Interim Results for Myasthenia Gravis – Resource Utilization, Epidemiology, Survival, and Treatment Patterns (MG-REST) Study in Ontario, Canada

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Abstract

Background: Reliable real-world data on the burden of myasthenia gravis (MG) is needed to inform Canadian clinical and policy decisions in the era of new MG therapeutics, including neonatal fragment crystallizable receptor (FcRn) inhibitors. Given the lack of recent Canadian data on MG disease burden, the MG-REST Study aims to estimate the clinical burden of MG in Ontario, Canada.

Methods: Ontario health administrative data held by ICES were utilized for a retrospective population-based cohort study of adults with MG identified through a validated algorithm (April 2013-March 2019) and followed for up to seven years (March 2020) to determine myasthenic crisis characteristics and overall survival (OS).

Results: The MG cohort (n=2,601) had an average age of 65.7 years and 53.3% were males. Incidence of first myasthenic crisis was 9%, with 87% of events occurring at/after diagnosis. MG OS was 89%, 85% and 75% at 1-year, 2-years and 5-years, respectively, while OS after first crisis was 60%, 52%, and 39% for the same years.

Conclusions: Despite the availability of conventional therapies throughout the study, MG crisis remains a serious, common complication of MG, with decreased survival at 1-year post-crisis (29% difference versus 1-year OS following MG diagnosis). Study highlights MG burden and unmet need for new effective therapies for MG treatment.

Background & Rationale

- Myasthenia gravis (MG) is a rare immunoglobulin G mediated autoimmune neuromuscular disorder, which results in involuntary muscle weaknesses in the respiratory muscles and those that control the eyes, mouth, throat and limbs.
- Myasthenic crisis is characterized by respiratory failure requiring intubation and mechanical ventilation which can lead to death, if untreated.
- In 2016, Breiner *et al.* published a validated algorithm to identify MG patients in the ICES database with high sensitivity (81.6%), specificity (100%), positive predictive value (80%) and negative predictive value (100%) to estimate incidence and prevalence.[1] However, published Canadian data on detailed demographics, clinical characteristics, myasthenic crisis, and survival rates of MG patients are limited, absent or outdated.
- To address these knowledge gaps, the MG-REST study utilized real-world evidence (RWE) from Ontario's Institute for Clinical Evaluative Sciences (ICES) to evaluate the clinical burden of MG patients. The results presented here are interim results.

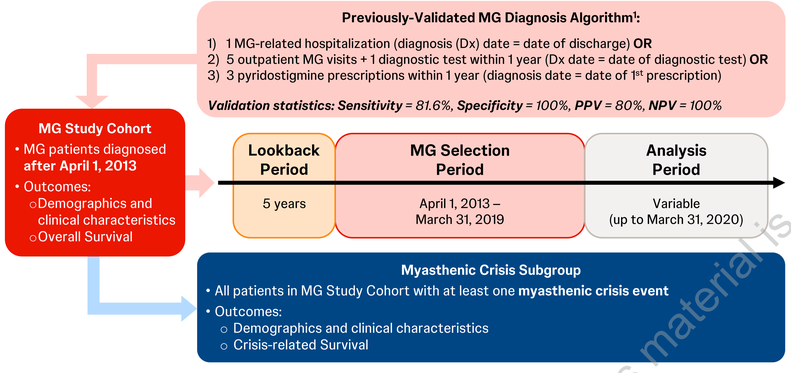
Objective

- To understand the clinical burden of MG by examining the demographics and clinical characteristics, myasthenic crisis characteristics, and survival of MG patients in Ontario, Canada

Methods

- This was an observational, retrospective cohort study using the ICES data repository based on adult patients who were identified with MG using a previously-validated algorithm developed for MG.[1] Validated algorithm diagnosis criteria and key study dates can be found in **Figure 1**.

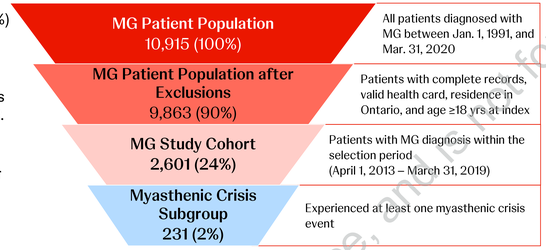
Figure 1. MG-REST Study Overview



Note: *Study analysis period ended in March 2020 to remove the effects of the COVID-19 pandemic. MG diagnosis date was assigned based on healthcare interactions observed within administrative data*

- The MG Study Cohort consisted of 2,601 patients who met the study inclusion and remained after applying exclusion criteria. Of these patients, 231 (9%) experienced myasthenic crisis and were included in the Myasthenic Crisis Subgroup (**Figure 2**).
- Categorical variables were reported in terms of frequency and percentage, while continuous variables were reported in terms of mean, SD, median, and IQR.
- Overall survival in both the MG Study Cohort and Myasthenic Crisis Subgroup was estimated from MG diagnosis date until date of death using Kaplan-Meier methodology with right censoring at end of study period (March 31, 2020).

Figure 2. Waterfall Diagram illustrating Cohort Selection



Results

- At baseline, the average age of the MG Study Cohort and the Myasthenic Crisis Subgroup was 42-47% female, with an average age of 65.7 and 67.6 years old, respectively.
- A larger proportion of the Myasthenic Crisis Subgroup had 3 or more Charlson Comorbidities, and also had higher prevalence of both autoimmune and non-autoimmune comorbidities compared to the MG Study Cohort (**Table 1**).

Table 1. Demographics and Clinical Characteristics at Baseline

Variable		MG Study Cohort (n=2,601)	Myasthenic Crisis Subgroup (n=231)
Sex	Female (%)	1,215 (46.7%)	98 (42.4%)
Age	Mean age ± SD, years	65.7 ± 16.0	67.6 ± 14.4
	Median age (IQR), years	69 (58-77)	70 (62-77)
Age Group	18-39 years (%)	230 (8.8%)	14 (6.1%)
	40-64 years (%)	702* (27.0%)	51 (22.1%)
	≥65 years (%)	1,672* (64.2%)	166 (71.9%)
Charlson Comorbidity Index (CCI)	0 (%)	495 (19.0%)	44 (19.0%)
	1 (%)	211 (8.1%)	24 (10.4%)
	2 (%)	203 (7.8%)	27 (11.7%)
	≥3 (%)	250 (9.6%)	37 (16.0%)
	No hospitalizations in past 5 years (%)	1,442 (55.4%)	99 (42.9%)
Autoimmune Comorbidities	Ankylosing spondylitis (%)	15 (0.6%)	3* (1.3%)
	Multiple sclerosis (%)	41 (1.6%)	7 (3.0%)
	Psoriasis/psoriatic arthritis (%)	35 (1.3%)	3* (1.3%)
	Rheumatoid arthritis (%)	84 (3.2%)	6 (2.6%)
	Systemic lupus erythematosus (%)	84 (3.2%)	8 (3.5%)
	Other autoimmune disease (%)	50 (1.9%)	11 (4.8%)
Other Key Comorbidities	Anxiety (%)	732 (28.1%)	59 (25.5%)
	Chronic obstructive pulmonary disease (%)	537 (20.6%)	66 (28.6%)
	Depression (%)	795 (30.6%)	66 (28.6%)
	Diabetes mellitus (%)	791 (30.4%)	80 (34.6%)
	Heart Disease (%)	527 (20.3%)	63 (27.3%)
	Hypertension (%)	1,620 (62.3%)	158 (68.4%)

Note: *Values marked with "*" have undergone cell suppression to either reduce the risk of patient re-identification through small cells (values from 1-5) or to prevent the back-calculation of small cells. Values marked with "~" have the midpoint value shown and were used to calculate the percentages.*

- A large proportion (n=200, 86.5%) of myasthenic crisis patients had their first myasthenic crisis event at index or after MG diagnosis. When pre-diagnosis events are excluded, the average time from diagnosis to myasthenic crisis was 9.1 months (**Table 2**).

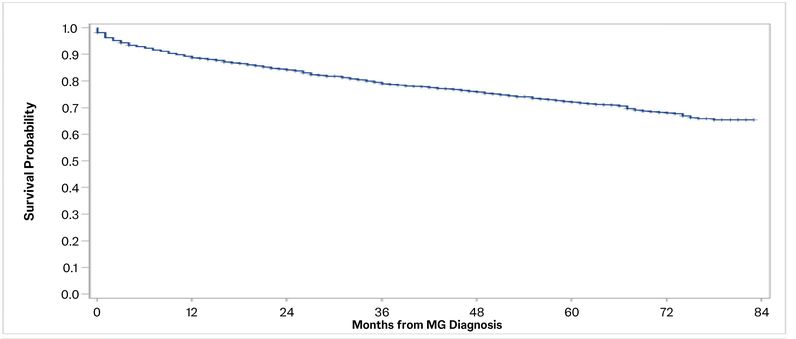
Table 2. Incidence and Timing of Myasthenic Crisis

Variable		Myasthenic Crisis Subgroup (n=231)
Myasthenic Crisis Timing	Pre-Diagnosis, n (%)	31 (13.4%)
	At Index, n (%)	117 (50.6%)
	Post-Diagnosis, n (%)	83 (35.9%)
Diagnosis to Myasthenic Crisis* (excluding pre-diagnosis events)	Mean ± SD, months	9.1 ± 15.5
	Median (IQR), months	0.8 (0-9.8)
	Min – Max, months	0 – 72.8

Note: *Patients could have multiple crisis events in this calculation.*

- For the 2,601 patients in the MG Study Cohort probability of overall survival was around 89%, 85%, and 75% at 1 year, 2 years, and 5 years following diagnosis, respectively (**Figure 3**). Median overall survival was not reached after 84 months (7 years).

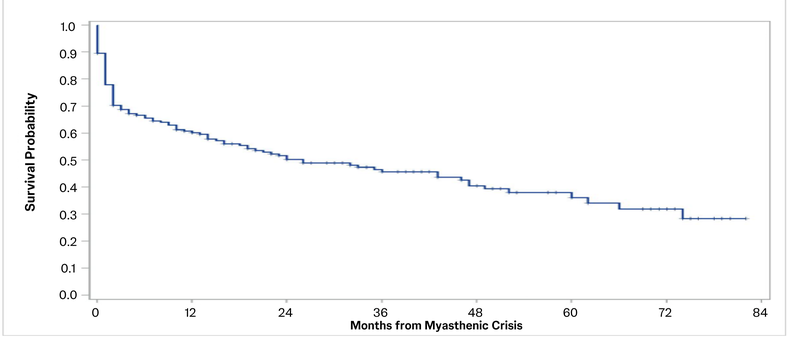
Figure 3. Kaplan Meier Curve for Overall Survival, MG Study Cohort (N=2,601)



Months	0	12	24	36	48	60	72	84
Patients at Risk	2,601	2,320	1,821	1,353	941	547	285	0

- For the 200 patients with their first myasthenic crisis (at or following their index date), the probability of overall survival was around 60%, 52%, and 39% at 1, 2, and 5 years after myasthenic crisis, respectively (**Figure 4**). Median overall survival was reached at 26 months after crisis.

Figure 4. Kaplan Meier Curve for Overall Survival after Myasthenic Crisis, Myasthenic Crisis Subgroup (N=200)



Months	0	12	24	36	48	60	72	84
Patients at Risk	200	109	77	55	38	20	12	0

Note: Survival analysis is based on patient's first myasthenic crisis. The 31 patients who had myasthenic crisis before index date were excluded from this analysis.

Conclusion

- Despite the availability of conventional therapies throughout the study, myasthenic crisis remains a serious, common complication of MG.
- This is the first study to examine MG survival in Canada. The study found patients with a myasthenic crisis have a decreased survival (29% difference) at 1-year post-crisis (60%) versus 1-year OS following MG diagnosis (89%)
- This study highlights the burden of MG in Canada and the unmet need for novel therapies for MG treatment and disease management.

References

1. Breiner A, Widdifield J, Katzberg HD, Barnett C, Bril V, Tu K. Epidemiology of myasthenia gravis in Ontario, Canada. Neuromuscular disorders : NMD. 2016;26(1):41-46.