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Evaluation of clinical features and prognosis of myasthenia gravis in adults based on the age of onset: A retrospective study from a single center of 30 years MG registry

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Abstract

Objective: We aimed to evaluate the demographic, clinical, and immunological features of myasthenia gravis (MG) in adults according to the age of onset and to investigate the effect on prognosis. *Methods:* A total of 332 patients with MG were included in the study. Patients were classified into three age subgroups: early-onset MG (EOMG), late-onset MG (LOMG), and very late-onset MG. Complete stable remission, pharmacological remission, and minimal manifestations for 1 year were assessed as a good prognosis on the MGFA-PIS scale. Improved, unchanged, worse, exacerbation and death due to MG were assessed as having a poor prognosis. *Results:* There were 177 (53.3%) female and 155 male (46.7%) patients with a mean age of 55.3 ± 17.4. A total of 176 patients (53%) were classified as EOMG, 94 patients (28.3%) as LOMG, 62 (18.7%) as very late-onset MG, 282 patients (84.9%) as anti-AChR positive, 21 patients (6.3%) as anti-MuSK positive, and two patients (0.6%) as anti-AChR and anti-MuSK double-positive. While 95.6% of patients with a good prognosis had MGFA-1 at the onset of the disease, 40.3% of patients with a poor prognosis had MGFA-2B. At the end of the clinical follow-up, the MGFA-PIS score was evaluated, 55.1% of the patients had a good prognosis, while 44.9% had a poor prognosis.
Conclusions: Age at disease onset was not associated with prognosis. Presence of generalized MG subtype and thymoma, anti-MuSK positivity, hospitalization in the intensive care unit, myasthenic crisis, IVIG administration, plasmapheresis, comorbidity, 2 or more comorbidities were found to have significant association with poor prognosis.

Keywords: Prognosis, early-onset myasthenia gravis, late-onset myasthenia gravis, very late-onset myasthenia gravis

INTRODUCTION

Myasthenia gravis (MG) is an autoimmune, neuromuscular disease with antibodies directed against the skeletal muscle nicotinic acetylcholine receptor (AChR), the muscle-specific kinase (MuSK), and likely other proteins concentrated at the neuromuscular junctions.[1] Approximately 15% of MG patients do not show antibodies to AChR or MuSK and are known as seronegative MG (SNMG).[2] Recently, it has been shown that new antibodies such as anti-LRP4 and anti-cortactin can be found in SNMG.[3,4] In MG, the weakness increases with the use of the muscles and improves with rest. Weakness can be seen in the eye, facial, oropharyngeal, axial, and extremity muscles. Eye muscle weakness at the onset of MG is evident in the vast majority of patients and often causes diplopia and ptosis. The distribution and severity of the affected muscles vary.[5] Initially, MG was a disease mostly seen in women under the age of 40, but in recent years, its incidence has increased in both men and women over 65 years of age.[6] The prevalence is estimated at 15-179 patients per million population and several investigators have reported an increasing incidence of late-onset MG (LOMG). There are clinical forms of MG: ocular MG (OMG) and generalized MG (GMG). If the muscle weakness is limited to the eyelids and extraocular muscles only, the disease is called 'Ocular Myasthenia'. In generalized myasthenia gravis, limb-girdle weakness is typically more prominent in the proximal muscles than in the distal muscles.[7] Myasthenic crisis is defined as respiratory distress caused by disease-related

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muscle weakness and is seen in approximately 15% of patients. Patients are generally classified into 2 subgroups according to age at onset: early-onset MG (EOMG), when they are under 50 at disease onset, and LOMG, when they are aged 50 or older at onset.[8]

Several studies show that the clinical features of MG disease differ among age groups. While EOMG was found to be more common in women with thymic hyperplasia and high anti-AChR titers, LOMG was found to be seen with the presence of thymoma and more severe forms of the disease.[9] In addition, anti-AChR positive antibodies and ocular subtype of MG disease were found to be more common in late-onset patients.[10] It has been shown that the presence of anti-MuSK and anti-titin ab do not have a negative effect on the prognosis of the disease in elderly people.[11]

The aim of this study is to describe the demographic, clinical, and immunological features of MG patients, compare these features among the age groups, and evaluate the effect on the prognosis of the disease.

METHODS

A total of 332 MG patients followed in the Neurology Clinic of Karadeniz Technical University were included in the study. Follow-up information was updated every 6 months and whenever a significant clinical event occurred. In this retrospective study, we selected all patients in the MG registry who had onset of MG between July 10, 1992, and July 29, 2021.

The diagnosis of MG was based on a combination of clinical and laboratory criteria. Inclusion criteria consisted of fluctuating voluntary muscle weakness throughout the day and one or more of the following laboratory results: (1) Positive response to anticholinesterase drugs; (2) More than 7% decrement in the nasalis and orbicularis oculi muscles, or more than 10% in the abductor digiti minimi and trapezius muscles in the repetitive nerve stimulation; (3) Increased jitter or neuromuscular block on Single-Fiber Electromyography (SFEMG); (4) Presence of AChR antibody (anti) and anti-MuSK in the serum.

All patients who met the diagnostic criteria for MG were included in the study. We also excluded patients who failed to appear for follow-ups and those for whom relevant information was missing. In this study, we classified patients into 3 subgroups according to age: EOMG, when they were younger than 50 years at onset; LOMG, when they were 50–64 years of age at onset; and very-late-onset MG, when they were 65 years or older at the onset. The third group was formed based on epidemiological data showing an increased incidence of MG disease in those aged 65 and over.[12]

The following variables were analyzed in this study: demographic characteristics, AChR and MuSK antibodies positivity at disease onset, presence of comorbidity, presence of 2 or more comorbidities, presence of hypertension (HT) and diabetes mellitus (DM), the severity of disease and distribution of muscle weakness according to the Myasthenia Gravis Foundation of America (MGFA) clinical classification at the onset which is defined as patients with a focal ocular form of the disease at onset (MGFA-I) but generalized (MGFA-II or higher), treatment regimens include intravenous immunoglobulin (IVIG) plasmapheresis and thymectomy, frequency of myasthenic crises and days in the intensive care unit (ICU) to achieve weaning from mechanical ventilation, thymus anomalies viewed by thorax computed tomography, thymus histopathology results of patients undergoing thymectomy, clinical outcome according to the MGFA postintervention status (MGFA-PIS), and any diseases accompanying MG. 'Complete stable remission (CSR), pharmacological remission (PR), and minimal manifestations (MM)' for 1 year were assessed as a good prognosis on the MGFA PIS scale. 'Improved (I), unchanged (U), worse (W), exacerbation (E), and death of MG (D of MG)' were assessed as poor prognosis.

Approval for the study was obtained from Karadeniz Technical University Faculty of Medicine Ethics Council (Research Ethics Committee no. 2021/354 dated 09.12.2021). Informed consent was obtained from all individual participants included in the study.

Statistical analysis

The SPSS 22.0 statistical package program was used in the analysis of the data. Descriptive statistics of evaluation results were given as numbers and percentages for categorical variables, mean, standard deviation, and interquartile range for numerical variables. Comparisons of numerical variables between two independent groups were made with the Student-test when the normal distribution condition was met and the Mann-Whitney U test when it was not. The Chi-Square Test was used to compare qualitative data. Statistical alpha significance level was taken as $p<0.05$.

RESULTS

A total of 332 patients who met the inclusion criteria were included in this study. There were 177 (53.3%) female and 155 (46.7%) male patients, with a mean age of 55.3 ± 17.4 (from18 to 98 years). The mean age of disease onset was 47.7±17.6 (from 8 to 89 years). MG was found in the family history of 9 (2.7%) patients. 187 of the patients (56.3%) were OMG, 145 (43.7%) of the MG patients were GMG; 282 patients (84.9%) were anti-AChR positive, 21 patients (6.3%) were anti-MuSK positive, and 2 patients (0.6%) were anti-AChR and anti-MuSK double-positive.

Also, 176 patients (53%) were classified as EOMG, 94 patients (28.3%) as LOMG, and 62 patients (18.7%) as very late-onset MG. The age of disease onset was higher in late and very late-onset groups than in the early onset group (p<0.001). The frequency of men was higher in the very late-onset group than in the early-onset and late-onset groups (p= 0.033).

According to the results of thoracic CT, thymic hyperplasia was detected in 31 patients (9.3%) and thymoma in 63 patients (19%). Table 1 shows the clinical and demographic characteristics of MG patients.

Thymoma evaluated with thoracic CT was found to be higher in the early-onset group than in the late and very late-onset groups (p<0.001). According to thymic histopathology, the most common thymoma types among 332 MG patients were thymoma type-A (28.6%) and thymoma type-B2 (28.6%). The rate of undergoing thymectomy operation was also found to be higher in the early-onset group than in the late and very late-onset groups (p< 0.001).

The patients were evaluated with MGFA-PIS at the end of their clinical follow-up, and minimal manifestations-3 (MM-3) is the most common in all three age groups. There was no significant difference among all three groups in terms of myasthenic crisis and hospitalization in the intensive care unit. Comorbidity and 2 or more comorbidities were detected at a higher rate in the very late-onset group (p< 0.001). It was determined that 9.1% of EOMG, 11.7% of LOMG, and 8.1% of very late-onset MG were accompanied by autoimmune disease and no significant difference was found among all three groups (p=0.706).

There was no statistically significant difference among all three groups in terms of anti-AChR and anti-MuSK positivity. The double seropositivity of anti-AChR and anti-MuSK was observed only in the late and very late-onset groups and not in the early-onset group. Table 2 shows the comparison of clinical and demographic characteristics in early-onset, late-onset, and very late-onset MG.

While 98.4% of the patients with a good prognosis had OMG and 1.6% had GMG, 55.1% of the patients with a poor prognosis had OMG and 44.9% had GMG (p< 0.001). There was no difference between patients with a good and poor prognosis in terms of gender, disease duration, and age of onset of MG (p-values: 0.571; 0.486; 0.724, respectively). Among the patients evaluated with thorax CT, thymoma was found in 13.1% of patients with a good prognosis, and 26.2% of patients with a poor prognosis (p=0.005). While 42 patients (22.9%) with a good prognosis had undergone thymectomy operation, 27 patients (18.1%) with poor prognosis had undergone (p=0.003).

Eighty-three point six percent of patients with good prognosis and 86.6% of patients with poor prognosis were anti-AChR positive. (p=0.550). 0.5% of patients with good prognosis and 13.4% of patients with poor prognosis were anti-MuSK positive (p<0,001). 15.8% of patients with good prognosis and 1.3% of patients with poor prognosis were anti-AChR and anti-MuSK double-seronegative (p<0,001).

A total of 61.7% of the patients with poor prognosis had a history of hospitalization in the intensive care unit and 61.1% of the patients had a myasthenic crisis (p-values, respectively: 0.001; 0.001). 71.1% had a history of IVIG administration and 8.1% of them had a history of plasmapheresis (p-values: 0.001; 0.004, respectively); 66.4% of the patients with poor prognosis had comorbidities, 42.3% of them had 2 or more comorbidities (p-values 0.002; 0.036, respectively). Of the patients with poor prognosis, 30.9% had HT, 18.8% had DM and 12.8% had a concomitant autoimmune disease (p-values: 0.625; 0.329; 0.122, respectively).

Among these clinical data are; the presence of GMG subtype and thymoma in thorax CT, anti-MuSK positivity, hospitalization in the intensive care unit, myasthenic crisis, IVIG administration, plasmapheresis, comorbidity, 2 or more comorbidities were found to have significant effects on poor prognosis. Ocular MG, the presence of double seronegativity and a history of thymectomy were found to be of significant importance in the development of good prognosis. Table 3 shows the effects of demographic and clinical features on prognosis.

Table 1: Demographic, clinical and immunological features of all MG patients

Variable	Value (number of patients, %, year, mean)
MG type	
OMG	187 (56.3)
GMG	145 (43.7)
Gender	
Female	177 (55.3)
Male	155 (46.7)
MG type according to onset age	9 (2.7)
Early-onset	176 (53)
Late-onset	94 (28.3)
Very late-onset	62 (18.7)
Age	55.3 ± 17.4
Age of disease onset	47.7 ± 17.6
Family history	9 (2.7)
Disease duration	7.5 ± 5.4
Thoracic CT findings	
Normal	238 (71.7)
Thymic hyperplasia	31 (9.3)
Thymoma	63 (19)
Histopathological findings of patients who underwent thymectomy	
Normal	11 (15.7)
Thymic hyperplasia	9 (12.9)
Thymoma type-A	20 (28.6)
Thymoma type-B1	5 (7.1)
Thymoma type-B2	20 (28.6)
Thymic carcinoma	3 (4.3)
Multiloculated thymic cyst	1 (1.4)
Thymus tissue showing reactive lymphoid hyperplasia	1 (1.4)
Antibody status	
Seronegative	31 (9.3)
Anti-AChR	282 (84.9)
Anti-MuSK	21 (6.3)
Double seropositive	2 (0.6)
Myasthenic crisis	98 (29.5)
Hospitalization in the intensive care unit	98 (29.5)
IVIG administration	131 (39.5)
Plasmapheresis	14 (4.2)
Comorbidity	190 (57.2)
2 or more comorbidities	120 (36.1)
Hypertension	98 (29.5)
Diabetes mellitus	54 (16.3)
Concomitant autoimmune disease	32 (9.6)

MG: Myasthenia gravis, OMG: Ocular myasthenia gravis, GMG: Generalized myasthenia gravis, IVIG: Intravenous immunoglobulin, Anti-AChR: Acetylcholine receptor antibody, Anti-MuSK: Muscle-specific kinase antibody

Table 2: Comparison of demographic, clinical and immunological features of patients with early-onset, late-onset, and very late-onset myasthenia gravis

Variable	Early-onset MG (18 to 50 years) (n=176)	Late-onset MG (50 to 65 years) (n=94)	Very late-onset MG (≥65 years) (n=62)	p-value
Gender				
Female	105 (59.7)	46 (48.9)	26 (41.9)	**0.033**
Male	71 (40.3)	48 (51.1)	36 (58.1)	
Age (year, SD)	42.3±11.2	64.0±5.6	79.2±7.5	**<0.001**
Age of onset (year, SD)	33.8±9.8	57.3±4.1	72.9±6.3	**<0.001**
MG type				
OMG	144 (81.8)	73 (77.7)	45 (72.6)	0.290
GMG	32 (18.2)	21 (22.3)	17 (27.4)	
Family history	6 (3.4)	1 (1.1)	2 (3,2)	-
Antibodies				
Anti-AChR positive	148 (84.1)	78 (83.0)	56 (90.3)	0.409
Anti-MuSK positive	8 (4.5)	7 (7.4)	6 (9.7)	0.314
Double seronegative	20 (11.4)	10 (10.6)	1 (1.6)	0.067
Double seropositive	-	1 (1.1)	1 (1.6)	-
MGFA-CC at disease onset				
MGFA-1	105 (59.7)	62 (66.0)	36 (58.1)	
MGFA-2A	26 (14.8)	9 (9.6)	4 (6.5)	
MGFA-2B	33 (18.8)	13 (13.8)	18 (29.0)	
MGFA-3A	3 (1.7)	2 (2.1)	-	
MGFA-3B	9 (5.1)	7 (7.4)	3 (4.8)	
MGFA-4A	-	1 (1.1)	1 (1.1)	
MGFA-PIS at the end of clinical follow up				
Complete stable remission	12 (6.8)	4 (4.3)	1 (1.6)	
Pharmacologic remission	2 (1.1)	-	2 (3.2)	
Minimal manifestation -1	1 (0.6)	-	2 (3.2)	
Minimal manifestation -2	16 (9.1)	18 (19.1)	5 (8.1)	
Minimal manifestation -3	63 (35.8)	33 (35.1)	24 (38.7)	
Improved	18 (10.2)	9 (9.6)	6 (9.7)	
Unchanged	19 (10.8)	6 (6.4)	7 (11.3)	
Worse	45 (25.6)	24 (25.5)	15 (24.2)	
Thoracic CT findings				
Normal	105 (59.7)	78 (83.0)	55 (88.7)	
Thymic hyperplasia	27 (15.3)	3 (3.2)	1 (1.6)	**<0.001**
Thymoma	44 (25)	13 (13.8)	6 (9.7)	
Thymectomy status	50 (28.4)	14 (14.9)	5 (8.1)	**0.001**
Histopathological findings of patients who underwent thymectomy				
Normal	8 (15.7)	3 (21.4)	-	
Thymic hyperplasia	9 (17.6)	-	-	
Thymoma type-A	16 (31.4)	3 (21.4)	1 (20.0)	
Thymoma type-B1	3 (5.9)	1 (7.1)	1 (20.0)	
Thymoma type-B2	11 (21.6)	7 (5.0)	2 (40.0)	
Thymic carcinoma	2 (4)	-	1 (20.0)	
Multiloculated thymic cyst	1 (1.9)	-	-	
Thymus tissue showing reactive lymphoid hyperplasia	1 (1.9)	-	-	
Hospitalization in the intensive care unit	50 (28.4)	29 (30.9)	19 (30.6)	0.895
Myasthenic crisis	50 (28.4)	29 (30.9)	19 (30.6)	0.895
IVIG administration	65 (36.9)	39 (41.5)	27 (43.5)	0.587
Plasmapheresis	9 (5.1)	3 (3.2)	2 (3.2)	-
Comorbidity	78 (44.3)	59 (62.8)	53 (85.5)	**<0.001**
2 or more comorbidities	38 (21.6)	40 (42.6)	42(67.7)	**<0.001**
Hypertension	26 (14.8)	32 (34.0)	40 (64.5)	**<0.001**
Diabetes mellitus	16 (9.1)	19 (20.2)	19 (30.6)	**<0.001**
Concomitant autoimmune disease	16 (9.1)	11 (11.7)	5 (8.1)	0.706

MG: Myasthenia gravis, OMG: Ocular myasthenia gravis, GMG: Generalized myasthenia gravis, Anti-AChR: Acetylcholine receptor antibody, Anti-MuSK: Muscle-specific kinase antibody, MGFA-CC: Myasthenia Gravis Foundation of America Clinical Classification, MGFA-PIS: Myasthenia Gravis Foundation of America post-intervention status, IVIG: Intravenous immunoglobulin

Table 3: Effects of demographic, clinical and immunological features on prognosis

Variable	Good prognosis (n=183) (%)	Poor prognosis (n=149) (%)	p-value
Age (year. SD)	55.0±18.0	55.7±16.8	0.756
Age of onset (year. SD)	47.8±17.9	47.6±17.4	0.947
Disease onset age groups			
Early-onset	94 (51.4)	82 (55.0)	0.724
Late-onset	55 (30.1)	39 (26.2)	
Very late-onset	34 (18.6)	28 (18.8)	
Disease duration (year. SD)	7.2±5.0 (4-9)	8.0±5.9 (4-10)	0.486
Gender			
Female	95 (51.9)	82 (55.1)	0.571
Male	88 (48.1)	67 (44.9)	
Antibodies			
Anti-AChR positive	153 (83.6)	129 (86.6)	0.550
Anti-MuSK positive	1 (0.5)	20 (13.4)	**<0.001**
Double seronegative	29 (15.8)	2 (1.3)	**<0.001**
Double seropositive	-	2 (1.3)	0.201
MGFA-CC at disease onset			
Group 1	175 (95.6)	28 (18.8)	
Group 2A	3 (1.6)	36 (24.2)	
Group 2B	4 (2.2)	60 (40.3)	
Group 3A	-	5 (3.4)	
Group 3B	1 (0.5)	18 (12.1)	
Group 4A	-	2 (1.3)	
MGFA-PIS at the end of clinical follow up			
Complete stable remission	17 (9.3)	-	
Pharmacologic remission	4 (2.2)	-	
Minimal manifestation -1	3 (1.6)	-	
Minimal manifestation -2	39 (21.3)	-	
Minimal manifestation -3	120 (65.6)	-	
Improved	-	33 (22.1)	
Unchanged	-	32 (21.5)	
Worse	-	84 (54.6)	
MG type at disease onset			
OMG	180 (98.4)	82 (55.1)	**<0.001**
GMG	3 (1.6)	67 (44.9)	
Thymectomy	42 (22.9)	27 (18.1)	**0.003**
Thoracic CT findings			
Normal	144 (78.7)	94 (63.1)	**0.005**
Thymic hyperplasia	15 (8.2)	16 (10.7)	
Thymoma	24 (13.1)	39 (26.2)	
Hospitalization in the intensive care unit	6 (3.3)	92 (61.7)	**<0.001**
Myasthenic crisis	25 (13.7)	106 (71.1)	**<0.001**
IVIG administration	25(13.7)	106(71.1)	**<0.001**
Plasmapheresis	2 (1.1)	12 (8.1)	**0.004**
Comorbidity	91 (49.7)	99 (66.4)	**0.002**
2 or more comorbidities	57 (31.1)	63 (42.3)	**0.036**
Hypertension	52 (28.4)	46 (30.9)	0.625
Diabetes mellitus	26 (14.2)	28 (18.8)	0.329
Concomitant autoimmune disease	13 (7.1)	19 (12.8)	0.122

Good prognosis: Minimal manifestation or better (minimal manifestation, pharmacologic remission, complete stable remission) in MGFA-PIS

Poor prognosis: Improved, unchanged, worse in MGFA-PIS

MG: Myasthenia gravis, OMG: Ocular myasthenia gravis, GMG: Generalized myasthenia gravis, Anti-AChR: Acetylcholine receptor antibody, Anti-MuSK: Muscle-specific kinase antibody, MGFA-CC: Myasthenia Gravis Foundation of America Clinical Classification, MGFA-PIS: Myasthenia Gravis Foundation of America post-intervention status, IVIG: Intravenous immunoglobulin

DISCUSSION

The prognosis of MG disease can be affected by many factors such as the presence of the age of onset of the disease, the age of the patient, thymic pathology, antibodies responsible for the disease, and the affected muscles. Recognition of these factors is of great importance in the management of the disease and in determining treatment strategies. We aimed to evaluate the demographic, immunological, and clinical characteristics of three different age groups with MG and to investigate their effects on prognosis.

Recent epidemiological and clinical studies have reported an increase in MG disease in the elderly, therefore, the incidence of LOMG is increasing worldwide. Although the reason for this increase is not known exactly, it is thought that this may be related to a biological phenomenon, increased awareness of MG disease, age-related changes in the immune system, prevalence of anti-AChR, and other antibody measurements, and prolongation of lifespan. There are some differences between EOMG and LOMG in terms of demographic, clinical, and serological characteristics.[7,13] There are differences between the genders in terms of age of onset in MG disease. It has been determined that EOMG is more prevalent in women and LOMG is more prevalent in men.[6,11,12,14] In our study, it was determined very late-onset MG was more common in males than EOMG and LOMG, and this respect; it is similar to previous studies.

Previous studies have shown that LOMG often has an ocular onset (MGFA-I.).[6,8,10,11,14] In our study, as shown in other studies, ocular onset was most common in all three age groups. MGFA 3a and above was observed very rarely in all three age groups at the onset of the disease. According to these results, all three age groups show similar characteristics in terms of initial symptoms evaluated with MGFA.

Despite the high rate of life-threatening events at the onset of LOMG, these patients generally respond well to medical treatments. It was determined that the patients over 65 years of age were better than the early-onset patients in terms of drug requirements and drug resistance.[6] At the end of the clinical follow-up of the patients with LOMG, it was reported that there was an improvement of more than 80%.[12,15] In another study, it was stated that older age is not an independent risk factor for a worse prognosis in MG disease.[13] In our study, it was found that MM-3 was seen at a higher rate at the end of clinical follow-up in all three age groups, which was consistent with previous studies. PR and MM-1 were found to be at a higher rate in the very late-onset group than in the early-onset and late-onset groups.

In 50% of MG patients, thymic hyperplasia occurs during childhood or after adolescence. Thymoma is frequently observed in MG patients whose age of onset is over 40.[9] In another study, thymoma was found to be more common in LOMG.[16] In our study, thymoma evaluated with thoracic CT was seen at a higher rate than thymic hyperplasia in all three age groups. This result was evaluated in contrast to other studies for the early-onset group and was consistent with other studies for the late and very late-onset groups. When evaluated in terms of thymus histopathology in patients undergoing thymectomy, thymic hyperplasia was the most common thymic pathology in the early-onset group, and in the very late-onset group, thymoma type B1, thymoma type B2, thymic carcinoma were observed at a higher rate than the early and late-onset groups, which is similar to other studies.

Studies have shown that the mean age at presentation with myasthenic crisis is approximately 59 years. In one study, although myasthenic crisis was seen in more patients in the very late-onset group than in the early and late-onset groups, no statistically significant difference was found.[6] In another study, myasthenic crisis was found with similar frequency in EOMG and LOMG.[11] In our study, consistent with other studies, no significant difference was found among all three age groups in terms of myasthenic crisis.

The course of myasthenia gravis and the outcome of treatment may be affected by accompanying autoimmune diseases common in the general population, or other conditions associated with tumors.[17,18] In a study, it has been shown that diseases accompanying MG are more common in LOMG than in EOMG.[11] In another study, it has been determined that diseases accompanying MG such as extrathymic malignancy were more common in late-onset MG.[8] In our study, consistent with other studies, comorbidity and 2 or more comorbidities were seen more frequently in the very late-onset group than in the early- and late-onset groups.

Studies have shown that AChR antibodies are more common in very late-onset MG and LOMG.[6,11,12] In another study, in contrast to other studies, no significant difference was found in EOMG, non-elderly LOMG, and elderly LOMG groups in terms of anti-AChR positivity. In our

study, antibodies against AChR were observed at the highest rate in very late-onset MG, but no statistically significant difference was observed among all three age groups.

One study showed that age of onset below 40 was an important predictor of MG disease remission, but gender was not a predictive factor of remission.[19,20] In another study, it was found that older age of onset was associated with an increased risk for the development of secondary generalization.[9,21] In another study, it was found that the age of onset and gender were not associated with secondary generalization.[22] In our study, it was found that gender was not associated with prognosis, which is consistent with previous studies. In addition, the age of onset was not found to have an effect on the prognosis. This may be related to the fact that the cut-off age at onset was 40 in some studies and 50 in some studies.

In previous studies, it was shown that thymectomy has a significant association with remission in MG.[20,23] In our study, it was determined that thymectomy had an effect on the development of a good prognosis, which is consistent with the previous study.

One study has shown that the presence of thymoma had no effect on the severity of the disease.[19,20] In other studies, it has been shown that the presence of thymoma has an increased risk in secondary generalization.[21-23] On the other hand, in another study, it was shown that the presence of thymic hyperplasia is associated with complete stable remission in MG.[22] Among these clinical data of MG patients, presence of thymoma in thorax CT, thymectomy status, hospitalization in the intensive care unit, myasthenic crisis, IVIG administration, use of plasmapheresis, 2 or more comorbidities were found to be statistically significant in the development of poor prognosis.

Studies have found that autoimmune diseases accompanying MG have a less favorable prognosis.[24,25] In our study, it was determined that the presence of HT, DM, and accompanying autoimmune diseases were not associated with poor prognosis.

The clinical pattern and prognosis of anti-Musk-associated MG are generally more severe than those associated with anti-AchR antibody MG.[26] In our study, in accordance with the literature, anti-Musk positivity was found to be associated with poor prognosis.

In conclusion, presence of GMG subtype and thymoma in thorax CT, anti-MuSK positivity, hospitalization in the intensive care unit, myasthenic crisis, IVIG administration, plasmapheresis, 2 or more comorbidities were associated with poor prognosis. Ocular MG, the presence of double seronegativity and a history of thymectomy were found to be of significant importance in the development of good prognosis however, age at disease onset, gender, and concomitant autoimmune disease was not associated with prognosis.

These results are of potential importance for recognizing similarities and differences in clinical features in EOMG, LOMG, and very late-onset MG, determining MG disease management strategy and prognosis.

DISCLOSURE

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