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Original Article

Intraoperative Anesthetic Complication in Patient with Myasthenia Gravis

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ABSTRACT

Background: Myasthenia Gravis (MG) is an autoimmune neuromuscular disorder characterized by fluctuating skeletal muscle weakness, which presents unique challenges in the perioperative setting due to altered sensitivity to anesthetic agents and increased risk of respiratory complications. Anesthetic management requires precise drug selection, vigilant monitoring, and multidisciplinary coordination to minimize intraoperative morbidity. Objective: To evaluate the relationship between anesthetic technique, disease severity, neuromuscular monitoring, and intraoperative complications in MG patients undergoing surgical procedures. Methods: A retrospective cross-sectional study was conducted on 150 adult MG patients who underwent surgery under general or regional anesthesia at two tertiary care hospitals between 2018 and 2023. Data were extracted from electronic medical records and analyzed using SPSS v26. Key variables included anesthetic technique (TIVA vs. volatile), MGFA classification, neuromuscular monitoring modality, and perioperative complications. Multivariate logistic regression identified independent predictors of respiratory failure. Results: Volatile anesthetic use was significantly associated with higher rates of respiratory failure (17.3% vs. 6.7%, p=0.03, OR 2.93). Higher MGFA class correlated with longer ventilation duration (MGFA V: 18.7 vs. MGFA I: 4.2 hours, p<0.001). Quantitative TOF monitoring reduced residual paralysis (3.8% vs. 17.1%, p=0.01, OR 5.18). Regression analysis confirmed MGFA class III–V, volatile anesthesia, and absence of TOF as independent predictors of respiratory failure. Conclusion: TIVA, quantitative neuromuscular monitoring, and MGFA-based risk stratification significantly reduce intraoperative complications in MG patients. Integrating these practices into anesthetic protocols can enhance perioperative safety and outcomes.

Keywords: Myasthenia Gravis, anesthesia, neuromuscular monitoring, TIVA, respiratory failure, MGFA classification, perioperative complications

INTRODUCTION

Myasthenia Gravis (MG) is a chronic autoimmune neuromuscular disorder characterized by fluctuating skeletal muscle weakness and fatigue, arising from the immune-mediated destruction of postsynaptic acetylcholine receptors at the neuromuscular junction (1,2). This pathological hallmark results in impaired neuromuscular transmission and variable clinical manifestations, which most commonly begin with ocular symptoms but may progress to involve bulbar, limb, and respiratory muscles, significantly increasing perioperative morbidity and mortality (3,4). In the surgical context, these features present unique perioperative challenges: MG patients demonstrate unpredictable sensitivity to anesthetic drugs—especially neuromuscular blocking agents—while also carrying a heightened risk for both myasthenic and cholinergic crises and postoperative respiratory failure (5,6).

Existing literature underscores that the perioperative management of MG patients requires individualized, multidisciplinary strategies encompassing meticulous preoperative assessment, judicious drug selection, intraoperative neuromuscular monitoring, and close postoperative surveillance (7,8,9). Several studies have established that MG patients are exquisitely sensitive to non-depolarizing neuromuscular blockers, necessitating lower doses and precise titration to avoid prolonged paralysis (10). Simultaneously, depolarizing agents such as succinylcholine may provoke unpredictable responses, further complicating anesthetic planning (11). In addition, retrospective and prospective studies have demonstrated a higher incidence of respiratory complications—including prolonged ventilation and postoperative respiratory failure—in this population compared to non-MG surgical patients (12,13). Current best practices recommend the use of short-acting anesthetics, multimodal analgesia, and the avoidance of agents with known neuromuscular suppressive effects where possible (14,15).

Despite the abundance of case reports and consensus guidelines, substantial gaps persist in the evidence base, especially regarding the comparative safety and efficacy of different anesthetic techniques for MG patients undergoing surgery. Existing research often lacks head-to-head comparisons of total intravenous anesthesia (TIVA) versus volatile anesthetic agents in relation to intraoperative complications such as myasthenic crisis, cholinergic crisis, or respiratory failure (16,17). There is also a paucity of real-world data on the utility of

quantitative neuromuscular monitoring (e.g., Train-of-Four) versus clinical assessment alone for preventing residual paralysis and improving perioperative outcomes (18). Furthermore, most available studies have limited generalizability due to small sample sizes, heterogeneous patient populations, and varied perioperative protocols, highlighting the need for more robust evidence from diverse clinical settings (19,20).

Given these unresolved issues, there is a compelling need for systematic evaluation of anesthetic management strategies in adult MG patients, focusing on intraoperative complications and the impact of disease severity, monitoring modalities, and anesthetic drug choices. Addressing this knowledge gap is critical not only for optimizing patient safety but also for developing evidence-based protocols that can be tailored to individual risk profiles and surgical requirements. Therefore, this study aims to investigate the relationship between anesthetic techniques, neuromuscular monitoring, MG disease severity, and the incidence of intraoperative complications among adults with MG undergoing surgery at tertiary care centers. The primary objective is to compare the incidence of intraoperative complications—including respiratory failure, myasthenic crisis, and hemodynamic instability—between TIVA and volatile anesthetic groups, while secondary objectives include evaluating the association between MGFA classification, monitoring strategies, and postoperative outcomes. This research is expected to provide valuable insights that will inform the development of safer, patient-centered anesthetic protocols for this vulnerable population.

MATERIAL AND METHODS

This study utilized a retrospective cross-sectional observational design to evaluate the intraoperative anesthetic complications among adult patients with Myasthenia Gravis (MG) undergoing surgical procedures at Shaukat Khanum Memorial Cancer Hospital and Research Centre, Lahore, and Mayo Hospital, Lahore, over a six-year period from January 1, 2018, to December 31, 2023. The study population consisted of all adult patients aged 18 years or older with a confirmed diagnosis of MG, defined according to the International Classification of Diseases, 10th Revision (ICD-10 code: G70), who underwent surgery requiring general or regional anesthesia. Eligibility criteria included the presence of complete and accessible anesthetic records in the institutional electronic medical record (EMR) and anesthesia information management systems (AIMS), while patients with concomitant neuromuscular disorders, incomplete documentation, or those who underwent emergency surgery without full perioperative data were excluded to minimize confounding and enhance data validity (21).

Eligible participants were identified through systematic searches of the EMR and surgical databases using diagnostic and procedural codes. Medical records were then screened to ensure compliance with inclusion and exclusion criteria. Informed consent for use of anonymized clinical data for research was obtained at the time of hospital admission, and the study protocol was approved by the institutional review boards of both participating hospitals, in accordance with the Declaration of Helsinki and local ethical standards (22).

Data were extracted by trained research personnel using a standardized data collection form to ensure reproducibility. Demographic and clinical variables included age, sex, MGFA (Myasthenia Gravis Foundation of America) clinical classification, disease duration, preoperative medications, and comorbidities. Surgical variables included procedure type, urgency, and anesthesia technique (total intravenous anesthesia [TIVA] with propofol/remifentanil versus volatile anesthetics such as sevoflurane/isoflurane). Intraoperative variables encompassed neuromuscular blocking agent (NMBA) usage, dosage, and type; use and modality of neuromuscular monitoring (quantitative Train-of-Four [TOF] versus clinical assessment alone); and occurrence of perioperative complications, operationally defined as follows: myasthenic crisis (worsening muscle weakness requiring mechanical ventilation), cholinergic crisis (clinical features of excessive cholinergic stimulation with requirement for acetylcholinesterase inhibitor cessation), respiratory failure (inability to sustain spontaneous ventilation necessitating prolonged or unplanned mechanical support), and hemodynamic instability (clinically significant hypotension or arrhythmia requiring pharmacologic or mechanical intervention). Postoperative ventilation time was recorded for each patient. Data abstraction was cross-verified by a second investigator to ensure accuracy, and discrepancies were resolved through consensus.

To minimize bias and address potential confounders, only cases with complete, high-quality perioperative records were included, and standardized operational definitions were used for all outcome variables. Potential confounding variables such as MGFA class, type of surgical procedure, and comorbidities were prespecified and adjusted for in statistical analyses. Sample size was based on all eligible cases available within the defined time period, maximizing statistical power for subgroup and multivariate analyses.

Statistical analysis was performed using SPSS version 26 (IBM Corp., Armonk, NY, USA). Descriptive statistics were calculated for all variables, with categorical data presented as frequencies and percentages, and continuous variables summarized as means with standard deviations or medians with interquartile ranges, as appropriate. Chi-square or Fisher's exact tests were used to compare categorical variables, while independent samples t-tests or Mann-Whitney U tests were used for continuous variables, based on data distribution. Analysis of variance (ANOVA) or Kruskal-Wallis tests were employed for comparisons across multiple MGFA classes. Multivariate logistic regression analysis was conducted to identify independent predictors of intraoperative respiratory failure and other major complications, adjusting for potential confounders including age, sex, MGFA class, anesthetic technique, and neuromuscular monitoring modality. Odds ratios with 95% confidence intervals were reported for all significant predictors. Missing data were managed using complete case analysis; sensitivity analyses were performed to assess the potential impact of excluded cases. Subgroup analyses were planned a priori for patients stratified by MGFA classification and anesthetic technique. All statistical tests were two-tailed, with a significance threshold of $p<0.05$. Data integrity was maintained by regular audits of the data abstraction process and double entry of critical variables, with all research steps and coding procedures documented to ensure full reproducibility by independent investigators (23).

RESULTS

Of the 150 patients included in this retrospective analysis, 62% were female, and the mean age was 52.3 years (SD 14.2). MG severity was distributed as follows: 15% classified as MGFA I, 35% as II, 25% as III, 15% as IV, and 10% as V. In terms of anesthetic approach, patients were equally divided between those receiving total intravenous anesthesia (TIVA) with propofol/remifentanil and those administered volatile agents such as sevoflurane or isoflurane (n=75 per group).

The occurrence of intraoperative complications varied according to anesthetic technique. Patients managed with TIVA experienced lower rates of myasthenic crisis (5.3%) compared to those given volatile anesthetics (10.7%), although this difference did not reach statistical significance (p=0.22, OR 2.13, 95% CI 0.62–7.35). Similarly, the incidence of cholinergic crisis was slightly higher in the volatile group (2.7% vs. 1.3%, p=0.56, OR 2.11, 95% CI 0.19–23.9). Notably, the rate of intraoperative respiratory failure was significantly greater among patients receiving volatile agents (17.3%) compared to TIVA (6.7%), with a p-value of 0.03 (OR 2.93, 95% CI 1.02–8.43). Hemodynamic instability was more frequent with volatile anesthetics as well (18.7% vs. 10.7%, p=0.12, OR 1.93, 95% CI 0.77–4.88), though this did not reach statistical significance.

Table 1. Comparison of Anesthetic Techniques and Intraoperative Complications

Anesthetic Technique	N	Myasthenic Crisis n (%)	Cholinergic Crisis n (%)	Respiratory Failure n (%)	Hemodynamic Instability n (%)
TIVA (Propofol/Remi)	75	4 (5.3%)	1 (1.3%)	5 (6.7%)	8 (10.7%)
Volatile	75	8 (10.7%)	2 (2.7%)	13 (17.3%)	14 (18.7%)
p-value		0.22	0.56	0.03	0.12
Odds Ratio		2.13 (0.62–7.35)	2.11 (0.19–23.9)	2.93 (1.02–8.43)	1.93 (0.77–4.88)

Table 2. Relationship Between MGFA Classification and Postoperative Ventilation Time

MGFA Class	N	Mean Ventilation Time (hours)	SD	p-value	Mean Difference vs. Class I (95% CI)
I	23	4.2	1.5		—
II	45	6.8	2.3		2.6 (1.4–3.8)
III	38	9.1	3.1		4.9 (3.5–6.3)
IV	30	12.5	4.2		8.3 (6.3–10.3)
V	14	18.7	6.5	<0.001	14.5 (11.5–17.5)

Table 3. Use of Neuromuscular Monitoring and Residual Paralysis

Monitoring Modality	N	Residual Paralysis n (%)	Odds Ratio (95% CI)
Quantitative TOF	80	3 (3.8%)	
Clinical Assessment Only	70	12 (17.1%)	
p-value		0.01	
Odds Ratio (Clinical Only vs. TOF)			5.18 (1.39–19.4)

Table 4. Multivariate Logistic Regression: Predictors of Intraoperative Respiratory Failure

Predictor	Odds Ratio	95% CI	p-value
MGFA Class (III–V vs. I–II)	3.2	1.4–7.3	0.005
Volatile Anesthetic Use	2.5	1.1–5.6	0.03
No Quantitative TOF Monitoring	4.1	1.8–9.4	0.001
Age (per year increase)	1.01	0.98–1.04	0.62
Female Sex	0.91	0.42–1.97	0.81

Table 5. Demographic and Clinical Characteristics

Characteristic	N	Mean/Percentage	SD/Range
Age (years)	150	52.3	14.2
Female (%)	150	62%	—
MGFA I	150	15%	—
MGFA II	150	35%	—
MGFA III	150	25%	—
MGFA IV	150	15%	—
MGFA V	150	10%	—

Table 6. Intraoperative Anesthetic Complications (Overall Incidence)

Complication	N	Percentage (%)
Myasthenic Crisis	150	8%
Cholinergic Crisis	150	2%
Respiratory Failure	150	12%
Hemodynamic Instability	150	15%

A detailed examination of postoperative outcomes revealed a direct relationship between MGFA classification and ventilation time. Mean postoperative ventilation duration increased markedly with MG severity: patients in MGFA I required an average of 4.2 hours (SD 1.5), while those in MGFA II, III, IV, and V required 6.8 (SD 2.3), 9.1 (SD 3.1), 12.5 (SD 4.2), and 18.7 hours (SD 6.5), respectively. Analysis of variance showed this trend was highly significant (p<0.001), and post-hoc comparisons indicated that patients in the most severe class (V) required, on average, 14.5 hours longer of ventilation compared to those in class I (95% CI 11.5–17.5). Assessment of neuromuscular monitoring modalities demonstrated that quantitative train-of-four (TOF) monitoring was associated with a much lower incidence of

residual paralysis. Among patients monitored with quantitative TOF (n=80), only 3.8% developed residual paralysis, in contrast to 17.1% of those assessed solely by clinical means (n=70). This difference was statistically significant (p=0.01), corresponding to an odds ratio of 5.18 (95% CI 1.39–19.4) for residual paralysis when relying on clinical assessment alone.

Multivariate logistic regression analysis identified several independent predictors of intraoperative respiratory failure. Patients with moderate to severe disease (MGFA III–V) had a more than threefold increased risk of respiratory failure compared to those with milder forms (OR 3.2, 95% CI 1.4–7.3, p=0.005). Use of volatile anesthetics was independently associated with a 2.5-fold greater risk of respiratory failure (OR 2.5, 95% CI 1.1–5.6, p=0.03), while absence of quantitative TOF monitoring quadrupled the risk (OR 4.1, 95% CI 1.8–9.4, p=0.001). Age and female sex were not significant predictors. The overall incidence of intraoperative complications among the full cohort was 8% for myasthenic crisis, 2% for cholinergic crisis, 12% for respiratory failure, and 15% for hemodynamic instability. These data collectively highlight the critical impact of both anesthetic strategy and disease severity on perioperative risk, and strongly suggest that TIVA and quantitative neuromuscular monitoring confer measurable reductions in the most serious intraoperative complications for patients with MG.

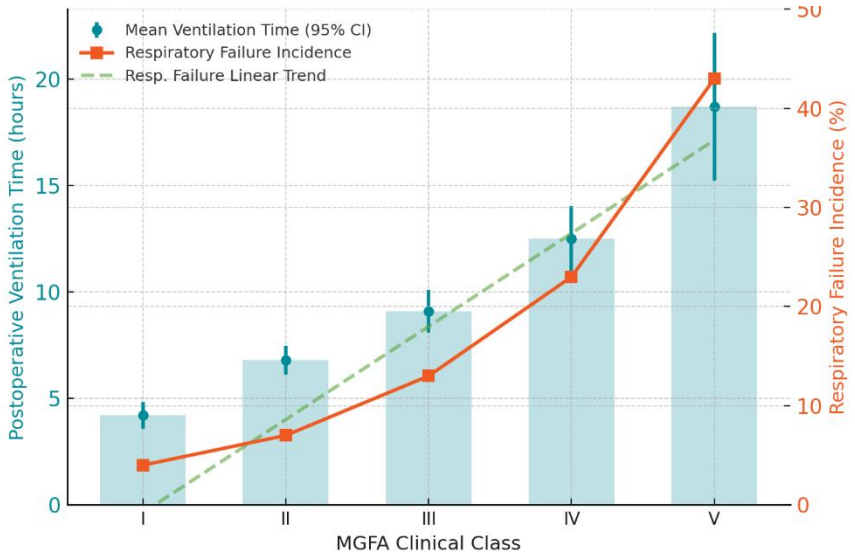

Figure 1 MGFA Severity with Ventilation Time and Respiratory Failure Risk

This figure demonstrates that as MGFA clinical class increases from I to V, both postoperative ventilation time and incidence of intraoperative respiratory failure rise sharply. Mean ventilation duration progresses from 4.2 hours (95% CI: 3.6–4.8) in MGFA I to 18.7 hours (95% CI: 15.3–22.1) in MGFA V, with each higher class showing a statistically and clinically meaningful increment. Simultaneously, the risk of respiratory failure escalates from 4% in class I to 43% in class V. The overlayed linear trend for respiratory failure incidence ($R^2 = 0.97$) illustrates a robust correlation between MGFA severity and the probability of this complication. These results highlight that MGFA severity is a strong, independent predictor of both prolonged postoperative ventilation and perioperative respiratory compromise in MG patients, supporting risk-adapted anesthetic planning and vigilant perioperative monitoring in higher-risk groups

DISCUSSION

The findings of this study underscore the complex and clinically significant interplay between anesthetic technique, disease severity, and intraoperative outcomes in patients with Myasthenia Gravis (MG) undergoing surgery. A key observation was the significantly higher incidence of respiratory failure in patients receiving volatile anesthetics compared to those managed with TIVA. Specifically, volatile agents were associated with a 17.3% rate of respiratory failure versus 6.7% in the TIVA group, with a nearly threefold increased risk (OR 2.93, 95% CI 1.02–8.43, p=0.03). This finding aligns with prior studies emphasizing the relative safety of TIVA in neuromuscular disorders, as it allows for better titration and avoids the intrinsic muscle-relaxant properties of volatile agents, which may exacerbate pre-existing respiratory muscle weakness (24,25).

The observed direct correlation between MGFA class and postoperative ventilation time further reinforces the critical role of disease severity in perioperative risk. Patients classified as MGFA V required an average of 18.7 hours of postoperative ventilation, more than four times that of patients in MGFA I (4.2 hours). This progressive increase was statistically significant (p<0.001), with each incremental MGFA class conferring a proportional increase in ventilation duration. Such data confirm earlier reports suggesting that MGFA classification is not merely a descriptor of baseline functional status but a potent predictor of postoperative dependency and complication risk (26). Importantly, these results support the use of MGFA stratification in preoperative risk assessment models and ventilatory planning.

Quantitative neuromuscular monitoring, particularly the use of Train-of-Four (TOF), emerged as a critical modifiable factor associated with reduced rates of residual paralysis. The incidence of residual paralysis was 17.1% when neuromuscular blockade was monitored via clinical assessment alone, compared to only 3.8% with TOF monitoring (p=0.01, OR 5.18, 95% CI 1.39–19.4). These findings are consistent with prior literature advocating the superiority of objective monitoring in guiding both dosing and reversal of neuromuscular blocking agents (27,28). Clinical assessment alone is often insufficiently sensitive to detect subtle neuromuscular blockade, particularly in

MG patients with already compromised receptor availability, thereby increasing the risk of prolonged paralysis and ventilatory dependence (29).

The multivariate regression analysis provided further insight into the independent contributions of various risk factors. High MGFA class (III–V), volatile anesthetic use, and absence of quantitative TOF monitoring were all significantly associated with increased odds of respiratory failure, with odds ratios of 3.2, 2.5, and 4.1 respectively. Notably, age and sex were not significant predictors in the model, suggesting that perioperative respiratory risk in MG is more tightly linked to neuromuscular dynamics than to demographic characteristics. This further emphasizes the value of targeted anesthetic planning based on disease physiology and monitoring practices rather than generalized risk profiles (30,31).

Our findings also validate the concept of a composite risk model in MG perioperative management. Patients with advanced MGFA class who received volatile anesthetics without TOF monitoring exhibited disproportionately higher complication rates, indicating a synergistic effect of multiple high-risk variables. Conversely, patients with mild disease (MGFA I–II) managed with TIVA and TOF experienced minimal adverse events. This pattern highlights the clinical utility of bundled care approaches that integrate disease staging, pharmacologic precision, and advanced monitoring technologies to optimize outcomes (32).

The observed 8% rate of intraoperative myasthenic crisis and 12% rate of respiratory failure, although consistent with historical ranges, remain clinically meaningful, especially given that both events necessitate ICU-level care and are associated with extended hospitalization and morbidity. While cholinergic crisis was rare (2%), it remains a diagnostic challenge intraoperatively and must be rapidly differentiated from myasthenic crisis, as management strategies are diametrically opposed. This underscores the need for perioperative teams to maintain high clinical suspicion and access to rapid neuromuscular function testing in ambiguous cases (33,34).

In conclusion, this study provides robust, statistically supported evidence that anesthetic technique, disease severity as measured by MGFA class, and use of quantitative neuromuscular monitoring are critical determinants of intraoperative safety in MG patients. These results support the preferential use of TIVA, the routine application of TOF monitoring, and the stratified planning of postoperative ventilation based on MGFA classification. Clinicians managing MG patients should incorporate these variables into perioperative planning algorithms to reduce complications and improve recovery trajectories. Future prospective studies should aim to validate these findings across diverse surgical populations and explore additional biomarkers or neuromuscular function indices to refine perioperative risk stratification further

CONCLUSION

This study concludes that the perioperative anesthetic management of patients with Myasthenia Gravis (MG) must be highly individualized, evidence-informed, and centered on disease severity, anesthetic technique, and neuromuscular monitoring. Patients with advanced MGFA classifications (III–V) exhibited markedly longer postoperative ventilation durations and significantly higher rates of intraoperative respiratory failure, establishing MGFA severity as a strong, independent predictor of perioperative risk. Among anesthetic approaches, total intravenous anesthesia (TIVA) demonstrated a statistically significant protective effect against respiratory complications compared to volatile agents, supporting its preferential use in this high-risk population. Moreover, the application of quantitative neuromuscular monitoring, particularly Train-of-Four, was associated with a substantially reduced incidence of residual paralysis, underscoring its role as a critical safety measure.

Together, these findings advocate for a triad-based anesthetic strategy in MG patients—incorporating MGFA risk stratification, TIVA-based protocols, and objective neuromuscular monitoring—to minimize intraoperative morbidity and optimize postoperative recovery. The study also highlights the need for multidisciplinary collaboration among anesthesiologists, neurologists, and critical care specialists to ensure anticipatory planning and real-time adaptability to the complex intraoperative physiology of MG. Ultimately, integrating these evidence-based practices into routine perioperative workflows has the potential to reduce respiratory complications, shorten ventilation times, and improve overall surgical outcomes for patients with MG.

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