 11**), with a far less prevalence for NETT (2-3%) (**12,**

13). We have no clear explanation for this prevalence difference in our database. The difference might result from geographic distribution, dedicated referral or improved pathologic expertise in differentiating B3 thymomas from thymic carcinoma. The tumor distribution is also different form the one we observed in the ESTS retrospective database (1990-2010), where we reported a prevalence of 88% for thymoma, 9% for thymic carcinoma, and 2% for the neuroendocrine thymic tumors (**14, 15**).

In the present report information about the new IASLC/ITMIG TNM classification was available in more than 200 patients. A good stage stratification was observed, although a wider discrepancy between cTNM and pTNM was observed (particularly for early stages) as compared to clinical vs. pathological Masaoka stage.

Surgical approach and management

A complete resection was performed in the vast majority of the patients (89%) and this reflects the relatively high prevalence of Stage I-II disease (67%). The extent of thymectomy consisted in resection of the thymic tumor only (thymomectomy) in 7.5% of the cases overall, and in 6.6% of early stages (Stage I-II).

Controversy still exists in the literature whether in early stage (Stage I-II) non-myasthenic patients thymomectomy alone (limited thymectomy) may be considered instead of the standard complete thymectomy + thymomectomy. A recent paper from the JART database (**16**) found that 22.5% (N=289/1286) patients with Stage I-II Masaoka stage actually received thymomectomy only, leaving residual thymic tissue behind. A similar figure (24%, N=251/1047) was reported by Gu and associates (**17**) enquiring the ChaRT database. An even higher rate of thymomectomies alone vs. thymothymomectomy (39%, N=295/762) was reported by Narm and associates exploring the KART database (**18**). The JART and ChaRT studies found no recurrence rate differences between the two techniques. In the KART study, no recurrence rate difference was found in Stage I, although a significantly higher recurrence rate was observed in patients with Stage II undergoing limited thymectomy. The lower percentage of limited thymectomies (thymomectomy) in the ESTS thymic database may reflect the traditional standard approach which has been used in Europe

over the last decades, with a general perception that limited thymectomy may predispose to postoperative MG or a higher recurrence rate.

Comparison of clinic-pathologic characteristics between the ESTS retrospective and prospective databases.

Table 4 shows the clinico-pathologic characteristics of the patient population in the ESTS retrospective and prospective thymic databases. The comparison may help clarify the trends over time in the ESTS community about presentation and management of thymic tumors spanning over almost 30 years (1990 to 2017). Median age, gender distribution, association with Myasthenia Gravis, stage distribution (Masaoka stage), tumor size at resection, and complete resection rate remained similar in the two databases. On the other hand, a significantly different distribution in the tumor types (thymoma, thymic carcinoma, NETT) was reported in the prospective dataset, with an increased prevalence in thymic carcinomas and NETT. As for the surgical approach, a significantly increased use of minimally invasive techniques (VATS and RATS) was reported (from 4% to 20% for VATS and from 2% to 13% for RATS) with a consequent decrease of open accesses. This is in line with most recent series from the largest international databases (**19**) demonstrating a steady increase in the use of minimally invasive technique for thymic tumors in the last years. A recent paper investigating the JART database report that currently 30% of thymectomies in Japan are performed by VATS (**20**). A 20% prevalence of VATS was reported in a recent paper from the ChART database from 1994 to 2010, with an increase up to 40% in the last three years (**21**). Finally, in the ITMIG database, out of 2514 patients undergoing thymectomy for thymoma from 1997 to 2012, 461 (18%) received a minimally-invasive approach (VATS or RATS), with more than 70% in the last 2 years (**22**). As for the use of perioperative treatments, we observed a wider use of chemotherapy in the prospective database, both as induction and as adjuvant therapy (from 9% to 15% and from 2% to 16% respectively). The progressive increase in the use of induction chemotherapy over the last years is in support of the conclusions of some recent large series (**23**) and meta-analysis (**24**) and it reflects the wider compliance from the contributing institutions to the current guidelines (**25**). Radiotherapy was similarly used in both

database, although with a slight reduction in the prospective data (25% vs. 29% in the retrospective database). This indicates a general perception among the ESTS members of a positive effect of postoperative radiotherapy after resection of thymic tumors which has not changed over the last decades and which seems to be confirmed by two recent meta-analysis (**26, 27**).

The international involvement of the ESTS prospective thymic registry.

The ESTS thymic working group and the ESTS database committee have been actively involved in the international big effort on thymic tumors which took place in the first decade of this millennium. The leading thymic organization worldwide is the International Thymic Malignancies Interest Group (ITMIG) which was founded in 2010 with the aim to promote and facilitate the integration among disciplines, societies and organizations with an interest in thymic tumors and to provide infrastructures and platforms to advance the clinical and basic research in these rare malignancies. A number of thymic organizations are also active worldwide working in collaboration with ITMIG: among these there are the Japanese Association for Research on the Thymus (JART), the Chinese Alliance on Research in Thymomas (ChART), the Korean Association for research on the Thymus (KART), and the Réseau Tumeurs THYMiques et Cancer (RYTHMIC). The ESTS thymic working group was established in 2010 as a permanent working group of the Society. In the same year the group launched the thymic retrospective database calling for the participation of any interested ESTS Institution. The structure of the retrospective database was designed in conjunction with ITMIG in order to have as many common datafields as possible to facilitate future common studies. The response to the retrospective thymic database was enthusiastic and 35 centers joined the project. In few months the largest retrospective database of thymic tumors for that time was collected. At the same time, IASLC called for the participation of international thymic organizations for the second phase of the IASLC staging project for the 8th edition of the TNM classification of thymic tumors. As a consequence of the call, a total of more than 10,000 cases were collected, including 1814 from ESTS. The ESTS contribution to the 8th edition of the TNM

staging classification was recognized by IASLC. The ESTS thymic retrospective database provided material for several studies, both alone (**14, 15**) and in association with ITMIG (**10,11**). In 2013 times were mature for the creation of the prospective thymic database. The ESTS Council and the ESTS Database committees approved and funded the prospective thymic database project as a satellite database of the ESTS Registry, using the official ESTS platform (Dendrite, later KData Clinical). The great advantage of the prospective database is the more complete collection of data and an overall increased data quality. The ESTS prospective database is online, user-friendly (see ~~***Appendix***~~ ***Supplemental file 2*** for instructions to access), free to all ESTS members, it is periodically-maintained, it uses a standardized risk factors and outcomes, and it has the possibility to export data for internal use from individual institutions, acting as institutional database. It also represents a benchmark of performance and data quality for the individual surgeon and for the Institution. The ESTS prospective database also represents a unique opportunity for any ESTS contributor to propose studies using the data from the ESTS thymic registry. This is a great opportunity among the ESTS members to contribute to thymic research using one of the largest thymic databases in the world. A study draft illustrating the scope of the project and the expected results should be sent to the ESTS Database Committee. The draft will be discussed by the Committee and, if accepted, the contributor will receive the data for the analysis. Our co-authorship policy includes that one person from each center which substantially contributed to the ESTS thymic registry will be included in any manuscript submitted using the ESTS thymic database under a list which allows each contributor to be linked to PubMed.

The structure of the ESTS thymic prospective database was designed from the retrospective database while adding new datafields about imaging, pathology and the new TNM staging system. Also, a big effort was undertaken in conjunction with ITMIG to harmonize the two databases, similarly to what was done for the retrospective database, for common projects. The result was the creation of a set of variables considered essential for the use of the record which are identical in format and wording between the two databases.

A major issue in all databases, and particularly in multi-institutional databases, is the completeness rate of the datafields, which in most clinical databases ranges from 20% to 85% depending on the

variables. The inputing of the data in the online prospective databases is very often a stepwise process in different periods of time, usually done by trainees or junior doctors. This results in the presence of many missing values which decrease the quality of the database. The 2015 ESTS Database Annual report of the thymic prospective registry indicated a mean completeness rate of 40% (range 29%-90%) which was considered suboptimal. To address the issue we introduced the concept of the “minimum dataset” which includes a set of variables which are considered essential in order to use the record. The contributors are informed that their data cannot be used for studies in case of incomplete information of the minimum dataset. Another tool to increase the completeness rate was the institution of the Clinical Care Analysis (CCA) dashboard, which gives the contributor a visual representation (in a dashboard) of his/her own data and their completeness. Finally, periodical timely reminders to the contributors (twice a year) were also considered of help to keep the momentum among the contributors. These implementations (the minimum dataset, the CCA dashboard and the biannual reminders) were proposed to the contributors and were introduced in 2016; as a consequence, the thymic report presented in the 2017 ESTS Database Annual Report resulted in a significant increase of the median completeness rate (65%, range 42%-95%) as compared to the previous year (median 51%, range 27%-92%). This positive trend was also evident at the last evaluation for the present analysis as of November 2017 (**Figure 1**)

The ESTS prospective thymic database is presently one of the three prospective thymic databases in the world, along with ITMIG and RYTHMIC.

IASLC has recently launched the third phase of the IASLC staging Project for the 9th edition of the TNM classification of thoracic malignancies, including thymic tumors (**28**). Once again, ESTS was asked to provide the data from the prospective thymic database to be analysed, along with those from the largest thymic organizations worldwide (ITMIG, JART, KART, RHYTMIC). The results of this big collaborative global effort will provide a solid background for the next revision of the TNM staging system of thymic tumors, expected in 2024.

Finally it is worth mentioning that, similarly to what has been done for the Core ESTS Dataset for lung cancer, a possible further collaboration with Eepithor is under discussion and it is likely to be finalized in the near future.

Strenghts and limitations.

Some limitations are associated with the present report. First, although prospective, the data collection remains heterogeneous and reflects different individual expertises, including a lack of a centralized pathologic review, and a non-uniform attitude towards perioperative treatments. Also, the relatively few cases with a detailed TNM classification makes it difficult to provide sound evidence about the applicability and the effectiveness of the new staging classification. Finally, although a significant increase in the completeness rate was observed during the last years, some datafields still include a considerable numbers of missing information, which may limit the use of these records for analysis.

On the other hand, the present report presents the results of one of the currently largest prospective thymic databases in the world. The potential impact of the information and the continuous data upload provided by the use of the official ESTS platform guarantee a good data reliability.

In conclusion, the preliminary results of the ESTS thymic prospective database confirm the general changes in presentation, diagnosis and management of thymic tumors which have been reported in the current literature, including a trend towards a widespread use of minimally-invasive resection techniques, and an increase adoption of chemotherapy both in the induction and in the adjuvant setting. The information of the present database may represent a valuable source of data which can be used for collaborative studies with other major thymic organizations and for the 9th revision of the TNM classification of thymic tumors.

CONFLICT OF INTEREST: None

TABLES.

Table 1.

ESTS Thymic Minimum dataset – Minimum standard datafields to be completed for data analysis

- Gender (Male/Female)
- Date of Birth
- Date of surgery
- Paraneoplastic associated syndromes (MG*, etc)
- Final pathologic diagnosis (thymoma, thymic carcinoma, NETT**)
- WHO histology
- Thymic carcinoma histology
- Neuroendocrine Thymic Tumor (NETT) histology
- Pathologic Masaoka Stage
- Final pathologic resection status (R0, R1, R2§)
- Pathologic TNM stage (IASLC/ITMIG staging, 8th Ed. TNM)
- Outcome at discharge (Alive/dead)
- Chemotherapy (Intent, Date initiated)
- Radiotherapy (Intent, Date initiated)
- Date of death or last follow-up date
- Vital status

*Myasthenia Gravis
**Neuroendocrine Thymic Tumors
§ R0: Complete resection; R1: Incomplete resection (microscopic); R2: Incomplete resection (macroscopic)

Table 2.

Distribution of European contributors to the ESTS thymic prospective database by country.

Country	No. of centers
Italy	14
Spain	11
Hungary	9
Belgium	5
Portugal	4
Greece	3
Romania	3
Austria	2
Germany	2
The Netherlands	2
Croatia	1
Switzerland	1
United Kingdom	1

Table 3.

Patients characteristics of the ESTS thymic prospective database.

	Number	%*
Gender		
Male	563	50.2
Female	559	49.8
Age (Mean, range)	54 (5-91)	
Associated paraneoplastic syndromes		
None	431	63.8
Myasthenia Gravis	216	32.0
Hypogammaglobulinemia	6	0.9
Red cell aplasia	1	0.1
Other autoimmune	24	3.6
Previous malignancy		
None	475	86
Breast	13	2.4
Lung	6	1.1
Colon	10	1.8
Prostate	9	1.6
Skin	3	0.5
Lymphoma	3	0.5
Other	38	7
Preoperative diagnosis required		
No	434	79
Yes	116	21
Histology		
Thymoma	484	65
• *A*	58	13.3
• *AB*	116	26.6
• *B1*	79	18.1
• *B2*	112	25.7
• *B3*	71	16.3
Thymic carcinoma	207	28
Neuroendocrine thymic tumor (NETT)	49	6.6
Tumor size		
< 3cm	116	16.3
3-5 cm.	196	27.6
>5 cm.	399	56.1
Clinical Masaoka Stage		
I	328	60
IIa	51	9.3
IIb	42	7.7
III	77	14.1

IVa	37	6.8
IVb	13	2.4
Pathologic Masaoka Stage		
I	248	34.7
IIa	134	18.8
IIb	101	14.1
III	100	14.0
IVa	45	6.3
IVb	25	3.5
Clinical TNM		
T1	140	70.0
T2	31	15.5
T3	21	10.5
T4	8	4
N0	205	95.7
N1	8	3.7
N2	1	0.5
M0	193	92.7
M1	15	7.3
Pathological TNM		
T1	126	56.2
T2	51	22.7
T3	37	16.5
T4	10	4.4
N0	213	96.8
N1	3	1.3
N2	4	1.8
M0	205	92.3
M1	17	7.6
Completeness of resection		
Complete (R0)	710	89.0
Microscopic residual (R1)	61	7.6
Macroscopic residual (R2)	20	2.5
Chemotherapy		
No	309	69.1
Induction	61	13.6
Adjuvant	63	14.1
Palliative	6	1.3
Both pre/post	8	1.8
Radiotherapy		
No	472	72.6
Induction	11	1.7
Adjuvant	158	24.3
Palliative	3	0.5
Both pre/post	6	0.9
Surgical approach		
Sternotomy	389	47.7
Thoracotomy	93	11.4
Clamshell/Hemiclamshell	26	3.2
VATS	167	20.5
Robotic (RATS)	109	13.4

Transcervical	7	0.9
Transcervical + sternal split	10	1.2
Sterno-thoracotomy	15	1.8
Extent of thymectomy		
Thymomectomy only	682	92.4
Thymothymomectomy	56	7.5
Recurrence		
One episode	38	10.8
More than one episode	11	

*Net of missing

Table 4.

Comparison between the prospective vs. the retrospective ESTS thymic database.

	Retrospective database	Prospective database
Years of collection	1990-2010	2007-2017
No. of patients	2151	1122
No. of Institutions	35 (27 from Europe)	75 (62 from Europe)
Age (median)	56	54
Males/Females (No./%)	1042/1109 (51%/49%)	563/559 (50%/50%)
Myasthenia Gravis	629 (35%)	216 (32%)
T size (median)	6	5.5
Stage (Masaoka) I II III IV	 672 (34%) 699 (35%) 410 (20%) 215 (11%)	 248 (38%) 235 (36%) 100 (15%) 70 (11%)
WHO Histology Thymoma low-grade (A-AB-B1) Thymoma high-grade (B2-B3) Thymic carcinoma NETT	 1018 (50%) 780 (38%) 191 (9%) 41 (2%)	 253 (58%) 183 (42%) 207 (28%) 49 (7%)
Surgical approach Open Simple° Extended° VATS RATS	N=1956 1824 (93%) 1716 (88%) 96 (5%) 88 (4%) 44 (2%)	N=816 540 (66%) 499 (61%) 41 (5%) 167 (20%) 109 (13%)
Complete resection (R0)	1709 (88%)	710 (89%)
Mean No. of pts treated by center (Yearly) <4 (19 centers, 54%) 5-9 (11 centers, 31%) >10 (5 centers, 14%)	 532 (26%) 680 (33%) 818 (40%)	
Induction therapy CT alone RT alone CT + RT	239 (13%) 170 (9%) 12 (1%) 57 (3%)	86 (17%) 69 (15%) 17 (3%) NA
Adjuvant therapy CT alone RT alone CT + RT	853 (44%) 54 (2%) 566 (29%) 243 (12%)	235 (43%) 71 (16%) 164 (25%) NA

Figure legends.

Figure 1.

Completeness rate for the datafields of the minimum dataset. Comparison between 2016 and ~~November~~ 2017.

Appendix 1

Contributing Institutions to the ESTS prospective thymic database.

Central Chest Institute of Thailand, Thailand (A. Omchai)
Istanbul University Medical School, Istanbul, Turkey (A. Toker)
Istanbul University, Cerrahpasa Medical Faculty, Istanbul, Turkey (A.Turna)
Marmara University Hospital, Istanbul, Turkey (H. Batirel)
University Hospital of Lung Disease,"Shefqet Ndroqi" (F. Gradica)
Otto Wagner Hospital, Vienna, Austria (M. Muller)
Medical University of Vienna, Vienna, Austria (B. Moser)
University Hospital of Antwerp, Antwerp, Belgium (P. Van Schil)
Hopital Academique Erasme, Belgium (M. Cappello)
University Hospitals Leuven, Belgium (D. Van Raemdonck)
ZOL St. Jan Genk, Belgium (G. Lauwers)
St Augustinus, Antwerp, Belgium (Deloersnijder)
Hospital Júlia Kubitscheck (L. Rodrigues)
Sainte Marguerite University Hospital, Aix Marseille University, Marseille, France (P. Thomas)
AHEPA University Hospital, Thessaloniki, Greece (C. Foroulis)
Evangelismos Hospital, Athens, Greece (C. Zisis)
Theagenio Hospital, Greece (Barbetakis)
Klinik Thoraxchirurgie, Klinikum Delmenhorst gGmbH, Germany (Esch)
University Medicine Essen – Ruhrlandklinik , Essen, Germany (C. Aigner)
Department of Thoracic Surgery "Jordanovac" University Hospital Zagreb, Croatia (Rokotov)
Department of Thoracic Surgery, University of Pecs, Hungary (Z. Szanto)
University of Szeged, Department of Surgery , Hungary (J Furak)
National Institute of Oncology, Hungary (Kocsis)
Pamok GyÖr Hungars, Hungary (T. Molnar)
Bács-Kiskun County Teaching Hospital, Hungary (Kovacs)
Semmelweis Teaching Hospital - Miskolc Hungary (Toth)
Markusovszky University Hospital, Hungary (Laszlo)
Koranyi National Institute for Pulmonology and Semmelweis University, Hungary (Vagvolgyi)
Debreceni Egyetem Orvos- és Egészségtudományi Centrum, Hungary (Enyedi)
Umberto I Regional Hospital Ancona, Italy (A. Brunelli)
University of Milan. Ca' Granda Foundation Ospedale Maggiore Policlinico, Milan, Italy (M.Nosotti)
Città della salute e della Scienza, University of Torino, Italy (F. Guerrera)
Ospedali Riuniti, Università di Foggia, Italy (F. Sollitto)
University Hospital Parma, Italy (M. Rusca)
University of Rome "Sapienza", Policlinico Umberto I, Rome, Italy (C. Poggi)
ASST Santi Paolo e Carlo, Milan, Italy (F. Raveglia)
Catholic University of Rome, University Hospital "Agostino Gemelli" (S. Margaritora)
AOU Careggi, SOD Chirurgia Toracica, Firenze (L. Voltolini)
AOU S. Maria Della Misericordia, Italy (F. Londero)
National Cancer Institute, Pascale Foundation, Naples, Italy (G. Rocco)
European Institute of Oncology, Milan, Italy (L. Spaggiari)
VUMC Department of Surgery, The Nederlands (J. Oosterhuis)
Amphia Hospital, The Nederlands (E. Veen)
Santa Martha Hospital, Lisbon, Portugal (I. Gomes Bravio)
Centro Hospitalar de Vila Nova de Gaia Espinho – Portugal (J. Miranda)
Luz Hospital, Lisbon, Portugal (P. Martelo)
Marius Nasta Institute of Pneumonology, Romania (C. Bolca)
Clinical Muncipal Emergency Hospital, Romania (A. Nicodin)
Institute of Oncology Bucharerst , Romania (C. Motas)
University Hospital of Salamanca, Spain (N. Novoa)

ha formattato: Inglese (Stati Uniti)

ha formattato: Inglese (Stati Uniti)

ha formattato: Inglese (Stati Uniti)

~~Hospital general Universitario Gregorio Maranon, Spain (R. Penalver)~~
~~H. Clinico San Carlos, Spain (Hernando)~~
~~Sagrat Cor University Hospital, Barcelona, Spain (J. Fibla)~~
~~HHUU Virgen del Rocio, Madrid, Spain (P.Moreno)~~
~~General University Hospital, Valencia, Spain (Figueroa)~~
~~Hospital Clinic, Barcelona University, Spain (L. Molins)~~
~~University Virgen Macarena Hospital, Spain (M. Congregado)~~
~~H Universitari Son Espases, Palma, Spain (J. Torrecilla)~~
~~University Hospital Donostia, San Sebastian, Spain (J. Iker)~~
~~Ramon y Cajal University Hospital, Madrid, Spain (Nico)~~
~~Kantonspital St. Gallen, Sweden (Dutly)~~
~~University College London Hospital, UK (M. Scarci)~~
~~Hospital das Clinicas da Faculdade de Medicina da Universidade de Sao Paulo, Brazil (R. Terra)~~
~~Hospital São Lucas da PUCRS, Brazil (M. Tsukazan)~~
~~Pavilhão Pereira Filho - Santa Casa de Porto Alegre, Brazil (S. Camargo)~~
~~Hospital de Base do Distrito Federal - Asa Sul, Brasília, Brazil (Humberto)~~
~~Hospital Santa Isabel - Nazaré, Salvador, Brazil (G. Fortunato)~~
~~Hospital Brasília, Lago Sul, Brasília, Brazil (N. Ferreira de Lima)~~

ha formattato: Inglese (Stati Uniti)

ha formattato: Inglese (Stati Uniti)

ha formattato: Inglese (Stati Uniti)

Appendix 2.

Instructions for access to the online ESTS thymic prospective database.

Eligibility criteria: ESTS active member (ESTS membership status is checked before providing database credentials)

1. Log in at http://www.ests.org
2. Click on “Collaboration” -> European Database.
3. Click on “Database Registration Form” -> Registration Form.
4. Download the Registration form.
5. Complete the form with the required information and send it to the addresses provided (KData Clinical Administrators)
6. You will receive the credentials for your Institutions for logging into the Database.

7. Direct access to the ESTS Registry: log in at https://ests.kdataclinical.it

Once logged into the Database:

8. Click on “Search/Add” -> “Add new patient”
9. You need to complete the fields with the demographics data.
10. Then you will see a menu with the thymic sections (Preop Thymus, Op Thymus, Postop Thymus, F.up Thymus).
11. Start completing the fields.
12. The mandatory fields (i.e. the minimum dataset fields) are highlighted.

561
562
563

564

565

REFERENCES

1. Detterbeck F, Stratton K, Giroux D, Asamura H, Crowley J, Falkson C, et al. The ITMIG/IASLC thymic epithelial tumors staging project: proposal for an evidence-based stage classification system for the forthcoming (8th) edition of the TNM classification of malignant tumors. J Thor Oncol 2014; 9 (9 Suppl 2):S65–S72.

2. Salati M, Brunelli A, Dahan M, Rocco G, Van Raemdonck DEM, Varela G et al. Task-independent metrics to assess the data quality of medical registries using the European Society of Thoracic Surgeons (ESTS) Database. Eur J Cardiothorac Surg 2011;40:91–98.

3. Salati M, Falcoz PE, Decaluwe H, Rocco G, Van Raemdonck D, Varela G et al. The European thoracic data quality project: an aggregate data quality score to measure the quality of international multi-institutional databases. Eur J Cardiothorac Surg 2016;49:1470–1475.

4. Detterbeck F, Zeeshan A. Thymoma: current diagnosis and treatment. Chin Med J. 2013;126:2186-2191.

5. Detterbeck FC, Parsons AM. Thymic tumors. Ann Thorac Surg 2004; 77: 1860-9.

6. Ruffini E, Weder W, Filosso PL. Thymic Tumors. In : The IASLC multidisciplinary approach to thoracic oncology. Aurora, CO, USA. International Association for the Study of Lung Cancer, 2014 : 787-811.

7. Filosso PL, Galassi C, Ruffini E, Margaritora S, Bertolaccini L, Casadio C, et al. Thymoma and the increased risk of developing extrathymic malignancies: a multicenter study. Eur J Cardiothorac Surg. 2013;44:219-224

8. Ruffini E, Van Raemdonck D, Detterbeck F, Rocco G, Thomas P, Venuta F; European Society of Thoracic Surgeons Thymic Questionnaire Working Group. Management

ha formattato: Inglese (Stati Uniti)

of thymic tumors: a survey of current practice among members of the European Society of Thoracic Surgeons. J Thorac Oncol 2011; 6:614-23

9. Venuta F, Anile M, Diso D, Vitolo D, Rendina EA, De Giacomo T, et al. Thymoma and thymic carcinoma. Eur J Cardiothorac Surg 2010; 37:13–25.

10. Ahmad U, Yao X, Detterbeck F, Huang J, Antonicelli A, Filosso PL, et al. Thymic carcinoma outcomes and prognosis: results of an international analysis. J Thorac Cardiovasc Surg 2015; 149:95-100

11. Filosso PL, Yao X, Ruffini E, Ahmad U, Antonicelli A, Huang J, et al. Comparison of outcomes between neuroendocrine thymic tumours and other subtypes of thymic carcinomas: a joint analysis of the European Society of Thoracic Surgeons and the International Thymic Malignancy Interest Group. Eur J Cardiothorac Surg 2016; 50:766-771

12. Filosso PL, Yao X, Ahmad U, Zhan Y, Huang J, Ruffini E, et al. Outcome of primary neuroendocrine tumors of the thymus: a joint analysis of the International Thymic Malignancy Interest Group and the European Society of Thoracic Surgeons databases. J Thorac Cardiovasc Surg. 2015; 149:103-109

13. Cardillo G, Rea F, Lucchi M, Paul MA, Margaritora S, Carleo F, et al. Primary neuroendocrine tumors of the thymus: a multicenter experience of 35 patients. Ann Thorac Surg 2012; 94:241-245;

14. Ruffini E, Detterbeck F, Van Raemdonck D, Rocco G, Thomas P, Weder W, et al. Tumours of the thymus: a cohort study of prognostic factors from the European Society of Thoracic Surgeons database. Eur J Cardiothorac Surg 2014; 46:361-368

Codice campo modificato

Codice campo modificato

Codice campo modificato

15. Ruffini E, Detterbeck F, Van Raemdonck D, Rocco G, Thomas P, Weder W, et al. Thymic carcinoma: a cohort study of patients from the European Society of Thoracic Surgeons database. J Thorac Oncol 2014; 9:541-548

16. Gu Z, Fu J, Shen Y, Wei Y, Tan L, Zhang P, et al. Thymectomy versus tumor resection for early-stage thymic malignancies: a Chinese Alliance for Research in Thymomas retrospective database analysis. J Thorac Dis 2016; 8:680-686.

17. Nakagawa K, Yokoi K, Nakajima J, Tanaka F, Maniwa Y, Suzuki M, et al. Is Thymomectomy Alone Appropriate for Stage I (T1N0M0) Thymoma? Results of a Propensity-Score Analysis. Ann Thorac Surg 2016;101:520–526.

18. Narm KS, Lee CY, Do YW, Jung HS , Byun GE, Lee JG, et al. Limited thymectomy as a potential alternative treatment option for early-stage thymoma: A multi-institutional propensity-matched study. Lung Cancer 2016; 101: 22-27.

19. Hess NR, Sarkaria IS, Pennathur A, Levy RM, Christie NA, Luketich JD. Minimally invasive versus open thymectomy: a systematic review of surgical techniques, patient demographics, and perioperative outcomes. Ann Cardiothorac Surg 2016; 5:1-9.

20. Agatsuma H, Yoshida K, Yoshino I, Okumura M, Higashiyama M, Suzuki K, et al. Video-Assisted Thoracic Surgery Thymectomy Versus Sternotomy Thymectomy in Patients With Thymoma. Ann Thorac Surg. 2017; 104: 1047-1053.

21. Wang H, Gu Z, Ding J, Tan L, Fu J, Shen Y, et al. Perioperative outcomes and long-term survival in clinically early-stage thymic malignancies: video-assisted thoracoscopic thymectomy versus open approaches. J Thorac Dis. 2016; 4:673-679.

Codice campo modificato

Codice campo modificato

22. Burt BM, Yao X, Shrager J, Antonicelli A, Padda S, Reiss J, et al. Determinants of Complete Resection of Thymoma by Minimally Invasive and Open Thymectomy: Analysis of an International Registry. J Thorac Oncol 2017; 12: 129-136.

23. Cardillo G, Lucchi M, Marulli G, Infante M, Leuzzi G, Mussi A, et al. Induction therapy followed by surgical resection in Stage-III thymic epithelial tumors: Long-term results from a multicentre analysis of 108 cases. Lung Cancer 2016; 93:88-94.

24. Hamaji M, Ali SO, Burt BM. A meta-analysis of induction therapy for advanced thymic epithelial tumors. Ann Thorac Surg. 2015; 99:1848-1856.

25. Girard N, Ruffini E, Marx A, Faivre-Finn C, Peters S; ESMO Guidelines Committee.Thymic epithelial tumours: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. Ann Oncol 2015; 26(Suppl 5):v40-55.

26. Zhou D, Deng XF, Liu QX, Zheng H, Min JX, Dai JG. The Effectiveness of Postoperative Radiotherapy in Patients with Completely Resected Thymoma: A Meta-Analysis. Ann Thorac Surg. 2016; 101:305-310.

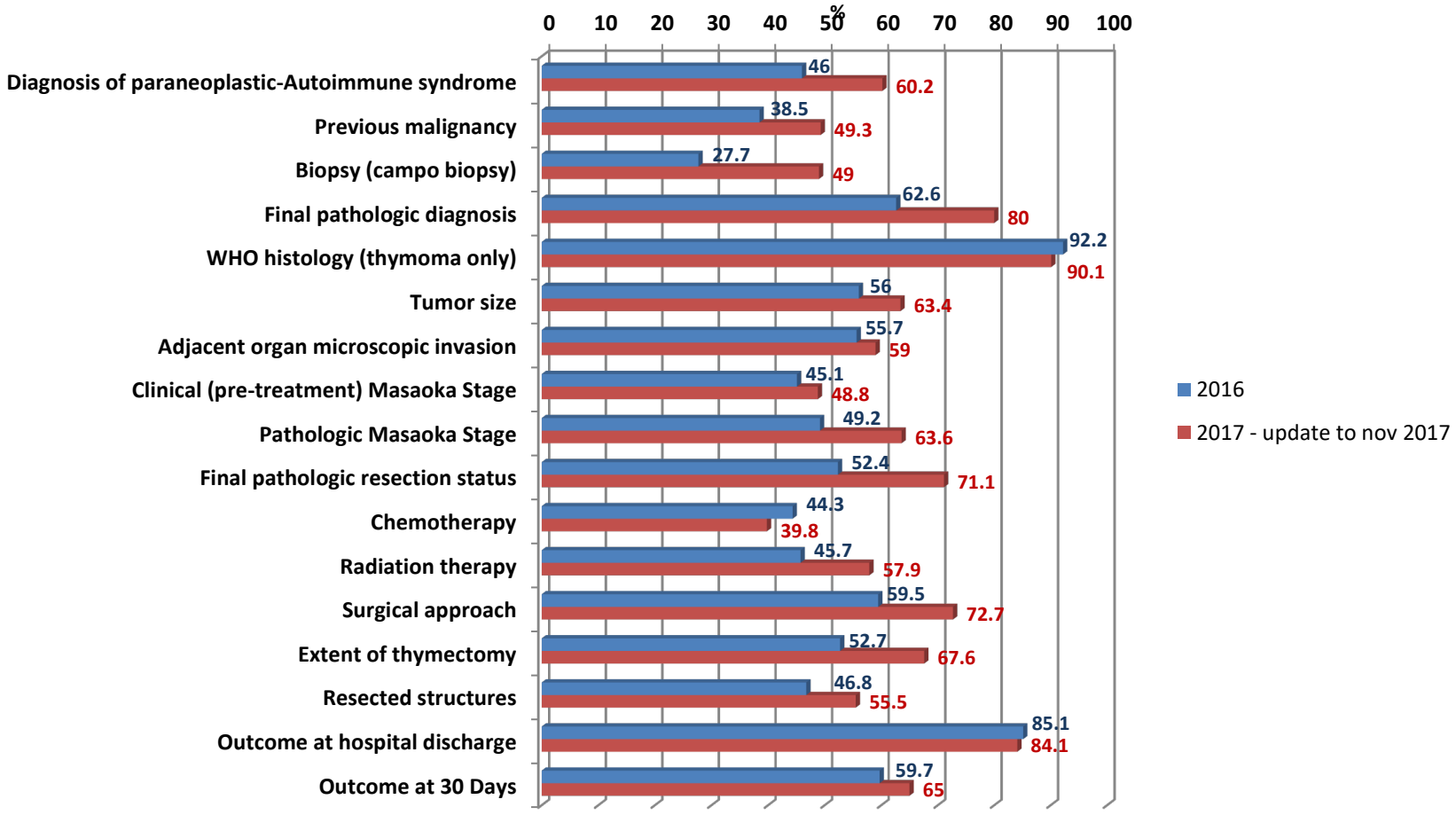
27. Hamaji M, Shah RM, Ali SO, Bettenhausen A, Lee HS, Burt BM. A Meta-Analysis of Postoperative Radiotherapy for Thymic Carcinoma. Ann Thorac Surg 2017; 103:1668-1675.

28. Giroux DJ, Van Schil P, Asamura H, Rami-Porta R, Chansky K, Crowley JJ, et al. The IASLC Lung Cancer Staging Project: A Renewed Call to Participation. J Thorac Oncol 2018; ~~Feb 21. pii: S1556-0864(18)30131-X (Epub ahead of print)~~13(6): 801-809.

Codice campo modificato

Codice campo modificato

675
676
677
678
679
680
681
682
683


%
0
10
20
30
40
50
60
70
80
90
100
Diagnosis of paraneoplastic-Autoimmune syndrome
46
60.2
Previous malignancy
38.5
49.3
Biopsy (campo biopsy)
27.7
49
Final pathologic diagnosis
62.6
80
WHO histology (thymoma only)
92.2
90.1
Tumor size
56
63.4
Adjacent organ microscopic invasion
55.7
59
Clinical (pre-treatment) Masaoka Stage
45.1
48.8
Pathologic Masaoka Stage
49.2
63.6
Final pathologic resection status
52.4
71.1
Chemotherapy
44.3
39.8
Radiation therapy
45.7
57.9
Surgical approach
59.5
72.7
Extent of thymectomy
52.7
67.6
Resected structures
46.8
55.5
Outcome at hospital discharge
85.1
84.1
Outcome at 30 Days
59.7
65
2016
2017 - update to nov 2017

Appendix 1

Contributing Institutions to the ESTS prospective thymic database.

Central Chest Institute of Thailand, Thailand (A. Omchai)
Istanbul University Medical School, Istanbul, Turkey (A. Toker)
Istanbul University, Cerrahpasa Medical Faculty, Istanbul, Turkey (A.Turna)
Marmara University Hospital, Istanbul, Turkey (H. Batirel)
University Hospital of Lung Disease,"Shefqet Ndroqi" (F. Gradica)
Otto Wagner Hospital, Vienna, Austria (M. Muller)
Medical University of Vienna, Vienna, Austria (B. Moser)
University Hospital of Antwerp, Antwerp, Belgium (P. Van Schil)
Hopital Academique Erasme, Belgium (M. Cappello)
University Hospitals Leuven, Belgium (D. Van Raemdonck)
ZOL St.-Jan Genk, Belgium (G. Lauwers)
St Augustinus, Antwerp, Belgium (Deleersnijder)
Hospital Júlia Kubitscheck (L. Rodrigues)
Sainte Marguerite University Hospital, Aix-Marseille University, Marseille, France (P. Thomas)
AHEPA University Hospital, Thessaloniki, Greece (C. Foroulis)
Evangelismos Hospital, Athens, Greece (C. Zisis)
Theagenio Hospital, Greece (Barbetakis)
Klinik Thoraxchirurgie, Klinikum Delmenhorst gGmbH, Germany (Esch)
University Medicine Essen - Ruhrlandklinik , Essen, Germany (C. Aigner)
Department of Thoracic Surgery “Jordanovac” University Hospital Zagreb, Croatia (Rokotov)
Department of Thoracic Surgery, University of Pecs, Hungary (Z. Szanto)
University of Szeged, Department of Surgery , Hungary (J Furak)
National Institute of Oncology, Hungary (Kocsis)
Pamok GyÖr Hungars, Hungary (T. Molnar)
Bács-Kiskun County Teaching Hospital, Hungary (Kovacs)
Semmelweis Teaching Hospital - Miskolc Hungary (Toth)
Markusovszky University Hospital, Hungary (Laszlo)
Koranyi National Institute for Pulmonology and Semmelweis University, Hungary (Vagvolgyi)
Debreceni Egyetem Orvos- és Egészségtudományi Centrum, Hungary (Enyedi)
Umberto I Regional Hospital Ancona, Italy (A. Brunelli)
University of Milan. Ca' Granda Foundation Ospedale Maggiore Policlinico, Milan, Italy (M.Nosotti)
Città della salute e della Scienza, University of Torino, Italy (F. Guerrera)
Ospedali Riuniti, Università di Foggia, Italy (F. Sollitto)
University Hospital Parma, Italy (M. Rusca)
University of Rome “Sapienza”, Policlinico Umberto I, Rome, Italy (C. Poggi)
ASST Santi Paolo e Carlo, Milan, Italy (F. Raveglia)
Catholic University of Rome, University Hospital "Agostino Gemelli" (S. Margaritora)
AOU Careggi, SOD Chirurgia Toracica, Firenze (L. Voltolini)
AOU S. Maria Della Misericordia, Italy (F. Londero)
National Cancer Institute, Pascale Foundation, Naples, Italy (G. Rocco)
European Institute of Oncology, Milan, Italy (L. Spaggiari)
VUMC Department of Surgery, The Nederlands (J. Oosterhuis)
Amphia Hospital, The Nederlands (E. Veen)
Santa Martha Hospital, Lisbon, Portugal (I. Gomes Bravio)
Centro Hospitalar de Vila Nova de Gaia Espinho – Portugal (J. Miranda)
Luz Hospital, Lisbon, Portugal (P. Martelo)
Marius Nasta Institute of Pneumonology, Romania (C. Bolca)

Clinical Muncipal Emergency Hospital, Romania (A. Nicodin)
Institute of Oncology Bucharerst , Romania (C. Motas)
University Hospital of Salamanca, Spain (N. Novoa)
Hospital general Universitario Gregorio Maranon, Spain (R. Penalver)
H. Clinico San Carlos, Spain (Hernando)
Sagrat Cor University Hospital, Barcelona, Spain (J. Fibla)
HHUU Virgen del Rocio, Madrid, Spain (P.Moreno)
General University Hospital, Valencia, Spain (Figueroa)
Hospital Clinic, Barcelona University, Spain (L. Molins)
University Virgen Macarena Hospital, Spain (M. Congregado)
H Universitari Son Espases, Palma, Spain (J. Torrecilla)
University Hospital Donostia, San Sebastian, Spain (J. Iker)
Ramon y Cajal University Hospital, Madrid, Spain (Nico)
Kantonspital St. Gallen, Sweden (Dutly)
University College London Hospital, UK (M. Scarci)
Hospital das Clinicas da Faculdade de Medicina da Universidade de Sao Paulo, Brazil (R. Terra)
Hospital São Lucas da PUCRS, Brazil (M. Tsukazan)
Pavilhão Pereira Filho - Santa Casa de Porto Alegre, Brazil (S. Camargo)
Hospital de Base do Distrito Federal - Asa Sul, Brasília, Brazil (Humberto)
Hospital Santa Isabel - Nazaré, Salvador, Brazil (G. Fortunato)
Hospital Brasília, Lago Sul, Brasília, Brazil (N. Ferreira de Lima)

Appendix 2.

Instructions for access to the online ESTS thymic prospective database.

Eligibility criteria: ESTS active member (ESTS membership status is checked before providing database credentials)

1. Log in at http://www.ests.org
2. Click on “Collaboration” - > European Database.
3. Click on “Database Registration Form” -> Registration Form.
4. Download the Registration form.
5. Complete the form with the required information and send it to the addresses provided (KData Clinical Administrators)
6. You will receive the credentials for your Institutions for logging into the Database.

7. Direct access to the ESTS Registry: log in at https://ests.kdataclinical.it

Once logged into the Database:

8. Click on “Search/Add” -> “Add new patient”
9. You need to complete the fields with the demographics data.
10. Then you will see a menu with the thymic sections (Preop Thymus, Op Thymus, Postop Thymus, F.up Thymus).
11. Start completing the fields.
12. The mandatory fields (i.e. the minimum dataset fields) are highlighted.