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The Relationship Between Lung Function and Health-Related Quality of Life in Patients With Generalized Myasthenia Gravis

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OBJECTIVE: To study lung function abnormalities and health-related quality of life (HRQL) in a group of patients diagnosed with generalized myasthenia gravis, and to analyze the relationship between these 2 sets of variables.

PATIENTS AND METHODS: In a prospective study of 20 patients diagnosed with generalized myasthenia gravis, the following parameters were measured: spirometry, static lung volumes, breathing pattern, maximal respiratory pressures, and maximum voluntary ventilation. HRQL was assessed using the 36-item short form general health questionnaire (SF-36).

RESULTS: The mean (SD) age of the patients was 64 (11) years. Patients were classified into 2 groups depending on whether they had IIa (12 patients) or IIb (8 patients) type disease. A small decrease in total lung capacity (86%) and slight reductions in maximal inspiratory pressure (88%) and maximum voluntary ventilation (63% in group IIb) were observed. The HRQL domains most affected were those related to physical activity and self-perceived health status in all groups, although women were more affected. The scores relating to vitality and physical activity were found to be significantly associated with forced vital capacity and lung volumes. Tidal volume was associated with maximal inspiratory and expiratory pressures, inspiratory capacity, and maximum voluntary ventilation. The respiratory rate to tidal volume ratio was inversely associated with the first three of these variables.

CONCLUSIONS: A very slight restrictive pattern and a reduction in inspiratory muscle strength were observed. The HRQL domains most affected were those related to physical activity and the patients' self-perceived health status. The weakness of the respiratory muscles contributes to the abnormalities observed in lung function and to the deterioration of health-related quality of life.

Key words: *Lung function. Maximal respiratory pressures. Health-related quality of life (HRQL). Myasthenia gravis.*

Relación entre función pulmonar y calidad de vida relacionada con la salud en la miastenia *gravis* generalizada

OBJETIVO: Estudiar las alteraciones de la función pulmonar y de la calidad de vida relacionada con la salud (CVRS), así como las relaciones entre ambas áreas, en un grupo de pacientes diagnosticados de miastenia *gravis* generalizada.

PACIENTES Y MÉTODOS: Se ha realizado un estudio prospectivo en 20 pacientes diagnosticados de miastenia *gravis* generalizada. Se evaluaron la espirometría, los volúmenes pulmonares estáticos, el patrón respiratorio, las presiones respiratorias máximas y la ventilación voluntaria máxima. La CVRS se valoró con el cuestionario general de salud SF-36.

RESULTADOS: La edad media (± desviación estándar) de los pacientes fue de 64 ± 11 años. Se clasificaron en IIa (12 pacientes) y IIb (8 pacientes). Se observaron una leve disminución de la capacidad pulmonar total (86%) y una ligera reducción de la presión inspiratoria máxima (88%) y de la ventilación voluntaria máxima (un 63% en el grupo IIb). Los dominios más afectados de la CVRS fueron los relacionados con la actividad física y la percepción general de la salud en todos los grupos, pero con mayor intensidad en el sexo femenino. Se observaron relaciones estadísticamente significativas entre las áreas de vitalidad y actividad física, la capacidad vital forzada y los volúmenes pulmonares. También se encontraron relaciones entre la presión inspiratoria máxima, la presión espiratoria máxima, la ventilación voluntaria máxima, la capacidad inspiratoria con volumen circulante y el índice volumen circulante.

CONCLUSIONES: Se observaron un patrón restrictivo muy ligero y reducción de la fuerza muscular inspiratoria. Los ámbitos de la CVRS más afectados fueron los relacionados con la actividad física y la percepción general de la salud. La afectación muscular respiratoria contribuye a una alteración en las variables de la función pulmonar y al deterioro de la calidad de vida relacionada con la salud.

Palabras clave: *Función pulmonar. Presiones respiratorias máximas. Calidad de vida relacionada con la salud (CVRS). Miastenia* gravis.

Introduction

Myasthenia gravis (MG) is an autoimmune disease characterized by muscle weakness and fatigue, especially after repetitive exercise. While its etiology is unknown, MG is attributable to a defect in neuromuscular transmission.[1-3] Most patients diagnosed with MG, and especially those with the generalized form of the disease, are affected by this muscle weakness and fatigue.[4,5]

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The classification devised by Osserman and Genkins[6] categorizes patients with MG into 5 classes—I, IIa, IIb, III, and IV—according to how fast symptoms develop, the severity of the patient's condition, and which muscular groups are affected. Approximately 70% of patients with MG fall into classes IIa and IIb, and their condition is known as generalized MG. While respiratory muscle involvement is observed in only 1% to 4% of patients in the early stages of the disease, these muscles are clinically impaired in between 60% and 80% of patients with more advanced disease. Between 30% and 40% of patients with generalized MG develop some kind of respiratory complication during the course of their illness. Our study was, therefore, restricted to patients with generalized MG excluding those in class I (who by definition do not have respiratory problems) and those in classes III and IV (who may have bulbar involvement).[7]

Persistent muscular weakness and fatigue gives rise to ventilatory impairment. This defect, which is initially restrictive, is characterized by respiratory insufficiency caused by hypoventilation as well as obvious abnormalities in the breathing pattern of these patients. The characteristics of the disease, and in particular its chronic and progressive nature, give rise to well known psychological and family problems, and the combination of muscle impairment and respiratory dysfunction has a negative impact on the patients' health-related quality of life (HRQL).[8]

In recent years, several authors have analyzed lung function in patients with generalized MG,[9-11] and HRQL has also been assessed recently in patients of this type.[8,12] However, despite the fact that both lung function and HRQL will inevitably deteriorate in patients with MG, the relationship between the two has not been investigated.

Our objective was to study the changes in lung function (and in particular those related to muscle function) and HRQL, and to analyze the relationship between the two in a sample group of patients with generalized MG.

Patients and Methods

This was a consecutive study of 20 patients who did not have respiratory insufficiency or polysomnographic abnormalities. All the participants had been clinically stable for at least 6 months before enrollment in the study (no myasthenic crises); this was confirmed by the neurologist in charge of their care. The patients were referred from a specialized MG clinic attached to our hospital's neurology department. The diagnosis of generalized MG had been reached on the basis of the patients' medical history, pharmacological tests (Tensilon/Prostigimine), electrophysiological study, and detection of anti-AchR antibodies. All the participants were volunteers, and the study protocol was approved by the hospital ethics committee.

Lung function, respiratory muscle function, lung volumes, breathing pattern, and HRQL were measured under baseline conditions, at the same time of day, and allowing a sufficient interval to ensure that the results would not be influenced by medication.

Lung Function Tests

Lung function tests included forced spirometry—forced vital capacity (FVC), forced expiratory volume in 1 second (FEV_1), and the ratio of FEV_1 to FVC—and maximum voluntary ventilation (MVV). These variables were measured with a Datospir-92 spirometer (SibelMed, Barcelona, Spain) in accordance with the recommendations of the Spanish Society of Pulmonology and Thoracic Surgery (SEPAR).[13] The reference values used for forced spirometry were obtained from a study thoroughly validated for the Spanish population.[14] The following static lung volumes were also measured: functional residual capacity (FRC), residual volume, expiratory reserve volume, total lung capacity (TLC), and inspiratory capacity. The method of measurement used was multiple breath helium dilution. Static lung volumes were measured with a PFL-2450 (SensorMedics, California, USA) in accordance with the SEPAR procedure manual. Two measurements were obtained for each patient and these were complemented by a third when the difference between the first 2 FRC measurements exceeded 200 mL.[15] The result used was the mean of the 2 measurements or the mean of the 2 closest results when 3 measurements were made. Lung volumes were calculated using reference values for a Spanish population.[16] Using the same PFL-2450 equipment, the following breathing pattern variables were measured during spontaneous room-air breathing: minute volume, tidal volume (V_t), respiratory frequency (f_R), and total duration of the respiratory cycle; the f_R/V_t ratio was also calculated. Breathing pattern was assessed after 20 minutes' rest with the patient seated comfortably. The mean values obtained from 10 breathing cycles measured in the resting patients were used in the analysis of the breathing pattern results. Maximum inspiratory pressure (PI_{max}) and maximum expiratory pressure (PE_{max}) were also measured under static conditions using a manometer (model 163; SibelMed, Barcelona, Spain) and following a previously described procedure.[17] Arterial blood gases (pH, PaO_2, and $PaCO_2$) were measured at rest with an ABL 500 (Radiometer, Copenhagen, Denmark) in accordance with SEPAR guidelines.[18] Values in the following ranges were considered normal: 7.35-7.45 for pH; 80-100 mm Hg for PaO_2; and 35-45 mm Hg for $PaCO_2$.

Health-Related Quality of Life

The questionnaire used to assess HRQL was a validated Spanish translation of the SF-36.[19] It comprised 36 items grouped into 8 subscales or domains and generated an overall mean score. There were 4 possible answers to each question. The first scale (10 questions) comprised the items relating to the patient's physical functioning; the second (2 questions) dealt with social functioning; the third (4 questions) with physical limitations; the fourth (3 questions) with emotional limitations; the fifth (4 questions) evaluated the patient's vitality (energy and fatigue); the sixth (2 questions) assessed pain; the seventh (5 questions) quantified the individual's overall perception of his or her own health; and the eighth was a single question designed to evaluate changes in health over time. The general SF-36 is an efficient tool for discriminating between patients with different diseases and for quantifying the differences between populations with and without diseases. The scores for all items were converted to percentages, with 0 indicating maximum abnormality and 100 an absence of abnormality. The results are shown as absolute values and as percentages of previously published norms for the healthy population.[20]

Statistical Analysis

The anthropometric characteristics of the group and the results for lung function, respiratory muscle function, lung volumes, breathing pattern, and HRQL are all expressed as means (SD). All the variables were analyzed for the group as a whole and by disease classification (IIa or IIb). The HRQL values were analyzed for the group as a whole, by disease classification (IIa and IIb), and by sex. The Student *t* test for independent samples was used to determine differences between subgroups IIa and IIb in the quantitative variables (lung function, respiratory muscle function, lung volumes, and breathing pattern) and to compare the results for HRQL domains with the reference values for a healthy population. Correlations were tested by Spearman nonparametric correlation (ρ). We did not test correlations for subgroups IIa and IIb or their variables because of the small number of patients studied. The statistical analysis was carried out using the SPSS statistical package (Chicago, Illinois, USA), version 11 for Windows. A *P* value less than .05 was considered statistically significant.

Results

Patients

Of the 20 patients with generalized MG studied, 12 were in class IIa (5 men and 7 women with a mean age of 67 [12] years and a mean body mass index of 28.2 [3] kg/m^2). The other 8 patients were in class IIb (3 men and 5 women, with a mean age of 61 [15 years] and a mean body mass index of 30.2 [4] kg/m^2). All of the participants were clinically stable, free of respiratory symptoms, and had arterial blood gas values within normal limits. Four of the 20 patients (20%) had undergone a thymectomy within 2 years of being diagnosed with MG. The mean time since diagnosis of the disease was 6 [2.5] years. Fifteen patients (75%) were being treated with prednisone, 14 (70%) with pyridostigimine, and 7 (35%) with azathioprine. Five patients (25%) were taking all 3 drugs, and the others were on a 2-drug regimen. Table 1 shows age and anthropometric characteristics for the group as a whole and for subgroups IIa and IIb.

Lung Function Tests

Many patients had abnormally low lung function results. Values under 80% of predicted were observed for FVC in 10 patients (50%) with a mean of 2.2 (0.4) L (66% of predicted); for FEV_1 in 9 patients (45%), with a mean of 1.5 (0.3) L (61% of predicted); for inspiratory capacity in 9 patients (45%), with a mean of 1.6 (0.1) L (69% of predicted); for TLC in 5 patients, with a mean of 3.4 (0.8) L (69% of predicted); and for FRC in 9 patients (45%), with a mean of 1.9 (0.3) L (72% of predicted). PI_{max}, PE_{max}, and MVV were slightly low in a considerable number of patients. Values under 80% of predicted were observed in 9 (45%) patients for PI_{max} (46 [9] cm H_2O, 62% of predicted), in 5 patients (25%) for PE_{max} (67 [17] cm H_2O, 68% of predicted), and in 9 patients (45%) for MVV (50 [9] L, 57% of predicted).

TABLE 1
Characteristics of the Study Group as a Whole and of Groups IIa and IIb: Spirometry, Lung Volumes, Maximal Respiratory Pressures, Maximum Voluntary Ventilation, and Breathing Pattern*

	All Patients	IIa	IIb
No. of patients	20	12	8
Sex, M/F	8/12	5/7	3/5
Age, years	64 (11)	67 (12)	61 (15)
BMI, kg/m^2	29 (3)	28.2 (3)	30.2 (4)
FVC, L	2.7 (0.7); 79%	2.94 (0.9); 86%	2.5 (0.8); 68%†
FEV_1, L/s	2 (0.6); 79.8%	2.1 (0.7); 87%	1.8 (0.7); 67%†
FEV_1/FVC	74%	71%	72%
IC, L	2.2 (0.6); 88%	2.2 (0.7); 91%	2.1 (0.5); 82%†
FRC, L	2.2 (0.3); 82%	2.2 (0.4); 82%	2.16 (0.4); 82%
TLC, L	4.33 (0.76); 86%	4.52 (1); 91%	4.0 (1); 79%†
RV, L	1.6 (0.25); 85%	1.6 (0.36); 85%	1.6 (0.22); 86%
pH	7.42 (0.01)	7.43 (0.02)	7.41 (0.01)
PaO_2, mm Hg	84.4 (9)	84.4 (11)	84.5 (10)
$PaCO_2$, mm Hg	41.3 (4)	41.3 (5.2)	41.3 (5.7)
ERV	0.61 (0.22)	0.62 (0.22)	0.58 (0.35)
PI_{max}, cm H_2O	62 (22); 88%	71 (38); 98%	56 (16); 73%†
PE_{max}, cm H_2O	112 (33); 109%	123 (51); 118%	96 (23); 95%†
MVV, L/min	109 (30); 74%	82 (32); 87%	63 (32); 70%†
VE, L	10.8 (3)	10.7 (3.7)	10.7 (2.2)
V_t, L	0.6 (0.2)	0.66 (0.2)	0.52 (0.1)
f_R, cycles/min	19.5 (77)	18 (7)	21 (7)
Ttot, s	3.6 (1.5)	3.9 (1.6)	3.1 (1.3)
f_R/V_t, cycle/L·min	39.5 (12.4)	39 (10)	46 (25)

*Data are means (SD) of absolute value, followed by percentage of published reference values.
M indicates male; F, female; BMI, body mass index; FVC, forced vital capacity; FEV_1, forced expiratory volume in 1 second; IC, inspiratory capacity; FRC, functional residual capacity; TLC, total lung capacity; RV, residual volume; ERV, expiratory reserve volume; PI_{max}, maximal inspiratory pressure; PE_{max}, maximal expiratory pressure; MVV, maximum voluntary ventilation; VE, minute volume; V_t, tidal volume; f_R, respiratory frequency; and Ttot, total duration of the respiratory cycle.
†P<.05.

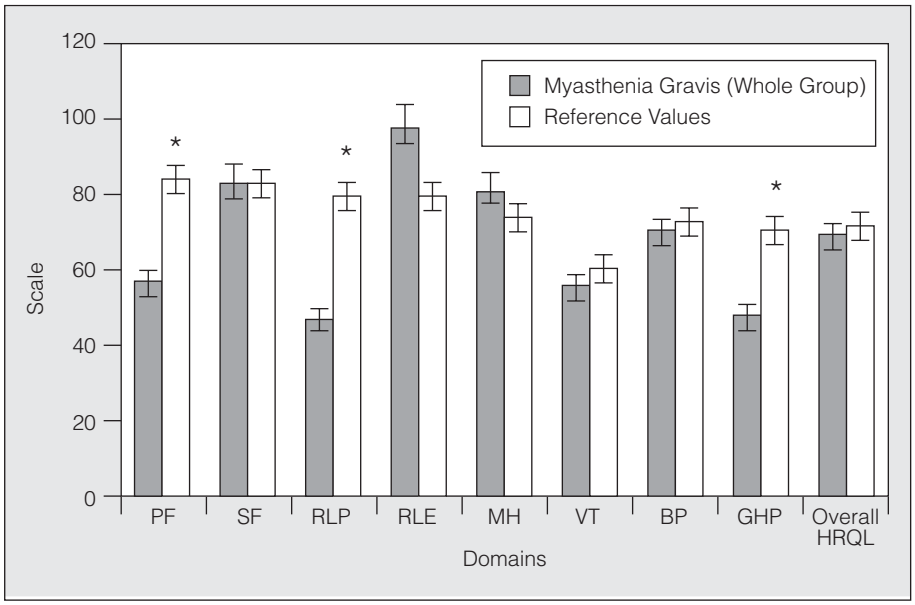

Figure. Health-Related Quality of Life (HRQL) Measured Using the 36-Item Short Form General Health Questionnaire (SF-36). PF indicates physical functioning; SF, social functioning; RLP, role limitations due to physical problems; RLE, role limitations due to emotional problems; MH, mental health; VT, vitality; BP, bodily pain; and GHP, general health perceptions.
***P<.01.**

Patients in class IIb had significantly lower values for FVC, FEV_1, inspiratory capacity, TLC, maximal respiratory pressures, and MVV than patients in class IIa (P<.05). The overall results for the breathing pattern variables fell within the predicted range, and although patients in the class IIb group tended to have slightly more abnormal results than those in class IIa, no statistically significant difference was observed. The most noteworthy result was the statistically significant difference observed between the 2 groups in the following variables: FVC, FEV_1, inspiratory capacity, TLC, PI_{max}, PE_{max}, and MVV. Mean values for the study as a whole and for each of the 2 subgroups are shown in Table 1.

Health-Related Quality of Life

Table 2 shows the mean HRQL values for the study group as a whole, by sex, and for each of the 2 subgroups. For the following domains the results for all the groups were lower than the reference values: physical functioning, role limitation due to physical problems, and general health perceptions (Table 2). Significant differences were found between the results for the study group as a whole and the reference values in the following domains: physical functioning (57 [22] as against a reference value of 84.5 [22.9], P<.01), role limitations due to physical problems (47 [40] as against 81.2 [33.8], P<.01), and general health perceptions (49 [11] as against 72.2 [20.2], P<.01) (Table 1, Figure). Scores on the scale measuring vitality tended to be below the reference values for the women and for the IIb subgroup. The scores for general health perceptions were lower than the reference values in all the groups. Results for all the remaining groups and domains were higher than or only slightly below the reference values for a healthy population.[20]

TABLE 2
Health-Related Quality of Life (HRQL) for the Whole Study Group, by Sex, and by Disease Classification in Comparison to Reference Values*

Scale	All Patients	Men	Women	IIa	IIb
No. of patients	20	8	12	12	8
Physical functioning	57 (22)†; 67%	67 (17); 79%	50 (23); 59%	59 (25); 70%	53 (28); 64%
Social functioning	84 (15); 100%	83 (17); 99%	84 (13); 100%	85 (17); 102%	81 (16); 97%
Role limitation, physical	47 (40)†; 58%	66 (28); 80%	35 (28); 43%	48 (44); 57%	65 (44); 56%
Role limitation, emotional	100 (123)	100 (123)	100 (123)	100 (123)	100 (123)
Mental health	82 (12); 110%	82 (15); 109%	82 (9); 110%	84 (18); 112%	80 (11); 108%
Vitality	55 (23); 91%	70 (17); 114%	46 (22); 75%	67 (23); 109%	38 (28); 63%
Bodily pain	72 (21); 96%	82 (21); 109%	66 (18); 87%	71 (26); 101%	74 (25); 106%
Health perceptions	49 (11)†; 67%	46 (7); 63%	50 (12); 69%	52 (13); 73%	42 (14); 59%
Overall HRQL	72 (16); 97%	64 (3); 88%	64 (11); 88%	70 (13); 97%	67 (16); 92%

*Data are shown as means (SD) followed by percentages of published reference values for a healthy population.[20]
†Significantly different with respect to the reference values (P<.01).

TABLE 3
Correlations Between Lung Function and Health-Related Quality of Life*

	Physical Functioning	Vitality	Role limitations (Physical)
FVC	0.465†	0.481†	0.288
TLC	0.525†	0.655‡	0.488†
FEV_1	0.387	0.401	0.384
FRC	0.630†	0.687†	0.570†
ERV	0.591‡	0.234	0.230
IC	0.265	0.492†	0.563‡
RV	0.211	0.570‡	0.441

*FVC indicates forced vital capacity; TLC, total lung capacity; FEV_1, forced expiratory volume in 1 second; FRC, functional residual capacity; ERV, expiratory reserve volume; IC inspiratory capacity; and RV, residual volume.
†P<.05; ‡P<.01.

TABLE 4
Correlation Between Muscular Function, Inspiratory Capacity (IC), and Breathing Pattern*

	V_t, L	f_R/V_t, Cycle/L × min)
PI_{max}	0.603†	–0.554‡
PE_{max}	0.694†	–0.581†
MVV	0.519‡	–0.403
IC	0.594†	–0.460‡

*Correlations for the whole group (sample of 20 patients). The data are expressed as ρ values. V_t indicates tidal volume; f_R, respiratory frequency; PI_{max}, maximal inspiratory pressure; PE_{max}, maximal expiratory pressure; and MVV, maximum voluntary ventilation.
†P<.05; ‡P<.01.

Associations Between Lung Function and HRQL

Tables 3 and 4 show the statistically significant correlations found between lung function and HRQL. No significant associations were found between HRQL and respiratory muscle function (PI_{max}, PE_{max}, and MVV). Significant correlations were, however, found between physical functioning and FVC (ρ=0.465, P<.05), TLC (ρ=0.525, P<.05), FRC (ρ=0.630, P<.01), and expiratory reserve volume (ρ=0.591, P<.01); vitality and FVC (ρ=0.481, P<.05), TLC (ρ=0.655, P<.01), FRC (ρ=0.687, P<.01), inspiratory capacity (ρ=0.492, P<.05), and residual volume (ρ=0.570, P<.01); and between the domain of role limitations due to physical problems and TLC (ρ=0.488, P<.05), FRC (ρ=0.570, P<.05), and inspiratory capacity (ρ=0.563, P<.01). Significant relationships were also found between V_t and PI_{max} (ρ=0.603, P<.01), PE_{max} (ρ=0.694, P<.01), MVV (ρ=0.519, P<.05), and inspiratory capacity (ρ=0.594, P<.01). The f_R/V_t ratio was inversely associated with PI_{max} (ρ=–0.554, P<.05), PE_{max} (ρ=–0.581, P<.01), and inspiratory capacity (ρ=–0.460, P<.05).

Discussion

The principal findings of the present study confirm that the general weakness found in patients with generalized MG also affects the respiratory musculature, and that these patients (classified as class IIa and IIb) present a slight restrictive ventilatory defect. At the same time, the HRQL domains most affected are those related to the patient's physical condition in general and muscular condition in particular. The most notable relationship is the association between the HQRL subscales relating to the patient's physical state and both lung function variables and lung volumes—2 groups of parameters that are also related to physical strength and the condition of the respiratory musculature.

MG is a chronic neuromuscular disease that affects various muscle groups. The generalized form of the disease usually affects the respiratory muscles to a greater or lesser degree, and in the final stages it can result in respiratory insufficiency caused by failure of the ventilatory pump.[1,2] In the present study of class IIa and IIb patients, we found only slight impairment of respiratory muscle strength (maximal respiratory pressures) and endurance (MVV). These findings are similar to those reported by other authors.[4,5,9-11,21-24] In any event; analysis of data from small numbers of patients (20 in our study) is highly influenced by extreme values. In our study, lung function values in 4 patients were much higher than those usually found in individuals with neuromuscular disease. This anomaly can probably be attributed to the fact that these patients had started pharmacological treatment at an early stage.

In a recent study, García Río et al[10] assessed respiratory pressures, forced spirometry, and breathing pattern in a group of 24 patients. Using a study design similar to ours, they allocated the patients to 2 subgroups (IIa and IIb). The patients in that study had better spirometry results, a similar breathing pattern, and more abnormal respiratory pressures than our study group. While our PI_{max} results were similar to those observed by García Río and colleagues, PE_{max} results were higher in our study for both subgroups. In another similar study, Díez Tejedor et al[9] analyzed maximal respiratory pressures in a series of 23 patients with MG (12 class IIa, 6 class IIb, and 5 class I). In comparison with their results, respiratory muscle strength was better preserved in both subgroups in our study, although the PI_{max} values reported by that study for patients in class IIb were very similar to those we found in the corresponding group. Muñoz-Fernández et al[4] and Radwan et al[24] found very slight impairment of respiratory muscle strength in their studies, and the degree of respiratory muscle involvement observed by Spinelli et al[11] and Keenan et al[23] was very similar to that observed in our study, especially for patients in class IIb. These differences in results between studies are, for the most part, attributable to differences in the timing of diagnosis, the duration of treatment, and to the difficulties involved in classifying patients with MG in a uniform and systematic way. In fact, Keenan et al[23] provided little or no information on the mean time elapsed since diagnosis or the mean duration of treatment for the patients in their study.

Our patients' breathing pattern was very similar to the pattern discussed in a recent review of the

literature[25] and described by other authors.[8,9] It was characterized by rapid shallow breathing, and evidenced by a practically normal f_R and V_t. The breathing pattern of the group of patients in class IIb was somewhat less efficient. This is reflected in the high f_R/V_t ratio observed in this group; these patients presented a slight increase in f_R and a decline in V_t.

Our HRQL results revealed a greater negative impact on the scales directly related to general physical activity and the patients' perception of their own health. Our results were very similar to those reported by Paul et al,[12] although that study included recently diagnosed patients who had not yet received appropriate medication. In a study carried out in Italy, Padua et al[8] report quality-of-life scores much lower than those found either by Paul and colleagues or in our study. The only explanation we can find for this discrepancy is that in most cases in the Italian study HRQL was assessed when the patients were hospitalized because of deterioration in their clinical condition due to myasthenic disease.

In view of the associations between functional respiratory abnormalities and HRQL, it can be deduced that—in the domains dealing with the patients' general health—the aspects most affected are those that involve muscle activity in general and the respiratory musculature in particular. Patients have to cope with the physical limitations caused by neuromuscular dysfunction and experience the fatigue associated with this situation. Furthermore, loss of pulmonary volume can also contribute to a higher incidence of this perception of fatigue. The positive correlation between FRC and the domains of physical functioning and role limitation (physical) leads us to believe that the higher the score obtained on these subscales, the better the patient's FRC will be. Conversely, patients with a more abnormal FRC will tend to score lower in these 2 domains. The same conclusions could be drawn about the relationship between these 2 HRQL domains and both TLC and inspiratory capacity—2 lung function variables that could hypothetically be related to the presence or development of respiratory muscle fatigue. The fact that no significant association was found between the HRQL domains and respiratory pressures or MVV may be attributable to the interindividual variability of muscle function within the groups. It is possible that, in a larger sample of patients, such relationships might be consolidated. Although it is only speculation, the associations we found between HRQL and lung function allow us to hypothesize about the mechanisms by which lung function affects HRQL. It is possible that respiratory muscle weakness may lead to a loss of lung volumes and consequently to episodes of impaired ventilatory efficiency evidenced by a decrease in breathing pattern values. In patients with MG, it is presumed that, although the breathing pattern is not very abnormal, the respiratory muscles—and particularly the diaphragm—require a longer recovery period to recuperate physiologically after a muscular contraction.[26] In fact, the associations identified between, on the one hand, respiratory muscle strength (PI_{max} and PE_{max}) and MVV and, on the other, the breathing pattern variables V_t and the f_R/V_t ratio support the hypothesis that muscular weakness is the triggering factor in all the lung function alterations. Weakness of the respiratory musculature leads to a decrease in the ventilatory efficiency of the respiratory cycle, evidenced by lower V_t, a higher f_R/V_t ratio, and a higher f_R. Moreover, in the long term, breathing pattern abnormalities will result in modifications of lung volumes and eventually—as a result of diaphragmatic dysfunction and changes in arterial blood gases—will lead to hypercapnic respiratory insufficiency.[27,28]

The greatest limitation of the present study was perhaps the small size of our sample, although patients with generalized MG represent, according to a recent Spanish epidemiological study, 69% of all MG patients.[29] It is also worth posing the question whether the changes in lung function are associated with functional abnormalities from the standpoint of ability to tolerate exercise. In a study published recently,[30] our group was able to demonstrate that submaximal exercise tolerance—measured using the 6-minute walk test—was within normal limits in a sample of patients with generalized MG very similar to the group that participated in the present study.[30] In our opinion, more studies with larger numbers of patients are necessary to study the evolution of lung function, respiratory muscle function, and HRQL from the time of diagnosis in order to measure linearly the extent of respiratory impairment.

In summary, our results coincide with those reported in the literature with respect to the type and degree of abnormality in lung function and the respiratory musculature. This deterioration is also related to the degree and extent of the progression of the disease. HRQL is slightly and particularly affected in the domains related to physical activity, the perception of having the energy to engage in such activity, and the patients' general perceptions about their health. Lung function studies allow us to assess the evolution of respiratory function and, to some degree, the progression of the disease since generalized MG is associated with considerable respiratory complications. The evaluation of lung function also contributes to an understanding of the extent of the problem, especially with respect to progressive functional impairment of the respiratory musculature.

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