

Is thymectomy in non-thymomatous myasthenia gravis of any benefit?

Andres Diaz^{a,*}, Edward Black^a and Joel Dunning^b

^a Department of Cardiothoracic Surgery, John Radcliffe Hospital, Oxford, UK

^b Department of Cardiothoracic Surgery, James Cook University Hospital, Middlesbrough, UK

* Corresponding author. Tel/fax: +44-7793211085; e-mail: andres.diazramirez@ouh.nhs.uk; adiazmd@yahoo.co.uk (A. Diaz).

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Abstract

A best evidence topic in thoracic surgery was written according to a structured protocol. The question addressed was if thymectomy in non-thymomatous myasthenia gravis was of any benefit? Overall, 137 papers were found using the reported search, of which 16 represented the best evidence to answer the clinical question. The authors, journal, date and country of publication, patient group studied, study type, relevant outcomes and results of these papers are tabulated. The outcome variables were similar in all of the papers, including complete stable remission (CSR), pharmacological remission, age at presentation, gender, duration of symptoms, preoperative classification (Oosterhius, Osserman or myasthenia gravis Foundation of America (MGFA)), thymic pathology, preoperative medications (steroids, immunosuppressants), mortality and morbidity. We conclude that evidence-based reviews have shown that relative rates of thymectomy patients compared with non-thymectomy patients attaining outcome indicate that the former group of patients is more likely to achieve medication-free remission, become asymptomatic and clinically improve (54%, $P < 0.01$), particularly patients with severe and generalized symptoms ($P = 0.007$). Patients with generalized myasthenia gravis showed 11% stronger association with favourable outcomes after thymectomy. Some studies show early remission rates (RRs), as early as 6 months post-thymectomy, of 44%. Overall, the reported remission rate for non-thymomatous myasthenia gravis is between 38 and 72% up to 10 years of follow-up. Among these patients, those with thymic hyperplasia show the best complete stable remission rates (42%, $P < 0.04$) in the majority of studies. Age showed variability across the studies and the cut-off was also different among them. Overall age < 45 years showed a higher probability of achieving complete stable remission during follow-up (81% benefit rate (BR), $P < 0.02$). Pharmacological improvement is reported between 6 and 42%. However, the certainty of these benefits has not been established due to factors such as the confounding differences between myasthenia gravis patients receiving and not receiving thymectomy, the non-randomized nature of class II studies and the lack of Class I evidence to support its use. There is currently a randomized trial ongoing looking at thymectomy by sternotomy vs controls and the results are eagerly awaited.

Keywords: Myasthenia gravis • Thymectomy • Non-thymomatous myasthenia gravis • Complete stable remission

INTRODUCTION

A best evidence topic was constructed according to a structured protocol. This is fully described in *ICVTS* [1].

THREE-PART QUESTION

In [non thymomatous Myasthenia Gravis] is [Thymectomy] of [any benefit].

CLINICAL SCENARIO

You see a 28-year old female in the outpatient clinic with a diagnosis of MGFA class III myasthenia gravis (MG), who has been referred to you by a neurologist. He wants to know your opinion on whether thymectomy will help control her symptoms and reduce the need for long-term immunosuppression. You feel that thymectomy could offer her a good outcome. You carry out a review of the literature.

SEARCH STRATEGY

Medline 1950 to May 2013 using OVID interface [thymectomy] AND [myasthenia OR myasthenia gravis] AND [improved outcome OR beneficial OR postoperative].

SEARCH OUTCOME

One hundred and thirty-seven papers were found using the reported search. From these, 16 papers were identified. That provided the best evidence to answer the question. These are presented in Table 1.

RESULTS

Mantegazza *et al.* [2] in their large multicentre follow-up reported a complete stable remission (CSR) of 11% at the 5-year follow-up. They concluded that thymectomy raised the remission rate (RR) in patients operated shortly after diagnosis, generalized mild-to-moderate MG and involuted thymus.

Table 1: Best evidence papers

Author, date, journal, country Study type (level of evidence)	Patient group	Outcomes	Key results	Comments/weakness
Mantegazza <i>et al.</i> (1990), J Neurol, Italy [2] Retrospective study (level 2b)	1152 patients with MG from 6 centres	Complete remission (CR) with thymectomy	11%	Thymectomy seemed to raise the RR mostly for patients operated shortly after the diagnosis, generalized mild-moderate MG and normally involuted thymus Study period not specified, not clear indications for thymectomy; different and unspecified surgical techniques used; patients with missing data were included
	829 (72%) underwent thymectomy, 531 transcervical, 249 trans-sternal and 49 unspecified	Pharmacological remission	6%	
	Osserman classes I-IV were included Mean follow-up was 4.9 years			
Frist <i>et al.</i> (1994), Ann Thorac Surg, USA [3] Retrospective study (level 2b)	A total of 46 MG patients from 1971 until 1992 operated at a single institution with combined surgical and medical therapy	Age Sex	Patients <45 years had a better outcome ($P = 0.0044$) Female patients showed a better outcome ($P = 0.06$)	Thymectomy for MG is an effective therapeutic modality. Of the total, 87% patients had improvement and 28% achieved permanent remission Close correlation between postoperative status at 1, 6 and 12 months and status at last follow-up. Once patients clinically improve, they maintain that clinical state over time. Status at 1 month post-thymectomy strongly correlates with long-term outcome Retrospective uncontrolled study; small number of patients. Thymoma patients included
	The surgical approach was trans-sternal for all patients	Preoperative stage	Response to thymectomy improved dramatically with a more advanced preoperative stage ($P = 0.02$)	
	NT $n = 42$			
	Thymoma $n = 4$	Duration of symptoms	No significant influence on outcome	
	Mean follow-up 75 months	Mortality and morbidity	No operative/hospital deaths No recurrent nerve injuries	
	Oosterhius classification used			
Masaoka <i>et al.</i> (1996), Ann Thorac Surg, Japan [4] Retrospective study (level 2b)	384 MG patients (286 non-thymomatous, 98 thymomatous) operated at 2 institutions from 1973 until 1993	Remission rate (RR) % (3 months, 6 months, 1 year, 3 years, 5 years, 10 years, 15 years, 20 years)	15.2, 15.9, 22.4, 36.9, 45.8, 55.7, 67.2, 50	Extended thymectomy is an excellent operative procedure in both non-thymomatous and thymomatous MG. The RR in the non-thymomatous group of patients continued to rise even after 5 years. PRs were stable after 3 years. These data suggest that the longer the postoperative period, the better are the results Thymoma patients included use of own classification system for disease severity; different protocols used for steroid administration
	Surgical approach for all non-thymomatous patients was trans-sternal extended thymectomy (<i>en bloc</i> resection of anterior mediastinal fat tissue, around upper poles of thymus, both brachiocephalic veins and on pericardium)	Palliation rate (PR) % (3 months, 6 months, 1 year, 3 years, 5 years, 10 years, 15 years, 20 years)	74.2, 79.5, 86.3, 91.6, 92.2, 98.2, 91.7	
	Age at time of operation	<34 years old showed better RR ($P < 0.05$)		
	Duration of disease	<23 months showed better RR		
	Preoperative steroids	No difference in outcome when comparing patients who received steroids preoperatively and patients who did not receive them		
	Severity of disease by their own MG classification system			
	Mean age 35 years			
	Female predominance	Mortality	No operative deaths	
Follow-up to 20 years				

Continued

Table 1: (Continued)

Author, date, journal, country Study type (level of evidence)	Patient group	Outcomes	Key results	Comments/weakness
Venuta <i>et al.</i> (1999), Eur J Cardiothorac Surg, Italy [5] Retrospective study (level 2b)	A total of 217 patients [155 with non thymomatous myasthenia gravis (NTMG)] underwent thymectomy over a 27-year period at a single institution MG was graded as per Osserman classification 3 surgical techniques were used (cervicotomy, partial upper sternal splitting and complete sternotomy) Female predominance Follow-up 6–234 months (mean 119)	Complete remission	25%	Thymectomy is effective in the management of patients with MG at all stages with low morbidity
		Reduction of medication and/or clinical improvement	46%	
		Stable disease	18%	
		Age at operation	<45 years old correlated with remission or clinical improvement	An upper split incision was favoured by this group as it allows extensive removal of thymic tissue; offers reduced surgical trauma with shorter length of stay
		Duration of symptoms	<18 months' duration correlated with increased RR ($P = 0.049$) and PR ($P = 0.041$)	Patients with thymoma present a less favourable outcome
Gronseth <i>et al.</i> (2000), Neurology, USA [6] Meta-analysis (level 2a)	A definitive study of the effectiveness of thymectomy has never been done A Medline search was carried out to find studies (controlled non-randomized and uncontrolled case series) describing outcomes in patients with or without thymectomy Patients with thymoma were excluded	Survival	Positive associations in most studies between thymectomy and MG remission and improvement	For patients with NTMG, thymectomy is recommended as an option to increase the probability of remission or improvement (Class II)
		Improvement since diagnosis		
		Asymptomatic on or off medication	There are confounding differences in baseline characteristics of prognostic importance between thymectomy and non-thymectomy patient groups in all studies	There is no conclusive evidence of the superiority of one surgical technique to another as RRs data comes from uncontrolled studies
		Asymptomatic off medication		
		MG severity		
Budde <i>et al.</i> (2001), Ann Thorac Surg, USA [7] Retrospective study (level 2b)	A total of 113 patients underwent thymectomy for MG between 1974 and 1999 at a single institution 2 surgical techniques were employed - T incision limited upper sternotomy in 84% (2 × 2 in. T-shaped skin incision with the horizontal limb over the second intercostal space and vertical limb from the	Remission	21%	Thymectomy may be safely performed by a limited T upper sternal incision. The proportion of overall improvement (75%) compares favourably with other large studies. The RR of 21% is slightly lower. However, comparison among studies is often difficult because of different exclusion criteria Complete stable remission (CSR) was achieved in patients
		Improved	54%	
		Remission + improvement ('benefit')	75%	
		Unchanged	14%	
		Worse	11%	
Symptom duration	did not correlate with outcome (average length of symptoms for worse patients was the lowest)			

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Table 1: (Continued)

Author, date, journal, country Study type (level of evidence)	Patient group	Outcomes	Key results	Comments/weakness
	midpoint of the T down to the fourth intercostal space. A superior skin flap is created and the sternum is divided from the notch to the fourth intercostal space)	Osserman classification	Class 2 of 3 tended to benefit more (79%)	at an average of 66 ± 71 months postoperatively, which is longer than the average follow-up of 51 months
	- Full sternotomy in 16%	Age	<50 years (81% benefit vs 55% if >50 years, <i>P</i> = 0.02)	Multivariate analysis of patient sex was not statistically significant (<i>P</i> = 0.34)
	Both NTGM and thymoma patients were included	Sex	Improved outcome for female patients in univariate analysis	Preoperative stabilization of the disease included different regimes given along the period of study
	Follow-up was obtained in 92 patients (81%). Mean follow-up 51 ± 59 months	Thymic pathology	No difference in non-thymomatous MG	Two surgical techniques were employed
		Preoperative treatment	No significant correlation with the outcome	
		Mortality	1 patient (2 weeks post-operatively of unknown causes)	The number of patients within each group is not clearly defined
		Morbidity	14%	
De Perrot <i>et al.</i> (2001), Respiration, Switzerland [8] Retrospective study (level 2b)	A total of 35 patients underwent thymectomy between 1979 and 1999 at a single institution (23 patients with non-thymomatous MG)	Age	The cut-off was 40 years of age. Remission and improvement were not statistically significant (<i>P</i> = 0.8 and 0.7, respectively)	The large majority of patients (81%) improved after surgery. Postoperative clinical improvement was greater when extensive myasthenic involvement was present preoperatively
	Complete follow-up available for 33 patients, with a mean of 96 months	Sex	There was no statistically significant difference between male and female rates for remission and improvement (<i>P</i> = 0.4 and 0.8, respectively)	RR was greater in patients with stage I and IIA (not statistically significant but this finding has been observed by other authors)
	Modified Osserman classification was employed	Duration of symptoms	No statistically significant difference for remission or improvement (<i>P</i> = 0.4 and 0.9, respectively)	Shorter duration of symptoms did not affect the RR in contrast to several other reports
	4 different surgical techniques employed: transcervical (preferred), median sternotomy (if thymoma was suspected or complete thymectomy could not be performed through a cervicotomy), right or left thoracotomy (for tumours extending into the pleural cavity)	Osserman stage	Greater clinical improvement in IIB, III, IV Class patients (<i>P</i> = 0.04)	Small series including thymomatous and non-thymomatous MG
		Histological findings	RRs better in the presence of thymic hyperplasia (<i>P</i> = 0.04)	Different surgical approaches
		Mortality	None for the non-thymomatous group	
Gronseth <i>et al.</i> (2002), Neurology, USA [9] Review	Patients with MG from non-randomized trials dating back to 1953	Measured outcomes included survival, improvement since diagnosis, becoming asymptomatic on medication and medication-free remission	No Class I studies of the effectiveness of thymectomy have been performed. Most Class II studies demonstrated higher MG. RRs in patients undergoing thymectomy. However, these studies were consistently confounded by differences between MG patients	MG patients undergoing thymectomy in most studies were more likely to achieve medication-free remission, become asymptomatic and improve Due to the confounding differences between MG patients receiving and not receiving thymectomy, a benefit of thymectomy in MG patients has not been established
Mantegazza <i>et al.</i> (2003), J Neuro Sci, Italy [10]	A total of 206 NTMG patients Video assisted thoracoscopic extended thymectomy (VATET)	CSR at the 6-year follow-up	Thymic hyperplasia, treatment with anticholinesterase drugs and age of onset <40 years	The absence of perioperative mortality and very low morbidity during the

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Table 1: (Continued)

Author, date, journal, country Study type (level of evidence)	Patient group	Outcomes	Key results	Comments/weakness
Prospective cohort study (1b)	n = 159 (transcervical incision with removal of thymic tissue in the neck. Subsequently, the sternum is lifted and trocars are introduced in the left pleural cavity to proceed via video-assisted thoracoscopy) Extended trans-sternal n = 47 Osserman classification I-V patients were included 6-year follow-up	Mortality	were associated with a significantly greater probability of achieving CSR (P = 0.0001, <0.0001 and 0.037, respectively) Sex, time of onset to surgery, presence of anti-Ach-R antibody and type of surgery did not affect CSR 0	postoperative period demonstrate that VATET is safe CSR was achieved in 53.9% of patients at 6 years
Tansel <i>et al.</i> (2003), Surg Today, Turkey [11]	A total of 204 NTMG patients underwent thymectomy between 1980 and 2001	Preoperative classification	No significant correlation was found (P = 0.43) although patients with Class I and IIc2 tended to benefit more	The early RR (44%) achieved after thymectomy had increased significantly by the end of the first year (72%, P = <0.001)
Retrospective study (level 2b)	Surgical technique via partial median sternotomy (94%) and median sternotomy (6%) Modified Osserman classification employed Medical treatment included anticholinesterase therapy, steroids, combination of both, steroids + immunosuppressant or no medication Mean follow-up 7.2 ± 1.2 years with last follow-up in 79% of patients	Preoperative treatment Age Duration of symptoms Gender Histological findings.	Not significant influence on outcome (P = 0.35) Did not influence remission or improvement rates (P = 0.42) Did not influence remission or improvement rates (P = 0.67) No influence on remission (P = 0.97) Favourable trend towards remission in patients with thymic hyperplasia (P = <0.001)	Early and late RRs of 6 months and 1 year seem arbitrary
El-Medany <i>et al.</i> (2003), Asian Cardiovasc Thorac Ann, Saudi Arabia [12]	A total of 100 MG patients at a single institution between 1986 and 2001 (93 non-thymomatous and 7 thymoma-associated MG)	Mortality	No perioperative deaths	
Retrospective study (level 2b)	Surgical technique: maximal thymectomy (combined transcervical and trans-sternal approach. Through the transcervical incision, thymic and fatty tissue anterior and anterolateral to the trachea from below the thyroid gland to the superior mediastinum is removed. In the mediastinum, the removal of tissue extends fatty tissue extending down to the diaphragm, between phrenic nerves, cardiophrenic tissue, retroinnominate and AP window) Osserman classification employed	CR BR Age Sex Duration of symptoms (<1 year) Preoperative steroids Histology	38.7% at last point of follow-up (increased progressively to reach a peak of 75% at 15 years) 86% (increased to 100% at 15 years) <50 years had better outcome (P = 0.0044) No statistically significance between female and male (BR 85 vs 75%) No significant correlation found with CR (36 vs 35.5%) CR in 27% of patients on steroids compared with 40% not on steroids (not statistically significant) CR in 42% of patients with hyperplastic thymus	Maximal thymectomy is an effective and safe procedure for treatment of MG The CR and total BR are prone to increase over time Univariate analysis showed that age, histology and ectopic thymic tissue are significant prognostic factors for outcome

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Table 1: (Continued)

Author, date, journal, country Study type (level of evidence)	Patient group	Outcomes	Key results	Comments/weakness
	Follow-up 8–180 months (mean 91 months)	Ectopic thymic tissue	Poor prognostic factor ($P = 0.0001$)	
Kawaguchi <i>et al.</i> (2007), Clin Neurol Neurosurg, Japan [13]	A total of 34 late-onset (age of onset >50 years) NTMG patients were selected	Minimal symptoms	Present in 50% of thymectomy group patients at the end of the follow-up period	Thymectomy is a potentially effective treatment for late-onset NTMG with mild generalized symptoms
Retrospective study (level 2b)	20 patients underwent thymectomy (approach not specified) and 14 medical treatment	Generalized symptoms (thymectomy group vs non-thymectomy)	30 vs 75% ($P < 0.05$)	Small sample, only assessing subgroup analysis
	Clinical grade evaluated according to MGFA	Clinical remission	50 vs 17% ($P = 0.11$)	
	Subgroup analysis of MGFA Class 2 was performed			
	Clinical course and outcomes over 2 years			
	Mean follow-up for thymectomy patients was 11.7 years and 7.8 years for non-thymectomy patients			
Sonett <i>et al.</i> (2008), Ann N Y Acad Sci, USA [14]	Review attempting to clarify some of the controversial issues concerning the selection of a thymectomy technique in the treatment of NTMG and to make limited recommendations based on the best available evidence	Extent of thymic tissue removal	The more thymus removed, the higher the RR	At 5 years maximal thymectomy continues to produce the most effective overall response
Review		Remission	51 and 50% at 5 years for VATET and combined transcervical–trans-sternal	Controlled well-designed studies are required to begin to resolve the many conflicting statements and unanswered questions that exist concerning the selection of thymectomy in the treatment of MG
	This analysis consists of uncontrolled retrospective studies with an extense number of confounding factors making the analysis speculative	Disease severity	Less severe disease has better outcomes	
		Duration of symptoms	Better outcomes for shorter duration	
		Surgical technique	Combined transcervical and trans-sternal maximal thymectomy should remain the benchmark	
Pompeo <i>et al.</i> (2009), Eur J Cardiothorac Surg, Italy [15]	A total of 32 patients with NTMG underwent extended thoracoscopic thymectomy (4-trocars access with removal of the entire thymus, anterior mediastinal perithymic tissues, fatty tissue in the aortocaval groove, AP window, cardiophrenic sinuses and lower cervical area)	Sex	No significant difference between male and female ($P = 0.1$)	Extended thymectomy results in highly satisfactory long-term outcome in non-thymomatous MG with a 10-year remission of 50% and an overall response rate of 90%
Retrospective study (level 2b)		Symptom duration (<12 months)	Shorter duration significantly correlated with CR and improvement ($P = 0.006$)	
	MGFA clinical classification was used	MGFA class	Did not impact on CR or improvement ($P = 1.0$)	Patients who did not respond to thymectomy had a positive titre of anti-MuSKab (predictor of no response at univariate analysis)
	CR and symptomatic improvement were assessed	Oropharyngeal involvement	No involvement significantly correlated with CR and improvement ($P = 0.01$)	Results of thymectomy continue to improve over time and adequate length of follow-up is needed to assess
		Histology	No statistically significant difference ($P = 0.06$)	

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Table 1: (Continued)

Author, date, journal, country Study type (level of evidence)	Patient group	Outcomes	Key results	Comments/weakness
	Follow-up 60–156 months (median 119)	Ectopic thymic tissue	Presence was associated with negative impact on CR and improvement ($P = 0.05$)	the efficacy of any thymectomy technique Small cohort
		Anti-AChRab	Does not influence outcome ($P = 0.12$)	
		Anti-MuSKab	Significant correlation with CR and improvement ($P = 0.0007$)	
		Mortality	None	
Lin <i>et al.</i> (2010), Eur J Cardiothorac Surg, Taiwan [16] Retrospective study (level 2b)	A total of 60 NTMG patients underwent thymectomy from 1995 to 2004 at a single institution Preoperative status was classified according to MGFA classification Two surgical approaches were employed (trans-sternal thymectomy $n = 22$ and video assisted thoracoscopic surgery (VATS) thymectomy $n = 38$) Follow-up range 12–131 months (median 44 months)	Crude CSR rate Sex, disease duration, MGFA classification, anti-AchR antibody, preoperative plasma exchange, preoperative medication and operative method Age of onset (<40 years), presence of hypothyroidism and thymic hyperplasia Mortality Morbidity	32% at 38.5 month mean follow-up Did not influence CSR rate ($P = 0.7, 0.21, 0.79, 0.32, 0.88, 0.3, 0.91$, respectively) Higher probability of achieving CSR ($P = 0.022, 0.003, 0.041$, respectively) 0 5%	VATS thymectomy is an advantageous procedure for treating NTMG patients compared with trans-sternal approach offering equivalent CSR rates The acceptable CSR, high improvement rate, short hospital stay, low conversion rate, low morbidity rate and no mortality demonstrate that VATS thymectomy is a safe and effective method for NTGM patients The role of thymectomy for ocular MG remains controversial Small sample including 2 surgical techniques and comparing data between them MGFA classification was different in both groups
Spillane <i>et al.</i> (2013), J Neurol, UK [17] Retrospective study (level 2b)	A total of 89 MG patients underwent extended trans-sternal thymectomy over a 12-year period (1999–2011) Thymoma and non-thymoma patients included MGFA classification used for preoperative assessment of disease severity and post-intervention status Follow-up 0.5–11 years, last clinical review mean of 3.8 years	CSR (at last clinical review) PR Improved status Steroid requirement after thymectomy Duration of symptoms (<2 years) Thymic histology (hyperplasia vs other histology) Mortality Morbidity	34% 33% 13% Fell from 73% preoperatively to 47% ($P < 0.01$) CSR 40 vs 33% ($P = 0.19$) CSR 42 vs 26% ($P < 0.05$) 0 9%	Thymectomy is a safe and well-tolerated procedure generally followed by a long-term substantial improvement in myasthenic symptoms in the majority of patients. No correlation between duration of symptoms and response to thymectomy

Frist *et al.* [3] reported that age <45 years ($P = 0.004$), female sex ($P = 0.03$) and preoperative stage ($P = 0.021$) had a positive impact on outcome.

Masaoka *et al.* [4] found in their study an RR of 67.2% at 15 years and 50% at 20 years after extended thymectomy. Age <34 years ($P < 0.05$) and shorter duration of symptoms (<2 years, $P < 0.05$) were favourable prognostic factors.

Venuta *et al.* [5] in their 27-year experience review reported a 25% CSR at the 10-year follow-up. CSR in patients with <18 months' duration of symptoms preoperatively was 26.8 vs 17.1% ($P = 0.049$). More importantly, palliation (improvement in activities and/or receiving less medication) in this group of patients was also significant (51.8 vs 19.5%, $P = 0.041$).

Gronseth *et al.* [6] reviewed the literature available before the year 2000 and developed evidence-based recommendations. After systematically reviewing the non-randomized studies describing outcomes, they recommended thymectomy as an option to increase the probability of remission or improvement. In patients who underwent thymectomy for severe MG (symptoms and Osserman >2b) relative rates of better outcomes were higher ($P = 0.06$ and 0.007 , respectively).

Budde *et al.* [7] conducted a retrospective review on 113 patients after radical thymectomy and found a 21% CSR, 54% improvement and total benefit of 75%. Patients <50 years (81 vs 55%, $P = 0.02$) and female sex correlated with better outcome ($P = 0.045$).

De Perrot *et al.* [8] found that 81% of their patients improved after thymectomy. Postoperative improvement was greater in patients with advance MG and thymic hyperplasia ($P = 0.04$).

Gronseth *et al.* [9] reported in 2002 yet with another review. They concluded that because of confounding differences between surgical and non-surgical therapies for MG the role of thymectomy remains controversial. However, patients with severe MG who undergo thymectomy show better outcomes.

Mantegazza *et al.* [10] reported that video assisted thoracoscopic extended thymectomy (VATET) is a safe procedure for the treatment of non thymomatous myasthenia gravis (NTMG) with CSR rate of 53.9% at 6 years. It offers similar efficacy to extended trans-sternal approach. They found that thymic hyperplasia, age ≤40 years and anticholinesterase medications were associated with greater probability of achieving CSR ($P = 0.0001$, $P < 0.0001$, $P = 0.037$, respectively).

Tansel *et al.* [11] found early and late postoperative RRs of 44.6 and 73%, respectively. They found no correlation between sex, age, duration of symptoms and preoperative classification. However, symptomatic improvement increased in late follow-up.

El-Medany *et al.* [12] reported that patients <50 years had better outcome ($P = 0.0044$). CSR and benefit rate (BRs) achieved a peak of 75 and 100% at 15 years, respectively.

Kawaguchi *et al.* [13] reported on a small series of patients with late-onset MG (>50 years old). They performed subgroup analysis on MGFA Class II patients showing a better clinical RR although this was not statistically significant ($P = 0.11$).

Sonett *et al.* [14] made recommendations on the best surgical approach based on the best evidence available. The data favour the use of combined trans-sternal-transcervical maximal thymectomy. However, they acknowledge that due to the lack of stronger evidence it is not possible to state with certainty which is the best technique.

Pompeo *et al.* [15] reported a 44% RR after 119 months of follow-up. They found thoracoscopic extended thymectomy a reliable alternative to standard open procedures.

Lin *et al.* [16] analysed the prognostic factors of VATS thymectomy vs trans-sternal thymectomy. Owing to the small numbers of patients in each cohort they found no statistically significant difference in achieving CSR ($P = 0.91$).

Spillane *et al.* [17] reported CSR in 34% of their patients at a mean follow-up of 3.8 years and 33% pharmacological remission. Hyperplastic thymus was associated with better outcome ($P < 0.05$).

CLINICAL BOTTOM LINE

A definitive study on the effectiveness of thymectomy in NTMG patients has not been done. Therefore, the role of this procedure remains uncertain after its introduction by Blalock in 1936. The evidence we have currently is from Class II studies that are affected by different classification systems and reporting crude rates of remission and improvement. Moreover, patients selected for thymectomy usually have aggressive preoperative medication regimes. Also, retrospective studies do not assess the heterogeneity of MG. Terminology employed such as remission and improvement was widely used with different meanings and only recently these terms have been standardized. A comparative analysis based on existing data is therefore difficult to perform. The existing data seem to support an extended resection that removes as much thymic tissue as possible. The ideal method to overcome these problems is a prospective randomized trial, Class I evidence. As highlighted by Gronseth [9], thymectomy in this group of patients should only be considered as an option to increase the chances of remission or improvement. There is an ongoing trial of thymectomy vs no thymectomy in patients receiving steroids. Results are eagerly awaited.

Conflict of interest: none declared.

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