LONG TERM PROGNOSTIC FACTORS AND HEALTH-RELATED QUALITY OF LIFE IN OCULAR MYASTHENIA GRAVIS (OMG)

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Introduction

Autoimmune Myasthenia Gravis (MG) is heterogeneous in clinical features and outcomes.[1-3] From 50% to 90% of patients with ocular MG (OMG) may evolve to Generalized Myasthenia Gravis (GMG) within 3 years.[4] Limited information are available about evolution and prognosis of OMG. The aim of this study was to identify factors predictive of prognosis and generalization, as well as their impact on health-related Quality of Life in our cohort of 200 Caucasian patients affected by OMG at the onset, evaluated throughout a follow up ranging from 12 to 158 months.

Patients and methods

Two hundreds Caucasians were followed between September 2000 and November 2014. Diagnosis of OMG was based on the association of clinical history, signs of fluctuating weakness and fatigability and at least one of the following clinical criteria: electrophysiological signs of neuromuscular transmission impairment, immunological confirmation by means of antibody status, unequivocal response either to i.v. edrophonium chloride/neostigmine injection or to symptomatic treatment.[3,5,6] Patients with signs of generalized involvement at diagnosis or with a follow up shorter than 12 months were excluded from the study. Considered prognostic factors were gender, age of onset, electrophysiological results, presence of antibodies against AChR and their titers, thymic abnormalities, thymectomy and treatments. As outcome measures we considered: variations in Physical (PCS) and Mental (MCS) Scores of Short Form health survey 36 (SF-36),[7-9] worsening of Quantitative Myasthenia Gravis (QMG) subscores, Ocular (O-QMG) and Total (T-QMG),[6] and development of generalization, i.e. when patients reached 10 or more points in T-QMG score.[10]

Results

Demographic characteristics are summarized in **Table 1**. The considered outcome measures are shown in **Table 2**. O-QMG was found to be significantly different between the beginning and the end of the follow up (p = 0,0002). Ptosis significantly worsened (p = 0,004) while diplopia did not (p = 0,08). T-QMG, PCS and MCS showed no statistically significant changes throughout the follow up (p = 0,3217; p = 0,4283; p = 0,7186 respectively). MCS improvement was significantly related to older age of onset (i.e. 65 years or more) None of the considered variables influenced PCS improvement. Generalization was significantly more frequent among female and anti-AChR Abs seropositive patients. Finally, none of the independent variables significantly affected O-QMG and T-QMG worsening. Survival analysis showed that factors influencing generalization were sex, age of onset and anti-AChR Abs seropositivity, i.e. longer stability in male, younger and seronegative patients (**Table ; Graphics 1, 2 and 3**).

Discussion and Conclusions

In our cohort of patients, factors influencing generalization were sex, age of onset and anti-AChR Abs seropositivity. Female patients, late-onset patients and anti-AChR Abs seropositive patients had higher risk of generalization, confirmed on multivariate analysis. Survival analysis showed longer stability in male, younger and seronegative patients.

1. *Vincent A, Palace J and Hilton-Jones D.* Myasthenia gravis. *Lancet* 2001; 357: 2122-2128.
2. *Meriggioli MN and Sanders DB.* Autoimmune myasthenia gravis: emerging clinical and biological heterogeneity. *Lancet Neurol* 2009; 8: 475-490.
3. *Berrih-Aknin S, Frenkian-Cuvelier M and Eymard B.* Diagnostic and clinical classification of autoimmune myasthenia gravis. *J Autoimm* 2014; 48-49: 143-148.
4. *Grob D, Brunner N, Namba T, et al.* Lifetime course of myasthenia gravis. *Muscle Nerve* 2008; 37: 141-149.
5. *Benatar M.* A systematic review of diagnostic studies in myasthenia gravis. *Neuromuscular Disorders* 2006; 16: 459–467.
6. *Jaretzki A 3rd, Barohn RJ, Ernstoff RM, et al.* Myasthenia gravis: recommendations for clinical research standards. *Neurology* 2000; 55: 16-23.
7. *Paul RH, Nash JM, Cohen RA, et al.* Quality of life and well-being of patients with myasthenia gravis. *Muscle Nerve* 2001; 24: 512-516.
8. *Padua L, Evoli A, Aprile I, et al.* Quality of life in patients with myasthenia gravis. *Muscle Nerve* 2002; 25: 466-467.
9. *Raggi A, Leonardi M, Antozzi C, et al.* Concordance between severity of disease, disability and health-related quality of life in myasthenia gravis. *Neurol Sci* 2010; 31: 41-45.
10. *Katzberg HD, Barnett C and Bril V.* Predictors of response to immunomodulation in patients with myasthenia gravis. *Muscle Nerve* 2012; 45: 648-652.

Demographic and clinical characteristics of the overall sample (200 patients)		
Median age of onset (yrs)		65 (11-88)
Median duration of follow up (months)		40 (12-158)
Sex	Males	115/200 (57,5%)
	Females	85/200 (42,5%)
Age at onset	Early-onset (< 50 yrs)	38/200 (19,0%)
	Late-onset (≥ 50 yrs)	162/200 (81,0%)
	Elderly-onset (≥ 65 yrs)	105/200 (52,5%)
Electrophysiological tests	RNS (positive)	37/113 (32,7%)
	SFEMG (positive)	103/116 (88,8%)
	All tests (positive)	132/183 (72,1%)
Antibody status	AChR-Abs (positive)	76/194 (39,2%)
	Mean value of AChR-Abs (pmol/ml)	29,5 (± 48,2)
	AChR ≥ 29,5 pmol/ml	22/76 (29,0%)
	Titin-Abs (positive)	36/178 (20,2%)
Thymic status	Thymoma	11/200 (5,5%)
	Thymic hyperplasia or residual gland	22/200 (11,0%)
	Thymectomy	17/200 (8,5%)
Concurrent diseases	Extra-thymic malignancies	48/200 (24,0%)
	Autoimmune diseases	37/200 (18,5%)
	Thyroid gland diseases	50/200 (25,0%)
Initial symptoms	Ptosis	114/200 (57,0%)
	Diplopia	10/200 (5,0%)
	Ptosis + diplopia	69/200 (34,5%)
	None	7/200 (3,5%)
Treatments	Pyridostigmine bromide only	16/200 (8%)
	Steroids only	38/200 (19%)
	Pyridostigmine bromide + Steroids	93/200 (46,5%)
	Combinations including Azathioprine	11/200 (5,5%)
	Combinations including IVIG/PLEX	11/200 (5,5%)
	Non-treated patients	34/200 (17,0%)
	Overall treated patients	166/200 (83,0%)

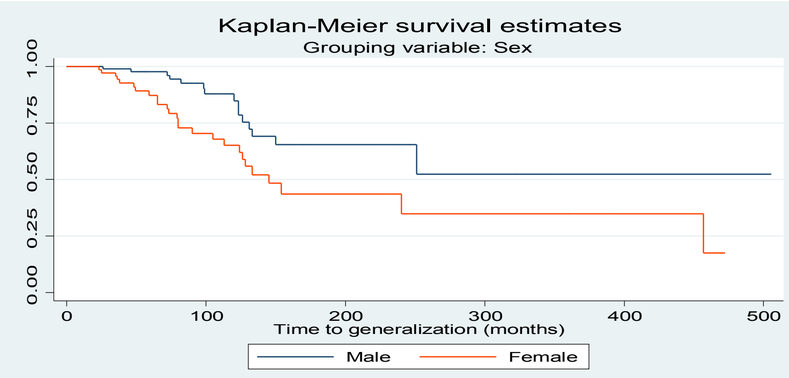
Table 1. Overall demographic characteristics of the whole sample (200 patients). The percentage values are given in parenthesis. *RNS:* Repetitive motor Nerve Stimulation; *SFEMG:* Single Fiber ElectroMyoGraphy; *AChR-Abs:* antibodies directed against the acetylcholine receptor; *Titin-Abs*: antibodies directed against titin; *IVIG:* infusion of IntraVenous ImmunoGlobulines; *PLEX:* PLasma EXchange, in case of generalization.

Overall outcome data throughout the follow up (200 patients)		
Health-related Quality of Life (SF-36)	Improved PCS patients	35/147 (23,8%)
	Improved MCS patients	31/147 (21,1%)
Ocular QMG score	Worsened patients	20/200 (10,0%)
	Improved patients	51/200 (25,5%)
	Stable patients	129/200 (64,5%)
Total QMG score	Worsened patients	49/200 (24,5%)
	Improved patients	40/200 (20,0%)
	Stable patients	111/200 (55,5%)
Generalization	Generalized patients	41/200 (20,5%)
	Median time to generalization (months)	34 (1-450)

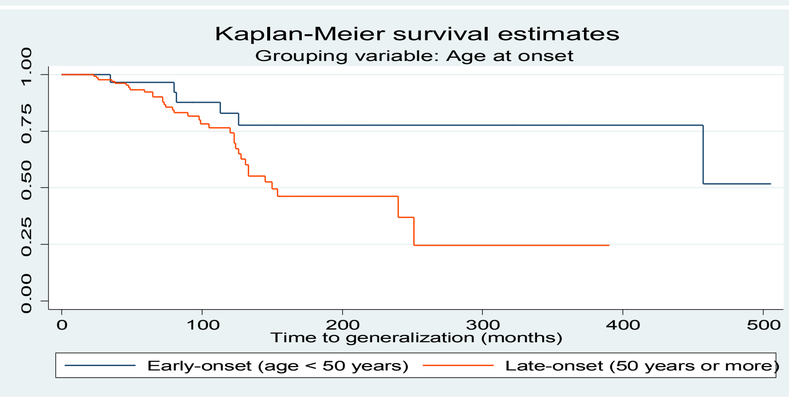
Table 2. Overall outcome data 200 patients. *PCS and MCS:* Physical and Mental Composite Subscores of the Short-Form 36 (*SF-36*) questionnaire about health-related Quality of Life; *QMG:* Quantitative Myasthenia Gravis score; *Generalization:* were considered as generalized those patients with a score of 10 or more in T-QMG.

Multivariate Cox survival analysis - Outcome: Generalization				
Independent variable	Adjusted HR	95% CI		p value
Sex (female)	2,975849	1,553557	- 5,700258	0,001
Late-onset (50 years or more)	3,723748	1,399923	- 9,905048	0,008
Anti-AChR Abs seropositivity	2,477898	1,306340	- 4,700138	0,005

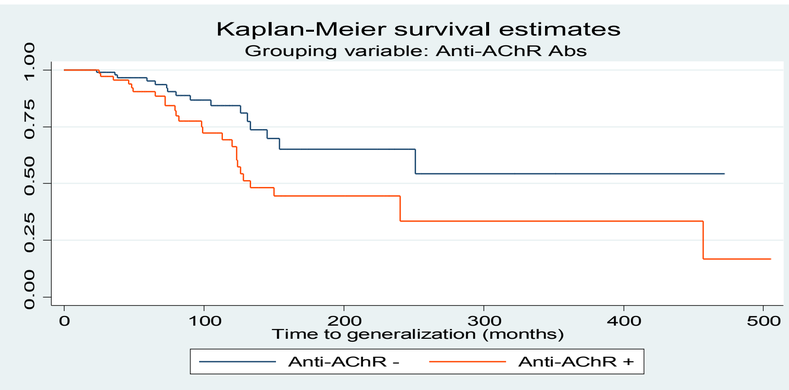
Table 3. Multivariate Cox analysis reporting adjusted Hazard Ratio (*HR*) of Generalization in respect to sex, onset at the age of 50 years or more and presence of anti-AChR Abs. None of the other considered variables significantly affected this outcome.



Graphic 1. Kaplan-Meier survival estimates of Generalization in respect to the sex of the patient.



Graphic 2. Kaplan-Meier survival estimates of Generalization in respect to Age at Onset. *Early-onset:* onset before the age of 50 years; *Late-onset:* onset at the age of 50 years or more.



Graphic 3. Kaplan-Meier survival estimates of Generalization in respect to anti-AChR Abs in serum.

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