Machine Learning for Predictive Modeling of Hospitalization Risk in Myasthenia Gravis Patients Using the MGFA Global Patient Registry: Addressing Imbalanced Data in Real-World Evidence Scenarios

MSR86

AUTHORS

Amaia Zurinaga
Alira Health, Barcelona, Spain

Richard Nowak
Yale School of Medicine, CT, USA

Kelly Gwathmey
Virginia Commonwealth University, VA, USA

Jean-François Ricci
Alira Health, Basel, Switzerland

Minjee Park
Alira Health, Basel, Switzerland

OBJECTIVE

Myasthenia Gravis (MG) is an autoimmune condition where antibodies target neuromuscular junctions.[1] MG may occasionally worsen resulting in hospitalizations for exacerbations and crises. The study aims to develop predictive models for identifying the risk of all cause overnight hospitalization.

METHODOLOGY

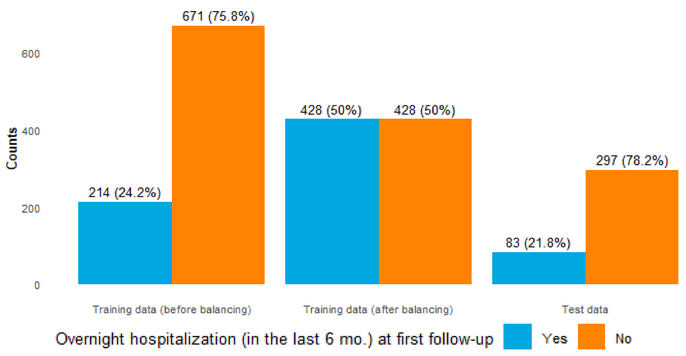
> **Data source:** Myasthenia Gravis Foundation of America Global MG Patient Registry (MGFAPR) is an online longitudinal patient-reported registry. Data collected between July 2013 and March 2025 were used in this study.

> **Inclusion criteria:** Participants aged 18 years and older, with a self-reported (and physician-confirmed) MG diagnosis, who had completed the first follow-up within 12 months of enrollment were included (n=1,350). Participants with incomplete response to overnight hospitalization at first follow-up were excluded (n=85).

> **Analysis:**

- Descriptive analysis (chi-square tests and ANOVA) was performed to compare patients with and without overnight hospitalization in the last 6 months at first follow-up, along with correlation analysis to check for multicollinearity and select variables for the prediction model (selected variables for the model are shown in Table 1).
- Multiple imputation was applied to the selected variables with less than 30% missing data.
- The data was split (70% training, 30% testing). To address class imbalance in hospitalization outcomes, the training dataset was balanced through oversampling the minority class (hospitalized) and undersampling the majority (not hospitalized) (Figure 1). Categorical variables were transformed to numerical using one-hot encoding.
- eXtreme Gradient Boosting (XGBoost) and K-Nearest Neighbor algorithm (KNN) classifier were used to build the predictive model.
- Model performance was evaluated using cross-validation, accuracy, sensitivity, specificity, precision, F1-score, and Area Under the Curve (AUC).

Figure 1. Outcome Distribution Pre- and Post-balancing in the Training Dataset



RESULTS

Table 1. Demographic and Disease Characteristics

Variable, mean (SD) or %	Overall (N = 1,265)	Hospitalization Yes (N = 297)	Hospitalization No (N = 968)	p-value
Age (years)[c]	59.00 (13.91)	56.16 (15.01)	59.87 (13.45)	<0.001*
Gender (female)	718 (57%)	184 (62%)	534 (55%)	0.046*
BMI	31.04 (7.39)	32.01 (7.12)	30.74 (7.44)	0.002*
Employment status (unemployed)	765 (60%)	187 (63%)	578 (60%)	0.005*
Alcohol consumption				0.005*
Never consumed	446 (35%)	120 (40%)	326 (34%)	
Rarely consumed	361 (29%)	95 (32%)	266 (27%)	
Occasionally consumed	223 (18%)	38 (13%)	185 (19%)	
Frequently consumed	235 (19%)	44 (15%)	191 (20%)	
Time since diagnosis (years)[c]	6.38 (9.39)	4.86 (8.36)	6.84 (9.63)	<0.001*
Antibody status[b]				<0.001*
AChR+	468 (37%)	94 (32%)	374 (39%)	
MuSK+	37 (2.9%)	12 (4.0%)	25 (2.6%)	
Double Seronegative (AChR- & MuSK-)	121 (9.6%)	48 (16%)	73 (7.5%)	
Unknown or missing	639 (51%)	143 (48%)	496 (51%)	
History of thymectomy (yes)[b]	309 (24%)	90 (30%)	219 (23%)	<0.001*
Exacerbation (yes)	396 (31%)	121 (41%)	275 (28%)	<0.001*
Psychological disorders (yes)[b]	836 (66%)	224 (75%)	612 (63%)	<0.001*
Treatments currently (yes)				
AChEIs	979 (77%)	253 (85%)	726 (75%)	<0.001*
Corticosteroids	553 (44%)	158 (53%)	395 (41%)	<0.001*
IVIg/SCIg	1,039 (82%)	218 (73%)	821 (85%)	<0.001*
PLEX	49 (3.9%)	22 (7.4%)	27 (2.8%)	<0.001*
MG-ADL score	6.11 (3.87)	7.90 (3.78)	5.57 (3.73)	<0.001*
Feeding-tube (yes)	128 (10%)	50 (17%)	78 (8.1%)	<0.001*
Number of times at ER	0.53 (1.01)	1.10 (1.31)	0.35 (0.82)	<0.001*
Number of times at ICU (in the last 5 years)				<0.001*
0	905 (72%)	172 (58%)	733 (76%)	
1	187 (15%)	68 (23%)	119 (12%)	
2	53 (4.2%)	24 (8.1%)	29 (3.0%)	
3 or more	44 (3.5%)	19 (6.4%)	25 (2.6%)	

[a] All variables captured at enrollment unless other wise indicated. [b] Antibody status, history of thymectomy and psychological disorders data were taken from enrollment and first follow-up. [c] Age and time since diagnosis data were taken from first follow-up. **BMI**, Body Mass Index; **AChR**, acetylcholine receptor; **MuSK**, muscle-specific tyrosine kinase; **AChEI**, acetylcholinesterase inhibitor; **IVIg**, intravenous immunoglobulin; **SCIg**, subcutaneous immunoglobulin ; **PLEX**, plasma exchange **MG-ADL**, Myasthenia Gravis Activities of Daily Living. **Psychological disorders** (anxiety and depression) was taken from enrollment and first follow-up.

Figure 2. Confusion Matrices (XGBoost; left, KNN; right)

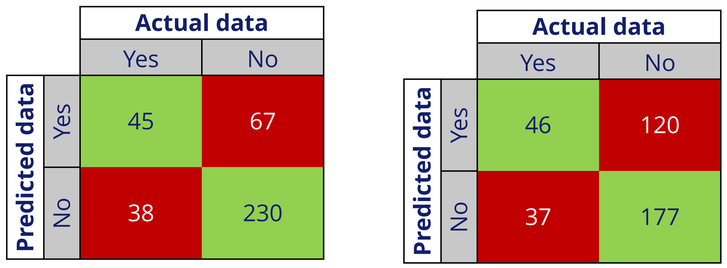
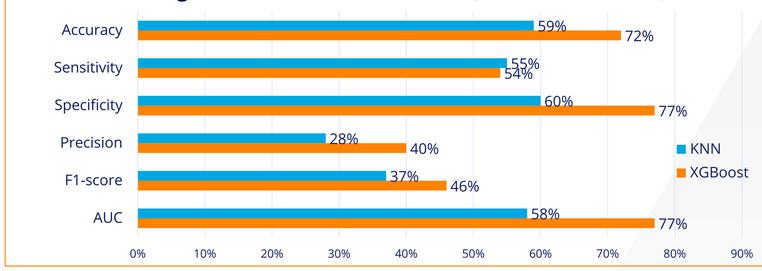


Figure 3. Performance Metrics (XGBoost and KNN)



> Figures 2 and 3 compare XGBoost and KNN models for predicting MG hospitalization. XGBoost outperforms KNN across all metrics: higher accuracy (72% vs. 59%), specificity (77% vs. 60%), precision (40% vs. 28%), F1-score (46% vs. 37%), and AUC (77% vs. 58%), with similar sensitivity (~55%).

> Confusion matrices (Figure 2) show XGBoost had fewer false positives for a similar number of false negatives than KNN, therefore exhibiting a lower error rate (28% vs. 41%, respectively).

Table 2. Odds ratios for patients ever hospitalized for MG (yes/no) in multivariate analysis

	OR	95% CI	p-value
Alcohol consumption at enrollment			
Occasionally consumed vs. Never consumed	0.62	0.39, 0.97	0.041*
Time since diagnosis at follow-up (years)	0.97	0.95, 0.99	0.006*
Antibody status			
Double Seronegative (AChR- & MuSK-) vs. AChR+	1.74	1.06, 2.85	0.028*
History of thymectomy			0.005*
Yes vs. No	1.72	1.21, 2.44	0.002*
MG-ADL score at enrollment	1.10	1.06, 1.16	<0.001*
Feeding-tube at enrollment			
Yes vs. No	1.60	1.00, 2.54	0.049*
Number of times at ER at enrollment	1.54	1.33, 1.79	<0.001*

Non-significant factors not shown: age at follow-up; gender; BMI; Employment status at enrollment; Alcohol consumption at enrollment (vs. Never consumed): Rarely consumed, Frequently consumed; Antibody status (vs. AChR+): MuSK+, Unknown or missing; Psychological disorders (Yes vs. No); AChEIs at enrollment (Yes vs. No); Corticosteroids at enrollment (Yes vs. No); IVIg/SCIg at enrollment (Yes vs. No); PLEX at enrollment (Yes vs. No); Number of times at ICU at enrollment (vs. 0): 1, 2, 3 or more.

> Occasional alcohol consumption, compared to never drinking, (OR 0.6, 95% CI 0.39-0.97) and longer time since diagnosis (OR 0.9 per year, 95% CI 0.95-0.99) were associated with lower odds of hospitalization.

> Factors linked to increased hospitalization risk include double seronegative antibody status (AChR− & MuSK−) compared to AChR+ (OR 1.7, 95% CI 1.06-2.85), history of thymectomy (OR 1.72, 95% CI 1.21-2.44), higher MG-ADL score at enrollment (OR 1.10 per point, 95% CI 1.06-1.16), presence of a feeding tube (OR 1.60, 95% CI 1.00-2.54), and more frequent emergency room visits (OR 1.54, 95% CI 1.33-1.79).

> Logistic regression performed like XGBoost, with an AUC of 76%.

CONCLUSION

> XGBoost achieved the highest AUC (77%), followed closely by logistic regression (76%), while KNN lagged behind with an AUC of 58%, suggesting XGBoost as the best-performing model in this context.

> As a proof-of-concept investigation, odds of hospitalization risk and factors identified are not necessarily definitive and further validation is needed as next step.

> Accurately predicting hospitalization risk using real-world evidence remains challenging due to limited sample sizes and imbalanced outcomes.

REFERENCES

1. García DA, Pardo, J. Myasthenia gravis. Update on diagnosis and therapy. *Medicina clínica*. 2023;161(3), 119–127.

AliraHealth

mg MYASTHENIA GRAVIS FOUNDATION OF AMERICA

DOWNLOAD THE DIGITAL VERSION!