



Review

Optimal surgical approach to thymic malignancies: New trends challenging old dogmas



Enrico Ruffini*, Pier Luigi Filosso, Francesco Guerrera, Paolo Lausi, Paraskevas Lyberis, Alberto Oliaro

Thoracic Surgery, University of Torino, Torino, Italy

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ABSTRACT

Until recently, the surgical approach to thymic tumors has remained basically unchanged. The collaborative effort led by ITMIG with the collaboration of regional and society-based interest groups (ESTS, JART) produced an enthusiastic surge of interest in testing the new technological advances in thoracic surgery and many historical dogmas in thymic surgery have been questioned and challenged. The present review addresses the new trends in the optimal surgical management of thymic tumors based on the review of the current literature. 1. Minimally-invasive techniques (MIT) including video-assisted thoracic surgery (VATS) and robotic-assisted thoracic Surgery (RATS) are now to be considered the standard of care in early-stage thymic tumors. MIT are no inferior to open approaches in terms of postoperative complications, loco-regional recurrence rates and survival. MIT are associated with a shorter length of stay, reduced intraoperative blood loss and better cosmetic results. 2. The adoption of the ITMIG/IASLC TNM staging system for thymic tumors requires a paradigm shift among thoracic surgeons to include regional lymphadenectomy according to the IASLC/ITMIG nodal map in the surgical management of thymic tumors. 3. A limited thymectomy instead of total thymectomy along with the removal of the thymic tumor in nonmyasthenic Stage I–II tumors has been proposed by some authors, although the results are not uniform. Until more mature data is available, adherence to the current guidelines recommending total thymectomy in addition to thymomectomy is always indicated. 4. In locally-advanced Stage IVa patients with pleural involvement, major pleural resections, including pleurectomy/decortication or extrapleural pneumonectomy are indicated, provided a complete resection of the pleural deposits is anticipated, usually in a multidisciplinary setting, with excellent long-term results. The incorporation of these new concepts and techniques in the surgical armamentarium of the thoracic surgeons dealing with thymic malignancies will certainly be of help in the optimal management of these patients.

1. Introduction

Thymic tumours are rare tumors with a reported annual incidence from 1.3 to 3.2/million [1,2]. They still represent the most common anterior mediastinal tumors in the adults. Thymic tumors are classified using the recommendations of the World Health Organization (WHO) into thymomas – further divided into low-grade (A,AB) and high-grade (B1,B2,B3), thymic carcinomas (TC) and thymic tumors with neuroendocrine features (NETT) [3–5].

After few decades of relatively indolent progress in the study of thymic malignancies, the last decade witnessed a new interest which led to tremendous advancements in the diagnosis, classification, staging and management of these rare tumors [6].

The key of this success was the collaborative effort among

Institutions, scientific societies, countries and continents which put together their resources in producing an extraordinary global effort. The foundation in 2010 of the International Thymic Malignancies Interest Group (ITMIG) was a landmark step [7]. In few years ITMIG produced recommendations for the standardization of terminology, outcome measures [8] and pathology [4], along with a large retrospective database [9]. In addition to ITMIG, regional society or country-based interest groups flourished, the most active being the Japanese Association for Research on the Thymus (JART) and the European Society of Thoracic Surgeons (ESTS) thymic working group. Very recently, the Chinese Alliance for Research in Thymomas (ChART) and the Korea Association for Research on the Thymoma (KART) were added. Thanks to the collaborative work of ITMIG, JART and ESTS, under the supervision of the International Association for the Study of Lung Cancer

* Corresponding author at: Thoracic Surgery, University of Torino, Italy, 14, Corso Dogliotti, 10126, Torino, Italy.
E-mail address: enrico.ruffini@unito.it (E. Ruffini).

Table 1a
TNM classification of thymic malignancies – 8th edition (IASLC/ITMIG).

T	Descriptor
T1	Tumor encapsulated or extending into the mediastinal fat, may involve the mediastinal pleura T1a No mediastinal pleura invasion T1b Direct invasion of the mediastinal pleura
T2	Tumor with direct involvement of the pericardium (partial or full thickness)
T3	Tumor with direct invasion into any of the following: lung, brachiocephalic vein, superior vena cava, phrenic nerve, chest wall, or extrapericardial pulmonary artery or vein
T4	Tumor with direct invasion into any of the following: aorta (ascending, arch or descending), arch vessels, intrapericardial pulmonary artery, myocardium, trachea, esophagus
N	Descriptor
N0	No regional lymphnode metastasis
N1	Metastasis in anterior (perithymic) lymph nodes
N2	Metastasis in deep intrathoracic or cervical lymph nodes
M	Descriptor
M0	No pleural, pericardial or distant metastasis
M1	Distant metastasis M1a Separate pleural or pericardial nodule(s) M1b Distant metastasis beyond the pleura or pericardium

Table 1b
Stage grouping.

Stage I	T1	N0	M0
Stage II	T2	N0	M0
Stage IIIA	T3	N0	M0
Stage IIIB	T4	N0	M0
Stage IVA	Any T	N1	M0
	Any T	N0, N1	M1a
Stage IVB	Any T	N2	M0, M1a
	Any T	Any N	M1b

(IASLC), the largest retrospective database of thymic tumors was collected and analysed, and formed the basis for the IASLC/TNM staging system of thymic tumors (Tables 1a and 1b) which was included in the 8th edition of the TNM international staging system of thoracic malignancies [10–12] and which should replace the Masaoka-Koga staging system [13,14]. Preliminary validation studies have demonstrated the value of the IASLC/ITMIG staging system [15,16].

Along with the major advancements in the diagnosis and staging, the standard surgical management of thymic tumors – which had remained basically unchanged for decades, was progressively adapted to the new thoracic surgical techniques (Video-assisted thoracic surgery – VATS, Robotic-assisted Thoracic Surgery – RATS) and new concepts have emerged and proposed for an optimal surgical approach of these rare tumors.

The present review paper will address the most recent concepts and techniques about the optimal surgical management of thymic tumors.

2. Optimal surgical approach to thymic tumors

Surgery still represents the treatment of choice in thymic tumors, despite the lack of robust evidence based on prospective, randomized trials [17] and complete resection has consistently been found to represent a powerful prognostic factor [18,19]. The anatomical location of the thymus in the anterior mediastinum has undisputedly convinced the thoracic surgeons that sternotomy was the only possible surgical approach which may provide a complete resection of the tumor. Few attempts to remove thymic tumors through cervicotomy only, or through a thoracotomy were criticized in the past for the perceived high chance not to achieve a complete resection. Very often the operation consisted only in removal of the tumor without any lymphadenectomy, under the assumption that lymphnodal spread was uncommon in thymic tumors and of little prognostic impact.

Surgical resection of capsulated or minimally invasive tumors (Masaoka Stage I–II) are usually easily achieved with a complete resection rate of nearly 100%. Resection of locally-advanced Stage III tumors is more challenging, and the decision to operate on upfront is based on the perception from the surgeon that the tumor can be completely resected. Excellent complete resection rates can be obtained even in case of tumors invading the neighboring structures (pericardium, venous great vessels, lung parenchyma), ranging from 50% to 80% [20–23]. The use of induction therapy and postoperative radiotherapy have been found to be of value in case of tumors deemed to be unresectable upfront, which is the case in most high-grade thymomas (B2–B3), thymic carcinomas and neuroendocrine thymic tumors [24–27]. Surgery in Stage IVa tumors with pleural spread in the form of pleural nodules or a diffuse carcinosis has long been considered by most surgeons of little efficacy, particularly in aggressive thymic tumors, and many authors were reluctant to extend the resection to the pleura in case of Stage IVa tumors, also based on the dismal results obtained in other tumors with pleural involvement.

This standard surgical approach has remained basically unchanged over the last 30 years with few minor changes until the first decade of the XXI century.

Then, the amazing collaborative effort led by ITMIG with the collaboration of regional and society-based interest groups (ESTS, JART and recently ChART and KART) produced an enthusiastic surge of interest in testing the new technological advances in thoracic surgery (VATS, RATS) and many historical dogmas of thymic surgery have been questioned and challenged.

The present review will focus on 4 “hot topics” in the optimal surgical approach to thymic tumors: 1. Minimally-invasive surgical techniques vs. the standard open techniques; 2. The role of lymphadenectomy in the surgical management of thymic malignancies. 3. The need of total thymectomy vs. thymomectomy only in early-stage non-myasthenic thymomas; 4. The efficacy of major pleural resection techniques in the management of Stage IVa locally-advanced thymic tumors with pleural involvement.

3. Minimally-invasive surgical techniques for thymic tumors: state-of-the-art

Surgical treatment with complete resection is the standard of care in the management of thymic tumors [19]. Traditionally, this has been achieved with open procedures. Among these, median sternotomy, either total or partial, and thoracotomy have been proposed in the past and have been proved to be successful in achieving optimal outcomes [20,28].

More recently, due to the widespread use of minimally invasive techniques (MIT) in different aspects of surgery and in thoracic surgery (Video-assisted thoracic surgery, VATS), there has been a progressive adoption of these techniques in thymic surgery. The even more recent introduction of the Robotic-assisted Thoracic surgery (RATS) has prompted many surgeons to explore the use of the robot for the resection of thymic tumours.

The debate about which technique, open surgery or MIT is the most appropriate for the treatment of thymic tumors resulted in a number of manuscripts in the last decade, most of which are retrospective case series. Unfortunately, no randomized clinical trial has been designed to address the issue and it seems unlikely, due to the rarity of the condition, that this can be done in the near future.

The correct indication of the surgical approach in thymic tumors depends on several factors: 1. The tumor stage, 2. The tumor dimension, 3. Tumor histology and 4. The individual patient’s clinical characteristics.

According to the European Society of Medical Oncology (ESMO) guidelines on thymic tumors, [29], the standard surgical approach in resectable disease remains median sternotomy (Grade IV, level A). Resectable tumors include all Stage I/II disease (according to Masaoka-

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