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ORIGINAL ARTICLE

Dysphagia in myasthenia gravis: the tip of the Iceberg

Ebru Karaca Umay[1] · Fatih Karaahmet[2] · Eda Gurcay[1] · Fatma Balli[1] · Erhan Ozturk[1] · Ozgur Karaahmet[1] · Yasemin Eren[3] · Tijen Ceylan[4]

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Abstract
We evaluated swallowing function in patients with myasthenia gravis (MG) with or without dysphagia symptoms using different evaluation parameters and compared the results with those of healthy subjects. A total of 36 patients with MG and 25 healthy volunteers were included in the study. The subjects were classified into three groups; patients without dysphagia (group 1), patients with dysphagia (group 2), and healthy participants (group 3). The presence and severity of dysphagia, the oropharyngeal, pharyngeal, pharyngoesophageal, and esophageal phases were assessed using a screening test, manometric test, electrophysiologic studies [electroneuromyography (EMG)], fiberoptic endoscopic evaluation of swallowing (FEES), and barium swallow pharyngeal esophagography (BSPE), respectively. There was a significant difference between group 1 and group 3 in terms of BSPE ($p = 0.001$) and manometry tests ($p = 0.001$). A significant difference was found in all methods between group 2 and group 3 ($p = 0.001$, for all). In the comparison of the patient groups, although the number of patients with dysphagia in group 2 was significantly higher in the clinical tests ($p = 0.007$), FEES ($p = 0.001$), and EMG ($p = 0.043$) than in group 1, no difference was detected for BSPE ($p = 0.119$) and manometry ($p = 0.644$). Swallowing functions in patients with MG may be affected even without symptoms. This condition should be considered in their follow-up.

Keywords Myasthenia gravis · Dysphagia · Electroneuromyography · Fiberoptic endoscopic evaluation swallowing · Barium swallow pharyngeal esophagography · Manometry

Introduction

Myasthenia gravis (MG) is an autoimmune disease caused by disordered transmission of acetylcholine (Ach) due to antibodies directed against acetylcholine receptors (anti-AchR) at neuromuscular junctions in striated skeletal muscle [1]. As a result, muscle control and neural communication are disrupted [2]. The characteristic features of MG include fluctuating fatigability and weakness in muscles and diurnal variation in the severity of symptoms, which peak at the end of the day and with physical exercise, emotional factors or repeated activity [1]. Most patients with MG (60–70%) have ocular symptoms at presentation; involvement may be limited to ocular muscles in 15% of patients [3]. However, other striated muscles can be involved and MG may become generalized in 85–90% of patients.

Dysphagia is frequently seen and can be the initial symptom of MG in 6–15% of patients, but it is rarely seen as a sole manifestation [4–9]. During the entire MG course, 40–60% of patients experience oropharyngeal and esophageal dysphagia due to striated muscle weakness with varying degrees of involvement, particularly toward the end of a meal or when foods require considerable chewing [7, 10].

In the literature, oropharyngeal phase disorders have been reported as characteristic dysphagia involvement for MG [11, 12]. The commonly reported symptoms and findings are difficulty in chewing, bolus formation, and swallowing; delayed swallowing trigger; and residue [11, 12]. In addition,

✉ Ebru Karaca Umay
ebruumay@gmail.com

[1] University of Health Sciences, Ankara Diskapi Yildirim Beyazit Training and Research Hospital, Physical Medicine and Rehabilitation Clinic, Altindag, Ankara, Turkey

[2] Ankara Education and Research Hospital, Gastroenterology Clinic, Ankara, Turkey

[3] University of Health Sciences, Ankara Diskapi Yildirim Beyazit Training and Research Hospital, Neurology Clinic, Ankara, Turkey

[4] University of Health Sciences, Ankara Diskapi Yildirim Beyazit Training and Research Hospital, Otolaryngology-Head & Neck Surgery Clinic, Ankara, Turkey

dysphagia can worsen in patients with advanced stage, and some esophageal symptoms can be seen due to upper esophageal sphincter (UES) disorders such as cricopharyngeal sphincter achalasia or megaesophagus [12–16]. It has been reported that the severity of dysphagia increases with the severity of MG [9, 13, 15]. Dysphagia is a significant problem because it may result in aspiration, which may cause mortality and morbidity [6]. Therefore, diagnosis and follow-up of dysphagia in the early period are important even if other symptoms improve. Furthermore, understanding the pathogenesis of dysphagia in patients with MG is key for the management of complications, as well as developing efficient treatment modalities.

Despite the frequent use of clinical examinations in diagnosis, this method alone is not sufficient to detect dysphagia in MG. Dysphagia is demonstrated through additional methods such as barium swallow pharyngeal esophagography (BSPE) or videofluoroscopy (VF), which show swallowing function, and the fiberoptic endoscopic evaluation of swallowing (FEES) test evaluates both the anatomy and function of swallowing function in patients [6, 17]. Routine use of these methods is recommended in addition to clinical examinations [6, 17–22].

Although FEES and VF are reported as the primary diagnostic methods of dysphagia, a few studies and case reports have reported that electrophysiologic [electroneuromyography (EMG)], manometric, and scintigraphic evaluations may also be useful in patients with MG because esophageal motility disorders may also be seen in these patients [2, 12–15]. To the best of our knowledge, no studies have evaluated swallowing function in patients with ocular "localized" MG without dysphagia symptoms. Therefore, our aim was to answer the following questions:

1. Is there any disorder in swallowing function in patients with MG without dysphagia compared with healthy subjects and patients with dysphagia?
2. When considering the comprehensive array of methodologic evaluation techniques, which method should be chosen early in MG, even if there are no symptoms?

Materials and methods

This study comprised 36 patients with MG who were admitted to our Neuromuscular Disease Unit and 25 healthy volunteers from among the patients' relatives. We included subjects aged between 30 and 60 years who were diagnosed as having class 1 or 2b MG in accordance with the Myasthenia Gravis Foundation of America (MGFA) classification [23] (Table 1), who had a disease duration of at least 1 year, had not undergone drug changes for the past three months, and had previously been treated for swallowing problems.

The exclusion criteria included causes of swallowing disorder malignancy (including thymoma); facial, cervical or thoracic surgery and/or trauma; metabolic or endocrine disease such as diabetes mellitus; progressive central and peripheral neurologic disorders such as stroke, multiple sclerosis and neuropathy; respiratory distress; smoking; and alcoholism. Additionally, the exclusion criteria for FEES and manometry methods were the presence of serious contagious or infectious diseases such as HIV and hepatitis, patients with risk for bleeding, and decompensated heart disease. Also, subjects with motor and mental disabilities who could not comprehend/cooperate with the researchers were not included.

Subjects were informed about the study and their written consents were obtained at the beginning of the study. Approval of the Ethics Board of the hospital was obtained, and the study was conducted in accordance with the principles of the Helsinki Declaration.

Demographic and disease characteristics

Demographic and disease characteristics including age, sex, education, comorbidities, disease duration, and classification class according to the MGFA, as well as the presence of anti-acetylcholine receptor antibodies (anti-AchR) were recorded for all patients.

Table 1 MGFA clinical classification

Class	Explanation
Class 1	Any ocular muscle weakness; may have weakness of eye closure. All other muscle strength is normal
Class 2	Mild weakness affecting muscles other than ocular muscles; may also have ocular muscle weakness of any severity
2a	Predominantly affecting limb, axial muscles, or both. May also have lesser involvement of oropharyngeal muscles
2b	Predominantly affecting oropharyngeal, respiratory muscles, or both. May also have lesser or equal involvement of limb, axial muscles, or both

MGFA Myasthenia Gravis Foundation of America

Evaluation methods

The evaluation methods were performed on the same day, after an 8-h fasting period, with at least a 30-min rest period between methods, and as a clinical screening test, manometry, EMG, FEES, and BSPE, respectively. The presence and severity of dysphagia, and the oropharyngeal, pharyngeal, pharyngoesophageal, and esophageal phases were assessed using these methods.

Ten-item eating assessment tool (Eat-10)

Eat-10 was used to evaluate dysphagia symptoms and severity [24]. This tool is a self-administered, symptom-specific outcome instrument consisting of 10 questions. Each question's score ranges from 0 (no problem) to 4 (severe problem). If the Eat-10 score is ≥ 3, it is considered as "presence of dysphagia."

Fiberoptic endoscopic evaluation of swallowing (FEES)

Endoscopy was used to evaluate swallowing. Endoscopic evaluation of patients was performed by the same specialist (a member of the dysphagia team in our hospital) using a 3.4-mm diameter non-ducted fiberoptic nasopharyngoscope, a light source, camera, monitor, and DVD recorder (Karl Storz GmbH & Co KG, Tuttlingen, Germany) while the patient was in the vertical sitting position. Local anesthetics were not used so as not to interfere with oral and pharyngeal function. To determine residue, aspiration or penetration up to 90 milliliters of water was used. Yoghurt and a piece of biscuit were used as semisolid and solid foods. The findings were recorded as video images and examined to score the dysphagia levels of our patients between 1 and 6 using the Dzeiwas endoscopic evaluation protocol [25]. Scores of 1 were considered as "normal swallowing function," whereas scores from 2 to 6 were considered as "dysphagia," graded between minimal and severe.

Electrophysiology (dysphagia limit)

A dysphagia limit (DL) was determined to assess the adequacy of coordination and strength of oropharyngeal muscles. The DL was assessed by the same specialist. EMG was performed using 10-channel Medelec Synergy equipment (Oxford, UK) and records were taken from submental electrodes. A laryngeal piezoelectric sensor was also fixed between the cricoid and thyroid cartilages. All electroneuromyography records were filtered (band pass 100 Hz–10 k Hz), amplified, rectified, and integrated. Patients were subsequently provided with 1, 3, 5, 10, 15, and 20 mL of water and were asked to swallow following a command. The study was discontinued in the existence of any repetition and/or indications of aspiration during swallowing within 8 s in any of these quantities. Three successive recordings were collected for each type of swallow, and the signals on single, superimposed, and averaged traces were examined and analyzed. According to the DL, patients were separated as "dysphagic—with existence of any repetition and/or indications of aspiration during swallowing within 8 s in any of each type of swallow," and "normal—those who could drink 20 mL of water in one swallow" [26].

Barium swallow pharyngeal esophagography (BSPE)

Twenty milliliters of liquid with barium (60% barium sulfate solution) was administered in one bolus under the intermittent fluoroscopic scanner. Spot films of the pharynx, larynx and anterior esophagus, and lateral and bilateral oblique projections were taken in both erect and prone positions, using the double-contrast technique. Motion recordings of the pharynx in the frontal and lateral positions during swallowing were included. This procedure was performed and evaluated by the same specialist. Patients were considered "dysphagic" according to the presence of premature leak, retention in the pyriform and vallecular, and tertiary contraction in the esophagus.

Esophageal manometry

Manometric evaluation was used to measure the different factors that play a role in the motility and function of the upper and lower esophageal sphincter and body of the esophagus. The procedure was performed using an 8-F air-charged disposable silicone manometry catheter (4-channel, solid-state system) according to a standardized technique. The catheter was inserted through the nasal cavity and advanced 50 cm with swallowing. After moving the patient to the supine position, the pressure inversion point and lower esophageal sphincter was found using the 0.5-cm interval stationary pull-through technique. Thereafter, by swallowing 10 times with 5 mL of water, the resting pressure, relaxation time, percentage of relaxation of the upper and lower esophageal sphincter and esophagus body pressure were measured. Patients were considered as "dysphagic" or "normal" according to the criteria of Pandolfino et al. [27].

Study protocol

The Eat-10 scale and EMG were performed by two separate blinded physiatrists, and endoscopic, radiologic, and manometric evaluations were conducted by blinded otolaryngology, radiology, and gastroenterology specialists. All subjects were evaluated as "normal" or "dysphagic" in accordance with the evaluation methods and were classified as group 1

(class 1 patients), group 2 (class 2b patients), and group 3 (healthy volunteers).

Statistical analysis

The Statistical Package for the Social Sciences (SPSS 22.0 for Windows) software was used in the analysis of the data. Continuous variables were evaluated using the Kolmogorov–Smirnov test to determine whether they exhibited normal distribution. In descriptive statistics, data are expressed as mean ± standard deviation for continuous variables, and as frequencies and percentages (%) for nominal variables, which were assessed using the Chi-square test. Statistically significant differences between the groups in terms of normal undistorted continuous variables were analyzed using the Mann–Whitney *U*-test and among the groups with the Anova test and Kruskal–Wallis test. The significance of differences for nominal variables was analyzed using Fisher's exact test. Values of $p < 0.05$ were considered as statistically significant.

Table 2 The distribution of demographic and disease characteristics of the patients

	$n = 36$ Mean ± SD, *n* (%)
Age (years)	52.22 ± 11.61
Sex	
Female	20 (55.6)
Male	16 (44.4)
Comorbidities	
No comorbidity	33 (88.9)
Hypertension	2 (5.6)
Hyperlipidemia	3 (8.3)
Disease duration (month)	25.14 ± 10.36
MGFA clinic classification	
Class 1	24 (66.7)
Class 2b	12 (33.3)

SD standard deviation, *MGFA* Myasthenia Gravis Foundation of America

Results

The mean age of the 61 subjects in the study was 54.35 years (SD 10.58), 34 (55.7%) were female and 27 (44.3%) were male. The disease duration of the patients was 25.14 months (SD 10.36). The mean age of the healthy volunteers was 53.12 years (SD 9.11), 14 (56%) were female and 11 (44%) were male; 2 (8%) had additional comorbidities (hypertension). The distribution of demographic and disease characteristics of the patients is shown in Table 2.

Most of the patients ($n = 24$, 66.7%) were class 1 according to the MGFA, and the anti-AchR titers of all patients ($n = 36$, 100%) were positive.

Seventeen patients (47.2%) had normal swallowing according to Eat-10; 13 (36.1%) of these patients scored 0 points indicating no dysphagic symptoms. Dysphagia was present in 19 (52.8%) patients.

In the FEES evaluation, 25 (69.4%) patients were found as normal and 11 (30.6%) had dysphagia. Eight (72.7%) of the 11 patients had minimal dysphagia and 3 (27.3%) had mild dysphagia.

Electrophysiologic findings showed normal results for 26 patients (72.2%) and dysphagia for 10 (27.8%).

On radiologic evaluation using BSPE, 23 patients (63.9%) were assessed as normal and 13 (36.1%) were dysphagic.

Seven (38.9%) patients were normal and 29 (80.6%) were dysphagic with the manometric assessment. Upper esophageal sphincter (UES) pressure was lower than normal in 8 (27.6%) of these patients. All patients with dysphagia were class 2b and met the diagnostic criteria of motility disorders and peristaltic abnormalities (weak peristalsis and frequent failed peristalsis.

In the control group, only one (4%) patient had defined peristaltic abnormalities and 1 (4%) had a low electrophysiologic dysphagia limit (15 mL).

The distribution of the presence of dysphagia in the patients according to the evaluation methods is shown in Table 3.

Two (5.6%) patients had no swallowing impairment, two (5.6%) had symptoms of swallowing disturbance only in the screening test, nine (25%) only had manometric dysphagia associated with peristalsis abnormalities, and four (11.1%) showed dysphagia with all methods.

The distribution of the presence of dysphagia in subjects according to the groups is demonstrated in Table 4.

In the comparison of evaluation methods according to the groups, although there were significant differences between group 1 and the control group in terms of BSPE ($p = 0.001$) and manometry ($p = 0.001$), there were no significant differences with respect to Eat-10 ($p = 0.072$), FEES ($p = 0.999$), and EMG ($p = 0.827$). Also, there were significant differences between group 2 and the control group in all evaluation methods ($p = 0.001$ for all).

In the comparison of the patient groups, although the number of patients with dysphagia in group 2 was significantly higher as per Eat-10 ($p = 0.007$), FEES ($p = 0.001$), and EMG ($p = 0.043$) results than in group 1, no differences were detected for BSPE ($p = 0.119$) and manometry ($p = 0.644$).

Table 3 The distribution of presence of dysphagia in patients according to the evaluation methods

Patient number	MGFA class	Eat-10	FEES	EMG	BSPE	Manometry
1	1					+
2	1	+				+
3	1	+			+	+
4	1					+
5	1	+			+	+
6	1					+
7	1	+				+
8	1					
9	1					+
10	1					+
11	1			+		+
12	1					+
13	1					+
14	1	+				
15	1					+
16	1	+			+	+
17	1					
18	1	+				
19	1					+
20	1	+				+
21	1				+	+
22	1			+	+	+
23	1	+			+	+
24	1					+
25	2b	+	+	+	+	+
26	2b	+	+	+		
27	2b	+	+		+	+
28	2b			+		+
29	2b	+	+			
30	2b	+	+	+	+	+
31	2b	+	+	+	+	+
32	2b	+	+		+	+
33	2b	+	+	+		+
34	2b	+	+	+	+	+
35	2b		+	+		
36	2b	+	+		+	+

+ presence of dysphagia, *Eat-10* 10-item eating assessment tool, *FEES* flexible fiberoptic endoscopic evaluation of swallowing, *EMG* electroneuromyography, *BSPE* barium swallow pharyngeal esophagography

Table 4 The distribution of presence of dysphagia in subjects according to the groups

	Eat-10 ($n = 19$), n (%)	FEES ($n = 11$), n (%)	EMG ($n = 10$), n (%)	BSPE ($n = 13$), n (%)	Manometry ($n = 29$), n (%)
Group 1 ($n = 24$)	9 (37.5)	0	2 (8.3)	6 (25)	20 (83.3)
Group 2 ($n = 12$)	10 (83.3)	11 (91.7)	8 (66.7)	7 (58.3)	9 (75)
Group 3 ($n = 25$)	2 (8)	0	1 (4)	0	1 (4)

Eat-10 10-item eating assessment tool, *FEES* flexible fiberoptic endoscopic evaluation of swallowing, *EMG* electroneuromyography, *BSPE* barium swallow pharyngeal esophagography

Discussion

Swallowing is a complex behavior that occurs through the coordinated and synergistic work of the oral, pharyngeal, laryngeal, and esophageal muscles. Dysphagia defines all disorders during the transport of food from the mouth to the stomach, and three phases of swallowing can be affected [28]. In oral dysphagia, bolus preparation or positioning of food in the oral cavity is affected by reduced strength or abnormal coordination of the oral muscles. Pharyngeal dysphagia occurs due to the absence of or a delayed swallowing reflex trigger, and esophageal dysphagia is caused by mechanical dysfunction of the esophagus or esophageal sphincter [29].

In the literature, disturbance of the pharyngeal phase has been reported as the most common swallowing abnormality in patients with mild-to-moderate MG [2, 12, 18]. Videofluoroscopy, FEES, and electrophysiologic studies in patients with dysphagia have shown that these disorders occur due to weakness and fatigue of the submental, suprahyoid, and pharyngeal constructor muscles, which enable the laryngeal elevation and transportation of the bolus by a secondary support, particularly the pumping activity of the tongue [2, 12, 18, 30].

Electrophysiologic studies that evaluated DL reported that the difficulty to take a bolus as large as 20 mL and prolongation of the swallowing time were probably due to weakness of the muscles in patients with MG [2, 12]. Moreover, these studies reported that a lower DL may be a compensation mechanism for weakness muscles [2, 12].

In our study, clinical, electrophysiologic, and endoscopic evaluations showed that oral and pharyngeal phase involvement were found significantly more in patients with MG and dysphagia compared with healthy subjects and patients without dysphagia.

The patients without dysphagia and with normal clinical findings were not different from the healthy controls in terms of electrophysiologic and endoscopic methods, especially regarding oropharyngeal phase disorders. Our results are compatible with studies in the literature that showed that clinical symptoms and dysphagia severity were correlated in patients with MG with oropharyngeal phase involvement, as evaluated using endoscopic and videofluoroscopic methods [6, 12, 17, 18, 30].

An important point should be emphasized here. Some patients had a localized form of MG; patients with class 1 MG are supposed to have no dysphagia symptoms, yet we found that 37% had dysphagia symptoms using Eat-10. The MGFA classification is based on muscle strength measurements. Unlike the MGFA classification, Eat-10 examines the presence of swallowing difficulty symptoms as well as influences on personal expectations, emotional state, and the social lives of patients (three questions). Accordingly, we do not think that the Eat-10 test examines muscle strength objectively.

The particularly interesting results of our study were the consequences of evaluation methods involving the esophageal phase. All patients with and without dysphagia were noted to have decreased esophageal motility at a level that would give a significant difference compared with healthy controls. Hypomotility in the medial and mid-parts of the esophagus (except the lower esophageal sphincter) has been demonstrated in manometry studies of patients with MG with various degrees of dysphagia. In these patients, pharyngeal contraction pressures were normal and UES pressures were found to be slightly low, although they showed good relaxation in coordination with pharyngeal contraction [13, 15]. There are also some case reports showing that patients with severe dysphagia symptoms and findings had low UES pressure and that motility disorders could go as far as aperistaltism [14, 31].

It has been reported that motility of the medial and distal esophageal segments, which consist only of smooth muscles, may gradually deteriorate due to the block of the neuromuscular transmission in the UES formed by striated muscle in patients with MG with dysphagia. In our study, UES pressure was slightly lower in eight patients, all of whom had dysphagia. As stated in previous studies, the greater the severity of dysphagia symptoms, the more the UES may be affected. However, the real question that requires answering: Why did almost all of our non-dysphagic patients with class 1 MG have motility disorders without being affected by UES pressures? We could not compare some of our results because of the lack of studies evaluating patients without dysphagia. Nevertheless, we think the phenomenon may be due to a number of reasons: the pharynx, UES, and varying lengths of the esophagus below the UES are composed exclusively of striated muscle. The LES and remaining esophageal segment are composed of smooth muscle. The two types contain a region that transitions from striated to smooth musculature with a variable length at the mid-esophagus. Esophageal peristalsis has been traditionally considered to start with a primary contraction of the UES and continues throughout the entire length of the esophagus. It can be concluded that the smooth muscle disorder in our patients may be the result of functional (not-anatomic) involvement of the voluntary muscles of the esophagus with repeated activity. Electrophysiologic studies have reported one or more abnormalities in almost all striated swallowing muscles, even if there are no dysphagia findings [2, 12]. Disco-ordination of these muscles, which constitute the biomechanical force required for UES opening, may cause hypomotility [32].

In line this evidence, peristalsis in smooth muscles first needs activation of the UES and UES dysfunction may

not be compensated, contrary to the compensation resulting from increased swallow intervals in the oropharyngeal phase because there are differences in the peristalsis mechanisms between the upper (striated) and the lower (smooth) esophagus. In the striated muscle segment, peristalsis is produced by consecutive firing of lower vagal motor neurons such that upper segments contract primarily and move distal segments subsequently. In the smooth muscle segment, neurons of the myenteric plexus can independently create peristalsis, but this peristalsis is a delayed contraction response secondary to distention if there is no stimulation from the striated muscles. The hypomotility in our patients may occur due to secondary peristalsis and dysfunction of the upper esophagus.

Another interesting point in our study was that despite the significant change in manometry, there was no similar level of change in BSPE. This may be related to the number of swallows in the manometric study. Unlike the BSPE, which is performed with a single swallow, the manometry study per se, in which swallowing occurred 10 times, may have been enough to trigger fatigue and weakness in striated muscles.

The limitations of our study are the lack of the following evaluation parameters: needle EMG on UES muscles, and more accurate methods such as high-resolution manometry and scintigraphy. Additionally, the small sample size may have posed limitations to the study. We believe that the results of future studies, including the above methods, will make our results clearer.

Conclusion

This study has taken previous studies a step further by showing that dysphagia including esophageal phase involvement may even be present in patients with MG who have no clinical dysphagia symptoms and signs or pathology in the striated swallowing muscles, as per classic assessment methods. It is not always possible to determine the esophageal involvement of patients at the time of examination. We suggest that all patients with MG should be checked for dysphagia at certain intervals through clinical examinations or procedures that focus on oropharyngeal phase disorders and using methods that evaluate repetitive swallowing activities and the esophageal phase.

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Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

References

1. Bettini M, Chaves M, Cristiano E, Pagotto V, Perez L, Giunta D et al (2017) Incidence of autoimmune myasthenia gravis in a health maintenance organization in buenos aires, Argentina. Neuroepidemiology 48(3–4):119–123
2. Hsu CC, Chen WH, Chiu HC (2013) Using swallow sound and surface electromyography to determine the severity of dysphagia in patients with myasthenia gravis. Biomed Signal Process Control 8(3):237–243
3. Akaishi T, Suzuki Y, Imai T, Tsuda E, Minami N, Nagane Y et al (2016) Response to treatment of myasthenia gravis according to clinical subtype. BMC Neurol 16:225
4. Gwathmey KG, Burns TM (2015) Myasthenia gravis. Semin Neurol 35(4):327–339
5. Ramalho S, Pereira S, Oliveira P, Morais H, Lima N, Condé A (2014) Dysphagia as a presenting symptom of myasthenia gravis-case report. IJOHNS 3:23–25
6. Juan HC, Tou I, Lo SC, Wu IH (2010) Efficacy of postural techniques assessed by videofluoroscopy for myasthenia gravis with dysphagia as the presenting symptom: a case report. J Med Case Rep 4:370
7. Rajeshwari A, Somayaji G, Deviprasad S (2011) A rare cause of dysphagia: a case report. Indian J Otolaryngol Head Neck Surg 63:83–84
8. Breen E, Bleich L, Loeser C (2014) Myasthenia gravis presenting with dysphagia in an elderly male: a case report. Am J Med 127(9):e7–e8
9. Klair JS, Rochlani YM, Meena NK (2014) Myasthenia gravis masquerading as dysphagia: unveiled by magnesium infusion. BMJ Case Rep. https://doi.org/10.1136/bcr-2014-204163
10. Suzuki Y (2015) Clinical features and associated conditions of myasthenia gravis. Nihon Rinsho 7:477–481
11. Altman KW, Richards A, Goldberg L, Frucht S, McCabe DJ (2013) Dysphagia in stroke, neurodegenerative disease, and advanced dementia. Otolaryngol Clin N Am 46(6):1137–1149
12. Ertekin C, Yüceyar N, Aydogdu I (1998) Clinical and electrophysiological evaluation of dysphagia in myasthenia gravis. J Neurol Neurosurg Psychiatry 65(6):848–856
13. Linke R, Witt TN, Tatsch K (2003) Assessment of esophageal function in patients with myasthenia gravis. J Neurol 250(5):601–606
14. Joshita Y, Yoshida M, Yoshida Y, Kimura K (1990) Manometric study of the pharynx and pharyngoesophageal sphincter in myasthenia gravis. Rinsho Shinkeigaku 30(9):944–951
15. Huang MH, King KL, Chien KY (1998) Esophageal manometric studies in patients with myasthenia gravis. J Thorac Cardiovasc Surg 95(2):281–285
16. Desuter G, Van Parijs V, Gardiner Q (2015) Megaesophagus associated with myasthenia gravis: a rare condition in humans. B-ENT 11(1):63–66
17. Coscarelli S, Verrecchia L, Coscarelli A (2007) Endoscopic evaluation of neurological dysphagic patients. Acta Otorhinolaryngol Ital 27(6):281–285
18. Higo R, Nito T, Tayama N (2005) Videofluoroscopic assessment of swallowing function in patients with myasthenia gravis. J Neurol Sci 231(1–2):45–48
19. Oda AL, Chiappetta AL, Annes M, Marchesan IQ, Oliveira AS (2002) Clinical, endoscopical and manometric evaluation of swallowing in patients with acquired autoimmune myasthenia gravis. Arq Neuropsiquiatr 60(4):986–995
20. Colton-Hudson A, Koopman WJ, Moosa T, Smith D, Bach D, Nicolle M (2002) A prospective assessment of the characteristics of dysphagia in myasthenia gravis. Dysphagia 17(2):147–151

21. Aoki Y, Yamamoto T, Ogata K, Oya Y, Ogawa M, Murata M (2007) Videofluorographic evaluation of dysphagia in a patient with myasthenia gravis. Rinsho Shinkeigaku 47(10):669–671
22. Hou LZ, Xu W, Han DM, Zhang L, Jing Y (2007) Laryngopharyngeal characteristics of myasthenia gravis. Zhonghua Er Bi Yan Hou Tou Jing Wai Ke Za Zhi 42(4):263–267
23. Sanders DB, Wolfe GI, Benatar M, Evoli A, Gilhus NE, Illa I et al (2016) International consensus guidance for management of myasthenia gravis. Neurology 87:1–7
24. Belafsky PC, Mouadeb DA, Rees CJ, Pryor JC, Postma GN, Allen J et al (2008) Validity and reliability of the eating assessment tool (EAT-10). Ann Otol Rhinol Laryngol 117:919–924
25. Dziewas R, Warnecke T, Olenberg S, Teismann I, Zimmermann J, Kramer C (2008) Towards a basic endoscopic assessment of swallowing in acute stroke-development and evaluation of a simple dysphagia score. Cerebrovasc Dis 26(1):41–47
26. Umay EK, Unlu E, Saylam GK, Cakcı A, Korkmaz H (2013) Evaluation of dysphagia in early stroke patients by bedside, endoscopic and electrophysiological methods. Dysphagia 28(3):395–403
27. Pandolfino JE, Ghosh SK, Rice J, Clarke JO, Kwiatek MA, Kahrilas PJ (2007) Classifying esophageal motility by pressure topography characteristics: a study of 400 patients and 75 controls. Am J Gastroenterol 102:1–11
28. Shaw SM, Martino R (2013) The normal swallow muscular and neurophysiological control. Otolaryngol Clin N Am 46:937–956
29. Matsuo K, Palmer JB (2008) Anatomy and physiology of feeding and swallowing—normal and abnormal. Phys Med Rehabil Clin N Am 19(4):691–707
30. Xu W, Han D, Hou L, Hu R, Wang L (2009) Clinical and electrophysiological characteristics of larynx in myasthenia gravis. Ann Otol Rhinol Laryngol 118(9):656–661
31. Llabre's M, Molina-Martinez FJ, Miralles F (2005) Dysphagia as the sole manifestation of myasthenia gravis. J Neurol Neurosurg Psychiatry 6:1297–1300
32. Goyal RK, Chaudhury A (2008) Physiology of normal esophageal motility. J Clin Gastroenterol 42(5):610–619