Adaptation of the Glucocorticoid Toxicity Index-Metabolic Domains Instrument to Evaluate Glucocorticoid Toxicity in Adults with Myasthenia Gravis using Electronic Health Records in the United States

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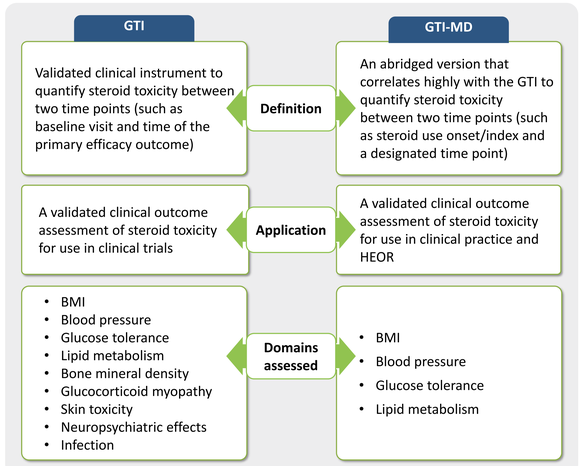
Introduction and Purpose

- Myasthenia gravis (MG) is an autoimmune disorder characterized by autoantibody-mediated defective transmission at the neuromuscular junction.[1]
- For patients with MG and other disorders, glucocorticoids (also referred to as corticosteroids or steroids) are considered first-line therapy due to their fast onset of action and their anti-inflammatory and immunosuppressant effects.[2,3]
- Nevertheless, the clinical benefits of steroid therapy are tempered by the potential for short- and long-term drug-related adverse effects, including osteoporosis, hyperglycemia, and adrenal suppression. However, quantifying the toxicity of glucocorticoids in the past has been challenging.[4,5]
- The Glucocorticoid Toxicity Index (GTI) is the only weighted, standardized clinical outcome assessment (COA) of glucocorticoid toxicity that uses 9 health domains in the calculation of its scores.
- An abbreviated version, the GTI-Metabolic Domains (GTI-MD), which was developed for use in clinical practice can assess steroid toxicity using 4 metabolic domains captured directly from electronic health records (EHR) including body mass index (BMI), blood pressure, glucose tolerance, and lipid metabolism.[7] The GTI-MD correlates highly with the GTI.
- The objective of the current study was to quantify steroid toxicity with GTI-MD in patients with MG using EHR data.

GTI versus GTI-MD

- While GTI uses 9 domains to evaluate steroid toxicity, GTI-MD uses 4 domains commonly collected in routine clinical practice, making it a practical COA to incorporate in datasets in less time (**Figure 1**).

Figure 1. Overview of GTI and GTI-MD

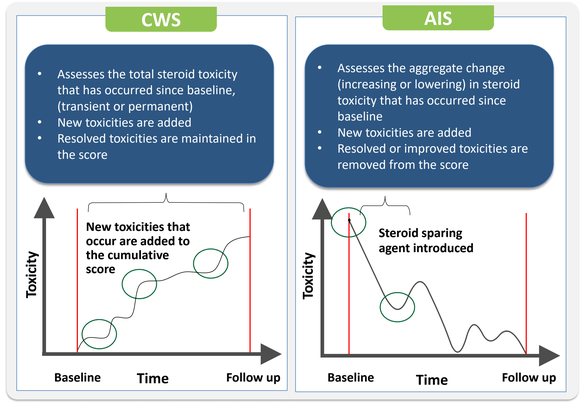


BMI, body mass index; GTI, Glucocorticoid Toxicity Index; GTI-MD Glucocorticoid Toxicity Index-Metabolic Domains; HEOR, health economics and outcomes research.

Cumulative Worsening Score (CWS) and Aggregate Improvement Score (AIS)

- The GTI measures toxicity effectively using two scores, the CWS and the AIS (**Figure 2**).

Figure 2. Cumulative worsening score and aggregate improvement score

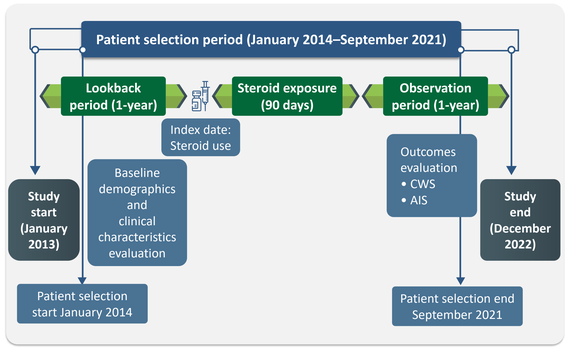


AIS, Aggregate Improvement Score; CWS, Cumulative Worsening Score.

Methods

- A retrospective, real-world study was conducted using Optum® de-identified Electronic Health Record data set (Optum® EHR) (comprised of lab values needed for the GTI-MD algorithm) with data from January 2013 to December 2022 (**Figure 3**).

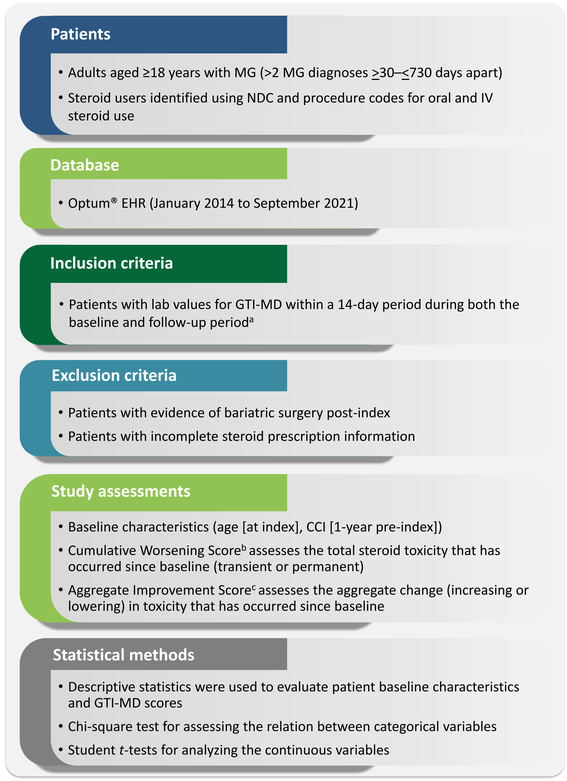
Figure 3. Study design



AIS, Aggregate Improvement Score; CWS, Cumulative Worsening Score.

- Adult patients aged ≥18 years with MG (≥2 MG diagnoses ≥30–≤730 days apart) were included (**Figure 4**).
- Index dates were defined as first steroid for steroid initiators (MG-SI; intervention) and assigned by age/gender-matched counterpart in MG-SI for patients with steroid naïve (MG-SN; control).

Figure 4. Study overview



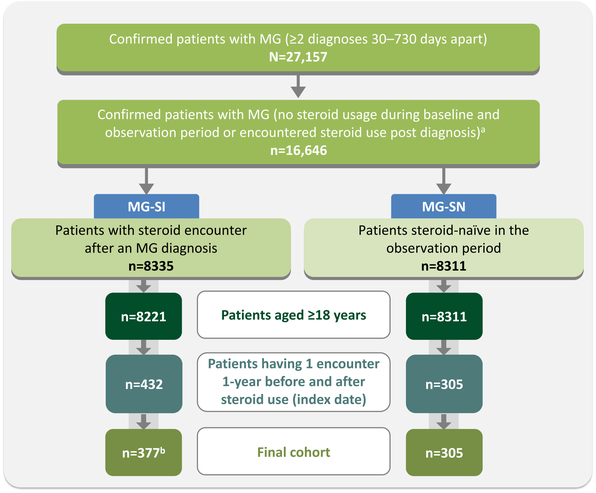
[a]The baseline period was 1-year pre-index, and the follow-up period was 1-year post-90-day steroid exposure period post-index. The limits of GTI-MD domains include LDL: 20–400 mg/dL; BMI: 15–50 Kg/m²; HbA1c: 3%–20%; BP: 40–250 mmHg (systolic) and 30–150 mmHg (diastolic). [b]CWS assessed the worsening of glucocorticoid-induced adverse events, assessing cumulative glucocorticoid toxicity, regardless of whether the toxicity has lasting effects or is transient; [c]AIS assessed improvement and/or worsening of glucocorticoid-induced AEs.

AE, adverse event; AIS, Aggregate Improvement Score; BP, blood pressure; BMI, body mass index; CCI, Charlson Comorbidity Index; CWS, Cumulative Worsening Score; GTI-MD, Glucocorticoid Toxicity Index-metabolic domains; EHR, electronic health records; HbA1c, hemoglobin A1c; IV, intravenous; LDL, low-density lipoprotein; MG, myasthenia gravis; NDC, National Drug Code.

Results

- Of 27,157 adult patients with MG, 377 were MG-SI, and 305 were MG-SN (**Figure 5**).

Figure 5. Patient flow



[a]10,511 patients were excluded as they had 1-year of steroid-free usage. [b]36 patients excluded for bariatric surgery and incomplete steroid information.
MG, myasthenia gravis; MG-SI, MG-steroid initiators; MG-SN, MG-steroid naïve.

- The mean (standard deviation [SD]) age was 68.7 (10.3) and 71.5 (9.0) years, and the Charlson Comorbidity Index (CCI) was 2.6 (2.2) and 2.2 (1.9), for MG-SI and MG-SN cohorts, respectively. Majority of patients were male (62%; MG-SI: 57%; MG-SN: 67%; **Table 1**).
- Almost half of the patients had CCI score 1–2 (MG-SI: 46%; MG-SN: 47%).

Table 1. Baseline demographics and characteristics

Characteristics	Total (N=682)	MG-SI (n=377)	MG-SN (n=305)	p value
Age, years, mean (SD)	70.0 (9.8)	68.7 (10.3)	71.5 (9.0)	<0.05
Gender, n (%)				
Male	420 (62)	216 (57)	204 (67)	<0.05
Female	262 (38)	161 (43)	101 (33)	
CCI, mean (SD)	2.4 (2.1)	2.6 (2.2)	2.2 (1.9)	<0.05
CCI range	0-12	0-12	0-9	
CCI category[a], n (%)				
0	91 (13)	45 (11)	46 (15)	
1–2	322 (47)	179 (46)	143 (47)	
3–4	167 (24)	91 (26)	76 (25)	
≥5	102 (15)	62 (18)	40 (13)	
GT-SNAPSHOT score[b], mean (SD)	90.6 (31.9)	90.2 (31.1)	88.8 (32.8)	0.19

[a]CCI can range from 0-24 with higher scores indicating presence of comorbidities with higher mortality rates.
[b]GT-SNAPSHOT score is an assessment of glucocorticoid toxicity at a single point in time (contrasting with the CWS and AIS, which measure change in toxicity between two points in time). CCI, Charlson Comorbidity Index; MG-SI, myasthenia gravis-steroid initiators; MG-SN, myasthenia gravis-steroid naïve; SD, standard deviation.

- GTI-MD mean (SD) scores were higher in MG-SI compared with MG-SN (**Table 2**).

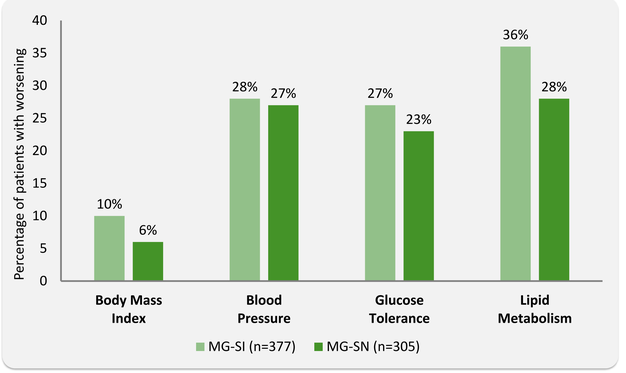
Table 2. CWS and AIS

GTI-MD score	Total (N=682)	MG-SI (n=377)	MG-SN (n=305)	p value
CWS				
Mean (SD)	20.8 (22.2)	22.6 (22.8)	18.7 (21.2)	<0.05
Range	0–95	0–95	0–93	
AIS				
Mean (SD)	3.5 (34.4)	4.9 (34.5)	1.9 (34.3)	0.27
Range	-119–93	-119–93	-107–93	

AIS, Aggregate Improvement Score; CWS, Cumulative Worsening Score; GTI-MD, Glucocorticoid Toxicity Index-Metabolic Domains; MG-SI, myasthenia gravis-steroid initiators; MG-SN, myasthenia gravis-steroid naïve; SD, standard deviation.

- MG-SI cohort experience a significant difference in worsening for the BMI domain compared to MG-SN in the follow-up period (**Figure 6**).

Figure 6. GTI-MD domains in patients with worsening for MG-SI and MG-SN



BMI, body mass index; GTI-MD, Glucocorticoid Toxicity Index-Metabolic Domains; MG-SI, myasthenia gravis-steroid initiators; MG-SN, myasthenia gravis-steroid naïve.

- MG-SI had a greater proportion of patients exceeding the minimal clinically important difference (MCID) compared to MG-SN (**Table 3**). The difference is significant for CWS at the 10- and 20-point thresholds.

Table 3. Minimal clinically important difference

MCID	MG-SI (n=377)	MG-SN (n=305)	p value
CWS, n (%)			
≥10 points	256 (68)	180 (59)	<0.05
≥20 points	167 (44)	110 (36)	<0.05
≥30 points	141 (37)	98 (32)	0.15
AIS, n (%)			
≥10 points	171 (45)	137 (45)	0.91
≥20 points	118 (31)	84 (28)	0.29
≥30 points	84 (22)	69 (23)	0.92

AIS, Aggregate Improvement Score; CWS, Cumulative Worsening Score; MG-SI, myasthenia gravis-steroid initiators; MG-SN, myasthenia gravis-steroid naïve.

Conclusions

- **GTI-MD utilizes readily available clinical data (BMI, blood pressure, glucose tolerance, lipid metabolism), reducing the assessment burden.**
- **GTI-MD offers a practical tool for monitoring glucocorticoid-related adverse effects in patients with MG, facilitating informed treatment decisions.**
- **Our results demonstrated that the GTI-MD score was higher in patients with MG-SI compared to patients with MG-SN suggesting steroid toxicity is quantifiable utilizing EHR data.**
- **Further research is warranted to explore the applicability of GTI-MD in predicting glucocorticoid toxicity to reduce long-term effects of steroid burden in other therapeutic areas.**

Limitations

- Small cohort size and incomplete steroid dosing capture in EHR data.
- A longer follow-up period might be needed to assess the long-term effectiveness of the GTD-MD tool in predicting complications.

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