Institutional report - Thoracic non-oncologic
Extended videoscopic robotic thymectomy with the da Vinci telemanipulator for the treatment of myasthenia gravis: the Vienna experience

Tatjana Fleck, Michael Fleck, Michael Müller, Helmut Hager, Walter Klepetko, Ernst Wolner, Wilfried Wisser.

Abstract

Surgical treatment of myasthenia gravis should include the complete resection of the thymus with the whole fatty tissue adherent to the pericardium for immunologic as well as oncologic reasons. The aim of the current study was to investigate the efficacy and safety of robotic approach. A total of 18 patients with myasthenia gravis (mean age 44 years) have been operated robotically via a left-sided approach. Preoperative MGFA (Myasthenia Gravis Foundation of America) classification was: Class I n=4, Class Ila n=4, Class IIb n=5, and Class IIIa n=3, IIIb n=2. Total endoscopic resection was feasible in 17/18 patients. One patient had to be converted due to bleeding. In the remaining patients, operative time was 175 min, intensive care unit (ICU) one day, hospital stay four days. In all patients it was possible to perform an extended thymic resection. MGFA post-intervention status after a mean of 18 months follow-up showed complete stable remission n=5, pharmacologic remission n=4, minimal manifestations n=5, unchanged n=1. Complete endoscopic thymus surgery with the da Vinci surgical system enables a complete and extended resection of all thymic tissue in the mediastinum. Due to the minimal trauma, patients can return to full activity within a short time.

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Keywords: Myasthenia gravis; Thymectomy; Robotics; Outcomes; Minimal invasive surgery

1. Introduction

Myasthenia gravis is an autoimmune disorder, due to the presence of acetylcholine receptor antibodies generated in the thymus, which results in weakness of striated muscle fibers.

Symptoms range from only mild weakness of certain muscle groups to severe generalized weakness involving the respiratory muscles.

In 1941, Alfred Blalock established thymectomy as a treatment for myasthenia gravis [1]. Since then, various operative approaches have emerged, however, with none being the gold standard. There is considerable evidence to suggest that the more extensive the resection is, the outcome is generally better [2, 3].

Surgical therapy of myasthenia gravis necessitates the complete removal of all thymic tissue as well as fatty tissue in the anterior mediastinum, as it has been shown that ectopic thymic isles may be found in the fatty mediastinal tissue [2, 3].

However, one has to balance between the extent of resection, morbidity, patient acceptance and results.

It was the aim of this study to evaluate whether the above-mentioned goals can be achieved with videoscopic robotic resection.

2. Material and methods

From December 2004 to January 2008, a total of 18 patients (female n=11, male n=7) with a mean age of 42±19 years, ranging from 14 to 82, underwent a thymectomy using a left-sided approach with the da Vinci telemanipulator (Intuitive Surgical, Sunnyvale, California, USA) at the department of cardiothoracic surgery at the Medical University of Vienna.

Diagnosis was based on clinical criteria, as well as by electromyography, tensilon test and the presence of acetylcholinesterase antibodies.

Preoperative evaluation included neurologic assessment, CT-scan, lung function test. Unfortunately, we were not able to retrieve information about the duration of symptoms. In 12 patients (71%) the acetylcholinesterase antibodies (ACR AK) were positive with a mean of 9.035±11 pmol/ml.

Preoperative and postoperative clinical staging was assessed by the MGFA (Myasthenia Gravis Foundation of America) classification [4].
MGFA clinical classification preoperatively is depicted in Table 1.

Preoperative medication consisted of anticholinesterase agents and/or steroids in 14 (82%) patients. Details are displayed in Table 2.

### 2.1. Operative technique

We used a left-sided approach in all patients.

Under general anesthesia and selective single lung ventilation the patient was positioned in a left-sided 30% elevated lateral decubitus position.

Port placement consisted of the camera port in the fourth ICR anterior axillary line. Instrument ports were placed in the third ICR midaxillary line and fifth ICR midclavicular space. A 30° camera endoscope was introduced and CO₂ inflation with a target pressure between 6–12 mmHg was started.

Dissection began at the left pericardiophrenic angle along the left phrenic nerve.

The left inferior horn of the thymus was located and dissected from the pericardium and the thymic gland was dissected from the retrosternal area.

Thereafter, preparation of the thymic veins after locating and isolating the innominate vein was performed.

This was followed by preparation of the pericardiophrenic angle on the right side and the dissection of both upper thymic poles.

At conclusion, exploration of the right pleura after locating the right phrenic nerve was done.

Then the specimens were placed in 1–3 endobags and removed over the left port.

One 24Fr chest tube was inserted through the left port incision. The left lung was inflated under direct vision.

### 3. Results

In 17 out of 18 patients (success rate 95%) the procedure was carried out endoscopically, with the extent of resection described in the material and methods section.

Mean operating time was 175±6 min, ranging from 105 to 210 min, which was dependent on the amount of fatty tissue.

Ventilation time after the end of operation was a mean 120±262 min, with the intention to extubate the patient in the operating room. However, this was not possible in all patients due to logistic reasons (safe transfer of the patient, time to clear the operating room).

Intensive care unit (ICU) stay was one day in all patients and hospital stay was a mean of 4±1.8 days. Chest tubes could be removed after one day, with a mean output of 150±50 ml.

<table>
<thead>
<tr>
<th>Table 1</th>
<th>MGFA clinical classification preoperatively n=18</th>
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</thead>
<tbody>
<tr>
<td>Class I</td>
<td>n=4                                      22%</td>
</tr>
<tr>
<td>Class IIA</td>
<td>n=2                                     11%</td>
</tr>
<tr>
<td>Class IIB</td>
<td>n=6                                     33%</td>
</tr>
<tr>
<td>Class IIa</td>
<td>n=3                                     17%</td>
</tr>
<tr>
<td>Class IIIb</td>
<td>n=2                                    11%</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Table 2</th>
<th>Preoperative medication</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cholinesterase inhibitors</td>
<td>n=13</td>
</tr>
<tr>
<td>Daily dosage</td>
<td></td>
</tr>
<tr>
<td>120 mg</td>
<td>n=1 (8%)</td>
</tr>
<tr>
<td>180 mg</td>
<td>n=5 (40%)</td>
</tr>
<tr>
<td>240 mg</td>
<td>n=3 (24%)</td>
</tr>
<tr>
<td>300 mg</td>
<td>n=4 (36%)</td>
</tr>
<tr>
<td>Prednisolone</td>
<td>n=1</td>
</tr>
</tbody>
</table>

Mortality was 0% and two patients (12%) experienced a major morbidity, namely a bleeding from the innominate vein, which required conversion to sternotomy and a chylothorax, which resolved with diet.

Minor morbidity was observed in 5 (27%) patients and was due to pain at the port incisions sites (lasting for a mean of four weeks). There were no wound infections and no nerve injuries.

Histology revealed a normal thymus in nine patients, thymic hyperplasia n=2, and thymoma in six patients (Masaoka stage I n=2, and Masaoka II n=4).

In these patients the thymoma was further defined as Masaoka and the corresponding WHO classification: II-B2, I-B2, II-B3, I-B2, II-B3 and II-B2-3.

In these cases there was no evidence of thymoma in the preoperative CT-scan.

Evidence of ectopic thymic tissue in the mediastinal fat was present in n=3.

Follow-up was a median of 18 months (ranging from 2 to 33 months) and in 84% (15/18) complete, as one patient was converted and two patients were lost.

MGFA therapy status after 16 months (n=15) was no therapy in seven patients (47%), seven patients were still on a reduced dose of cholinesterase inhibitors (47%) and one patient was on a triple therapy with cholinesterase inhibitors, prednisolone and imurek (7%). Refer to Table 3. MGFA change in status (after 16 months) was improved n=14 (93%) and unchanged n=1 (7%).

MGFA post-intervention status after 16 months follow-up (n=15): four patients were in complete stable remission (27%), pharmacologic remission was present in n=6 (40%) and minimal manifestations were detectable in n=5 (33%) (Table 3).

Regarding quality of life, patients had pain at the incision site for approximately one month. Return to sedentary work was possible after one week and light sports activity was possible after a mean of one month (2 weeks–3 months) in 17/18 patients.

<table>
<thead>
<tr>
<th>Table 3</th>
<th>MGFA post-intervention status after 16 months follow-up (n=15, 2 patients were lost to follow-up, 1 converted)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Complete stable remission (CSR)</td>
<td>n=4 27%</td>
</tr>
<tr>
<td>Pharmacologic remission (PR)</td>
<td>n=6 40%</td>
</tr>
<tr>
<td>Minimal manifestations (MA)</td>
<td>n=5 33%</td>
</tr>
<tr>
<td>MGFA therapy status</td>
<td></td>
</tr>
<tr>
<td>No therapy (NT)</td>
<td>n=7 47%</td>
</tr>
<tr>
<td>Cholinesterase inhibitors (CH)</td>
<td>n=7 47%</td>
</tr>
<tr>
<td>CH and PR and IM</td>
<td>n=1 7%</td>
</tr>
</tbody>
</table>

PR, prednisolone; IM, immunosuppression.
Thymectomy is suggested as a proven therapeutic option in the treatment of myasthenia gravis. However, the surgical approach and extent of resection is still a matter of debate. Even though consensus exists, regarding that, the entire thymus gland and possible ectopic tissue in the anterior mediastinum has to be removed, the approach to accomplish these goals remains controversial.

When we look into the literature, we learn that transcervical thymectomy is limited to the removal of the intracapsular portion of the central cervical mediastinal lobes. Therefore, it is associated with a high residual thymus rate and hence, a high reoperation rate [3].

Extended transcervical thymectomy with a special manubrium retractor as proposed by Cooper et al. [4], wanted to overcome this problem. It has the same extension as transsternal resection, but does not remove mediastinal pleura sheets.

Video-assisted thymectomy unilateral (classic VATS) or bilateral (VATET) appear to be less extensive as the transsternal approach, or at least equal [6, 7].

Transsternal thymectomy, standard or extended, is limited to the removal of the cervical-mediastinal lobes as originally proposed by Blalock and Keynes. Findings of residual tissue in the neck and mediastinum, however, often result in an incomplete resection [8].

Therefore, combined transternal and cervical thymectomy was implemented, which consists of en bloc removal of all thymus in the neck and mediastinum. It is the benchmark operation, where other approaches are to be compared with [8].

The negative aspect of this maximal invasive operation are the certain aspects of myasthenia patients, namely:

- Patients are often under immunosuppressive medication which leads to a delayed wound healing.
- Myasthenia gravis patients have a reduced respiratory function caused by alveolar hypoventilation which increases the risk of atelectases and the risk of pneumonia [12].
- The cosmetic aspect in these often young patients.

The da Vinci system (Intuitive Surgical, Mountain View, CA) consists of a master console and a surgical manipulator (slave unit) with two instrument arms and one camera arm. The surgeon operates the master handles at the console, which translate the position and motion of the hands over highly sensitive motion sensors to the end of the instruments at a remote location. System load especially at the entry points is minimized by remote center kinematics.

The instrument arms have a total of six degrees of freedom. The system provides motion scaling, tremor filter and the possibility to disconnect the slave from the master to enhance precision and to ensure optimal hand–eye alignment. The camera consists of two 3D CDD cameras with 800 pixel resolution.

The extended thymectomy with the da Vinci system with the above-mentioned advantages facilitates thoracoscopic thymectomy and leads to a more radical resection with minimal (less) invasive impact for the patient. The system has the advantage of articulating instruments and which is superior over the fixed instruments in VATS surgery, as they imitate the human wrist and enable free motion in a three-dimensional space [9].

This might also be the reason for the low conversion rates in robotic thymectomy. We had to convert one patient (1.8%) which is in the range of the other robotic groups [9, 12]. In contrast, VATS procedures are associated with a conversion rate of around 19% [15].

We used a left-sided approach based on a paper by Rückert et al., who investigated the radicality of thymectomy depending on a right- or left-sided approach by an anatomical study. He favors the left-sided approach because the larger side of the thymus is on the left side and the aortopulmonary window is easier to reach, which is a frequent side of ectopic thymic tissue [10, 11]. Furthermore, it is easier to identify the left phrenic nerve, which is mandatory in this patient population, as a phrenic nerve injury might exacerbate the already compromised alveolar function as mentioned by Rea et al. [12].

Our follow-up period is relatively short, but there is a trend towards improvement of symptoms as defined by the MGFA which is in accordance with a paper by Cakar et al. who followed their patients 13 months after robotic thymectomy [13].

It is interesting to note, that we did not find a correlation between the change of status in comparison to the underlying histology, e.g. thymoma vs. non-thymoma MG. This might be caused by the relatively short follow-up in our series and has to be determined in a longer follow-up study.

The complication rate in our cohort was very low, with no mortality and only one case of conversion. This bleeding incidence from the innominate vein occurred early in our experience, and would not be a cause for conversion in our present experience. Especially no wound infections occurred in our cohort, which is a frequent problem in the maximal invasive approaches.

Our remission rate was 27% after 16 months which is slightly better than reported in the literature, however, depending on the surgical approach used.

Tomulescu et al. evaluated 107 patients after unilateral thoracoscopic resection and had a remission rate of 15% after 24 months [14], whereas Manulu et al. had a 22.2% (after 69 months) remission rate (n=36) after the same procedure [15].

The advantage of the robotic system is the fact that it enables optimum access and visibility to the anatomic structures, so that a radical and complete resection can be performed without injuring a vital structure.

The two upper poles of the thymus can be completely visualized and resected and all the cervical portion of the thymus radically removed, thus isolating the innominate vein and carotid artery. A radical and complete resection can be performed without injuring a vital structure. In addition, all the mediastinal fat on the pericardium down to the diaphragm can be accessed easily through the same approach.
5. Conclusion

Minimal invasiveness does not necessarily lead to minimal accessibility. The ultimate goal of thymectomy, namely the resection of the entire thymus as well as ectopic tissue, is often the limiting factor in maximal invasive approaches. However, this can be easily accomplished with the da Vinci system as it combines an optimal access and radical resection with minimal invasiveness.

This less invasive approach might lower the threshold of neurologists to refer their patients to surgery. Furthermore, re-entry into the chest can be easily accomplished after a robotic procedure.

We are aware of the limitations in our study, namely the small patient number and the short follow-up.

References