Long-term Use of Oral Corticosteroids and Overall Survival Among Patients with Myasthenia Gravis: A Nationwide Population-based Study

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Introduction

- Myasthenia gravis (MG) is a rare autoimmune neuromuscular disorder characterized by muscle weakness and fatigability, significantly impacting patients' quality-of-life[1]
- Oral corticosteroids (OCS) are a cornerstone in the management of MG, and are frequently used to reduce symptom severity and prevent disease exacerbations[2]
- However, long-term OCS use is associated with well-documented adverse effects, including osteoporosis, diabetes, and cardiovascular complications
  - Furthermore, the impact of prolonged oral OCS exposure on overall survival (OS) in patients with MG remains poorly understood[3]
- Understanding the long-term effects of oral OCS use in patients with myasthenia gravis (MG) is essential for optimizing treatment strategies and improving patient outcomes

Objective

- To assess the association between long-term OCS exposure and OS among patients with MG

Methods

Data collection

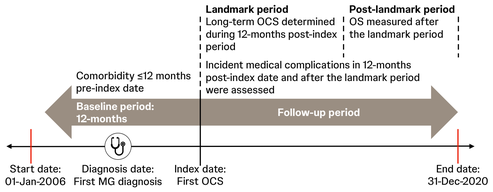
- Data were derived from 4 linkable, longitudinal, nationwide population-based Swedish registries
  - National Patient Register (NPR)[4]
  - Prescribed Drug Register (PDR)[5]
  - Cause of Death Register (CDR)[6]
  - The Longitudinal Integration Database for Health Insurance and Labor Markets Studies (LISA)
- For adult patients with ≥1 primary diagnosis of MG (ICD-10-SE G70.0) provided by neurologist from 01-Jan-2006 to 31-Dec-2020

ICD-10-SE=International Classification of Diseases, 10th Revision, Swedish Edition.

Study design

Patients

- ≥18 years of age
- ≥1 primary diagnosis of MG (ICD-10-SE G70.0)
- ≥1 OCS prescription on or after MG diagnosis
- ≥12-month follow-up period



Note: The Swedish edition of the International Classification of Diseases Version 10 (ICD-10-SE) was used to define indications or comorbidities of interest. The Anatomical Therapeutic Chemical (ATC) classification system was used to identify dispensed prescriptions of interest. Procedure codes were used to define the procedures or surgeries of interest. ICD-10-SE=International Classification of Diseases, 10th Revision, Swedish Edition; MG=myasthenia gravis; OCS=oral corticosteroids; OS=overall survival.

Duration of OCS use

- Long-term OCS use was defined as continuous use for ≥3 consecutive months and without gaps of >60 days between prescriptions or end of data availability during the 12 months after MG diagnosis (landmark period)
- Short-term OCS use was defined as use not meeting these criteria

Statistical analysis

- OS was assessed in patients with long-term and short-term OCS users from the end of landmark period to end of follow-up
- Kaplan-Meier estimates and log-rank tests were used to evaluate OS
- OS rates were adjusted with baseline covariates (e.g., age, gender) and variables during landmark period (e.g., Charlson Comorbidity Index (CCI), OCS-related complication/time-to-complication) in Cox-regression models

TABLE 1: Time window definitions and study measures

Time window	Definition	Study measures	
Index date	Date of the first OCS claim	Demographic characteristics	
Baseline period	12 months prior to index date	Clinical characteristics	
Follow-up period	**From index date to date of death, date of last record, or the data cut-off date, whichever the earliest**		
Landmark period	12 months after index date	Long-term OCS use	OCS-related incident medical complications were measured during the 12-month post-index period and after the end of landmark period
Post-landmark	From end of landmark to end of study period	OS, compared between long-term versus (vs) short-term OCS users with adjustment of covariates in landmark (e.g., CCI) and baseline (e.g., age, gender as of index) period	

CCI=Charlson Comorbidity Index; OCS=oral corticosteroids; OS=overall survival.

Results

Among the total of 1,942 patients, 1,236 patients used OCS

- Long-term OCS users: 272 (22%) patients
- Short-term OCS user: 964 (78%) patients

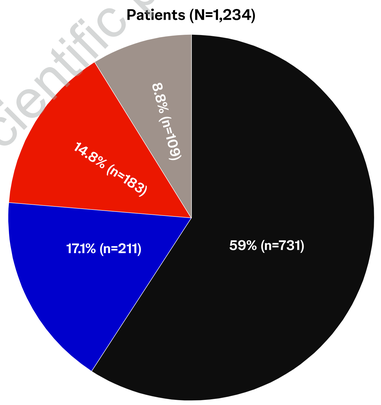
TABLE 2: Demographics and baseline characteristics during 12-month pre-index period

	Long-term OCS users n=272	Short-term OCS users n=964
Age, mean (SD), years	65.2 (17.1)	63.4 (17.0)
Female (%)	48.5	47.4
Time from MG diagnosis to index OCS, mean (SD)*, days	236.12 (559.61)	478.09 (820.08)
Charlson comorbidity index, mean (SD)	0.67 (1.05)	0.61 (1.26)
Medication use during 12-month pre-index period, %		
AChEi	69.12	70.85
OCS	20.22	18.57
IST	13.97	13.69
Length of study follow-up in years, mean (SD)	6.59 (3.68)	6.88 (3.60)

*Index Date: Date of the first OCS claim, and for non-OCS users it is a randomly assigned date based on the distribution of time interval for MG diagnosis date to the index date among OCS-users. AChEi=acetylcholinesterase inhibitor; IST=immunosuppressive treatment; MG=myasthenia gravis; OCS=oral corticosteroids; SD=standard deviation.

- Among all OCS users, the mean standard deviation (SD) average daily dose of OCS was 23.8 mg (18.75)
- About 3% (n=31/1,236) of the OCS users in the study dataset were on long-term high-dose [average daily dose (ADD) ≥40 mg/day for ≥3 months)] OCS usage

FIGURE 1: OCS average daily dose

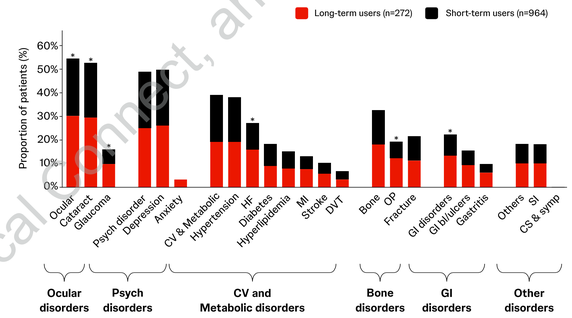


Note: Two patients with missing dose not shown here.

OCS=oral corticosteroids.

- Post-index, bone, gastrointestinal and ocular medical conditions were significantly higher in long-term OCS users than short-term users (p<0.05)

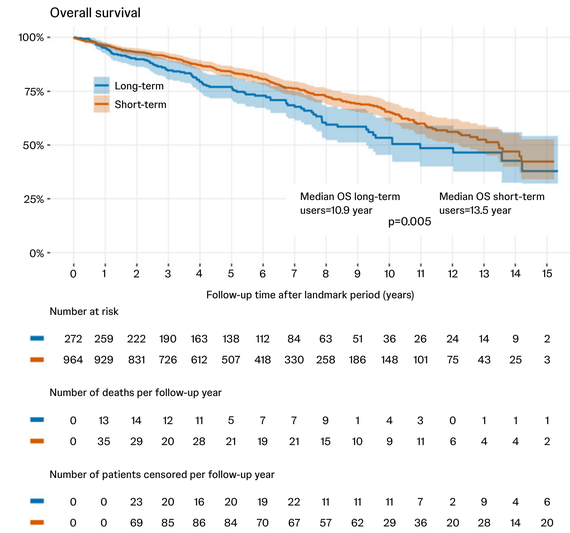
FIGURE 2: Patients with incident medical conditions during entire post-index period



*p≤0.05
BI=bleeding; CV=cardiovascular; CS & symp=Cushing Syndrome and related symptoms; DVT=deep vein thrombosis; GI=gastrointestinal; HF=heart failure; MI=myocardial infarction; OP=osteoporosis; Psych=psychiatric; SI=systemic infection.

- The median OS among long-term OCS users was 10.9 years and 13.5 years in short-term OCS users (P<0.01) (Figure 3)
- After covariate adjustment, long-term OCS users had a significantly higher risk (42%) of death vs short-term users (adjusted hazard ratio (HR): 1.42; 95% CI: 1.10–1.83; p=0.0079)

FIGURE 3: KM curve for overall survival in patients with long-term vs short-term OCS use



p-value from log-rank test
CI=confidence interval; KM=Kaplan-Meier; OCS=oral corticosteroids; OS=overall survival.

Key Takeaway

Long-term OCS use among patients with MG in Sweden was associated with lower OS, emphasizing the need for safer, more effective treatment alternatives and strategies to reduce OCS utilization for better patient outcomes

Conclusions

Long-term OCS use was associated with lower OS among patients with MG in Sweden, highlighting the potential limitations of OCS use in this population

These findings also highlight the need for safer and more effective treatment alternatives for MG management in Sweden, particularly for patients requiring long-term therapy

Findings from this study could potentially guide treatment protocols, strategies to reduce OCS utilization and help to optimize outcomes in the management of MG

Limitations

- The study used a 12-month landmark period following OCS initiation to define long-term vs short-term OCS use
- It is possible that short-term users continued OCS use beyond the 12-month period and became long-term users
- Due to this limitation, the HR estimate of long-term OCS users vs short-term OCS users was conservative

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Disclosures

Qian Cai, Kavita Gandhi, Maria Ait-Tihyaty, and **Winghan Jacqueline Kwong**: Are/were employees of Janssen; may hold stock or stock options in Johnson & Johnson. **Nurgul Batyrbekova** and **Gabriel Isheden:** are employees of SDS Life Science- a Cytel company, Uppsala, Sweden

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Autoantibody: gMG