

Differences in Mortality Among Medicare Beneficiaries With and Without Generalized Myasthenia Gravis

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Background

Generalized myasthenia gravis (gMG) demonstrates a bimodal age of onset distribution, affecting individuals in young adulthood (20–40 years) and in later life (55–75 years)¹

Older adults with gMG are particularly vulnerable to poor outcomes, as they often have multiple comorbid conditions that may exacerbate symptoms or complicate treatment selection and tolerability²

There are limited real-world data on mortality among older adults with gMG, most of whom are covered under Medicare in the United States³

Objectives

To assess differences in mortality between Medicare beneficiaries with gMG and those without myasthenia gravis (MG), and to identify predictors of mortality among Medicare beneficiaries with gMG

Methods

Study Design and Data Source

- This retrospective, observational study evaluated Medicare beneficiaries using the 100% Medicare Fee-for-Service database from January 1, 2018, to December 31, 2023
- The study included a cohort of patients with prevalent active gMG and a comparison cohort of patients without MG
- For the gMG cohort, the index date was a randomly selected MG diagnosis date; for the non-MG cohort, it was a randomly selected medical encounter within the study period
- The baseline period consisted of the 12 months preceding the index date and was used to assess patient characteristics, including demographics, comorbidities, MG clinical events, and gMG-related treatments
- The follow-up period spanned from the index date until the earliest of death, end of continuous Medicare eligibility, or end of data availability

Patient Selection Criteria

- Patients in the gMG cohort met the following criteria:
 - At least one MG diagnosis (International Classification of Diseases, Tenth Revision, Clinical Modification [ICD-10-CM] codes G70.00, G70.01)
 - Evidence of active gMG on the index date or during baseline, defined as:
 - At least one MG diagnosis by a neurologist, *and*
 - At least one MG-related inpatient admission or two or more MG-related outpatient visits ≥ 30 days apart, *and*
 - No claims for congenital MG (ICD-10-CM code G70.2)
- Patients in the non-MG cohort met the following criteria:
 - No claims for MG (ICD-10-CM codes G70.00, G70.01, G70.2) during the study period
- Both cohorts additionally met the following criteria:
 - ≥ 18 years old on the index date
 - ≥ 12 months of continuous Medicare Parts A, B, and D eligibility prior to the index date

Statistical Analysis and Outcomes

- Patients without MG were matched 10:1 to patients with gMG by age and index year
- Overlap propensity score weighting balanced potential baseline confounders between cohorts, including demographics, key comorbidities, and Quan-Charlson Comorbidity Index (standardized difference $< 10\%$ was considered balanced)⁴
- Mortality during the follow-up period was evaluated using Kaplan–Meier analysis with the log-rank test and Cox proportional hazards models censoring survivors at the end of follow-up
- A multivariable Cox proportional hazards model was used to assess predictors of all-cause mortality among the gMG cohort
- Statistical significance was determined using a 5% threshold ($p < 0.05$)

Results

Patient Characteristics

Baseline demographics and clinical characteristics were well balanced in weighted cohorts

Characteristic*	gMG Cohort (N=37,321)	Non-MG Cohort (N=373,210)	Std. diff. (%)
Age at index date, years	74.2 \pm 10.3 [75.0]	74.4 \pm 9.9 [75.0]	1.5
Sex, female	17,592 (47.1)	176,150 (47.2)	0.1
Race/ethnicity			
Non-Hispanic White	32,080 (86.0)	320,534 (85.9)	0.2
Black	1,896 (5.1)	19,099 (5.1)	0.2
Hispanic	1,520 (4.1)	15,262 (4.1)	0.1
Asian	668 (1.8)	6,736 (1.8)	0.1
Multiple or other	345 (0.9)	3,460 (0.9)	0.0
Unknown	813 (2.2)	8,119 (2.2)	0.0
Geographic region			
South	14,929 (40.0)	149,229 (40.0)	0.0
Midwest	8,628 (23.1)	86,257 (23.1)	0.0
Northeast	7,521 (20.2)	75,192 (20.1)	0.0
West	6,201 (16.6)	62,103 (16.6)	0.1
Other or unknown	41 (0.1)	415 (0.1)	0.0
Dual eligibility with Medicaid	5,661 (15.2)	57,004 (15.3)	0.3
Year of index date			
2019	6,576 (17.6)	65,778 (17.6)	0.0
2020	7,087 (19.0)	70,883 (19.0)	0.0
2021	6,663 (17.9)	66,624 (17.9)	0.0
2022	7,292 (19.5)	72,917 (19.5)	0.0
2023	9,703 (26.0)	97,008 (26.0)	0.0
Common physical comorbidities			
Hypertension	30,306 (81.2)	286,898 (76.9)	10.6*
Dyslipidemia	28,284 (75.8)	278,278 (74.6)	2.8
Cardiac arrhythmias	15,470 (41.5)	133,606 (35.8)	11.6*
Diabetes	15,246 (40.9)	123,511 (33.1)	16.1*
Obesity	13,946 (37.4)	102,561 (27.5)	21.1*
Chronic pulmonary disease	11,483 (30.8)	114,740 (30.7)	0.1
Renal failure	9,095 (24.4)	90,890 (24.4)	0.0
Valvular disease	8,848 (23.7)	88,391 (23.7)	0.1
Heart failure and cardiomyopathy	8,094 (21.7)	80,895 (21.7)	0.0
Solid tumor without metastasis	6,901 (18.5)	68,943 (18.5)	0.0
Liver disease	4,023 (10.8)	40,191 (10.8)	0.0
Acute myocardial infarction	3,742 (10.0)	37,388 (10.0)	0.0
Pulmonary circulation disorder	3,375 (9.0)	33,718 (9.0)	0.0
Quantitative CCI, excluding rheumatoid disease	2.2 \pm 2.4 [2.0]	2.2 \pm 2.5 [2.0]	0.1
MG characteristics ⁵			
≥ 1 MG exacerbation	12,863 (34.5)	–	–
≥ 1 Myasthenic crisis	608 (1.6)	–	–
Treatments			
AChE inhibitor	25,175 (67.5)	–	–
Systemic corticosteroid	21,798 (58.4)	–	–
Nonsteroidal immunosuppressant	12,614 (33.8)	–	–
Immunoglobulin	4,097 (11.0)	–	–
Inpatient surgical procedure	10,479 (28.1)	–	–

*Data are presented as mean \pm SD [median] or n (%). **MG characteristics and treatments were reported only among the gMG cohort. *Indicates a Std. diff. $\geq 10\%$. AChE=acetylcholinesterase, gMG=generalized myasthenia gravis, MG=myasthenia gravis, Quan-CCI=Quan-Charlson Comorbidity Index, SD=standard deviation, Std. diff.=standardized difference.

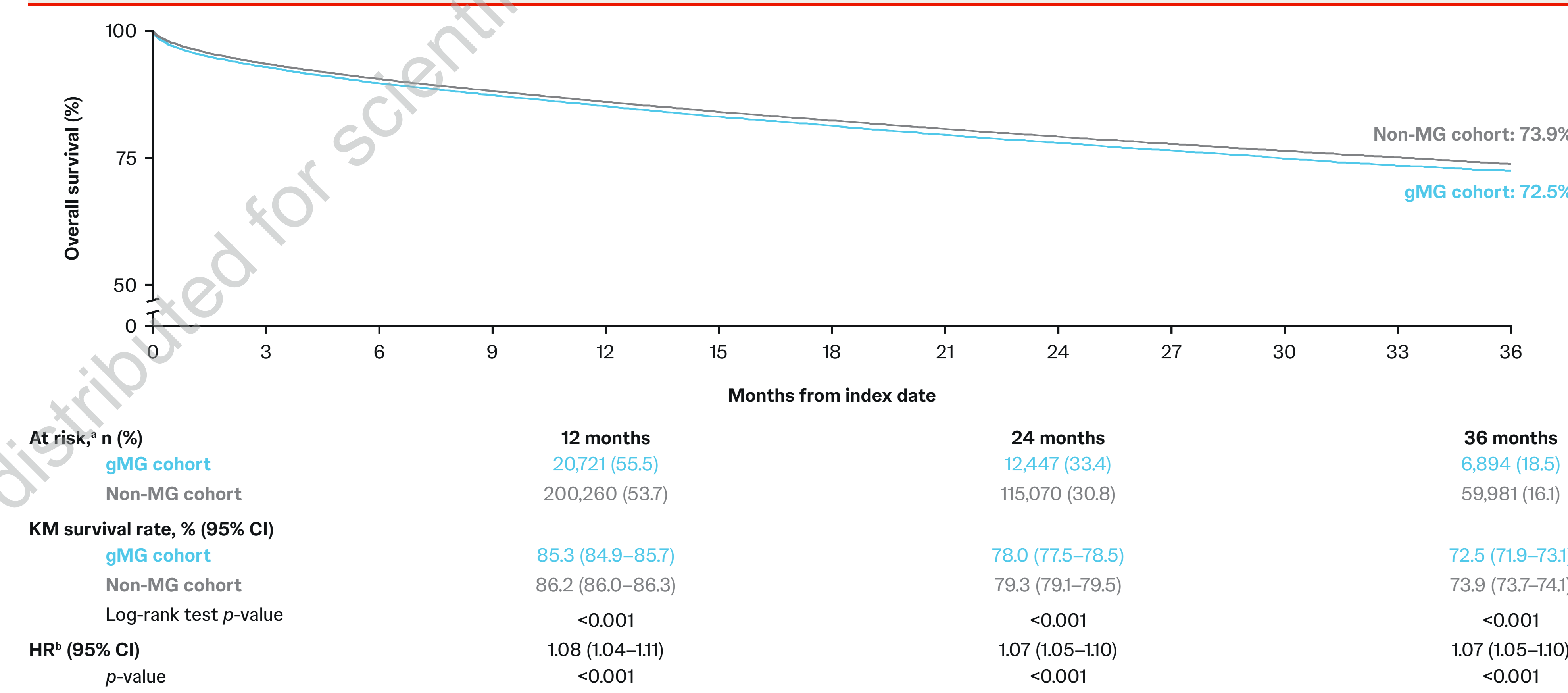
The gMG Cohort Had a Higher Risk of Death Than the Non-MG Cohort

- The mean follow-up duration was 18.9 and 18.1 months in the gMG and non-MG cohorts, respectively, with corresponding observed mortality of 19.9% and 15.8%
- Survival rates were significantly lower in the gMG versus the non-MG cohort (Figure 1)
 - The gMG cohort had an 8% higher risk of death at 12 months (hazard ratio, 1.08) and a 7% higher risk at 24 and 36 months (hazard ratio, 1.07 for both; all $p < 0.001$)

Among the gMG Cohort, Mortality Was Higher in Males, Older Patients, Those With More Severe Baseline gMG, and Those With Serious Comorbidities

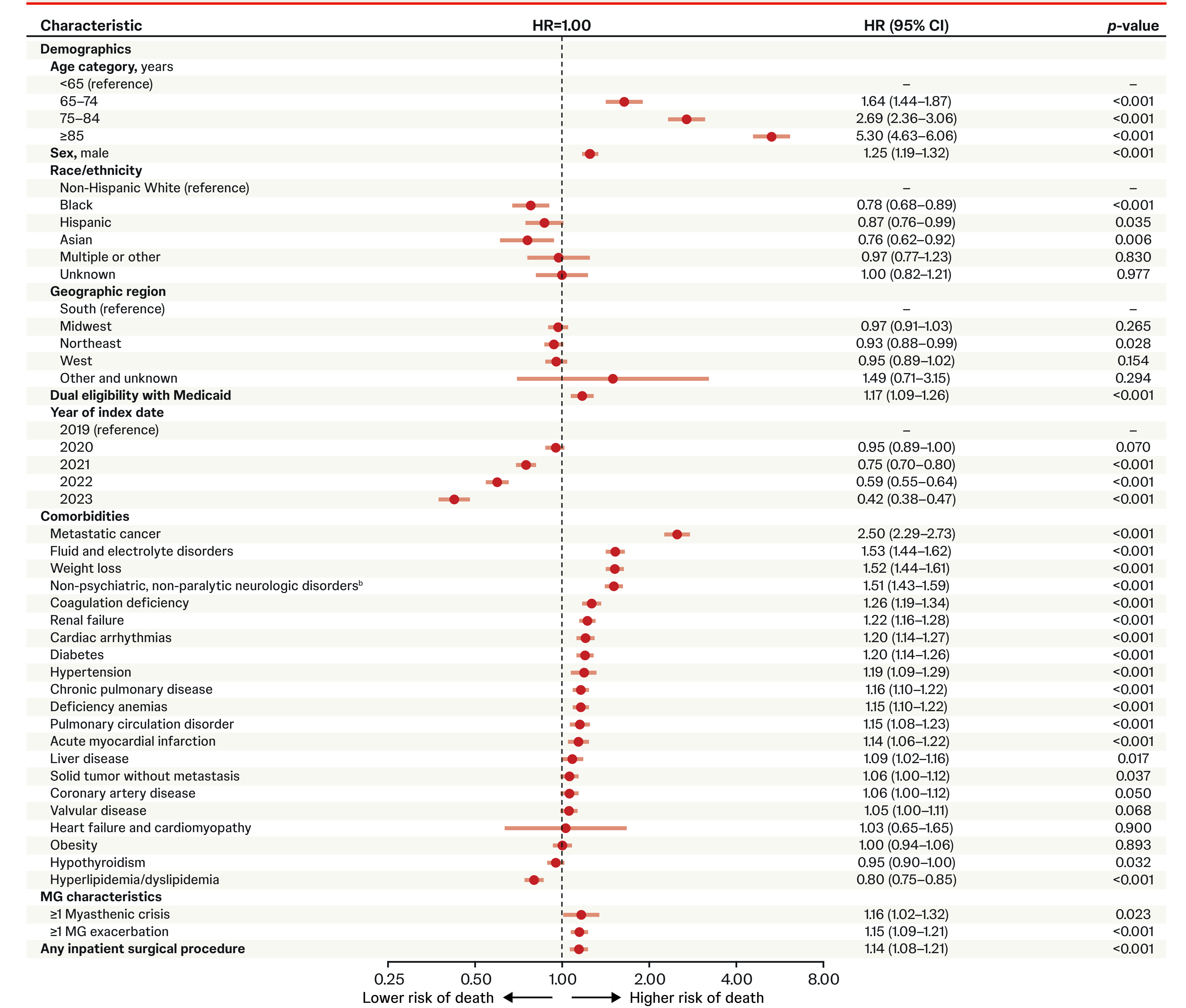
- Demographic predictors of mortality included male sex with 25% higher risk, older age (75–84 vs < 65 years) with 169% higher risk, and dual eligibility for Medicare–Medicaid with 17% higher risk (all $p < 0.001$) (Figure 2)
- MG exacerbation during baseline was associated with 15% higher risk of mortality ($p < 0.001$), and baseline myasthenic crisis was associated with 16% higher risk ($p = 0.022$)
- Any baseline inpatient surgical procedure was associated with 14% higher risk of mortality ($p < 0.001$)
- Comorbidities with $\geq 20\%$ higher risk of mortality included metastatic cancer (150% increase); fluid and electrolyte disorders (53% increase); weight loss (52% increase); non-psychiatric, non-paralytic neurologic disorders (51% increase); coagulation deficiency (26% increase); renal failure (22% increase); cardiac arrhythmias (20% increase); and diabetes (20% increase; all $p < 0.001$)

Figure 1. Overall survival among the weighted gMG (N=37,321) and non-MG (N=373,210) cohorts



*Includes the number and percentage of patients who remained at risk after the given period. **HRs were based on Cox proportional hazard models comparing mortality in the weighted gMG vs non-MG cohort. HR > 1 indicates a higher mortality rate among the gMG vs non-MG cohort. CI=confidence interval, gMG=generalized myasthenia gravis, HR=hazard ratio, KM=Kaplan–Meier, MG=myasthenia gravis.

Figure 2. Selected characteristics associated with all-cause mortality among the gMG cohort*



*Baseline characteristics in the multivariable Cox proportional hazard model omitted from the figure included ESRD eligibility, DSM-5 conditions, gMG-related treatments, and HRR. **Conditions included degenerative, seizure, neuromuscular, and demyelinating disorders. CI=confidence interval, DSM-5=Diagnostic and Statistical Manual of Mental Disorders, 5th Edition, ESRD=end-stage renal disease, gMG=generalized myasthenia gravis, HR=hazard ratio, HRR=healthcare resource utilization, MG=myasthenia gravis.

Key Takeaways

- Medicare beneficiaries with gMG had a consistently higher risk of mortality compared with those without MG
- Within the gMG cohort, higher mortality risk was associated with male sex, older age, MG clinical events, and a range of comorbid conditions
- These findings highlight the importance of gMG management strategies that optimize disease control and proactively address comorbidities to improve survival outcomes in this vulnerable patient population

Limitations

- Because no ICD-10-CM code specifically identifies gMG, an MG diagnosis made by a neurologist was used as a proxy for gMG status
- Despite adjusting for observable confounders, residual confounding may have remained between cohorts due to unmeasured factors such as lifestyle characteristics and social support
- As gMG onset likely occurred prior to Medicare eligibility for many patients, the observed mortality reflects outcomes in a prevalent gMG population and should not be interpreted as mortality starting from disease onset
- Cause of death could not be ascertained from the claims dataset



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