

Diagnosis of Lambert-Eaton Myasthenic Syndrome (LEMS) may be Missed among Patients with Myasthenia Gravis and Autonomic Dysfunction: Results from a US Database Analysis

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Conclusions



- LEMS should be suspected in patients diagnosed as MG with autonomic dysfunction, especially in those with SCLC.
- Based on our analyses, at least 2% of this MG population may have the diagnosis of LEMS and be appropriate for alternative treatments.

Clinical relevance



- Delayed diagnosis of Lambert-Eaton myasthenic syndrome (LEMS), an underrecognized syndrome, can worsen morbidity, including delayed recognition of associated small cell lung cancer.
- This observational data analysis examined autonomic dysfunction in patients in the US with presumably seronegative myasthenia gravis, who may have the diagnosis of LEMS and be appropriate for alternative treatments.

Acknowledgements

This study was funded by Catalyst Pharmaceuticals (Coral Gables, FL, USA).

Disclosures

DM - employee, shareholder of Catalyst Pharmaceuticals; GS, RG - consultants to Catalyst Pharmaceuticals; SV - consultant for argenx, Antag, and CSL Behring; DSMB for Alletty; research support from Takeda, Dysautonomia International, Grifols and NIH; JR - Advisory consultant to argenx, MTPA, Biogen, NeuroSense, Annexion, ML Bio and Amylyx



Background

- Myasthenia gravis (MG) and Lambert-Eaton myasthenic syndrome (LEMS) are both characterized by muscle weakness, but autonomic dysfunction is more common with LEMS.
 - Comorbid autonomic dysfunction has been reported to occur in over 90% of patients with LEMS but is uncommon among patients with MG.¹
- LEMS patients may initially be diagnosed as MG. In observational studies, a diagnosis of MG was reported in up to 1/3 of patients with LEMS.¹⁻⁶
- Autonomic dysfunction in patients diagnosed with MG may indicate a missed LEMS diagnosis.

Objective

We evaluated the potential for missed diagnoses of LEMS and autonomic dysfunction among patients with MG in the United States (US).

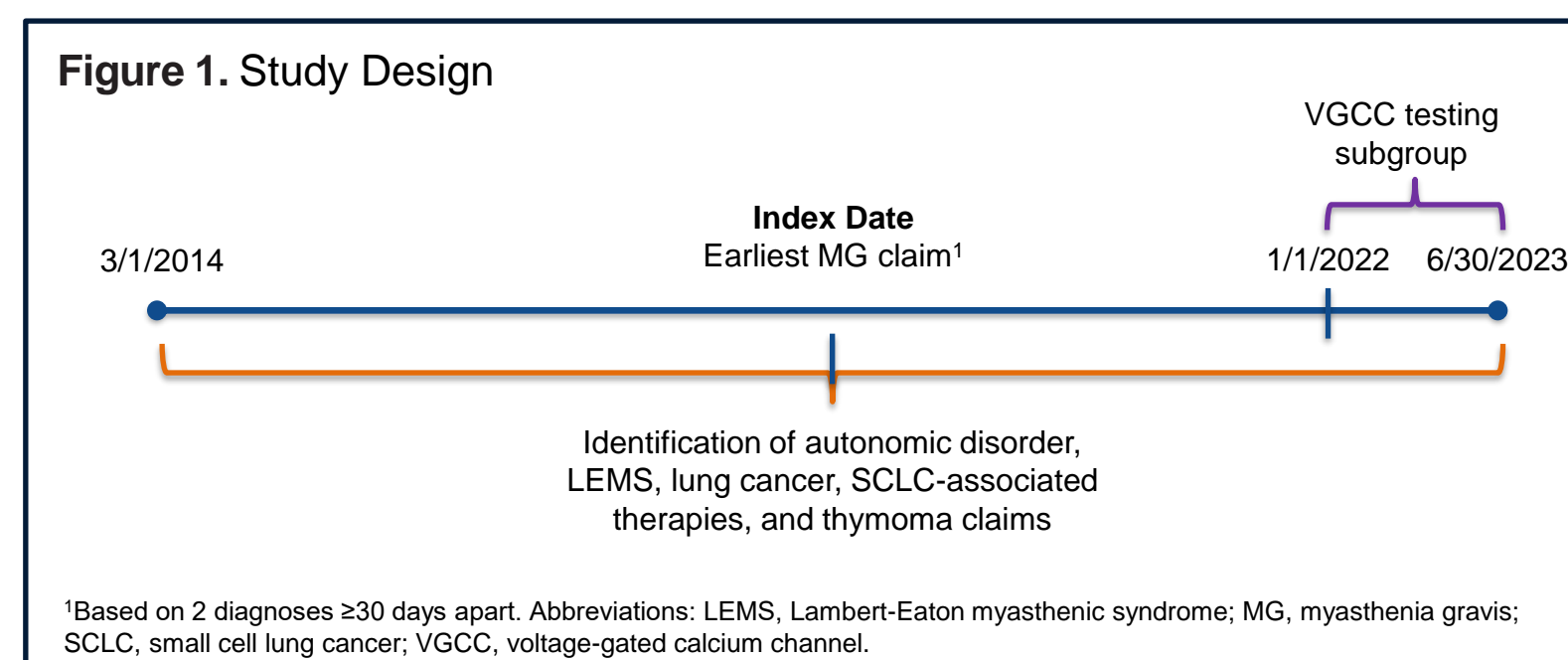
Design/Methods

Study design and data source

- Retrospective, observational cohort study.
- Longitudinal pharmacy and medical claims from a large US de-identified dataset (Symphony Health's PatientSource[®]) between March 1, 2014-June 30, 2023 were analyzed.
- Eligible patients had ≥ 2 claims ≥ 30 days apart for MG. (Figure 1)

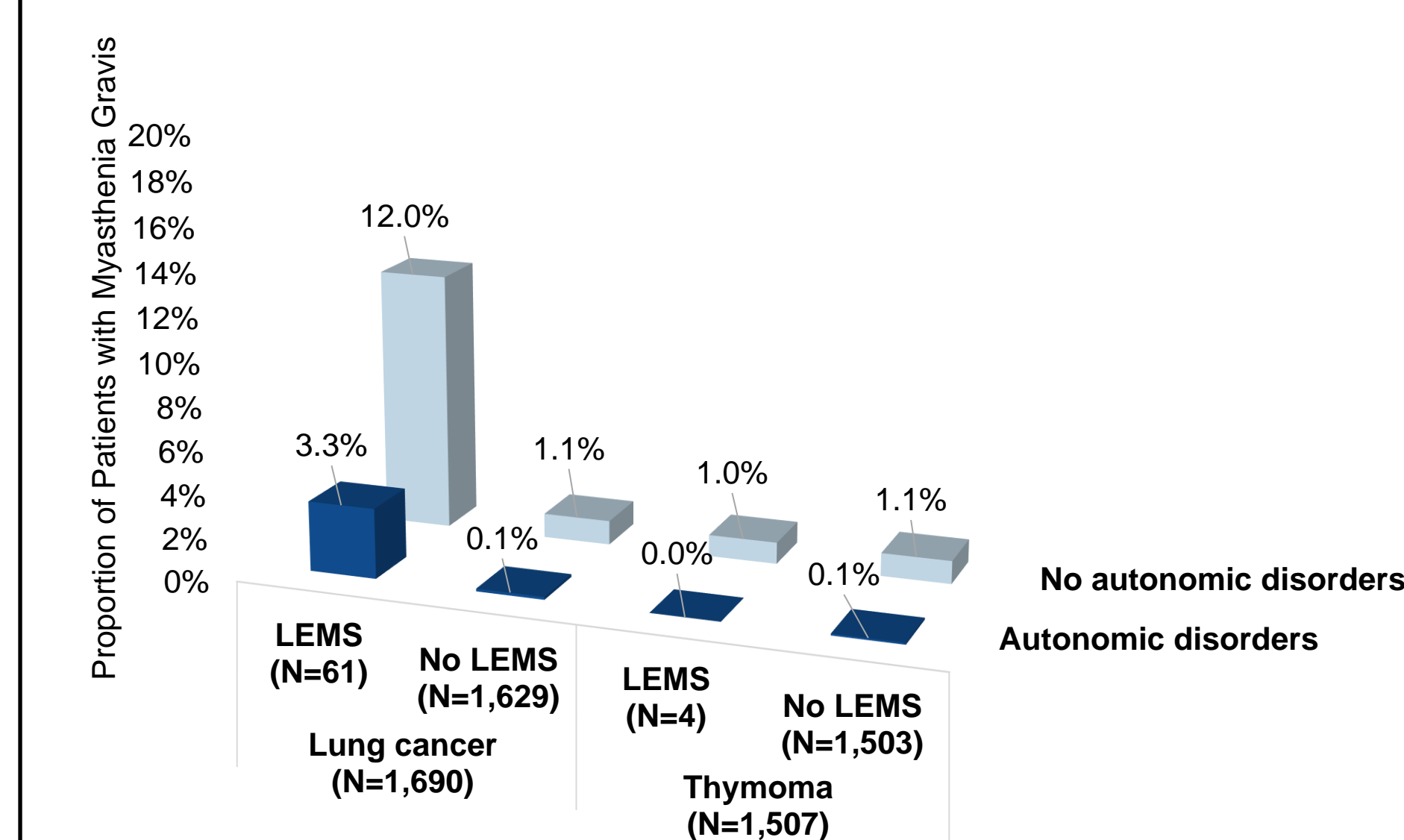
Analysis

- Patients with MG were assessed for autonomic disorders, defined as ≥ 2 claims ≥ 30 days apart with the same diagnostic code for disorders of the autonomic nervous system, hypotension, and/or orthostatic hypotension.
 - Diagnoses of LEMS, lung cancer, and prescriptions for SCLC-associated therapies (etoposide + platinum-based chemotherapy) were identified and descriptively analyzed according to the presence of autonomic disorder claims.
 - As thymoma occurs in 10-15% of patients with MG⁷ and is uncommon in LEMS, claims associated with thymoma diagnoses were evaluated.
- Claims for LEMS-specific VGCC antibody tests were evaluated among patients diagnosed with MG 1/1/2022 or later.



Results

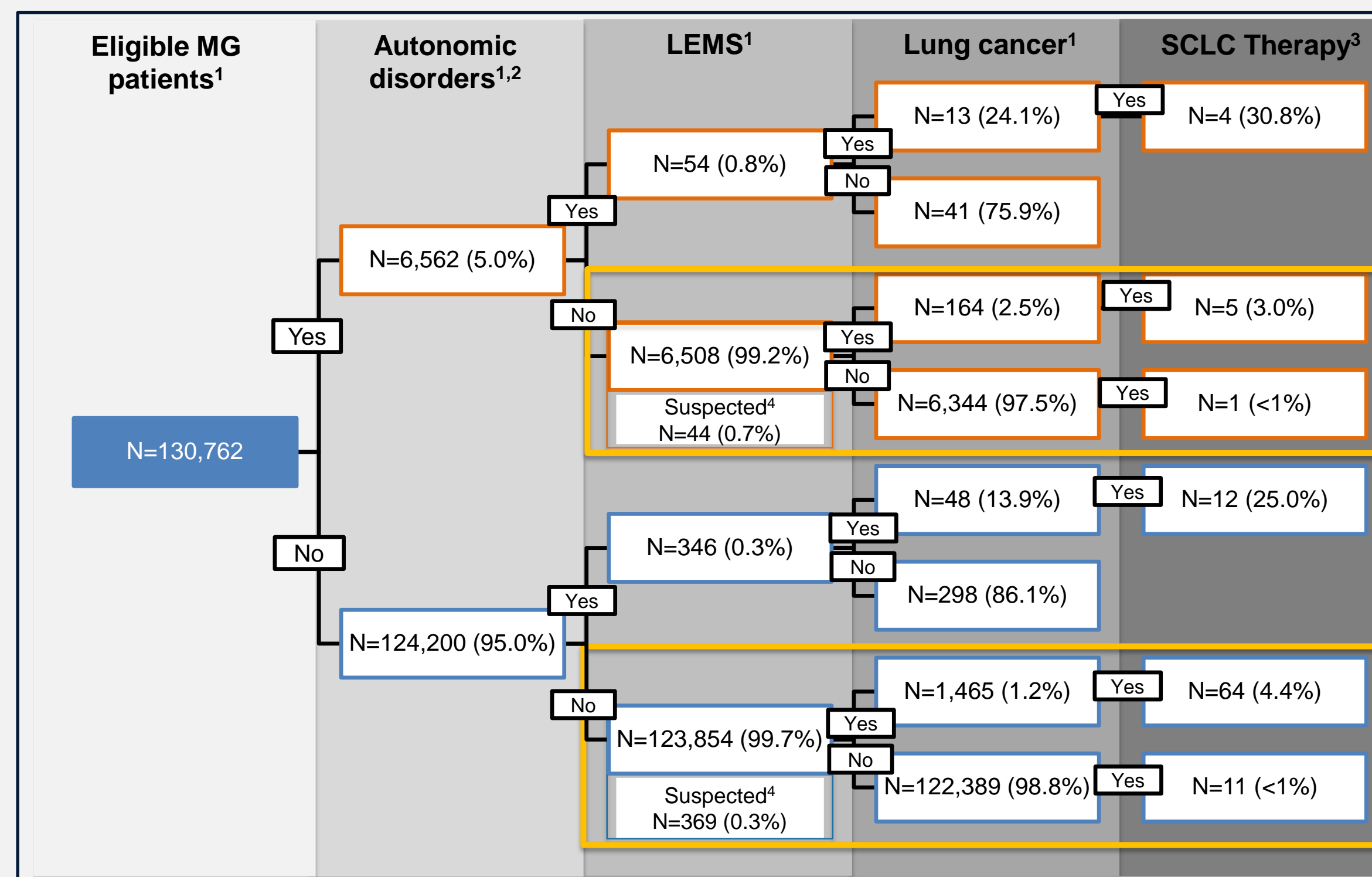
Figure 2. Frequency of Lung Cancer and Thymoma among Patients with MG According to the Presence of LEMS and Autonomic Disorders¹



¹Based on ≥ 2 diagnoses ≥ 30 days apart. Abbreviations: LEMS, Lambert-Eaton myasthenic syndrome; MG, myasthenia gravis.

Results

Figure 3. Frequency of LEMS and Lung Cancer According to the Presence of Autonomic Disorders among Patients with MG



Potential missed LEMS diagnosis

Potential missed LEMS diagnosis

Figure 4. Frequency of Thymoma According to the Presence of Autonomic Disorders among Patients with MG

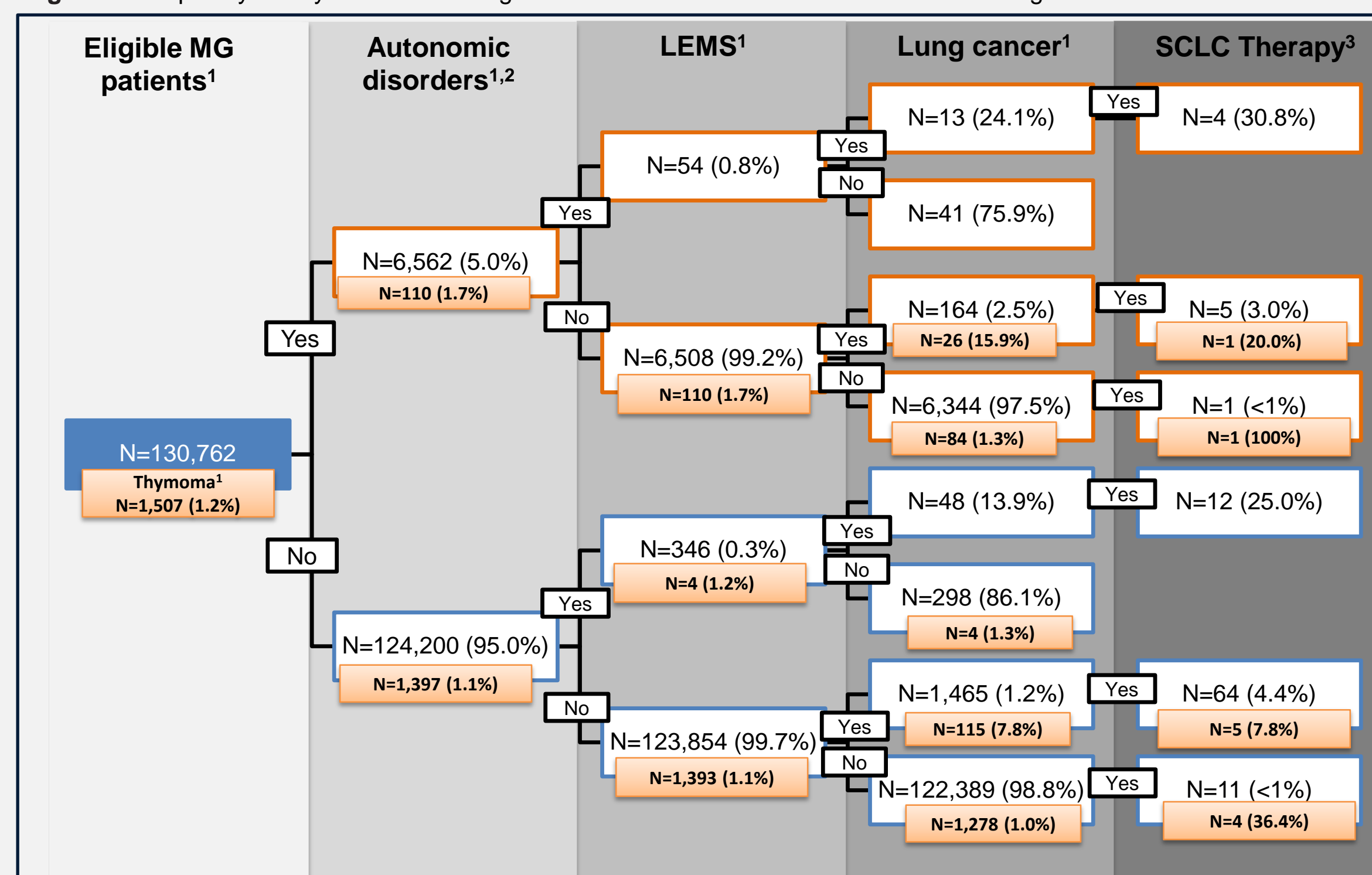
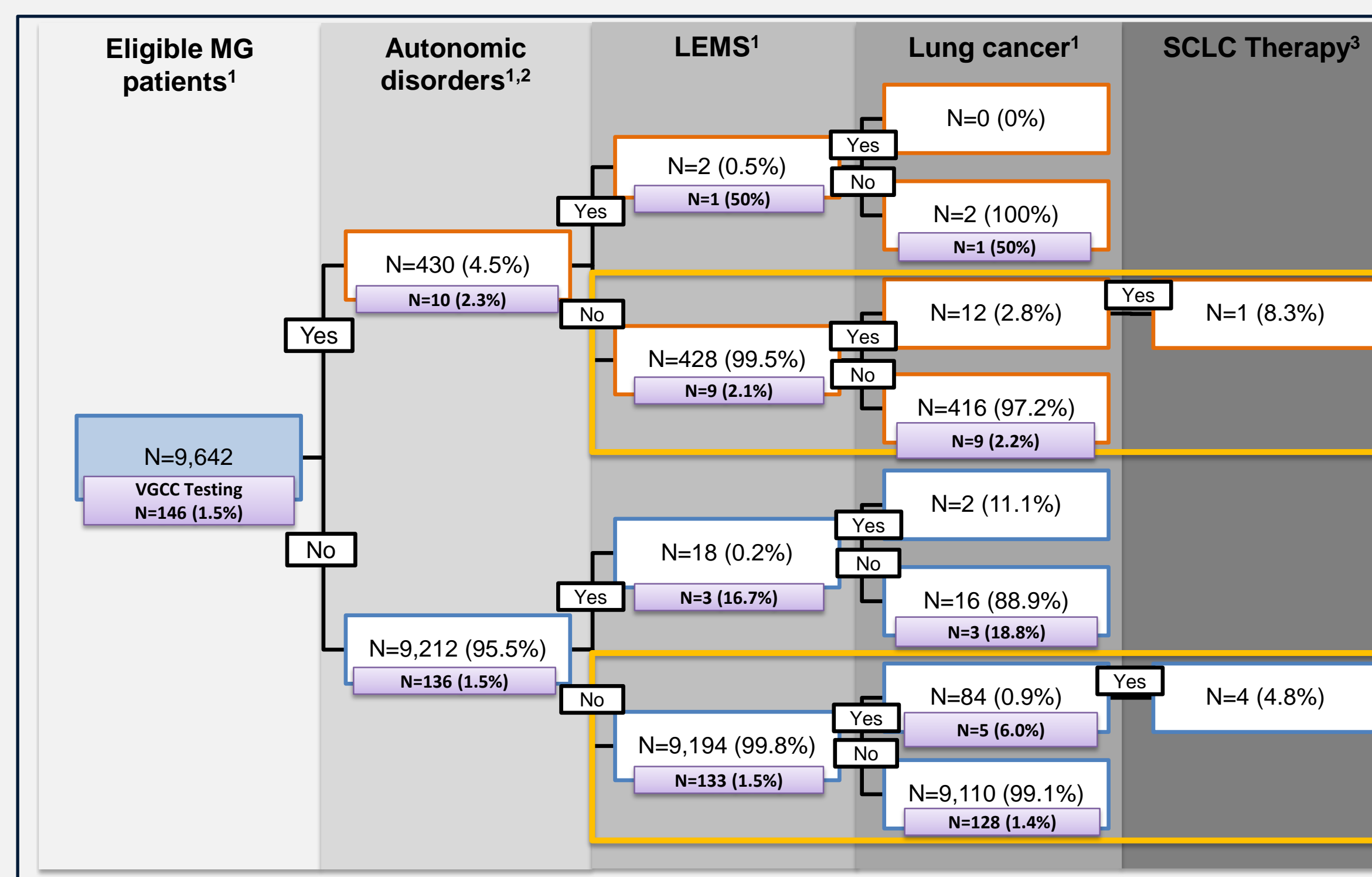


Figure 5. Frequency of VGCC Testing among Patients with an Index MG Diagnosis 1/1/2022 or Later



Potential missed LEMS diagnosis

Potential missed LEMS diagnosis

¹Based on ≥ 2 diagnoses ≥ 30 days apart; ²Includes disorders of the autonomic nervous system, hypotension, and/or orthostatic hypotension; ³SCLC-associated therapies include etoposide and platinum-based chemotherapy; ⁴Defined as a single LEMS claim. VGCC, voltage-gated calcium channel.

Study cohort

- 130,762 patients with MG (51% female) were eligible for inclusion in the study.
 - Patients with LEMS diagnoses accounted for 0.3% of patients with MG, whereas patients with MG diagnoses accounted for 20% of patients with LEMS.
 - Autonomic dysfunction claims were observed in 5.0% of patients with MG.
- 1,690 patients (1.3% of patients with MG) had lung cancer claims.
 - Lung cancer claims were ~10x more frequent among patients with MG with LEMS diagnoses vs. those without LEMS diagnoses, while thymoma occurred at a similar frequency. (Figure 2)

Autonomic disorders

- LEMS diagnoses were more frequent in patients with MG and autonomic dysfunction (0.8%) than in patients with MG without autonomic dysfunction (0.3%). (Figure 3)
- Autonomic dysfunction was more common among patients with LEMS diagnoses (13.5%) than among patients without LEMS diagnoses (5.0%).
- Claims for lung cancer were more frequent in patients with autonomic dysfunction and without LEMS (2.5%) relative to those without autonomic dysfunction and without LEMS (1.2%).
 - This difference in the rate of lung cancer suggests a group of patients who are more likely to have a missed diagnosis of LEMS.

Thymoma-related diagnoses

- The evaluation of thymoma-related diagnoses and autonomic dysfunction among patients with MG are illustrated in Figure 4.
 - No thymoma-related diagnoses were observed among patients with autonomic symptoms and LEMS.
 - On balance, while some (n=4) thymoma claims were observed among patients with LEMS, these analyses were generally consistent with thymoma occurring among patients with MG who did not have LEMS diagnoses.
- Among 6,508 patients with MG and autonomic dysfunction, without a LEMS diagnosis, 138 patients were diagnosed with non-thymoma lung cancer.
 - Among them, of those who received SCLC therapies (n=4/138), none had LEMS codes in their claims history.

LEMS diagnostic testing

- In a subset of 9,642 patients with MG diagnoses 1/1/2022 or later, VGCC antibody testing claims were infrequent but more common when autonomic dysfunction was present (2.3% vs 1.5%). (Figure 5)
- Among 146 patients with MG who received VGCC tests, 2.7% were diagnosed with LEMS.
 - VGCC positivity appeared higher among patients with autonomic disorders: 10% in MG with autonomic disorders vs. 2.2% in MG without autonomic disorders.

Limitations

- The claims data used in this analysis relies upon ICD coding and may not capture all diagnoses or symptoms. In addition, cash-paying and uninsured patients are not captured in the database.
- Diagnoses of MG and LEMS were limited to those observed during the study window.
- Autonomic disorder evaluation was limited by the definition applied in our analyses and may have missed patients with autonomic symptoms including dry mouth.
- AChR status was not available in the administrative claims database; MG patients with autonomic symptoms may be seronegative.
- Results of VGCC testing were not available in the administrative claims database; however, the predictive value of this test is implied by corresponding LEMS diagnoses.

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