Factors influencing exacerbations and crisis in generalized myasthenia gravis: Findings from a claims database study

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Introduction

- Generalized myasthenia gravis (gMG) is a rare, chronic autoantibody disease characterized by muscle weakness and fatigue
- Worsening symptoms can manifest as MG exacerbations and/or life-threatening myasthenic crisis, which often require emergency treatment and hospitalization[1,2]

Objective

- To estimate the occurrence of MG exacerbations and myasthenic crisis and explore their association with select patient characteristics among individuals with gMG

Methods

- This was a retrospective cohort study using US healthcare claims data from Optum's de-identified Clinformatics® Data Mart database
- Inclusion criteria for the study population included:
  - ≥1 myasthenia gravis (MG) claim between January 2017 and March 2023, based on International Classification of Diseases, 10th Revision, Clinical Modification (ICD-10-CM) diagnosis codes G70.00 and G70.01
  - Diagnosis code for MG in the primary billing position for an inpatient visit, or ≥2 claims between 1 and 60 days apart with a diagnosis code for MG in any billing position for an outpatient, emergency department, or other type of visit
  - Age ≥18 years on the index date
    - The date of the first MG-related claim that met the inclusion criteria was defined as the index date
  - ≥12 months of continuous health plan enrollment prior to the index date
- Patients who had no claims with MG diagnosis codes during the 12-month baseline period before the index date were included in the newly diagnosed (incident) gMG cohort; otherwise, they were included in the prevalent gMG cohort
  - In the incident gMG cohort, patients were defined as having early-onset gMG if they were <50 years of age or late-onset gMG if they were ≥50 years of age at disease onset
- Patients were excluded if the MG-related claims occurred only on visits with ophthalmologists; otherwise claims could occur on visits with any other provider type (not limited to neurologists)
- All eligible patients were followed up from the index date until the earlier of the date of discontinued health plan enrollment or the end of the study period (March 31, 2023)
- Outcome events were defined as:
  - MG exacerbation: a hospitalization event with MG (ICD-10-CM code G70.0*) as one of the admitting diagnoses
  - Myasthenic crisis: an MG exacerbation with an intensive care unit service (except for surgical purposes)
- Rates of outcome events were summarized per 100 patient-years
- A nested case–control design embedded within the existing gMG cohort was applied to assess the association between the patient characteristics of interest and outcome events
  - Patients experiencing outcome events during follow-up were classified as cases, and patients without events served as controls
  - Correspondingly, patient characteristics of interest were collected over the 12 months preceding the event (cases), or the 12 months preceding the follow-up end date (controls)
- Regression models yielding odds ratios (OR) and 95% confidence intervals (95% CI) assessed the association between demographic and clinical characteristics, as well as the occurrence of MG exacerbations and crisis during follow-up for the prevalent and incident gMG populations

*G70.01 became the effective code number as of October 1st, 2023

Results

- In total, 12,813 patients with prevalent and 3748 patients with incident gMG were identified (**Table 1**)
  - Overall, the mean age was 69.6 years, 49.9% of patients were female, and 73.1% of patients were White

TABLE 1: Patient demographics and clinical characteristics for the prevalent and incident gMG groups

Characteristic	Prevalent gMG patients (n=12,813)	Incident gMG patients (n=3748)
Female sex, n (%)	6317 (49.3)	1955 (52.2)
Mean age, years (SD)	69.8 (13.6)	68.9 (14.1)
Age group, n (%)		
18–44 years	826 (6.4)	294 (7.8)
45–54 years	810 (6.3)	259 (6.9)
55–64 years	1686 (13.2)	460 (12.3)
≥65 years	9491 (74.1)	2735 (73.0)
Race, n (%)		
Asian	333 (2.6)	93 (2.5)
Black	1268 (9.9)	378 (10.1)
Hispanic	1139 (8.9)	323 (8.6)
Unknown	741 (5.8)	181 (4.8)
White	9332 (72.8)	2773 (74.0)
Quan-Charlson Comorbidity Index score, mean (SD)	1.8 (2.1)	1.7 (2.2)
Health plan type, n (%)		
Health Maintenance Organization	3100 (24.2)	755 (20.1)
Preferred Provider Organization	726 (5.7)	223 (5.9)
Other	6690 (52.2)	1951 (52.1)
Point of Service	1810 (14.1)	661 (17.6)
Missing	487 (3.8)	158 (4.2)
Source of healthcare coverage, n (%)		
Commercial	2673 (20.9)	931 (24.8)
Medicare	10,140 (79.1)	2817 (75.2)
Previous[a] myasthenic crisis, n (%)	292 (2.3)	0
Previous[a] MG exacerbation, n (%)	572 (4.5)	0
Late onset of gMG (at ≥50 years of age), n (%)[b]	–	3331 (88.9)
Comorbidity (in >10% of gMG populations), n (%)		
Hypertension	9222 (72.0)	2562 (68.4)
Diabetes	4590 (35.8)	1225 (32.7)
Obesity	3644 (28.4)	1043 (27.8)
Hypothyroidism	3486 (27.2)	929 (24.8)
Chronic pulmonary disease	3379 (26.4)	918 (24.5)
Deficiency anemia	3222 (25.1)	808 (21.6)
Other neurological disorders	3162 (24.7)	988 (26.4)
Any autoimmune disease	2945 (23.0)	840 (22.4)
Depression	2558 (20.0)	742 (19.8)
Fluid and electrolyte disorders	2482 (19.4)	669 (17.8)
Renal failure	2223 (17.3)	587 (15.7)
Valvular heart disease	2058 (16.1)	623 (16.6)
Congestive heart failure	1737 (13.6)	476 (12.7)
Solid tumor without metastasis	1601 (12.5)	457 (12.2)

[a]Patient characteristics of interest were collected over the 12 months preceding the event (cases), or the 12 months preceding the follow-up end date (controls). [b]Diagnosis date unknown for patients in the prevalent gMG cohort.
gMG, generalized myasthenia gravis; **MG**, myasthenia gravis; **SD**, standard deviation.

- MG exacerbations occurred during follow-up in 12.2% and 22.0% of patients with prevalent and incident gMG, respectively; rates were 19.2 and 33.9 per 100 patient-years, respectively (**Table 2**)
- Myasthenic crisis occurred during follow-up in 6.0% and 12.4% of patients with prevalent and incident gMG, respectively; rates were 3.5 and 7.5 per 100 patient-years, respectively (**Table 2**)

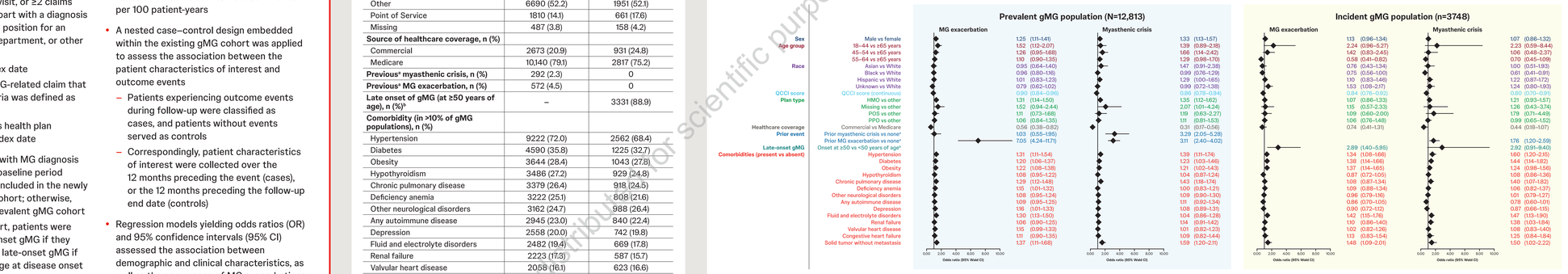
TABLE 2: Occurrences of MG exacerbations and myasthenic crisis during follow-up

Patient group	Number of patients with event	Proportion of patients with event (%)	Rate (100 person years)[a]	95% confidence interval
MG exacerbation				
Prevalent gMG	1567	12.2	19.2	17.5–21.0
Incident gMG	823	22.0	33.9	29.6–38.8
Myasthenic crisis				
Prevalent gMG	763	6.0	3.5	3.0–3.9
Incident gMG	463	12.4	7.5	6.3–8.9

[a]Patients could have multiple events.
gMG, generalized myasthenia gravis; **MG**, myasthenia gravis.

- Associations between patient characteristics and outcome events (**Figure 1**) were demonstrated as follows:
  - Among patients with prevalent gMG, male (vs female) sex was associated with MG exacerbation and myasthenic crisis (OR 1.25 and 1.33, respectively)
  - Among patients with prevalent gMG, being in the 18–44 years age group (vs ≥65 years) was associated with MG exacerbation (OR 1.52); for the incident gMG cohort, being in the 55–64 years age group (vs ≥65 years) was associated with reduced likelihood of MG exacerbation (OR 0.58)
  - In both gMG populations, higher Quan-Charlson Comorbidity Index score (reflecting higher predicted risk of death within 1 year due to specific comorbid conditions) was associated with a lower chance of experiencing MG exacerbation or myasthenic crisis (OR range 0.80–0.90)
  - For patients in the prevalent gMG group, prior MG exacerbation was associated with future exacerbation (OR 7.05) and prior myasthenic crisis was associated with a future episode (OR 9)
  - For the incident gMG cohort, late-onset gMG (onset at ≥50 years of age) was associated with MG exacerbation (OR 2.89)
  - Across one or both of the study populations, the occurrence of comorbid conditions, including hypertension, diabetes, obesity, chronic pulmonary disease, deficiency anemia, depression, fluid and electrolyte disorders, and solid tumor without metastasis, was significantly associated with MG exacerbation and/or myasthenic crisis

FIGURE 1: Patient demographics and clinical characteristics and their association with the occurrence of MG exacerbations and myasthenic crisis during follow-up in the prevalent and incident gMG cohorts in case–control analyses



Not all characteristics analyzed are shown in the figure. The list of presence/absence of comorbidities also includes pulmonary circulation disorders, paralysis, liver disease, chronic peptic ulcer disease, lymphoma, metastatic cancer, coagulation deficiency, weight loss, blood loss anemia, alcohol abuse, drug abuse, and psychoses. Other variables analyzed included geographic region of the United States (Midwest, Northeast, South, West, or Unknown), and treatment ever received (acetylcholinesterase inhibitor, corticosteroid, monoclonal antibody, Fc receptor antagonist, nonsteroidal immunosuppressant, intravenous immunoglobulin, subcutaneous immunoglobulin, MG-related thymectomy, or MG-related plasmapheresis; yes vs no). Solid tumor without metastasis, obesity, fluid and electrolyte disorders, deficiency anemia, depression, any autoimmune disease: present vs absent), geographic region of the United States and treatment ever received.
[a]Analyses were based on the case–control design, not when patients entered the cohorts; therefore, some patients with incident gMG developed exacerbations after entering the cohort during follow-up (but none had myasthenic crisis).
[b]Late onset of gMG was not analyzed for the prevalent gMG cohort as the diagnosis date was unknown for these patients.
CI, confidence interval; **gMG**, generalized myasthenia gravis; **HMO**, Health Maintenance Organization; **MG**, myasthenia gravis; **POS**, Point of Service; **PPO**, Preferred Provider Organization; **QCCI**, Quan-Charlson Comorbidity Index.

Limitations

- Results may not be generalizable to patients without health insurance
- gMG was identified based on a combination of diagnoses, treatment settings, and physician specialties
- The models are subject to omitted variable bias as certain clinical characteristics were unavailable

Conclusions

- MG exacerbations and myasthenic crisis occur at a notable rate among patients with gMG
- Prior history of these events is a strong predictor of future occurrences
- Comorbidities, such as hypertension, diabetes, and chronic pulmonary disease, are also associated with MG exacerbation and myasthenic crisis
- These findings suggest there is a need for gMG treatments that provide stable disease control while avoiding MG exacerbations and myasthenic crisis, which are costly to health systems and disruptive and damaging to patients

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Disclosures

LJ, **ZL**, **JP**, **AKC**, and **ZC** are employees of Janssen Scientific Affairs, LLC, a Johnson & Johnson Company, the sponsor of this study. **AEB** and **QC** are employees of Janssen Global Services, LLC, a Johnson & Johnson Company. **NS** reports no conflicts of interest.

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