Clinical Report

Journal of INTERNATIONAL MEDICAL RESEARCH

Journal of International Medical Research
2016, Vol. 44(6) 1524–1533

DOI: 10.1177/0300060516669893
imr.sagepub.com
SAGE

Predictors of extubation outcomes following myasthenic crisis

Zhenguo Liu[1], Shiyuan Yao[1], Qian Zhou[2], Zhensheng Deng[1], Jianyong Zou[1], Huiyu Feng[3], Hua Zhu[4] and Chao Cheng[1]

Abstract

Objective: Myasthenic crisis (MC) is considered the most severe adverse event in patients with myasthenia gravis. The present retrospective study was performed to evaluate the predictors of clinical outcomes in patients with MC.

Methods: The medical charts of 33 patients (19 women, 14 men) with 76 MC attacks from 2002 to 2014 were retrospectively reviewed. Early extubation (≤7 days) and prolonged ventilation (>15 days) during the MC were used to assess patient outcomes.

Results: Among the 33 patients, 24 (72.7%) had positive acetylcholine receptor antibody test results and 20 (60.6%) experienced recurrent MC attacks (≥2 episodes) during follow-up (median 83.6 months, range 1.5–177 months). Plasma exchange during an MC was significantly associated with early extubation. Male sex, older age (>50 years), atelectasis, and ventilator-associated pneumonia significantly contributed to prolonged ventilation. In 22 patients who underwent thymectomy, both the duration between MC attacks and the mean number of MC attacks were significantly reduced after surgery.

Conclusions: Plasma exchange during MC attacks was found to be important for early extubation; older patients and those with atelectasis or ventilator-associated pneumonia were more vulnerable to prolonged ventilation. Thymectomy may be useful to prevent recurrence of MC.

Keywords

Myasthenia gravis, myasthenic crisis, early extubation, thymectomy, plasma exchange, prolonged ventilation, surgery

Date received: 6 March 2016; accepted: 26 August 2016

[1]Department of Thoracic Surgery, The First Affiliated Hospital of Sun Yat-sen University, Guangzhou, People's Republic of China
[2]Clinical Trials Unit, The First Affiliated Hospital of Sun Yat-sen University, Guangzhou, People's Republic of China
[3]Department of Neurology, The First Affiliated Hospital of Sun Yat-sen University, Guangzhou, People's Republic of China
[4]Department of Surgery, Davis Heart and Lung Research Institute, The Ohio State University Wexner Medical Center, Columbus, OH, USA

Corresponding author:
Chao Cheng, Department of Thoracic Surgery, The First Affiliated Hospital of Sun Yat-sen University, 58 Zhongshan 2nd Road, Guangzhou 510080, P.R. China.
Email: drchengchao@163.com.

Introduction

Myasthenia gravis (MG) is an autoimmune disease caused by antibodies to acetylcholine receptors on the postsynaptic motor endplate in the neuromuscular junction, leading to generalized or localized muscle weakness.[1,2] Myasthenic crisis (MC) is a severe presentation of MG in which patients experience a rapid deterioration of muscle control. In its most severe form, MC leads to paralysis of the respiratory or upper airway muscles, resulting in respiratory failure that requires mechanical ventilation and intensive care unit management.[2,3] MC is considered the most severe life-threatening but reversible neurological emergency in patients with MG. The lifetime prevalence of MC in patients with MG ranges from 20% to 30% and most frequently occurs within the first year of illness.[3–5]

An MC can result from many different aetiologies, including respiratory tract infections, drug abuse, electrolyte imbalances, or other unidentifiable factors.[2,3,6] The management of MC is challenging because of its fluctuant nature.[7–9] With improvement in respiratory care and intensive care unit management, the MC-associated mortality rate has declined from >40% in the early 1960s to approximately 5% today.[2,5] Immunologic therapies, including plasma exchange (PE), intravenous immunoglobulin (IVIG), and corticosteroids, are considered the mainstays of treatment during an MC; however, no consensus or standardized management for these patients has been established.[2,4,7] Additionally, thymus dysfunction is pathogenically linked to MG, and thymectomy has been widely performed as part of the treatment of general MG. However, little is known about the influence of thymectomy on MC attacks. Therefore, the present retrospective chart review was performed to evaluate 33 patients with 76 episodes of MC at the Myasthenia Gravis Research Center of the First Affiliated Hospital of Sun Yat-sen University, China from 2002 to 2014. In this cohort of Chinese patients, the authors analysed potential factors affecting the outcomes of MC and studied the potential relationship between thymectomy and MC attacks.

Patients and methods

Patients

The medical charts of 33 Chinese patients with MG with a history of MC diagnosed and treated from May 2002 to December 2014 at the Myasthenia Gravis Research Center of the First Affiliated Hospital of Sun Yat-sen University were retrospectively reviewed. This retrospective study was approved by the Ethics Committee and Institutional Review Board of the First Affiliated Hospital of Sun Yat-sen University. MG was diagnosed by experienced neurologists using previously reported standard diagnostic criteria.[10] MC was defined as a rapid deterioration of MG characterized by neuromuscular respiratory failure requiring ventilator support and airway protection.[11] Patients with MG undergoing a surgical procedure requiring intubation and who experienced delayed extubation of >24 h after the procedure were also considered to have experienced an MC.[4,6] Long-term follow-up was continued through outpatient clinic visits or telephone interviews, and the interval between two consecutive follow-up visits was <6 months.

Treatments

A multidisciplinary protocol was required for the management of MC.[2,12] Experienced intensive care unit neurologists managed the patients and their complications with a combination of general critical care treatment, respiratory support (intubation and mechanical ventilation, noninvasive positive-pressure ventilation), and medications

including cholinesterase inhibitors and specific immunotherapies (e.g., PE, IVIG, corticosteroid treatment). All patients initially underwent standard intubation and mechanical ventilation; tracheostomy was performed when the duration of intubation was ≥2 weeks. Typically, guidelines for extubation in patients without MG include a vital capacity of ≥15 ml/kg, maximal inspiratory pressure of ≤−20 cm H_2O, expiratory pressure of >40 cm H_2O, and tidal volume of ≥5 ml/kg.[12] However, there is a lack of clinical criteria for when and how to safely extubate patients with MG because of their tendency to develop fluctuating weakness and pulmonary complications. Therefore, the decision to extubate patients with MG relies mostly on the clinical judgment of the intensive care unit neurologist.

Clinical responses

The duration of ventilation during an MC is an important indicator of treatment efficacy.[2,12,13] In the present study, early extubation and prolonged ventilation were considered the primary outcome measures. Early extubation was defined as intubation and ventilation support for <7 days; prolonged ventilation was defined as the requirement for mechanical ventilation for >15 days.[13] For patients with MG who underwent thymectomy, the severity and frequency of MC before and after thymectomy were also evaluated during the long-term follow-up.

Statistical analysis

Statistical analysis was performed with SPSS 18.0 software (IBM, Armonk, NY, USA). Continuous variables are presented as median with interquartile range. Categorical data are presented as counts and proportions. Categorical variables were compared by the chi-square test or Fisher's exact test. Paired variables in Table 5 were analysed by the paired McNemar test. The duration of intubation during MC attacks was evaluated by Kaplan–Meier analysis using the Wilcoxon test. Statistical significance was set at $P < 0.05$.

Results

Patient profile

Thirty-three patients with MG (19 women, 14 men) with 76 documented episodes of MC managed at the Myasthenia Gravis Research Center were included in the analysis. The median age at MG onset was 33 years (range 2.8 – 75 years), and the median interval from disease onset to first MC was 6 months (range 0.5 – 60 months). Twenty-two patients (66.7%) underwent thymectomy. Eight patients (24.2%) were diagnosed with concurrent thymoma. Twenty-four patients (72.7%) were acetylcholine receptor antibody-positive. The main comorbid diseases were hyperthyroidism (4 patients), hypertension (2 patients), and pulmonary tuberculosis (2 patients). The characteristics of the study cohort are summarized in Table 1. Within the follow-up period (median 83.6, range 1.5 – 177 months), 20 of 33 patients (60.6%) experienced recurrent MCs (≥2 episodes).

Early extubation and prolonged ventilation

Early extubation (ventilation of ≤7 days) and prolonged ventilation (ventilation of >15 days) were evaluated as outcome measures, and the potential risk factors affecting these outcomes in patients with MC were assessed. First, the outcomes following each patient's first MC were analysed. The following variables were included in the analysis: sex, age at the time of MC onset, comorbid hyperthyroidism, any identifiable triggers of MC, immunotherapies administered for treatment, atelectasis, and ventilator-associated pneumonia (VAP). Using univariate analysis, patients who underwent

Table 1. Demographic and clinical characteristics of 33 patients with myasthenic crisis.

Variables	Descriptions	
Sex		
Female	19	57.6
Male	14	42.4
Age at MG onset, years	33	(2.8–75)
Interval from MG onset to first MC, months	6	(0.5–60)
Thymoma	8	24.2
Thymectomy	22	66.7
Comorbid diseases		
Hyperthyroidism	4	12.1
Hypertension	2	6.1
Pulmonary tuberculosis	2	6.1
AchR antibody-positive status	24	72.7
Episodes of MC	76	(1–8)
Follow-up time, months	83.6	(1.5–177)

Data are presented as n (%) or median (range) with the exception of episodes of MC, which are presented as total (range). MG, myasthenia gravis; MC, myasthenic crisis; AchR, acetylcholine receptor.

early PE were more likely to be successfully extubated early ($P = 0.049$). There were no differences among the use of PE, IVIG, or corticosteroid treatments in patients with prolonged ventilation. Male sex ($P = 0.047$), an age of >50 years ($P = 0.023$), atelectasis ($P = 0.008$), and VAP ($P = 0.004$) occurred significantly more frequently in patients with prolonged ventilation. Identifiable causes of MC and the anti-acetylcholine receptor antibody status were not associated with early extubation or prolonged ventilation. These results are summarized in Tables 2 and 3. The results of a comparison of patients in the early extubation group (n = 11) and prolonged extubation group (n = 8) were consistent with the above-described conclusion: younger female patients with PE tended to undergo successful early extubation, while older male patients with atelectasis or VAP tended to have poor outcomes (Table 4). In an effort to determine whether the role of PE during the first MC attack of each patient with MG could be generalized to other types of MC, 55 episodes of MC were analysed (n = 28 for early extubation, n = 27 for prolonged extubation); the results also showed that PE might contribute to successful early extubation (Supplementary Table 1) Furthermore, Kaplan–Meier analysis using the Wilcoxon test revealed that male sex ($P = 0.024$), atelectasis ($P = 0.013$), and VAP ($P < 0.001$) were associated with prolonged ventilation, and the use of PE ($P = 0.068$) seemed to be a good predictor of early extubation (Figure 1).

Thymectomy and MC attacks

The relationship between thymectomy and MC in patients with MG undergoing surgical treatment is shown in Table 5. The severity of MC, including the duration of ventilation, rate of early extubation, and prolonged ventilation, was analysed in these patients. There was no difference in the duration of ventilation between patients who developed MC before and after thymectomy. Additionally, patients who underwent thymectomy had significantly fewer MC episodes ($P = 0.016$) and a longer duration between MC attacks (median, 46 vs. 9 months, $P = 0.036$) than did patients who did not undergo thymectomy. Therefore, thymectomy seemed to be associated with a decreased risk of MC recurrence but not severity.

Discussion

Myasthenia gravis is a rare disease with an estimated prevalence of 5 to 15 per 100 000 individuals. Of those diagnosed with MG, 20% to 30% will experience an MC.[3–5,14] Although an MC is a severe, life-threatening event in patients with MG, few prospective studies on MCs in large cohorts have been performed. The current understanding of

Table 2. Analysis of potential factors affecting early extubation (≤7 days) during a myasthenic crisis.

Variables	No.	Ventilation ≤7 days n = 11 (33.3%)	Ventilation >7 days n = 22 (66.7%)	*P*-value*
Sex				0.105
Male	14	2 (18.2)	12 (54.5)	
Female	19	9 (81.8)	10 (45.5)	
Age at MC onset				0.141
≤50 years	23	10 (90.9)	13 (59.1)	
>50 years	10	1 (9.1)	9 (40.9)	
Comorbid hyperthyroidism				0.586
Yes	4	2 (18.2)	2 (9.1)	
No	29	9 (81.8)	20 (90.9)	
Causes of MC				0.903
Pulmonary infectious	20	6 (54.5)	14 (63.6)	
DRPS	6	2 (18.2)	4 (18.2)	
Electrolyte imbalance	3	1 (9.1)	2 (9.1)	
Unknown	4	2 (18.2)	2 (9.1)	
Treatment during MC				
Plasma exchange				0.049
Yes	16	8 (72.7)	8 (36.4)	
No	17	3 (27.3)	14 (63.6)	
IVIG				0.794
Yes	22	7 (63.6)	15 (68.2)	
No	11	4 (36.4)	7 (31.8)	
Corticosteroid				1.000
Yes	24	8 (72.7)	16 (72.7)	
No	9	3 (27.3)	6 (27.3)	
Atelectasis				0.143
Yes	5	0 (0.0)	5 (22.7)	
No	28	11 (100.0)	17 (77.3)	
Ventilator-associated pneumonia				0.026
Yes	18	3 (27.3)	15 (68.2)	
No	15	8 (72.7)	7 (31.8)	
Anti-AchR antibody status				1.000
Positive	24	8 (72.7)	16 (72.7)	
Negative	9	3 (27.3)	6 (27.3)	

Data are presented as n (%).

Pulmonary infections included aspiration pneumonitis, bacterial pneumonia, and nonspecific upper respiratory infection. MC, myasthenic crisis; IVIG, intravenous immunoglobulin; DRPS, drug-related problems, including discretionary or non-prescribed drug withdrawal or administration; AchR, acetylcholine receptor.

*Chi-square test.

the clinical course, complications, treatments, and outcomes of MC is mostly based on retrospective reports.[2,5,13,15,16] Therefore, the present retrospective study of a relatively large cohort of Chinese patients with MG and a history of MC was performed to further investigate this life-threatening disease. The study showed that 33.3% of patients with MC achieved early extubation (≤7 days), and only 24.2% of patients needed prolonged ventilation (>15 days). Treatment with PE ($P = 0.049$)

Table 3. Analysis of potential factors affecting prolonged ventilation (>15 days) in patients with a myasthenic crisis.

Variables	No.	Ventilation ≤15 days (n = 25, 75.8%)	Ventilation >15 days (n = 8, 24.2%)	*P*-value*
Sex				0.047
Male	14	8 (32.0)	6 (75.0)	
Female	19	17 (68.0)	2 (25.0)	
Age at MC onset				0.023
≤50 years	23	20 (80.0)	3 (37.5)	
>50 years	10	5 (20.0)	5 (62.5)	
Comorbid hyperthyroidism				1.000
Yes	4	3 (13.6)	1 (12.5)	
No	29	22 (86.4)	7 (87.5)	
Causes of MC				0.954
Pulmonary infectious	20	15 (60.0)	5 (62.5)	
DRPS	6	5 (20.0)	1 (12.5)	
Electrolyte metabolism imbalance	3	2 (8.0)	1 (12.5)	
Unknown	4	3 (12.0)	1 (12.5)	
Treatment during MC				
Plasma exchange				0.225
Yes	16	14 (56.0)	2 (25.0)	
No	17	11 (44.0)	6 (75.0)	
IVIG				0.315
Yes	22	15 (60.0)	7 (87.5)	
No	11	10 (40.0)	1 (12.5)	
Corticosteroid				1.000
Yes	24	18 (72.0)	6 (75.0)	
No	9	7 (28.0)	2 (25.0)	
Atelectasis				0.008
Yes	5	1 (4.0)	4 (50.0)	
No	28	24 (96.0)	4 (50.0)	
Ventilator-associated pneumonia				0.004
Yes	18	10 (40.0)	8 (100.0)	
No	15	15 (60.0)	0 (0.0)	
Anti-AchR antibody status				0.229
Positive	24	20 (80.0)	4 (50.0)	
Negative	9	5 (20.0)	4 (50.0)	

Data are presented as n (%).

Pulmonary infections included aspiration pneumonitis, bacterial pneumonia, and nonspecific upper respiratory infection. MC, myasthenic crisis; IVIG, intravenous immunoglobulin; DRPS, drug-related problems, including discretionary or non-prescribed drug withdrawal or administration. AchR, acetylcholine receptor.

*Chi-square test.

may be useful for early extubation. However, male sex ($P = 0.047$), age of >50 years ($P = 0.023$), atelectasis ($P = 0.008$), and VAP ($P = 0.004$) were significantly associated with prolonged ventilation. This conclusion was further confirmed by comparison between patients in the early extubation group (n = 11) and prolonged

Table 4. Potential factors affecting ventilation time (≤7 or >15 days) in patients with a myasthenic crisis.

Variables	No.	Ventilation ≤7 days (n = 11)	Ventilation >15 days (n = 8)	*P*-value*
Sex				0.024
Male	8	2 (25.0)	6 (75.0)	
Female	11	9 (81.8)	2 (18.2)	
Age at MC onset				0.041
≤50 years	13	10 (76.9)	3 (23.1)	
>50 years	6	1 (16.7)	5 (83.3)	
Comorbid hyperthyroidism				1.000
Yes	3	1 (66.7)	1 (33.3)	
No	16	9 (56.2)	7 (43.8)	
Causes of MC				0.961
Pulmonary infectious	11	6 (54.5)	5 (45.5)	
DRPS	3	2 (66.7)	1 (33.3)	
Electrolyte metabolism imbalance	2	1 (50.0)	1 (50.0)	
Unknown	3	2 (66.7)	1 (33.3)	
Treatment during MC				
Plasma exchange				0.070
Yes	10	8 (80.0)	2 (20.0)	
No	9	3 (33.3)	6 (66.7)	
IVIG				0.338
Yes	14	7 (50.0)	7 (50.0)	
No	5	4 (80.0)	1 (20.0)	
Corticosteroid				1.000
Yes	14	8 (57.1)	6 (42.9)	
No	5	3 (60.0)	2 (40.0)	
Atelectasis				0.018
Yes	4	0 (0.0)	4 (100.0)	
No	15	11 (73.3)	4 (26.7)	
Ventilator-associated pneumonia				0.003
Yes	11	3 (27.3)	8 (72.7)	
No	8	8 (100.0)	0 (0.0)	
Anti-AchR antibody status				0.377
Positive	12	8 (66.7)	4 (33.3)	
Negative	7	3 (42.9)	4 (57.1)	

Data are presented as n (%).

Pulmonary infections included aspiration pneumonitis, bacterial pneumonia, and nonspecific upper respiratory infection. MC, myasthenic crisis; IVIG, intravenous immunoglobulin; DRPS: drug-related problems, including discretionary or non-prescribed drug withdrawal or administration; AchR, acetylcholine receptor.

*Fisher's exact test.

extubation group (n = 8). In addition, there was evidence that thymectomy may be related to a reduction in MC recurrence.

Plasma exchange and IVIG are often used during an MC. However, because of the lack of evidence and clinical consensus, the choice of which immunomodulating treatment to use relies on the judgment of the treating physician.[2,7,12,17–19] The present study showed that PE is an effective treatment for MC. The use of PE was associated with a significantly higher rate of early

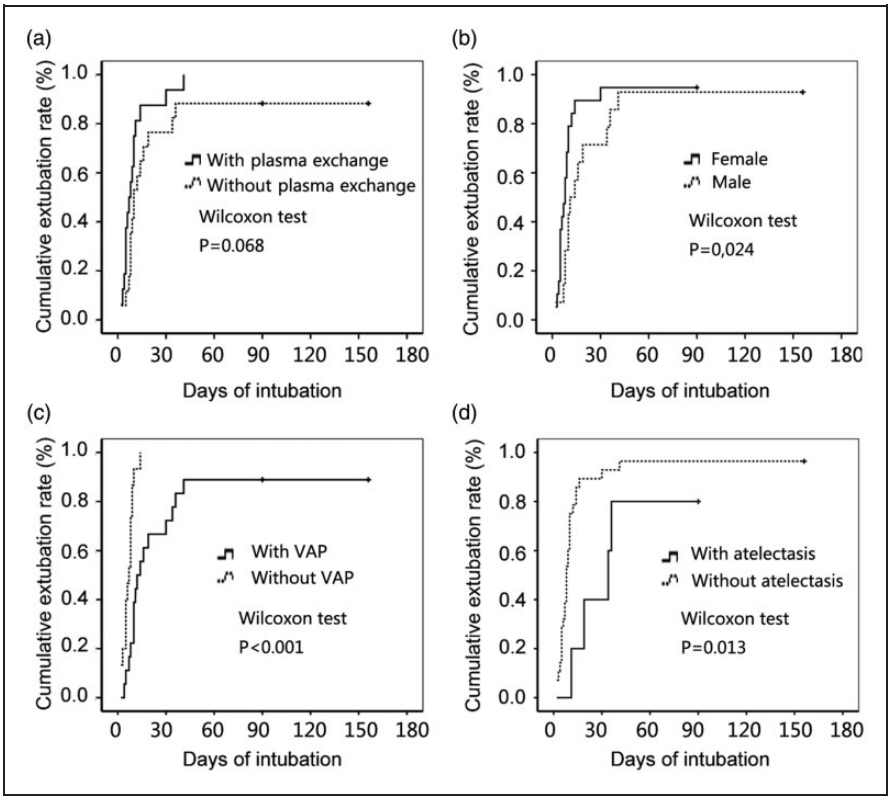

Figure 1. Kaplan–Meier curves of extubation in patients with myasthenia gravis during a myasthenic crisis. (a) The use of plasma exchange during each crisis seemed to positively contribute to early extubation. (b) Male sex, (c) ventilator-associated pneumonia, and (d) atelectasis after intubation were significantly associated with delayed extubation. A *P*-value of <0.05 was considered statistically significant.

Table 5. Relationship between thymectomy and myasthenic crisis in patients with myasthenia gravis undergoing surgical treatment.

Variables	MCBT	MCAT	*P*-value*
Severity of MC			
Days of ventilation, median (IQR)	8 (5–14)	5 (3–12)	0.140
Early extubation, $\leq$7 days (n)	7	10	0.453
Prolonged ventilation, $>$15 days (n)	3	2	1.000
Frequency of MC			
Months between MC attacks (mean, range)	9 (7–24)	46 (11.6–61.7)	0.036
Number of episodes, mean (range)	1 (1–3)	1 (1–1)	0.016
Number of episodes, total (range)	29 (1–6)	17 (1–2)	–

MCBT, myasthenic crisis before thymectomy; MCAT, myasthenic crisis after thymectomy.
*Paired variables were analysed by the paired McNemar test.

extubation, whereas the use of IVIG was not significant. As demonstrated in previous studies, PE can rapidly eliminate the pathological autoantibodies that lead to the phenotypic expression of MG.[20] The mechanism by which IVIG acts is less clear, and it may take longer for IVIG to reach its maximal effect.[21–23] However, further clarification with randomized controlled clinical trials is needed.

Respiratory complications often affect the prognosis of MC.[2,12,24] In the present cohort, VAP occurred in 18 of 33 (54.5%) patients and was an independent adverse prognostic factor for early extubation ($P = 0.026$). In previous reports, VAP was common and identified as a main cause of prolonged intubation or reintubation during MC.[24] Strategies aimed at preventing VAP are needed to improve MC therapy and allow for early extubation. Interventions that reportedly prevent VAP include suction, intermittent positive-pressure breathing, bronchodilators, and chest physiotherapy.[25] Additionally, five patients (15.2%) in the present study developed pulmonary atelectasis during their MC; atelectasis was significantly associated with prolonged ventilation ($P = 0.008$).

The current study also showed that thymectomy was related to a reduced frequency but not severity of MC. A limited number of studies have reported a relationship between thymectomy and MC.[26–28] A study of 20 patients from Iran concluded that thymectomy decreased the rate of MC in patients with non-thymomatous MG.[27] Massine et al.[26] also reported that thymectomy reduced the rates of MC. However, because of small sample sizes and lack of long-term follow-up, conclusive evidence has not yet been provided. The present study involved a relatively large cohort with a long-term follow-up. Despite the evidence suggesting a relationship between thymectomy and a decreased risk of MC, the retrospective study design does not allow for causal conclusions regarding the association of thymectomy with the risk of MC recurrence and ventilator prognosis.

This study is the first comprehensive analysis of predictors of early extubation and prolonged ventilation during MC in a Chinese cohort. Because of the retrospective and observational nature of the study, the results are subject to limitations. First, as a retrospective analysis, the study is vulnerable to selection bias. Second, various physicians treated and evaluated the patients based on personal clinical judgments. Third, the analysis is limited by the sample size and inability to stratify patients into more specific clinical categories for comparison. Nevertheless, to the best of our knowledge, this is the first cohort of Chinese patients with MC to be studied in aggregate. The results indicate that the use of PE and prevention of VAP and atelectasis are important for early extubation. Thymectomy may be useful for the prevention of MC recurrence, but more research on this topic is required. A multicentre randomized controlled trial is needed to confirm these conclusions.

Acknowledgments

The authors thank Fenghua Xu for providing assistance with the statistical analysis. The authors also thank Honghe Luo and Fotian Zhong for providing administrative support in this study.

Declaration of conflicting interests

The authors declare that there is no conflict of interest.

Funding

The work was supported by grants from the China National Natural Sciences Foundation (No. 81572391 to C. Cheng), the Guangdong Natural Sciences Foundation (No. S2012010008678 to C. Cheng), and the Research and Development

Program of Sun Yat-sen University (No. 10YKPY09 to C. Cheng).

References

1. Drachman DB. Myasthenia gravis. *N Engl J Med* 1994; 330: 1797–1810.
2. Thomas CE, Mayer SA, Gungor Y, et al. Myasthenic crisis: clinical features, mortality, complications, and risk factors for prolonged intubation. *Neurology* 1997; 48: 1253–1260.
3. Lacomis D. Myasthenic crisis. *Neurocrit Care* 2005; 3: 189–194.
4. Juel VC. Myasthenia gravis: management of myasthenic crisis and perioperative care. *Semin Neurol* 2004; 24: 75–81.
5. Cohen MS and Younger D. Aspects of the natural history of myasthenia gravis: crisis and death. *Ann N Y Acad Sci* 1981; 377: 670–677.
6. Chaudhuri A and Behan PO. Myasthenic crisis. *QJM* 2009; 102: 97–107.
7. Jani-Acsadi A and Lisak RP. Myasthenic crisis: guidelines for prevention and treatment. *J Neurol Sci* 2007; 261: 127–133.
8. Bershad EM, Feen ES and Suarez JI. Myasthenia gravis crisis. *South Med J* 2008; 101: 63–69.
9. Kirmani JF, Yahia AM and Qureshi AI. Myasthenic crisis. *Curr Treat Options Neurol* 2004; 6: 3–15.
10. Liu Z, Feng H, Yeung SC, et al. Extended transsternal thymectomy for the treatment of ocular myasthenia gravis. *Ann Thorac Surg* 2011; 92: 1993–1999.
11. Bedlack RS and Sanders DB. On the concept of myasthenic crisis. *J Clin Neuromuscul Dis* 2002; 4: 40–42.
12. Godoy DA, Mello LJ, Masotti L, et al. The myasthenic patient in crisis: an update of the management in neurointensive care unit. *Arq Neuropsiquiatr* 2013; 71: 627–639.
13. Liu N, Liu Q, Wu X, et al. Predictors of outcome of myasthenic crisis. *Neurol Sci* 2015; 36: 801–802.
14. Nicolle MW. Myasthenia gravis. *Neurologist* 2002; 8: 2–21.
15. Gracey DR, Divertie MB and Howard FM, Jr. Mechanical ventilation for respiratory failure in myasthenia gravis. Two-year experience with 22 patients. *Mayo Clin Proc* 1983; 58: 597–602.
16. Sellman MS and Mayer RF. Treatment of myasthenic crisis in late life. *South Med J* 1985; 78: 1208–1210.
17. Graves M and Katz JS. Myasthenia gravis. *Curr Treat Options Neurol* 2004; 6: 163–171.
18. Qureshi AI, Choudhry MA, Akbar MS, et al. Plasma exchange versus intravenous immunoglobulin treatment in myasthenic crisis. *Neurology* 1999; 52: 629–632.
19. Gajdos P, Chevret S and Toyka K. Intravenous immunoglobulin for myasthenia gravis. *Cochrane Database Syst Rev* 2003; 63: 845–848.
20. Antozzi C, Gemma M, Regi B, et al. A short plasma exchange protocol is effective in severe myasthenia gravis. *J Neurol* 1991; 238: 103–107.
21. Howard JF Jr. Intravenous immunoglobulin for the treatment of acquired myasthenia gravis. *Neurology* 1998; 51(6 Suppl 5): S30–S36.
22. Zivkovic S. Intravenous immunoglobulin in the treatment of neurologic disorders. *Acta Neurol Scand* 2015; 133: 84–96.
23. Ballow M. Mechanisms of immune regulation by IVIG. *Curr Opin Allergy Clin Immunol* 2014; 14: 509–515.
24. Rabinstein AA and Mueller-Kronast N. Risk of extubation failure in patients with myasthenic crisis. *Neurocrit Care* 2005; 3: 213–215.
25. Varelas PN, Chua HC, Natterman J, et al. Ventilatory care in myasthenia gravis crisis: assessing the baseline adverse event rate. *Crit Care Med* 2002; 30: 2663–2668.
26. El Hammoumi M, Arsalane A, El Oueriachi F, et al. Surgery of myasthenia gravis associated or not with thymoma: a retrospective study of 43 cases. *Heart Lung Circ* 2013; 22: 738–741.
27. Soleimani A, Moayyeri A, Akhondzadeh S, et al. Frequency of myasthenic crisis in relation to thymectomy in generalized myasthenia gravis: a 17-year experience. *BMC Neurol* 2004; 4: 12.
28. Nam TS, Lee SH, Kim BC, et al. Clinical characteristics and predictive factors of myasthenic crisis after thymectomy. *J Clin Neurosci* 2011; 18: 1185–1188.