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Predictive Value of Perioperative Blood Lactic Acid Levels for Postoperative Crisis in Myasthenia Gravis Patients Undergoing Thymectomy

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ABSTRACT

Introduction/Aims: Postoperative myasthenic crisis (POMC), which occurs specifically after thymectomy in myasthenia gravis (MG) patients, is a serious complication with known risk factors such as prior myasthenic crisis. However, the predictive value of perioperative blood lactic acid levels (BLAL) for POMC remains unclear. This study aims to determine whether changes in perioperative BLAL can predict POMC in MG patients undergoing thymectomy.

Methods: A total of 340 patients diagnosed with MG and undergoing thymectomy at the First Affiliated Hospital of Sun Yat-sen University were enrolled (January 2008–September 2018). Multivariate logistic regression analyses were employed to discern independent factors linked with POMC.

Results: Among the patients with POMC, notable differences including higher Myasthenia Gravis Foundation of America (MGFA) stage, and history of preoperative myasthenic crisis were observed. Higher postoperative lactic acid levels and the extent of changes were more prevalent in the POMC group. The multivariate analysis unveiled history of myasthenic crisis (odds ratio, OR: 67.18), postoperative BLAL change ratio greater than 50% (OR: 2.86), the video-assisted thoracoscopic surgery (VATS) approach (OR: 4.33), and higher preoperative BLAL (OR per unit: 2.68) were associated with POMC. Both continuous and grouped lactic acid models demonstrated a good predictive capability, yielding area under the curve (AUC) values of 0.84 and 0.83, respectively. The optimal threshold for 24-h postoperative BLAL was 1.98 mmol/L.

Discussion: These findings offer valuable insights for clinical decision-making and monitoring of prognosis in managing patients with MG. Future research should explore further the underlying mechanisms linking elevated lactate levels to POMC.

Abbreviations: AChR-Ab, acetylcholine receptor antibody; AUCs, area under the curve; BLAL, blood lactic acid levels; FEV1, forced expiratory volume in 1 s; FVC, forced vital capacity; MG, myasthenia gravis; MGFA, Myasthenia Gravis Foundation of America; OR, odd ratio; POMC, postoperative myasthenic crisis; QMGS, quantitative myasthenia gravis score; ROC, receiver operating characteristic; VAT, video-assisted thoracoscopic.

Jianyong Zou, Xiaojing Yao, and Zhihao Liu contributed equally in this study.

1 | Introduction

Current guidelines recommend thymectomy for patients with AChR ab+ generalized myasthenia gravis (MG), particularly those under 65 years of age with nonthymomatous AChR ab+ MG, as it improves clinical outcomes compared to prednisone alone [1]. MG is strongly associated with the thymus, with thymic abnormalities found in 80%–90% of patients, most commonly thymic hyperplasia and thymoma [2–4]. Thymectomy can alleviate symptoms but may also trigger postoperative myasthenic crisis (POMC), which occurs in 2%–30% of MG patients after surgery [5, 6]. POMC is a major contributor to postoperative mortality, yet no biomarkers exist to predict it effectively.

Research has shown that lactate levels serve as an indicator of tissue hypoxia and are an independent prognosticator factor for postoperative mortality in critically ill patients [7, 8]. Despite its relevance in critical care, the link between lactate levels and POMC remains unexplored. In 2020, Lin et al. [9] reported a patient with MG who developed hyperlactatemia and POMC post-thymectomy, highlighting stress and pain as potential triggers. While evidence connecting lactate accumulation to POMC is limited, systemic hypoxia observed in early POMC may contribute to lactate buildup. Lactate levels have been associated with the severity of MG, as shown in metabolomics studies [10] and in the context of COVID-19 [11]. Hypoxia-inducible factor HIF-1α, implicated in MG development, may also contribute to the imbalance of immune cells [12]. This study investigates the predictive value of perioperative blood lactate levels for POMC in MG patients undergoing thymectomy [4].

2 | Methods

2.1 | Study Population

In this retrospective study, clinical data were gathered from patients diagnosed with MG, all of whom underwent thymectomy at the First Affiliated Hospital of Sun Yat-sen University between January 2008 and September 2018. The patients were distinctly classified into two groups: the POMC group and the non-POMC group, based on the progression of their disease during their hospitalization, and in alignment with the established criteria for defining a myasthenic crisis (MC) [13].

Inclusion criteria were as follows: (1) clinical diagnosis of MG in accordance with the "Chinese Myasthenia Gravis Diagnosis and Treatment Guidelines", which includes the following diagnostic criteria: (a) clinical presentation: characteristic muscle weakness that worsens with activity and improves with rest; (b) antibody testing: positive acetylcholine receptor antibodies (AChR-Ab) test; (c) neurophysiological testing: positive results from repetitive nerve stimulation (RNS) or single-fiber electromyography (SFEMG) testing; (2) confirmation of thymic abnormalities through chest CT, thymic MRI, and thymic pathology, meeting the criteria for thymectomy outlined in the "Chinese Clinical Diagnosis and Treatment Guidelines for Thymic Epithelial Tumors (2021 edition)"; (3) availability of comprehensive clinical data encompassing demographic, physiological, and laboratory information; (4) having undergone thymectomy and possessing complete postoperative pathological findings.

Exclusion criteria were: (1) incomplete laboratory and clinical data in their medical records; (2) onset of POMC occurring more than 14 days after thymectomy; (3) respiratory failure arising from other factors like diaphragmatic paralysis, pneumonia or exacerbation of chronic obstructive pulmonary disease [14].

No patients with purely ocular MG underwent thymectomy. However, six patients who initially presented with generalized MG but were left with only ocular symptoms following non-surgical treatment were included in this cohort. These patients were deemed by the multidisciplinary team (MDT) to be at high risk for future symptom exacerbation, warranting the decision to proceed with thymectomy. None of the patients included in this study underwent preoperative optimization with intravenous immunoglobulin (IVIg) or plasma exchange (PLEX). No patients in this study had comorbid conditions that could have contributed to the development of POMC. This study was approved by the Ethics Committee of the First Affiliated Hospital of Sun Yat-sen University (Approval No. [2018]273). The need for written informed consent was waived by the IRB due to the retrospective design of the study.

2.2 | Data Collection

The following information was extracted from the medical records:

(1) Demographic details: including the patient's gender and age; (2) preoperative parameters: duration of disease (months); history of MC; involvement of bulbar muscles; lung function metrics: forced expiratory volume in 1 s (FEV1), forced vital capacity (FVC); severity assessment of myasthenia gravis: Myasthenia Gravis Foundation of America (MGFA) classification and quantitative myasthenia gravis score (QMGS). QMGS evaluations are routinely performed in all patients; daily dosage of pyridostigmine bromide (mg); serum AChR-Ab level (mmol/L). (3) Surgery-related variables: chosen surgical approach (transsternal or thoracoscopy); blood loss during surgery (measured in milliliters). (4) Thymus pathology: presence of thymoma or thymic hyperplasia. (5) Blood lactate measurements: at our center, lactate levels are routinely measured through blood gas analysis to assess both preoperative pulmonary function and postoperative oxygen status in MG patients. Preoperative blood gas analysis, including lactic acid levels, is conducted within 12 h prior to surgery, while postoperative analysis is performed 24 h after surgery. The following lactate-related data were collected for analysis: preoperative blood lactate level (mmol/l), 24-h postoperative blood lactate level (mmol/L), 24-h lactate change rate (%), lactate increase ratio (%) [15]. (6) Postoperative parameters: occurrence of postoperative complications: lung infection, incision infection.

2.3 | Definition

POMC was defined as encompassing patients necessitating endotracheal intubation or non-invasive mechanical ventilation for over 24 h within a 14-day span following surgery. It also included patients requiring re-intubation due to excessive secretions or inability to breathe post extubation [16]. Instances of respiratory failure attributed to other causes including

TABLE 1 | The demographic and clinical characteristics of patients.

Parameters	Postoperative MC		Difference (95% CI)	*p*
	No ($n=314$)	Yes ($n=26$)		
Characteristics				
Age (year)	25.69 ± 10.81	23.19 ± 8.08	−2.50 (−5.96 to 0.95)	1.000
Sex				1.000
Male	131 (41.72%)	13 (50.00%)	8.28% (2.83% to 13.73%)	
Female	183 (58.28%)	13 (50.00%)	−8.28% (−13.73% to −2.83%)	
Smoking history	9 (2.87%)	3 (11.54%)	8.67% (6.83% to 10.52%)	1.000
Preoperative features				
MGFA clinical classification				**< 0.001**
I + IIA + IIB	182 (57.96%)	5 (19.23%)	−38.73% (−44.19% to −33.27%)	
IIIA+IIIB	126 (40.13%)	15 (57.69%)	17.56% (12.14% to 22.99%)	
IVA + IVB + V	6 (1.91%)	6 (23.08%)	21.17% (19.65% to 22.68%)	
MGFA clinical classification				**< 0.001**
I	6 (1.91%)	0 (0.00%)	−1.91% (−3.43% to −0.40%)	
IIA	79 (25.16%)	2 (7.69%)	−17.47% (−22.27% to −12.67%)	
IIB	97 (30.89%)	3 (11.54%)	−19.35% (−24.46% to −14.24%)	
IIIA	78 (24.84%)	5 (19.23%)	−5.61% (−10.39% to −0.83%)	
IIIB	48 (15.29%)	10 (38.46%)	23.17% (19.19% to 27.16%)	
IVA	5 (1.59%)	3 (11.54%)	9.95% (8.56% to 11.33%)	
IVB	0 (0.00%)	1 (3.85%)	3.85% (−1.68% to 9.38%)	
V	1 (0.32%)	2 (7.69%)	7.37% (6.75% to 8.00%)	
Bulbar involvement	146 (46.50%)	16 (61.54%)	15.04% (9.52% to 20.56%)	1.000
Daily dose of pyridostigmine (mg)				1.000
< 240	130 (41.40%)	9 (34.62%)	−6.79% (−12.23% to −1.34%)	
≥ 240	184 (58.60%)	17 (65.38%)	6.79% (1.34% to 12.23%)	
Immunosuppressants				0.173
None	285 (90.76%)	19 (73.08%)	−17.69% (−20.89% to −14.48%)	
Azathioprine	18 (5.73%)	1 (3.85%)	−1.89% (−4.46% to 0.68%)	
Methotrexate	8 (2.55%)	3 (11.54%)	8.99% (7.25% to 10.73%)	
Tacrolimus	3 (0.96%)	3 (11.54%)	10.58% (9.51% to 11.66%)	
Use of prednisone	212 (67.52%)	20 (76.92%)	9.41% (4.23% to 14.59%)	1.000
Preoperative oral prednisone dose (mg)	100.00 ± 97.57	130.77 ± 108.70	30.77 (−8.75 to 70.28)	1.000
MC history	3 (0.96%)	9 (34.62%)	33.66% (32.58% to 34.74%)	**< 0.001**
MG onset to surgery (months)	17.93 ± 6.05	19.77 ± 4.35	1.84 (−0.55 to 4.22)	1.000
Elevated AchRAb level				1.000
No	0 (0%)	0 (0%)	0.00% (−5.53% to 5.53%)	
Yes	314 (100%)	26 (100%)	0.00% (−5.53% to 5.53%)	

(Continues)

TABLE 1 | (Continued)

Parameters	Postoperative MC		Difference (95% CI)	*p*
	No ($n=314$)	Yes ($n=26$)		
FEV1 (%)	65.79 ± 7.00	67.48 ± 7.42	1.69 (−1.13 to 4.51)	1.000
FEV1 ≤ 70%				1.000
No	99 (31.53%)	11 (42.31%)	10.78% (5.64% to 15.92%)	
Yes	215 (68.47%)	15 (57.69%)	−10.78% (−15.92% to −5.64%)	
FVC (%)	73.38 ± 7.86	75.67 ± 8.06	2.29 (−0.87 to 5.45)	1.000
FVC ≤ 75%				1.000
No	131 (41.72%)	13 (50.00%)	8.28% (2.83% to 13.73%)	
Yes	183 (58.28%)	13 (50.00%)	−8.28% (−13.73% to −2.83%)	
QMGS	16.72 ± 5.05	20.35 ± 6.07	3.62 (1.56 to 5.68)	0.094

Note: The *p* value has been adjusted using the Bonferroni correction to account for 29 univariate comparisons between two groups, and the bold font indicates a statistically significant *p* value.
Abbreviations: AChR-Ab, acetylcholine receptor antibody; ET, extended transsternal; FEV1, forced expiratory volume in 1 s; FVC, forced vital capacity; MC, myasthenic crisis; MGFA, Myasthenia Gravis Foundation of America; QMGS, quantitative myasthenia gravis score; VATS, video-assisted thoracoscopic surgery.

diaphragmatic paralysis, lung infection, or chronic obstructive pulmonary disease exacerbation were excluded [14].

Calculation of 24-h lactate change rate: the 24-h lactate change ratio was computed employing the formula: 24-h lactate change rate = ([postoperative lactate—preoperative lactate]/preoperative lactate) × 100%. A 24-h lactate change ratio exceeding 50% was classified as "lactate elevation positive," while a rate less than or equal to 50% was designated as "lactate elevation negative."

The MGFA clinical classification is provided in Table S1 [17].

QMGS criteria: the criteria for the QMGS are provided in Table S2 [18].

2.4 | Statistical Analysis

Continuous data are reported as mean ± SD (standard deviation) while categorical data are reported as number and percentage (%). For comparisons of means between groups, the Mann–Whitney U test or student's independent *t*-test was used depending on the normality assumption. Categorical data were tested using the Chi-square test or Fisher's exact test (if the expected value ≤ 5 was found). The difference for the between-group comparison and the 95% confidence interval (CI) were also reported. Bonferroni correction was used to prevent the inflation of type I error among multiple comparisons between groups. Univariate and multivariate logistic regression models were used to analyze the association between independent variables and survival results. Instead of univariate results, all independent variables were entered into a multivariate model with a forward procedure (Wald test). The estimated odds ratio (OR) and its 95% CI were reported in all logistic regression results. If a continuous variable was chosen by a multivariate model, the best cut-off was defined by the maximum Youden index in a receiver operating characteristic (ROC) analysis. ROC analysis was also further used to validate the probabilities generated from multivariate logistic regression models. The area under the curve (AUC) (95% CI), specificity (sp), and sensitivity (se) were reported. ROC analysis was used to investigate the cut-off point for postoperative lactic acid levels in predicting POMC; the coordinate with the maximum Youden index would be the cut-off point with the greatest discriminatory power. All the above analyses were performed using SPSS Version 26 (IBM, Armonk, NY). A *p* value of <0.05 was considered statistically significant. After the final multivariate model of POMC is confirmed, the variables associated with POMC were used to construct a nomogram, which was then be used to estimate the risk of POMC occurrence in individual patients. The nomogram was established through statistical software R (version 4.3.0) and package "RMS."

3 | Results

3.1 | Patient Demographic and Clinical Characteristics

A cohort of 340 patients, comprising 144 males and 196 females, was selected for study. Within this group, 26 patients developed POMC, while the remaining 314 patients were categorized as non-POMC cases. The detailed demographic and clinical characteristics are reported in Table 1.

Individuals with POMC demonstrated a significantly higher MGFA clinical classification and a higher incidence of preoperative MC (Table 1).

3.2 | Operative Indicators and Complications

Over 90% of the non-POMC group underwent extended transsternal (ET) thymectomy, while the proportion of patients in the POMC group who underwent video-assisted thoracoscopic surgery (VATS) thymectomy was descriptively higher than that of the non-POMC group (Table 2). No significance was found in blood loss, pathology results, and postoperative complications

TABLE 2 | The operative related index and postoperative complications of patients.

Parameters	Postoperative MC		Difference (95% CI)	*p*
	No ($n=314$)	Yes ($n=26$)		
Operative related index				
Surgical approach				0.534
ET	290 (92.36%)	20 (76.92%)	−15.43% (−18.37% to −12.49%)	
VATS	24 (7.64%)	6 (23.08%)	15.43% (12.49% to 18.37%)	
Blood loss (ml)				1.000
< 200	250 (79.62%)	20 (76.92%)	−2.69% (−7.15% to 1.76%)	
≥ 200	64 (20.38%)	6 (23.08%)	2.69% (−1.76% to 7.15%)	
Pathology results				1.000
Hyperplasia	242 (77.07%)	17 (65.38%)	−11.69% (−16.34% to −7.04%)	
Thymoma	72 (22.93%)	9 (34.62%)	11.69% (7.04% to 16.34%)	
Postoperative complications				
Pneumonia	12 (3.82%)	1 (3.85%)	0.02% (−2.10% to 2.15%)	1.000
Incision infection	9 (2.87%)	1 (3.85%)	0.98% (−0.87% to 2.83%)	1.000
Mediastinitis	8 (2.55%)	0 (0.00%)	−2.55% (−4.29% to −0.80%)	1.000
Sepsis	0 (0.00%)	3 (11.54%)	11.54% (6.01% to 17.07%)	**0.012**

Note: The *p* value has been adjusted using the Bonferroni correction to account for 29 univariate comparisons between two groups, and the bold font indicates a statistically significant *p* value.
Abbreviations: ET, extended transsternal; MC, myasthenic crisis; VATS, video-assisted thoracoscopic surgery.

TABLE 3 | The lactic acid level before and after operation.

Parameters	Postoperative MC		Difference (95% CI)	*p*
	No ($n=314$)	Yes ($n=26$)		
Preoperative lactic acid level (mmol/L)	1.30 ± 0.56	1.18 ± 0.77	−0.12 (−0.35 to 0.11)	1.000
PostoperativelLactic acid level (mmol/L) (24 h)	1.16 ± 0.61	1.58 ± 0.79	0.41 (0.16 to 0.66)	0.120
Ratio of lactic acid change (%)	22.53 ± 247.34	61.60 ± 104.38	39.08 (−57.14 to 135.30)	**0.004**
Lactic acid elevation (> 50%)				**0.002**
No	251 (79.94%)	12 (46.15%)	−33.78% (−38.21% to −29.35%)	
Yes	63 (20.06%)	14 (53.85%)	33.78% (29.35% to 38.21%)	

Note: The *p* value has been adjusted using the Bonferroni correction to account for 29 univariate comparisons between two groups, and the bold font indicates a statistically significant *p* value.
Abbreviation: MC, myasthenic crisis.

between non-POMC and POMC groups; however, there were three cases of sepsis in the POMC group, but none in the non-POMC group.

3.3 | Changes in Lactic Acid Levels

Preceding surgery, the baseline lactic acid levels were comparable between the two groups (Table 3). A day following the thymectomy, the POMC group displayed a greater elevation in lactic acid levels than the non-POMC group (Table 3). The POMC group also exhibited a greater increase in the ratio of lactic acid change and an elevation in lactic acid (> 50%) than the non-POMC group (Table 3).

3.4 | Independent Factors Associated With POMC

A logistic regression analysis was conducted to identify the independent factors associated with POMC (Table 4). The univariate logistic regression analysis revealed several variables that bore a significant connection to an elevated risk of POMC

TABLE 4 | Multivariate logistic regression analysis of independent factors associated with postoperative myasthenic crisis (POMC).

	Model 1		Model 2	
Parameters	**OR (95% CI)**	***p***	**OR (95% CI)**	***p***
MC history				
No	1	—	1	—
Yes	67.18 (14.43 to 312.87)	**< 0.001**	66.61 (14.70 to 301.83)	**< 0.001**
Lactic elevation				
≤ 50%	1	—	1	—
> 50%	2.86 (1.05 to 7.78)	**0.039**	3.79 (1.42 to 10.10)	**0.008**
Surgical approach				
ET	1	—	1	—
VATS	4.33 (1.26 to 14.83)	**0.020**	4.04 (1.19 to 13.74)	**0.026**
Postoperative lactic acid level (mmol/L) (24 h)	2.68 (1.30 to 5.51)	**0.007**		
Postoperative lactic acid level (mmol/L) (24 h)				
≤ 1.98			1	—
> 1.98			5.73 (1.69 to 19.43)	**0.005**

Note: The bold font indicates a statistically significant *p* value.
Abbreviations: ET, extended transsternal; MC, myasthenic crisis; OR, odds ratio; VATS, video-assisted thoracoscopic surgery.

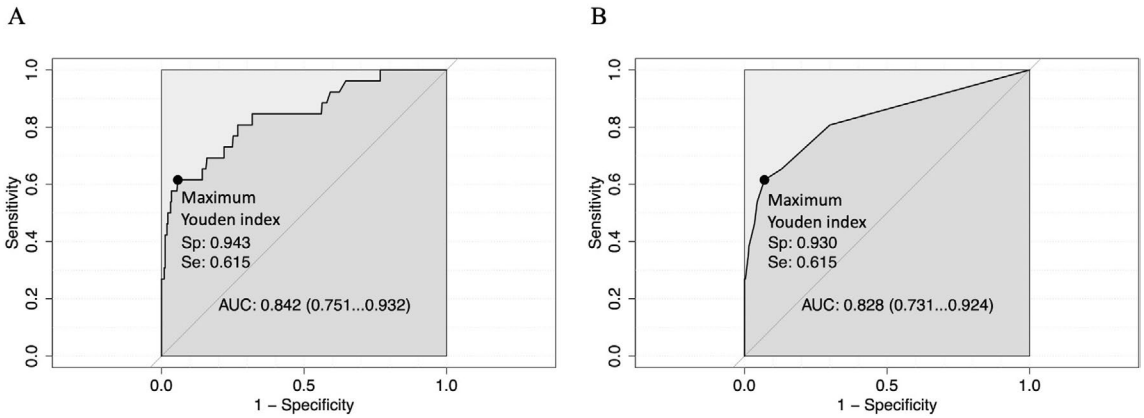

FIGURE 1 | The ROC outcomes of the multivariate models for predicting POMC. The first model incorporates continuous postoperative lactic acid levels (A), while the second model incorporates grouped postoperative lactic acid levels (cutoff: 1.98 mmol/L) (B).

(Table S3). These variables were higher MGFA clinical classification, a history of MC, a lactic acid increase exceeding 50% post-operation, selection of the VAT surgical approach, heightened preoperative lactic acid levels, and a higher QMGs score (all $p < 0.05$).

However, multivariate modeling through the forward procedure, as evaluated by the Wald test, revealed only four independent variables as significant in their association with the risk of POMC (Table 4, Model 1). The multivariate model demonstrated Cox and Snell R^2 and Nagelkerke R^2 indices of 15.41% and 36.92%, respectively, underlining its reliability in explaining the variance in the data.

Table 4 also presented a distinct multivariate model that incorporated a grouped postoperative lactic acid level (Model 2). The Cox and Snell R^2 and Nagelkerke R^2 indices for this model stood at 15.34% and 36.76%, respectively. While marginally smaller in comparison, these results exhibited a substantial degree of similarity to the preceding model, reinforcing the consistency of the findings.

3.5 | ROC Analysis and Nomograms

In the case of the continuous lactic acid model, the AUC emerged as 0.84 ($p < 0.001$, Figure 1A), attesting to its robust

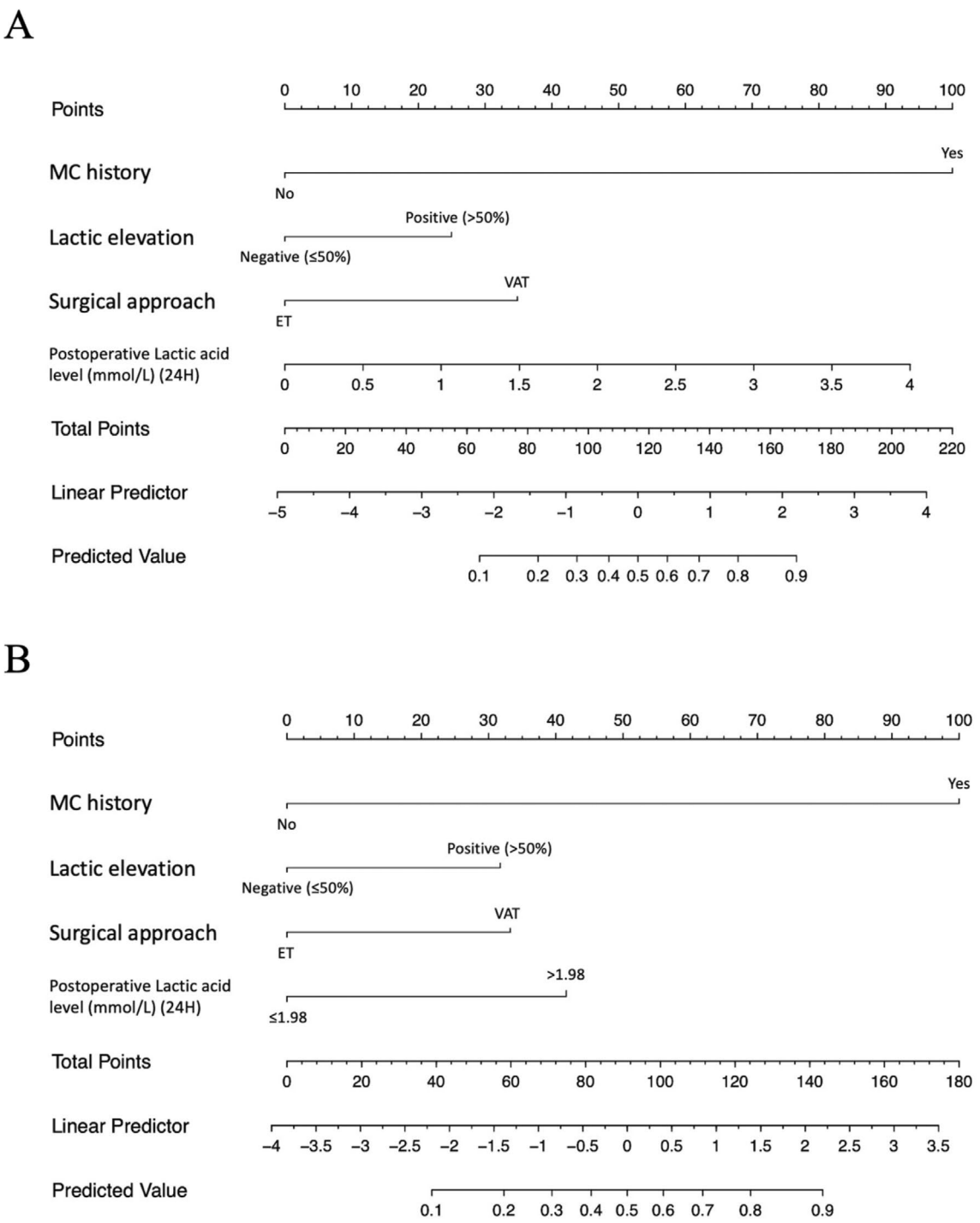

FIGURE 2 | The nomogram of the multivariate model that encompasses continuous postoperative lactic acid levels (A) or postoperative lactic acid levels (cutoff: 1.98 mmol/L) (B). Introduction to the use of a nomogram: (1) At the very top, "points" refers to the score. Below that, each variable can be marked according to the individual patient's data, and a corresponding score for that variable can be found. For example, if the MC history is "yes," it corresponds to 100 points, and a lactic elevation "positive" corresponds to 25 points. After mapping the patient's actual conditions to the results and points for each variable, calculate the total score. For instance, if a patient's total points are 160, then you would draw a vertical line at the 160 points position on the bottom part of the nomogram. This line would approximately intersect with the predicted value of 0.85, indicating that this patient's POMC risk estimate is 85%.

discriminatory ability. Similarly, the grouped lactic acid model generated an AUC of 0.83 ($p < 0.001$, Figure 1B), reaffirming its commendable diagnostic efficacy. Both models displayed a remarkable diagnostic performance, particularly notable in terms of specificity, with values of 0.94 and 0.93, respectively.

Through the ROC analysis centered on postoperative lactic acid level and its relation to POMC, a threshold of 1.98 mmol/L emerged as optimal, aligning with the highest Youden index.

To enhance the practical applicability of these findings in a clinical context, nomograms were constructed for both models. Figure 2A illustrates the continuous version, while Figure 2B depicts the grouped version, each serving as valuable tools for clinicians in their decision-making processes.

4 | Discussion

This study found that 7.6% of MG patients undergoing thymectomy experienced POMC. Both Liu et al. [5] and Watanabe et al. [19] found a correlation between POMC and factors such as thoracotomy and intraoperative blood loss exceeding 1000 mL. It is hypothesized that traditional thoracotomy, with its greater surgical impact, may increase patients' susceptibility to postoperative pulmonary infections and related complications, thereby potentially contributing to the development of POMC [20].

There was no significant difference in intraoperative blood loss between the two groups in this study. Of particular interest is the identification of the VATS surgical technique as an independent risk factor for POMC, with patients undergoing VATS surgery exhibiting a 4.33-fold heightened risk of developing POMC in contrast to those undergoing the ET approach. These findings diverge from earlier study outcomes [5, 19, 21, 22]. A possible explanation is the relatively limited utilization of VATS within this particular cohort, accounting for only 8.82% of the cases. This pronounced imbalance in case distribution could introduce bias into the analysis. A more comprehensive investigation featuring a balanced representation of both ET and VATS surgical approaches might yield a clearer and more accurate understanding of this phenomenon.

In this study, a significantly higher proportion of POMC patients had a history of MC. Multivariate logistic regression analysis confirmed that a history of MC is an independent risk factor for POMC, consistent with previous research [23]. Patients with a history of MC often require extensive medication and therapeutic interventions over a prolonged period to stabilize their condition. In the context of their already unstable disease state, the additional stress from surgical trauma and anesthesia further increases the risk of developing POMC.

This study introduces the lactate clearance rate as an observational parameter. This parameter is assessed through the 24-h lactate change ratio and the occurrence of significant elevation in blood lactate levels (> 50%). It has been incorporated as a variable under investigation to discern risk factors for POMC. The results revealed that the POMC group had significantly higher postoperative lactic acid levels at 24 h, an increased ratio of lactic acid change, and a higher incidence of lactic acid levels exceeding a 50% rise.

Both the continuous and grouped lactic acid models showed high diagnostic efficacy. Additionally, ROC analysis identified a postoperative lactic acid threshold of 1.98 mmol/L for POMC, aligning closely with the common clinical upper limit of normal lactate levels (2 mmol/L). While numerous clinical characteristics associated with POMC have been identified in prior investigations, perioperative biomarkers capable of predicting POMC have remained elusive. However, the current study introduces the potential significance of perioperative lactic acid levels and their dynamic alterations as valuable tools in predicting POMC. In our study, lactate elevation in the postoperative period was likely an early indicator of underlying hypoxia caused by respiratory muscle weakness, a hallmark of progressive POMC. This aligns with the established pathophysiology of MG, whereby respiratory compromise can lead to hypoxia and subsequent lactate accumulation. Lactate elevation itself may not act as a direct trigger for MG. Further research is needed to explore whether elevated lactate levels could exacerbate MG symptoms or contribute to the onset of MC in certain patient populations. Investigating whether lactic acid levels can be similarly employed in the context of other treatments for MG presents an avenue for further research.

The limitations of this study primarily stem from the relatively small sample size, particularly within the POMC group. This study was also retrospective, introducing the possibility of selection bias. The restricted number of covariates used in our analysis could potentially overlook confounding factors, such as pre-operative IVIg, which is sometimes administered to optimize symptoms before surgery. Although pre-operative IVIg can improve muscle strength and reduce postoperative complications [24], its impact on postoperative lactate levels has not been clearly established. Future prospective studies should address this and explore the relationship between pre-operative IVIg and postoperative lactate dynamics to refine predictive models for POMC.

5 | Conclusion

While the association between elevated postoperative lactic acid and POMC requires further validation, monitoring lactic acid levels through routine blood gas analysis may offer clinicians a practical tool to identify patients at risk for POMC. The nomograms we developed could assist in clinical decision-making and the early identification of patients who may benefit from preventive interventions. In forthcoming endeavors, a prospective study should be undertaken to validate this study's findings.

Author Contributions

Zhenguo Liu: resources, supervision, validation. **Haoshuai Zhu:** software, supervision, resources. **Xin Zhang:** methodology, validation. **Zhenguang Chen:** conceptualization. **Chunhua Su:** writing – original draft, writing – review and editing. **Jianyong Zou:** conceptualization, resources, writing – original draft. **Xiaojing Yao:** software, formal analysis, methodology. **Zhihao Liu:** conceptualization, investigation.

Conflicts of Interest

The authors declare no conflicts of interest.

Data Availability Statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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Supporting Information

Additional supporting information can be found online in the Supporting Information section.