Anaesthesia for thymectomy in adult and juvenile myasthenic patients

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Purpose of review
Myasthenia gravis, a chronic disease of the neuromuscular junction, is associated with an interaction with neuromuscular blocking agents (NMBAs). As thymectomy is often the method of choice for its treatment, anaesthetic management requires meticulous preoperative evaluation, careful monitoring, and adequate dose titration. The frequency of video-assisted thoracoscopic extended thymectomy (VATET) is also increasing, making the use of NMBA obligatory. The number of cases of the juvenile form has also increased over years; airway management in juvenile one-lung ventilation is another challenge.

Recent findings
Sugammadex appears to be a safe choice to avoid prolonged action of NMBA also in patients with myasthenia gravis, although this information has to be confirmed in further series. The number of VATETs is increasing so that the experience with sugammadex will also increase in time. In non-VATET operations, use of NMBA should and can be avoided as much as possible. New scoring systems are defined to predict a postoperative myasthenic crisis. For VATET in juvenile cases, blockers can be a good option for the airway management.

Summary
Anaesthetic management of thymectomy in myasthenia gravis requires experience concerning different approaches. Sugammadex should be considered as a possible further step toward postoperative safety.

Keywords
muscle relaxants, myasthenia gravis, one-lung ventilation

INTRODUCTION

The last review about myasthenia gravis in Current Opinion in Anaesthesiology was in 2001 [1]. Since then, a lot of things have changed in this topic: there is new information concerning it's pathology, which has also changed and improved the therapeutic approach. Regarding surgical treatment, not only the experience has improved, there are also new procedures which are associated with better outcome. Not at least, regarding the anaesthesiological approach, there are new solutions for classical problems. But overall, the multidisciplinary challenge of myasthenia gravis remains. This review will focus more on the anaesthesiological challenges, which include not only the intraoperative strategies, but also the perioperative management.

Myasthenia gravis is a well known neuromuscular junction disease, described first at the end of the 19th century. The paediatric or juvenile form of the disease was defined later in the middle of the 20th century. The term 'juvenile MG' (JMG) is currently accepted for patients between 0–19 years of age [2]. Neonatal myasthenia gravis, which is caused by passive transfer of maternal acetylcholine receptor (AChR) antibodies, cannot be included in JMG. Muscle weakness is relieved in 2–4 weeks, and therapy remains mostly symptomatic.

Prevalence and incidence of myasthenia gravis appears to be increased, probably caused by better diagnosis and better treatment [3]. The pooled incidence rate is reported to be about 5.3 per million person-years and the estimated pooled prevalence rate about 77.7 per million. For JMG, the incidence in Europe is about 0.1–0.5/100.000 per year [4–5].

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KEY POINTS

- Anaesthesiologists should have a key place regarding decisions concerning timing, strategy of operation and postoperative course in myasthenia gravis and JMG patients.
- Use or avoidance of neuromuscular blocking agents is still a question, but they appear to be absolutely indicated in video-assisted thoracoscopic extended thymectomies [because of one-lung ventilation].
- Sugammadex is a new reversal drug, and can be a reliable choice in this patient group.
- Postoperative care is of high importance, yet not necessarily in the ICU, but complete recovery of respiratory functions should be assured.

Myasthenia gravis is caused by pathogenic autoantibodies to components of the postsynaptic muscle endplate. A subgrouping based on the different antibodies has been defined recently [6▪▪]. This classification also affects the clinical approach, including surgery. Briefly, there are autoantibodies against the AChR, muscle-specific kinase, and lipoprotein-related protein 4. Myasthenia gravis with AChR antibodies are further divided to 'early' and 'late-onset' myasthenia gravis. Moreover, 'thymoma-associated', 'antibody-negative generalized', and 'ocular' types are also differentiated. Among them, 'early-onset myasthenia gravis with AChR antibodies' and 'thymoma-associated myasthenia gravis' can profit from surgical treatment. Generally, there is a close relationship between the indication for surgery and cellular abnormalities of thymic gland (hyperplasia or thymoma). JMG is often seropositive with anti-AChR [6▪▪].

DIAGNOSIS

Diagnosis is initiated with clinical suspicion of fluctuating muscle weakness. Definite diagnosis consists of the edrophonium test, electromyography and detection of antibodies.

Edrophonium is a short acting anti-acetylcholine esterase (AChE) drug. The test is positive if patient's muscle weakness is ameliorated 45 s after drug administration and this improvement continues for approximately 5 min. A decremental response of affected muscles for repetitive action potentials is a characteristic finding of myasthenia gravis in electromyography studies. These findings may also be seen in similar disorders, such as Lambert–Eaton syndrome, certain myotonies, or motor neuron diseases. The presence of anti-AChR antibodies is pathognomic for myasthenia gravis [7].

CLINICAL COURSE

Main feature of the disorder is muscle weakness, which improves at rest and which worsens with activity [8]. More than half of patients have ocular signs like diplopia or ptosis. Extremity muscles are also affected and result in fatigue more prominent at the end of the day. Proximal muscle groups are more frequently impaired. Dysphagia or dysarthria are present with bulbar impairment and indicate a more severe level of disease. Aspiration or malnutrition should be investigated in serious myasthenia gravis. In 1950s, Osserman suggested a clinical classification to evaluate the severity of the disease. This was modified by the Myasthenia Gravis Foundation of America in the 2000s (Table 1).

As an autoimmune disease myasthenia gravis can coexist with disorders, which possess dysimmune properties, among them endocrinopathies (thyroid disorders), rheumatoid arthritis, ulcerative colitis, and sarcoidosis are mostly encountered [9]. Hypothyroidism and malnutrition deserve special interest for perioperative recovery, as they have to be treated prior to surgery.

Some conditions may exacerbate the course of disease and may even cause need for mechanical ventilation. Infections, thyroid disorders, radiation, and extreme temperature are frequent pathological risk factors; however sleep disorders, pain, or menses may also worsen patient's status [6▪▪,9]. Drugs should be cautiously used in myasthenic patients as a large variety of drugs [antibiotic (e.g. aminoglycosides), antiarrhythmic (e.g. verapamil), neuropsychiatric] may aggravate the disease. Although corticosteroids are a part of the therapy, they may cause an early exacerbation of myasthenia gravis. If

Table 1. Myasthenia Gravis Foundation of America clinical classification of myasthenia gravis; a modification of Osserman score system

Stage	Clinical status
I	Only ocular involvement
II	Generalized mild muscle weakness
IIa	Predominantly affects limb and axial muscles
IIb	Predominantly bulbar involvement or respiratory weakness
III	Generalized moderate muscle weakness
IIIa	Predominantly affects limb and axial muscles
IIIb	Predominantly bulbar involvement or respiratory weakness
IV	Generalized severe muscle weakness
IVa	Predominantly affects limb and axial muscles
IVb	Predominantly bulbar involvement or respiratory weakness
V	Tracheal intubation or mechanical ventilation

surgery should be performed at the initial phase of steroid therapy, the anaesthetist must be aware of this worsening effect [10].

Apart from drugs, electrolyte imbalance may be associated with increased muscle weakness. Hypermagnesaemia is the most prominent as magnesium acts as an antagonist to calcium during neuromuscular transmission. Hypermagnesaemia is mostly iatrogenic as in preeclampsia/eclampsia therapy. Serum magnesium levels are not always consistent with clinical course, so weakness should be carefully assessed.

The myasthenic and the cholinergic crises

In a patient with myasthenia gravis, there is a risk of developing two kinds of crises: the myasthenic and the cholinergic. Both can interfere with the surgical/anaesthesiological approach. The myasthenic crisis can be considered an exacerbation. Factors like respiratory infections, emotional stress, and surgery can possibly cause or provoke this crisis.

The cholinergic crisis, on the other hand, is generally caused by an overdose with cholinesterase inhibitors and may show related symptoms (e.g. excessive salivation, sweating, abdominal cramps, urinary urgency, bradycardia, muscle fasciculations, or muscle weakness).

Clinically, it can be difficult to differentiate these two crises; a single dose of edrophonium may be useful: clinical findings would resolve in a myasthenic crisis, but they will worsen or be the same in a cholinergic crisis.

THERAPY

The treatment consists of medical and surgical modalities. For the anaesthesiologist, it is essential to have detailed information about the medical treatment of the patient, for it can be crucial in determining the optimal timing for the operation. The most important and common way of treatment is still symptomatic. Improving neuromuscular transmission is the key approach and is achieved with an anti-AChE drug, mainly pyridostigmine [7,11]. The drug results in increased Ach levels at the neuromuscular junction by decreasing Ach degradation. Patients with antimuscle-specific kinase are less likely to respond to pyridostigmine therapy [12]. To treat the muscarinergic side-effects of pyridostigmine, glycopyrronium bromide, atropine sulphate, and loperamide can be used.

Regarding the immunosuppressive therapy, corticosteroids have been shown to be beneficial in slowing the progression [13]. Other alternatives for immunosuppressive therapy are azathioprine, cyclophosphamide, cyclosporine A, and rituximab [6▪▪].

The myasthenic crisis is an emergency case and has to be treated under 'intensive care' conditions with respiratory support, treatment of infections, and monitoring of vital functions and mobilization. Intravenous immunoglobulin and plasma exchange are options for further treatment, both can be given in sequence if necessary, as patients can respond to one but not to the other [14].

Treatment of the cholinergic crisis includes endotracheal intubation, atropine, and cessation of cholinesterase inhibitors until the crisis is over.

Preoperative evaluation

Elective surgery for myasthenic patients should be reserved for a stable period of the disease, when the medication requirement is minimal. It is mandatory – although not sufficient – to obtain neurological optimization to ensure an early and safe recovery in the postoperative course. It should be kept in mind that vigilant preoperative assessment by an experienced anaesthesiologist is the first step to reduce complications and need for ICU admission. An experienced team can prepare alternative strategies for perioperative period. For acute cases with a high probability of developing a myasthenic crisis, more aggressive strategies such as plasmapheresis can be necessary during operative preparation [14].

Prediction of postoperative myasthenic crisis (POMC) would be very beneficial, both because of possible preventive approaches and also to plan a postoperative ICU admission. A recent article proposes a new predictive score of POMC (Table 2) [15▪▪]. Regarding this system, patients with a score of <2.5 have the probability of having a POMC of less than 10%, whereas a score of >4.0 is associated with a POMC probability of approximately 50%.

Anti-AChE therapy on the morning of surgery is associated with two different approaches. Suspension of anti-AChE therapy can reduce neuromuscular block requirement, whereas it may decre ase neuromuscular recovery in early postoperati ve period [16], maintenance of pyridostigmine is generally accepted as it is essential for physiologic recovery in adults [17,18].

Coexisting disease should be carefully investigated; especially those which would affect patient's recovery such as thyroid disturbances [7].

Routine premedication with opioids or common sedatives should be avoided or performed very carefully because they can depress respirati on; interactions of drugs having no effect on respiration (such as dexmedetomidine) have to be examined.

Table 2. A new predictive score for postoperative myasthenic crisis

Variables associated with POMC	Assigned points (range: 0.0–8.5)
Osserman stage	
Stage I–IIA	0
Stage IIB	1
Stage III–IV	3
Duration of myasthenia gravis (year)	
<1	0
1–2	1
>2	2
Lung resection	
No	0
Yes	2.5
BMI	
<28	
≥28	1

POMC, postoperative myasthenic crisis. Reproduced with permission from [15▪▪].

Surgery and perioperative anaesthetic management

Thymectomy in indicated patients can be performed either via sternotomy ('open') or with newer methods such as VATET or robotic surgery. The advantages of VATET over conventional 'open surgery', such as reduced stress, lowered pain scores, early mobilization, and diminished length of stay [19,20], have been demonstrated [21]. However, these methods develop a new challenge for the anaesthesiologist. The use of NMBAs is inevitable.

Indeed, in myasthenia gravis, use of NMBAs should be avoided. The use of succinylcholine is not recommended at all. Regarding the use of nondepolarizing agents, the effects and duration of action can vary depending on the preoperative management (such as maintenance or suspension of pyridostigmine). Several case series and case reports describe alternative methods such as high-dose desflurane [22] or thoracic epidural anaesthesia [23] to avoid the NMBAs in open thymectomy and in other surgeries aside thymectomy. In a recent cohort study, the success rate of anaesthetic management for myasthenia gravis without NMBA was found to be 71.1% [24▪]. However, in VATET, OLV is mandatory and as a consequence NMBAs are necessary for several reasons [18]:

(1) Successful positioning of double-lumen tubes can be very difficult in nonrelaxed patients.
(2) A totally 'silent' lung is necessary for a successful operation.
(3) Spontaneous breathing efforts are not suggested during OLV.

For lung isolation, successful applications of bronchial blockers have also been reported in complicated cases [25].

The differences in sensitivity between the different types of nondepolarizing NMBAs in myasthenia gravis appear to be very small. Mivacurium, a short acting NMBA, differs by elimination mechanism (hydrolysis by plasma choline-esterase). Pyridostigmine therapy was suspected to increase elimination of mivacurium. It has been shown that reduced dose of mivacurium is associated with adequate muscle relaxation and well tolerated extubation [18]. Intermediate acting NMBAs, such as rocuronium, cisatracurium, and vecuronium have similar effects on myasthenia gravis patients. Empirically, 50% of the standard dose is suggested to be adequate, albeit with an increased risk of prolonged recovery. A recent study has shown that baseline train-of-four (TOF) ratio and age at onset of disease are determinants of the increased response to rocuronium in myasthenia gravis [26▪].

Neuromuscular monitoring (i.e. TOF) is crucial both to achieve adequate relaxation and moreover to ensure safe recovery (TOF > 90) at the end of surgery. In adult myasthenia gravis, TOF is a part of standard monitoring independent of NMBA administration [18,27▪,28▪]. When reversal agents are available, TOF would be beneficial to assess timing and dosing.

Generally, drugs that can even potentially affect the respiratory effort [e.g. benzodiazepines and (long acting) opiates] should be avoided.

Sugammadex in myasthenia gravis

Sugammadex (approved in the European Union 2008; currently not approved by Food and Drug Administration) is a selective NMBA-binding agent designed to reverse the effect of the steroidal NMBAs rocuronium and vecuronium [9]. It decreases the amount of free NMBA molecules by binding the molecules, making them ineffective. The use of sugammadex in myasthenia gravis patients has been described in larger series in recent publications [27▪,28▪]. Generally, use of sugammadex after (diminished doses of) rocuronium showed faster reversal and no postoperative complications. However, it must be noted that there are some case reports showing that sugammadex was not effective in the reversal of rocuronim in myasthenia gravis [29,30]. Obviously, sugammadex is a new drug, and scientific and practical experience is still necessary in different patient populations including

myasthenia gravis. For now, it can be suggested as a potentially very beneficial improvement.

JUVENILE MYASTHENIA GRAVIS

Juvenile myasthenia gravis is often of the anti-AchR type and presumably responsive to thymectomy. As in adults, plasmapheresis or intravenous IgG are indicated for refractory myasthenia gravis or prior to operation [31].

The benefits of thymectomy in JMG have been reported in a recent series [32▪,33] and thoracoscopic approaches have been found to significantly decrease length of stay [34].

The largest series reported 40 children, with about one-half (17 of 40) assessed as severe myasthenia gravis [32▪]. For neuromuscular blockade a reduced (1 × ED95) dose of rocuronium was used. No prolonged (>1 h) reversal was observed. Sugammadex was used safely also in this patient group. TOF monitoring was a part of monitoring of JMG patients.

An additional challenge for the anaesthetic management of JMG is airway management for the paediatric OLV (this is actually also a general problem, even without myasthenia gravis). In one series, thoracoscopic thymectomy was managed without muscle relaxation in 20 children [35], whereby endotracheal intubation was achieved with a single lumen tube, which does not necessitate a deep muscle relaxation. On the other hand, the benefits and necessities of lung isolation should also be considered. Double lumen tubes (Left; no.: 28 or 32) are preferred among older children (i.e. above 30 kg). For smaller children, endobronchial blockers under guidance of a paediatric fiberoptic bronchoscope (3.7 mm) constitute a reliable alternative; however, the handling requires an experienced thoracic anaesthetist familiar with paediatric cases [32▪].

POSTOPERATIVE FOLLOW-UP

Postoperative follow-up for myasthenia gravis begins with total recovery of neuromuscular function. A TOF ratio of greater than 90% (or at least a head lift >5 s in the conscious patient) should be achieved for the decision to extubation. Apart from spontaneous breathing efforts, upper airway reflexes should be intact. Residual curarization should be prevented by TOF monitoring and by reversal drugs if needed.

Routine admission to the ICU with mechanical ventilation should be avoided for several reasons, such as increased infection risk, airway-associa ted morbidity, and not at least stress-induced myasthenic crisis. To prevent a POMC, an effective postoperative analgesia is also crucial. For VATET, paravertebral analgesia with long-acting local anaesthetics can be the method of choice. For open thymectomies and other operations, epidural analgesia/anaesthesia is associated not only with a decrease in perioperative NMBA application, but also an effective postoperative analgesia. Nonopioid analgesics are desirable; if systemic opioids are required, small doses of short-acting opioids should be preferred.

CONCLUSION

The increasing number of thymectomy and especially of VATET in myasthenia gravis and also in JMG necessitates an adequate knowledge of myasthenia gravis by the anaesthesiologist. The dilemma of using or avoiding NMBAs is on going, but sugammadex can be a reliable drug in cases requiring NMBA. Further studies are necessary regarding sugammadex in myasthenia gravis and in JMG. Neuromuscular monitoring should be considered as an obligatory part of the anaesthesia, especially in patients with myasthenia gravis.

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Conflicts of interest

There are no conflicts of interest.

REFERENCES AND RECOMMENDED READING

Papers of particular interest, published within the annual period of review, have been highlighted as:

- ▪ of special interest
- ▪▪ of outstanding interest

1. Stevens RD. Neuromuscular disorders and anesthesia. Curr Opin Anaesthesiol 2001; 14:693–698.
2. Evoli A. Acquired myasthenia gravis in childhood. Curr Opin Neurol 2010; 23:536–540.
3. Carr AS, Cardwell CR, McCarron PO, McConville J. A systemic review of population based epidemiological studies in myasthenia gravis. BMC Neurol 2010; 10:1–9.
4. McGrogan A, Sneddon S, de Vries CS. The incidence of myasthenia gravis: a systematic literature review. Neuroepidemiology 2010; 34:171–183.
5. Della Marina A, Trippe H, Lutz S, Schara U. Juvenile myasthenia gravis: recommendations for diagnostic approaches and treatment. Neuropediatrics 2014; 45:75–83.
6. ▪▪ Gilhus NE, Verschuuren JJ. Myasthenia gravis: subgroup classification and therapeutic strategies. Lancet Neurol 2015; 14:1023–1036.

The review focuses not only on the neurological, but also multidisciplinal challenges of Myasthenia Gravis and is therefore helpful for every clinician interesting in this issue.

7. Sieb JP. Myasthenia gravis: an update for the clinician. Clin Exp Immunol 2014; 175:408–418.
8. Abel M, Eisenkraft JB. Anesthetic implication of myasthenia gravis. Mt Sinai J Med 2002; 69:31–37.

9. Blichfeldt-Lauridsen L, Hansen BD. Anesthesia and myasthenia gravis. Acta Anesthesiol Scand 2012; 56:17–22.

10. Benzing G, Bove KE. Sedating drugs and neuromuscular blockade during mechanical ventilation. JAMA 1992; 267:1775.

11. Hirsch NP. Neuromuscular junction in health and disease. Br J Anaesth 2007; 99:132–138.

12. Ionita CM, Acsadi G. Management of juvenile myasthenia gravis. Pediatr Neurol 2013; 48:95–104.

13. Monsul NT, Patwa HS, Knorr AM, *et al.* J Neur Science 2004; 217:131–133.

14. Barth D, Nabavi N, Ng E, *et al.* Comparison of IVIg and PLEX in patients with myasthenia gravis. Neurology 2011; 76:2017–2023.

15. Leuzzi G, Meacci E, Cusumano G, *et al.* Thymectomy in myasthenia gravis:
■■ proposal for a predictive score of postoperative myasthenic crisis. Eur J Cardiothorac Surg 2014; 45:76–88.

From the point of view of an anaesthesiologist, one of the most important questions is the postoperative status, and the decision whether to send the patient to ICU or not. The study is at least a very important initiation dealing with this challenge.

16. Gritti P, Sgarzi M, Carrara B, *et al.* A standardized protocol for the perioperative management of myasthenia gravis patients. Experience with 110 patients. Acta Anesthesiol Scand 2012; 56:66–75.

17. Tripathi M, Kaushik S, Dubey P. The effect of use of pyridostigmine and requirement of vecuronium in patients with myasthenia gravis. J Postgrad Med 2003; 49:311–315.

18. Sungur Ulke Z, Sentürk M. Mivacurium in patients with myasthenia gravis undergoing video-assisted thoracoscopic thymectomy. Br J Anaesth 2009; 103:310–311.

19. Toker A, Tanju S, Sungur Z, *et al.* Videothoracoscopic thymectomy for nonthymomatous myasthenia gravis: results of 90 patients. Surg Endosc 2008; 22:912–916.

20. Diaz A, Black E, Dunning J. Is thymectomy in nonthymomatous myasthenia gravis of any benefit? Interact Cardiovasc Thorac Surg 2014; 18:381–389.

21. Toker A, Eroglu O, Ziyade S, *et al.* Comparison of early postoperative results of thymectomy: partial sternotomy vs. videothoracoscopy. Thorac Cardiovasc Surg 2005; 53:110–113.

22. Koda K, Kimura H, Uzawa M, *et al.* Desflurane anesthesia without muscle relaxant for a patient with myasthenia gravis undergoing laparoscopic high anterior resection: a case report. Masui 2014; 63:1135– 1138.

23. Rangasamy V, Kumar K, Rai A, Baidya D. Sevoflurane and thoracic epidural anesthesia for trans-sternal thymectomy in a child with juvenile myasthenia gravis. J Anaesthesiol Clin Pharmacol 2014; 30:276–278.

24. Fujita Y, Moriyama S, Aoki S, *et al.* Estimation of the success rate of anesthetic
■ management for thymectomy in patients with myasthenia gravis treated without muscle relaxants: a retrospective observational cohort study. J Anesth 2015; 29:794–797.

A unique study searching the success rate of the avoidance of NMBAs, and for possible reasons of the obligatory use of NMBAs.

25. El-Tahan MR, Doyle DJ, Hassieb AG. High-frequency jet ventilation using the Arndt bronchial blocker for refractory hypoxemia during one-lung ventilation in a myasthenic patient with asthma. J Clin Anesth 2014; 26:570–573.

26. Fujimoto M, Terasaki S, Nishi M, Yamamoto T. Response to rocuronium and its
■ determinants in patients with myasthenia gravis: a case-control study. Eur J Anaesthesiol 2015; 32:672–680.

The action of rocuronium is hard to predict in myasthenia gravis. This study searches the independent determinants affecting the action of rocuronium.

27. Sungur Ulke Z, Yavru A, Camci E, *et al.* Use of rocuronium and sugamma-
■ dex in patients with myasthenia gravis undergoing video-assisted thoracoscopic extended thymectomy. Acta Anesthesiol Scand 2013; 57:745–748.

These two studies (ref #27 and #28) are two reports of series showing the successful and reliable use of sugammadex in thymectomy.

28. De Boer H, Shields MO, Booij LHDJ. Reversal of neuromuscular blockade
■ with sugammadex in patients with myasthenia gravis undergoing video-assisted thoracoscopic extended thymectomy. Eur J Anaesth 2014; 31:708–721.

These two studies (ref #27 and #28) are two reports of series showing the successful and reliable use of sugammadex in thymectomy.

29. Sugi Y, Nitahara K, Shiroshita T, Higa K. Restoration of train-of-four ratio with neostigmine after insufficient recovery with sugammadex in a patient with myasthenia gravis. A A Case Rep 2013; 1:43–45.

30. Kiss G, Lacour A, d'Hollander A. Fade of train-of-four ratio despite administration of more than 12 mg kg(-1) sugammadex in a myasthenia gravis patient receiving rocuronium. Br J Anaesth 2013; 110:854–855.

31. Liew WK, Powell CA, Sloan SR, *et al.* Comparison of plasmapheresis and intravenous immunoglobulin as maintenance therapies for juvenile myasthenia gravis. JAMA Neurol 2014; 71:575–580.

32. Özkan B, Demir A, Kapdağlı M, *et al.* Results of videothoracoscopic thymect-
■ omy in children: an analysis of 40 patients. Interact Cardiovasc Thorac Surg 2015; 21:292–295.

This is the largest series of thymectomy in JMG for now. Anaesthesiological approach is also described.

33. Kitagawa N, Shinkai M, Take H, *et al.* Mediastinoscopic extended thymectomy for pediatric patients with myasthenia gravis. J Pediatr Surg 2015; 50:528–530.

34. Goldstein SD, Culbertson NT, Garrett D, *et al.* Thymectomy for myasthenia gravis in children: a comparison of open and thoracoscopic approaches. J Pediatr Surg 2015; 50:92–97.

35. Christison-Lagay E, Dharia B, Vajsar J, Kim PC. Efficacy and safety of thoracoscopic thymectomy in the treatment of juvenile myasthenia gravis. Pediatr Surg 2013; 29:583–586.