Multivariate determinants of the need for postoperative ventilation in myasthenia gravis

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Purpose: Following transsternal thymectomy, up to 50% of patients may require postoperative ventilation. The aim of this study was to identify the variables most useful in predicting the myasthenic patient who needs postoperative mechanical ventilation.

Methods: We applied multivariate discriminant analysis to preoperative physical, historical, laboratory and intraoperative data of 51 myasthenic patients who underwent transcervical-transsternal thymectomy to select those variables most useful in predicting the postoperative need for mechanical ventilation. The receiver operating characteristic (ROC) curve was also used to describe the discrimination abilities and to explore the trade-offs between sensitivity and specificity of the model.

Results: Discriminant analysis identified seven risk factors that correlated with the need for postoperative ventilation: FVC, $FEF_{25-75\%}$, $MEF_{50\%}$ and their percentages of the predicted values, as well as, sex. The model correctly predicted the actual ventilatory outcome in 88.2% of patients. The area under the ROC curve verified that our model correctly pre-

dicted the actual ventilatory outcome with a probability of 88.2%.

Conclusions: This model can be used for predicting the need for postoperative mechanical ventilation in myasthenia gravis patients.

Objectif: Après une thymectomie transternale, jusqu'à 50% des patients peuvent avoir besoin de ventilation postopératoire. L'objectif de cette étude était d'identifier les variables les plus utiles pour prédire le besoin de ventilation mécanique postopératoire chez le myasthénique.

Méthodes: L'analyse discriminante multifactorielle a été appliquée à l'examen physique préopératoire, à l'anamnèse, au laboratoire et aux données peropératoires de 51 myasthéniques qui ont subi une thymectomie transcervico-transternale dans le but de choisir les variables les plus utiles pour prédire le besoin postopératoire de ventilation mécanique. La courbe ROC (receiver operating characteristic) a aussi été utilisée pour décrire les capacités de discrimination et pour explorer les échanges entre la sensibilité et la spécificité du modèle.

Résultats: L'analyse discriminante a identifié sept facteurs de risque qui corrélaient avec le besoin de ventilation postopératoire: CVF, $FEF_{25-75\%}$, $FEM_{50\%}$ et leur pourcentage des valeurs prédites, ainsi que le sexe. Le modèle a prédit le résultat ventilatoire actuel chez 88,2% des patients. La surface sous la courbe a prédit correctement le résultat ventilatoire actuel avec une probabilité de 88,2%.

Conclusion: On peut utiliser ce modèle pour prédire le besoin de ventilation mécanique postopératoire chez des patients souffrant de myasthénie grave.

Key words

ANAESTHESIA: outcome;

COMPLICATIONS: myasthenia gravis;

NEUOMUSCULAR TRANSMISSION: myasthenia gravis;

STATISTICS: multivariate discriminant analysis, the receiver operating characteristic (ROC) curve;

SURGERY: thymectomy;

VENTILATION: postoperative, mechanical.

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The muscular weakness and fatigability that are the hallmarks of myasthenia gravis are due to antibodies against acetylcholine receptors at the neuromuscular junction. Myasthenic patients are at increased risk of developing postoperative respiratory failure. Following transsternal thymectomy, up to 50% of patients required prolonged postoperative ventilation.^{1,2}

Almost 15 yr ago, Leventhal *et al.*³ retrospectively applied multivariate discriminant analysis to preoperative data of 24 patients with myasthenia gravis undergoing thymectomy. They identified four risk factors felt to be of value in predicting the need for postoperative mechanical ventilation, namely: duration of myasthenia gravis ≥ 6 yr, chronic respiratory disease, pyridostigmine dosage ≥ 750 mg per day and vital capacity ≤ 2.9 L.³ When further tested in 18 patients at their institution, they reported that the model sensitivity was 78%.⁴ In contrast, Grant and Jenkins⁵ tested this predictive model in 27 patients who underwent thymectomy (four transcervical; 23 transsternal) and found it of limited value since it had a sensitivity of only 43%. Gracey *et al.*⁶ also failed to substantiate the criteria of Leventhal *et al.*³ Therefore, it is evident that the accurate prediction of postoperative respiratory failure in myasthenic patients has not been substantiated by this model.

Much has been learned in the past 15 years about myasthenia gravis. Optimization of the condition of the myasthenic patients can markedly decrease the risk of surgery and improve the outcome.⁷ In addition, different anaesthetic techniques including the balanced technique with the use of neuromuscular blocking drugs have been used with success in myasthenic patients undergoing thymectomies.^{8,9}

In this study, we applied multivariate discriminant analysis to preoperative physical, historical, laboratory and intraoperative data of 51 myasthenic patients who underwent transcervical-transsternal "maximal" thymectomy in order to select those variables most useful in predicting the myasthenic patient who needs postoperative mechanical ventilation.

Methods

The computerized database (in the Department of Thoracic Surgery) and the medical records of 51 patients with myasthenia gravis who were operated upon consecutively between July 1988 and April 1995 at King Khalid University Hospital, Riyadh, Saudi Arabia, were reviewed. The data entry was made on a prospective case-by-case basis. All the variables included in this study were present in the database. The diagnosis of myasthenia gravis was based on clinical features and one or more of the following factors: response to edrophonium chloride (Tensilon), electrophysiological studies, and demonstration of circulating antibodies directed against the acetylcholine receptor. All patients underwent transcervical-transsternal "maximal" thymectomy according to the technique described by Jaretzki and Wolff.¹⁰ Surgery was performed through separate transcervical and complete mid-sternotomy incisions. All operations were performed by the same surgical

team. Anaesthesia was managed according to the preference of each attending anaesthetist.

The variables collected for each patient include: age, sex, weight, duration of disease, highest severity score in patient's history (Osserman scale¹¹), severity of the disease at time of operation (Osserman scale), preoperative pyridostigmine daily doses, preoperative prednisone daily doses, number of preoperative plasmaphereses, history of respiratory failure, history of other chronic respiratory diseases, presence of other diseases, preoperative arterial blood gas values [PaO₂, PaCO₂ and oxygen saturation (%)], preoperative pulmonary function tests and their percentages from the predicted values [forced vital capacity (FVC), forced expiratory volume in 1 second (FEV₁), forced midexpiratory flow between 25 and 75% of the forced vital capacity (FEF_{25-75%}), maximum expiratory flow at 50% of the forced vital capacity (MEF_{50%}), and peak expiratory flow rate (PEFR)], results of serological tests (acetylcholine receptor-binding antibodies), type of anaesthetic (inhalational, balanced or regional), the use of neuromuscular blocking drugs, duration of anaesthesia, duration of mechanical ventilation postoperatively, and the presence of ectopic thymic tissue.

Patients characteristics

Of the 51 patients, 30 were female and 21 were male. Their age ranged from 10–61 (mean 27 [SD 11.4]) yr and body weight ranged from 30–120 (mean 64.2 [SD 17.4]) kg. Duration of myasthenia gravis ranged from 1–240 (mean 26.6 [SD 41.9]) months. Regarding the highest Osserman scale observed: seven patients had Osserman classification class I (ocular signs and symptoms only), 16 had class II (mild generalized weakness), 21 had class III (moderate generalized weakness with or without bulbar involvement), and seven had class IV (severe generalized weakness with or without bulbar involvement). All patients received pyridostigmine, and the preoperative dosages of pyridostigmine ranged from 60–360 (mean 208 [SD 68.5]) mg per day. Seventeen patients were receiving glucocorticoids and three were also receiving azathioprine. Preoperative plasmapheresis was performed in 37 of 51 patients with a mean of three sessions. At the time of operation, two patients had no symptoms, eight had Osserman class I, 32 had class II, seven had class III, and two had class IV. Seven patients had previous histories of myasthenic crises that required ventilatory support, and two patients needed preoperative mechanical ventilation up to the time of surgery. Fourteen patients had associated diseases: thyroid nodule (two patients), Hashimoto's thyroiditis (one patient), thyrotoxicosis (one patient), diabetes mellitus (four patients), hypertension (two patients), bronchial asthma

TABLE I Preoperative results of pulmonary function tests and arterial blood gas analyses

	Observed value (n = 51)	Percentage of the predicted value
FVC (L)	3.0 ± 0.9 (1.3–5.7)	76.2 ± 16 (42–120)
FEV ₁ (L)	2.7 ± 0.8 (1.2–4.6)	80.1 ± 16 (42–130)
FEF _{25–75%} (L · sec ⁻¹)	3.4 ± 1.0 (1.3–5.4)	80.8 ± 22 (40–129)
MEF _{50%} (L · sec ⁻¹)	4.0 ± 1.4 (1.7–7.4)	80.1 ± 21 (35–123)
PEFR (L · sec ⁻¹)	6.7 ± 2.6 (2.2–12.2)	91 ± 20 (51–127)
PaO ₂ (mmHg)	92 ± 10.7 (72–118)	–
PaCO ₂ (mmHg)	38.5 ± 4.7 (25–52)	–
O ₂ saturation (%)	95.6 ± 1.7 (92–98)	–

Values are mean ± SD (range).

(one patient), alopecia totalis (one patient), and depression (one patient). Serological tests were done in 39 patients. Acetylcholine receptor-binding antibodies were found in 24 (61.5%) of patients tested. Preoperative results of pulmonary function tests and arterial blood gas analyses are given in Table I. Thymus histology was recorded in 49 patients. It showed hyperplasia in 26 patients and hyperplasia with ectopic thymus tissue in 18 patients. In the remaining five patients the thymus was involuted.

Anaesthetic management

Premedication with either diazepam or lorazepam *po* was given to 39 patients approximately two hours before surgery. Pyridostigmine and steroid therapy was continued up to the time of surgery in 49 patients. Anaesthesia was induced with opioid and either thiopentone or propofol and was maintained with either halothane or isoflurane (16 patients) or with thoracic epidural analgesia (17 patients), supplemented with nitrous oxide in oxygen in addition to opioid and/or propofol infusion. In 25 patients, tracheal intubation was performed under topical analgesia without the use of neuromuscular blocking drugs. The remaining 26 patients received different neuromuscular blocking drugs: atracurium (14 patients), mivacurium (six patients), pancuronium (three patients), pipecuronium (two patients),¹² and *d*-tubocurarine (one patient).

Intraoperative monitoring included ECG, invasive arterial and central venous pressures, end-tidal concentration of carbon dioxide, pulse oximetry, temperature and multiple arterial blood gas determinations. Neuro-

muscular function was monitored in patients who received neuromuscular blocking drugs. Train-of-four (TOF) stimulation was applied to the ulnar nerve at the wrist at 12 sec intervals by means of a peripheral nerve stimulator. The resultant contraction of the adductor pollicis was recorded using either a force displacement transducer and neuromuscular function analyzer (Myograph 2000, Biometer International, Odense, Denmark), or an acceleration transducer and neuromuscular transmission monitor (Accelograph, Biometer International, Odense, Denmark). Residual neuromuscular block was antagonized in 22 patients with neostigmine or edrophonium mixed with atropine. Antagonism was considered adequate when the TOF ratio had reached ≥0.75.

After completion of the operation, the patient's respiratory status was assessed. Tracheal extubation was performed if the clinical and respiratory variables were judged to be adequate. The extubation criteria were: (a) adequate recovery of neuromuscular function (as judged by the TOF ratio), (b) tidal volume >5 ml · kg⁻¹ during unassisted spontaneous breathing and (c) inspiratory force of –20 cm H₂O or more. The duration of anaesthesia ranged from four to five hours. All patients were managed postoperatively in the intensive care unit. All patients received half of the preoperative pyridostigmine dose 24 hr after surgery. There were no operative or hospital deaths and no phrenic or recurrent nerve injuries in this patient population.

Data processing and statistical analyses

According to the postoperative outcome, the patients were divided into two groups: (1) those patients whose tracheas were extubated in the operating room or shortly (<six hours) after admission to the surgical intensive care unit (Group 1), and (2) those patients who were unable to have their tracheas extubated in <six hours postoperatively (Group 2).

All statistical analyses were carried out using the BMDP statistical package, release 7.01 (University of California Press, Berkeley, CA, USA, 1994). We subjected all the preoperative variables to multivariate discriminant analysis based on a stepwise, forward and backward selection of variables according to their predictive ability. An allocation rule based on the mean scores of each group was developed. Those variables that best predicted which patient tolerated early tracheal extubation and which patients needed postoperative ventilation for ≥6 hr were identified. These predictions were compared with the actual outcome.

The receiver operating characteristic (ROC) curve was also used to describe the discrimination abilities and to explore the trade-offs between sensitivity and specificity of our model. The ROC curve is constructed

TABLE II Demographic data

	Trachea readily extubatable (Group 1)	Needs ventilation (Group 2)
n	39	12
Sex (M/F)	(18/21)	(3/9)
Age (yr)	25.9 ± 10.1 (10–55)	30.9 ± 14.8 (18–61)
Weight (kg)	66.2 ± 18.4 (30–120)	58.0 ± 12.4 (37–80)
Height (cm)	159.9 ± 11.8 (121–179)	157 ± 12.1 (138–178)
Duration of symptoms (mo)	30.5 ± 46.9 (2–240)	14.3 ± 12.1 (1–36)

Values are mean ± SD (range).

from a set of (x,y) points, where x = the proportion of false positive results ($1 - \text{specificity}$) and y = the proportion of true positive results (sensitivity). The most commonly used quantitative index to describe the ROC curve is the area under the curve.¹³ The ROC area ranges from 0.5 (corresponding to a totally uninformative variable) to 1.0 (corresponding to a variable which classifies perfectly).

Results

Demographic data are shown in Table II. Thirty-nine (76.5%) patients had successful tracheal extubation in the immediate postoperative period (Group 1). In this group, the tracheas of 34 patients were extubated immediately after surgery, while in the five remaining patients tracheal extubation was performed one to four hours later. In Group 2, 12 patients (23.5%) needed ventilatory support for at least six hours (three patients required ventilatory support for six hours, two patients for eight hours, three patients for 12 hr, two patients for 18 hr, one patient for 24 hr, and one patient for 48 hr).

Discriminant analysis identified seven risk factors that correlated with the need for postoperative ventilation: FVC, $\text{FEF}_{25-75\%}$, $\text{MEF}_{50\%}$, and their percentages of the predicted values, as well as, sex. Classification functions for each group are shown in Table III. Pairwise test of equality of group means was statistically significant ($P = 0.02$).

Table III shows the coefficients of the classification functions for each group and the discriminant function coefficient (b_i) for allocating individuals to one of the two groups. The discriminant function (I) is, therefore, given by

$$I = -3.198 - 2.874 \text{ FVC} + 0.117 (\% \text{ of the predicted value of FVC}) + 2.491 \text{ MEF}_{50\%} - 0.17 (\% \text{ of the predicted value of MEF}_{50\%}) - 0.95 \text{ FEF}_{25-75\%} +$$

$$0.087 (\% \text{ of the predicted value of FEF}_{25-75\%}) + 0.623 \text{ sex}^*$$

Since the observed mean scores (Table III) for Group 1 is greater than those of Group 2 ($\bar{I}_1 > \bar{I}_2$), the allocation rule assigns an individual to Group 1 (i.e., tracheal extubation would be tolerated) if the numerical value (I) – after substitution in the above equation – is greater than zero and to Group 2 (i.e., needs ventilatory support) if the numerical value (I) is less than zero (see Appendix).

The posterior probability of group membership for each patient was used to compare the preoperative prediction with the actual postoperative respiratory outcome. In this model, the ventilatory outcomes were correctly classified in 88.2% of patients. Two patients were predicted as needing mechanical ventilation when actually their tracheas were extubated early, and four patients were falsely predicted to be ready for tracheal extubation. Examination of cases that were not classified correctly revealed that two out of the four patients that were falsely predicted to be ready for tracheal extubation were given large doses of pancuronium intraoperatively. Exclusion of these two cases from analysis did not affect the variables included in the model, but resulted in improvement of the predictability from 88.2% to 91.8%.

Several other preoperative variables, such as duration of disease, pyridostigmine or glucocorticoids dosage, Osserman scale, the presence of bulbar symptoms, previous histories of respiratory failure or associated diseases, arterial blood gas values, FEV_1 , PEFR , the titre of acetylcholine receptor-binding antibodies, type of anaesthetic (inhalational, balanced or regional), the use of neuromuscular blocking drugs, duration of anaesthesia, and the presence of ectopic thymic tissue, all failed to add a statistically significant increment to the predictive ability of the discriminant function of our model.

The receiver operating characteristic (ROC) plot and the area under the curve are shown in the Figure. The typical curve will be convex and located above the "chance line". The area under the ROC curve (based on the data of all patients), that measures the probability of the correct prediction of the model, was found to be 0.8822. This also verified that our model correctly predicted the actual postoperative respiratory outcome in myasthenic patients with a probability of 88.2%.

Discussion

The multivariate discriminant analysis used in this study identified seven variables (FVC, $\text{FEF}_{25-75\%}$, $\text{MEF}_{50\%}$, and their percentages of the predicted values, along with

*Males were given a numerical value (code) of 1 and females were given a numerical value of 2.

TABLE III Classification functions of the independent risk factors predicting the ventilatory outcome after maximal (transcervical-transsternal) thymectomy and the discriminant function coefficient (bi) for allocating individual patient to one of the two groups

Preoperative factor	Trachea readily extubatable (Group 1)	Needs ventilation (Group 2)	Discriminant function coefficient (bi) for allocation
FVC (L · sec ⁻¹)	3.2 ± 1.0 (1.3–5.7)	2.6 ± 0.8 (1.4–4.3)	
Coefficient	8.905	6.031	–2.874
FVC (% of the predicted value)	75.7 ± 15 (42–107)	77.8 ± 20 (44–120)	
Coefficient	–0.045	0.072	0.117
MEF _{50%} (L · sec ⁻¹)	4.1 ± 1.4 (1.6–7.2)	3.9 ± 1.6 (1.7–7.4)	
Coefficient	0.943	3.434	2.491
MEF _{50%} (% of the predicted value)	80 ± 21 (35–123)	80.2 ± 22 (51–114)	
Coefficient	0.121	–0.049	–0.17
FEF _{25–75%} (L · sec ⁻¹)	3.4 ± 1.0 (1.3–5.4)	3.3 ± 1.1 (1.4–4.9)	
Coefficient	–7.262	–8.212	–0.95
FEF _{25–75%} (% of the predicted value)	79.4 ± 20.6 (40–129)	85.5 ± 27.2 (43–129)	
Coefficient	0.283	0.370	0.087
Sex (M/F)	(18/21)	(3/9)	
Coefficient	15.668	16.291	0.623
Constant	–30.257	–33.455	–3.198

Values are mean ± SD (range).

*Males are given a numerical value (code) of 1 and females are given a numerical value of 2.

sex) that predicted respiratory outcome in post-thymectomy patients (Table III). Surprisingly, the risk factors previously identified by Leventhal *et al.*³ (duration of disease, pyridostigmine dosage and history of chronic respiratory disease) were found by our analysis to be unimportant. This difference could be attributed to several reasons. First, Leventhal *et al.*³ were not able to include the results of the preoperative pulmonary function tests because these data were missing from the medical records of many of their patients. Although ventilatory support sustains ventilation in the presence of muscle weakness, it does not compensate for an inadequate cough. Therefore, the objective assessment of pulmonary functions is of great value in the management of myasthenic patients. In addition, the preoperative dosages of pyridostigmine reported in Leventhal's study³ ranged from none to 1,290 mg per day, compared with 60–360 (mean 208 [SD 68.5]) mg per day in our patients. Furthermore, they identified a history of respiratory disease as a risk factor based on data from three patients only (three out of 24 patients).³ They also noted that the vital capacity (one of the risk factors identified in their model) had only slight importance.

Another important factor that should be considered is that the preoperative optimization of the patients' conditions may have improved over the past 15 yr. Pyridostigmine in combination with plasmapheresis was the prevalent mode of therapy in our patients. It was noted

that plasmapheresis was effective in treating ventilator-dependent myasthenia gravis patients.⁶ In our study, 12 patients (23.5%) needed postoperative ventilatory support with only two patients (3.9%) requiring prolonged mechanical ventilation for 24–48 hr. This is to be contrasted with the 33.3–50% reported after transsternal thymectomy in other series.^{1–3} In one study, 50% of patients ($n = 14$) required ventilation for 12 days or more.¹ Further, surgical approach to the thymus gland influences the need for postoperative ventilation. For example, the reported need for postoperative ventilation following transcervical thymectomy was 8.7%.¹⁴ This, however, can be expected since there is no disruption of the thoracic cage with its consequent decrease in vital capacity. Nevertheless, transcervical thymectomy is not as effective as transsternal thymectomy by the criteria of incidence and degree of remission.¹⁰

In our model, forced vital capacity (FVC) and forced midexpiratory flow between 25 and 75% of the forced vital capacity (FEF_{25–75%}) were noted to have large discrimination coefficients (bi) (Table III). The FVC is reduced by the same conditions that reduce vital capacity (VC).¹⁵ In healthy subjects, both VC and FVC usually result in nearly equal measured volumes.¹⁵ Loach *et al.*¹ reported that postoperative artificial ventilation was required in myasthenic patients when the preoperative VC was less than two litres. Younger *et al.*¹⁶ found that expiratory weakness was the main determinant for the

FIGURE The receiver operating characteristic (ROC) curve is a graphic representation of the relationship between sensitivity and specificity of the model described. The dotted line indicates the 50% "chance line" of no accuracy in prediction or discrimination. The area under this ROC curve is 0.8822 and it measures the probability of the correct risk rating. This indicates that our model correctly predicted the actual postoperative respiratory outcome in myasthenic patients with a probability of 88.2%.

need of postoperative supported ventilation in myasthenic patients. The expiratory muscles are needed to clear secretions and may be weaker than the inspiratory muscles in many patients.¹⁷ Ringqvist and Ringqvist¹⁷ assessed respiratory mechanics in a group of nine untreated myasthenia gravis patients. They found that maximum inspiratory force was decreased less than the maximum expiratory force.¹⁷ This finding has great implication for the ability to cough and to clear secretions. Maximum expiratory flow at 50% of the forced vital capacity (MEF_{50%}) was also one of the predictors in our model. The FEF_{25-75%} represents the average flow during mid-exhalation and is often referred to it as effort independent.¹⁵ It is also felt to reflect better the true physical state of the airways, especially small airways, in which airflow becomes primarily a function of the

net forces and geometric dimensions of the airway. Nevertheless, FEF_{25-75%} can be decreased by marked reductions in expiratory effort and by submaximal inspiration preceding the manoeuvre. Paradoxically, it may also decrease with truly maximal effort compared with slightly submaximal effort.¹⁸

In this series, 30 patients (59%) were female with a 1:1.4 male to female ratio. Furthermore, the proportion of females that needed ventilatory support was greater (M:F = 1:3). The influence of sex hormones on myasthenia gravis is evidenced by their effects on the incidence of myasthenia gravis,^{19,20} the variation of disease severity with the menstrual cycle in one third of women with myasthenia gravis,²⁰ and the increased number of oestrogen receptors on lymphocytes and thymocytes in patients with myasthenia gravis.²¹ Recently, Andrews *et al.*²² reported that sex influenced not only disease incidence but also disease severity, response to therapy, and outcome in myasthenia gravis patients.

Concern about anaesthesia for patients with myasthenia gravis has been focused on questions regarding the use of nondepolarizing neuromuscular blocking drugs. There is a reduction of the number of acetylcholine receptors at the neuromuscular junction²³⁻²⁵ and, hence, a reduction of the safety margin. This makes myasthenic patients sensitive to nondepolarizing neuromuscular blocking drugs. Some anaesthetists in the past have advocated avoiding all neuromuscular blocking drugs in these patients. Neuromuscular blocking drugs were not used in the series reported by Leventhal *et al.*³ In this study, different non-depolarizing neuromuscular blocking drugs were used in 26 patients (51%), and their use did not affect the respiratory outcome. Apart from the two patients who were given relatively large doses of pancuronium, our data demonstrated that, with titrated doses and adequate neuromuscular monitoring, intermediate- and short-acting nondepolarizing neuromuscular blocking drugs can be used safely in the myasthenic patient.^{8,9,12}

Plasmapheresis and pyridostigmine inhibit plasma cholinesterase activity.^{26,27} As most of our patients had on average three plasmaphereses, and they were receiving pyridostigmine preoperatively, plasma cholinesterase activity was less than 50% of the normal value (Naguib, unpublished data). However, all patients who had received mivacurium ($n = 6$), a drug that is metabolized by plasma cholinesterase, had their tracheas extubated at the end of surgery. This observation is in accordance with that reported by others.⁹

In avoiding the use of nondepolarizing neuromuscular blocking drugs in myasthenic patients, volatile anaesthetics may be associated with a slow recovery and postoperative respiratory depression. In addition, myas-

thenic patients are more sensitive than normal to the neuromuscular depressant effects of halothane and isoflurane.²⁸⁻³⁰

The receiver operating characteristic (ROC) curve (Figure) is a graphic representation of the relationship between sensitivity and specificity of our model. An important advantage of ROC analysis over traditional sensitivity and specificity analysis is that the area under the ROC curve is independent both of the cut-point criteria chosen and the prevalence of outcome of interest.¹³ This independence allows comparison of the ROC area across study populations where sensitivity and specificity would be distorted by differences in the prevalence of outcome of interest across populations.¹³

The model described in this study can be used in assisting the clinician to predict the need for postoperative mechanical ventilation in myasthenic patients undergoing maximal (transcervical-transsternal) thymectomy. The large ROC area noted in this study implies reproducibility. It is, however, not intended to be an absolute standard and further studies are needed for complete evaluation.

Appendix

The model described in this paper is:

$$I = -3.198 - 2.874 \text{ FVC} + 0.117 (\% \text{ of the predicted value of FVC}) + 2.491 \text{ MEF}_{50\%} - 0.17 (\% \text{ of the predicted value of MEF}_{50\%}) - 0.95 \text{ FEF}_{25-75\%} + 0.087 (\% \text{ of the predicted value of FEF}_{25-75\%}) + 0.623 \text{ sex}^*$$

In order to illustrate further how this model can be used clinically, two myasthenic patients are presented and are assessed using the formula.

Case one

A 22-yr-old woman, 154 cm in height and weighing 44.2 kg presented with a four-month history of myasthenic gravis, and was classified as an Osserman's Class IIb. Diagnosis was confirmed by the patient's rapid improvement after edrophonium chloride *iv* and by the presence of antibodies to acetylcholine receptors (12.3 nmol·L⁻¹; reference range is <0.25 nmol·L⁻¹). The patient was scheduled for transcervical-transsternal thymectomy. Preoperatively, she was taking pyridostigmine 60 mg *po* three times a day and she had three sessions of plasmapheresis. The results of her preoperative pulmonary function tests were as follows: FVC = 2.79 L·sec⁻¹ (79% of the predicted value), MEF_{50%} = 3.2

L·sec⁻¹ (68% of the predicted value) and FEF_{25-75%} = 3.03 L·sec⁻¹ (77% of the predicted value). Anaesthesia was induced with fentanyl and propofol and was maintained with thoracic epidural supplemented with propofol and 70% nitrous oxide in oxygen. Tracheal intubation was carried under topical anaesthesia of larynx and trachea (4 ml lidocaine 4%). No neuromuscular blocking drugs were used. This patient required postoperative mechanical ventilation for 12 hr.

If we substitute the values of the preoperative pulmonary function tests of this patient into the formula:

$$I = -3.198 - 2.874 (2.79) + 0.117 (79) + 2.491 (3.2) - 0.17 (68) - 0.95 (3.03) + 0.087 (77) + 0.623 (2) = -0.496$$

Since the numerical value of the discrimination function (*I*) is less than 0, the model correctly predicted that this patient would need postoperative ventilatory support.

Case two

A 19-yr-old man, 65 kg in weight and 148 cm in height, was scheduled for transcervical-transsternal thymectomy. He had a two year history of myasthenic gravis and was classified as an Osserman's Class IIa. The diagnosis had been confirmed by pharmacological testing. Preoperatively, he was taking pyridostigmine 60 mg *po* three times a day and he had three sessions of plasmapheresis. The results of his preoperative pulmonary function tests were as follows: FVC = 3.02 L·sec⁻¹ (63% of the predicted value), MEF_{50%} = 7.42 L·sec⁻¹ (86% of the predicted value) and FEF_{25-75%} = 4.02 L·sec⁻¹ (87% of the predicted value). Anaesthesia was induced with fentanyl and propofol and was maintained with propofol and 70% nitrous oxide in oxygen. Incremental doses of atracurium 50–100 µg·kg⁻¹ were used during the surgical procedure. Neuromuscular function was recorded as the evoked thenar mechanomyographic response to TOF stimulation of the ulnar nerve at 12 sec intervals. After completion of the operation, neostigmine was used to antagonize the residual neuromuscular block and tracheal extubation was carried out in the theatre after assessing the patient's respiratory status with the extubation criteria.

If we substitute the values of the preoperative pulmonary function tests of this patient into the formula:

$$I = -3.198 - 2.874 (3.02) + 0.117 (63) + 2.491 (7.42) - 0.17 (86) - 0.95 (4.02) + 0.087 (87) + 0.623 (1) = 3.729$$

Since the numerical value of the discriminant function (*I*) is greater than 0, the model correctly predicted that this patient would not require postoperative ventilatory support.

*Males are given a numerical value (code) of 1 and females are given a numerical value of 2.

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