Editorial

Contemporary treatment for thymic malignancies: what's the bottom line?

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The recent manuscript by Ruffini *et al.* entitled "Optimal surgical approach to thymic malignancies: new trends challenging old dogmas" highlights important points and principles regarding the appropriate surgical management of thymic masses (1). There are still questions which remain, however, in our goal of achieving a consensus view on various aspects of treatment. There are four topics which warrant discussion:

(I) Appropriate surgical approach for large tumors;
(II) Appropriateness of surgery for stage IV-A disease;
(III) Role of nodal dissection for thymic tumors;
(IV) Role of perioperative chemotherapy and radiation treatment.

Minimally invasive approaches

Thymic malignancies occur in approximately 0.13 per 100,000 people (2). Because this disease is relatively rare, the basis for disease management in most centers has arisen from retrospective studies in the literature. Prior to the advent of minimally invasive thoracic surgery, surgical approaches were usually sternotomy and/or thoracotomy. In the last decade, however, video-assisted thoracic surgery (VATS) and robotic-assisted thoracic surgery (RATS) have been used more frequently to resect thymic tumors. Historically, size had been an absolute contraindication to minimally invasive resection. But there have been numerous reports and case series which have shown good outcomes when resecting large anterior mediastinal masses using minimally invasive approaches (3,4). In experienced centers, these large tumors can be resected using minimally invasive approaches with no differences in rates of R0 resection, perioperative complication rate (5,6) and with a low conversion rate (7). Surgeons should individualize each case and use their comfort levels with minimally invasive techniques when deciding whether a tumor can be completely resected by VATS or RATS. As this decision is made, it should be understood that different surgeons and centers will have different comfort levels. As technology advances and surgeon experience with minimally invasive surgery increases, the average size of tumors resected and frequency of use of VATS and RATS is expected to increase as well.

Stage IV-A disease

Stage IV-A thymoma occurs in 7% of patients with thymic malignancies (8). There is a wide range of treatment options available for this stage of disease, and surgical resection is one of those options. Despite a limited amount of data, there is some literature which suggests that a subset of patients will have a survival benefit with surgery (9,10). When deciding between extrapleural pneumonectomy (EPP) and discrete pleural metastasectomy (DPM) for surgical treatment of stage IV-A disease, the goal should be to perform whatever surgery is required to resect all disease. In a series examining patients with stage IV-A

thymic neoplasms, EPP was found to demonstrate better local control and improved disease-free survival rates when compared to DPM (11). However, the increased morbidity of EPP should be considered when deciding whether to offer surgery. If preoperative tumor burden suggests that EPP will be needed to resect all disease but the patient does not have the functional reserve for an EPP, then surgery should not be offered. Performing a "debulking" procedure will likely create morbidity for the patient without a survival advantage.

Nodal dissection

The role of nodal dissection during resection of thymic tumors is a topic of debate. Lymph node dissection has typically been overlooked when treating patients with thymic malignancies, as one study one study using the Surveillance, Epidemiology, and End Results (SEER) database showed that only 19.8% of patients undergoing resection of a thymic mass had any lymph nodes resected (12). In that same study, it was shown that patients who had a positive lymph node experienced a 3-fold decrease in disease-specific survival compared to patients without nodal involvement. Although recent literature has focused on the importance of nodal sampling in stage II or above (13), we feel that lymph node sampling should be performed routinely when resecting thymic lesions. The morbidity from lymph node sampling is quite low and there will potentially be prognostic information gained from the addition of this procedure to the surgery.

Perioperative chemoradiation therapy

Regardless of the technical approach, the goal of surgery should be to resect the mass completely. When complete resection is not possible preoperative chemotherapy should be offered to reduce the mass to a size which will allow for complete resection. This scenario most often arises when there is significant great vessel or bony involvement. Cisplatin-based chemotherapy regimens have oftentimes resulted in reductions in tumor size significant enough to allow previously unresectable masses to be removed with an R0 resection. As mentioned above, there should be no attempt to "debulk" the tumor and then give adjuvant treatment, as this approach will significantly decrease the chances of cure and is not the optimal treatment for most patients.

Preoperative chemotherapy should also be considered if there is a chance that the extent of surgery will be greatly reduced by reducing the size of the tumor. As an example, a patient with a large tumor may be deemed to require a pneumonectomy to resect all disease. If a partial response to treatment could potentially lessen the extent of surgery, then chemotherapy should be given preoperatively. Each case should be individualized, and every patient with a large tumor should have his/her case discussed in a multidisciplinary conference prior to the initiation of any treatment. Coordinating a treatment plan with multiple service lines at the beginning of treatment will result in better overall outcomes for patients.

Because many large thymic tumors can be associated with very extensive resections, such as EPP, our center has tended to avoid preoperative radiation therapy. The increase in morbidity and technical challenge after radiation treatment appears to be greater than the benefit gained when radiation is given before surgery. We reserve radiation for cases in which complete resection was unable to be performed and there is a positive margin, or if surgery is never going to be offered. In tumors in which total resection was not performed, there may be a survival benefit when radiation treatment is added postoperatively (14).

In summary, the treatment of thymic malignancies has changed over time. More frequently, VATS and RATS can be used to resect disease completely. Size is not an absolute contraindication to resection using a minimally invasive approach if the tumor can be resected completely and safely by that surgeon. Some patients with stage IV-A disease will have a survival benefit associated with surgical resection. Lymph node sampling should be performed in all cases. Neoadjuvant chemotherapy should be offered if the tumor is considered "unresectable" or if the extent of surgery can be significantly lessened with a partial response to treatment. And radiation treatment should be offered only postoperatively if there is residual disease after surgery.

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Footnote

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

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