Perspective

Standardized definitions and policies of minimally invasive thymoma resection

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A wide range of technical approaches for the minimally invasive resection of thymus have been described. Most of the time, the benefits are superior cosmetic outcome and shorter duration of postoperative stay. Other demonstrable differences that have been reported include shorter duration of surgery, less intraoperative blood loss and less postoperative pleural drainage. Robotic surgery and video-assisted surgery (VATS) may become routinely used procedures in the treatment of stage I and II thymomas.

Keywords: Thymoma; video-assisted thoracoscopic surgery (VATS); robotics

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Surgical treatment of thymoma has been a controversial topic in the field of mediastinal surgery, due to the lack of proper definitions and standardization. However, the development of terms, definitions and policies for minimally invasive thymoma by the International Thymic Malignancy Interest Group (ITMIG), a worldwide collaborative organization of individuals interested in mediastinal tumors, has been able to change perspectives towards this procedure (1). Surgeons with experience in minimally invasive thymic resections were assembled to recommend standardized definitions, terms and procedures in the existing literature for minimally invasive thymoma resections. These recommendations were then discussed with a larger working group consisting of a diverse range of specialists in ITMIG, which was supported by the International Association for the Study of Lung Cancer, until an overall consensus was reached. This agreement has led to improved outcomes of both minimally invasive and open thymic resections.

There is a wide variety of technical approaches for minimally invasive thymic resections (2-5). Many types of incisions, methods of exposure, visualization, equipment via transcervical, extended transcervical, video-assisted thoracoscopy and robotic approaches (right and/or left, right and cervical, left and cervical, subxiphoid and right and left, cervical and subxiphoid) are currently considered as minimally invasive thymic resections (1). Some techniques may involve sternal lifting or rib spreading via soft tissue retractors. However, in the near future, only approaches that do not involve sternotomies (including partial sternotomy) or thoracotomy with rib spreading will be considered to be minimally invasive thymic resection (1).

Why minimally invasive thymoma resection?

The major benefits of minimally invasive thymic resections are improved cosmesis and shorter postoperative stays. However, other benefits include: shorter duration of surgery, less intraoperative blood loss and reduced postoperative pleural drainage (6). A study comparing outcomes of transsternal and video-assisted thoracoscopic surgery (VATS) thymectomy for thymoma demonstrated that patients undergoing VATS thymectomy have shorter hospital stays and potentially fewer complications compared to transsternal thymectomy. In addition, mid-term follow-up revealed that VATS thymectomy had comparable oncological outcomes with transsternal thymectomy in terms of adjuvant therapy received, disease progression, and

survival (7). Finally, there is a lack of complications from sternotomy in patients with corticosteroid dependency, due to the medications for myasthenia gravis (MG) and the need to have adjuvant radiotherapy.

Standard resection of a thymoma

A standard thymoma resection is defined as a complete en bloc resection of the tumor and complete thymectomy with removal of the upper cervical poles and the surrounding mediastinal fat (8). Resection also extends to structures invaded by the thymoma, which may include the pericardium, lung, phrenic nerve, superior vena cava, aorta and its main branches. However, there are reports that do not follow these recommendations, whereby only the thymic mass was resected, and not the thymus or mediastinal fat. A study showed that in early-stage nonmyasthenic thymoma patients, thymomectomy without thymectomy via thoracotomy or VATS is associated with lower morbidity and shorter hospitalization compared to thymomectomy with extended thymectomy (9). It also reported that MG did not develop in any of the patients enrolled in a study postoperatively, over a median follow-up of 57 months. Overall tumor recurrence rates were not significantly different between these two patient groups. Thymomectomy without thymectomy through thoracotomy or VATS is justified for early-stage nonmyasthenic thymoma patients, and further studies with longer follow-up periods are required to investigate the role of thymectomy in these patients (9).

Should lymph node resection be routine at the time of thymoma resection with minimally invasive surgery?

Until recently, it has been shown that the rate of lymph node metastases is 1.8% in patients with thymic epithelial tumors (10,11). Kondo and Monden's paper is the only publication to have reported the incidence and prognostic relevance of nodal metastases in patients with thymoma. However, a large database of patients from the United States was recently presented to demonstrate the incidence and prognostic significance of nodal metastases in patients with thymoma (12). According to this study, 2,227 patients with thymoma were entered into the Surveillance, Epidemiology and End-Result (SEER) database. Of these, 442 patients had lymph node resection in addition to thymoma resection. The median number of resected nodes was two. There were 59 patients (13.3%) found to have lymph node involvement. These patients were younger and tended to have smaller thymomas. Given that nodal metastases may occur more frequently than is currently recognized, evaluation of anterior mediastinal lymph nodes and pathologic analysis and reporting should be included in the routine investigation for a thymoma. In addition, younger and smaller thymoma patients are typically suitable candidates for minimally invasive thymoma resection. This study demonstrated a clinical need for mediastinal lymph node dissection or sampling in order to determine the proper staging and treatment of thymoma. The technical recommendations for this development have yet to be defined for minimally invasive resection of thymoma. Authors of this paper suggested the removal or sampling of at least the anterior mediastinal lymph nodes routinely.

In 2013, Park *et al.* (13) recommended routine resection of all mediastinal lymph nodes in patients with thymic resection. Furthermore, the ITMIG and International Association for the Study of Lung Cancer has produced a new TNM staging classification emphasizing the importance of lymph node status (14,15).

Minimum requirements of minimally invasive thymoma resection

Minimally invasive resection does not equate to minimal resection of the thymoma and mediastinal tissues. The actual resection should be the same as what is deemed appropriate for an open approach. Incomplete resection and debulking should not be considered acceptable in a minimally invasive procedure, and in such situations, conversion to open surgery is required (1). During the dissection, the innominate vein and both phrenic nerves should be visualized. Opening and resection of the contralateral pleura must be performed using a 30 degree or greater scope in order to visualize the contralateral phrenic nerve. Pulling the tissue towards the surgeon may further assist in identifying the phrenic nerve. Conversion to open surgery is required if oncologic principles are being compromised or violated: e.g., perforation of the capsule, incomplete resection possibility, risk of a discontinuous (not en bloc) resection, or disruption of the tissues exposing the tumor. The access incision for retrieval of the thymoma should be large enough to prevent specimen disruption. Trans-capsular invasion can be subtle and not be detected by the surgeon; therefore, the tumor should be resected with the surrounding thymus and fatty tissue rather than be shelled out. If the tumor projects into the

pleural space, pleural metastases may be present, and the entire pleural space should be subsequently searched for possible parietal and visceral metastases, which should be resected accordingly if present. Inspection of the pleural space may not be performed for a tumor that is completely contained within the thymus. The suggested procedure is a complete thymectomy for patients without MG, including nodes close to the tumor, and an extended thymectomy for patients with MG (removal of the contiguous right and left mediastinal pleura, mediastinal and pericardiophrenic fatty tissues, and dissection of aorta-pulmonary window in addition to complete thymectomy) (1). A maximal thymectomy may be performed with a neck dissection and sternal lifting methods (4). If the surgeon chooses to do so, the authors recommend removing all lymph nodes for documentation purposes. Lesions with a preoperative diagnosis such as thymic carcinoid tumour or thymic carcinoma may benefit from such a procedure, as a more aggressive lymph node dissection may be required in these circumstances. All tissue retrievals must be contained in the bag.

Upper limits of minimally invasive thymoma resection

According to our report, Masaoka stage 1 and 2 tumors may be resected safely and efficiently (16). It is well known that the learning curve in learning the technique is steep, and a level of expertise is essential in minimally invasive resection of a thymoma (17).

Clinical and radiographic findings can be used to select patients for a VATS thymoma resection; markers of invasion such as phrenic or recurrent laryngeal nerve palsy or major vessel invasion may be considered as reasons for open surgery. It has been proposed that involvement of the phrenic nerve, innominate vein or other major vessels is a contraindication to a minimally invasive approach when diagnosed preoperatively or intraoperatively. The ITMIG paper recommends avoiding minimally invasive resections of the phrenic nerve. However, I believe that phrenic nerve invasion, if diagnosed intraoperatively, can be evaluated and managed with a minimally invasive approach, taking appropriate steps to preserve the nerve if possible. I also recommend diaphragmatic plication in the same operation.

Experienced surgeons have demonstrated the feasibility of VATS resection in Masaoka stage 3 and 4a (18). Agasthian and colleagues [2011] selected patients with tumors smaller than 5 cm without major invasion on preoperative computed tomography. Out of 77 patients, there were 13 invasive thymomas (Masaoka stage III and IV). Limited resection of the phrenic nerve, pericardium, perithymic fat and a wedge of lung was performed en bloc with the tumor. Median hospital stay was 3.6 days. There was one case of wound infection and no operative mortality. The mean size of the thymomas was 34 mm (range, 23-55 mm). All patients had adjuvant radiotherapy. During follow-up of 4.9 years (range, 1-10 years), there was one local recurrence. Evidently, selected invasive thymomas detected during surgery can be removed safely without requiring open conversion (18). It must be understood that the invasiveness of thymoma may not necessarily correlate with thymoma size, as documented in our previous publication. Rather, it is the stage that indicates the feasibility of minimally invasive resection (16).

According to our experience, surgeons with expertise in VATS thymectomies can perform resection of Masaoka stage 3 thymomas. However, our study clearly demonstrated that patients with Masaoka stage 3 and higher did not benefit from the advantages of VATS resection (16). Conversion to open surgery is necessary if any pathological or surgical issue would be potentially compromised or inadequately managed by minimally invasive techniques (1).

In patients with thymoma resection, recurrences may occur many years later. We must be careful in firmly establishing outcomes of minimally invasive approaches first in straightforward cases before expanding the technical boundaries too rapidly.

Does robotic surgery provide any additional benefit?

In a recent study, 79 patients operated in four European centers for early-stage thymoma with robot-assisted thoracoscopic surgery (RATS) thymectomy were evaluated (19). In this study, one patient needed open conversion, one patient required a standard thoracoscopy following a robotic system breakdown, and five patients required an additional access incision. No vascular and neural injuries were recorded, and no perioperative mortality occurred. Median hospital stay was three days (range, 2-15 days). Median diameter of tumor resected was 3 cm (range, 1-12 cm), and Masaoka stage was stage I in 30 patients (38%) and stage II in 49 patients (62%). At a median follow-up of 40 months, 74 patients were alive and five had died (four patients from nonthymoma-related causes and one from a diffuse intrathoracic recurrence), with

a five-year survival rate of 90%. This report indicated that RATS thymectomy for early-stage thymoma is a technically sound and safe procedure with a low complication rate and a short hospital stay. While the oncologic outcomes appear acceptable, longer follow-up is needed to definitively consider this as a standard approach (19).

The short-term outcomes of 46 patients who underwent surgery for Masaoka stage I thymoma without MG were evaluated in another recent study (20). Of these patients, 25 received unilateral VATS, while the remaining 21 received unilateral RATS thymectomy. The duration of surgery and intraoperative blood loss did not significantly differ between the two groups. The postoperative hospital stay, however, was significantly shorter in the RATS group (3.7 *vs.* 6.7 days; P<0.01), and the postoperative pleural drainage duration of the RATS group was also significantly lower (1.1 *vs.* 3.6 days; P<0.01). No patients in the RATS group required conversion to open surgery, compared to one case of conversion in the VATS series. No surgical complications were observed except for one case of pulmonary atelectasis in the RATS group, and one patient who developed pneumonia after surgery. The use of robotics is more expensive than VATS (20). No early recurrence was observed in both groups. According to this study, the minor benefits of robotic surgery may be promising (20).

What is new after the proposals made by the ITMIG?

There are several points to be discussed in redefining minimally invasive thymoma resections, as follows:

(I) Could Masaoka stage 3 and 4a patients be candidates for minimally invasive resections? Resection of thymomas with invasion of lung, pericardium and phrenic nerve may be performed in experienced hands. However, our data did not show any functional benefit to parameters such as duration of hospital stay and duration of drainage. Nonetheless, the minimally invasive approach does provide a cosmetic benefit;

(II) Should a lymph node dissection be performed with a minimally invasive approach, considering the most recent proposals of ITMIG? Not yet, as we do not have a solid evidence-base. However, recent reports demonstrate that lymph node invasion is more common than has been reported. According to our personal experience with a long period of patient follow-up, we see more and more lymph node recurrences in the mediastinum after resection of thymomas. Subsequently, we believe that at least the anterior mediastinal nodes should be resected using minimally invasive techniques;

(III) Does robotic surgery have additional benefits? As the developments in minimally invasive surgery techniques, indications and capabilities continue, there will be a higher patient demand for minimally invasive surgery. Certainly, robotic surgery may be an attractive option, although there are very few reports showing its superiority to other minimally invasive approaches. However, as a surgeon performing an equal number of VATS and robotic surgeries, I still prefer VATS over robotic surgery for three main reasons. Firstly, most patients in this group are myasthenic, and in my experience, robotic surgery is more time-consuming in the resection of a thymoma, compared to VATS. Duration of surgery is extremely important in myasthenic patients. Secondly, most of the experience that I have gained in thymoma resections was during the pre-robotic era. Surgeons should operate with the technique that they are most comfortable with. Thirdly, VATS thymoma resection could be performed at the same cost as open surgery, whereas robotic surgery is more expensive.

Conclusions

Over the past few years, perceived benefits of shortened hospital stays and reduced pain have shifted the favor to minimally invasive surgery. However, the superiority of these approaches compared with open techniques has yet to be properly documented. Prospective collaborative data collection was provided in several platforms. The ITMIG and European Society of Thoracic Surgeons (ESTS) databases may assist in defining the future value of these techniques.

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Footnote

Conflicts of Interest: The author has no conflicts of interest to declare.

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