Robotic Mediastinal Surgery in Patients with Suspected Thymic Neoplasms: First Israeli Experience

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ABSTRACT: **Background:** Thymectomy is a reliable surgical method for treating patients with myasthenia gravis (MG) and benign tumors of the thymus. Despite the advantages of minimally invasive surgical approaches for resection of thymic neoplasms, there are still controversies regarding the superiority of one type of surgery over another.

Objectives: To report the results of our initial Israeli experience with robotic thymectomy in 22 patients with MG and suspected benign thymic tumors.

Methods: We retrospectively analyzed 22 patients (10 men, 12 women) who underwent robotic thymectomy by a left-sided (16) or right-sided approach (6) using the da Vinci robotic system at Assaf Harofeh Medical Center. Seven patients were diagnosed with MG before surgery and 14 had suspected benign thymic neoplasms.

Results: Average operative time was 90 minutes. There were no deaths or intraoperative complications. Postoperative complications occurred in two patients (dyspnea and pleural effusion). Median blood loss was 12.3 cc (range 5–35 cc), median hospital stay 2.9 days (range 2–5 days), and mean weight of resected thymus 32.1 grams. Seven patients had thymic hyperplasia, six a lipothymoma, one a thymic cyst. Seven each had thymomas in different stages and one had a cavernous hemangioma.

Conclusions: Robotic thymectomy is a safe, technically effective surgical method for resection of thymic neoplasms. The advantages of this technique are safety, short hospitalization period, little blood loss, and low complications. We have included this surgical procedure in our thoracic surgery residency program and recommend a learning curve program of 10 to 12 procedures during residency.

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Thymomas are rare intrathoracic neoplasms of the thymus with an annual incidence of approximately 0.15 per 100,000 person-years [1]. They are the most common primary tumor in the anterior mediastinum in adults. Conversely, the prevalence of myasthenia gravis (MG) is approximately 14–20 per 100,000 person-years [2]. Surgical intervention with safety margins remains the only curative treatment for thymomas in patients with or without MG and represents the most important prognostic factor [3]. It is traditionally performed through a median sternotomy, followed by complete resection of the thymus tumor, and thereafter resection of thymic cervical extensions and the surrounding perithymic and pericardial fat [4,5].

With the advent of improved optics and computer-assisted surgical systems, minimally invasive thymectomies by video-assisted surgery have become increasingly popular, especially since the early 1990s. The introduction of robotic-assisted techniques have added further precision and advantages in terms of technical skills and safety in working in difficult-to-reach anatomic regions, such as the mediastinum, and they overcome the limitations of conventional thoracoscopy, thus substantially improving clinical results [6]. The aim of our study was to review our initial experience with robotic thymectomy in patients with MG or benign thymic tumors without MG.

PATIENTS AND METHODS

The robotic thoracic surgery program at our hospital, which was initially created by cooperation between the hospital administration and the thoracic surgery department, included having staff members attend a robotic thoracic surgery training course in Los Angeles, CA, USA, which was conducted by Prof. Kemp Kernstine [7], as well as a robotic thymectomy training course in Berlin, Germany, coordinated by Prof. Jens C. Ruckeurt in March 2013 [8]. The program at Assaf Harofeh Medical Center was initiated in October 2013, after receipt of the appropriate certifications earned by completing the da Vinci System Training Course at the da Vinci Training Center, Ecole Européenne de Chirurgie (EEC) in Paris, France, as a consultant surgeon (MP).

We retrospectively reviewed our experience with robotic thymectomy for the treatment of 22 patients with thymic tumors in the department of thoracic surgery at Assaf Harofeh Medical Center between October 2013 and October 2016.

Preoperative evaluation included a neurologic assessment, electrocardiography, chest radiography, and computed tomography (CT) with contrast in all patients, and magnetic resonance imaging and spirometry in selected patients. Data on patient demographics, presence or absence of MG, intraoperative and postoperative data, complications, operative time, hospital stay, and other characteristics were collected. Preoperative CT demonstrated an anterior mediastinal tumor with features highly suggestive of thymoma. In all cases, the lesions were smaller than 5–6 cm in diameter and without signs of invasion of the surrounding structures. The criteria for patient selection followed the recommendations of Cheng et al. [8] and included an encapsulated tumor in the anterior mediastinum, a distinct fat plane between the tumor and mediastinal organs without signs of compression, the existence of normal appearing residual thymic tissue, and unilateral tumor predominance in tumors > 3 cm. Tumor size and invasion of surrounding structures were our most important criteria for selection of surgical approach. The Masaoka staging system was used to assess the pathologic stages in cases diagnosed with a thymoma [9] [Table 1, Table 2]. The new World Health Organization Histologic Classification System was used for definition of histology [10], and the Myasthenia Gravis Foundation of America clinical classification was applied to determine the preoperative class of MG and postoperative therapy status [11]. Microscopically, the histologic types of the thymus were described as hypertrophic, lipothymoma, and thymoma.

This retrospective study was approved by the Assaf Harofeh institutional review board.

Table 1. Patient baseline characteristics

Variables	Value	Percentage
Gender		
Female	12	54.5
Male	10	45.5
Age, years	Median 51.6 (range 18–74)	
Smoking history	11	50
Myasthenia gravis	7	31.8
Right-side robotic thymectomy	6	27.3
Left-side robotic thymectomy	16	72.7
Hospital stay, days	Mean 2.9 (range 2–5)	
Co-morbidities		
Chronic obstructive pulmonary disease	2	9.1
Hypertension	5	22.6
Ischemic heart disease	3	13.6
Non-insulin-dependent diabetes mellitus	2	9.1
Polyarteritis	3	13.6
Atrial fibrillation	1	4.6
Obesity	2	9.1
Peripheral vascular disease	1	4.6
Pulmonary embolism	1	4.6
Cerebrovascular accident	1	4.6
Hyperthyroidism	1	4.6

ANESTHESIA SURGICAL TECHNIQUE

All patients were anesthetized using a double-lumen tube for split-lung ventilation. A urinary catheter was introduced in all patients. We did not use epidural analgesia or a central venous pressure sensor catheter. Patients were placed left side or right side up at a 30° angle, according to the side of procedure, using a bean bag. The arm with the operating side extensions was positioned with partial extension so as to avoid damage to the brachial plexus. In all cases, the chest wall was prepared for possible transition to open sternotomy. In addition to general anesthesia, all patients were treated preoperatively with pectoral nerve block II (Pecs II) by injecting 30 ml of 0.25% bupivacaine.

SURGICAL TECHNIQUE

Robotic-assisted thymectomy with resection of all the anterior mediastinal fat tissue with four thymic poles was performed. The surgical team included two surgeons: the surgeon console controller and the patient-side robotic assistant. A three-arm da Vinci® Surgical System (Intuitive Surgical Inc., Sunnyvale, CA, USA) was used. The first incision was generally performed at the fifth intercostal space in the anterior axillary line. First, carbon dioxide was injected into the chest (up to a pressure of 8 to 10 mmHg) to enlarge the operating space and enable safe performance of the port incisions. The robotic camera with a 3-dimensional 30° stereo endoscope was inserted through a 15 mm incision to explore the chest cavity. Two other port incisions, at the third intercostal space and at the eighth intercostal space in the mid-axillary and min-clavicular lines, were made. In selected patients, an additional assistant 5 mm utility incision, which was used for suctioning, was made at the seventh intercostal space in the anterior axillary line. The controller's right robotic handheld Maryland bipolar forceps to perform the dissection, and the left handheld Cadiere forceps (EndoWrist; Intuitive Surgical, Inc, Sunnyvale, CA, USA), both of which are atraumatic instruments for grasping thymic tissue.

The resection borders were lower pericardium caudally, innominate veins cranially, and the phrenic nerves laterally. After inspection of the thymus gland and the thymoma, the dissection generally started inferiorly, first from the left side at the

Table 2. Postoperative characteristics*

Variable	Value	Percentage
Postoperative pathologic examination		
Hypertrophic thymus	7	31.8
Lipothymoma	6	27.2
Thymoma	7	31.8
Thymic cyst	1	4.5
Thymic cavernous hemangioma	1	4.5
Postoperative complication		
Dyspnea	1	4.6
Pleural effusion	1	4.6

Variable*

*Mean operative time: 90 minutes (range 45–135 minutes) pericardiophrenic angle; and then continued on the right side, from the retrosternal area. The right mediastinal pleura and right phrenic nerve were identified, permitting safe dissection of the right inferior horn under direct visualization of the nerve. Consequently, the dissection continued upward to the aorto-pulmonary window and to the neck until the superior horns were identified. The thymic veins were identified and separately clipped or dissected with Maryland bipolar forceps. The normal thymic tissue and perithymic fat were grasped first to reduce traction of the tumor, and thereafter to avoid direct manipulation of the tumor and minimize the risk of capsule damage to avoid seeding. The tumor with four superior and inferior thymic horns and surrounding thymic fat was mobilized en-bloc, and removed with the Endo Catch 10™ (Universal Intermodal Services, Inc, Cincinnati, OH, USA) from the cavity through the lower port incision in the mid-axillary region.

The 24 French chest tube was inserted generally through the accessory port or lower port incision. All thymus tissue and perithymic fat were dissected according to the Masaoka criteria [4], and the completeness of the thymectomy was assessed by macroscopic inspection of the thymic bed and the specimen after removal. After the surgery, extubation was attempted in the operating room in all patients. Operated patients remained in surgical intensive care for 24 hours and were then transferred to the department of thoracic surgery.

We also evaluated the duration of surgery, amount of intraoperative blood loss, duration of chest drainage, postoperative hospital stay, postoperative complications, and hospitalization costs. The diagnoses of all resected thymomas, surgical margins, and Masaoka stages were confirmed by histological examination. Size and weight, as shown by the maximal diameter of the tumor within the resected specimen, was measured. The chest tube was removed when the 24 hour drainage amount was less 100 ml. Follow-up was complete in all patients.

RESULTS

Twenty-two patients, 10 men (45.5%) and 12 women (54.5%), with a median age of 51.6 years (range 18–74 years) underwent surgery. Seven patients (31.8%) presented with MG. The robotic thymectomy was left sided in 16 patients (72.7%) and right sided in 6 patients (27.3%). All surgeries were conducted endoscopically with no conversion to an open surgical approach, no intraoperative complications, and no bleeding. No nerve or vascular injures were recorded and no perioperative mortality or morbidity occurred. Average blood loss was 12.3 cc (range 5–35 cc). All patients were extubated in the operating room immediately after the surgery. The mean operative time was 90 minutes (range 45–135 minutes) mean chest tube duration was 1.5 days (range 1–3 days), and mean hospitalization was 2.9 days (range 2–5 days). Postoperative complications occurred in two patients (9%): one patient with a thymoma and MG had postoperative dyspnea and one patient with a thymoma without MG had a moderate pleural effusion. These patients were successfully managed with conservative treatment. Pathologic examinations revealed seven cases (31.8%) of hypertrophic thymus, six cases (27.2%) of lipothymoma, one case (4.5%) of thymic cyst, seven cases (31.8%) of various stage thymomas (A,

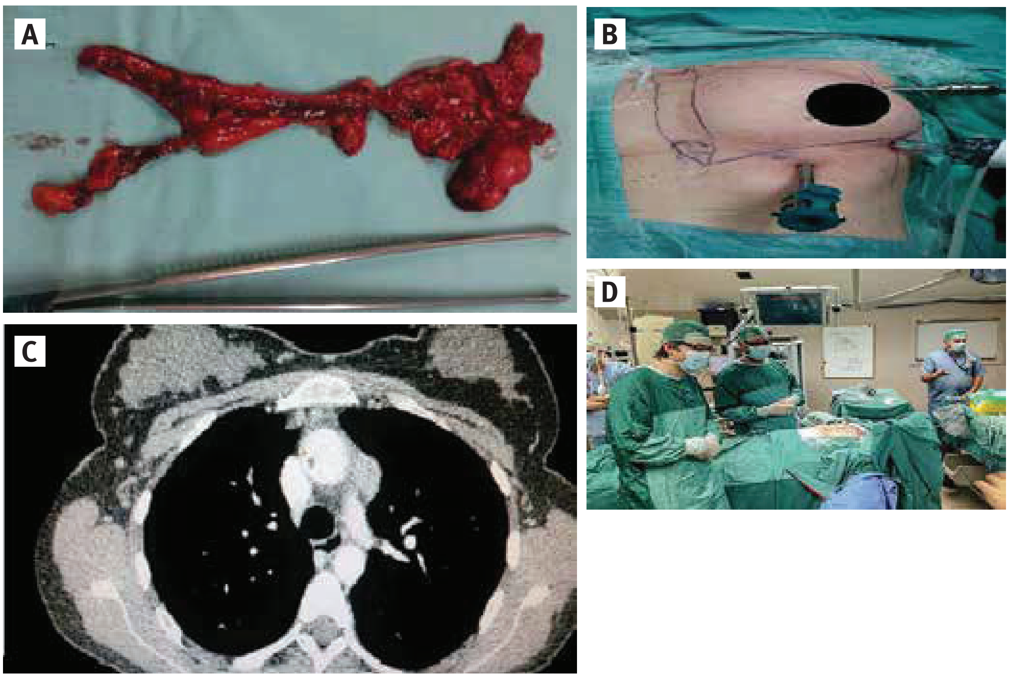

Figure 1. [A] Specimen after thymectomy, **[B]** Position of patient before surgery with location of three robotic ports, **[C]** Computed tomography scan of an early-stage thymoma, **[D]** Surgical room planning

B1, B2, AB, B3), and one case (4.5%) of cancerous hemangioma. Out of seven patients with MG, only one patient was diagnosed postoperatively with a thymoma type B1. Mean weight of the specimen (thymus and perithymic tissue together) was 32.1 grams. Postoperative radiation therapy was administered to two patients with stage B1 and B3 tumors with microscopic capsular invasion. Chest radiography was performed every 6 months in all cases. In patients with a thymoma, chest CT was performed every year. To date no patients with a thymoma have had tumor recurrence. Patients with MG were evaluated periodically by a neurologist. At the last follow-up (January 2017), all patients were in good general health.

DISCUSSION

Traditionally, thymic tumors and MG are basic indications for thymectomy. Several thymectomy techniques with different degrees of invasiveness have been described: from various kinds of sternotomy approaches to cervical and minimally invasive video-assisted and robotic-assisted techniques. The open surgical approach has generally been accepted as the gold standard for thymoma resection [12,13]. However, over the last decades, both thoracoscopic and, more recently, robotic approaches have been introduced into the thoracic field and have also been applied to thymectomy. Several reports were published regarding minimally invasive thymectomy, reporting good outcomes and emphasizing less operative trauma, shorter hospital stays, preserved pulmonary function, and superior cosmetic results [14-16].

According to the literature, if we compare thoracoscopic thymectomy with the robotic approach, both of them combine the advantages of minimally invasive techniques with a good view of the anterior mediastinum. However, disadvantages of the conventional thoracoscopic technique include a 2-dimensional view of the operative field and the fact that the arms do not articulate, making it difficult to operate in the mediastinum and especially in the contralateral mediastinum and the neck. The da Vinci surgical system consists of a master console and a robot with a camera and surgical arms. The camera consists of a device with 3-dimensional vision that affords the best possible view of the operative site. The robot, which has arms that can be articulated with seven degrees of freedom and 360 degrees of rotation, is perfectly suited for operations in the narrow space of the mediastinum, where there is a great danger of damage to major blood vessels or nerves. The da Vinci robotic surgical system enables surgeons to accurately dissect the left thymic lobe from right-sided and left-sided access in most patients by endo-wrists with articulated movements that permit improve maneuverability in the operation field [17]. Great care must be taken to avoid vascular and nerves injuries. Bleeding is the most serious complication and should be controlled during this surgery. Special care must be taken because venous drainage of the thymic gland to the innominate vein involves thin vessels; each must be isolated from the thymic veins, coagulated, and cut with an ultrasonic device to minimize the amount of bleeding or clamped. Moreover, the robotic system facilitates differentiation of a thymoma from normal thymic tissue thereby enabling safe manipulation.

In particular, not many studies have systematically reviewed the surgical results of minimally invasive robotic thymectomy for benign mediastinal tumors. Mussi and colleagues [18] demonstrated their experience of robotic thymectomy on 13 patients with a 7.7% conversion to sternotomy rate, 139 minutes mean operative time, and 4 days mean hospital stay. Marulli and co-authors [19] evaluated 79 patients, with a 1.3% conversion rate, 165 minutes mean operative time, and 4.4 days mean hospital stay.

In our series, our preference, based on anatomic considerations, was left-sided robotic thymectomy due to the fact that the larger part of the thymus is located in the left mediastinum [20], and right-sided robotic thymectomy was performed only for lesions located primarily on the right side. Our policy is to perform an extended thymectomy in all cases, as in the open approach. For patients with MG, all mediastinal fat tissue was removed, including an aortopulmonary window, which is frequently on the side of ectopic thymic tissue. We know that our study did not have a control group of patients with a transsternal approach, but our surgical results are good and show no mortality, no conversion rate, minimal blood loss, low hospital stay, and almost a complete lack of intraoperative and postoperative complications. Despite the recommendations that lesions smaller than 5 cm are generally considered oncologically acceptable for robotic thymectomy [21], we also operated on one patient with a larger tumor.

Another important advantage of robotic-assisted thoracic surgery is quick adaptation to the operating surgeon's technique. Thoracoscopic thymectomy is considered a technically challenging operation that requires a long learning curve [22]. However, compared to traditional transsternal thymectomy techniques, minimally invasive thoracoscopic techniques are superior due to low morbidity and mortality, a short hospital stay, good cosmetic results, minor surgical trauma, reduced postoperative pain, better preservation of pulmonary functions, and similar efficacy [14,23]. The introduction of robotic techniques and increasing experience is the next step in the introduction of less invasive surgical techniques that are reported to have low conversion rates (< 5%), low morbidity rates (< 10%), a short hospital stay (< 4 days), and a low rate of complications (<10%) [17,24]. Seong et al. [25] compared the results of robotic thymectomy with conventional sternotomy and found less tube drainage, less blood loss, earlier removal of chest drainage, and a shorter hospital stay without postoperative complications. Our research is not yet complete and is still continuing. There is only a small number of patients with a short follow-up period. This finding is also especially true for the oncologic outcome since at least 5 years of follow-up is needed in patients with thymoma to evaluate the survival and relapse rate. However, our initial experience has resulted in gained skills in robotic mediastinal surgery, and the main goal of achievement of safety and technical feasibility of the robotic approach for mediastinal diseases by one surgeon is accepted. After 12 to 15 robotic thymectomies, the second surgeon should be able to start the robotic mediastinal program under the guidance of the first, more experienced, surgeon.

CONCLUSIONS

Our study demonstrates that robotic mediastinal surgery is safe and efficient from the technical point of view, with no mortality, low morbidity, a short hospital stay, and acceptable costs. Robotic thymectomy has the advantage of being more easily and readily accepted by both neurologists and young patients because of good cosmetic results and a less invasive technique. We have achieved good results with the development of our mediastinal robotic surgery program and have introduced it into the residency program.

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"The life of every man is a diary in which he means to write one story, and writes another, and his humblest hour is when he compares the volume as it is with what he vowed to make it"

Sir James Matthew Barrie, 1st Baronet, (1860–1937), Scottish novelist and playwright, best remembered as the creator of Peter Pan

"It is hard to fail, but it is worse never to have tried to succeed"

Theodore "Teddy" Roosevelt, (1858–1919), 26th president of the United States of America

"What wisdom can you find that is greater than kindness?"

Jean Jacques Rousseau, (1712–1778), philosopher and author