Predictor for prolonged intubation after thymectomy in patients with myasthenia gravis

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Predictor for prolonged intubation after thymectomy in patients with myasthenia gravis

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TABLE OF CONTENTS

LIST OF TABLES

Abstract

Predictor for prolonged intubation after thymectomy in patients with myasthenia gravis

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Prolonged intubation with mechanical ventilation have resulted in pulmonary complications such as airway injury, pneumonia, and atelectasis in patients with myasthenia gravis. We performed this study to determine predictors for prolonged intubation in patients with myasthenia gravis (MG) after thymectomy in intensive care unit (ICU). Forty five patients with MG after extended thymectomy who were admitted to the ICU at a single university hospital from 2005 to 2006 were included. We reviewed and analysed medical records retrospectively to identify prognostic predictor for prolonged intubation. Median duration of intubation was 39.0 (12-644) hours. The patients extubated at the first postoperative day successfully were assigned to group I, and the patients extubated at the second day or later were assigned to group II. The patients classified as MGFA class $\geq$ IIIa were 3 of 20 in group I and 13 of 25 in group II. There were no significant differences in terms of age, sex, body surface area, preoperative medical treatment, preoperative vital capacity, and repetitive nerve stimulation test, except in the orbicularis oculi, between two groups. Seven (28%) patients in group I and one (5%) received

preoperative plamapheresis or intravenous immunoglobulin (IVIG) because of reduced pulmonary function or severe symptoms. The incidence of thymoma in group II (44%) was higher than that of group I (15%) significantly. The mean vital capacity at the first postoperative day in the group II (1036 ml) was smaller than that in the group I (1281 ml) significantly. The predictors of prolonged intubation were MGFA (Myasthenic Gravis Foundation of America) clinical class ≥ IIIa (odds ratio: 13.052, confidence interval: 1.606-106.082), presence of thymoma (odds ratio: 18.460, confidence interval: 1.551-219.665), higher titiers of acetylcholine receptor (AchR) binding antibodies (odds ratio: 0.834, confidence interval: 0.700-0.994) and female (odds ratio: 14.745, confidence interval: 1.479-147.033). The identified predictors such as MGFA clinical classification, thymoma, titers of AchR binding Ab, and female, will be useful for proper management of myasthenic crisis patients with mechanical ventilation after thymectomy.

Key words: Myasthenia gravis, prolonged intubation, predictors, clinical classification, thymoma, female, acetylcholine receptor antibody

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I. INTRODUCTON

Myasthenic crisis may be defined as respiratory failure requiring mechanical ventilation or delayed postoperative extubation resulting from myasthenic weakness.[1] Postoperative myasthenic crisis may cause from weakness of respiratory muscles which were influenced by surgical stress or anesthetics exposure through direct or immunologic mechanism. Prolonged intubation and mechanical ventilatory care have resulted in adverse complication such as infection, pneumonia or atelectasis.[1, 2]

Postoperative myasthenic crisis after surgery was defined as the need of

mechanical ventilation with prolonged intubation due to myasthenia gravis for more than 6, 24, 48 or 72 hours after surgery. [3-7]

Although there were many studies about risk factors related with prolonged intubation or mechanical ventilation, [1, 5, 8, 9] these still remains obscure because myasthenia gravis is relatively uncommon disease with the fluctuating nature.

We performed this study to identify the predictors of prolonged intubation and mechanical ventilation in myasthenia gravis after thymectomy. We divided myasthenic patient after thymectomy into two group. The group I include the patients extubated at POD 1 or earlier and the group II include the patients extubated at POD 2 or later. The patients who needed reintubation and mechanical ventilatory support for more than 48 hours were assigned to group II. To identify the predictor for prolong intubation with mechanical ventilation in myasthenia gravis after thymectomy will be helpful for proper management.

II. MATERIALS AND METHODS

1. Populations

All patients undergoing extended thymectomy in myasthenia gravis between November 1, 2005, and February 31, 2007 at Severance Hospital, Yonsei University Health System, Seoul, Korea, were identified retrospectively. They were managed by same medical team. All medical records were reviewed, and patients who needed mechanical ventilation with intubation for more than 6 hours after thymectomy were selected. All cases of myasthenic crisis without thymectomy and all patients transferred after extubation in operating room were excluded. Forty-eight patients undergoing extended thymectomy with myasthenia gravis needed mechanical ventilatory support with intubation for more than 6 hours after admission at ICU in our institution. Three patients from further analysis were excluded because of insufficient data.

2. Methods

Pertinent information for this study included the patient's age, sex, weight, height, duration of myasthenia gravis (months), and preoperative medical history including a history of ocular, bulbar, respiratory symptom, generalized weakness, and fatigue at baseline and after hospital admission. The preoperative clinical severity of myasthenia gravis was assessed using the Myasthenia Gravis Foundation of America (MGFA) classification: class I, characterized by ocular muscle weakness only, class II, mild weakness affecting other than ocular muscles, class III, moderate weakness affecting other than ocular muscle, class IV, severe weakness affecting other than ocular muscle, class V, defined by intubation, except when employed during routine postoperative management.[10] Patients including class II – IV can be subdivided by predominantly affecting limb and/or axial muscles (IIa – IVa) or predominantly oropharyngeal and/or respiratory muscles (IIb – IVb). A history of myasthenic crisis (defined as respiratory failure treated with

mechanical ventilation) and postoperative application of non-invasive positive pressure ventilation were sought from all patients, and ICU stay, hospital stay, the pre- and post-operative use and dosage of anticholine-esterase, and pre- and post-operative immunomodulation therapy were recorded.

The following laboratory data and examination results were recorded: preoperative forced vital capacity (FVC), preoperative repetitive nerve stimulation test (RNST), preoperative acetylcholine receptor (AchR) binding antibodies (Ab), vital capacity (VC) at the first postoperative day (POD 1), oxygenation index [a ratio of partial pressure of oxygen (PaO_2) to fraction of inspired oxygen (FiO_2), P/F ratio] and partial pressure of carbon dioxide ($PaCO_2$) at the first and second day after successful extubation or weaning in patients with tracheostomy. In RNST, the most severe decrement from the first to fifth compound muscle action potential (CMAP) comparing to initial CMAP was recorded following 2, 3, 5 Hz repetitive stimulation on each muscle group, trapezius, flexor carpi ulnaris (FCU), abductor digiti minimi (ADQ), nasalis,

and orbicularis oculi (OO).

Diagnosis of myasthenia gravis was established by a combination of clinical findings, improved symptoms with rest or injection of anticholinesterase durgs, RNST, and AchR binding Abs. All patients were being treated with pyridostigmine, of which administration was continued on the day of surgery. Preoperative plasmapheresis or infusion of IVIG was done, if pulmonary function was diminished. Thymectomy was avoided in the patients with acute exacerbations and myasthenic crisis, and thymectomy was delayed until the condition of patients was stabilized.

All patients except one patient underwent transsternal thymectomy by identical surgical team, except one patient by chamberlain approach. When the patients were admitted to the ICU after thymectomy, adaptive support ventilation (ASV) mode was applied by the Galileo Ventilator (Hamilton Medical, Reno, NY). Using intravenous fentanyl infusion for postoperative pain control, if needed, infusion of alfentanil and/or midazolam were added for

maintenance of visual analog pain score (VAS score) less than 4 and ramsay score less than 3.

Extubation criteria were: (1) normal chest radiographic findings and arterial blood gas analysis (PaO_2 > 90mmHg in 0.4 FiO_2, $PaCO_2$ less than or equal to 50mmHg, pH greater than or equal to 7.30) (2) postoperative vital capacity ≥ 50% of preoperative vital capacity and ≥ 15 ml/kg (3) pressure support ventilation (PSV) < 8cmH_2O (4) no surgical comlication or adverse medical conditions.

Reintubation criteria were: (1) tachypnea (respiratory rate greater than 40 breaths/min) (2) respiratory acidosis not due to narcotics (3) vital capacity less than or equal to 8ml/kg.

Complications at postoperative period in ICU was recorded, such as pneumonia (fever and new infiltrate on chest radiograph), atelectasis, bleeding, re-intubation, hoarseness, pneumothorax, hemothorax, congestive heart failure and cardiac arrest.

The patients were divided two groups according to duration of mechanical ventilation and intubation. Forty-five patients needed postoperative ventilatory support with intubation for at least 6 hours. (table 1) Twenty patients were extubated at POD 1 or earlier and assigned to group I. Twenty-five patients extubated at POD 2 or later were assigned to group II. The patients who needed reintubation and mechanical ventilatory support for more than 48 hours were assigned to group II. Median duration of intubation was 20 hours in group I and 49 hours in group II. In patients with prolonged intubation (group II), there were two cases of pulmonary complications such as atelectasis or pneumonia. There was fever in one patient. One of patients in group I and two in group II underwent thymectomy with unilateral phrenic nerve resection. In group I, there was pneumothorax in one patient and hemothorax in one patient. Because of postoperative bleeding, one patient underwent reoperation in group II. Pneumothorax, hemothorax, phrenic nerve resection, and chamberlain approach were categorized as surgical complicated

problem for logistic regression anaylsis. There were no operative or hospital deaths. Seventeen patients were applied non-invasive positive pressure ventilation (NIPPV, Galileo Ventilator, Hamilton Medical, Reno, NY) for 3 hours after extubation or more if needed.

There was none who underwent reintubation or tracheostomy in group I. Seven in group II underwent reintubation due to respiratory failure and two in group II underwent tracheostomy. The ICU length of stay and hospital length of stay in group II were longer than group I. There were no significant differences in terms of postoperative medication and dosage. However, five patients received IVIG and two patients had high dose steroid therapy in group II, because of postoperative myasthenic crisis.

Statistical analysis was performed using SPSS 11.5 software (SPSS, Inc, Chicago, Ill). Descriptive data are given as mean ± standard deviation, median (range), or number of patients. Independent t-test, Mann - Whitney U test, chi-square test, or Fisher's exact test was used for comparison between

group I and II. Variables were subjected to univariate analysis to identify factors that were associated with prolonged intubation. To ascertain which variables were independently associated with prolonged intubation, variables were subjected to step-wise multiple logistic regression analysis after defining prolonged intubation as being unable to extubate at POD 1 or earlier successfully.

Table 1. Patients grouping by postoperative course

	Group I	Group II
Duration of intubation (hours)	20.0 (12-29)	49 (37-644)
Postoperative pulmonary complication	0 (0%)	2 (8%)
Surgical complicated problem	3 (15%)	4 (16%)
NIPPV application	6 (30%)	10 (40%)
Reintubation	0 (0%)	7 (28%)
Tracheostomy	0 (0%)	2 (8%)
ICU length of stay (day)	3 (2-7)	5 (3-45)
Hospital length of stay (day)	12.5 (6-20)	16 (4-122)

Data are expressed as number of patients (percentage) or median (range). Group I, extubated at POD 1 or earlier; Group II, extubated at POD 2 or later, and/or reintubate and mechanical ventilatory support for more than 48 hours; ICU, intensive care unit; NIPPV, non-invasive positive pressure ventilation.

III. RESULTS

Table 2 displays the MGFA clinical classification at preoperative periods. The numbers of patients with preoperative MGFA clinical classifications of I, IIa, IIb, IIIa, IIIb, IVa, IVb were 1, 7, 9, 1, 2 , 0, 0 in group I and 0, 4, 8, 4, 5, 1,3 in group II. The variables were converted into binominal variable using the cufoff level decided for maximizing the difference between group I and II, and these cutoff values were the MGFA class $\geq$ IIIa.

The demographic data and characteristics of the patients enrolled in the study are shown in table 3. Mean age was 38.2 years and there were 29 females and 16 males. Mean body surface area (BSA) was 1.63 m^2. There were no significant differences between the two groups in terms of age, sex, BSA, duration of disease, and preoperative medication. The ratio of preoperative immunomodulating therapy such as plamapheresis, IVIG was higher significantly in goup II, because some patients with preoperative more severe clinical symptoms and reduced pulmonary function were included in group II.

FVC and the ratio of FVC to weight (FVC/weight) or the predicted FVC (FVC%) of patients in group I were larger than those in group II. However, there were no significant differences between two groups in terms of FVC and the ratio of FVC to weight (FVC/weight) or the predicted FVC (FVC%), as shown in table 4. Mean VC at POD 1 was 1281 ml of patients in group I, larger than 1036 ml in group II significantly. Mean value of PaO_2/FiO_2 ratio at 24 and 48 hours after extubation or weaning (in patients with tracheostomy) was 352.6 and 391.6, and mean of PaCO2 at 24 and 48 hours after extubation or weaning (in patients with tracheostomy) was 36.1 and 38.0. There were no differences between two groups. Appropriate P/F ratio and PaCO2 were maintained after successful extubation or weaning from the ventilator in patients with tracheostomy.

The serum level of AchR binding Ab of patients in group I was higher. However, there was no significant difference between two groups in terms of preoperative serum level of AchR binding Ab. In preoperative RNST, there

were no differences between two groups in each muscle group except orbicularis oculi. The incidence of thymoma in group II was higher than that of group I significantly. (table 5)

In univariate analysis, variables with *P* value of less than 0.05 between 2 groups were the histology of thymoma (odds ratio: 4.452, confidence interval: 1.035-19.162) and VC at POD 1 (odds ratio: 0.998, confidence interval: 0.996-1.000). Variables with *P* value less than 0.20 in univariate analysis are shown in table 6.

The variables included in multivariate analysis were sex, BSA, history of myasthenic crisis, preoperative immunomodulation therapy, AchR binding Ab, surgical complicated problem, postoperative bleeding, histology of thymoma, duration of disease, preoperative pyridostigmine dosage, decrement on trapezius, FCU, ADQ, nasalis, and OO. VC at POD 1 or VC at POD 1 for predicted VC (VC% at POD 1), and application of NIPPV after extubation were excluded, because these parameters were got immediately before or after extubation and

postoperative variables.

Multiple logistic regression analysis showed that MGFA class ≥ IIIa (odds ratio: 13.052, confidence interval: 1.606-106.082), histology of thymoma (odds ratio: 18.460, confidence interval: 1.551-219.655), AchR binding Ab (odds ratio: 0.834, confidence interval: 0.700-0.994), and female (odds ratio: 14.745, confidence interval: 1.479-147.033) were significant predictors for prolonged intubation. Acquired multiple logistic regression model is summarized in table 7.

Table 2. Preoperative MGFA clinical classification[10]

	Total	Group I	Group II
I	1 (2.2%)	1 (5.0%)	
II			
a	11 (24.4%)	7 (35.0%)	4 (16.0%)
b	17 (37.8%)	9 (45.0%)	8 (32.0%)
III			
a	5 (11.1%)	1 (5.0%)	4 (16.0%)
b	7 (15.6%)	2 (10.0%)	5 (20.0%)
IV			
a	1 (2.2%)		1 (4.0%)
b	3 (6.7%)		3 (12.0%)
V	0 (0%)		

Data are expressed as number of patients (percentage). Group I, extubated at POD 1 or earlier; Group II, extubated at POD 2 or later, and/or reintubate and mechanical ventilatory support for more than 48 hours; MGFA, Myasthenia Gravis Foundation of America.

Table 3. Preoperative clinical characteristics

	Group I (n = 20)	Group II (n = 25)	*p*-value
Age (y)	36.0 ± 11.9	40.0 ± 12.9	0.284
Sex (M/F)	9/11	7/18	0.237
BSA (m^2)	1.63 ± 0.18	1.63 ± 0.14	0.840
Duration of Disease (months)	15.5 (2–58)	5.0 (2–192)	0.336
Preoperative treatment			
Dose of pyridostigmine (mg)	480 (180–600)	480 (90–720)	0.972
Prednisolone maintenance	5 (25%)	7 (28%)	0.821
High dose steroid therapy	0 (0%)	2 (8%)	0.196
Plasmapheresis or IVIG	1 (5%)	7 (28.0%)	0.045

Data are expressed as mean ± standard deviation, number of patients (percentage), median (range). Group I, extubated at POD 1 or earlier; Group II, extubated at POD 2 or later, and/or reintubate and mechanical ventilatory support for more than 48 hours; BSA, body surface area; IVIG, intravenous immunoglobulin; Independent t-test, Mann-Whitney U test, or Fisher's exact test used for analysis.

Table 4. Preoperative and postoperative vital capacity

	Group I (n = 20)	Group II (n = 25)	*p*-value
Preoperative FVC (L)	3.28 ± 0.69	3.08 ± 0.79	0.416
Preoperative FVC/weight (ml/kg)	53.9 ± 9.4	48.8 ± 10.8	0.133
Preoperative FVC/predicted VC (%)	82.6 ± 12.5	82.9 ± 16.9	0.941
VC at POD 1 (mL)	1281 ± 285.8	1036 ± 395.5	0.020

Data are expressed as mean ± standard deviation. Group I, extubated at POD 1 or earlier; Group II, extubated at POD 2 or later, and/or reintubate and mechanical ventilatory support for more than 48 hours; FVC, forced vital capacity; VC, vital capacity; POD, postoperative day; Independent t-test, Mann-Whitney U test, or Fisher's exact test used for analysis.

Table 5. Laboratory data and pathology

	Group I	Group II	*P*-value
AchR binding Ab (nmol/L)	10.5 (0.24-17.52)	9.6 (0-20.28)	0.508
RNST			
Trapezius	25.0 ± 13.1	28.1 ± 19.6	0.549
FCU	34.1 ± 22.6	31.3 ± 24.8	0.705
ADQ	21.4 ± 19.2	21.7 ± 19.8	0.957
Nasalis	31.9 ± 20.0	32.9 ± 21.0	0.870
OO	35.5 ± 19.1	25.3 ± 14.2	0.046
Pathology: Thymoma	3 (15.0%)	11 (44%)	0.037

Data are expressed as mean ± standard deviation, number of patients (percentage), median (range). Group I, extubated at POD 1 or earlier; Group II, extubated at POD 2 or later, and/or reintubate and mechanical ventilatory support for more than 48 hours; AchR binding Ab, acetylcholine receptor binding antibody; RNST, repetitive nerve stimulation test; FCU, flexor carpi ulnaris; ADQ, abductor digiti minimi; OO, orbicularis oculi; Independent t-test, Mann-Whitney U test, or Fisher's exact test used for analysis.

Table 6. Univariate analysis

	Odds ratio	(95% CI)	*P* value
Preoperative MGFA class ≥ IIIa	5.063	(0.950-26.991)	0.079
Preoperative plasmapheresis or IVIG	7.389	(0.825-66.168)	0.059
Preoperative FVC/weight (ml/kg)	0.948	(0.883-1.018)	0.139
RNST : orbicularis oculi	0.963	(0.926-1.000)	0.053
VC at POD 1 (mL)	0.998	(0.996 –1.000)	0.034
VC at POD 1 (%predicted value)	0.956	(0.901 – 1.015)	0.139
Histology : Thymoma	4.452	(1.035 – 19.162)	0.037

Dependent variable: Prolonged intubation, extubated at POD 2 or later, and/or reintubate and mechanical ventilatory support for more than 48 hours; CI, confidence interval; MGFA, Myasthenia Gravis Foundation of America; IVIG, intravenous immunoglobulin; FVC, forced vital capacity; VC, vital capacity; POD 1, the first postoperative day

Table 7. Multivariate logistic regression analysis

	Coefficient ± SE	OR (95% CI)	*P* value
MGFA class ≥ IIIa	2.569 ± 1.069	13.052 (1.606-106.082)	0.016
Thymoma	2.916 ± 1.264	18.460 (1.551-219.655)	0.021
AchR binding Ab	-0.181 ± 0.089	0.834 (0.700-0.994)	0.043
Female	2.691 ± 1.173	14.745 (1.479-147.033)	0.022
Constant	-1.242 ± 1.055	0.289	0.239

Dependent variable: Prolonged intubation, extubated at POD 2 or later, and/or reintubate and mechanical ventilatory support for more than 48 hours; SE, standard error; OR, odds ratio; CI, confidence interval; MGFA, Myasthenia Gravis Foundation of America; AchR binding Ab, acetylcholine receptor binding antibodies.

IV. DISCUSSION

The multivariate logistic regression analysis used in this study identified four variables as predictors or risk factors of postoperative myasthenic crisis, which were MGFA clinical class ≥ IIIa, presence of thymoma, higher titer of AchR binding Ab, and female.

We classified the preoperative severity of disease using MGFA classification instead of Osserman's classification. MGFA clinical classification includes the criteria about severity of myasthenia gravis and division into only ocular, bulbar muscles and other general involved muscle groups.[10] MGFA classification seems to reflect the severity of disease and dominantly involved muscle groups. Preoperative moderate to severe weakness in bulbar or generalized muscle groups (MGFA clinical class ≥ IIIa) in spite of proper medical treatment was related with prolonged intubation after thymectomy. However, there are limitations that MGFA clinical classification is subjective assessments and can have no lack of quantification. MGFA classification was suggested as uniform

classification by Task Force of the Medical Scientific Advisory Board of the MGFA for meaningful comparison of data.[10] Modified Osserman's classification have been widely used since 1970's.[11] However, this classification include categories on the course and onset time of the disease. Categories based on the course of the disease, such as "acute fulminating" and "late severe", and categories for muscle atrophy and childhood onset cannot reflect the preoperative severity of disease, because overall clinical course and onset of disease is different from the severity of disease immediately before surgery in Myasthenia gravis with the fluctuating feature and thymectomy was delayed until the condition of patients was stabilized.[10]

There were several studies that presence or severity of preoperative bulbar symptoms was related with the need for postoperative ventilatory support or myasthenic crisis.[4, 5, 12, 13] Preoperative bulbar symptom and history of myasthenic crisis has been considered to increase the risk of myasthenic crisis and the need of postoperative ventilatory support.[4-6] Jaretzki[14] and Kas[15]

recommended that patients with respiratory insufficiency or oropharyngeal weakness preoperatively be made as free as possible for the postoperative complication and the use of plasmapheresis or IVIG can be considered. However, in these studies, overall clinical severity and disease status were not estimated immediately before surgery or after proper medical treatment.

In this study, the low serum concentration of AchR binding Ab was correlated to prolonged intubation in postoperative periods. However, Watanabe and coworkers[4] reported that preoperative higher serum level of AchR binding Ab was considered as risk factor of postoperative myasthenic crisis. In our study, less than 30 nmol/L of AchR binding Ab could be detected in all patients and relatively low concentration as compared with data in the study of Watanabe et al[4]. In the study of Watanabe et al[4], the mean value of preoperative AchR binding Ab was 35.5 nmol/L in the group without postoperative myasthenic crisis (108 patients) and 204.3 nmol/L in the group with postoperative myasthenic crisis (14 patients). Interestingly, median value was 5.2 in the

gourp without postoperative myasthenia crisis and 9.3 in the gourp with postoperative myasthenia crisis and the concentration of AchR binding Ab was less than 100 nmol/L in 105 of 122 patients (97/108 vs 8/14). It also is possible to be different clinical features according to the low or high titers of AchR binding Ab. AchR binding Ab can be detected in about 80 – 90 % of patients with myasthenia gravis and autoantibody-negative myasthenia gravis also is an antibody-mediated autoimmune that can not be detected by radioimmunoassay.[16] It has been considered that the serum concentration of AchR binding Ab does not correlate with the clinical severity of myasthenia gravis.[16, 17] However, investigators have identified the immunopathogenesis of myasthenia gravis related to AchR binding Ab and proved the key role of the immune response with AchR binding Ab in myasthenia gravis.[18-21] In addition, the clinical effect of AchR binding Ab or conventionally undetected antibody may be complicated, not simple because AchR binding Ab have very heterogenous and various epitope.

In our study, the patients with thymoma had a risk of prolonged intubation. This result was comparable with that of other studies. It has been considered that the patients with thymoma trace more fulminant courses as compared with non-thymoma patients.[22, 23] Thomas and coworkers[1] reported that 38% (10/26) of patients yonger than 55 years and 30% (8/27) of patients older than 55 years in myasthenia crisis had thymoma and showed higher incidence of thymoma in the myasthenic crisis, compared with the incidence of thymoma in the myasthenic patients undergoing thymectomy (15%).[24] Loach and coworkers[12] reported that the presence of thymoma was one of factors influenced myasthenic crisis.

This study showed that female patients had more risk of prolonged intubation. In this study, 29 patients (64%) were female and comparable with the proportion in other studies.[4, 7] The proportion of females in the group with prolonged intubation was 18 of 25 patients (72%) and significant predictor in multivariate logistic regression analysis, although not significantly higher

proportion compared with group I in univariate analysis. The incidence of myasthenia gravis has relation to age and sex.[25] There are two peaks bimodally distributed. Mostly women are affected in early peak age, the second and third decades, and mostly men in later peak age, the sixty and seventh decades.[25] In addition to incidence and severity of myasthenia crisis, it seems that women have the need for postoperative ventilatory support and risk of postoperative myasthenic crisis, as compared with men. Naguib and coworkers[7] reported that the proportion of females required ventilatory support was greater than the proportion of females including in that study.

There were no significant differences between two groups in terms of preoperative FVC, however, VC at POD 1 in the group II was significantly lower than that in the group I and lower VC at POD 1 was correlated with prolonged intubation in univariate analysis. This showed that the reduced reserve of pulmonary function may be masked with preoperative medical treatment and manifested after thymectomy. The VC at POD 1 may be

thought to be useful predictor for prolonged intubation.

This study has limitations because of subjective clinical classification and relatively small number of patients. It is needed that additional studies using more objective evaluation of disease severity such as quantitative myasthenia gravis score, in sufficient number of patients, and it seems necessary to develop and identify more practically useful tools reflecting the severity of disease.

V. CONCLUSION

Development in perioperative managements including surgical or anesthetic managements will lead to the reduced requirement of postoperative ventilatory support and many patients in myasthenia gravis undergoing thymectomy will be extubated early after surgery or in operating room. Consequently, it is important to identify the need of postoperative mechanical ventilatory support and the risk factors of prolonged intubation in preoperative period under current perioperative managements. The patients including in this study managed at the single institution during recent years. MGFA clinical class $\geq$ IIIa, presence of thymoma, higher titer of AchR binding Ab, and female were identified as predictors of prolonged intubation in this study. The predictors are thought to be useful for proper perioperative managemant. However, further study in larger population and by using more objective evaluation of disease severity is needed, for prolonged ventilation and its complication have to be prevent.

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ABSTRACT (IN KOREAN)

중증근무력증 환자에서 흉선절제술후 기관삽관기간에 영향을 미치는 인자

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중증근무력증 환자에서 기관내 튜브를 오래 거치하면 기도손상, 폐렴, 무기폐와 같은 호흡기계 합병증이 증가한다. 따라서 흉선절제술후 중환자실에 입실한 중증근무력증 환자에서 기관내 튜브를 통한 기계환기의 장기화와 관련된 인자를 알아보고자 한다. 2005년부터 2006년까지 흉선절제술후 본원 중환자실에 입실한 중증근무력증환자 중 45명의 의무기록을 후향적으로 조사, 분석하여 다변량 분석을 시행하였다. 기관내 튜브 거치기간은 중위값 39.0 시간, 범위는 12 – 644시간이었다. 수술후 1일째 성공적으로 발관한 환자들은 I 군으로, 수술후 2일 이후에 발관한 환자와 재삽관후 48시간 이상 기계환기를 적용한 환자는 II 군으로 분류하였다. MGFA class IIIa 이상으로 분류된 환자는 I 군 20명중 3명, II 군 25명중 13명이었고, 나이, 성별, 체표면적, 술전 약물치료, 술전 폐활량, orbicularis oculi를 제외한 반복신경자극검사결과에서 유의한 차이를 보이지 않았다. 폐기능 감소와 심한 임상증상 때문에 술전 plamapheresis나 정맥혈내 면역글로불린 투여를 받은 환자는 I 군 7명 (28%), II 군 1명 (5%) 이었다. 흉선종이 있는 환자는 I 군 15%, II 군 44% 으로 II 군에서 유의하게 많았다. 수술후 1일째 측정한 폐활량은 II 군에서 1036 ml로 1281 ml인 I 군에 비해 유의하게 적었다. 다변량 분석을 통하여 수술후 2일 이후부터 발관이 가능하거나 재삽관 및 총 48시간 이상 기도내관을 통한 기계환기가 이루어진 장기 기관내 튜브 거치는 MGFA (Myasthenic Gravis Foundation of America) clinical class ≥ IIIa (odds ratio: 13.052, confidence interval: 1.606-106.082), 흉선종 (odds ratio: 18.460, confidence interval: 1.551-219.665), acetylcholine receptor (AchR) binding

antibodies의 혈중농도 (odds ratio: 0.834, confidence interval: 0.700-0.994), 여성 (odds ratio: 14.745, confidence interval: 1.479-147.033)과 관련이 있었다. 위의 예측인자들은 흉선종 절제술후 기계환기를 받는 환자에서 발생한 myasthenic crisis에 대해 적합한 치료를 하는데 유용하리라 생각된다.

핵심되는 말: 중증근무력증, 장기간 기관내 삽관, 예측인자, MGFA clinical classification, 흉선종, 여성, acetylcholine receptor antibody