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Robotic thymectomy for thymomas: a retrospective follow-up study in the Netherlands

Running Head: Long-term outcomes after RATS

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Disclosures

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Abstract

Background: The Maastricht University Medical Center+ (MUMC+) is a Dutch center of expertise, appointed by the Netherlands Federation of University Medical Centres (NFU), for the treatment of thymomas. The aim of this study was to investigate the long-term oncological-, surgical-, and neurological outcomes of all patients who underwent a robotic thymectomy for a thymoma at the MUMC+.

Methods: We retrospectively analyzed the clinical-pathological data of all consecutive patients with a thymoma who underwent robotic thymectomy using the DaVinci® Robotic System at the MUMC+ between April 2004 and December 2018. Follow-up data were collected from 60 referring Dutch hospitals.

Results: In total, 398 robotic thymectomies were performed and 130 thymomas (32.7%) were found. Median follow-up time, procedure time and hospitalization were 46 months, 116 minutes and 3 days, respectively. In 8.4% of the patients a conversion was performed and in 20.8% a complication was registered. The majority of myasthenic patients with a thymoma went into remission, mostly within 12 to 24 months after thymectomy (81.0%). No statistical difference was found in the number of complications, conversions, incomplete resections or deaths between patients with myasthenia gravis and nonmyasthenic patients. Thirty-six patients (27.7%) underwent postoperative radiotherapy. The recurrence rate was 9.1% and the five-year thymoma-related survival rate was 96.6%.

Conclusions: Robotic thymectomy was found to be safe and feasible in early-stage thymomas, most advanced-stage thymomas and thymomatous myasthenia gravis. A national guideline could contribute to the improvement of the oncological follow-up of thymic epithelial tumors in the Netherlands.

Key words: thymomas, robotic thymectomy, follow-up
The Netherlands Federation of University Medical Centres (NFU) has appointed two academic hospitals as centers of expertise for the surgical care of patients with thymic epithelial tumors (TETs) for a total of population of 17.48 million people.\textsuperscript{1-3} The Maastricht University Medical Center+ (MUMC+) is one of these two centers, with a special interest in thymectomy by robotic-assisted thoracoscopic surgery (RATS). Indications for thymectomy include all mediastinal tumors that are suspected of being a thymoma, myasthenia gravis (MG), and thymic cysts.\textsuperscript{4-6} Minimally invasive approaches, such as RATS, are increasingly being performed for the resection of thymomas. Achieving a thymectomy with free margins is the most important prognostic factor for survival in patients with a thymoma.\textsuperscript{7} The aim of this study was to investigate the long-term oncological-, surgical-, and neurological outcomes of all patients who underwent RATS for a thymoma at the MUMC+.

**Material and Methods**

*Study population*

We retrospectively analyzed the clinical-pathological data of all consecutive patients with a thymoma who underwent RATS using the DaVinci® Robotic System at the MUMC+ between April 2004 and December 2018. Because most of the patients were referred to the MUMC+ for thymectomy only, the follow-up data were requested from eight referring Dutch university hospital centers and 52 general hospitals with the written consent of the patients. This study was approved by the ethics committee of the MUMC+ (METC number: 2018-0491 and amendment 2018-0491-A-9). Patients under 18 years old and patients with (radiological) suspected thymic carcinomas were excluded from this study. Patients were excluded from robotic surgery if they had insufficient lung capacity for single-lung ventilation (forced vital capacity <70%), all other patients were initially operated by RATS. If anti-AChR-antibodies were present, a neurological assessment was performed before thymectomy and patients were monitored more closely on respiratory failure after thymectomy. MG was subclassified as clinical MG or subclinical MG, depending on symptoms at the time of thymectomy.\textsuperscript{8} The clinical severity of MG was classified using the criteria of the Myasthenia Gravis Foundation of America (MGFA). Preoperative radiological evaluation was performed with at least one computed tomography (CT) scan or Magnetic Resonance Imaging (MRI) scan of the thorax. Positron emission tomography (PET) was not performed standardly, only when metastatic disease (e.g. thymic carcinoma or other mediastinal tumors) was suspected.

*Surgical technique*

Prior to surgery, the surgical strategy was discussed by a multidisciplinary team, including a pulmonologist, radiologist and surgeon. Surgical procedures were performed with the DaVinci® Robotic Surgical System (Intuitive Surgical, Sunnyvale, CA, USA). All robotic thymectomies were performed using a right-sided approach, except for thymomas located on the left side. The robotic procedures were performed by one or two surgeons trained in robotic surgery. The patients were
operated on under general anesthesia and intubated with a double lumen tube. Patients were placed in the supine position and the middle part of the thorax was elevated to 30 degrees at the incision site, taking care that the patient’s shoulder remained lying flat on the table to prevent interference with the movement of the robotic arm. Three ports in the anterior axillary line through the third, fourth and sixth intercostal space. The latter being used for removal of the specimen at the end of the procedure. Specimens were removed from the thoracic cavity using endobags with various sizes and strengths depending on the size of the tumor. In accordance with the guidelines of the International Thymic Malignancy Interest Group (ITMIG), the thymomas were resected using the ‘no-touch’ and ‘en bloc’ strategies.\(^7,9\) A small pleural drainage catheter was introduced through a separate stab incision. The procedure time was defined as the time from the first incision until the closure of the skin. Myasthenic patients were seen by a neurologists before thymectomy. The anesthesiologist took into account the patients’ history and use of medication and adapted according to this his anesthetic drug regimen. Patients were immediately weaned from the ventilator in the OR and subsequently taken care of in a postoperative care unit with special attention for the occurrence of a myasthenic crisis for two to three hours after which the patient was brought to the general ward.

**Postoperative care**

The period of hospitalization was recorded in days, from the day of surgery until discharge from hospital. Operative mortality was defined as death within 30 days after surgery or during the same period of hospitalization. Complications were registered and classified in accordance with the Clavien-Dindo classification.\(^10\) In myasthenic patients, worsening of symptoms or signs of a myasthenic crisis were reasons for consultation with a neurologist during hospitalization.

**Pathological evaluation**

Complete resection (R0) was defined as no evidence of residual tumor tissue. Incomplete resection was defined as microscopic (R1) or macroscopic (R2) evidence of residual tumor tissue. Thymomas were histologically classified by the WHO Histological Classification of Thymomas. Tumor invasion was classified by the Masaoka-Koga Staging System and TNM Classification of Malignant Tumors.\(^11\) Early-stage thymoma was defined as Masaoka-Koga stages I and II / TNM < T3N0M0, and advanced-stage thymomas was defined as Masaoka-Koga stages III and IV / TNM ≥ T3N0M0. All resection specimens were discussed by a multidisciplinary team including a pulmonologist, pathologist, radiologist, surgeon and radiation oncologist.

**Adjuvant therapy and follow-up**

In accordance with the ESMO guidelines, postoperative radiotherapy (PORT) was advised in B3 thymomas, incomplete surgical resection and after complete resection of stage III/IV thymomas.\(^5\) For oncological follow-up, a postsurgical CT scan was advised six weeks after thymectomy followed by a yearly CT scan for the first five years, and every other year for the following six years. In total, at least
11 years of follow-up was advised in all patients with a thymoma. Because most patients were referred to the MUMC+ for thymectomy only, the MUMC+ gave postsurgical advice about oncological treatment, and the referring hospitals carried out adjuvant therapy and follow-up. Improvement in MG status was quantified according to the MGFA post-intervention status classification. The interval from thymectomy to the recurrence, the disease-free interval (DFI) was defined as the period from the first thymectomy to the diagnosis of recurrence.

Statistical analysis

Descriptive statistics are reported as mean and standard deviation (SD), median and interquartile range (IQR). The survival probabilities were calculated by the Kaplan–Meier method from the date of the thymectomy until death. The differences in survival were evaluated with the log-rank test. Statistical significance was considered to have the probability value of p < 0.05. Statistical analysis was performed with SPSS statistical software (IBM SPSS Statistics for Windows, Version 25.0. Armonk, NY: IBM Corp).

Results

From April 2004 to December 2018, 398 robotic thymectomies were performed at the MUMC (Supplemental Figure 1). All 130 thymomas were included in this study. Seven patients (5.4%) did not provide informed consent for this study, and eight patients (6.2%) were lost to follow-up. Baseline characteristics are shown in Table 1. There was an equal gender distribution. Mean age was 58.9±13.4 years and nonmyasthenic patients were significantly older than patients with MG (65.6 vs. 55.9 years, p<0.001). Median follow-up time was 46 months (IQR: 50 months).

Surgical outcomes

All surgical outcomes are shown in Table 2. No perioperative deaths were reported. Median procedure time was 116 minutes (IQR: 63 minutes) and median hospitalization was 3 days (IQR: 2 days). An advanced-stage thymoma was found in 15.4% of the patients. A R0-resection was performed in 111 patients (85.4%), and more commonly in early-stage thymomas (94.5%). Incomplete resections were predominantly found in advanced-stage thymoma (68.4%) and B2/B3-thymoma (73.7%). Advanced-stage thymoma was found significantly more in patients with an incomplete resection (p<0.001). Median size of the thymomas was after resection 4.6 cm (0.5-19.0) and 43.1% of the thymomas was more than five centimeter. Resections of pericardium, lung and phrenic nerve were performed in 24 patients (18.5%), and patients with advanced-stage thymoma had significantly more extended resections (p<0.001). The presence of MG did not lead to a significant statistical difference in diameter or stage of the thymoma. No significant statistical difference was found in surgical outcomes between patients with MG and nonmyasthenic patients. The reasons for nine planned conversions were debulking of stage III
thymomas (in 3 patients, 2.3%), stage IV thymomas (in 2 patients, 1.5%), thymomas larger than 100mm (in 3 patients, 2.3%), and a difficult-to-reach location of the thymoma in the sinus of the diaphragm (in 1 patient, 0.8%). In one patient (0.8%) an unplanned conversion was registered due to a hemothorax (conversion to thoracotomy). Especially the microscopic camera view during RATS was a benefit to inspect the phrenic nerve and pleura carefully with a non-invasive technique, before conversion to an open approach took place. According to the Clavien-Dindo classification, the severity of complications was classified as Grade I (6 events), Grade II (17 events), Grade IIIA (6 events), Grade IIIB (2 events), Grade IVA (4 events), Grade IVB (0 events) and Grade V (0 events). Postsurgical diaphragmatic palsy as a result of manipulation or resection of the phrenic nerve was seen in 10 patients (7.7%). In four patients the phrenic nerve was consciously sacrificed and in three others an attempt was made to spare the phrenic nerve. In six patients diaphragmatic palsy was described in radiological follow-up and considered to be a permanent consequence of surgery. There was no difference in the number or severity of complications between patients with an early-stage thymoma and those with an advanced-stage thymoma. Moreover, there was no significant difference in the number or severity of perioperative complications between patients with MG and nonmyasthenic patients.

**Oncological outcomes**

All oncological outcomes are shown in Table 3. The oncological follow-up was available in 110 patients (84.6%). Neo-adjuvant chemotherapy was performed in six patients (4.6%), of which five patients underwent a biopsy before neo-adjuvant chemotherapy was started. All patients who received neo-adjuvant chemotherapy had a tumor size more than 10cm on imaging and in five patients extended invasion of surrounding tissue was reported. Patients with early-stage thymomas had a significantly smaller size thymoma compared with advanced-stage thymomas (p = 0.031). In 39 patients (30%) PORT was advised, and eventually performed in 36 patients. Patients with MG underwent PORT significantly more frequently than nonmyasthenic patients (37.1% vs. 7.3%, p<0.001). In three patients known with stage III/IV thymomas, adjuvant chemotherapy was advised in addition to PORT. In total, ten recurrences of thymoma were described. In 100 patients no recurrence has appeared and in 20 patients no data were available. Therefore, the recurrence rate in patients who had a complete follow-up was 9.1%. Three patients experienced a recurrence twice. The median disease-free interval (DFI) in patients with a recurrence of thymoma was 36 months (IQR: 44 months). The recurrences were either predominantly local or discovered in the pleura. One patient had extensive metastasis of the thymoma in the thoracic wall, lung, pleura, pericardium, diaphragm and lymph nodes. Three patients were treated for the recurrence by a resection, two by radiotherapy and five patients were given best supportive care. Patients with a history of an advanced-stage thymoma had significantly more recurrences than patients with early-stage thymoma (p<0.001). As shown in Figure 1, the five-year overall survival rate was 90.4%. The five-year thymoma-related survival rate was 96.6%. Patients with an early-stage thymoma had a significantly longer overall survival time compared with patients with an advanced-stage thymoma.
(127.3 vs. 84.0 months p=0.022) (Figure 2). The mean survival time of patients with MG was not significantly different to that of nonmyasthenic patients, as shown in Figure 3. The five-year thymoma-related mortality rate was 3.4%. In total, mortality after thymectomy was reported in 19 patients after a medium follow-up of 65 months (IQR: 61). There was no significant difference in the number of deaths, or time until death between myasthenic patients and nonmyasthenic patients.

Neurological outcomes
All neurological outcomes are shown in Table 4. In total, 89 patients (68.5%) were diagnosed with MG, of which 11 patients had subclinical MG. Follow-up data were available from 77 patients (86.5%). The majority of the patients had had positive anti-AChR-antibodies (97.8%), and symptoms of MG for less than 12 months (58.4%). At the time of thymectomy, the majority of the patients was treated with immunosuppressive therapy (49.4%) or cholinesterase inhibitor monotherapy (36.0%). In total, 48 patients (53.9%) went into remission at least once during follow-up. Most patients experienced remission within 24 months after thymectomy (81.0%), with the majority in the first year (54.8%). Overall, 49.4% had improved by the end of the follow-up, 11.2% had improved but suffered from exacerbations of MG, 16.9% had an unchanged clinical score, 7.9% had worsened symptoms and 1 patient (1.1%) died of a myasthenic crisis. All seven patients with CSR had mild-moderate MG (MGFA 0-IIB). Of the patients with worsened MG, subclinical MG was found in six out of seven patients.

Comment
In this study, we investigated the long-term outcomes of 130 patients with a thymoma who underwent a thymectomy by RATS. With a mean procedure time of two hours, no intraoperative mortality and a median hospitalization of three days, we conclude that a minimally invasive surgical technique such as RATS is particularly suitable and beneficial for the treatment of most thymomas. Neither patients with an advanced-stage thymoma nor those with myasthenia gravis (MG), had a higher complication rate than patients with early-stage thymomas and nonmyasthenic patients. Also, additional resections of pericardium, lung and phrenic nerve can successfully be performed with RATS. Previous literature shows that RATS is safe and feasible in patients with early-stage thymomas, large thymomas, and for selected advanced thymomas.13-16 Additionally, we conclude that RATS is also a safe and feasible procedure for patients with thymomatous MG.

The MUMC is a tertiary referral center in the Netherlands that is specialized in RATS for thymomas and myasthenia gravis. The transition from VATS and open approaches to robotics started in 2004 as at that time our first robotic surgical system became available to our surgeons, who were trained to perform minimally invasive cardiac and thoracic surgery. The high number of patients with myasthenia gravis (68.5%), advanced-stage thymomas (15.4%) and thymomas >5cm (43.1%) shown in our series is
probably caused by referral bias. The higher number of patients with PORT in the group with MG could be explained by the higher number of B3 thymomas. Subclinical MG was found in six out of seven patients whose MG worsened after thymectomy. In all probability this was due to the fact that the definition of subclinical MG states that patients do not have symptoms of MG at the time of the thymectomy. Therefore, this group was expected to have a higher risk of worsening than of improvement of the MG. In our opinion, the extensive presurgical and perioperative care for myasthenic thymoma patients at the MUMC led to a lower number of myasthenic complications and deaths than has previously been reported.

The five-year thymoma-related survival rate in this study was 96.6%. Although the survival rate is commonly high in thymomas on comparison with other oncological tumors, high morbidity due to paraneoplastic syndromes and recurrences is common. According to Ruffini et al, a recurrence of encapsulated and non-invasive thymomas is rare (0-5%). Luo et al found that the recurrence rate of invasive thymomas varies from 20-50%. These findings support the results of our study concerning the higher number of recurrences in incompletely resected advanced-stage thymomas. A recurrence diagnosis within 40 months after thymectomy is known to be a negative prognostic factor, whereas a local recurrence and a single recurrence imply a better prognosis. In conclusion, not only the thymectomy itself, but also the oncological follow-up is crucial for the best treatment of thymomas.

Adjuvant oncological treatment and follow-up were performed in the referring hospitals. Although the MUMC works in collaboration and in accordance with international guidelines, the lack of a national protocol could lead to fluctuations in the execution of the oncological advice of the MUMC in those hospitals that perform the oncological follow-up. Furthermore, due to the rare disorder, statistical analyses were not always feasible in this study as a result of small numbers. With an incidence of 0.17 per 100,000 population, thymic epithelial tumors are rare and not standard thoracic disease in clinical practice. In our opinion, thymomas should be treated in centers of expertise that participate in international research and in collaboration with other centers and panels with a high affinity with thymomas worldwide. We support the current setting of two surgical centers of expertise for thymomas in the Netherlands, and would prefer to develop a national system such as the Réseau tumeurs et THYMiques et Cancer (RYTMIC) in France, which provides a national platform for clinical cases of thymic epithelial tumors. Experts give advise about diagnostics, treatment, follow-up and physicians can share questions, doubts and considerations to provide the best care for patients with thymomas. Furthermore, we support the creation of a national protocol and guidelines for the oncological treatment and follow-up of thymomas in The Netherlands.

Conclusions
This retrospective single-center study demonstrates the long-term outcomes of patients with a thymoma after a robot-assisted thymectomy. A robotic thymectomy was found to be safe and feasible in early-stage thymomas, most advanced-stage thymomas and thymomatous myasthenia gravis. The majority of myasthenic patients with a thymoma went into remission, mostly within 12 to 24 months after thymectomy. No statistical difference was found in the outcomes between patients with myasthenia gravis and nonmyasthenic patients. A national guideline would contribute to the improvement of the oncological follow-up of thymic epithelial tumors in the Netherlands.

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Figure Legends

**Figure 1:** Overall survival.

**Figure 2:** Overall survival in early vs. advanced-stage thymomas. There is a significant difference in survival between patients with an early-stage thymoma vs. advanced-stage thymoma, in favor of early-stage thymoma. Early-stage thymoma: Masaoka-Koga stages I and II / TNM < T3N0M0. Advanced-stage thymoma: Masaoka-Koga stages III and IV / TNM ≥ T3N0M0

**Figure 3:** Overall survival in thymomas with/without myasthenia gravis. No statistical difference in survival was found between patients with myasthenia gravis and patients without myasthenia gravis.
Table 1: Baseline characteristics

|                                | Total thymomas N = 130 | Thymomas with Myasthenia Gravis | Thymomas without Myasthenia Gravis | p-value |
|--------------------------------|-------------------------|---------------------------------|------------------------------------|---------|
| Patients, n                    | 89                      | 41                              |                                    | 0.94    |
| Female, n (%)                  | 45 (50.6)               | 21 (51.2)                       |                                    | <0.001  |
| Age at surgery, mean years (SD)| 55.9 (±13.1)            | 65.6 (±11.7)                    |                                    | 0.71    |
| Length of follow-up, mean months (SD) | 52.8 (±38.9) | 50.5 (±39.3) |                                    | 0.09    |
| Neoadjuvant chemotherapy, n (%)| 2 (2.2)                 | 4 (9.8)                         |                                    | N/A     |
| Thymoma diameter >50mm, n (%)  | 34 (38.2)               | 22 (53.7)                       |                                    |         |
| WHO histological type, n (%)   |                         |                                 |                                    |         |
| A                              | 12 (13.5)               | 5 (12.2)                        |                                    | N/A     |
| AB                             | 17 (19.1)               | 16 (39.0)                       |                                    |         |
| B1                             | 2 (2.2)                 | 5 (12.2)                        |                                    |         |
| B2                             | 36 (40.5)               | 9 (22.0)                        |                                    |         |
| B3                             | 22 (24.7)               | 4 (9.8)                         |                                    |         |
| ‘Micronodular’                 | 0 (0.0)                 | 1 (2.4)                         |                                    |         |
| ‘Degenerated’                  | 0 (0.0)                 | 1 (2.4)                         |                                    |         |
| Staging, n (%)                 |                         |                                 |                                    | 0.71    |
| Early-stage thymomas*          | 76 (85.4)               | 34 (82.9)                       |                                    |         |
| Advanced-stage thymomas**      | 13 (14.6)               | 7 (17.1)                        |                                    |         |
| Other paraneoplastic syndromes besides MG, n |         |                                 |                                    | N/A     |
| Aplastic anemia                | 2                       | 0                               |                                    |         |
| Sjögren’s syndrome             | 2                       | 0                               |                                    |         |
| Thyroid diseases               | 2                       | 1                               |                                    |         |
| Rheumatoid arthritis           | 2                       | 1                               |                                    |         |
| Polymyalgia rheumatica         | 1                       | 0                               |                                    |         |
| Hypogammaglobulinemia:         | 0                       | 2                               |                                    |         |
| Inflammatory bowel disease      | 1                       | 1                               |                                    |         |
| Psoriasis                      | 0                       | 1                               |                                    |         |
| Systemic lupus erythematosus   | 0                       | 1                               |                                    |         |
| Vitiligo                       | 0                       | 1                               |                                    |         |

N/A: Not applicable
WHO: World Health Organisation
MG: myasthenia gravis
* Early-stage thymomas: Masaoka-Koga stages I and II / TNM < T3N0M0
**Advanced-stage thymomas: Masaoka-Koga stages III and IV / TNM ≥ T3N0M0
### Table 2: Surgical outcomes

|                                | Thymomas with Myasthenia Gravis N = 89 | Thymomas without Myasthenia Gravis N = 41 | p-value |
|--------------------------------|---------------------------------------|------------------------------------------|---------|
| Hospitalization from day of thymectomy, median days (IQR) | 2 (1-24) | 3 (1-35) | 0.20 |
| Surgical approach, n (%) | | | 0.98 |
| Right-sided RATS | 65 (73.0%) | 30 (73.2%) | |
| Left-sided RATS | 24 (27.0%) | 11 (26.8%) | |
| Additional resected tissue, n patients (%) | | | 0.83 |
| Lung | 13 | 3 | |
| Pericardium | 5 | 6 | |
| Phrenic nerve | 1 | 3 | |
| Great vessels | 0 | 1 | |
| Conversions, n (%) | | | N/A |
| Thoracotomy (planned) | 6 (6.7%) | 4 (9.8%) | |
| Thoracotomy (unplanned) | 0 | 1 | |
| Sternotomy (planned) | 3 | 1 | |
| Sternotomy (unplanned) | 0 | 0 | |
| Complications within 30 days after thymectomy, n (%) | | | 0.48 |
| Myasthenic crisis | 20 (22.5%) | 7 (17.1%) | |
| Increase in myasthenic symptoms | 3 | 0 | |
| Atrial fibrillation | 5 | 0 | |
| Pulmonary embolism | 3 | 2 | |
| Pneumonia | 2 | 0 | |
| Pneumothorax with drain | 1 | 0 | |
| Chylothorax | 1 | 1 | |
| Phlebitis | 1 | 0 | |
| Anemia with transfusion | 1 | 0 | |
| Hemothorax | 0 | 1 | |
| Acute tubular necrosis with dialysis | 0 | 1 | |
| Resection, n (%) | | | 0.59 |
| R0 (complete) | 75 (84.3%) | 36 (87.8%) | |
| R1 (microscopically incomplete) | 13 (14.6%) | 4 (9.8%) | |
| R2 (macroscopically incomplete) | 1 (1.1%) | 1 (2.4%) | |

N/A: Not applicable
Table 3: Oncological outcomes

|                                | Thymomas with Myasthenia Gravis (N = 89) | Thymomas without Myasthenia Gravis (N = 41) | p-value |
|--------------------------------|-----------------------------------------|---------------------------------------------|---------|
| Adjuvant radiotherapy performed, n (%) |                                          |                                             |         |
| Thymoma A                       | 33 (37.1%)                              | 3 (7.3%)                                    | <0.001  |
| Thymoma AB                      | 0                                       | 0                                           |         |
| Thymoma B1                      | 1                                       | 1                                           |         |
| Thymoma B2                      | 11                                      | 1                                           |         |
| Thymoma B3                      | 18                                      | 1                                           |         |
| Adjuvant/second-line chemotherapy, n (%) |                                          |                                             | N/A     |
| Yes: 7 (7.9%)                   | Yes: 3 (7.3%)                           |                                             | N/A     |
| No: 67 (75.3%)                  | No: 33 (80.5%)                          |                                             |         |
| N/A: 15 (16.9%)                 | N/A: 5 (12.2%)                          |                                             |         |
| Time to recurrence after thymectomy, median months (IQR) | 38 (78)                               | 24 (24)                                     | N/A     |
| Mortality after thymectomy, n (%) |                                          |                                             | 0.28    |
| Thymoma A                       | 2                                       | 0                                           |         |
| Thymoma AB                      | 0                                       | 6                                           |         |
| Thymoma B1                      | 0                                       | 0                                           |         |
| Thymoma B2                      | 7                                       | 0                                           |         |
| Thymoma B3                      | 2                                       | 2                                           |         |
| Time till death after thymectomy, median months (IQR) | 84 (60)                               | 49.5 (46)                                   | 0.18    |

N/A: Not applicable
Table 4: Neurological follow-up of patients with myasthenia gravis

| Total patients, n | 89 |
|-------------------|----|
| **Duration of MG before thymectomy, n (%)** |     |
| <12 months        | 52 (58.4%) |
| 12-24 months      | 15 (16.9%) |
| 25-36 months      | 3 (3.4%)   |
| 37-48 months      | 2 (2.2%)   |
| >60 months        | 6 (6.7%)   |
| Subclinical MG    | 11 (12.4%) |
| **Anti-AChR-antibodies, n (%)** |     |
|                  | 87 (97.8%) |
| **Therapy for MG at time of surgery, n (%)** |     |
| No therapy        | 13 (14.6%) |
| Cholinesterase inhibitor monotherapy | 32 (36.0%) |
| Immunosuppressive drugs | 44 (49.4%) |
| **Presurgical MGFA classification (at the latest two months before thymectomy), n (%)** |     |
| 0                 | 13 (14.6%) |
| I                 | 16 (18.0%) |
| IIA + IIB         | 44 (49.4%) |
| IIIA + IIIB       | 14 (15.8%) |
| IVA + IVB         | 1 (1.1%)   |
| V                 | 1 (1.1%)   |
| **Remission of MG after thymectomy, n (%)** |     |
| CSR               | 7 (7.9%)   |
| PR                | 10 (11.2%) |
| Minimal manifestations | 37 (41.6%) |
| No remission      | 23 (25.8%) |
| N/A               | 12 (13.5%) |
| **MGFA postoperative change score, n (%)** |     |
| Improved          | 44 (49.4%) |
| Improved with exacerbations | 10 (11.2%) |
| Unchanged         | 15 (16.9%) |
| Worsened          | 7 (7.9%)   |
| Died              | 1 (1.1%)   |
| N/A               | 12 (13.5%) |

*MG: Myasthenia gravis
MGFA: Myasthenia Gravis Foundation of America
CSR: Complete stable remission
PR: Complete stable pharmacological remission
N/A: Not applicable*
| TIME (MONTHS) | 0  | 12 | 24 | 36 | 48 | 60 | 72 | 84 | 96 | 108 | 120 | 132 | 144 | 156 | 168 |
|---------------|----|----|----|----|----|----|----|----|----|-----|-----|-----|-----|-----|-----|
| PATIENTS AT RISK, N | 150 | 115 | 101 | 77 | 65 | 53 | 36 | 27 | 19 | 13 | 9 | 8 | 4 | 1 | 0 |
| NUMBER OF DEATHS, N | 0  | 2  | 3  | 2  | 1  | 2  | 2  | 3  | 0  | 1  | 1  | 0  | 0  | 0  | 0  | 0  |
