Effectiveness of thymectomy in Very Late-Onset Myasthenia Gravis: a single-center experience

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Background

Myasthenia Gravis (MG) becomes increasingly prevalent with age. Recently, patients whose disease onset occurs after the age of 65 have been categorized as having very- late-onset MG (VLOMG), which presents with a different phenotype compared to early- and late-onset MG [1-2]. This evolving epidemiology raises the question of whether a different therapeutic approach is warranted, particularly concerning thymectomy. Most experts do not recommend the procedure for patients over 60 years of age due to concerns that the risks may outweigh the potential benefits, unless a thymoma is present. The primary aim of this study was therefore, to assess the efficacy and safety of thymectomy in patients with generalized VLOMG.

Table 1. Comparison of baseline characteristics of thymectomy and conservative VLOMG cohorts

	Thymectomy group n=12	Conservative group n=14	p value*
Sex n (%)			
Female	6 (50%)	4 (28.6%)	ns
Male	6 (50%)	10 (71.4%)	
Age at onset median (IQR)	70.5 (7) years	77.5 (8) years	**<0.001**
MGFA classification at onset n (%)			
1	3 (25%)	0	**0.047**
2A	0	0	ns
2B	5 (41.7%)	8 (57.1%)	ns
3A	0	0	ns
	4 (33.3%)	4 (28.6%)	ns
3B	0	1 (7.1%)	ns
4B	0	1 (7.1%)	ns
5			
MG treatment at baseline n (%)			
Prednisone	12 (100%)	13 (92.8%)	ns
Immunosuppressants	0	3 (21.4%)	ns
Dose of prednisone at baseline median (IQR)	25 (12.5) mg/die	13.75 (19.4) mg/die	**0.020**
Immunosuppressants at baseline n (%)	0	3 (21.4%)	ns
IVIG/PLEX at baseline n (%)	0	4 (28.6%)	**0.044**
MG ADL at baseline median (IQR)	4.5 (3)	2.5 (5)	ns
MGC score at baseline median (IQR)	6 (7)	3.5 (8)	ns

List of abbreviations: Δ = delta (i.e. change from baseline to last follow-up); MG ADL= Myasthenia Gravis Activities of Daily Living; MGC score= Myasthenia Gravis Composite score; CSR= complete stable remission; PR= pharmacological remission; SD=standard deviation; IQR= interquartile range; ns= not significant

Table 2 -Comparison of neurological outcomes in VLOMG

	Thymectomy group n=12	Conservative group n=14	p value*
Δ prednisone dosage median (IQR)	- 20 (12.5) mg/die	- 17.5 (25) mg/die	ns
Δ MG ADL median (IQR)	- 3 (4)	- 0 (3)	**0.009**
Δ MGC score median (IQR)	- 6 (5)	- 0 (9)	**0.004**
MGFA-PIS last follow-up n (%)			
CSR	5 (41.6%)	1 (7.1%)	**0.037**
PR	3 (25%)	1 (7.1%)	**0.006**
MM	2 (16.7%)	9 (64.3%)	**0.014**
U	0	2 (14.3%)	ns
W	2 (16.7%)	1 (7.2%)	ns

* Chi-square test for categorical variables, Mann-Whitney test for continuous variables

List of abbreviations: Δ = delta (i.e. change from baseline to last follow-up); MG ADL= Myasthenia Gravis Activities of Daily Living; MGC score= Myasthenia Gravis Composite score; CSR= complete stable remission; PR= pharmacological remission; MM= minimal manifestation; U= unchanged; W= worse; SD=standard deviation; IQR= interquartile range; ns= not significant

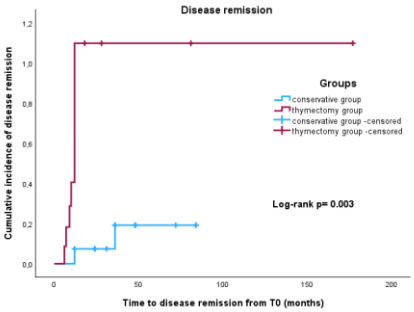
Methods

This was a retrospective, single-center, case-control study of VLOMG patients followed at the MG Clinic of Pisa University Hospital. Inclusion criteria were: a diagnosis of non-thymomatous generalized MG with anti-AChR antibodies, disease onset at age ≥65 years, and a minimum follow-up of 12 months. Neurological status was assessed using the MG-ADL and MGC scales, as well as daily steroid dosage. The primary outcome was evaluated according to the MGFA-PIS at the last available follow-up. The cumulative incidence of disease remission in the thymectomy and conservative groups was compared using Kaplan–Meier analysis with a log-rank test, and the effect of thymectomy on achieving remission was estimated using a Cox regression model, adjusting for confounding variables.

Results

We identified 26 VLOMG patients with a median follow-up of 48 months: 12 underwent thymectomy and 14 received medical therapy alone. The two groups differed at baseline in terms of age at onset, which was significantly higher in the conservative group (p<0.001). Conversely, ocular symptoms at onset and median baseline prednisone dosage were higher in the thymectomy group. After adjusting for age, sex, disease severity, and immunotherapy, thymectomy was associated with an 8.85-fold increased probability of achieving disease remission (HR = 8.85, 95% CI 1.05–74.3) compared to medical therapy alone.

Figure 1. Kaplan-Meier curves for cumulative incidence of disease remission in VLOMG



Kaplan-Meier curves of cumulative incidence of disease remission (PR+CSR) in the VLOMG patients who underwent thymectomy (thymectomy group) and those who did not (conservative group).

Discussion and conclusions

Despite the limitations related to the small sample size and retrospective design, our findings support the feasibility and potential benefit of thymectomy in this subgroup of MG patients. Compared to medical therapy alone, thymectomy appears to significantly increase the likelihood of achieving disease remission, without the need for immunosuppressive treatment. Although advanced age is associated with increased comorbidity burden and surgical risk, thymectomy should be considered a valid therapeutic option for appropriately selected VLOMG patients.

References:

1. Cortés-Vicente E, Álvarez-Velasco R, Segovia S, et al. Clinical and therapeutic features of myasthenia gravis in adults based on age at onset. Neurology. 2020;94(11).
2. Barnett C, Bril V. New insights into very-late-onset myasthenia gravis. Nat Rev Neurol. 2020;16(6):299-300.