JMSR
Journal of Medical and Surgical Research

Research Article

JMSR 2023 Vol X, n 2: 1247-1254

PREDICTIVE FACTORS FOR POSTOPERATIVE MYASTHENIC CRISIS AFTER THYMECTOMY IN MOROCCAN PATIENTS WITH MYASTHENIA GRAVIS: AN ANALYSIS OF 30 CASES.

Fatima Zahra Haddari, Soumaya Touzani, Abderrahim El Bouazzaoui, Nawfal Houari, Brahim Boukatta, Nabil Kanjaa.

Anesthesiology and Intensive Care Department A4, Hassan II[d] University Hospital, Fez, Morocco.

Corresponding address: Fatima Zahra Haddari, Anesthesiology and Intensive Care Department A4, Hassan II University Hospital, Sidi Mohammed Ben Abdellah University, Fez, Morocco;
E-mail: fatimazahrahaddari@gmail.com

doi: 10.46327/msrjg.1.000000000000250
Published in December, 2023

Abstract

Introduction: Myasthenia crisis (MC) occurs in 15 % to 20 % of myasthenia gravis (MG) patients. How to prevent post-operative myasthenic crisis (POMC) is of great importance to the treatment of post-surgery MG patients. **Methods**: Retrospective study including myasthenia patients who underwent thymectomy and were admitted to our unit from January 2013 to December 2019. Variables analyzed were age, gender, history of MC, duration of disease, diagnostic parameters, preoperative functional muscle and Leventhal scores, Ossermann classification, patient comorbidities, treatment, and outcomes. **Results**: Thirty patients were included in this study. The mean age was 36.86 years. The sex ratio M/F was 0.30. Twenty percent of the patients had a history of MC. Bulbar symptoms were present in 50 % of cases. Anti-acetylcholine receptor antibodies were positive in 93 % of cases. The functional muscle score varied between 60 and 100 points with a mean of 83.63 points. The mean vital capacity was 3.302 liters. The Leventhal score was greater than 10 in five patients. Curarization was necessary in 25 patients and monitored in four cases. Surgical approach was median sternotomy in 86.67 % of cases and mean surgery duration was 159.83 minutes. The univariate analysis identified 5 variables significantly ($p < 0.05$) associated with the occurrence of POMC: Leventhal score > 10, weak functional muscle score, low vital capacity, prolonged duration of surgery, and prolonged length of ICU stay. **Conclusion**: Leventhal score > 10, weak functional muscle score, low vital capacity and prolonged surgery duration were independent risk factors for POMC.

Keywords: Morocco, Myasthenia Crisis; Myasthenia Gravis; Risk Factors; Thymectomy.

Introduction

Myasthenia gravis is a rare disorder of neuromuscular transmission that involves generalized or localized weakness with fatigability. Extended thymectomy is the most effective treatment for generalized MG. [1-3]. POMC is a life-threatening complication after thymectomy [4, 5]. It is defined as a rapid onset of respiratory muscle failure requiring invasive or noninvasive mechanical ventilation, and leading to increased hospital stay and medical costs [6]. The incidence of POMC ranges from 6.2 % to 30.3 % [7, 8]. Greater symptomatic stage, bulbar deficiency, preoperative myasthenia crisis (MC), prolonged surgery duration, and thymoma were reported as independent risk factors for POMC in different studies [9-11]. To our knowledge, this is the first study to focus on risk factors of post-thymectomy myasthenic crisis in the Moroccan population and its aim is to update our local protocol for a better perioperative management of myasthenia patients.

Materials and methods

Study design and setting.

In this single-center retrospective observational study, we evaluated patients who underwent thymectomy for systemic myasthenia gravis in the central operating room of our University Hospital and were managed postoperatively in our intensive care unit (ICU) between January 2013 and December 2019. Postoperatively, admission to the ICU was systematic. Patients admitted to the ICU for myasthenic/ cholinergic crisis who did not receive thymectomy or whose records were incomplete and/or not usable were excluded from the analysis. The setting of the study was a 14-bed medico-surgical intensive care unit in a tertiary university hospital in Morocco (ICU A4- Hassan II University Hospital of Fez). POMC is defined as the necessity of prolonged ventilation or re-ventilation after surgery for respiratory failure due to muscle weakness related to myasthenic exacerbation [12]. In this study, the POMC was defined as postoperative respiratory failure requiring a stay in ICU with ventilatory support (invasive or non-invasive) for more than 48 hours or readmission to ICU within 45 days of the surgical intervention.

Data collection.

Study data was collected retrospectively from patients' paper and electronic medical records using the HOSIX electronic data entry tools hosted at our University Hospital. Variables collected included demographic information, diagnostic parameters, preoperative functional muscle and Leventhal scores, and Ossermann classification, patient comorbidities, management, and outcome.

Statistical analysis.

Statistical analysis of the parameters was carried out using SPSS 20 software in the epidemiology laboratory of our Faculty of Medicine and Pharmacy. Factors associated with the occurrence of POMC were analyzed by univariate analyses. Descriptive statistics were used to summarize the basic characteristics of the patients. Results were expressed as numbers and percentages for qualitative variables and as means ± standard deviations (SD) for quantitative variables. Comparison of quantitative and qualitative variables was based on the student t test and the FISHER exact test by univariate analysis, respectively. The threshold of statistical significance was determined at $p = 0.05$. Multivariate analysis was not carried out due to the small sample size.

Results

Characteristics of the study population (Table 1). A total of 30 patients were included in the study. There were 23 women and 07 men. The mean age was 36.86 ± 13.096 years (range 16-62 years), and 60 % of patients were younger than 40 years old.

The mean time from symptom onset to thymectomy was 25.96 months (range 2-120 months). Co morbidities other than myasthenia were reported in 50 % of patients. The most frequent ones were a history of arterial hypertension (6.7 %), asthma (6.7 %), diabetes (3.3 %), epilepsy (3.3 %), and thyroid pathology (10 %) including one case of autoimmune thyroiditis. Twenty percent of our patients had a history of intensive care stay for myasthenic crisis. The mode of discovery of myasthenia was progressive in the majority of cases (90 % versus 10 % of cases). Ocular involvement was present in 86.7 % of cases and ptosis was the most frequent sign. Pharyngo-laryngeal symptoms were present in 50 % of cases as following: dysphagia, dysphonia, nasal voice, false routes and chewing difficulties. Respiratory disorders were noted in 33 % of cases. Electromyogram showed a post-synaptic block of neuromuscular transmission in 87 % of cases and anti-acetylcholine receptor antibodies were positive in 93 % of cases. Pyridostigmine was the most frequently used anticholinesterase (27 cases). Eight patients had combined corticotherapy and one patient required immunosuppressors (Imurel®)). Intravenous immunotherapy and plasmapheresis were necessary preoperatively in 6 and 1 patient retrospectively. Preoperative assessment revealed: a mean functional muscle score of 83.63 points (range from 60 to 100 points), a mean vital capacity (VC) at respiratory functional of 3.302 liters, a Leventhal score less than or equal to 4 in 83 % of cases and greater than or equal to 10 in 5 patients. Anticholinesterase therapy and corticoids were maintained before surgery.

Table 1: Clinical features of patients with myasthenia gravis (*n* = 30).

Variables	Total cohort
Age, y/o	36.86 ± 13.09
Gender, n (%)	
Male	7 (23.3 %)
Female	23 (76.7 %)
Comorbidities, n (%)	
Diabetes	1 (3.3 %)
Hypertension	2 (6.7 %)
Asthma	2 (6.7 %)
Endocrine pathology	3 (10 %)
Smoking	2 (6.7 %)
Previous surgery	4 (13.3 %)
History of Myasthenia crisis	6 (20 %)
History of MG, *mo*	25.96 ± 25.43
Symptomatology, *n* (%)	
Occular disorder	26 (86.7 %)
Bulbar symptom	15 (50 %)
Facial diplegia	4 (13.3 %)
Generalized weakness	24 (80 %)
Respiratory disorders	10 (33.3 %)
Paraclinical tests	
Positive anti-AchR antibodies, n (%)	28 (93.3 %)
Post-synaptic block of neuromuscular transmission, n (%)	26 (86.7 %)
RFT: vital capacity, mean ± SD	3.30 ± 1.03
Preoperative hemoglobin, mean ± SD	13.44 ± 1.64
Symptomatic stage in accordance with modified Osserman's classification, n (%)	
I	4 (13.3 %)
IIa	7 (23.3 %)
IIb	10 (33.3 %)
III	9 (30 %)
LEVENTHAL score > 10, n (%)	5 (16.7 %)
Functional muscle score, mean ± SD	83.63 ± 12.03
Preoperative medical therapy, n (%)	
Mestinon n (%)/dose (mg), mean ± SD	27 (90 %)/224.44 ± 54.16
Mytelase n (%)/dose (mg), mean ± SD	6 (20 %)/ 26.66 ± 19.66
Corticosteroid, *n* (%)/dose (mg), mean ± SD	8 (26.7 %)/ 18.75 ± 14.07
Immunosuppressors, *n* (%)/dose (mg), mean ± SD	1 (3.3 %)/ 150
Immunoglobulins, *n* (%)	6 (20 %)
Plasmapheresis, *n* (%)	1 (3.3 %)
Curarization, n (%)	25 (83.3 %)
Rocuronium, mean ± SD	35.20 ± 9.06
Curarization monitoring, n (%)	4 (13.3 %)
Antagonization with sugammadex, n (%)/dose (mg), mean ± SD	15 (50 %)/ 182.66 ± 36.14
Surgical approach, n (%)	
Trans- sternotomy	26 (86.7 %)
Manubriotomy	01 (3.3 %)
Right triple approach	01 (3.3 %)
Left anterolateral thoracotomy	01 (3.3 %)
VATS	01 (3.3 %)
Epidural analgesia, n (%)	6 (20 %)
Duration of surgery, mean ± SD	159.83 ± 38.78
Postoperative complications, n (%)	8 (26.7 %)
POMC, n (%)	4 (13.3 %)
Length of intensive care unit stay, h	69.60 ± 109.04
Intra-hospital mortality, n (%)	01 (3.33 %)

MG: myasthenia gravis; mo: months; anti-AchR: anti-acetylcholine receptor; RFT: respiratory function test; VATS: video-assisted thoracoscopic surgery; POMC: postoperative myasthenia crisis.

All patients had respiratory physiotherapy and incentive spirometry. Premedication was based essentially on bronchodilators in asthmatic patients and antiepileptics in one epileptic patient. Perioperative antibiotic prophylaxis was not indicated in 56.7 % of our patients. Amoxicillin-clavulanic acid was used in 40 % of cases and cefalotin in only one patient (3.3 %). A list of

prohibited drugs for myasthenic patients was posted in the operating room and in the post-interventional surveillance room (PISR) and attached to the patient charts, to avoid prescription errors. Curarization without monitoring was used in 21 patients and rocuronium was administered at half conventional induction dose (0.3 mg/kg). Mean dose of rocuronium was of 37.14 mg. Curarization with train-of-four (TOF) monitoring (thumb adduction response) was used in 4 patients and mean dose of rocuronium required was of 25 mg. Maintenance of general anesthesia was provided by halogens in 27 patients (sevoflurane in 20 cases and isoflurane in 7 cases) and by propofol and fentanyl via target controlled infusion (TCI) in 3 patients. Perioperative warming and temperature monitoring was systematic. Operative access was done through 26 median sternotomies, one left anterolateral thoracotomy, one manubriotomy, one right triple approach and one video-assisted thoracoscopy (VATS). The surgical procedure consisted of a simple thymectomy in 27 cases and a thymectomy with radical mediastinal lymph node curage in the remaining 3 cases. Mean duration of surgery was 159.83 minutes (Ranges: 90 - 300 minutes). Nineteen patients were extubated in the operating room and 11 patients in the PISR. De-curarization was monitored in 4 cases and sugammadex was used in 15 patients. Early post-operative rehabilitation was applied to all patients on a routine basis and included early mobilization and feeding, respiratory physiotherapy, incentive spirometry and prophylactic non-invasive ventilation using a spontaneous ventilation mode with inspiratory aid and positive expiratory pressure (SV-IA-PEEP). This approach is implemented immediately in the post-operative recovery room. Anticholinesterase and corticosteroid therapies were maintained at the usual doses after surgery. According to our local protocol, all patients have a systematic 24-hour stay in the ICU. The postoperative follow up at 45 days noted complications in eight patients as shown in **table 2**.

Table 2: Postoperative complications.

Complication	Number of cases
Myasthenic crisis	03
Cardiorespiratory arrest post myasthenic crisis	01
Respiratory distress on bilateral postoperative atelectasis	01
Surgical site infection	02
Pericarditis without compression with positive salmonella typhi and paratyphi serologies and positive pleural fluid study for sensitive Pseudomonas aeruginosa.	01

Mean stay in the intensive care unit was 2.9 days. Intra-hospital mortality was 3.33 %. The death case occurred in a 36-year-old woman with a history of metastatic digestive cancer and pulmonary embolism. Follow-up at six months after hospital discharge was possible in only 23 cases. Twenty-one patients had a good evolution under medical treatment with 18 complete remissions, while two patients had a worsening of their condition with the occurrence of acute myasthenia exacerbation.

Univariate analysis of risk factors for the occurrence of postoperative myasthenic crisis. The univariate analysis identified 5 variables that were significantly ($p < 0.05$) associated with the occurrence of post-thymectomy myasthenic crisis in our population (***table 3***): a Leventhal score greater than 10, a reduced functional muscle score, a low vital capacity (VC) on respiratory function test, a prolonged duration of surgery, and a prolonged duration of hospitalization in the intensive care unit.

Table 3: Clinical findings in patients with and without myasthenic crisis after thymectomy.

Factors	POMC (*n* = 4)	Non- POMC (*n* = 26)	*P value*
Age, mean ± SD	45.25 ± 11.44	35.57 ± 13.04	0.137
Female gender, *n* (%)	4 (100 %)	19 (73.07 %)	0.548
Comorbidities, *n* (%)			
Diabetes	0 (0 %)	1 (3.84 %)	1.000
Hypertension	1 (25 %)	1 (3.84 %)	0.253
Endocrine pathology	0 (0 %)	3 (11.54 %)	1.000
Smoking	0 (0 %)	2 (7.69 %)	1.000
Previous surgery	0 (0 %)	4 (15.38 %)	1.000
History of Myasthenia crisis	0 (0 %)	6 (23.07 %)	0.557
History of MG, mo, mean ± SD	46.5 ± 18.57	22.80 ± 25.12	0.083
Symptomatology, *n* (%)			
Occular disorder	4 (100 %)	22 (84.61 %)	1.000
Bulbar symptom	4 (100 %)	11 (42.31 %)	0.100
Facial diplegia	1 (25 %)	3 (11.54 %)	0.454
Generalized weakness	3 (75 %)	21 (80.77 %)	1.000
Respiratory disorders	1 (25 %)	9 (34.61 %)	1.000
Paraclinical tests			
Positive anti-AchR antibodies, *n* (%)	3 (75 %)	24 (92.31 %)	1.000
RFT: vital capacity, mean ± SD	1.98 ± 0.28	3.50 ± 0.95	**0.004**
preoperative hemoglobin, mean ± SD	13.83 ± 2.55	13.40 ± 1.57	0.675
Severity scores			
Osserman's classification	-	-	0.427
LEVENTHAL score > 10, *n* (%)	3 (75 %)	2 (7.69 %)	**0.009**
Functional muscle score, mean ± SD	64.00 ± 2,94	86.65 ± 9,79	**0.0001**
Treatement			
Mestinon dose (mg), mean ± SD	220 ± 34.64	225 ± 56.64	0.884
Mytelase dose (mg), mean ± SD	30 ± 28.28	25 ± 19.14	0.804
Corticosteroid, *n* (%)	1 (25 %)	7 (26.92 %)	1.000
Immunosuppressors, *n* (%)	1 (25 %)	0 (0 %)	0.133
Immunoglobulins, *n* (%)	1 (25 %)	5 (19.23 %)	1.000
Plasmapheresis, *n* (%)	0 (0 %)	1 (3.84 %)	1.000
Intraoperative period			
Curarization, n (%)	4 (100 %)	21 (80.77 %)	1.000
Duration of surgery (min), mean ± SD	225 ± 51.96	149.80 ± 25.23	**0.0001**
Length of ICU stay, h	198 ± 271.08	49.84 ± 43.95	**0.009**

POMC: postoperative myasthenia crisis; MG: myasthenia gravis; anti-acetylcholine receptor; RFT: respiratory function test; ICU; intensive care unit

Discussion

Myasthenia gravis is an auto-immune disease, characterized by muscle weakness and the synthesis of anti-Acetylcholine-Receptor Antibodies (anti-AchR-Ab) [13]. Sixty percent of our patients were younger than 40 years old with a significant female predominance, which is in line with the literature [14]. In our study, the mean duration of MG symptoms before surgery was 25.96 ± 25.43 months, higher than that found in the study conducted by Ying Huang and al. (19.67 ± 45.77 months) [15]. Bulbar symptoms were present in 50 % of our patients; however, this percentage was higher in other studies (80.4 %) [15].

The current standard approach to treat generalized MG in patients with or without thymoma is extended thymectomy [2, 3, 16]. Thymectomy minimizes the occurrence of MC [10] - a potentially life-threatening MG complication - in most patients. However, in some cases, the MC can be a postoperative complication. In our study, 13.33 % of cases developed a POMC within 45 days after surgery, and this percentage is meaningfully lower than that reported in previous studies (18.08 - 29.5%) [5, 17-18]. This may be explained by the fact that ocular MG cases were included in the analysis because the occurrence of POMC in cases with ocular MG is significantly less than in patients with generalized MG [15].

With advances in resuscitation techniques, mortality due to POMC has significantly reduced, as reflected by the lack of death in our POMC cases during the clinical care (the only case of death was secondary to pulmonary embolism in a metastatic tumor setting). However, our study showed that POMC significantly prolonged ICU stay (2.03 days in the non-POMC group Vs 8.25 days in the POMC group), which is consistent with previous studies [15], hence the importance of knowing the risk factors for the occurrence of POMC in order to improve patient outcome. Given the absence of local or regional studies on the subject, we decided to carry out this study to identify our own risk factors, which will enable us to update our local protocol for perioperative management, in collaboration with

neurologists and thoracic surgeons, and thus improve the management of our patients.

The analysis identified potential factors predisposing to POMC (***table 4***). A history of MC, thymoma, generalized myasthenia, bulbar weakness, and coexisting complications were reported as risk factors for POMC in a recently published meta-analysis [19]. Some reports suggests that bulbar deficiency is highly correlated with POMC [18, 20]. In our cohort, bulbar weakness was present in 50 % of cases, and all patients who developed POMC had bulbar symptoms, suggesting that bulbar weakness may be an independent risk factor for POMC despite the absence of a statistically significant association. All publications included in the meta-analysis published by Geng et al [19] suggested that MG patients with a history of MC had a higher risk of POMC than those without a history of MC. Although the relationship between MC history and the occurrence of POMC was not statistically meaningful in our univariate analysis due to the low sample size, the presence of a history of MC should be assessed before thymectomy for patients with MG.

Table 4: Predictive factors of post-thymectomy myasthenic crisis in different studies.

Study	Design	Predictive factors of POMC
Ando T [17]	Japan 2014 55 patients cohort	unstable MG before surgery, history of MC
Zou J [31]	China 2016 541 patients cohort	preoperative MC, high dose of pyridostigmine, Pre-surgery anxiety, postoperative infection (pneumonia)
Luezzi G [32]	Italy 2014 177 patients cohort	Osserman-stage equal to or higher than IIB, BMI ≥ 28, previous history of MC, longer duration of MG and lung resection
Chu XY [11]	China 2011 243 patients cohort	higher Osserman stage (IIb + IIIb + IV), thymoma and major postoperative complications
Wu Y [33]	China 2015 77 patients cohort	history of MC, high dose of pyridostigmine > 360 mg, post-surgery pulmonary infection
Yu S [9]	China 2014 178 patients cohort	Bulbar symptoms, history of preoperative MC, and longer operation duration
Yamada [34]	Japan 2013 131 patients cohort	Perioperative high-dose prednisolone therapy
Li Y [5]	China 2017 173 patients cohort	Bulbar symptom, incomplete resection of thymoma
Kanai T [8]	Japan 2017 393 patients cohort	VC < 80%, duration of MG before thymectomy < 3 months, and bulbar symptoms immediately before thymectomy
Our study	Morocco 2022 30 patients cohort	Weak pulmonary function, LEVENTHAL score > 10, lower Functional Muscle Score & longer surgery duration

POMC: postoperative myasthenia crisis; MC: myasthenia crisis; AchR-Ab : acetylcholine receptor antibodies; MG: myasthenia gravis; BMI: body mass index; VC: vital capacity.

At the preoperative evaluation, the severity of the disease, which is essentially linked to respiratory function, is assessed by both respiratory function tests (RFT) and the functional score out of 100 points. Vital capacity assessment is included in the predictive scores of postoperative mechanical ventilation (Leventhal score), and the muscular functional testing evaluates the extent of the involved muscle groups [14]. In this study, a weak respiratory function, a Leventhal score higher than 10 and a weak functional score were significantly associated with the occurrence of POMC in the univariate analysis.

Epidural analgesia has been successfully used to provide analgesia to patients undergoing thymectomy. This technique, reducing the use of intravenous opioids and general anesthetics, is associated with better lung function in the postoperative period and may speed up patient recovery [21, 22]. Only 20 % of our patients had received epidural analgesia, so the association between the absence of epidural analgesia and the occurrence of POMC was not significant.

Given the physiopathology of MG, the sensitivity to non-depolarizing neuromuscular blockers agents (NMBA) is increased, corresponding to a reduction in requirements that varies according to the severity and evolution of the MG [23]. With neuromuscular monitoring, the required dose of NMBA can be adapted to each patient [24, 25], and sugammadex could be of particular interest in this neuromuscular pathology because of the absence of effect on acetylcholine metabolism. However, the use of sugammadex in no way exempts the need for neuromuscular monitoring [26] to prevent residual curarization. In our study, the neuromuscular monitoring became systematic after the acquisition of a curameter and this from January 2019, which

explains the low percentage of cases benefiting from neuromuscular monitoring. The latter allowed a reduction in the doses of NMBA used with a mean dose of 25 mg in patients with neuromuscular monitoring versus 37.14 mg in the group without neuromuscular monitoring. Twenty percent of our patients have received de-curarization with sugammadex. In limited resources facilities, reducing NMBA doses and sugammadex use as rescue therapy may be interesting in the absence of curarization monitoring that is considered the gold standard.

In the meta-analysis by Geng and al, the risk of myasthenia crisis increased with the duration of the procedure and blood loss [19]. Indeed, the association between long procedure duration and the occurrence of POMC was highly significant (p = 0.0001) in the present study. To date, video-assisted thoracoscopic surgery (VATS) has proved to be identical to trans-sternotomy (TS) in terms of complete resection of thymus malignancy [27]. In addition, VATS, the minimally invasive approach most widely used, was once considered as the way of less injury to chest wall, less blood loss, and therefore less POMC occurrence than TS [28]. But other studies also reported TS is similar with VATS regarding to the risk of POMC [29, 30]. In our center, TS was the surgical technique of choice (86.7 %). VATS is growing in importance lately as surgical teams are acquiring expertise.

This review presents some limitations. First, the low sample size because of the retrospective monocentric design and the infeasibility of performing multivariate analysis may restrict the inner validity of the outcomes. Second, anti-acetylcholine receptor antibody titers and the anatomopathologic nature of the resected specimen were not determined in the majority of observations. Still, this study allowed us to critically review and improve our care level.

Conclusion

This single-center retrospective study, analyzing the risk factors related to the occurrence of POMC in MG patients who underwent thymectomy, revealed that a Leventhal score greater than 10, a low functional muscle score, a low vital capacity on the respiratory function test, and a prolonged duration of surgery were independent risk factors for POMC. Furthermore, our study showed that POMC significantly prolonged the length of ICU stay. To prevent POMC, we adopted a protocol adapted to our context based on a multidisciplinary management (anesthesiologists, intensivists, neurologists and thoracic surgeons) with a systematic admission in postoperative ICU for an early rehabilitation, which explains our results and the low incidence of POMC. This study enabled us to update our management protocol.

Conflict of interest: No potential conflict of interest relevant to this article was reported.

Informed consent: The patient consent was waived because it is a retrospective study

References

1. Gilhus NE. Myasthenia Gravis. N Engl J Med. 2016; 375: 2570-2581.
2. Wolfe GI, Kaminski HJ, Aban IB, Minisman G, Kuo HC, Marx A, Ströbel P, Mazia C, Oger J, Cea JG, Heckmann JM, Evoli A, Nix W, Ciafaloni E, Antonini G, Witoonpanich R, King JO, Beydoun SR, Chalk CH, Barboi AC, et al. Randomized trial of thymectomy in myasthenia gravis. N Engl J Med. 2016; 375: 511-522.
3. Taioli E, Paschal PK, Liu B, Kaufman AJ, Flores RM. Comparison of conservative treatment and thymectomy on myasthenia gravis outcome. Ann Thorac Surg. 2016; 102: 1805-1813.
4. Chigurupati K, Gadhinglajkar S, Sreedhar R, Nair M, Unnikrishnan M; Pillai M. Criteria for postoperative mechanical ventilation after thymectomy in patients with myasthenia gravis: a retrospective analysis. J Cardiothorac Vasc Anesth. 2018; 32: 325-330.
5. Li Y, Wang H, Chen P, Chen Z, Su C, Luo C, Feng H, Liu W. Clinical outcome and predictive factors of postoperative myasthenic crisis in 173 thymomatous myasthenia gravis patients. Int J Neurosci. 2018; 128: 103-109.
6. Wong YS, Ong CT, Sung SF, Wu CS, Hsu YC, Su YH, Hung LC. Clinical Profile and outcome of myasthenic crisis in central Taiwan. Acta Neurol Taiwan. 2016; 25: 129-135.
7. Nam TS, Lee SH, Kim BC, Choi KH, Kim JT, Kim MK, Cho KH, Lee MC. Clinical characteristics and predictive factors of myasthenic crisis after thymectomy. J Clin Neurosci 2011; 18: 1185–8.
8. Kanai T, Uzawa A, Sato Y, Suzuki S, Kawaguchi N, Himuro K, Oda F, Ozawa Y, Nakahara J, Suzuki N, Takahashi YK, Ishibashi S, Yokota T, Ogawa T, Yokoyama K, Hattori N, Izaki S, Oji S, Nomura K, Kaneko J, et al. A clinical predictive score for postoperative myasthenic crisis. Ann Neurol 2017; 82: 841–9.
9. Yu S, Lin J, Fu X, Li J, Li Y, Chen B, Yang M, Zhang M, Bu B. Risk factors of myasthenic crisis after thymectomy in 178 generalized myasthenia gravis patients in a five-year follow-up study. Int J Neurosci. 2014; 124: 792-798.
10. Xue L, Wang L, Dong J, Yuan Y, Fan H, Zhang Y, Wang Q, Ding J. Risk factors of myasthenic crisis after thymectomy for thymoma patients with myasthenia gravis. Eur J Cardiothorac Surg. 2017; 52: 692-697.
11. Chu XY, Xue ZQ, Wang RW, Tan QY. Predictors of postoperative myasthenic crisis in patients with myasthenia gravis after thymectomy. Chin Med J (Engl). 2011; 124: 1246-1250.
12. Watanabe A, Watanabe T, Obama T, Mawatari T, Ohsawa H, Ichimiya Y, Takahashi N, Kusajima K, Abe T. Prognostic factors for myasthenic crisis after transsternal thymectomy in patients with

myasthenia gravis. J Thorac Cardiovasc Surg 2004; 127: 868–76.
13. Ciafaloni E, Sanders DB. Advances in myasthenia gravis. Curr Neurol Neurosci Rep 2002; 2: 89–95.
14. S. Lammens, B. Eymard, B. Plaud. Anesthésie et myasthénie. EMC (Elsevier Masson SAS, Paris), Anesthésie-Réanimation, 36-657-C-10, 2010.
15. Ying Huang, Lei Su, Yi Zhang, Julong Guo, Chunmei Wang. Risk Factors for Postoperative Myasthenic Crisis After Thymectomy in Patients With Myasthenia Gravis. Journal of surgical research. 2021; 262: 1-5.
16. Liu Z, Yao S, Zhou Q, Deng Z, Zou J, Feng H, Zhu H, Cheng C. Predictors of extubation outcomes following myasthenic crisis. J Int Med Res. 2016; 44: 1524-1533.
17. Ando T, Omasa M, Kondo T, Yamada T, Sato M, Menju T, Aoyama A, Sato T, Chen F, Sonobe M, Date H. Predictive factors of myasthenic crisis after extended thymectomy for patients with myasthenia gravis. Eur J Cardiothorac Surg. 2015; 48: 705-709. discussion 709.
18. Li KK, Qian K, Feng YG, Guo W, Tan QY, Deng B. Predictive factors of prolonged mechanical ventilation, overall survival, and quality of life in patients with post-thymectomy myasthenic crisis. World J Surg Oncol. 2017; 15: 150.
19. Geng Y, Zhang H, Wang Y. Risk factors of myasthenia crisis after thymectomy among myasthenia gravis patients: a meta-analysis. Medicine (Baltimore). 2020; 99: e18622.
20. Akaishi T, Motomura M, Shiraishi H, Yoshimura S, Abe M, Ishii T, Aoki M. Preoperative risks of post-operative myasthenic crisis (POMC): a meta-analysis. J Neurol Sci. 2019; 407: 116530.
21. Kirsch JR, Diringer MN, Borel CO, Hanley DF, Merritt WT, Bulkley GB. Preoperative lumbar epidural morphine improves postoperative analgesia and ventilatory function after transsternal thymectomy in patients with myasthenia gravis. Crit Care Med 1991; 19: 1474–9.
22. Liu XZ, Wei CW, Wang HY, Ge YH, Chen J, Wang J, Zhang Y. Effects of general-epidural anaesthesia on haemodynamics in patients with myasthenia gravis. West Indian Med J 2015; 64: 99–103.
23. Itoh H, Shibata K, Nitta S. Difference in sensitivity to vecuronium between patients with ocular and generalized myasthenia gravis. Br J Anaesth 2001; 87: 885-9.
24. Sungur Ulke Z, Yavru A, Camci E, Ozkan B, Toker A, Senturk M. Rocuronium and sugammadex in patients with myasthenia gravis undergoing thymectomy. Acta Anaesthesiol Scand 2013; 57: 745–8.
25. Murray MJ, DeBlock HF, Erstad BL, Gray Jr AW, Jacobi J, Jordan CJ, McGee WT, McManus C, Meade MO, Nix SA, Patterson AJ, Sands K, Pino RM, Tescher AN, Arbo ur R, Rochwerg B, Murray CF, Mehta S. Clinical practice guidelines for sustained neuromuscular blockade in the adult critically ill patient: 2016 update—executive summary. Am J Health-Syst Pharm 2017; 74: 76–8.
26. Cata JP, Lasala JD, Williams W, Mena GE. Myasthenia Gravis and Thymoma Surgery: A Clinical Update for the Cardiothoracic Anesthesiologist. Journal of Cardiothoracic and Vascular Anesthesia 2019; 33: 2537- 2545.
27. Burt BM, Yao X, Shrager J, Antonicelli A, Padda S, Reiss J, Wakelee H, Su S, Huang J, Scott W. Determinants of complete resection of thymoma by minimally invasive and open thymectomy: analysis of an international registry. J Thorac Oncol 2017; 12: 129–36.
28. Lee CY, Kim DJ, Lee JG, Park IK, Bae MK, Chung KY. Bilateral video-assisted thoracoscopic thymectomy has a surgical extent similar to that of transsternal extended thymectomy with more favorable early surgical outcomes for myasthenia gravis patients. Surg Endosc 2011; 25: 849–54.
29. He Z, Zhu Q, Wen W, Chen L, Xu H, Li H. Surgical approaches for stage I and II thymoma-associated myasthenia gravis: feasibility of complete videoassisted thoracoscopic surgery (VATS) thymectomy in comparison with trans-sternal resection. J Biomed Res 2013; 27: 62–70.
30. Gung Y, Zhang H, Li S. Sternotomy versus video-assisted thoracoscopic surgery for thymectomy of myasthenia gravis patients: a meta-analysis 2016; 9: 285–94.
31. Zou J, Su C, Lun X, Liu W, Yang W, Zhong B, Zhu H, Lei Y, Luo H, Chen Z. Preoperative anxiety in patients with myasthenia gravis and risk for myasthenic crisis after extended transsternal thymectomy: a CONSORT study. Medicine (Baltimore) 2016; 95: e2828.
32. Leuzzi G, Meacci E, Cusumano G, Cesario A, Chiappetta M, Dall'armi V, Evoli A, Costa R, Lococo F, Primieri P, Margaritora S, Granone P. Thymectomy in myasthenia gravis: proposal for a predictive score of postoperative myasthenic crisis. Eur J Cardiothorac Surg 2014; 45: e76–88.
33. Wu Y, Chen Y, Liu H, Zou S. Risk factors for developing postthymectomy myasthenic crisis in Thymoma Patients. J Cancer Res Ther 2015; 11 Suppl 1:C115–117.
34. Yamada Y, Yoshida S, Suzuki H, Tagawa T, Iwata T, Mizobuchi T, Kawaguchi N, Yoshino I. Efficacy of perioperative highdose prednisolone therapy during thymectomy in myasthenia gravis patients. J Cardiothorac Surg 2013; 8: 226.