



Robotic radical thymothymectomy for thymomatous myasthenia gravis in the elderly: case report and mini-review

François Montagne¹, David Delacour², Marion Fommarty¹, Zied Chaari^{1,2,3}, Eloise Papet¹, Jean-Marc Baste^{1,4}^

¹Department of General Thoracic Surgery, Rouen University Hospital, Rouen, France; ²Department of Radiology, Cardiac Imaging Unit, University Hospital of Rouen, Rouen, France; ³Department of Thoracic and Cardiovascular Surgery, Habib Bourguiba University Hospital, Sfax, Tunisia; ⁴INSERM U1096, Haute Normandie Research and Biomedical Innovation, Normandie University, Rouen, France

Contributions: (I) Conception and design: F Montagne, JM Baste; (II) Administrative support: F Montagne, D Delacour, JM Baste; (III) Provision of study materials or patients: F Montagne, D Delacour, JM Baste; (IV) Collection and assembly of data: F Montagne, JM Baste; (V) Data analysis and interpretation: F Montagne, JM Baste; (VI) Manuscript writing: All authors; (VII) Final approval of manuscript: All authors.

Correspondence to: Jean-Marc Baste, MD, PhD. Department of General Thoracic Surgery, Rouen University Hospital, 1 rue de Germont, 76000 Rouen, France. Email: jean-marc.baste@chu-rouen.fr.

Abstract: Thymectomy remains a therapeutic challenge in elderly patients with thymoma associated with myasthenia gravis (MG). Thymectomy, in the multimodality therapy of these patients should be discussed by multidisciplinary expert teams. Available data show that robotic thymectomy seems to be as safe and as effective as an open procedure with better short-term outcomes and with at least the same quality of oncologic resection. Nevertheless, data are limited on the safety and effectiveness of robotic thymectomy in elderly patients. We present here, our surgical technique of robotic radical *en bloc* thymothymectomy that we use in all our patients with thymoma associated with MG, with particularities related to elderly patients. We also review the medical and surgical literature on robotic thymectomy for thymoma and MG. The robotic platform allows us to “mimic an open procedure by a minimally invasive approach”, and thus, we are able to perform a complete and radical thymothymectomy comparable to open procedure with the same quality of oncologic resection, but with the advantages of a minimally invasive approach regarding short-term outcomes.

Keywords: Minimally invasive surgery; robotic thymectomy; myasthenia gravis (MG); thymomatous myasthenia gravis; case report

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Introduction

Despite technological progress and surgical advances, some procedures remain therapeutic challenges in some populations. Thymectomy in elderly patients with thymoma associated with myasthenia gravis (MG) is one such example.

Most thymomas are found in adult patients, with a peak incidence in the 7th decade of life, but thymomas associated with MG are typically diagnosed in the 5th decade. MG

is a rare autoimmune disorder characterized by muscle weakness caused by the production of autoantibodies against acetylcholine receptors or other molecular components at the neuromuscular junction. MG is the most common parathymic syndrome and occurs in 45% of patients with thymoma, more often B-type thymomas (1). MG incidence is increasing worldwide, and also in the elderly population (2).

The treatment of thymoma involves a combination

^ORCID: 0000-0002-1739-4523.

of surgery, radiotherapy and chemotherapy, and each therapeutic combination is guided by the stage of the disease (3). *En bloc* thymothymectomy is the surgical procedure recommended for stage I and II thymoma and is defined as the removal of the thymoma, the thymus with the anterior mediastinal fatty tissue, and the mediastinal pleura. For stage III and IV thymoma, according to the Masaoka Koga classification (4), surgery—*en bloc* resection of the tumor and of the adjacent overgrown structures—is one treatment in the overall multimodality therapy.

In thymoma associated with MG, the oncologic imperative of the thymoma remains, but there is also the question of MG with the existence of thymic islands located in the pericardial and perithymic fatty tissue. Thymectomy is performed as part of the multimodality therapy of MG since Blalock *et al.* (5) first reported a complete remission of MG after thymectomy in 1939. Thymectomy must always be adapted to the patient in order to perform the most “complete” or “radical”, but also the least morbid resection, and accounting for intensive care monitoring in case of a postoperative myasthenic crisis. The question of the preservation of the phrenic nerve is one such an example, it’s crucial to preserve it in cases of MG, but for advanced stages of thymoma, it could be spared, instead of being cut, at the expense of more local recurrences, but without affecting overall survival (6).

Many approaches have been described such as the “maximal” thymectomy by an *en bloc* transcervical-transsternal resection of Jaretzki *et al.* (7) during the 80’s. During the 90’s, at the beginning of minimally invasive surgery, video-assisted thoracoscopic surgery (VATS) thymectomy was developed (8,9), and at the end of the 90’s, Zielinski *et al.* (10) developed a transcervical-subxiphoid-videothoracoscopic approach for non-thymomatous MG. Yoshino *et al.* (11) were the first to report the successful use of the da Vinci robotic system with a thymothymectomy procedure for a stage I thymoma, and similarly for Ashton *et al.* (12) with a thymectomy for a non-thymomatous MG. Today, it is accepted that robotic-assisted thoracoscopic surgery (RATS) thymectomy is a safe procedure, with fewer complications and adverse events, with a lower positive margin rate for a comparable operative time compared to open thymectomy (13) for early-stage thymomas and also for larger thymomas superior to 6 cm wide (14). When compared to VATS, RATS allows the surgeon to mimic open thymectomy, with the benefits of both a minimally invasive approach and an open sternotomy.

There are few data concerning thymectomy for elderly MG patients. Recently Li *et al.* (2) reported good results in

favor of performing robotic thymectomy for MG patients older than 60 years with a statistically significant steroid-sparing effect. Our clinical case echoes the article of Li *et al.* (2), with a particular question, “How far to go?”. In an elderly patient with MG, with a lesion that seemed to be a thymoma on CT-scan, how should we perform the resection of the pericardial fatty tissue? What are the limits of our resection? Should we always be “maximalist” as Jaretzki for example? We present the following case in accordance with the CARE reporting checklist (available at <https://jovs.amegroups.com/article/view/10.21037/jovs-20-128/rc>).

Clinical case description

An 80-year-old woman, usually treated for high blood pressure, was referred to neurology unit. She presented a left eye ptosis associated with fluid dysphagia evolving for 4 months, and her clinical condition corresponded to Myasthenia Gravis Foundation of America (MGFA) grade IIIA (15). The diagnosis of MG was confirmed by laboratory investigation—sero-positivity for the autoantibody against acetylcholine receptor—and by electromyography—post-synaptic decrement signal. The first CT-scan only showed hyperplasia of the mediastinal fatty tissue, without thymoma-like tumor. Treatment with ammonium chloride allowed rapid correction of her symptoms. Six months later, she had a hip prosthesis, and was treated for a zona of the right buttock during her postoperative rehabilitation. Back home, 2 months after her hip surgery, she had an episode of myasthenic crisis with respiratory failure that required mechanical ventilation. She was intubated for 14 days, a tracheostomy was done and finally removed one month after symptoms onset. During the myasthenic crisis, she was treated with intravenous infusion of immunoglobulin for 3 days and corticotherapy was introduced. A new CT-scan was done—2 years after her first neurologic consultation—and described an anterior mediastinal tumor comparable to an early-stage thymoma, measuring 35 mm by 25 mm by 19 mm (*Figures 1,2*). Four months after the resolution of her myasthenic crisis, after multidisciplinary discussion, the patient was referred to our thoracic unit. Symptoms of MG were under control with ammonium chloride—10 mg 3 times a day—and a corticosteroid therapy—25 mg in the morning. We decided to perform a RATS radical thymothymectomy by a left-sided approach, with two objectives. The first one was to protect the patient from scalability of the thymoma and the second one was to stop her steroid therapy. The patient gave her informed consent

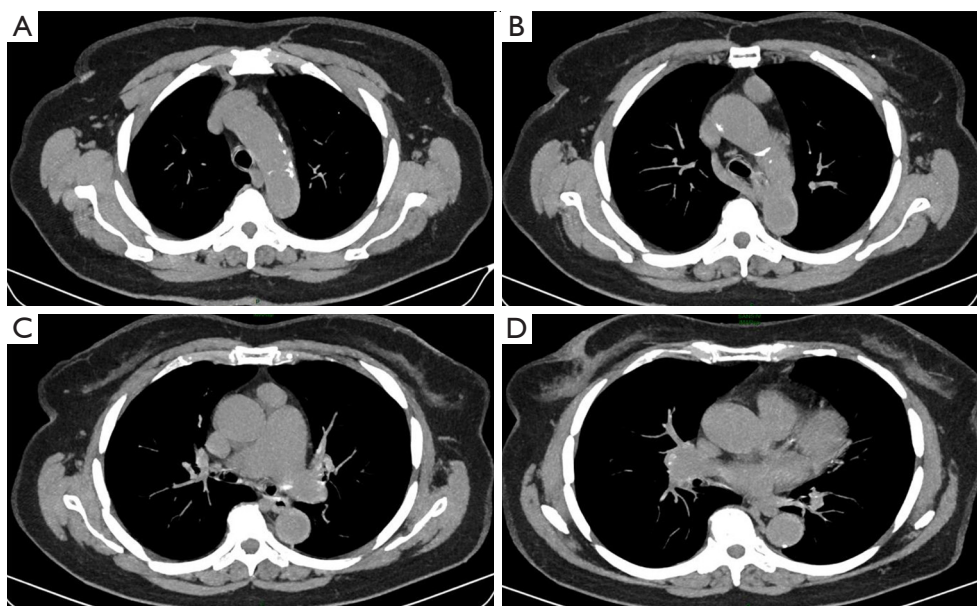


Figure 1 CT scan of our patient with transversal slides. (A) Drainage level of the left internal mammary vein in the superior vena cava; (B) upper part of the thymoma; (C) pulmonary artery trunk; (D) inferior part of the anterior mediastinal fatty tissue.

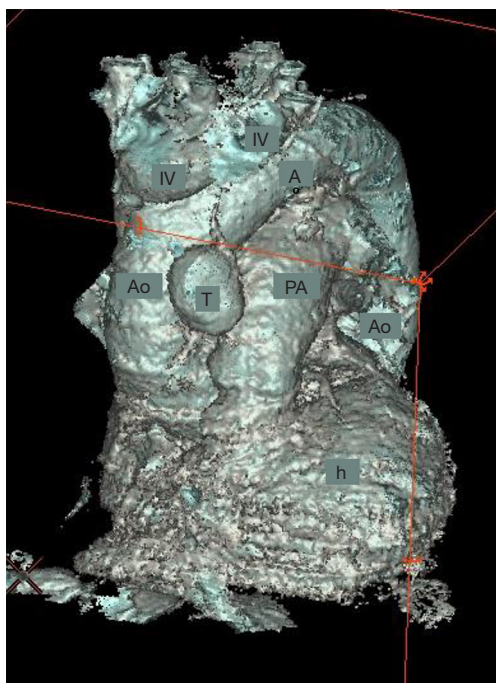


Figure 2 Three-dimensional representation of the thymoma (T) on the heart (h), and its vessels, with the pulmonary artery (PA), the aorta (Ao), and the innominate vein (IV).

to use and published medical information and the surgical procedure video recording. All procedures performed in this study were in accordance with the Helsinki Declaration (as revised in 2013).

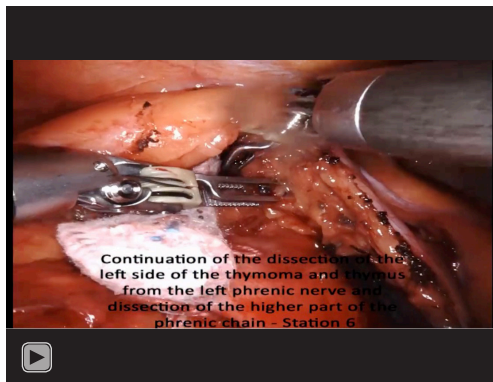
Pre-operative preparation

The choice of the side

The side approach is based on the presence of unilateral tumor predominance, the size and the shape of the thorax, the size of the heart and also the surgeon's experience. We usually perform a left-sided approach—for 80% of our patients—in order to better control the upper part of the left phrenic nerve, but, the disadvantage of the left approach is to dissect tangentially the innominate vein. Conversely, with a right-sided approach, the innominate vein may be dissected more safely but the left phrenic nerve may be injured during the dissection of the left upper horn due to its lateral situation. For this case of a left-sided thymoma, we performed a left-sided approach.

Patient installation

Under general anesthesia, the patient was ventilated through a left-sided double lumen endotracheal tube. The



Video 1 Robotic radical Thymothymectomy for a thymomatous myasthenia gravis in an elderly patient. Surgical procedure performed with the da Vinci X platform.

patient was placed supine with the body moved to the left edge of the operating table. Her left arm was parallel to the table, but in a lower position, in order to facilitate the left-sided thoracic access, and her right arm was placed alongside her body. The left shoulder should be positioned as low as possible. One of the most common technical issues is to have insufficiency clearance between the cranial trocar and the shoulder, when this arm is directed medially. The operative body position was “fixed” using a vacuum beanbag. The skin was marked at the position of the trocar incisions and the sternotomy incision. The operative field was scrubbed, sterilized, and draped exposing the chest from the left posterior axillary line to the right anterior axillary line to ensure enough area for the 3 robotic ports and the assistant port and also to convert to sternotomy if necessary.

Equipment preference and Robotic setting

We use now the da Vinci X System (Intuitive Surgical, Sunnyvale, CA, USA). We first placed an 8 mm port at the fifth intercostal space on the anterior axillary line and inserted the 8 mm 30° angled da Vinci camera before insufflating carbon dioxide (CO₂) to a pressure of 5 mmHg at the beginning through this port. Under vision control, with the 30° up camera, we placed the cranial port in the third intercostal space medially to the anterior axillary line, and the caudal port in the fifth intercostal space medially to the mid-clavicular line. If, there is insufficiency clearance between the cranial port and the shoulder, a long robotic port may be helpful. The 10 mm assistant-

port, dedicated to CO₂ insufflation using the iFS AirSeal™ system, was then inserted medially to the optical-trocar in the sixth intercostal space. Then, the patient-cart (Intuitive Surgical, Sunnyvale, CA, USA) was docked by aligning the thymoma, between the patient cart and the camera. Under vision control, with the 30° up camera, we introduced the Maryland bipolar forceps (Intuitive Inc., Sunnyvale, CA, USA) into the cranial port and the fenestrated bipolar forceps (Intuitive Inc., Sunnyvale, CA, USA) into the caudal port for a left-sided approach. The CO₂ insufflating pressure was increased to a maximum of 8 to 10 mmHg.

Surgical technique and procedure

Tips and tricks, “Basics of anterior mediastinal robotic dissection”

In our opinion, anterior mediastinal robotic dissection complies with 4 rules: “*en bloc*”; “no touch”; “stay and play”; “the right camera angle for each dissection area”.

We usually perform an *en bloc* resection of the thymus, and the thymoma with its fatty tissue and also use a “no-touch” thymectomy technique to minimize tumoral seeding and bleeding. We repress the thymus by using the Endowrist system and the back of our forceps and by using a rolled compress, rather than grasping it. When the optical camera is correctly placed, we usually “stay and play”, we dissect everything that can be easily dissected, before moving the camera, to reduce unnecessary and dangerous forceps movements. During each step of the dissection, it is important to use the right camera angulation. The 30° down camera is used during the dissection of the thymus from the pericardium, near the phrenic nerve, or in the contralateral pleural space cavity. The 30° up camera is used during the dissection of the thymus from the sternum, from the opposite mediastinal pleura, in the angle between the left phrenic nerve and the sternum and during the dissection of the upper thymic poles.

Surgical technique of a radical thymectomy and thymomectomy:

The first step is the exploration of the left thoracic pleural space, before beginning the resection. A radical thymectomy including a thymomectomy (*Video 1*) begins by dissecting the left-sided pericardiophrenic fatty tissue from the pericardium, the phrenic nerve, and the opposite mediastinal pleura. Before dissecting this fatty tissue from

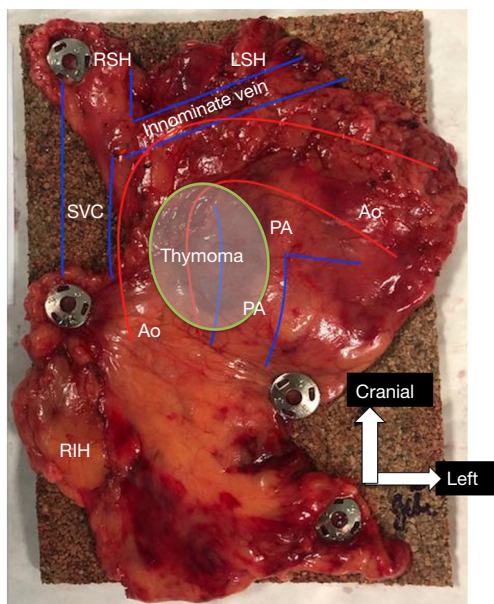


Figure 3 Specimen with anatomical landmarks: thymoma; innominate vein; aorta (Ao); pulmonary artery (PA); superior vena cava (SVC); right superior thymic horn (RSH); left superior thymic horn (LSH); right inferior thymic horn (RIH); and the pericardial anterior fatty tissue.

the sternum, it is important to completely dissect it from the pericardium as this facilitates its exposure. When the inferior side is dissected, the dissection can be continued on the contralateral mediastinal pleura and the sternum.

Going up, we continue the dissection of the thymus and the thymoma. We continue first on the pericardium side, then near the phrenic nerve and after against the contralateral mediastinal pleura and the sternum. During the dissection from the phrenic nerve, extreme caution is required to prevent any mechanical or thermal injury. We leave some fatty tissue on the nerve instead of resecting this nerve with the thymoma if the phrenic nerve is free of tumoral infiltration.

The dissection progresses cautiously in the angle between the left phrenic nerve and the sternum, and slowly, until the dissection of the innominate vein. In this area the phrenic nerve, the innominate vein, or the internal mammary veins could be injured. The dissection is done in the lower part, by taking care not to injure the thymic vein, and in its upper part by the resection of the left and the right upper horns and the fatty tissue from the thyrothymic ligament. Upper horns are dissected by gentle caudal traction and arteries and venous branches are electrocoagulated. When the

upper thymic horns are completely dissected, the dissection of the innominate vein is continued in the direction of the superior vena cava by gentle caudal traction of the thymus. During this step, the thymus can be gently removed from the right pleural space. To improve the visualization of the phrenic nerve, the left angle between the phrenic nerve and the sternum, or the pericardium side, the dissected specimen can be mobilized in the right pleural space.

The dissection is continued in the angle between the innominate vein and the superior vena cava and the sternum, until the end of the dissection. In order to prevent any right-sided phrenic nerve, the 30° down camera can be used at the end of the dissection of the fatty tissue from the superior vena cava.

End of the robotic procedure

The *en bloc* specimen of radical thymectomy including the thymoma is placed at the left apical pleural cavity. The operating field is examined to ensure that there is no bleeding, no innominate injuries or no phrenic nerve injuries. An Endobag (Applied, Rancho Santa Margarita, CA, USA) is used to extract the specimen. It is important to perform an accurate utility thoracotomy incision in order to avoid any capsule breach of the thymoma. This incision is made by removing the assistant trocar. A 20 Portex® (Smiths Medical, Minneapolis, MN, USA) chest tube is inserted and placed transmediastinally in order to drain the two pleural cavities. Finally, the left lung is inflated under vision control. Thoracic drainage can be avoided by removing the thoracic chest tube at the last skin suture in straightforward cases if the patient is free of chronic obstructive pulmonary disease or emphysema. But for MG patients, the chest tube can be removed at postoperative day 1 because they will be monitored in ICU and in our thoracic unit. Port incisions are closed with absorbable sutures. The specimen (*Figure 3*) is disposed on an anatomical support.

Post-operative management

After surgery, the patient was monitored in the postoperative intensive care unit during the first 24 hours and then in our thoracic unit before she was discharged home at postoperative day 4. The chest tube was removed at postoperative day 1. The patient ate early in a chair at postoperative day 0, and walked at postoperative day 1. The patient's treatment for MG was not changed during her hospital stay.

Discussion

An *en bloc* extended thymothymectomy should be performed by an experienced thoracic surgeon (16) in MG patients with a thymoma in order to completely remove the tumor. Minimally invasive procedures as VATS and RATS remain controversial for thymic malignancies (17) due to the fear of a possible breach of the tumor capsule precipitating local and pleural seeding and the uncertainty of acquiring sufficient oncologic margins.

Marulli *et al.* (18) in 2016 reported a multi-institutional European experience of robotic thymectomy for thymoma, including 134 RATS procedures, 52% with MG. Twelve patients (8.9%) were converted to open surgery for technical reasons, but there was no vascular or nerve involvement. Postoperative complication rate was 17.1%. The mean diameter of the resected thymoma was 4.4 cm, with Masaoka stage I for 46 patients (34.4%), stage II for 71 patients (52.9%), stage III for 11 patients (8.3%) and IVa/b for 6 patients (4.4%). The 5-year survival rate was 97% and only one patient had a pleural recurrence.

In a recent meta-analysis and systematic review including 30 studies with 2,038 patients with thymic malignancies, VATS and RATS approaches allowed safe resection with the same oncologic outcomes compared to an open procedure (17) in Masaoka stage I and II thymic malignancy. In the minimally invasive group, authors observed significantly less blood loss ($P<0.001$) and a shorter length of hospital stay ($P<0.001$) but not a significantly lower rate of postoperative pulmonary ($P=0.64$) and cardiac complications ($P=0.52$) with VATS and RATS thymectomy compared to the open group. Nevertheless, VATS and RATS allowed the same quality of oncologic resection, without differences observed in R0 margin resections ($P=0.60$) and locoregional recurrences ($P=0.46$) compared to open procedure. Moreover, in the subset of patients with Masaoka stage I or II thymic malignancies, there was no difference in R0 margin resections ($P=0.88$) and locoregional recurrence rate ($P=0.39$). When RATS thymectomy was compared to VATS thymectomy, there was no statistical difference concerning short-term outcomes reported as blood loss, conversion rate, postoperative complications and hospital length of stay except a longer operating duration in the RATS group (19,20).

RATS offers the advantages of a minimally invasive approach as VATS, but its ergonomic benefits overcome the technical and methodological limitations of VATS (20), and finally RATS allows surgeons to “mimic an open

procedure by a minimally invasive approach”. The robotic surgical system with its high-resolution, three-dimensional vision, and its improved dexterity of instruments with 7 degrees of freedom allowing complex three-dimensional movements, has significantly increased the safety and the oncologic effectiveness of robotic thymectomy. Moreover, for large thymomas exceeding 4 cm, the robotic approach is safe and effective (14) compared to open procedure, with less blood loss ($P=0.001$), shorter length of hospital stay ($P=0.034$), low conversion rates, 15%, without any major vascular injuries, and one of the most important criteria of oncologic quality, no difference concerning R0 margins ($P=0.62$). Rather than the absolute size of the thymoma, it is important to evaluate the ratio between the size of the thymoma and the size and the shape of the thorax. Thus, a lesion of the same size, for example 4 cm, could be easily removed from a patient with a large chest, e.g., in a young man of 185 cm, but represent a surgical challenge in a patient with a thinner thorax, e.g., in an elderly woman of 160 cm with a “big heart”.

Tips and Pitfalls, and other surgical considerations of our case warrant discussion. A robotic approach was obvious for this elderly patient with early-stage thymoma associated with MG, and the real challenge was to perform the adequate resection of the thymoma, the thymus and the anterior mediastinal fatty tissue with the least possible risk. Our functional priority here was, and still is to preserve the left and right phrenic nerves. Therefore, we decided to keep a small margin of fatty tissue between the nerve and our resection in order to prevent any lesion. Our first priority is to prevent any vascular injury. This same margin should also be kept in the innominate vein and the superior vena cava if there is a high risk of vascular injury. The dissection of the cranial fatty tissue should be cautious, millimeter per millimeter to avoid any bleeding complications. During the dissection of the innominate vein, we usually electro coagulate thymic veins away from the innominate vein keeping a stump that can be compressed if necessary. Our second priority is oncology, by preventing tumor seeding by a capsule wound. Therefore, we usually perform a “no touch technique” and only manipulate fatty tissue so that the thymoma is never exposed, except on its pericardial side. Moreover, we manipulate the thymus and the fatty tissue with great caution. In elderly patients, the resection of the thymoma is first and foremost essential and there is no need to take any extra risk by dissecting the phrenic nerves, the innominate vein and the superior vena cava. At the end of the procedure when we extract the thymoma, we always use

a bag, and we enlarge the incision of the assistant trocar in order to facilitate the extraction of the resected specimen to avoid any capsule breach that may complicate the pathology analysis.

Some medical considerations of our case also warrant discussion. A robotic approach was obvious for this elderly patient with early-stage thymoma associated with MG to facilitate recovery. At the present time, her corticosteroid therapy was interrupted without any complications. The pathology analysis revealed a B1/B2 thymoma, stage I according to the Masaoka-Koga classification and stage pT1aN0 according to the WHO classification. The nodes were free of metastasis. Many microscopic thymic cysts were observed around the thymoma.

Conclusions

Robotic radical thymothymectomy seems to be safe and effective in the multimodality therapy of thymoma associated with MG in elderly patients. These patients should be evaluated by a multidisciplinary team, and then referred to an expert surgical team. This procedure must be well prepared and performed in compliance with 4 rules: “no touch”, “*en bloc* resection”, “stay and play”, and “the right camera angle for each surgical area”. RATS allows us to “mimic an open procedure by a minimally invasive approach”, and thus, we are able to perform a complete and radical thymothymectomy comparable to open procedure with the same quality of oncologic resection, but with the advantages of a minimally invasive approach regarding short-term outcomes.

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Footnote

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Ethical statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. All procedures performed in this study were in accordance with the Helsinki Declaration (as revised in 2013). The patient gave her informed consent for this publication.

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