Factors Associated with Exacerbations or Crises in Generalized Myasthenia Gravis

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Introduction

Generalized myasthenia gravis (gMG), a rare chronic autoimmune condition, is a more widespread form of myasthenia gravis (MG) causing weakness in the ocular, limb and respiratory muscle groups[1]

Without proper control or prevention, gMG symptoms can progress to exacerbations, and in more severe cases, to myasthenic crises, which are life-threatening events characterized by compromised respiratory function[2]

Exacerbations and crises in gMG require more intensive management, which are associated with increased healthcare resource utilization (HRU) and costs[3]

Identifying characteristics and symptoms of at-risk patients is essential to optimize resource allocation to preventative strategies

Objective

To evaluate factors associated with exacerbations or crises among patients with gMG in the United States

Methods

Data source

- Data from Komodo Research Database were used (01/2017 - 09/2023)
- Data were de-identified and complied with requirements of the Health Insurance Portability and Accountability Act

Study design

- A retrospective observational design was used
- The index date was the first MG diagnosis confirmed by a neurologist
- The baseline period was the 12-month period before the index date
- The follow-up period spanned from the index date until the end of continuous insurance eligibility or data availability for ≥12 months and was used to identify MG-related clinical events

Patient selection

- ≥1 diagnosis of MG (ICD-10-CM: G70.00, G70.01) by a neurologist during study period (01/01/2017 - 09/30/2023)
- ≥18 years old on the index date
- ≥12 months of continuous insurance eligibility starting before the first MG diagnosis and ≥12 months after the index date
- No claim for congenital MG (G70.2) during the baseline period

MG-related clinical events

- MG-related clinical events included exacerbation and crisis:
  - **MG exacerbation** was defined based on MG diagnoses as follows:
    - MG diagnosis with exacerbation (G70.01) in any setting or position, or
    - MG diagnosis without exacerbation (G70.00) in primary position in inpatient or emergency setting
  - **MG crisis** was defined based on procedures for intubation, tracheostomy or mechanical ventilation with any MG diagnosis in inpatient or intensive care unit setting

Statistical Analysis

- A multivariable Cox proportional hazards model was used to assess the association between baseline characteristics and the first MG-related clinical event during the follow-up period
- Patients were followed from index date to the first MG-related clinical event; patients without an event were censored at end of insurance or data end
- Baseline characteristics considered in the Cox proportional hazard models included:
  - Demographic characteristics (e.g., age, sex, race/ethnicity)
  - Baseline comorbidities
  - Baseline gMG symptoms
  - Baseline gMG-related treatments
  - Baseline HRU

Key Takeaways

- **Nearly 50% of patients with gMG experienced exacerbations or crises, occurring on average 5 months after neurologist-confirmed gMG diagnosis**
- **gMG symptoms — dysarthria, generalized or other weaknesses, dysphagia, dyspnea, ptosis — and use of immunoglobulin before the neurologist-confirmed gMG are key factors associated with future exacerbations or crises**
- **These findings suggest the need for more effective symptom management and proactive disease control**

Results

Demographic characteristics

- *A total of 6,195 patients with gMG were included (mean age: 61.1 years; female: 49.1%)*
- *The mean follow-up lengths were 33.4 months (maximum: 68.7 months) in the gMG with clinical event cohort and 32.1 months (maximum: 69.0 months) in the gMG without clinical event cohort*
- *3,045 (49.2%) patients experienced an MG-related clinical event during the follow-up period*
  - *3,026 (48.8%) experienced at least one exacerbation*
  - *190 (3.1%) experienced at least one crisis*
- *Among those with an event:*
  - *The first event was exacerbation in 97.9% patients and crisis in 2.1% patients*
  - *Mean time from index date to the first event was 5.4 months*
- *The breakdown of baseline characteristics among patients with and without a clinical event are found in Table 1*

Factors associated with a clinical event

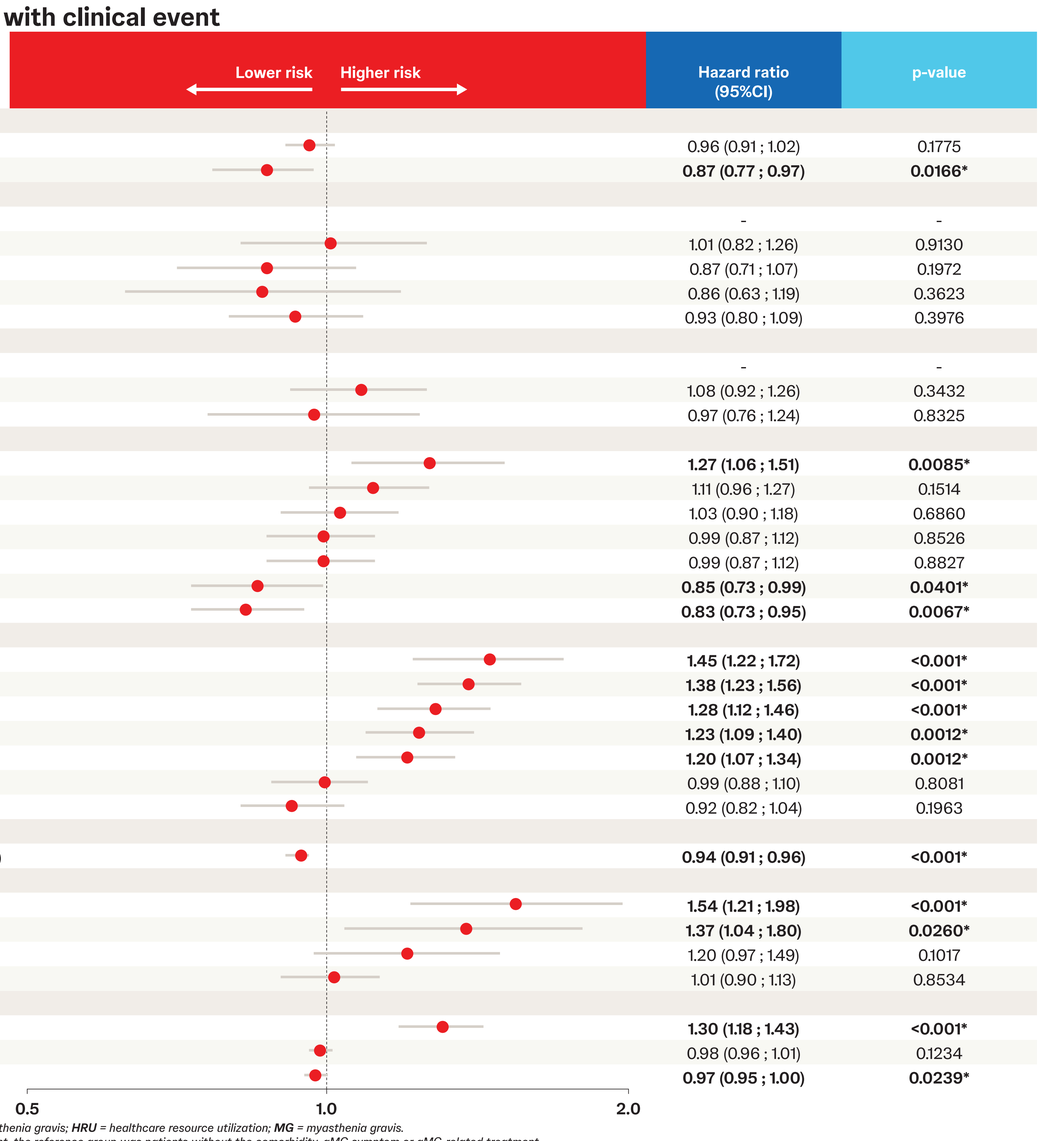
- *Male patients had 15% higher risk of an MG-related clinical event compared with female patients (p=0.017; Figure 1)*
- *Several baseline gMG symptoms were also associated with significantly higher risk of an MG-related clinical event, including:*
  - *Dysarthria → 45% higher risk (p<0.001)*
  - *Generalized or other weaknesses → 38% higher risk (p<0.001)*
  - *Dysphagia → 28% higher risk (p<0.001)*
  - *Dyspnea → 23% higher risk (p=0.0012)*
  - *Ptosis → 20% higher risk (p=0.0012)*
- *Other baseline factors were associated with a significantly higher risk of clinical event, including:*
  - *Use of immunoglobulin → 54% higher risk (p<0.001)*
  - *Use of non-steroidal immunosuppressants → 37% higher risk (p=0.026)*
  - *All-cause emergency visits → each additional 10 visits associated with 30% higher risk (p<0.001)*
  - *Weight loss → 27% higher risk (p=0.009)*
  - *No neurological disorder other than gMG → 20% higher risk (p=0.0067)*
  - *No comorbid autoimmune disease → 18% higher risk (p=0.040)*
  - *Shorter time from MG diagnosis to neurologist visit (index date) → each fewer month associated with a 6% higher risk (p < 0.001)*

Table 1: Baseline characteristics

Mean ± SD [median] or n (%)	gMG with clinical event N=3,045	gMG without clinical event N=3,150
Demographic characteristics		
Age at index date (years)	61.3 ± 15.7 [62.7]	61.0 ± 15.1 [62.4]
Female	1,435 (47.1)	1,605 (51.0)
Race/ethnicity		
White	1,953 (64.1)	1,955 (62.1)
Black or African American	228 (7.5)	212 (6.7)
Hispanic or Latino	234 (7.7)	255 (8.1)
Asian or Pacific Islander	90 (3.0)	104 (3.3)
Other or unknown	540 (17.7)	624 (19.8)
Payer		
Commercial	1,581 (51.9)	1,726 (54.8)
Medicare Advantage	1,289 (42.3)	1,248 (39.6)
Medicaid or unknown	175 (5.7)	176 (5.6)
Baseline comorbidities		
Weight loss	296 (9.7)	179 (5.7)
Hypertension	1,877 (61.6)	1,798 (57.1)
Obesity	1,099 (36.1)	1,056 (33.5)
Hyperlipidemia/dyslipidemia	1,734 (56.9)	1,771 (56.2)
Diabetes	817 (26.8)	799 (25.4)
Other autoimmune disorder	576 (18.9)	603 (19.1)
Other neurological condition	733 (24.1)	691 (21.9)
Baseline gMG symptoms		
Dysarthria	340 (11.2)	163 (5.2)
General and other weaknesses	1,145 (37.6)	811 (25.7)
Dysphagia	834 (27.4)	516 (16.4)
Dyspnea	968 (31.8)	783 (24.9)
Ptosis	1,226 (40.3)	1,140 (36.2)
Diplopia	1,142 (37.5)	1,215 (38.6)
Malaise and fatigue	920 (30.2)	810 (25.7)
Baseline gMG-related treatments		
Immunoglobulin	91 (3.0)	40 (1.3)
Non-steroidal immunosuppressant	64 (2.1)	53 (1.7)
Systemic corticosteroid	352 (11.6)	244 (7.7)
Acetylcholinesterase inhibitor	1,074 (35.3)	990 (31.4)
Baseline HRU (per-patient-per-year)		
Number of emergency visits	1.5 ± 5.0 [1.0]	1.0 ± 1.7 [0.0]
Number of outpatient visits	26.8 ± 28.1 [19.0]	25.3 ± 27.6 [18.0]
Number of inpatient days	3.7 ± 12.5 [0.0]	2.9 ± 16.2 [0.0]

*Abbreviations: **gMG** = generalized myasthenia gravis; **HRU** = healthcare resource utilization; **MG** = myasthenia gravis; **SD** = standard deviation.*

Figure 1: Factors associated with clinical event



*Abbreviations: **CI** = confidence interval; **gMG** = generalized myasthenia gravis; **HRU** = healthcare resource utilization; **MG** = myasthenia gravis.*
[1] For each comorbidity, gMG symptom and gMG-related treatment, the reference group was patients without the comorbidity, gMG symptom or gMG-related treatment.

Strengths

- The large sample size and long follow-up period requirement allowed for a robust time-to-event analysis
- Komodo Research Database included provider specialty for each encounter, which enabled the identification of neurologist visits as a confirmation of gMG

Limitations

- Exacerbations and crises were classified using claims data, which may be less precise than medical notes
- Claims data are limited by availability and potential coding errors
- Certain information was not observed in the data, such laboratory test results, lifestyle or education and this information remains unaccounted for in the model
- Findings may not be generalizable to uninsured populations

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