COMORBIDITIES IN MYASTHENIA GRAVIS IN THE US NATIONAL VETERANS AFFAIRS HEALTH NETWORK

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INTRODUCTION AND OBJECTIVE

Introduction

- Myasthenia gravis (MG) is a neuromuscular autoimmune disorder characterized by muscle weakness and fatigue.[1]
- Patients diagnosed with MG commonly have comorbidities such as cardiovascular disease, metabolic and endocrine disorders (hyperlipidemia, hypertension, diabetes mellitus, thyroid disease), respiratory disorders and autoimmune diseases. Some comorbidities (thymoma, thyroid disease, diabetes mellitus, dyslipidemia, and arterial hypertension) can worsen the MG prognosis.[2-5]
- Managing MG with comorbidities poses challenges such as increased exacerbations, hospitalizations, and healthcare resource utilizations and negatively impacts disease outcomes, especially in cases with multiple comorbidities.[3-5]
- There are limited data on the incidence of comorbidities and their impact on the patients' clinical course to better inform patient care in the US.

Study Objective

- The purpose of this study was to compare the cumulative incidence of 14 common comorbidities in individuals diagnosed with MG versus matched controls.

METHODS

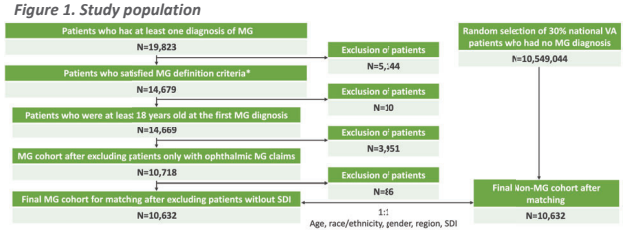
Study Design and Data Source

- This was a retrospective cohort study using de-identified data extracted from the National Veterans Affairs (VA) Health Care Network database from January 1999 to March 2022.
- The database contains electronic medical record (EMR) data from over 1,700 sites of care serving ~8.76 million veterans.

Study Population (Figure 1)

- Adult patients with confirmed MG diagnosis and continuous enrollment in VA Health Network.[6]
- A 1:1 matched control cohort was developed, matching on key baseline characteristics including age, index year, gender, race, region, and social deprivation index (SDI).
- Patients were followed from index date (defined as the first diagnosis of MG for the MG cohort and a randomly chosen date for non-MG cohort) until enrollment end date, end of the study (03/15/2022) or death.

Figure 1. Study population



*Study population diagnosis criteria referenced the best performing algorithm based on Lee et al. Muscle & Nerve 2021[6]
Abbreviations: MG=myasthenia gravis; SDI=social deprivation index; VA=Veterans Affairs

Study endpoints

- Patient demographics and disease characteristics were assessed during the baseline period, defined as one year prior to the index date.
- 14 common comorbidities associated with MG, including anxiety, autoimmune conditions, cardiovascular disease, depression, diabetes, gastroesophageal reflux disease (GERD), glaucoma, hyperlipidemia/hypercholesterolemia, hypertension, infections, malignancy, osteoporosis, sleeping disorders, and thyroid disorders were included in the analysis.

Statistical Analysis

- Descriptive statistics were used to compare the baseline characteristics between patients with MG and the non-MG matched cohort.
- Kaplan-Meier (KM) analysis and log-rank tests were performed to compare the cumulative incidence of comorbidities from the index date between MG vs. the non-MG matched cohort.

RESULTS

Patient Characteristics

- A total of 10,632 patients with MG and 10,632 matched controls were identified with a 7.8-year follow-up for each cohort (**Table 1**).
- Demographic characteristics were similar between the MG and non-MG cohorts after the 1:1 matching.
- Although baseline composite CCI score was similar between cohorts, compared to the non-MG matched cohort, the MG cohort exhibited significantly higher incidences of many of the specific comorbidities evaluated.

Table 1. Key baseline characteristics

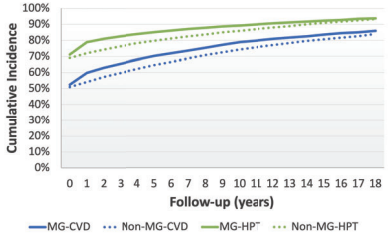
Characteristics	MG (N=10,632)	Non-MG (N=10,632)	p-value*
Time to index date by year, (mean, SD)	8.43 (5.27)	8.43 (5.27)	1
Median (IQR) follow-up in time to index date	7 (4-12)	7 (4-12)	
Follow-up in years (Mean, SD)	7.77 (4.91)	7.78 (4.91)	0.91
Age at diagnosis			
Age at index date (mean, SD)**	70.47 (11.53)	70.30 (11.56)	0.45
Median, IQR	71.92 64.35-78.63	71.92 64.24-78.50	
Gender			
Male (N, %)	10,178 (95.73%)	10,178 (95.73%)	1
Race/ethnicity (N, %)			
Caucasian	7,890 (74.21%)	7,890 (74.21%)	1
African-American	817 (7.68%)	817 (7.68%)	
Hispanic	447 (4.20%)	447 (4.20%)	
Other (Asian, Native American, Unknown)	1478 (13.90%)	1478 (13.90%)	
SDI (mean, SD)	46.98 (26.40)	48.05 (26.62)	0.0032
BMI (mean, SD)	30.18 (5.87)	29.24 (5.70)	<0.0001
CCI (mean, SD)	0.68 (1.23)	0.67 (1.20)	0.60
Comorbidities before index date, N %			
Hypertension	7,580 (71.29%)	7,359 (69.22%)	0.0009
Hyperlipidemia/hypercholesterolemia	6,971 (65.57%)	6,872 (64.64%)	0.15
Infections	5,836 (54.89%)	5,537 (52.08%)	<.0001
Cardiovascular disease	5,578 (52.46%)	5,421 (50.99%)	0.03
Diabetes	3,906 (36.74%)	3,483 (32.76%)	<.0001
GERD	3,721 (35.00%)	3,319 (31.22%)	<.0001
Depression	2,562 (24.10%)	2,463 (23.17%)	0.11
Malignancy	1,864 (17.53%)	1,946 (18.30%)	0.14
Glaucoma	1,809 (17.01%)	1,500 (14.11%)	<.0001
Thyroid-related disorders	1,657 (15.59%)	1,089 (10.24%)	<.0001
Autoimmune-associated conditions	1,035 (9.73%)	879 (8.27%)	0.0002
Sleeping disorder	862 (8.11%)	655 (6.16%)	<.0001
Osteoporosis	530 (4.98%)	346 (3.25%)	<.0001
Anxiety	386 (3.63%)	310 (2.92%)	0.0034

* p-value compared MG to non-MG cohort: Two-sample t-tests were performed for continuous variables and Chi-square tests were performed for categorical variables to determine statistical significance. ** first MG diagnosis date for the MG cohort and the random assigned proxy date for the non-MG cohort. Abbreviations: BMI=body mass index; CCI=Charlson Comorbidity Index; IQR=interquartile range; MG=myasthenia gravis; SD=standard deviation; SDI=social deprivation index

Comorbidity Characteristics

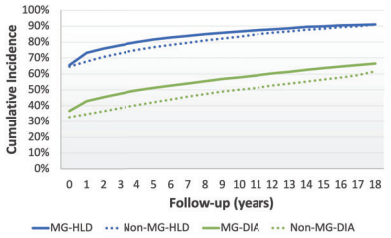
- The analysis demonstrated that across all 14 comorbidities examined, patients with MG displayed a significantly higher cumulative incidence of individual comorbidities (p's <0.001) (**Figures 2-7**).
- The unadjusted Cox model demonstrated that patients in the MG cohort developed new onset comorbidities significantly faster than those in the matched non-MG cohort (HR's >1, p's <0.001).

*Figure 2. Incidence of CVD and hypertension comorbidities in patients with MG vs non-MG**



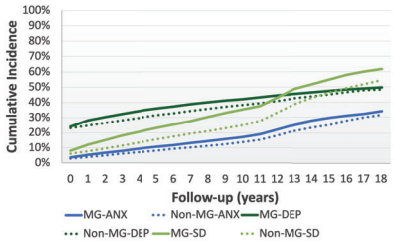
*Log rank test p<0.0001. Abbreviations: CVD=Cardiovascular Disease; HPT=Hypertension

*Figure 3. Incidence of diabetes and hyperlipidemia in patients with MG vs non-MG**



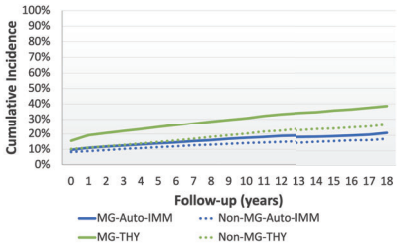
*Log rank test p<0.0001. Abbreviations: DIA=Diabetes; HLD=Hyperlipidemia / Hypercholesterolemia

*Figure 4. Incidence of anxiety, depression and sleep disorder in patients with MG vs non-MG**



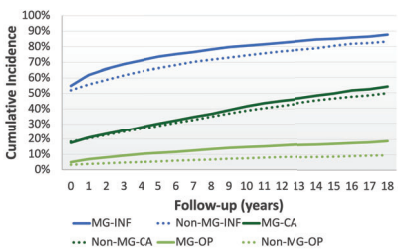
*Log rank test p<0.0001. Abbreviations: ANX=Anxiety; DEP=Depression; SD=Sleep Disorders

*Figure 5. Incidence of auto-immune and thyroid related disorders in patients with MG vs non-MG**



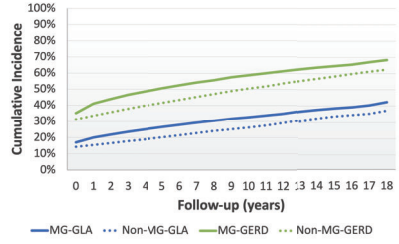
*Log rank test p<0.0001. Abbreviations: Auto-IMM=Auto-immune Associated Conditions; THY=Thyroid-related Disorders

*Figure 6. Incidence of infections, malignancy and osteoporosis in patients with MG vs non-MG**



*Log rank test p<0.0001. Abbreviations: CA=Cancer / Malignancy; INF=Infections; OP=Osteoporosis

*Figure 7. Incidence of GERD and glaucoma in patients with MG vs non-MG**



*Log rank test p<0.0001. Abbreviations: GLA=Glaucoma; GERD=Gastro Esophageal Reflux Disease; gastro=gastrointestinal

CONCLUSIONS

- Patients diagnosed with MG in the US were at significant risk to develop comorbidities commonly associated with MG and the onset occurred at a faster rate compared to the non-MG cohort.
- These findings underscore the association between MG and an elevated risk of specific comorbidities.

References

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