Management of Thymic Tumors

A Survey of Current Practice among Members of the European Society of Thoracic Surgeons

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Introduction: Management of thymoma has largely been based on single-institution retrospective, observational studies. The European Society of Thoracic Surgeons (ESTS) Thymic Working Group has investigated the current practice among ESTS members.

Methods: A questionnaire divided into seven sections with 24 questions was designed, and it was delivered to ESTS members.

Results: Forty-four centers replied to the questionnaire. The results indicate that there is a general agreement concerning (1) the value of computed tomography scan for preoperative assessment; (2) the uselessness of a routine histologic confirmation before surgery; (3) the role of the World Health Organization classification; (4) the importance of complete and extended resection; (5) the role of surgery for recurrent disease; and (6) the need of a multidisciplinary team, including thoracic surgeons, pathologists, medical, and radiation oncologists. On the other hand, there is still a considerable debate about (1) the role of positron emission tomography scan for preoperative assessment; (2) a consistent and reliable staging system; (3) the usefulness of postoperative treatments for stages II and III diseases; (4) the management of type C thymoma; and (5) the role of extrapleural pneumonectomy for stage IVA thymoma.

Conclusions: The survey provides a large, multiinstitutional overview of the clinical practice in the management of thymic tumors by ESTS members. Responses show some areas of agreement along with several areas of controversy. It is conceivable that a consequent step forward will be the creation of a collaborative effort within the ESTS and with other organizations for the creation of standard recommendations and guidelines for the management of thymic malignancies.

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Disclosure: The authors declare no conflicts of interest.

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ISSN: 1556-0864/11/0603-0614

Key Words: Thymoma, Thymic carcinoma, Surgery, Survey.

(*J Thorac Oncol.* 2011;6: 614–623)

Thymoma is the most frequent epithelial tumor in the anterior mediastinal compartment in adults, with an overall incidence of 0.15 cases per 100,000 (National Cancer Institute Surveillance, Epidemiology and End Results program).[1] Because of the indolent course and sporadic occurrence of these lesions, management has largely been based on single-institution retrospective, observational studies. Despite the large body of literature, no uniformly accepted guidelines are available so far. Complete surgical resection, when feasible, is currently considered the gold standard; however, the role of chemo-radiotherapy (RT), histology, and staging is still to be clearly defined. The European Society of Thoracic Surgeons Thymic Working Group (ESTS-TWG) distributed an electronic survey among the members of the Society to collect an overview of current thymoma management.

MATERIALS AND METHODS

An e-mail was sent to all ESTS members encouraging the ESTS community to join the ESTS thymic group and its activities indicating the intention to launch the questionnaire.

Questionnaire Design

The questionnaire was designed by the ESTS-TWG steering committee and was delivered by e-mail to ESTS members who were interested to participate to retrospective and prospective studies. The questionnaire included 25 points organized in seven sections:

- Volume of activity
- Preoperative assessment
- Histology and staging system
- Extent of surgical resection
- Pre- and postoperative treatment of stages II and III diseases according to the Masaoka classification
- Treatment of stage IV tumors, recurrence, and type C thymoma
- Local multidisciplinary organization and logistics

The centers were also allowed to add personal comments after each question to clarify their answer and implement understanding.

After 2 months, 52 centers showed interest, and 44 answered the survey. The contributors were primarily from not only academic hospitals ($N = 29$, 66%) but also community hospitals, and private institutions were well represented. The geographical distribution is presented in Table 1: 33 were from Europe, four from Asia (Israel, one; Japan, one; Saudi Arabia, one; and Turkey, one), five from the United States, one from Canada, and one from South America (Brazil). Most of the European countries were represented: Italy (14), Austria (two), France (two), Germany (two), Poland (four), Spain (two), Belgium (one), Czech Republic (one), Greece (one), Portugal (one), Netherland (one), the United Kingdom (one), and Switzerland (one). The analysis was performed using basic statistics. Proportion differences were tested using the χ^2 method (Fisher's exact test when appropriate). Statistical analysis was performed using STATISTICA (Statsoft, Italy, release 7.1) software.

RESULTS

The results are reported for each section separately, referring to each of the 25 questions.

Section 1: Volume of Activity and Time Period (Table 2)

1. **How many thymoma resections are performed at your center yearly?** 1 to 5; 6 to 10; 11 to 20; and more than 20.
2. **What is the overall number of patients operated at your center?** less than 20; 21 to 50; 51 to 100; 101 to 300; and more than 300.
3. **In how many years?** less than 10; 11 to 20; and more than 20.

TABLE 1. Geographic Distribution of the Respondents

Country	Respondents (No.)
Europe	33
Italy	14
Poland	4
Austria	2
France	2
Germany	2
Spain	2
Belgium	1
Czech Republic	1
Greece	1
Portugal	1
Switzerland	1
The Netherlands	1
United Kingdom	1
The United States and Canada	6
The United States	5
Canada	1
Asia	4
Israel	1
Japan	1
Saudi Arabia	1
Turkey	1
South America	1
Brazil	1

TABLE 2. Volume of Activity among the Different Centers

Question	Response Count	Response %
1. How many thymoma resections are performed at your center yearly?		
1–5	3	7
5–10	23	52
10–20	14	32
>20	4	9
2. What is the total number of patients with thymoma operated at your center?		
<20	1	2
20–50	13	30
50–100	16	36
100–300	11	25
>300	3	7
3. In which time period?		
<10 yr	21	48
10–20 yr	16	36
>20 yr	7	16

Half of the centers ($N = 23.52\%$) perform from 5 to 10 thymoma resections per year; one third ($N = 14$, 32%) from 10 to 20, four centers (9%) more than 20, and three (7%) perform less than five resections per year. Most of the centers (16/18.89%) performing more than 10 resections per year are academic institutions. Sixteen centers (36%) have performed between 50 and 100 thymoma resections. Thirty percent ($N = 13$) have performed between 20 and 50 resections; 25% ($N = 11$) between 100 and 300; and three centers (7%) have performed more than 300 operations. Seven centers (16%) had a long tradition of thymoma surgery (more than 20 years), 16 (36%) have been practicing thymoma surgery for 10 to 20 years, and 21 centers (48%) have started in the last decade. Therefore, this survey covers a wide range of experiences from different centers in different countries from all over the world, in terms of the number of procedures per year, the overall number of operations, and length of activity.

Section 2: Preoperative Assessment (Table 3)

1. **Do you perform total body computed tomography (CT) scan before surgery?** All centers rely on CT for preoperative evaluation, but only 19 (43%) use total body CT scan. The remaining 25 centers consider either chest or chest + upper abdomen CT scan sufficient. This confirms what reported in the international literature[2–4]: chest CT scan with intravenous contrast administration is the radiographic examination of choice for the evaluation of all anterior mediastinal masses. The radiological features are diagnostic, especially for early-stage lesions and when calcifications are associated;

TABLE 3. Preoperative Assessment

Question	Response Count	Response %
1. Do you perform total body CT scan before resection?		
Yes	19	43
No	25	57
2. Do you use PET (or integrated PET/CT) scan in patients with thymoma?		
Yes	22	50
No	22	50
3. Do you always try to obtain histologic confirmation before surgical resection?		
Yes	4	9
No	40	91

PET, positron emission tomography; CT, computed tomography.

problems of differential diagnosis may occur at more advanced stages, when local aggressiveness may mimic lymphoma or germ cell tumors. The use of abdominal CT scan may be indicated in the latter situation or for accurate staging before induction treatment.

2. **Do you use positron emission tomography (PET) (or PET/CT) scan for preoperative assessment?** The experience of the different centers about the use of PET or integrated PET/CT scan in patients with thymoma was evenly distributed: 22 (50%) centers reported to use PET, and 22 (50%) do not use it. This probably reflects the slowly increasing availability of PET and its role in the diagnosis of thoracic malignancies. Only one center indicates that the reason why they do not use PET is related to the unavailability of the equipment at their institution. Many centers indicate that they routinely use PET to assess response to induction therapy before planning surgical resection. Others comment that they use PET only on a selective basis, depending on stage. One center indicates that they use PET only when pleural dissemination is suspected. No center mentioned the potential role of standard uptake value in their comments.
3. **Do you always try to obtain histological confirmation before surgical resection?** The answers to this question are quite interesting. Forty centers (91%) do not routinely look for histological confirmation when thymoma is suspected. This apparently does not match with the current general opinion about always attempting to obtain diagnosis before surgical resection. As mentioned before, there was a possibility to add comments; the most frequent addendum was that in case CT scan strongly suggests thymoma (small, resectable, capsulated lesions with no radiological sign of invasion) or when myasthenia gravis is associated, no preoperative histological diagnosis should be required. One center stated that they always require intraoperative frozen sections before proceeding to resection. In few cases, it has been also stated that complete resection of a small mediastinal mass through a minimally invasive approach is appropriate even in case of lymphoma, as it provides adequate material for the pathologist. Other comments reported the potential increased risk of tumor spread through the needle biopsy site or in the pleura during video-assisted thoracic surgery. Most of the comments stated that surgical biopsy should be preferred (anterior mediastinotomy or video-assisted thoracic surgery) and should be performed only if lymphoma is suspected at CT, when neoadjuvant treatment is to be planned, or the lesion looks unresectable.

Section 3: Histologic Classification and Staging (Table 4)

1. **Do you use the World Health Organization (WHO) pathologic classification? If not which classification do you use?** All centers except one (98%) use the WHO histologic classification proposed in 1999[5] and updated in 2004[6]; this system classifies thymoma on the base of morphology and lymphocyte to epithelial cells ratio using letters and numbers (A, AB, B1, B2, B3, and C). C tumors have been recently completely separated and are currently considered as a different entity.[7] It is, therefore, clear that the WHO classification has gained wide acceptance as the standard histologic classification for thymic malignancies. The single center reporting not to use the WHO system did not provide any information about what classification they currently use.
2. **Do you use the Masaoka staging system? If not, what system are you currently using?** The centers were asked to choose among four proposed staging systems including the standard Masaoka system,[8] the modified Masaoka-Koga,[9] the tumor, nodes, and metastasis (TNM) system,[10] and the Groupe d'Etude des Tumeurs Thymique (GETT) system.[11] Most (33 centers, 75%) stated to favor the standard Masaoka staging system, which divides thymoma into four stages based on clinicosurgical criteria of invasion (stages I–IV). Of the remaining 11 centers, eight reported to use the modified Masaoka-Koga system (stage II and stage III are divided into A and B subgroups) (one in Germany, France, Austria, and Portugal each and two in Italy and

TABLE 4. Histologic Classification and Staging

Question	Response Count	Response %
Do you use the WHO pathologic classification?		
Yes	43	98
No	1	2
Do you use the Masaoka staging system?		
Yes	33	75
No	11	25
If not, which staging system do you use?		
Masaoka-Koga	8	
TNM	2	
GETT	1	

WHO, World Health Organization; TNM, tumor, node, and metastasis; GETT, Groupe d'Etude des Tumeurs Thymique.

the United States each). Two centers indicated that they still use the TNM staging system either routinely or on some occasion (one in Italy and one in Switzerland), and one (France) reported that they use the GETT system that takes into consideration also the extent and completeness of resection. It may, therefore, be concluded that there is still no uniform consensus about the optimal staging system in patients with thymoma.

Section 4: Extent of Surgical Resection (Table 5)

1. **Do you strive to obtain complete resection even if it requires extension to neighboring organs?**
2. **Do you extend the resection to the pericardium, lung, and great vessels for stage III thymoma?**

All centers but two (95%) agree that complete resection is crucial and should include all the adjacent structures, if they are involved and if they are technically resectable (and reconstructable, when required). Extended resections, including pericardium, lung, diaphragm, and great vessels are often feasible; however, only 42 (95%) centers reported to perform them. When asked to make comments, many of them appropriately indicate notable exceptions to extended resections: three centers indicate that they do not perform resection of the great vessels (without stating what great vessels), and they prefer to leave residual disease to be treated with postoperative RT. Also, some others stated that they do not resect both phrenic nerves in case of bilateral involvement. From the present survey, it appears a general agreement on the need to achieve complete resection when technically feasible; concern exists about invasion of the great vessels and bilateral phrenic nerve involvement.

Section 5: Pre- and Postoperative Treatment in Stage II Thymic Tumors (Table 6)

1. **Do you administer adjuvant treatment in Masaoka stage II thymoma? If yes, what type of treatment?** Twenty-seven centers (61%) report that they tend to administer postoperative treatment at this stage. They use postoperative RT in most of the cases; only three centers use combined radio and chemotherapy. Twenty of them routinely administer postoperative treatment; the others consider it on a case-by-case basis related to histology (only in B2–B3 and C types), staging (only in case of stage IIB according to the modified Masaoka-Koga staging system), or completeness of resection (incomplete resections are treated). Seventeen centers (39%) clearly stated not to use any postoperative treatment after resection of stage II thymoma in any case, independently from the pathological report, invasion of the capsule, or potential incomplete resection. Thus, it seems that this issue still poses many important questions to be addressed.
2. **Do you administer induction chemotherapy for stage III thymoma?** Induction chemotherapy is used by the majority of the centers (33 centers, 75%), whereas 11 do not. It is not clear from the survey whether at these centers they proceed with surgery upfront or whether they use RT to downstage the tumor. The centers with more experience tend to use induction.
3. **Do you administer postoperative chemotherapy, RT, or a combination of both after resection of stage III thymoma?** All centers but three use postoperative treatments after resection of stage III thymoma. Three centers do not use any kind of postoperative treatment in case of macro- and microscopic complete resection or indicate postoperative therapy only in case of incomplete resection. Twenty-nine centers use either chemotherapy or RT without stating in their comments how do they select them. Chemotherapy alone was administered only at three centers, whereas postoperative RT alone was used in 26. Finally, 25 centers use an association of radio- and chemotherapy; some centers reported that they use it based on WHO histology (B2–B3 and C types). There is clearly a heterogeneous approach to postoperative treatment after resection of invasive

TABLE 5. Extent of Surgical Resection

Question	Response Count	Response %
Do you strive to obtain a total resection even in case of anticipated extended resection to neighboring structures?		
Yes	42	95
No	2	5
Do you perform extended resection of the pericardium, lung, diaphragm, and great vessels in case of stage III thymoma?		
Yes	42	95
No	2	5

TABLE 6. Induction and Adjuvant Treatments in Stages II to III Thymomas

Question	Response Count	Response %
Do you use induction treatment for stage III thymoma?		
Yes	33	75
No	11	25
Do you administer adjuvant treatment for stage II thymoma?		
Yes	27	61
No	17	39
Do you administer adjuvant chemotherapy only for stage III thymoma?		
Yes	3	7
No	41	93
Do you administer adjuvant radiotherapy only for stage III thymoma?		
Yes	26	59
No	18	41
Do you administer adjuvant chemo-radiotherapy (together) for stage III thymoma?		
Yes	25	57
No	19	43

TABLE 7. Treatment of Stage IV, Recurrence, and Type C Tumors

Question	Response Count	Response %
1. Do you administer induction chemotherapy for stage IV thymoma?		
Yes	38	86
No	6	14
2. Do you consider extrapleural pneumonectomy for stage IV thymoma?		
Yes	18	41
No	26	59
3. In case of locoregional recurrence, do you think surgery may be indicated?		
Yes	40	91
No	4	9
4. Do you treat type C thymoma differently?		
Yes	23	52
No	21	48

(stage III) thymoma; most centers administer RT or radio-chemotherapy, whereas chemotherapy alone is rarely used.

Section 6: Treatment of Stage IV Thymoma, Recurrences, and Type C Tumors (Table 7)

1. **Do you administer induction chemotherapy for stage IVA thymoma?**
2. **Do you perform extrapleural pneumonectomy (EPP) for stage IVA thymoma?** Treatment of advanced thymoma (stage IVA) with pleural dissemination is still controversial. Most of the centers (38.86%) administer induction chemotherapy at this stage with subsequent surgical resection of the pleural implants. In case of extended pleural and lung involvement, EPP or pleurectomy/decortication (P/D) has been advocated by some authors. From our survey, 18 centers (41%) agree to perform EPP or P/D in case of major pleural involvement to achieve complete resection. Only one group performed intrapleural hyperthermic chemotherapy after surgical resection. The remaining 26 centers (59%) do not consider EPP indicated in this setting.
3. **In case of locoregional recurrence, do you think surgery should be indicated?** The questionnaire included one question about thymoma recurrence and the potential surgical treatment. Forty centers (91%) agree that recurrence should be removed when complete resection is feasible; some of them reported to have already performed multiple subsequent resections in case of repeated recurrence. Many centers added in their comments that a correct patient selection is crucial and that they proceed to resection only when complete resection may be anticipated.
4. **Do you treat type C thymoma (thymic carcinoma) differently from other histologic subtypes?** The results of the survey indicate that the majority of the centers ($N = 23.52\%$) use a different treatment policy in case of type C thymoma. In particular, some of them added in their comments that, with this histology, they always administer induction chemotherapy before surgery, even in case of stage I disease; others simply stated to use a different chemotherapeutic regimen.

TABLE 8. Multidisciplinary Organization

Question	Response Count	Response %
Do you have a dedicated pathologist?		
Yes	36	82
No	8	18
Do you have a dedicated medical oncologist?		
Yes	37	84
No	7	16
Do you have a dedicated radiation oncologist?		
Yes	29	66
No	15	34

Section 7: Multidisciplinary Organization and Logistics (Table 8)

1. **Do you have a dedicated pathologist for thymic malignancies?**
2. **Do you have a dedicated medical oncologist for thymic malignancies?**
3. **Do you have a dedicated radiation oncologist for thymic malignancies?**

Thirty-six centers (82%) indicated that they have a dedicated pathologist, 37 (84%) a dedicated medical oncologist, and 29 (66%) a dedicated radiation oncologist for thymic tumors. Some centers added that they have a dedicated tumor board to discuss management of thymic neoplasms.

High-Volume versus Low-Volume Centers

Further analysis was undertaken stratifying the surveyed centers by the volume of activity. Two groups were identified: those performing more than 10 thymoma resections per year (high-volume group, $N = 18$) and those performing less than 10 thymoma resections per year (low-volume group, $N = 26$); the answers in the two groups were compared (Table 9), including the following variables: the use of standard Masaoka staging, the use of PET scan, postoperative treatment at stage II, the administration of induction treatment at stage III, postoperative treatments at stage III (further divided into chemotherapy, RT, and combined radio-chemotherapy), the need to pursue complete resection and extended resections to neighboring structures, the use of induction therapy and EPP at stage IV, a different policy to treat type C thymoma, and the presence of a dedicated team. The results of our analysis indicate that high-volume centers less frequently use combined radio-chemotherapy after resection of stage III thymoma ($p = 0.01$) and less frequently use postoperative treatment after resection

TABLE 9. Comparison of Different Responses in High-Volume ($N = 18$) vs. Low-Volume ($N = 26$) Groups

	High-Volume Group		Low-Volume Group	
Variables	**Yes**	**No**	**Yes**	**No**
Masaoka staging	14	4	19	7
Use of PET scan	10	8	16	10
Total resection	18	0	24	2
Extended resection	17	1	25	1
Postoperative treatment in stage II	7	11	20	6
Preoperative treatment in stage III	15	3	18	8
Postoperative treatment in stage III				
Chemotherapy	0	18	3	23
Radiotherapy	11	7	10	16
Chemo-radiotherapy	4	14	14	12
Preoperative chemotherapy in stage IV	16	2	22	4
EPP in stage IV	8	10	10	16
Different policy in type C thymoma	12	6	11	15
Dedicated pathologist	16	2	19	7
Dedicated medical oncologist	15	3	21	5
Dedicated radiation oncologist	13	5	16	10

PET, positron emission tomography; EPP, extrapleural pneumonectomy.

of stage II thymoma ($p = 0.03$), when compared with low-volume centers.

DISCUSSION

The present survey provides insights on the management of thymic malignancies coming from 43 centers belonging to the ESTS community. The analysis supports the need of an extended discussion and clarification on several points to achieve a uniform approach.

The results of the questionnaire indicate that there is a general agreement concerning the following issues: (1) the role of CT scan; (2) the uselessness of a routine histologic confirmation before surgery; (3) the role of the WHO classification; (4) the need to achieve complete resection extending surgery to the neighboring organs, if required; (5) the role of surgery for recurrent disease; and (6) the positive role of a multidisciplinary team including thoracic surgeons, pathologists, medical, and radiation oncologists to approach thymic tumors in a dedicated tumor board. On the other hand, there is still a considerable debate about (1) the role of PET scan for preoperative assessment; (2) the staging system; (3) the administration of postoperative treatments at stages II and III; (4) the management of type C thymoma; and (5) the role of EPP at stage IVA.

Thymic neoplasms are rare; the large body of literature available on this topic is based on retrospective, mostly single-institutional, observational studies. Several strategic decisions are still controversial and are often based on personal experience and individual practice. There are no guidelines concerning optimal management. For this reason, our survey may represent a good platform to start a collaborative effort and provide insights into those problems still awaiting a definitive answer.

The questionnaire was grouped into seven sections, each of which covers a particular aspect in thymoma management; each section deserves discussion.

1. Volume of activity and time period: This section was designed to obtain a snapshot about the type of institutions involved in the survey and to improve interpretation of the results. Interestingly, all types of institutions were present including well-known word-recognized centers of excellence, academic Institutions, and smaller hospitals. This surely adds strength to our study and provides support to extend the results to the scientific community.
2. Preoperative assessment: There is a general agreement that the new generation CT scans offers a reliable and appropriate diagnostic tool. The potential extension of the examination beyond the chest is still debated; more than half of the centers perform total body CT scan, which may be of help to differentiate thymoma from other mediastinal disorders, in particular lymphoma. Despite the little evidence in the literature about the value of PET or integrated PET-CT scan,[12,13] half of the centers does use PET scan, although mostly on a selective basis, with three major indications: (a) potentially invasive thymoma, (b) pleural dissemination, and (c) assessment of response after induction therapy. It sounds clear that the role of PET scan in the management of patients with thymoma needs to be discussed, but this will certainly require prospective studies.
   Histologic confirmation before resection was not considered crucial at almost all centers. When the lesion is small, capsulated, calcified, or cystic, with radiological characteristics clearly excluding lymphoma, and if the clinical presentation is not suggestive of lymphoma, all centers agree to proceed directly to surgery; the presence of myasthenia gravis also helps in this direction. Histology is required for invasive lesions, before induction therapy, if the tumor is clearly unresectable or when the radiological features do not allow to exclude other mediastinal disorders requiring a different approach. The potential pleural or transthoracic seeding during biopsy is also a major concern, although this fear is not substantiated in the literature.[14]
3. Histologic classification and staging: There is a general agreement that the WHO classification proposed should be worldwide accepted. This assumption is clearly supported by the international literature, reporting it as an independent prognostic factor.[15–17] Only one center stated that they do not use it without reporting their system. Concerning the staging system, the questionnaire proposed four options: the standard Masaoka system, the modified Masaoka-Koga, the TNM, and the GETT classification. The standard Masaoka is still used in most of the cases, followed by the modified Masaoka-Koga. The TNM and GETT classifications are used only by three centers. Also, this point is consistent with the international literature.[18–22] Nevertheless, as

we will see in the analysis of the following section, both histology and staging, although uniformly accepted, do not uniformly impact treatment modalities, and potentially also on long-term results. Thus, the WHO and Masaoka classifications should be the object of prospective studies to improve their role in patient and treatment modality selection.

4. Extent of surgical resection: Complete resection is clearly the most important prognostic factor and should be aimed even if the neighboring organs are involved. This also appear from the international literature,[18,19,23–25] and it is so important that the GETT staging system has included this variable. Extended resections are often feasible and associated with satisfactory survival rates[26–28]; the lung, great vessels, and, in particular, the superior vena cava, the pericardium, and the diaphragm are to be removed along with the tumor when they are involved and if the required reconstruction is feasible. Nevertheless, some concern still exists about resection and reconstruction of the great vessels. Some centers reported that they prefer leaving residual tumor and refer the patient for adjuvant treatment. It is not clear from the answers and comments whether this concern is restricted only to the ascending aorta and main pulmonary artery or whether it is also referred to the superior vena cava. The other exception is referred to bilateral involvement of both phrenic nerves, in the fear of postoperative respiratory failure and ventilator dependence; this is even more crucial in myastenic patients; in such cases, incomplete resection on one nerve is advisable.
5. Pre- and postoperative treatment for stage II thymoma and stage III thymoma: This is the most controversial issue coming out from our survey, and it echoes the debate in the literature.[19,29–33] In stage II thymoma, although 60% of the surveyed centers administer RT after surgical resection, most of them stressed that the indication to RT should be raised selectively, based on (a) histology (only B2, B3, and C types), (b) the perceived completeness of resection by the surgeon, or (c) staging according to the Masaoka-Koga system. The subdivision of stage II into IIA (microscopic transcapsular invasion) and IIB (macroscopic invasion into the surrounding mediastinal fat tissue or nontransmural adherence to the mediastinal pleura) was specifically designed to indicate the need for postoperative RT, and it seems, therefore, superior to the standard Masaoka system. Nonetheless, 40% of the centers stated that they do not use RT after resection of stage II thymoma. This leaves field to an open discussion, but an answer will be able only through prospective randomized trials.
   On the other hand, there is an almost unanimous consensus concerning postoperative treatment after resection (either complete or not) of stage III thymoma. There are, however, three centers stating that they do not administer any postoperative treatment in case of complete resection; incomplete resection poses indication to RT. Postoperative chemotherapy alone is rarely administered, and in most of the cases, the association of chemo-RT or RT alone seems preferable. Also, the international literature reflects the impossibility to standardize this approach as results with postoperative administration of RT have never been analyzed in prospective trials, and cases with and without postoperative treatment are usually mixed in the reports without any rule.
   The interpretation of the results concerning induction treatment for stage III tumors is easier; this treatment modality is clearly accepted in the international literature[3,33–35] in case of invasive tumors potentially unresectable, and this is what was also performed by most of the centers answering the survey.
6. Treatment of stage IVA thymoma, recurrence, and type C thymoma: Masaoka stage IVA is a challenging situation. The indolent biologic behavior of thymoma and the predictable response to chemotherapy encourage to seek long-term survival without surgery[36,37]; on the other hand, recent reports support an increasing evidence that complete resection of pleural implants, along with mediastinal dissection and even EPP is effective in prolonging disease-free survival in this subset of patients.[38–42] Interestingly, most of the centers agree to consider surgery for stage IVA thymoma, and almost all administer induction chemotherapy before resection. Approximately 40% perform EPP or P/D to achieve a complete macroscopic resection of the pleural implants. The remaining centers rely on discrete resection of pleural metastases, and only one center use intracavitary hyperthermic chemotherapy. It is clear that there is a tendency toward a more aggressive attitude in stage IVA thymoma, although most of the EPP were performed at "high volume" institutions.
   Concerning locoregional recurrence, there is no doubt from the recent literature that surgery plays a major role in a multidisciplinary approach.[42–46] Reresections are also indicated in case of subsequent recurrences. Also, as most centers correctly pointed out, a proper patient selection is crucial, as incomplete resection of recurrence is a poor prognostic factor.
   Management of thymic carcinoma is not standardized in the literature,[47–50] and this clearly emerges also from our survey. Half the centers reported to approach type C thymoma similarly to other types of thymoma, whereas the remaining half indicated that they use a completely different protocol. The latter group added in their comments that they always perform a multidisciplinary approach with induction therapy (chemotherapy or combined chemo-RT) even in apparently completely resectable disease or stage I tumors and use a different chemotherapeutic schedule (however, this was not reported in the comments). Once again, this issue needs to be further clarified as conflicting practice exists even among experienced centers.
7. Multidisciplinary organization and logistics: There is a clear evidence that almost all centers support the idea of a dedicated team including thoracic surgeons, pathologists, medical, and a radiation oncologists experienced

in this field. Most centers pointed out that all cases should be discussed in a dedicated tumor board.

8. High-volume and low-volume centers: Interestingly, management of thymic malignancies looks quite similar at high- and low-volume centers. The most important difference consists in the use of preoperative and postoperative treatments at stage II and III disease. High-volume centers tend not to use RT after resection of stage II thymoma, and they tend to rely more on postoperative RT than combined chemo-RT after resection of stage III tumors. The relatively small number of centers answering the questionnaire suggests a word of caution in the interpretation of these results, which surely deserve confirmation in a larger sample size.

Survey studies have distinctive characteristics and several limitations, and the present one is not an exception. A limit of this study may be considered as the geographical distribution among the centers and the issue of the representative among the ESTS community; it should be noted, however, that the proposal of the project was offered by e-mail to all the ESTS community, and all ESTS members had, therefore, the opportunity to join the project; also, the overrepresentation of Italian centers may result from the longstanding tradition in the management of thymic neoplasms from Italian centers and the general interest in thymic neoplasms in this country. Another important limitation is related to the preparation of the list of questions. The questionnaire is made of close-ended questions, specifically designed to be easy to understand, not time consuming, and direct; this is crucial to obtain a high response rate. As a consequence, some details are difficult to be extrapolated, and the final result is, therefore, a general overview of the current practice. A second limitation is that surveys are unavoidably biased toward those who reply, ignoring those (usually most) who do not answer for whatever reason (they do not perform thymic surgery, they are not willing to participate, they disagree with most of the questions, they have no time, etc.). There are no data about how many ESTS members really perform thymic surgery, and this represents a major bias. A third limitation results from the body of data: as the questionnaire is filled out with "self-response" data, we do not know how accurate and true they are, and theoretically, a possible bias may result if the respondent simply tries to adhere to the literature instead of reporting his/her true clinical practice. Finally, it should be emphasized that the results of a survey are not to be taken as a recommendation, as they lack the required statistical validation from the very beginning.

On the other hand, the value of the present survey is that it represents a large, multiinstitutional, clear, comprehensive overview of the clinical practice in the management of thymic tumors. It is an up-to-date picture of the state of the art. An added value of this study includes the possibility to identify areas of agreement and areas where a considerable debate remains because of the variability in the responses. As a consequence, it provides a stimulus to identify specific issues needing further discussion, to prompt retrospective studies in areas of controversy, to design prospective studies on specific areas of interest, and, finally, to form the backbone to set up guidelines and recommendations.

In conclusion, the present survey from the ESTS-TWG is currently the largest report concerning the overall approach to this disease so far. The next move will be the creation of a collaborative effort within the ESTS and with other organizations for research projects, to eventually achieve standardized guidelines.

ACKNOWLEDGMENTS

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