RESEARCH ARTICLE

Hospitalizations and Mortality From Myasthenia Gravis

Trends From 2 US National Datasets

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Abstract

Background and Objectives

Myasthenia gravis (MG) is a rare neuromuscular disorder where IgG antibodies damage the communication between nerves and muscles, leading to muscle weakness that can be severe and have a significant impact on patients' lives. MG exacerbations include myasthenic crisis with respiratory failure, the most serious manifestation of MG. Recent studies have found MG prevalence increasing, especially in older patients. This study examined trends in hospital admissions and in-hospital mortality for adult patients with MG and readmissions and post-discharge mortality in older (65 years or older) adults with MG.

Methods

Data from the Nationwide Inpatient Sample (NIS), an all-payer national database of hospital discharges, were used to characterize trends in hospitalizations and in-hospital mortality related to MG exacerbations and MG crisis among adult patients aged 18 years or older. The Medicare Limited Data Set, a deidentified, longitudinal research database with demographic, enrollment, and claims data was used to assess hospitalizations, length of stay (LOS), readmissions, and 30-day postdischarge mortality among fee-for-service Medicare beneficiaries aged 65 years or older. The study period was 2010–2019. Multinomial logit models and Poisson regression were used to test for significance of trends.

Results

Hospitalization rates for 19,715 unique adult patients and 56,822 admissions increased from 2010 to 2019 at an average annualized rate of 4.9% (MG noncrisis: 4.4%; MG crisis: 6.8%; all $p < 0.001$). Readmission rates were approximately 20% in each study year for both crisis and noncrisis hospitalizations; the in-hospital mortality rate averaged 1.8%. Among patients aged 65 years or older, annualized increases in hospitalizations were estimated at 5.2%, 4.2%, and 7.7% for all, noncrisis, and crisis hospitalizations, respectively (all $p < 0.001$). The average LOS was stable over the study period, ranging from 11.3 to 13.1 days, but was consistently longer for MG crisis admissions. Mortality among patients aged 65 years or older was higher compared with that in all patients, averaging 5.0% across each of the study years.

Discussion

Increasing hospitalization rates suggest a growing burden associated with MG, especially among older adults. While readmission and mortality rates have remained stable, the increasing hospitalization rates indicate that the raw numbers of readmissions—and deaths—are also increasing. Mortality rates are considerably higher in older patients hospitalized with MG.

Introduction

Myasthenia gravis (MG) is a rare neuromuscular disorder where IgG antibodies damage the communication between nerves and muscles, leading to muscle weakness that can be severe

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Glossary

FFS = fee-for-service; **HCUP** = Health care Cost and Utilization Projects; **LDS** = Limited Data Set; **LOS** = length of stay; **MG** = Myasthenia gravis; **MGAE** = MG with acute exacerbation; **NIS** = Nationwide Inpatient Sample; **NRD** = Nationwide Readmissions Database.

and have a significant impact on patients' lives. Estimated prevalence has varied widely and increased over time, with estimates of approximately 10–35 per 100,000 in the United States.[1-5] The increase in MG prevalence is likely due to improved case identification, better treatment, and an aging population with increased life expectancy.[1,2,6] In particular, while incidence has remained stable, improvements in health care and life expectancy have led to greater burden of MG among older age groups.[7] Environmental and genetic factors may also play a role in the increasing prevalence.[6]

Myasthenic crisis with respiratory failure (MG crisis) is the most serious manifestation of MG, requiring mechanical ventilation and measures to alleviate the neuromuscular blockade including treatment/removal of triggering factors, use of plasma exchange, and IV immunoglobulin.[8]

A recent analysis of the Health care Cost and Utilization Projects (HCUP) National Inpatient Sample (NIS) found the annual number of discharges for MG with acute exacerbation (MGAE) increased >70% from 2004 to 2014, peaking at 6,365. The increase was the greatest for the 65–84 years age group, followed by ages 45–64 years.[9] The increasing prevalence in older patients is concerning because this vulnerable group is more likely to face delayed or incorrect diagnosis and has a greater chance of mortality from MG.[10-12] Older age and respiratory failure are associated with increased risk of death.[13]

Nationally representative studies of US mortality due to MG are limited, and based on existing literature, seem lower than other countries. Using the NIS data, one study found the rate of in-hospital death for MGAE varied from 1.5% to 2.6% from 2004 to 2016,[9] while another study estimated a higher rate of 4.5% between 2000 and 2005 (2.2% for MG overall, that is, with or without acute exacerbation).[13] A retrospective multicenter German study using rigorous criteria for case selection identified a 12% mortality rate among patients experiencing myasthenic crisis and requiring ventilatory support.[14] A population-based study of Chinese hospitals from 2016 to 2018 found an even higher mortality rate of 14.7%.[15]

Readmission rates for patients experiencing MGAE or MG crisis are scarce. Previous estimates using Nationwide Readmissions Database (NRD) of the HCUP found 30-day readmission rates of 16%–17% for patients with MG (with or without acute exacerbation or crisis) using data through 2014, with greater comorbidities associated with increased risk of readmission.[16,17]

Current estimates on hospital admissions, readmissions, and mortality in patients with MG, particularly MGAE and MG crisis, are limited. Differences in these outcomes by age group, especially among older vs younger adults, are largely unexamined. The goals of this study were to examine hospital admissions and in-hospital mortality for patients with MG and readmissions and postdischarge mortality in older adults. We also assessed outcomes for hospitalizations involving MG crisis, the most severe clinical event. In addition to using HCUP data, ours is the first study to examine trends in MGAE and MG crisis hospitalization outcomes using the Medicare Limited Data Set (LDS), which allows examination of patient-level readmissions and postdischarge mortality in older patients.

Methods

Data Sources

The National (Nationwide) Inpatient Sample

The Health care Cost and Utilization Project (HCUP) is a collection of databases sponsored by the Agency for Health care Research and Quality. It includes the largest collection of longitudinal hospital data in the United States and includes all payers and data at the encounter level. Data are collected from a 20% stratified sample of community hospitals and are weighted to be nationally representative. The National (Nationwide) Inpatient Sample (NIS) is one of the component databases of the HCUP and provides information on more than 7 million hospital stays each year. Weights are provided to allow nationally representative estimates. The NIS data are reported at the hospitalization level and cannot be used to follow-up patients over time or track readmissions.[18] Outcomes examined using the NIS were the number of MG discharges and in-hospital mortality.

The Medicare Limited Dataset

The Medicare LDS is a deidentified, longitudinal database publicly available to researchers through the Centers for Medicare & Medicaid Services. The LDS data include enrollment and demographic information, including mortality, and adjudicated claims covered by Medicare Part A (inpatient care) and Part B (physician services and other outpatient care). These data allow individuals to be followed up over time because hospitalizations, other health care encounters, enrollment, and demographic data are reported at the patient level. In the Medicare LDS data, demographic and enrollment information, including mortality, are reported in the Master Beneficiary Summary file, with deaths and death dates

Table 1 ICD-9 and ICD-10 Diagnosis and Procedure Codes for Patient Selection and Identification

	ICD-9	ICD-10	Code description
Principal diagnosis	358.01	G70.01	Myasthenia gravis with (acute) exacerbation[a]
	358.00	G70.00	Myasthenia gravis without (acute) exacerbation[a]
Secondary diagnosis of respiratory failure	518.81	J96.00	Acute respiratory failure, unspecified whether with hypoxia or hypercapnia[a]
		J96.01	Acute respiratory failure with hypoxia[a]
		J96.02	Acute respiratory failure with hypercapnia[a]
Endotracheal intubation	96.04	0BH17EZ	Insertion of endotracheal airway into trachea, through natural or artificial opening
		0BH13EZ	Insertion of endotracheal airway into trachea, percutaneous approach
		0BH18EZ	Insertion of endotracheal airway into trachea, through natural or artificial opening endoscopic
CPAP or BiPAP noninvasive ventilation	93.90	5A09357	Assistance with respiratory ventilation, less than 24 consecutive hours, continuous positive airway pressure
		5A09457	Assistance with respiratory ventilation, 24–96 consecutive hours, continuous positive airway pressure
		5A09557	Assistance with respiratory ventilation, greater than 96 consecutive hours, continuous positive airway pressure
		5A1935Z	Respiratory ventilation, less than 24 consecutive hours
		5A1945Z	Respiratory ventilation, 24–96 consecutive hours
		5A1955Z	Respiratory ventilation, greater than 96 consecutive hours
		Z99.11	Dependence on respirator [ventilator] status[a]

[a] Indicates diagnosis code; remaining codes are procedure codes.

primarily validated from the Social Security Administration. Approximately 96% of death dates are validated.[19] This is in contrast to deaths recorded in the NIS, which are taken only from hospital discharge records.[20]

This analysis used LDS 100% claims data from January 2010 to December 2020. These data include all hospitalizations for fee-for-service (FFS) Medicare beneficiaries but exclude Medicare Advantage patients; the proportion of FFS Medicare patients has steadily declined over time, reaching 61% of all Medicare-covered individuals in 2020.[21] We restricted the sample to age-eligible (65 years or older) beneficiaries to focus on older adults. Outcomes examined using the LDS data were number of discharges, 30-day readmission rates, in-hospital mortality, and 30-day postdischarge mortality.

Patient Selection Criteria

Patients with MGAE were identified through ICD-9 or ICD-10-CM MG diagnosis codes in the principal position (ICD-9-CM: 358.01; ICD-10-CM: G70.01). The principal position diagnosis is "the condition established after study to be chiefly responsible for the admission."[22] We limited patients to those with a principal position diagnosis for MG to ensure that our study focused on patients hospitalized for MG.

In addition to selecting patients with MGAE, we identified patients experiencing myasthenic crisis (MG crisis). Myasthenic crisis was identified by a principal diagnosis of MG (with or without exacerbation) plus at least one of a secondary diagnosis of respiratory failure, a procedure code for endotracheal intubation, or a procedure code for CPAP/BiPAP noninvasive ventilation. We segmented our study sample into 2 groups: MGAE without crisis (MGAE) and MG with crisis (MG crisis). Our study thus defined a person as having MG crisis even if the ICD-9 or ICD-10 code indicates "without exacerbation" so long as they have additional codes indicating respiratory failure. Table 1 summarizes the ICD-9 and ICD-10 codes used in the study. For analyses using the NIS data, patients with MG were excluded if they were younger than 18 years, if their admission type indicated a transfer to another short-term hospital, or if their age or sex had a missing value. For the analyses using the LDS data, we limited to patients older than 65 years to focus on hospitalizations for older patients.

Outcomes

For purposes of comparison, we analyzed LDS and NIS admission characteristics and outcomes for years 2010–2019, the years that are available in both datasets. We then analyzed outcomes for 2020 LDS admission separately.

Sample Characteristics

For each dataset, we examined characteristics of hospitalizations for MGAE and myasthenic crisis (MG crisis), including age, sex, race, region, payer, and the proportion of admissions

Table 2 Patient and Admission-Level Characteristics Across All Years of Sample

Admission characteristic	LDS admission level (2010–2019), N = 19,715	NIS admission level[a] (2010–2019), N = 56,822
Age group (%)		
18–44		12,827 (22.6)
45–64		17,613 (31.0)
65–84	17,243 (87.5)	23,391 (41.2)
85+	2,472 (12.5)	2,992 (5.3)
Sex (%)		
Female	9,069 (46.0)	32,823 (57.8)
Region (%)		
Northeast	3,718 (18.9)	10,845 (19.1)
Midwest	4,514 (22.9)	10,880 (19.1)
South	8,712 (44.2)	24,876 (43.8)
West	2,735 (13.9)	10,222 (18.0)
Unknown	36 (0.2)	N/A
Race (%)		
White	18,177 (92.2)	37,430 (65.9)
Black	769 (3.9)	9,742 (17.1)
Asian	154 (0.8)	1,011 (1.8)
Hispanic	246 (1.2)	5,162 (9.1)
North American Native	64 (0.3)	176 (0.3)
Other	172 (0.9)	1,310 (2.3)
Unknown	133 (0.7)	N/A
Crisis admissions (%)		
% with MG crisis	5,574 (28.3)	12,558 (21.1)

Abbreviation: MG = Myasthenia gravis; NIS = Nationwide Inpatient Sample.
[a] NIS statistics are weighted to be nationally representative.

with crisis. For the NIS dataset, these statistics are reported at the admission level due to the lack of patient-level data. For the LDS data, the statistics are reported at the beneficiary level, and for comparison with the NIS, at the admission level as well.

MG Discharges

Using the NIS data, hospitalizations for MGAE and MG crisis were counted by year. The total number of discharges were reported overall and by age group (18–44, 45–64, 65–84, and older than 85 years) and the presence of MG crisis.

Using the LDS data, hospitalizations were also counted by year and the total number of discharges reported overall, by age group (65–84, older than 85 years) and the presence of MG crisis.

Length of Stay

For LDS admissions, we calculated LOS as the difference between admission and discharge date. If a discharge and new admission occurred on the same date or 1 day apart, they were considered a single hospitalization.

Readmissions

Using the LDS data, readmissions were defined as admission for any reason within 30 days after an MG hospitalization discharge. Claims with an admission date that was equal to or 1 day after a discharge date were counted as an admission, not a readmission.

Mortality

In-hospital mortality was calculated separately using the NIS and LDS data sources. In the NIS, in-hospital death is confirmed through the discharge disposition of the patient as recorded by the hospital. In the Medicare data, deaths are confirmed by reference to Social Security deaths and reported in 3 fields. The NCH patient status indicator code (NCH_PTNT_STATUS_IND_CD) is reported on inpatient claims and indicates whether the beneficiary was discharged, died, or was still a patient. The patient discharge status code (PTNT_DSCHRG_STUS_CD) reports the status of the patient as of the claim through date. Beneficiary death dates are also recorded in the Medicare Master Beneficiary Summary File. In-hospital death for the LDS was defined as a death recorded in any of these sources on or before the discharge date.

In addition to in-hospital mortality, the LDS allowed us to examine 30-day postdischarge mortality because we could follow-up patients over time. Thirty-day mortality included death within the hospital and a death date within 30 days of discharge. Mortality was reported for NIS and LDS analyses both overall and by age group and the presence of MG crisis.

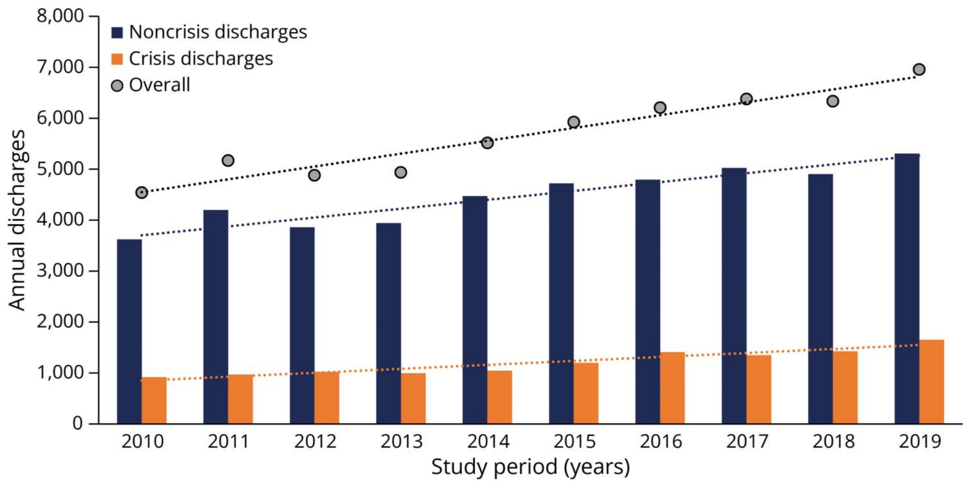
Data Analysis

Descriptive results were generated and reported for demographic characteristics of admissions and hospitalization outcomes. Due to the overlapping samples in the LDS and NIS data and the inability to identify admissions from the same patient in the NIS data, differences in results between the 2 datasets were not statistically tested.

To test for the significance of trends over time, we modeled discharges with a linear time trend. For the NIS data, we used a multinomial logit model to predict MG admissions by age group and the presence of crisis after controlling for admission-level characteristics including age, sex, race, region, and payer. For the LDS data, we used a Poisson regression to predict counts of MG admissions by the presence of crisis. The log of total admissions was included as a covariate to control for the trends in overall sample characteristics and number of admissions.

Due to the overlapping samples in the LDS and NIS data and the inability to identify admissions from the same patient in

Figure 1 Annual MGAE Discharges, With and Without Crisis (NIS)



the NIS data, differences in results between the 2 datasets were not statistically tested. A standard significance threshold of $p < 0.05$ was used for testing of trends.

Data Availability

The NIS and LDS data sources used in this study are deidentified and publicly available to researchers.

Results

Patient and Hospitalization Characteristics

Table 2 contains demographic information for the NIS and LDS hospitalized patients. In the NIS sample, slightly more than half of hospitalizations were for patients between ages 18 and 64 years, and more than half (57.8%) were for female patients, likely reflecting the higher incidence of MG among younger women, with a female to male ratio of 3:1 for early-onset MG (before 40 years of age).[4] Approximately two-third of all MG hospitalizations in the NIS data were for White patients; 17% were for Black, and 9% for Hispanic. Approximately 1 in 5 (21.1%) of all hospitalizations were for MG crisis.

In the LDS sample, where hospitalizations were limited to those for patients aged 65 years or older, just under half (46.1%) were for female patients. The regional distribution of these hospitalizations was similar to the NIS, but a larger proportion were for White patients; far fewer were for Black (3.8%) or Hispanic (1.2%) patients. Nearly 3 in 10 (28.7%) hospitalizations for these older patients were for MG crisis, a higher rate than in the NIS data.

MG Discharges

NIS MG Discharges (All Ages)

As shown in Figure 1, using the NIS data, hospitalizations increased substantially over our study period, growing 53%, from a low in 2010 of 4,540 discharges to a high in 2019 of 6,955 discharges. With an unadjusted linear trend, this is an average annual increase of 4.6% per year. After controlling for patient characteristics using a multinomial logit regression, there was a statistically significant annualized increase of 4.9% from 2010 to 2019 ($p < 0.001$). Noncrisis discharges formed the majority of MGAE discharges, averaging 78.9% of the discharges across all years.

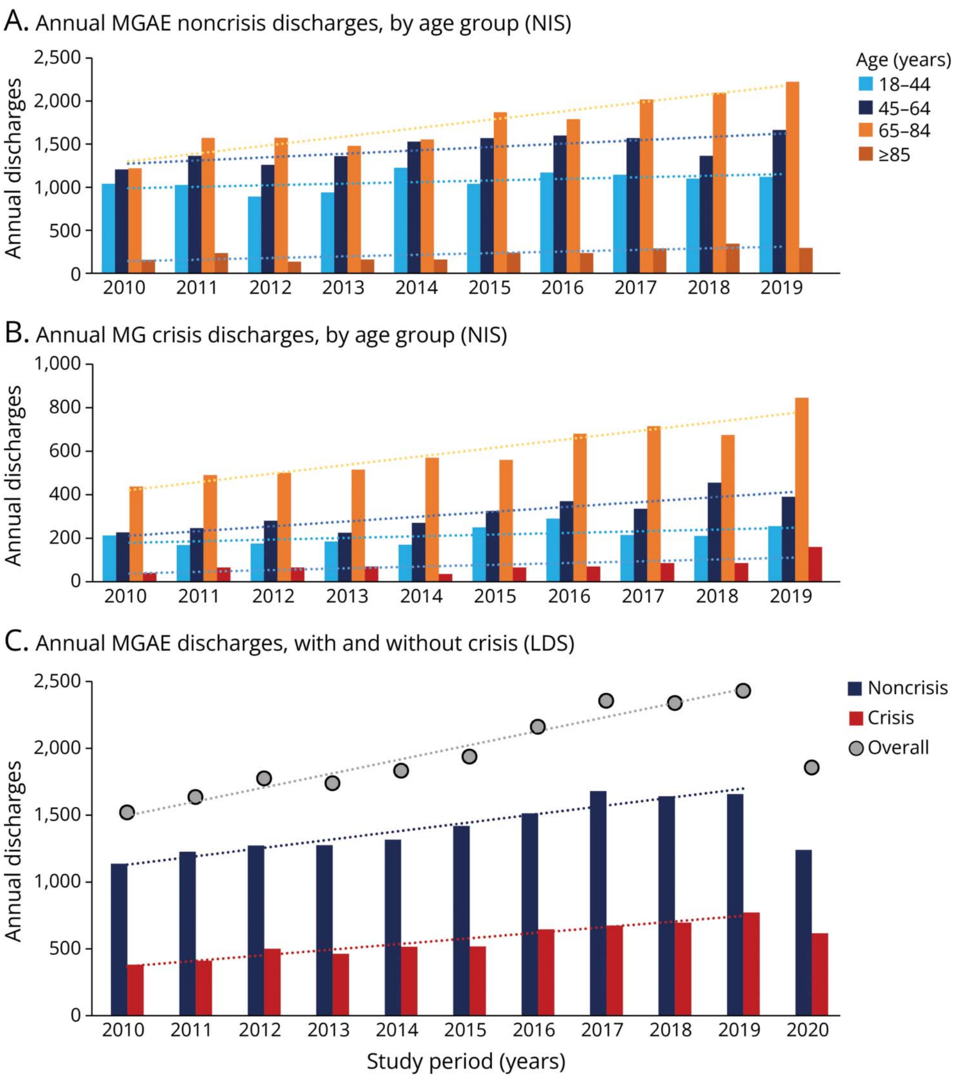
Both MG crisis and noncrisis discharges showed upward trends as well. MGAE noncrisis discharges increased 46%, from a low of 3,623 in 2010 to a high of 5,305 in 2019. With an unadjusted linear trend, this is an average annualized increase of 4.0% per year. After adjusting for patient characteristics, the modelled trend showed a statistically significant annualized increase of 4.4% ($p < 0.001$).

MG crisis discharges increased 80%, from a low of 917 in 2010 to a high of 1,650 in 2019. With an unadjusted linear trend, this is an average increase of 9.2% per year. The modelled trend for this period showed an annualized increase of 6.8% in MG crisis discharges ($p < 0.001$).

Regression results and fit criteria are available on request. As shown in Figure 2A, MGAE noncrisis discharges increased over our study period in all age groups, with the largest increases in the oldest patients. Hospitalizations for patients in the 65–84 years and 85 years or older age groups nearly doubled over the period, increasing 91% and 87%, respectively. Hospitalizations for individuals aged 65–84 years were the largest proportion of all MGAE noncrisis discharges, at 38.8%, and drove the overall increase in noncrisis discharges.

After controlling for patient characteristics in a multinomial logit model, trends for all age groups were statistically significant, showing an average annualized increase of 2.7% for

Figure 2 Annual Discharges for MGAE With and Without Crisis By Age Group From the NIS Between 2010 and 2019, and MGAE Without and With MG Crisis From the Medicare LDS Between 2010-2020



ages 18–44 years, 3.0% for ages 45–64 years, 5.5% for ages 65–84 years, and 14.1% for ages 85 years or older ($p = 0.012$; $p = 0.001$; $p < 0.001$; and $p < 0.001$, respectively). Regression results are available on request.

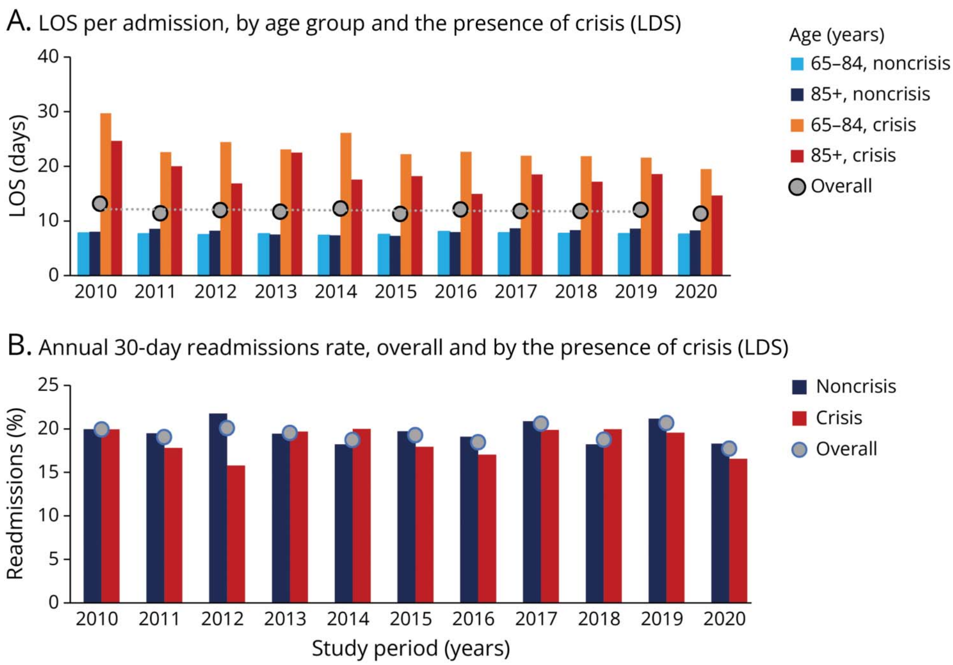
As shown in Figure 2B, MG crisis discharges also increased in all age groups over our study period. The greatest increase was in hospitalizations for the oldest patients (aged 85 years or older), with 4 times as many hospitalizations in 2019 compared with those in 2010. As with MGAE noncrisis discharges, hospitalizations for individuals in the 65–84 years age group were more numerous than in any other age group, with a 1.8-fold increase from 2010 to 2019.

After controlling for patient characteristics in a multinomial logit model, trends for all age groups were statistically significant, showing an average annualized increase of 3.7% for ages 18–44 years, 7.5% for ages 45–64 years, 6.4% for ages 65–84 years, and 17.6% for ages 85 years or older ($p = 0.045$; $p < 0.001$; $p < 0.001$; and $p < 0.001$, respectively). Regression results are available on request.

LDS: MG Discharges (Age 65 Years and Older)

Using the LDS data, we examined overall, crisis, and noncrisis discharges for individuals aged 65 years and older, from 2010 through 2020. As shown in Figure 2C, the numbers of total, noncrisis, and crisis hospitalizations in 2019 compared with those in 2010 were 1.6, 1.5, and 2.0 times higher, respectively, corresponding to average annualized increases of 5.0%, 4.1%, and 7.1%. MG crisis admissions as a proportion of the total also grew over the period, from 25.1% in 2010 to 31.8% in 2019. The LDS data are available through 2020, and notably, the year 2020 saw a marked drop in discharges, with a decline of 23.6% from the prior year (20.2% for noncrisis and 25.2% for crisis). This decline likely reflected the COVID-19 pandemic.

Figure 3 Length of Stay and Hospital Readmission Rates Amongst Patients Admitted With and Without MG Crisis From the Medicare LDS Between 2010 and 2020



After controlling for trends in all-cause admissions with Poisson regression, the average annualized increases from 2010 to 2019 in total, noncrisis, and crisis discharges were 5.2%, 4.2%, and 7.7%, respectively (all $p < 0.001$). Regression results are available on request.

LDS Discharges: Length of Stay

Figure 3A shows length of stay (LOS) per admission for older patients, stratified by age group and the presence of MG crisis. The average LOS was relatively stable over the study period, ranging from 11.3 in 2015 to 13.1 in 2010. LOS was consistently longer for MG crisis admissions, with the longest LOS for patients aged 65–84 years. While LOS showed more variation for crisis admissions than for noncrisis, it was shorter at the end of the study period, compared with the start (age 65–84 years: 29.7 days in 2010 vs 21.6 days in 2019 vs 19.5 days in 2020; age 85 years or older: 24.6 days in 2010 vs 18.6 days in 2019 vs 14.7 days in 2020).

LDS: 30-Day All-Cause Readmissions

The Medicare LDS data were used to examine all-cause 30-day readmissions among patients aged 65 years or older, as shown in Figure 3B. The combined 30-day readmission rate for MGAE and MG crisis averaged 19.5% from 2010 to 2019. The average readmission rates following an admission for MG crisis were slightly lower than those for noncrisis (18.8% vs 19.8%). While the number of admissions dropped in 2020, the absolute number of readmissions also dropped, leading to a relatively stable readmissions rate over all years of our study period. However, the lowest readmission rate of 10.7% occurred in 2020. The readmission rate did not show a strong trend by crisis or noncrisis admission.

Readmission rates for 2010 through 2019 were slightly higher for noncrisis patients aged 65–84 years, compared with those older than 85 years, on average (19.3% vs 17.8%), with a larger difference in readmissions following MG crisis hospitalizations (aged 65–84 years: 19.3% vs aged older than 85 years: 15.3%).

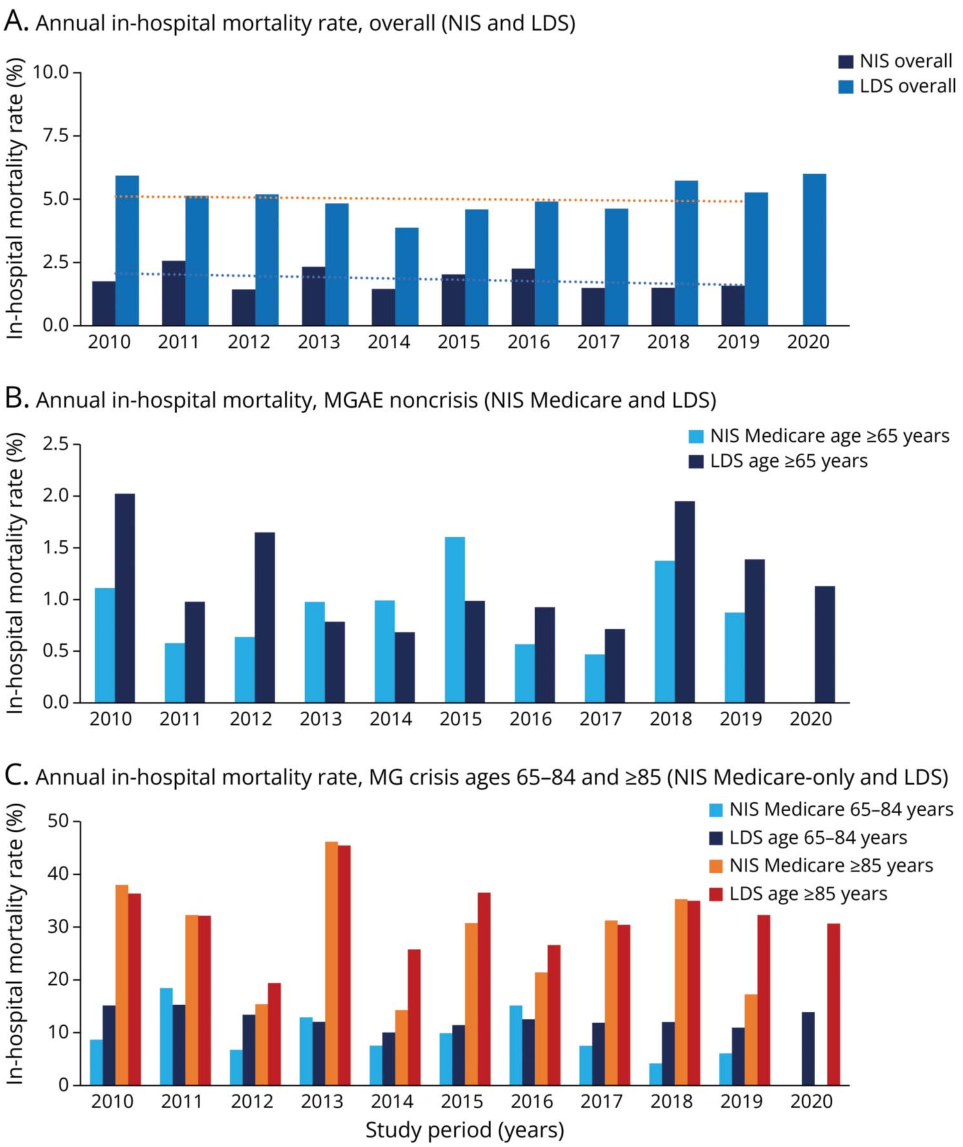
NIS and LDS: Mortality

In-Hospital Mortality

The NIS overall in-hospital mortality rate averaged 1.8% from 2010 to 2019, reflecting mortality across hospitalizations for individuals in all age groups. The LDS rate for these years, which reflected mortality for patients aged 65 years or older only, was considerably higher, averaging 5.0% (Figure 4A). The mortality rate declined slightly for admissions from both data sources for the years 2010–2019. Notably, the LDS data study period extended through 2020. The observed in-hospital death rate was 6.0% in that year, higher than any other, and coinciding with the first year of the COVID-19 pandemic in the United States.

When the NIS data were limited to MGAE noncrisis patients aged 65 years or older with Medicare coverage, the in-hospital death rate averaged 0.9% from 2010 to 2019, higher than for all ages, but lower than the 1.2% reported in the LDS data. There was a slight downward trend in both data sources. In-hospital mortality for patients aged 65–84 years and 85 years

Figure 4 Comparison of Annual In-Hospital Mortality Amongst Older (≥65 years) Patients From the NIS and Medicare LDS Between 2010 and 2020



or older was higher, on average, in the LDS data, compared with the NIS data for both age groups.

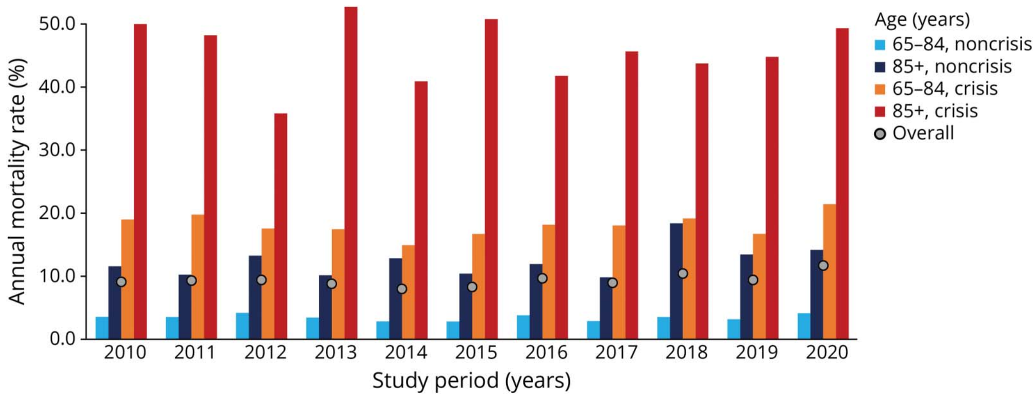
Notably, the numbers of both MGAE noncrisis admissions and in-hospital deaths reported in LDS decreased in 2020, leading to an in-hospital mortality rate that was within the range of previous years. Figure 4B shows the in-hospital mortality rate age group and data source.

Among patients aged 65 years or older with Medicare coverage hospitalized with MG crisis, in-hospital mortality rates were higher in the LDS data for years 2010–2019, compared with the NIS. Specifically, in the 65–84 years age group, the NIS rate was 9.4% vs 12.2% in the LDS. In the 85 years or older age group, the average NIS rate across all years in the sample was 27.4% vs 31.5% in the LDS. The mortality rates varied widely among patients aged 85 years or older in each data source, ranging from 17.2% to 46.2% in the NIS data and from 19.4% to 45.5% in the LDS data, reflecting relatively small numbers of patients and a high variance outcome in this age group. Figure 4C shows the annual in-hospital mortality rate by age group and data source.

30-Day Postdischarge Mortality

Using the LDS data, we examined 30-day postdischarge mortality. As shown in Figure 5, the average 30-day postdischarge mortality rate from 2010 to 2019 for admissions in the LDS sample was 9.2%, but this varied by the presence/absence of crisis and was highest in the oldest patients. For noncrisis admissions, the 30-day mortality rate was 3.3% for ages 65–84 years and 12.3% for ages 85 years or older. For crisis admissions, the average rate was 17.7% for ages 65–84 years and

Figure 5 Annual 30-Day Post-discharge Mortality Rate, Overall and by Age Group (LDS) Between 2010 and 2020



49.3% for ages 85 years or older. Figure 5 shows the annual rates for each age group and by the presence of MG crisis.

While there was not a clear trend by year, the highest overall annual rate of 11.7% was in 2020, with the COVID-19 pandemic. The highest rate for all groups occurred in this year except for ages 85 years or older with crisis.

Discussion

Discharges for MGAE and MG crisis have increased overall and in all age groups since 2010. After controlling for changing patient characteristics and the overall upward trend in hospitalization, discharges with and without crisis and in all age groups showed statistically significant and meaningful increases. Notably, hospitalizations for patients aged 65–84 years have continued to be greater in numbers than for any other age group, have increased substantially over the study period, and underlie much of the overall increase.

Previous literature has noted an increasing trend in MG incidence.[1-4] Our study demonstrates that this increase is associated with increasing numbers of MG hospitalizations, especially for older patients, who are vulnerable to misdiagnosis, treatment delays, and worse outcomes.[10-12] Some of this increase may reflect demographic changes in the United States because the number of individuals aged 65 years or older increased 38.6% during our study period, from 40.3 million in 2010 to 55.8 million in 2020.[23] Increases in longevity in the United States and other countries, coupled with greater awareness of MG, may also underlie the increase in MG hospitalizations that we observed.[5] It is also possible that new therapeutics such as checkpoint inhibitors have led to a surge in iatrogenic MG/myositis and other neurologic effects.[5,24,25]

Readmission rates are also high for older patients. Using the LDS data, we found overall 30-day readmission rates for MGAE of 19.5% from 2010 to 2019 in patients aged 65 years and older. This estimate is in line with previous estimates using the 2014 Nationwide Readmissions Database of the HCUP, which found readmission rates for patients with MG of all ages of 16%–17%.[16,17] Our estimates, however, are somewhat higher because we restricted to patients with MGAE or MG crisis. These rates are similar to other chronic conditions with acute crises that impose a large burden on the health system. An analysis of the NRD from 2010 to 2018 found a 30-day readmission rate of 19.4% for people with diabetes type 1 after admission for diabetic ketoacidosis.[26] A study of people with heart failure in the same database from 2010 to 2017 found a 30-day readmission rate of 18.2%.[27] All-cause 30-day readmissions rates for Medicare patients aged 65 years or older with any condition were 12.0% in 2018.[28]

The slightly lower readmission rates and the shorter average LOS among the oldest patients (age 85 years or older) may reflect their higher mortality rates. In addition, the large drop in MG admissions and readmissions for older patients in 2020 likely reflected the COVID-19 pandemic. It is possible that patients with MG were less likely to seek treatment in 2020; were discouraged from coming to the hospital when they did; were more cautious with their health due to the immunocompromised states; were treated in the emergency department and discharged without an admission; or MG codes were less likely to be found in the primary position due to the pandemic. It is also possible that hospitalizations were limited to sicker patients over this time.[29]

Our estimates of in-hospital mortality are similar to those previously reported, with global rates varying from 2%–16%, and mortality for MG crisis in the US hospital system estimated at approximately 4.5%.[29] A study using the NIS data from 2000 to 2005 reported an in-hospital mortality rate of 2.2% for patients hospitalized with MG.[13] Our estimate using the NIS data from 2010 to 2019 is lower (1.8%), with the lowest rates in 2016–2019, suggesting that in-hospital mortality for MG may be declining. Our estimates are considerably lower than those from a population-based study of MG admissions in China, where in-hospital MG mortality rates were estimated at 14.7%.[15]

Our analyses of mortality in older patients further highlight the high burden of MG among the older individuals both in the United States and other countries.[29] Among patients with MG crisis hospitalized in Germany, whose median age was 72 years, in-hospital mortality was estimated at 12%, consistent with our estimates for older patients with MG crisis.[14] Among patients with MG hospitalized in China, in-hospital mortality was also considerably higher among those aged 65 years or older.[15]

Our findings suggest that previous literature using the NIS may underestimate MGAE in-hospital mortality in the oldest patients. Using the Medicare LDS data, we found higher in-hospital death rates in Medicare patients aged 65 years or older compared with the NIS, with a 2010–2019 average of 5.0% vs 3.6%. It is possible that the lower rates in NIS reflect the different sampling method and population, with the LDS including all Medicare FFS beneficiaries and the NIS including both traditional and Medicare Advantage beneficiaries while sampling from community hospitals only.[20]

We observed an increase in mortality in 2020, the first year of the COVID-19 pandemic. It is possible that the higher mortality rate reflected admissions for sicker patients who were more likely to die. In addition, the pandemic led to a shortage of intubation equipment, which may have led to delayed or reduced treatment for patients with MG crisis.[30] Furthermore, COVID-19 infection has been shown to exacerbate MG conditions and lead to increased health care utilization and mortality.[31,32] Given the reduction in MG admissions in 2020, it is also possible that some patients with MG died outside the hospital without being admitted. Future studies examining retrospective claims or registry data may be able to estimate the potentially large impact of the COVID-19 pandemic on patients with MG and hospitalizations.

Our study has limitations. While discrepancies in results from the NIS and LDS datasets may be due to data collection and covered population differences and the NIS weighting methodology, we cannot directly compare the 2 study populations. In addition, hospitalization coding practices may vary over time, and across hospitals, affecting our estimates from both datasets. Furthermore, we identified patients with MG with MG diagnosis codes in the principal position only; if diagnoses were recorded differently across MG admissions for contextual or administrative reasons, MG hospitalizations could have been underestimated or misidentified. It is also possible that some patients hospitalized for MG were treated with noninvasive ventilation for coexisting conditions such as sleep apnea, potentially leading to an overestimation of MG crisis hospitalizations and an underestimation of MGAE hospitalizations, particularly among older patients. Excluding these hospitalizations, however, could exclude true crisis patients treated with NIV, leading to underestimation. Results should therefore be treated as estimates only. Finally, our data do not include clinical details, and we cannot definitively identify the reasons underlying the increases in hospitalizations over our study period.

We also did not examine costs of MG admissions, readmissions, and deaths. Given the growing number of MGAE and MG crisis discharges, the high readmission rate, the long LOS, and the high mortality and greater frequency of crisis among older patients, the health and economic burden of MG is likely large and growing.

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