



Li, F., Takahashi, R., Bauer, G., Yousef, M-S., Hotter, B., Swierzy, M., McAleenan, A., Ismail, M., Meisel, A., & Rückert, J-C. (2019). Results of Robotic Thymectomy Performed in Myasthenia Gravis Patients Older Than 60 Years at Onset. *Annals of Thoracic Surgery*, *108*(3), 912-919. https://doi.org/10.1016/j.athoracsur.2019.02.016

Peer reviewed version

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Link to published version (if available): 10.1016/j.athoracsur.2019.02.016

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Results of robotic thymectomy performed in myasthenia gravis patients older than 60 years at onset

**Running Head:** Robotic thymectomy in MG patients > 60 years at onset

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#### Meeting Presentation: No.

Classifications: Robotics; Thymectomy; Myasthenia gravis; Thymoma, thymic carcinoma

#### Word Count: 4552

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# Abstract

**Background** Data are limited on the safety and efficacy of robotic thymectomy in myasthenia gravis (MG) patients older than 60 years at onset.

**Methods** Patients older than 60 years at MG onset who underwent robotic thymectomy in Charite Universitaetsmedizin Berlin between 2003 and 2017 were potentially eligible for inclusion. The main outcomes were perioperative complications and clinical outcome according to the MG Foundation of America Post-Intervention Status (MGFA-PIS).

**Results** Sixty-eight (25 females, 43 males) of 580 MG patients who underwent robotic thymectomy were eligible for perioperative analyses (median age at MG onset 67 years [range 61-85]). The perioperative morbidity rate was 13.2% and the only perioperative mortality was due to aortic dissection. Fifty-one patients were available for further analysis with a median follow-up time of 60 months (range 12-263). The complete stable remission (CSR) rate was 7.8%, the improvement rate was 68.6% and the overall mortality rate was 11.8%. Compared with preoperative use, the average daily dose of corticosteroids was significantly reduced at the last follow-up (17.6 $\pm$ 23.6 VS 2.6 $\pm$ 6.1 mg, *P*=0.0001) without increased use of azathioprine (35.9 $\pm$ 61.9 VS 42.7 $\pm$ 59 mg, *P*=0.427). After excluding two patients seronegative for the antiacetylcholine receptor (AChR) antibody, 10 out of 49 seropositive patients achieved "good outcome" (including four CSR, three pharmacologic remission and three minimal manifestations 0) which was predicted by being free of concomitant disease (OR: 7.307, 95% CI (1.188-44.937), *P*=0.032) and MGFA classification I prethymectomy (OR: 6.696, 95% CI (1.259-35.620), *P*=0.026).

**Conclusion** Robotic thymectomy seems to be safe and effective in MG patients older than 60 years at onset with a significant steroid-sparing effect.

### Introduction

Myasthenia gravis (MG) is a rare autoimmune disorder characterized by muscle weakness caused by the production of autoantibodies against acetylcholine receptors (AChR) or other related molecules at the neuromuscular junction. The annual incidence of MG is estimated at 8 to 10 per million population and the prevalence at 150 to 250 per million (1). During the last few decades the incidence of MG in the elderly has been increasing worldwide (2-3).

Thymectomy has become an indispensable option in the multidisciplinary management of MG since Blalock et al. first reported a complete remission of MG after thymectomy about 80 years ago (4). Since then, thymectomy has gained increasing acceptance and many approaches have been described (5, 6). As the latest advance of minimally invasive thymectomy, robotic thymectomy has been performed in patients with MG since 2003 (7). Available data have shown that minimally invasive thymectomy via video-assisted thoracoscopic surgery (VATS) approach or robotic-assisted approach can result in equivalent clinical outcome with reduced postoperative pain, less perioperative complications, quicker recovery and shorter hospital stay, when compared with extended transsternal thymectomy (8-10). Recently, a randomized controlled trial in MG patients aged between 18 and 65 years old demonstrated better clinical outcomes in patients who underwent extended transsternal thymectomy compared to those who did not (11). Regarding thymectomy in elderly MG patients, however, most researchers consider it as a risky and less effective intervention.

In this study, we aimed to investigate the safety and efficacy of robotic thymectomy in MG patients older than 60 years at onset, providing evidence to counsel these patients who are contemplating undergoing thymectomy.

#### **Patients and Methods**

This is a monocentric observational retrospective study. The ethics approval for this study was granted by the Ethics Committee of Charite Universitaetsmedizin Berlin (Berlin, Germany). Written informed consent was obtained from each patient included in this study.

We included patients with a confirmed diagnosis of MG, with disease onset after 60 years of age, who underwent robotic thymectomy at the thoracic surgery department in the Charite Universitaetsmedizin Berlin between 2003 and 2017. We excluded patients who were 60 years or younger at disease onset and patients with unspecified age at onset.

The diagnosis of MG was confirmed by the presence of relevant clinical symptoms and either seropositive autoantibody status (mostly anti-AChR antibody [above 0.45 nM] or anti-muscle-specific kinase [MuSK] antibody [above 0.4 U/ml]); response to acetylcholinesterase inhibitors; or positive electrophysiologic electrophysiologic findings (including repetitive nerve stimulation and single fiber electromyography) (12). Since thymoma is associated with MG in about 15% patients (13), a computed tomography (CT) scan of the chest was performed before thymectomy in all patients to screen for thymoma. Indication for thymectomy was not limited by age but poor general condition and geriatric multimorbidity, such as severe coagulopathy, recent myocardial infarction, pleural symphysis and poor lung function (FEV1 <30% and/or DLCO <30%).

Patients without a suspected thymoma have been operated by a left-sided three-trocar approach for robotic thymectomy, in patients with a suspected thymoma a unilateral approach was chosen according to the location of the lesion. In rare cases, an extra trocar at subxiphoid was used to ensure the complete removal of the specimen. Typically, an enbloc resection including the thymus, thymoma (if any) and all mediastinal fatty tissue was performed by the authors. The "no touch" surgical technique was used in patients with a suspected thymoma.

Preoperative and perioperative data were collected retrospectively from the hospital information system, including the presence of concomitant disease (defined here as hypertension, dyslipidemia, diabetes mellitus [DM], coronary heart disease [CHD] and arrhythmia). Perioperative complications were reported according to a standardized classification system after thoracic surgery (14). We divided patients into two subgroups according to the presence of a thymoma, preoperative clinical parameters and perioperative parameters were compared between the two subgroups.

After excluding patients with a follow-up less than 1 year, we assessed clinical status of the patients at a final follow-up using a structured telephone interview based on a questionnaire. In the case of patients who were not able to answer the questionnaire, we interviewed close family members who were familiar with the disease course. Based on the response to the questionnaire, we assessed the clinical state of the patients according to the MG Foundation of America Post-Intervention Status (MGFA-PIS), and divided patients into those who experienced a "good outcome" (defined as complete stable remission [CSR], pharmacologic remission [PR] and minimal manifestations 0 [MM-0]), or "poor outcome" (minimal manifestations 1-3 [MM 1-3]).

SPSS 21.0 software (IBM Corp., Armonk, NY, USA) and GraphPad Prism 5.0 software (GraphPad Software, Inc., La Jolla, CA, USA) were used to perform the statistical analyses. Continuous variables were summarized as median (range) and analyzed by Mann Whitney test, whilst categorical variables were summarized as proportions and analyzed by Chi-Squared test or Fisher's Exact test. Missing data were treated as unknown data points, but the medications of the six deceased patients at the last follow-up were handled via last observation carried forward approach. Binary logistic regression models were performed to determine the association of clinical characteristics with "good outcome" of robotic thymectomy in MGpatients older than 60 years at onset. Variables with a *P* value smaller than 0.1 on univariate analyses were included in the multivariable binary logistic regression model and *P*<0.05 was considered statistically significant.

# Results

Five hundred and eighty patients with MG underwent robotic thymectomy in the Charite Universitaetsmedizin Berlin between 2003 and 2017 (Figure 1). After excluding 395 patients who were 60 years or younger at MG onset and 117 with unspecified age at onset, 68 patients were older than 60 years at MG onset. The series comprised 25 females (37%) and 43 males (63%) with a median age at MG onset of 67 years (range 61-85). Table 1 shows the detailed preoperative clinical parameters of patients with thymomatous MG and non-thymomatous MG. In our series, the female:male ratio was significantly different between thymomatous MG (1.27:1) and non-thymomatous MG (0.34:1) (P=0.012). There were also statistical differences between the two groups in symptoms at onset (P=0.036), thymectomy delay (P=0.022) and medications (P=0.010).

Table 2 summarizes perioperative clinical parameters in patients with thymomatous MG and non-thymomatous MG. There were no significant differences. One out of 68 patients underwent a conversion to median sternotomy for the injury of the left innominate vein. The median length of hospital stay in our series was 5 days (range 2-77). The patient with a 77 days of hospital stay experienced worsening symptoms after thymectomy and died of MG. Perioperative complications occurred in 9 out of 68 patients and are described in Table 3 according to Seely et al. (14). Among the nine patients with perioperative complications, one also experienced perioperative MG crisis and was treated with plasmapheresis. Thymic follicular hyperplasia occurred in six (14%) non-thymomatous MG patients, leaving 37 (86%)

findings of involution. In 25 thymomatous MG, follicular hyperplasia was found in six (24%) residual glands, and involution was found in the rest (76%).

After excluding 4 patients with a follow-up less than 1-year and 13 patients who were lost to the last follow-up, 51 patients were available for further analyses with a median follow-up time of 60 months (range 12-263). There were no significant differences between the two subgroups with regard to clinical outcomes (Table 4). Ten patients had a "good outcome" at the last follow-up: four CSR, three PR and three MM-0. Thirty-five of 51 (68.6%) patients showed improvement after robotic thymectomy, leaving eight unchanged, four worse and four died of MG. The other two death were due to stroke 39 months after surgery and myocardial infarction 42 months after surgery (Table 5).

The average number of medications required for MG decreased at the last follow-up, compared with the preoperative period (Figure 2A,  $1.9\pm0.9$  VS  $1.5\pm0.8$ , P=0.025). Although the average daily dose of corticosteroids decreased significantly (Figure 2C,  $17.6\pm23.6$  VS  $2.6\pm6.1$  mg, P=0.0001), the average daily doses of cholinesterase inhibitors (Figure 2B,  $252.7\pm183.2$  VS  $205.5\pm176.0$  mg, P=0.154) and azathioprine (Figure 2D,  $35.9\pm61.9$  VS  $42.7\pm59.0$  mg, P=0.427) did not change statistically between the preoperative period and at the last follow-up. However, three patients who used to take azathioprine were taking mycophenolat mofetil at the last follow-up because of the side effects of azathioprine (leukopenia and liver function test abnormalities), and medications of the six deceased patients at the last follow-up were replaced by their last observational ones.

Since there were only two patients seronegative for anti-AChR antibody, we conducted binary logistic regression models to identify clinical parameters associated with "good outcome" in forty-nine seropositive patients. Univariate analyses identified being free of concomitant disease (Table 6, OR: 5.583, 95% CI (1.138-29.899), P=0.034), purely ocular symptoms at onset (Table 6, OR: 5.575 (1.076-30.720), P=0.041) and MGFA classification I prethymectomy (Table 6, OR: 5.500(1.210-25.005), P=0.027) as potential predictors of "good outcome". In a multivariable analysis, being free of concomitant disease (Table 6, OR: 7.307, 95% CI (1.188-44.937), P=0.032) and MGFA classification I prethymectomy (Table 6, OR: 6.696, 95% CI (1.259-35.620) P=0.026) persisted as independent predictors of "good outcome" after thymectomy. Besides, the predictive factors remained the same when we added back the two seronegative cases in the analyses.

# Comment

To our knowledge, this monocentric retrospective study is the largest series describing the safety and efficacy of robotic thymectomy in patients older than 60 years at MG onset. In our series, men (n=43) outnumbered women (n=25), mainly due to more men developing non-thymomatous MG, which is in line with previous report (3). Besides, patients with thymomatous MG had a shorter thymectomy delay (P=0.022), smaller probability of purely ocular symptoms at onset (P=0.036) and required fewer immunosuppressive medications (P=0.010) compared with patients with non-thymomatous MG, similar to a previous study (15). In our series, the percentage (70.6%) of the MG patients older than 60 years at onset who required immunosuppressive medications was comparable with that (65% to 82.1%) reported previously (16-18). Therefore, it would be advantageous if evidence on steroid-sparing effect of robotic thymectomy in this population could be provided.

The rate of open conversion in our series was 1.5%, which was similar to that (2.4%, 3.1%) reported in previous publications (19, 20). The only conversion in our series occurred in a 73 years male with a 7.7cm Masaoka-Koga stage III thymoma because of the injury of the left innominate vein. The perioperative complication rate of 13.2% was similar to that (15.4%) in a non-robotic thymectomized series including 34 patients older than 50 years at MG onset (21),

but higher than that (5%) in a thoracoscopic thymecomized series with an average age of 29 years at MG onset (22). Another study of 28 cervicomediastinal thymectomized patients older than 55 years also reported a pulmonary complication rate of 5.5% and one mortality because of a pulmonary embolism 3 days after discharge from the hospital (23). The overall mortality rate in our series was 11.8% with a MG specific mortality of 7.8%, which is in line with that (13%) reported in another elderly series (24), but higher than that (0%) in a younger series (22). Therefore, from our experience, robotic thymectomy in MG patients older than 60 years at onset seems to be as safe as non-robotic thymectomy, although might not be as safe as in a non-elderly population. However, comorbidities should be carefully evaluated and considered in the decision making towards thymectomy in patients with non-thymomatous MG. Patients with multimorbidity increasing perioperative risk or reducing the long-term prognosis substantially should be excluded from thymectomy (25).

In 1975, Perlo et al. found 9 cases with involuted thymic tissues and 11 without thymic tissues in 20 autopsies from patients older than 60 years, concluding that thymecotmy is not likely to be effective in this population (26). However, in recent thymectomy series, thymic hyperplasia was seen in 5/39 (12.8%) patients older than 50 years at MG onset (21), in 8/28 (28.6%) patients older than 55 years at onset (23) and in 4/25 (16%) patients older than 60 years at onset (24). Similarly, the rate of thymic hyperplasia in our non-thymomatous MG was 6/43 (14%). Although most of the non-thymomatous MG patients older than 60 years at onset were likely to present with involuted thymus, the authors did not see refusal reasons for thymectomy in this population. First, it is still controversial whether evoluted thymus plays a prognostic role in MG patients (27, 28). Second, MG patients with involuted thymus could be seropositive for anti-AChR antibodies and previous studies have demonstrated that ectopic thymic tissue is likely to be the place where the antibodies are produced in these patients (29-32). Third, although thymectomy was deemed less effective in late-onset MG than in early-onset MG patients, data comparing clinical outcomes between surgical patients and non-surgical controls in MG patients older than 60 years at onset are still limited.

In our series, four patients (7.8%) achieved CSR and 35 patients (68.6%) showed improvement after thymectomy according to the MGFA-PIS, which is comparable with outcomes reported previously in series of elderly patients who underwent extended thymectomy or cervicomediastinal thymectomy (23, 24). Although the rate of remission in elderly MG patients after thymectomy was lower than that reported in non-elderly patients, the rate of improvement was still comparable (22). Importantly, we found that the average daily corticosteroids dose had statistically decreased (P=0.0001) after thymecomy without increasing the average daily dose of azathioprine (P=0.427), which was the most commonly used steroid-sparing drug in our series. Therefore, we deemed that robotic thymectomy was effective for MG patients older than 60 years at onset regarding the long-term neurologic outcome and the steroid-sparing effect.

Being free of concomitant disease and MGFA classification I prethymectomy were independently associated with "good outcome" in our patients. A systematic review also found that preoperative mild disease severity is the most repeatedly reported predictor of remission (28). Although many researchers believe that patients with thymic follicular hyperplasia are more likely to benefit from thymectomy (33-34), neither thymic follicular hyperplasia nor thymoma was associated with "good outcome" in our series, which is also in line with the findings of the systematic review (28).

This study has some limitations. Data were collected retrospectively from the hospital information system, and most missing data were treated as unknown data points. This is a single arm case series, the absence of the comparison is a major limitation of our research. We have not systematically assessed the number of patients having refused thymecomy which

is a further limitation of our study. Besides, 13 out of 64 (20.3%) patients were lost to followup, which also introduced selection bias in this study. Furthermore, patients were not treated by the same neurologist after thymectomy. Also, at the last follow-up, azathioprine was replaced by mycophenolat mofetil in three patients due to side-effects and data for six deceased patients were handled via the last observation carried forward approach, which might introduce bias when evaluating the steroid-sparing effect in this study. Since myasthenic symptoms could be changing over time and some patients might even re-suffer from the symptoms after reaching complete stable remission, this adds difficulty in interpreting the results of our research and is another limitation of our research. Finally, the sample size was too small to draw solid conclusions. However, considering the rarity of the disease, it is virtually impossible to conduct a randomized controlled trial in MG patients older than 60 years at onset, and this is a relatively large series of patients treated using the same surgical technique at a single center. In addition, all patients were well documented during their treatment and followed based on a well-constructed questionnaire.

Robotic thymectomy seems to be safe and effective in patients older than 60 years at MG onset with a significant steroid-sparing effect. In this population, being free of concomitant disease and MGFA classification I prethymectomy appear to be independently associated with "good outcome".

Acknowledgments and Disclosures: None reported.

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Clinical parameters	Total	MG with or w	MG with or without Thymoma		
	(N=68)	Thymomatous MG (n=25)	Non- thymomatous MG (n=43)	-	
Gender, no. (%)				0.012	
Male Female	43(63.2%) 25(36.8%)	11(44%) 14(56%)	32(74.4%) 11(25.6%)		
Age at onset, median	67 (61-85)	68 (61-85)	67 (61-82)	0.601	
(range), yrs BMI ª , median (range), Kg/m²	26 (18.1- 51.1)	24.5 (18.1- 51.1)	26.6 (19.2-39.8)	0.090	
Anti-AChR Ab, no. (%)				0.292	
Positive Negative	65(95.6%) 3(4.4%)	25(100%) 0(0%)	40(93%) 3(7%)		
OAID, no. (%)				0.074	
Yes No	21(30.9%) 47(69.1%)	11(44%) 14(56%)	10(23.3%) 33(76.7%)		
Concomitant disease, no. (%)				0.305	
Yes No	57(83.8%) 11(16.2%)	19(76%) 6(24%)	38(88.4%) 5(11.6%)		
Symptoms at onset, no. (%)				0.036	
Purely ocular symptoms Others Unknown	32(47.1%) 34(50%) 2(2.9%)	8(32%) 17(68%) 0(0%)	24(55.8%) 17(39.5%) 2(4.7%)		
MGFA classification, no. (%)	2(2.070)	0(070)	2(4.770)	0.204	
I I-V	13(19.1%) 55(80.9%)	7(28%) 18(72%)	6(14%) 37(86%)		
MG crisis, no. (%)				1.000	
Yes No	12(17.6%) 56(82.4%)	4(16%) 21(84%)	8(18.6%) 35(81.4%)		
ThX delay, median (range), Mons	9 (1-168)	4 (1-35)	13 (2-168)	0.022	
Medications, no. (%)	- /	- /		<b>0.010</b> <sup>b</sup>	
No medications Cholinesterase inhibitors Corticosteroids Steroid-sparing drugs Both	3(4.4%) 17(25%) 24(35.3%) 5(7.4%) 19(27.9%)	3(12%) 9(36%) 9(36%) 1(4%) 3(12%)	0(0%) 8(18.6%) 15(34.9%) 4(9.3%) 16(37.2%)		
Plasmapheresis and/or IVIg, no. (%)	9(13.3%)	3(12%)	6(14%)	1.000	

 Table. 1 Preoperative clinical parameters of 68 patients older than 60 years at MG onset

a. Data were available for 59 patients (21 thymomatous MG and 38 non-thymomatous MG).

b. Patients who received immunosuppressive medications vs. patients did not, calculated

by Chi-Squared test.

BMI = body-mass-index; Anti-AChR Ab = antibody against acetylcholinesterase receptor; OAID = other autoimmune disease; ThX = thymectomy; IVIg = IV immunoglobulin.

Clinical parameters	Total	MG with or wit	hout Thymoma	P
	(N=68)	Thymomatous MG (n=25)	Non- thymomatous MG (n=43)	value
Open conversion				0.368
Yes No	1(1.5%) 67(98.5%)	1(4%) 24(96%)	0(0%) 43(100%)	
Length of hospital stay, median (range), d Complications <sup>a</sup> , no. (%)	5(2-77)	6(3-20)	5(2-77)	0.085 0.272
None Yes Minor Major Mortality	59(86.8%) 9(13.2%) 5(55.6%) 3(33.3%) 1(11.1%)	20(80%) 5(20%) 3(60%) 2(40%) 0(0%)	39(90.7%) 4(9.3%) 2(50%) 1(25%) 1(25%)	0.272
Weight of the specimen <sup>b</sup> , median (range), g	102 (20 280)	- 87.5 (35-280)	116 (20-274)	0.299
Pathology of the thymus <sup>°</sup> , no. (%) Involution Follicular hyperplasia	56(82.4%) 12(17.6%)	19(76%) 6(24%)	37(86%) 6(14%)	0.335

**Table. 2** Perioperative clinical parameters of 68 patients older than 60 years at MG onset

a. Documented according to Seely et al. (14).

b. Data were available for 54 patients (20 thymomatous patients and 34 non-thymomatous patients).

c. In thymomatous MG, pathology of the residual gland was detected.

Gender	Age at onset, yrs	Delay of ThX, mons.	MGFA class	Thymic pathology	Complication	Grade	Conconmitant disease preThX
Male	79	6	I	Involution	Delirium	I	No
Male	72	3	lla	Thymoma with involution	Tachycardias	II	Hypertension
Male	73	1	llb	Thymoma with involution	Atrial fibrillation	II	No
Male	66	2	llb	Involution	Atrial fibrillation	II	CHD, DM, Hypertension, Arrhythmia
Female	66	14	lla	Thymoma with involution	Pulmonary artery embolism	II	Hypertension
Male	70	15	llb	Hyperplasia	Bradycardia	Illa	DM
Male	72	3	I	Thymoma with involution	Pleural effusion and MG crisis	Illa	Hypertension
Female	62	4	I	Thymoma with involution	Respiratory failure	IVa	Hypertension, DM
Male	74	9	llb	Hyperplasia	Type A aortic dissection	V	Hypertension

 Table. 3 Clinical parameters of 9 patients who experienced postoperative complications

ThX = thymectomy.

Clinical parameters	Total	MG with or without Thymoma		Р
	(N=51)	Thymomatous MG (n=19)	Non- thymomatous MG (n=32)	— value
MGFA-PIS				1.000
Good outcome Poor outcome	10(19.6%) 41(80.4%)	4(21.1%) 15(78.9%)	6(18.8%) 26(81.2%)	
Change in status Improved Unchanged Worse Died of MG	35(68.6%) 8(15.7%) 4(7.8%) 4(7.8%)	12(63.2%) 4(21.1%) 2(10.5%) 1(5.3%)	23(71.9%) 4(12.5%) 2(6.3%) 3(9.4%)	0.517 ª
Medications, no. (%)				0.517 <sup>b</sup>
No medications Cholinesterase inhibitors Corticosteroids Steroid-sparing drugs Both	5(9.8%) 11(21.6%) 9(17.6%) 21(41.2%) 5(9.8%)	1(5.3%) 6(31.6%) 4(21.1%) 6(31.6%) 2(10.5%)	4(12.5%) 5(15.6%) 5(15.6%) 15(46.9%) 3(9.4%)	

**Table. 4** Clinical outcome of 51 patients older than 60 years at MG onset

a. Improved vs. others calculated by Chi-Squared Test.

b. Patients received immunosuppressive medications vs. patients did not, calculated by Chi-Squared Test.

MGFA-PIS = Myasthenia Gravis Foundation of America Post-Intervention Status.

Gender	Age at onset, yrs	ThX delay, mons.	MGFA classification	Thymic pathology	Specific reason of death	Overall survival <sup>a</sup> , mons.
Male	74	9	llb	Hyperplasia	MG	9
Male	69	3	llb	Thymoma with involution	MG	14
Male	78	5	I	Involution	Stroke	44
Female	81	7	llb	Thymoma with involution	Myocardial infarction	49
Male	78	10	IIIb	Involution	MG	51
Male	71	168	V	Involution	MG	180

Table. 5 Clinical parameters of the six deceased patients

a. From disease onset to death.

ThX= thymectomy

	Univariate analysis		Multivariable anal	ysis
Variable	OR (95% CI)	P value	OR (95% CI)	P value
Age at onset, yrs	1.063(0.953-1.186)	0.270	NA	NA
Female	0.400(0.075-2.143)	0.285	NA	NA
BMI, kg/m <sup>2</sup>	0.891(0.725-1.095)	0.272	NA	NA
Being free of OAID	4.500(0.513- 39.436)	0.174	NA	NA
Being free of concomitant disease	5.833(1.138- 29.899)	0.034	7.307(1.188- 44.937)	0.032
Purely ocular symptoms at onset	5.575(1.076- 30.720)	0.041	NA	NA
ThX delay, mons	0.958(0.877-1.046)	0.339	NA	NA
MGFA classification I preThX	5.500(1.210- 25.005)	0.027	6.696(1.259- 35.620)	0.026
Thymic follicular hyperplasia <sup>a</sup>	1.333(0.113- 15.704)	0.819	NA	NA
Thymoma	1.095(0.262-4.572)	0.901	NA	NA

**Table. 6** Binary logistic regression of clinical parameters associated with a "good outcome" in

 49 patients seropositive for anti-AChR antibody

a. Reference = thymic involution

OR = odds ratio; CI = confidence interval; NA = not applicable; BMI = body-mass-index; OAID = other autoimmune disease; ThX = thymectomy.

**Figure 1.** Age split of MG patients who underwent robotic thymectomy between 2003 and 2017 in Charite Universitaetsmedizin Berlin. Five hundred and eighty patients with MG underwent robotic thymecotmy, among whom 463 patients had documented age at disease onset. Sixty-eight out of 463 patients were older than 60 years at MG onset.

**Figure 2.** Average daily medications of the MG patients older than 60 years at onset during the preoperative period and at last follow-up (n=51). Medications of the six deceased patients were handled via Last Observation Carried Forward approach. A. Average number of daily medications for MG during the preoperative period and at the last follow-up. B-D. Average daily dose of cholinesterase inhibitors (B), corticosteroids (C), azathioprine (D) during the preoperative period and at the last follow-up.