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The correlation between FVC, FEV_1, and FEVR with voice handicap index of myasthenia gravis patients

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ABSTRACT

Background and objectives. Dysarthrophonia due to weakness of bulbar muscles are one of the common manifestations of Myasthenia Gravis (MG), in the form of hypernasal voice, vocal fatigue, harshness, breathiness, monopitch, monoloudness, as well as impaired articulation and speaking fluency. This voice disorder affects the quality of life of MG patients, especially those who use their voices a lot in their daily lives and professions. Lung function is closely related to vocal function because sound comes from exhaled air

which passes through the voice box and vibrates the vocal cords. This study aims to analyze the correlation between lung function and voice-related quality of life in MG patients.

Materials and Methods. This cross-sectional study involved 23 patients (7 men; 16 women), aged 18-59, with mild to moderate stable MG. Pulmonary function assessed was Forced Vital Capacity (FVC), Forced Expiratory Volume in 1 second (FEV_1), and Forced Expiratory Volume Ratio (FEVR), measured using a portable digital spirometer. Voice-related quality of life was assessed with the Voice Handicap Index (VHI-30) questionnaire.

Results. There was no significant correlation between FVC, FEV1, and FEVR with VHI (CI 95%, $p > 0.05$).

Conclusions. There is no relationship between FVC, FEV1, and FEVR with VHI in MG patients. Further research is needed to analyze the factors influence voice-related quality of life in MG patients.

Keywords: myasthenia gravis, dysarthrophonia, voice handicap index, lung function

Abbreviations:

BMI	: Body Mass Index
EOMG	: Early Onset Myasthenia Gravis
FEV_1	: Forced Expiratory Volume in 1 second
FEVR	: Forced Expiratory Volume Ratio
FVC	: Forced Vital Capacity
gMG	: Generalized Myasthenia Gravis
HRQL	: Health-Related Quality of Life
LOMG	: Late Onset Myasthenia Gravis
MG	: Myasthenia Gravis
MGC	: Myasthenia Gravis Composite
MGFA	: Myasthenia Gravis Foundation of America
MoCA-INA	: Montreal Cognitive Assessment Indonesia Version
MPT	: Maximum Phonation Time
oMG	: Ocular Myasthenia Gravis
VHI	: Voice Handicap Index
VHI-E	: Voice Handicap Index Emotional
VHI-F	: Voice Handicap Index Functional
VHI-P	: Voice Handicap Index Physical
VRQOL	: Voice-Related Quality of Life

INTRODUCTION

Myasthenia Gravis (MG) is an autoimmune disease characterized by symptoms such as muscle weakness and fatigue, which worsen with repetitive activity [1]. The symptoms experienced by MG patients can vary from mild to severe in each individual, affecting ocular muscles, limb muscles, and even bulbar muscles [2]. The manifestation of MG in bulbar muscles can lead to symptoms such as dysarthria, dysphonia, dysphagia, and in severe cases can cause respiratory disturbances. Dysarthria can be the first or even the only symptom in 6-27% of MG cases, and as the disease progresses, it can affect around 60% of patients [3]. A study in Brazil in 2010 found that the presence of dysphonia symptoms in MG patients over 50 years old was as common as diplopia symptoms [3].

The function of the voice is closely related to respiratory function. Disorders in the laryngeal, respiratory, or orofacial organs can affect voice outcomes, such as decreased speech rate, volume, Maximum Phonation Time (MPT), and voice stability. As a result, complaints such as hoarseness, crackling, breathiness, tension, tremor, and vocal fatigue can arise [4]. Myasthenia Gravis is a chronic disease that often requires lifelong treatment, so the quality of life is significantly affected [5]. Voice complaints are also common among MG patients and can affect their quality of life, especially for those who rely on their voice in their daily lives or profession.

The Voice Handicap Index (VHI) is a questionnaire used as a tool to assess quality of life and severity of voice disorders, where patients subjectively evaluate complaints related to voice problems. A study by Konstantopoulos et al. found a significant difference ($p<0.01$) in VHI scores between MG subjects and controls. This indicates that MG subjects perceive voice complaints affecting their quality of life [6].

So far, there have been no studies linking the results of lung function measurements using a spirometer with the quality of life of MG patients related to voice. Considering the significant number of voice complaints in MG patients and their impact on quality of life, this study was conducted to determine whether there is a relationship between lung function and quality of life related to voice in MG patients.

MATERIALS AND METHODS

This study used cross-sectional design with consecutive sampling. It was conducted at Physical Medicine and Rehabilitation Outpatient Clinic from April to June 2023.

Participants in this study were MG patients with a total of 23 participants. (Figure 1)

Ethical approval was obtained before the study begin from Hospital ethical committee with ethical clearance number 0601/KEPK/II/2023. The following are the criteria for

inclusion: 1) confirmed myasthenia gravis patients class I - IIb based on Myasthenia Gravis Foundation of America (MGFA), 2) Men or women aged 18-59 years, 3) patient is cooperative and able to follow instructions, 4) normal cognitive function (Montreal Cognitive Assessment Indonesia Version / MoCA-INA Score ≥ 26), 5) receive myasthenia gravis treatment at RSUD Dr. Soetomo and approved by neurologist to join the study, 6) willing to join the study and sign the informed consent. The exclusion criteria were: 1) myasthenia crisis, 2) has had a speech or voice disorder since childhood or unrelated to the MG condition, 3) diagnosed with tumors of the larynx, mediastinum or lung, 4) have contraindications to spirometry, such as stroke or heart attack in the last 3 months, intracranial SOL (space occupying lesion), cerebral aneurysm, retinal detachment, history of surgery (eye, brain, chest, stomach) in the last 3 months, hemoptysis in the last 1 month, pneumothorax, hernia (scrotal, inguinal, umbilical), hernia of the nucleus pulposus, suspected or confirmed infectious disease (tuberculosis, influenza, pneumonia, etc.).

This study collected data on lung function and voice related quality of life. Portable digital spirometer (CONTEC SP10, Contec Medical, China) was used to assess lung function parameters namely Forced Vital Capacity (FVC) and Forced Expiratory Volume in 1 second (FEV_1). While Forced Expiratory Volume Ratio (FEVR) was calculated using the FEV_1/FVC formula and expressed as a percentage [7]. Voice Handicap Index (VHI-30) Questionnaire was used to assess voice related quality of life, which consists of 30 queries on 3 distinct subscales, including physical, functional, and emotional. The possible score for each subscale between 0 and 40, so that the total score for all subscales was between 0 and 120. The higher scores reflected a greater decline in quality of life [7].

Statistical analysis

All data obtained in this study were analysed using SPSS version 26 (SPSS Inc., Chicago, USA). The data obtained will be analyzed descriptively in the form of mean, standard deviation, minimum, maximum, and percentage. Using the Monte Carlo test for normality assumption, the distribution of the quantitative data was analyzed. Pearson correlation coefficients was used to analyzed correlation between lung function test and voice related quality of life. Statistical significance was defined as $p < 0.05$ with a 95% confidence interval.

RESULTS

Characteristics of the patients

Majority of participants were female (69.6%) with mean age 47.87 ± 6.12 years old. According to MGFA classification, all subjects were class II MG type (generalized type), consist of 56.5% type IIA and 43.5% type IIB. Mean MGC score of the participants was 4.87 ± 3.2. The majority of participants have a normal BMI (56.5%), while some others were underweighted (13.0%), obese grade I (21.7%), and 4.3% each for overweight and obese grade II. The most common comorbidity among the participants was hypertension (13.0%), although the majority do not have any comorbidities (56.5%). While others had dyslipidemia (8.6%), asthma (4.3%), hypertension and asthma (4.3%), hypertension and nephrolithiasis (4.3%), valvular heart disease (4.3%), and uterine myoma (4.3%). (Table 1)

Results of voice handicap index and spirometry according to MG type

The VHI score in MG type IIA ranged from 0-66 with an average of 21.85 ± 23.24, while in MG type IIB the VHI score ranged from 0-50 with an average value of 19.80 ± 20.60. The mean values of FEV1 in MG type IIA was 72.54 ± 10.80, while in type IIB MG the mean was 53.15 ± 10.25. The mean FVC values in MG type IIA was 75,60 ± 7,11, whereas in type IIB MG was 53,57 ± 5,71. The mean FEVR values in MG type IIA was 79,67 ± 8,33, whereas in type IIB MG was 82,33 ± 10,92. (Table 2)

Correlation between spirometry and voice handicap index results in MG patients

All independent and dependent data exhibit normal distribution according to Monte Carlo test, thereby meeting the criteria for using Pearson test to assess correlation between FVC, FEV1, and FEVR with VHI. Table 3 showing the result of Pearson correlation test between spirometry results and VHI, both the total and VHI subscales. There was no correlation between spirometry results (FVC, FEV_1, and FEVR) with VHI (total VHI, VHI-F, VHI-P, and VHI-E) ($p>0.05$). (Table 3)

DISCUSSION

The majority of subjects had Early-onset MG (EOMG), which is MG with an onset age below 50. In this EOMG group, there is a predominance of women with a female-to-male ratio of 3:1 [9]. A study by Bubuioc *et al.* in Asian population reported more cases of EOMG compared to LOMG (Late-onset MG), in accordance with the characteristic profile of the subjects in this study which the onset age ranged between 19-52 years old [10].

This study did not obtain participants with type I MG or ocular type (Ocular MG/oMG). All participants had generalized MG (gMG), which consist of MG type IIA and IIB. This is

consistent with the theory that around 70% of MG patients are categorized as IIA and IIB [11]. Other research indicates that almost 90% of oMG patients will advance to gMG within 2-3 years of symptom onset [9,12]. The findings of this research suggest that the participants had received MG treatment for a period ranging from 2 to 24 years since onset, indicating a strong possibility that those who initially presented with oMG have now transitioned to gMG.

The results of this study show that the most common comorbidity is hypertension (13.0%), followed by hypertension and asthma (4.3%), hypertension and nephrolithiasis (4.3%), as well as dyslipidemia, valvular heart disease, and uterine myoma, each with a percentage of 4.3%. A 2022 retrospective cohort study of more than 1,000 MG patients in England reported common comorbidities associated with MG include cardiovascular disease, hyperlipidemia, hypertension, diabetes mellitus, respiratory diseases, and other autoimmune diseases [13]. A meta-analysis study by Yingchoncharoen *et al.* (2021) found that asthma patients are 1.4 times more likely to suffer from MG [14].

The number of MG subjects with obesity in this study is fewer compared to the previous study by Chang *et al.*, which found 40% of MG subjects with obesity, but consistent with the study by O'Connor *et al.*, which found that 26% of its subjects had obesity [15,16]. The MG process damages the structure and function of the neuromuscular junction, leading to muscle weakness and changes in body composition, including a decrease in muscle mass, an increase in adipose tissue, and an increase in the frequency of obesity [15].

As 90% of MG patients are generalized MG, and of these 30-40% will develop respiratory complications, it is important to perform pulmonary function tests in all types of MG [11]. Among other things, pulmonary function tests are performed to assess ventilatory function. One of the simple and routine modes of pulmonary function testing is spirometry [17]. The results of this study show that the average values of FEV1 and FVC are lower than the normal values, which are ≥ 80%. This finding is consistent with the study by Octaviana *et al.* (2023) that assessed spirometry results in 70 MG patients at a National Referral Hospital in Indonesia and found significantly lower FEV1 and FVC values in MG subjects compared to controls [18].

This study shows an average FEV1% value of 64.11 ± 14.26 and an FVC value of 66.02 ± 12.87. These values are lower compared to the study conducted by Calik-Kutukcu *et al.* (2019) on 28 MG subjects, where an average FEV1 value of 74.72 ± 17.93 and an FVC of 71.60 ± 16.71 were obtained [19]. This difference may be due to the chronic use of prednisone in the majority of subjects in that study (65%), whereas in this study, only 2 out of 23 subjects (8.69%) were consuming methylprednisolone. Prednisone works to

reduce inflammation in the airways, which can affect spirometry results. Another study by Fregonezi *et al.* (2006) found an average FVC value of 66% and an FEV1 value of 61%, which are consistent with the results of this study [20].

This study indicates that the values of FEV1 and FVC are lower in subjects with MG type IIB compared to type IIA. These findings are consistent with previous studies that show subjects with MG type IIB have significantly lower values of FVC, FEV1, inspiratory capacity, total lung capacity, maximal respiratory pressure, and maximum ventilation volume compared to type IIA [20].

Generalized MG patients often show restrictive results on pulmonary function examination [11,16]. Accordingly, the results of this study showed a restrictive spirometry pattern in 69.6% of subjects, followed by mixed (13.0%), obstructive (8.7%), and normal (8.7%) patterns. These results differ from a study by Oliveira *et al.* on 15 MG subjects where only 2 subjects (13.3%) showed abnormalities in their spirometry results even though both were also restrictive patterns [11]. Obstructive and mixed pattern in this study are very likely due to the presence of comorbid asthma and a history of other respiratory disorders. Additionally, one of the cholinergic effects of pyridostigmine is spasm and excessive mucus production in the airway so that it can cause obstructive respiratory disorders [21].

Myasthenia Gravis can also affect bulbar muscles, such as the laryngeal muscles. The manifestation of MG in the bulbar muscles can result in symptoms such as dysarthria, dysphonia, dysphagia, and in severe cases, can lead to respiratory difficulties [2]. A study in Brazil in 2010 found that the presence of dysphonia symptoms in MG patients over the age of 50 was as common as diplopia symptoms [3]. Voice plays a very important role in communication in daily life, so any disruption in speaking will affect a person's quality of life.

This study uses the Voice Handicap Index (VHI-30) questionnaire, which consists of 30 statements, covering the functional, physical, and emotional domains of voice disorders in daily activities [8]. Generally, the VHI score will increase as the degree of voice disturbance increases. The results of this study showed that only 8.7% of the subjects felt severe impairment in their voice-related quality of life while the majority of the subjects felt mild impairment (52.2%), the rest felt moderate impairment (17.4%), and 21.7% did not feel impaired. VHI scores in this study ranged from 0-66 with a mean value of 20.96 ± 21.66.

Another study by Konstantopoulos *et al.* obtained a mean VHI score in 12 MG subjects of 21.750 ± 19.027, in accordance with the VHI score obtained in this study [6]. It was explained that the presence of voice disorders in MG patients is a manifestation of

neuromuscular junction dysfunction. Muscle weakness and fatigue lead to incoordination of muscle synergy and decreased strength of plica vocalis movement, resulting in the inability to maintain adequate plica vocalis adduction, causing disturbances in the voice component [6].

A study by Hwang *et al.* assessed VHI in 48 subjects with stroke where in stroke subjects with voice disorders the mean VHI score was 65.1 ± 21.4, while in stroke subjects without voice disorders the score was 7.4 ± 4.8 [22]. The VHI score of MG subject in this study was lower compared to that study because in this study not all subjects had voice disorders so that the mean value of the VHI score was lower.

This study showed no significant correlation between the lung function parameters (FEV1, FVC and FEVR) and the total VHI score as well as the functional, physical and emotional components. This result could be due to the fact that dysphonia in MG is caused more by bulbar muscle weakness than by weakness in the respiratory muscles. The subjective nature of the VHI questionnaire is highly influenced by personal factors such as occupation, economic status, and educational level. This can be seen from the comparison of VHI scores between subjects with MG type IIA and IIB which are not much different even though MG type IIB shows a higher level of bulbar muscle involvement. (Table 2) To date, there have been no previous research publications assessing the relationship between pulmonary function and voice-related quality of life in MG patients.

Past studies have shown a significant relationship between FVC and Health-Related Quality of Life (HRQL) of MG patients assessed using SF-36 questionnaire [20]. This questionnaire assesses the patient's quality of life in terms of global health, consisting of 8 domains namely physical function, social function, physical limitation, social limitation, mental health, vitality (energy and fatigue), pain, and perception of overall health. Factors that influence HRQL are disease severity, age, age at onset, BMI, type of employment, educational status, and physical activity [23]. This assessment of HRQL is broader and more multidimensional compared to the assessment of voice-related quality of life. It could be argued that voice problems are only one-dimensional part of the overall health condition assessed by the HRQL.

A study in subjects with Chronic Obstructive Pulmonary Disease (COPD) proved a significant moderate negative correlation between voice-related quality of life assessed using the Voice-Related Quality of Life (VRQOL) questionnaire and Peak Expiratory Flow (PEF) [24]. Peak expiratory flow is one of the parameters of pulmonary function tests to assess breath effort, which can be obtained by forced expiratory maneuver on spirometry or with a peak flow meter [7,25]. Many sources state the relationship between

PEF and FEV1, but in general FEV1 is a more reliable indicator of airflow disorders because it reflects the caliber of both large and small airways [26].

This study has limitations, as the subjects in this study were only mild-moderate MG patients, and not all of them had voice disorders. In the future, another research is needed to analyze the factors affecting voice-related quality of life in MG patients.

CONCLUSION

There is no relationship between FVC, FEV1, and FEVR with VHI in MG patients.

Conflict of interest:

No conflicts of interest were revealed about this article's authorship and publishing.

Author's contributions:

Methodology, resources, data collection/processing, literature search, and writing - original draft preparation, project administration: N.A., Conceptualization, writing - review and editing, data curation, supervision, data analysis/data interpretation, critical reading: I.S., D.P., M.A., P.S., S.M. All authors have read and agreed to the published version of the manuscript.

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REFERENCES

1. Corrado B, Giardulli B, Costa M. Evidence-Based Practice in Rehabilitation of Myasthenia Gravis. A Systematic Review of the Literature. J Funct Morphol Kinesiol. 2020;5(4):71. doi:10.3390/jfmk5040071
2. Jayam Trouth A, Dabi A, Solieman N, Kurukumbi M, Kalyanam J. Myasthenia gravis: a review. Autoimmune Dis. 2012;2012:874680. doi:10.1155/2012/874680
3. Ayres A, Winckler PB, Jacinto-Scudeiro LA, Rech RS, Padovani MMP, Jotz GP, et al. Speech characteristics in individuals with myasthenia gravis: a case control study. Logoped Phoniatr Vocol. 2022;47(1):35-42. doi:10.1080/14015439.2020.1834614
4. Cielo CA, Pascotini FS, Ribeiro VV, Gomes AM, Haeffner LSB. Vocal Phonotherapy and Respiratory Physical Therapy with Healthy Elderly People: Literature Review. Rev CEFAC. 2016;18(2):533-543. doi:10.1590/1982-021620161822415
5. Anggarini YD, Subadi I, Andriana M, Poerwandari D, Sugianto P, Kartika L, *et al*. The correlation between functional capacity and quality of life in patients with myasthenia gravis. Rom. J. Neurol., 2023;22(3):196-202. doi:10.37897/RJN.2023.3.4
6. Konstantopoulos K, Christou YP, Vogazianos P, Zamba-Papanicolaou E, Kleopa KA. A quantitative method for the assessment of dysarthrophonia in myasthenia gravis. J Neurol Sci. 2017;377:42-46. doi:10.1016/j.jns.2017.03.045
7. CDC. Respiratory Health Spirometry Procedures Manual [Internet]. 2008. Available from: https://www.cdc.gov/nchs/data/nhanes/nhanes_07_08/spirometry.pdf
8. Jacobson BH, Johnson A, Grywalski C, Silbergleit A, Jacobson G, Benninger MS, *et al*. The Voice Handicap Index (VHI): Development and Validation. *Am J Speech Lang Pathol*. 1997;6:66-70. doi:10.1044/1058-0360.0603.66
9. Dresser L, Wlodarski R, Rezania K, Soliven B. Myasthenia Gravis: Epidemiology, Pathophysiology and Clinical Manifestations. *J Clin Med*. 2021;10(11):2235. doi:10.3390/jcm10112235
10. Bubuioc AM, Kudebayeva A, Turuspekova S, Lisnic V, Leone MA. The epidemiology of myasthenia gravis. *J Med Life*. 2021;14(1):7-16. doi:10.25122/jml-2020-0145
11. Oliveira EF, Nacif SR, Foncesa NT, Apostólico N, Urbano JJ, Guimarães LL, et al. Pulmonary Function and Respiratory Muscle Strength in Myasthenia Gravis.

Man. Ther., Posturology Rehabil. J., 2014;1-8. doi:10.17784/mtprehabjournal.2014.12.198

12. Fan L, Ma S, Yang Y, Yan Z, Li J, Li Z. Clinical differences of early and late-onset myasthenia gravis in 985 patients. *Neurol Res*. 2019;41(1):45-51. doi:10.1080/01616412.2018.1525121
13. Harris L, Graham S, MacLachlan S, Exuzides A, Jacob S. A retrospective longitudinal cohort study of the clinical burden in myasthenia gravis. *BMC Neurol*, 2022;22(1), 172. doi:10.1186/s12883-022-02692-4
14. Yingchoncharoen P, Charoenngam N, Ponvilawan B, Thongpiya J, Chaikijurajai T, Ungprasert P. The Association Between Asthma and Risk of Myasthenia Gravis: A Systematic Review and Meta-analysis. *Lung*. 2021;199(3):273-280. doi:10.1007/s00408-021-00444-8
15. Chang CC, Chen YK, Chiu HC, Yeh JH. Changes in Physical Fitness and Body Composition Associated with Physical Exercise in Patients with Myasthenia Gravis: A Longitudinal Prospective Study. *J Clin Med*. 2021;10(17):4031. doi:10.3390/jcm10174031
16. O'Connor L, Westerberg E, Punga AR. Pattern of Habitual Physical Exercise in Myasthenia Gravis Patients. *J Neuromuscul Dis*. 2019;6(1):85-91. doi:10.3233/JND-180355
17. Uyainah A, Amin Z, Thufeilsyah F. Spirometri. *Ina J Chest Crit and Emerg Med*, 2014;1(1),35-38
18. Octaviana F, Safri AY, Wiratman W, Indrawati LA, Fadli N, Hakim M. Pulmonary Function Assessment in Myasthenia Gravis Patients in a National Referral Hospital in Indonesia. *Int J Gen Med*. 2023;16:4477-4483. doi:10.2147/IJGM.S426321
19. Calik-Kutukcu E, Salci Y, Karanfil E, Fil-Balkan A, Bekircan-Kurt CE, Armutlu K. Expiratory muscle strength as a predictor of functional exercise capacity in generalized myasthenia gravis. *Neurosciences (Riyadh)*. 2019;24(2):95-100. doi:10.17712/nsj.2019.2.20180024
20. Fregonezi GA, Regiane-Resqueti V, Pradas J, Vigil L, Casan P. Relación entre función pulmonar y calidad de vida relacionada con la salud en la miastenia gravis generalizada [The relationship between lung function and health-related quality of life in patients with generalized myasthenia gravis]. *Arch Bronconeumol*. 2006;42(5):218-224. doi:10.1016/s1579-2129(06)60449-7

21. Elsais A, Johansen B, Kerty E. Airway limitation and exercise intolerance in well-regulated myasthenia gravis patients. *Acta Neurol Scand*. 2010;122: 12-17. doi:10.1111/j.1600-0404.2010.01369.x
22. Hwang H, Lee S, Park HY, Lim HY, Park KH, Park GY, et al. Investigating the Impact of Voice Impairment on Quality of Life in Stroke Patients: The Voice Handicap Index (VHI) Questionnaire Study. *Brain Neurorehabil*. 2023;16(1):e10. doi:10.12786/bn.2023.16.e10
23. Szczudlik P, Sobieszczuk E, Szyluk B, Lipowska M, Kubiszewska J, Kostera-Pruszczyk A. Determinants of Quality of Life in Myasthenia Gravis Patients. *Front Neurol*. 2020;11:553626. doi:10.3389/fneur.2020.553626
24. da Silva GDAP, Feltrin TD, Pichini FDS, Cielo CA, Pasqualoto AS. Quality of Life Predictors in Voice of Individuals With Chronic Obstructive Pulmonary Disease. *J Voice*. 2024;38(6):1530.e7-1530.e13. doi:10.1016/j.jvoice.2022.05.017
25. National Asthma Council Australia. Spirometry Quick Reference Guide. Melbourne; 2017.
26. Goel A, Goyal M, Singh R, Verma N, Tiwari S. Diurnal Variation in Peak Expiratory Flow and Forced Expiratory Volume. *J Clin Diagn Res*. 2015;9(10):CC05-CC7. doi:10.7860/JCDR/2015/15156.6661

TABLES

Table 1. Demographic features of the participants included in the study (n = 23)

Variable	Min	Max	Mean ± SD	Frequency (%)
Age (year)	36	57	47.87 ± 6.12	-
Onset age (year)	19	52	37.96 ± 8.53	-
Medication duration (year)	2	24	8.70 ± 6.14	-
BMI (kg/m^2)	15.38	34.70	23.08 ± 4.35	-
Dose of pyridostigmine 60 mg/day (tab)	0	6	3.39 ± 1.50	-
MGC Score	0	10	4.87 ± 3.21	-
Sex				7 (30.4)
Male				16 (69.6)
Female				
BMI Category				3 (13.0)
Underweight				13 (56.5)
Normoweight				1 (4.3)
Overweight				5 (21.7)
Obese grade I				1 (4.3)
Obese grade II				
Comorbidities				13 (56.5)
None				3 (13.0)
Hypertension				2 (8.6)
Dyslipidemia				1 (4.3)
Asthma				1 (4.3)
Hypertension, asthma				1 (4.3)
Hypertension, nephrolithiasis				1 (4.3)
Valvular heart disease				1 (4.3)
Uterine myoma				
MGFA Classification				13 (56.5)
Type IIA				10 (43.5)
Type IIB				
Thymectomy				19 (82.6)
No				4 (17.4)

Yes	
Spirometry Pattern	16 (69.6)
Restrictive	2 (8.7)
Obstructive	3 (13.0)
Mixed	2 (8.7)
Normal	
VHI results	12 (52.2)
Mild disabilities	4 (17.4)
Moderate disabilities	2 (8.7)
Severe disabilities	5 (21.7)
Normal	

Min: Minimum, Max: Maximum; SD: Standard deviation; BMI: Body Mass Index; kg: kilogram; m: meter; mg: miligrams; MGC: Myasthenia Gravis Composite; MGFA: Myasthenia Gravis Foundation of America; VHI: Voice Handicap Index

Table 2. Descriptive Analysis of VHI and Spirometry results based on MG type

Variable	MG type IIA (n = 13)			MG type IIB (n = 10)		
	Min	Max	Mean ± SD	Min	Max	Mean ± SD
Total VHI	0	66	21.85 ± 23.24	0	50	19.80 ± 20.60
Spirometry						
FEV_1 (%)	55.09	87.51	72.54 ± 10.80	30.35	68.34	53.15 ± 10.25
FVC (%)	64.69	84.80	75.60 ± 7.11	46.38	65.27	53.57 ± 5.71
FEVR (%)	68.33	92.47	79.67 ± 8.33	55.64	94.77	82.33 ± 10.92

MG: Myasthenia Gravis; VHI: Voice Handicap Index; FEV_1: Forced Expiratory Volume in 1 second; FVC: Forced Vital Capacity; FEVR: Forced Expiratory Volume Ratio

Table 3. Correlation between spirometry and VHI results in MG patients

	Pearson	VHI	VHI-F	VHI-P	VHI-E
FEV_1 (%)	Correlation Coefficient	-0.072	-0.116	0.018	-0.130
	Sig. (2-tailed)	0.744	0.598	0.936	0.553
	N	23	23	23	23
FVC (%)	Correlation Coefficient	-0.062	-0.106	0.040	-0.138
	Sig. (2-tailed)	0.778	0.632	0.856	0.529
	N	23	23	23	23
FEVR (%)	Correlation Coefficient	-0.014	-0.006	-0.015	-0.030

	Sig. (2-tailed)	0.949	0.979	0.947	0.891
	N	23	23	23	23

VHI: Voice Handicap Index; VHI-F: VHI Functional; VHI-P: VHI Physical; VHI-E: VHI Emotional; FEV_1: Forced Expiratory Volume in 1 second; FVC: Forced Vital Capacity; FEVR: Forced Expiratory Volume Ratio

FIGURES

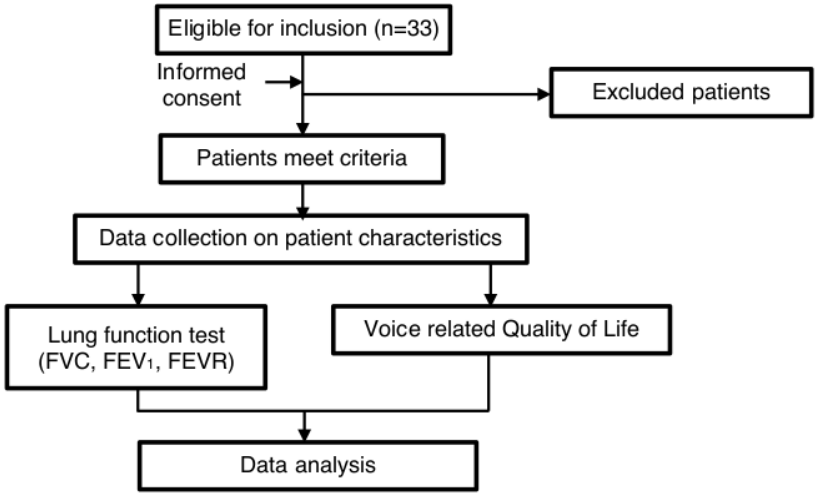

Figure 1. Study flowchart

FVC: Forced Vital Capacity; FEV_1: Forced Expiratory Volume in 1 second; FEVR: Forved Expiratory Volume Ratio