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Abstract

Background: EBUS-TBNA is an established technique for diagnostically sampling intrathoracic masses and lymph nodes. While the procedure is commonly conducted under general anesthesia (GA), little is known regarding the association between anesthetic management and perioperative respiratory complications. Here, we aim to evaluate this association among patients presenting for EBUS-TBNA.

Methods: 586 patients receiving GA for EBUS-TBNA between 2012 and 2018 were retrospectively evaluated. The primary endpoint was the occurrence of perioperative respiratory complications and the secondary endpoint was procedure end to OR exit time (minutes). Respiratory complications were defined as episodes of severe (SpO₂ <85%) or prolonged (SpO₂ <90% for >5 min) hypoxemia, bronchospasm, and postoperative ventilation that could not be directly attributed to procedural invasiveness.

Results: Among all patients, 79 (13.5%) had respiratory complications. Four patient characteristics were associated with respiratory complications: home oxygen use (OR 2.39; 95% CI 1.26–4.45; P = 0.007), pre-existing respiratory disease (OR 2.01; CI 1.21–3.29; P = 0.005), ASA class (P = 0.03), and albuterol administration intra-operatively (OR 2.22; CI 1.23–3.92; P = 0.007). No anesthetic factors were found to be statistically significant. Procedures with respiratory complications had a longer duration (mean time 88.7 min vs. 111.8 min; P = 0.00009), prolonged time to extubation (mean time 11.9 min vs. 14.2 min; P = 0.039), and stayed in the room longer after extubation (mean time 18.4 min vs. 23.1 min; P = 0.0016). When comparing types of GA, there were no significant differences between volatile anesthetics versus TIVA (12.7% vs. 14.6%, P = 0.54).

Conclusions: Pre-existing patient characteristics, as opposed to anesthetic factors, are associated with respiratory complications during EBUS-TBNA.

Keywords: General anesthesia, EBUS-TBNA, Respiratory complications, Interventional pulmonology

1. Introduction

Endobronchial Ultrasound-guided Transbronchial Needle Aspiration (EBUS-TBNA) is a minimally invasive and highly accurate technique for sampling intrathoracic masses and lymph nodes to diagnose non-malignant and malignant pulmonary diseases.^{1–4} Comparative studies have shown that EBUS-TBNA is superior to conventional TBNA as well as mediastinoscopy for lung cancer staging,

and as a consequence EBUS-TBNA has become widely adopted.^{5–7} Most EBUS-TBNA studies define primary outcomes of diagnostic accuracy, yield, and efficacy.^{8–10} However, there have been few significant studies focused on procedural safety with the aim of quantifying the incidence of and risk factors for perioperative complications. In these studies, the complications are addressed broadly in range and scope, with no focused assessment of complications that cannot be

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attributed to the invasiveness of the surgical procedure itself.^{7,11–14}

Patients undergoing EBUS-TBNA often receive anesthesia with varying degrees of success. It has been reported previously in the literature that minimal, moderate, and deep sedation are safe and efficacious.^{15–19} In both retrospective and prospective studies of sedation techniques, continuous propofol infusion, midazolam, meperidine, ketamine-midazolam, ketamine-propofol, propofol-midazolam, and midazolam-fentanyl have all shown similar effectiveness.^{15,20–23} However, Cases-Viedma et al. demonstrated fewer respiratory and non-respiratory complications when combined midazolam-propofol and combined midazolam-fentanyl were used for patient sedation.¹⁵ Additionally, bispectral index monitoring has been shown to decrease the number of adverse events, including hypoxia and hypotension, when administering sedation for EBUS-TBNA.²⁴

Compared to sedation, there are few studies that have demonstrated the safety and efficacy of various general anesthetic techniques for EBUS-TBNA. Zamparelli et al. has demonstrated that general anesthesia (GA) can be safely administered utilizing an endotracheal tube (ETT) or an LMA for EBUS-TBNA. Further, it has been shown that minor complications of a procedural, respiratory, or cardiac nature are less likely to occur with GA compared to sedation.^{25,26} However, the 2013 AQUIRE registry study notably determined both deep sedation and GA are risk factors for escalation of care post-procedure and that evidence is lacking regarding any strong recommendation favoring one method of GA over another.¹² Additionally, inherent mechanisms underlying GA can contribute to respiratory complications via decreased functional residual capacity, impaired ventilatory drive leading to respiratory depression, and increased ventilation-perfusion mismatch.^{27,28}

Due to the lack of recommendations regarding perioperative management of patients presenting for EBUS-TBNA, we retrospectively analyzed the perioperative course of 586 patients undergoing EBUS-TBNA with GA at our institution over a six-year period. Specifically, we assessed their perioperative courses for the occurrence of respiratory complications that could not be directly attributed to the invasiveness of the procedure. The primary objective was to quantify the incidence of, and risk factors for, respiratory complications with a focus on anesthetic management and how selection of agents may influence procedural outcomes. The secondary outcome of this study was to assess whether anesthetic management influenced the duration of time

Abbreviation list

ASA	American Society of Anesthesiologists
BAL	Bronchoalveolar Lavage
COPD	Chronic obstructive pulmonary disease
EBUS-TBNA	Endobronchial ultrasound-guided transbronchial needle aspiration
ETT	Endotracheal tube
FRC	Functional residual capacity
GA	General Anesthesia
LMA	Laryngeal Mask Airway
OR	Operating Room
OSA	Obstructive Sleep Apnea
SpO ₂	Oxygen saturation
TB	Tuberculosis
TIVA	Total intravenous anesthesia

the patient needed to be monitored post-procedurally prior to operating room (OR) exit.

2. Materials and methods

We performed a retrospective analysis of 586 patients undergoing bronchoscopy with lymph node sampling by EBUS-TBNA under GA from 2012 to 2018 at a single university hospital center. Approval was obtained from the university's Institutional Review Board (Protocol HP-00076323), with waiver of consent obtained in accordance with institutional guidelines. All patients who underwent EBUS-TBNA under GA during this time interval were included in this study. All procedures were performed using Olympus™ EBUS bronchoscopes (BF-UC180F) and Olympus™ ViziShot EBUS-TBNA needles (21G and 22G). Patient selection for GA was based on patient co-morbidities, anticipated length of procedure, patient preference, and resource allocation. The needle gauge used during the procedure was selected at the discretion of the bronchoscopist. The anesthetic regimen used during the procedure was selected at the discretion of the anesthesiologist.

Information extracted from patient charts included demographics, clinical characteristics, sedation and general anesthetic information, procedural information, pathology results, complications, and outcomes of complications. The presence of pre-existing respiratory disease among patients was defined as any chronic pulmonary condition diagnosed prior to the patient's EBUS-TBNA procedure. Conditions included, but were not limited to, the following: asthma, chronic obstructive pulmonary disease, pulmonary tuberculosis, pulmonary sarcoidosis, obstructive sleep apnea, and emphysema.

The primary outcome was respiratory complication, defined as any of the following events: severe (any desaturation to SpO₂ <85%) or prolonged

($\text{SpO}_2 < 90\%$ for > 5 min) hypoxemia, bronchospasm, or postoperative ventilation. The timing and degree of desaturation for all hypoxemia events was tracked through MetaVision (iMDsoft, Needham, MA), an electronic anesthesia medical recording software. MetaVision automates the intraoperative recording of the American Society of Anesthesiologists standard monitors in real-time at 1-min intervals including heart rate, blood pressure, oxygen saturation (SpO_2) and temperature. Bronchospasm was assessed by physical exam, auscultation, and peak airway pressures (if available). If a case was described in the procedural notes as having had a complication (respiratory or otherwise) due to the procedure itself or the actions of the proceduralist, then it was deemed a procedural complication and excluded from this study. Any respiratory complication documented by anesthesia providers or tracking software, in the setting of complication-free procedural records, was counted as a respiratory complication for the purposes of this study. The secondary outcome was time from procedure end to OR exit. All outcomes were defined prior to performing any data analysis.

2.1. Statistical analysis

In the bivariate analysis, categorical data were compared using the Fisher's exact test and Pearson's Chi-squared test. Non-categorical data were compared using the Mann–Whitney U test. Multivariable linear and logistic regression was used to examine the association of outcomes with patient, clinical, and anesthetic characteristics. For the multivariable logistic regression analysis, we decided *a priori* that variables with P values < 0.05 in the bivariate analysis would be the candidate variables in the multivariable logistic regression model. These selected variables included home oxygen use, pre-existing respiratory disease, albuterol use intra-operatively, ASA class, total procedure duration, procedure end to extubation time, and procedure end to OR exit time post-extubation. For the multivariable linear regression model, we decided *a posteriori* to select variables known to extend or influence operative times under other circumstances. These variables included weight (kg), ketamine, fentanyl dosage, age, total intravenous anesthesia (TIVA), ASA class, total procedure duration, home oxygen use, succinylcholine use, rocuronium use, and rocuronium redosing. P-values < 0.05 were considered statistically significant. All tests were two sided. Statistical analyses were performed utilizing GraphPad Prism 8, Python 3.4, and R 3.5.2.

3. Results

A total of 586 patients were enrolled in this retrospective study from one institution. Baseline patient characteristics and GA factors are summarized in [Table 1](#).

3.1. Respiratory complications

Among the 586 patients, 79 (13.5%) had respiratory complications of EBUS-TBNA that could not be directly attributed to the invasiveness of the procedure ([Table 2](#)). These respiratory complications include severe or prolonged hypoxemia, or bronchospasm. Three of the 79 patients (3.8%) also required post-operative ventilation as well as subsequent unplanned hospital admission. Notably, 62% of patients who experienced a respiratory complication also had at least one pre-existing chronic respiratory disease, while 21.5% had home oxygen requirements.

[Table 3](#) shows the bivariate analysis for categorical patient, clinical, and anesthetic characteristics evaluated in this study. Notably, home oxygen use was associated with an increased risk of respiratory complications (24.6%), compared with 12% among those who did not (OR 2.39; 95% CI 1.26–4.45; $P = 0.007$). Additionally, pre-existing respiratory disease (OR 2.01; CI 1.21–3.29; $P = 0.005$), ASA class ($P = 0.03$), and albuterol administration intra-operatively (OR 2.22; CI 1.23–3.92; $P = 0.007$) were also associated with increased respiratory complications ([Table 3](#)). However, diagnosis with multiple chronic respiratory diseases, as opposed to one, was not associated with a statistically significant increased risk of perioperative respiratory complications (12.9% vs. 16.9%; $P = 0.38$).

Procedures with respiratory complications had a longer duration (mean time 88.7 min vs. 111.8 min; $P = 0.00009$) and a prolonged time to extubation after the procedure (mean time 11.9 min vs. 14.2 min; $P = 0.039$). Furthermore, these patients stayed in the OR longer after the conclusion of the procedure (mean time 18.4 min vs. 23.1 min; $P = 0.0016$) ([Table 4](#)). In multivariable logistic regression analysis, only total procedure duration (OR 0.016; CI 1.008–1.024, $P = < 0.0001$) and intra-operative albuterol use (OR 1.83; CI 1.007–3.226; $P = 0.041$) were independent variables predictive of respiratory complications ([Table 5](#)). Home oxygen use, pre-existing respiratory disease, ASA class, procedure end to extubation time, and procedure end to OR exit time were not statistically significant predictors.

Table 1. Patient demographics, clinical and anesthetic characteristics.

Variable	Value
Total Number of Patients	586
Age, years	
Mean \pm SD	63.7 \pm 12.8
Median	65
>65	296 (50.5%)
Male	336 (57.3%)
Female	250 (42.7%)
Smoking Status	
Current	157 (26.8%)
Former	281 (48.0%)
Never	148 (25.2%)
Pack Years, Mean \pm SD	39.9 \pm 28.7
Weight, kg	
Mean \pm SD	79.7 \pm 20.9
Median	77
Home O ₂ Use	69 (11.8%)
Pre-existing Respiratory Disease	
= 1	276 (47.1%)
>1	83 (14.2%)
Number of TBNA passes	
Mean \pm SD	4.1 \pm 2
Median	4
Total Procedure Duration (minutes)	
Mean \pm SD	91.9 \pm 41.3
Median	86
Procedure End to Extubation (minutes)	
Mean \pm SD	12.3 \pm 8.6
Median	11
Procedure End to OR exit (minutes)	
Mean \pm SD	19 \pm 11.6
Median	17
Prior EBUS/Bronchoscopy	125 (21.3%)
LMA	35 (6.0%)
Sevoflurane	305 (52.0%)
Isoflurane	18 (3.1%)
Desflurane	8 (1.4%)
Nitrous Oxide	10 (1.7%)
Inhaled maintenance of anesthesia	347 (59.2%)
TIVA	239 (40.8%)
Rocuronium	489 (83.4%)
with neostigmine	152 (31.1%)
with sugammadex	282 (57.7%)
with no reversal	55 (11.2%)
Rocuronium re-dosed	176 (30.0%)
Succinylcholine	122 (20.8%)
Vecuronium	16 (2.7%)
Neostigmine	286 (48.8%)
Sugammadex	162 (27.6%)
Etomidate Induction	14 (2.4%)
Propofol Induction	571 (97.4%)
Propofol Infusion	377 (64.3%)
Fentanyl	519 (88.6%)
Remifentanyl	241 (41.1%)
Glycopyrrolate	299 (51.0%)
Dexamethasone	134 (22.9%)
Albuterol	92 (15.7%)
Ketamine	16 (2.7%)

(continued on next column)

Table 1. (continued)

Variable	Value
ASA physical status	
1	3 (0.5%)
2	115 (19.6%)
3	411 (70.2%)
4	57 (9.7%)

Data are presented as Total Number of Patients (%) unless otherwise indicated. ASA = American Society of Anesthesiologists. TBNA = transbronchial needle aspiration. EBUS = endobronchial ultrasound. LMA = laryngeal mask airway. TIVA = total intravenous anesthesia.

We also assessed the association of neuromuscular blockade and reversal agent choice with respiratory complications. Rocuronium use occurred in 83.4% of all patients with 31.1% of those patients receiving neostigmine, 57.7% receiving sugammadex, and 11.2% receiving no reversal (Table 1). Respiratory complications were not associated with the use of neostigmine or sugammadex for reversal (16.4% and 12.1%, $P = 0.24$) (Table 3). When we assessed the GA regimen overall, we found that there were no significant associations between respiratory complications and the use of inhalation maintenance versus total intravenous anesthesia (TIVA) (12.7% vs. 14.6%, $P = 0.54$). With regards to opiate use intraoperatively, respiratory complication rates were more common with remifentanyl use as opposed to fentanyl but not to a statistically significant degree (21.6% vs. 11.7%; $P = 0.35$).

3.2. Time to operating room exit

Table 6 presents the independent variables that are predictive of prolonged post-extubation time to OR exit. In a multivariable linear regression analysis, weight (Estimate 0.052; $P = 0.029$), fentanyl dosage (Estimate 0.013; $P = 0.028$), and ketamine dosage (Estimate 9.09; $P = 0.0018$) were positively associated with longer OR exit times. Age, TIVA, ASA class, succinylcholine, rocuronium, rocuronium redosing, case length, and home oxygen use were not statistically significant predictors.

4. Discussion

EBUS-TBNA is a minimally invasive and highly accurate technique for sampling intrathoracic masses and lymph nodes for diagnostic purposes. While this procedure is considered safe, there are very few studies that investigate the effects of GA on

Table 2. Respiratory complications following EBUS-TBNA

Respiratory Complications	Number of Patients
Total number of patients with respiratory complications	79
• Severe Hypoxemia (<85%)	55 (69.6%)
• Prolonged Hypoxemia (<90% for >5 min)	6 (7.6%)
• Severe and Prolonged Hypoxemia	8 (10.1%)
• Bronchospasm	5 (6.3%)
• Bronchospasm with severe and prolonged hypoxemia	2 (2.5%)
• Bronchospasm requiring post-operative intubation	2 (2.5%)
• Severe hypoxemia requiring post-operative intubation	1 (1.4%)

Data are presented as Total Number of Patients (%) unless otherwise indicated.

Table 3. Categorical patient, clinical, and anesthetic characteristics by occurrence of respiratory complications.

Variable	No Complication n = 507	Yes Complication n = 79	P-value ^a	OR (95% CI) ^b
Age			0.47	1.19 (0.73–1.95)
<65	254 (87.6%)	36 (12.4%)		
>65	253 (85.5%)	43 (14.5%)		
Sex			0.63	0.87 (0.53–1.42)
Female	214 (85.6%)	36 (14.4%)		
Male	293 (87.2%)	43 (12.8%)		
Smoking Status			0.62	— ^b
Current	133 (84.7%)	24 (15.3%)		
Former	247 (87.9%)	34 (12.1%)		
Never	127 (85.8%)	21 (14.2%)		
Home O ₂ Use	52 (75.4%)	17 (24.6%)	0.007	2.39 (1.26–4.45)
Pre-Existing Respiratory Disease	227 (82.2%)	49 (17.8%)	0.005	2.01 (1.21–3.29)
Multiple (>1) Respiratory Diseases	69 (83.1%)	14 (16.9%)	0.38	0.73 (0.39–1.37)
Prior EBUS/Bronchoscopy	103 (82.4%)	22 (17.6%)	0.14	1.51 (0.88–2.65)
ASA Score			0.03	— ^b
1	3 (100%)	0 (0%)		
2	108 (93.9%)	7 (6.1%)		
3	345 (83.9%)	66 (16.1%)		
4	51 (89.5%)	6 (10.5%)		
Sevoflurane	269 (88.2%)	36 (11.8%)	0.23	0.74 (0.46–1.22)
Isoflurane	16 (88.9%)	2 (11.1%)	1.00	0.79 (0.13–3.33)
Desflurane	5 (62.5%)	3 (37.5%)	0.08	3.95 (0.81–16.5)
Nitrous Oxide	8 (80%)	2 (20%)	0.63	1.62 (0.24–7.59)
TIVA vs. Inhalation			0.54	1.18 (0.72–1.95)
Inhalation	303 (87.3%)	44 (12.7%)		
TIVA	204 (85.4%)	35 (14.6%)		
Rocuronium	422 (86.3%)	67 (13.7%)	0.87	1.12 (0.58–2.28)
Rocuronium Redosed	147 (83.5%)	29 (16.5%)	0.19	1.42 (0.85–2.33)
Succinylcholine	101 (82.8%)	21 (17.2%)	0.18	1.45 (0.83–2.57)
Vecuronium	13 (81.3%)	3 (18.7%)	0.46	1.49 (0.36–5.32)
Neostigmine	252 (88.1%)	34 (11.9%)	0.28	0.76 (0.47–1.26)
Sugammadex	135 (83.3%)	27 (16.7%)	0.18	1.43 (0.84–2.37)
Neostigmine vs. Sugammadex			0.24	0.69 (0.39–1.24)
Neostigmine	127 (83.6%)	25 (16.4%)		
Sugammadex	248 (87.9%)	34 (12.1%)		
Propofol Bolus	494 (86.5%)	77 (13.5%)	1.00	1.01 (0.22–6.39)
Propofol Infusion	323 (85.7%)	54 (14.3%)	0.45	1.23 (0.74–2.06)
Etomidate	13 (92.9%)	1 (7.1%)	0.71	0.49 (0.02–3.09)
Fentanyl	453 (87.3%)	66 (12.7%)	0.13	0.61 (0.31–1.19)
Remifentanil	204 (84.6%)	37 (15.4%)	0.27	1.31 (0.81–2.13)
Ketamine	13 (81.3%)	3 (18.7%)	0.46	1.49 (0.36–5.32)
Fentanyl vs. Remifentanil			0.35	— ^b
Fentanyl	278 (88.3%)	37 (11.7%)		
Remifentanil	29 (78.4%)	8 (21.6%)		
Both	175 (85.8%)	29 (14.2%)		
None	25 (83.3%)	5 (16.7%)		
Glycopyrrolate	260 (87.2%)	38 (12.8%)	0.63	0.88 (0.55–1.43)
Dexamethasone	111 (82.8%)	23 (17.2%)	0.19	1.46 (0.83–2.52)
Albuterol	71 (77.2%)	21 (22.8%)	0.007	2.22 (1.23–3.92)

Categorical data are presented as Total Number of Patients (%) unless otherwise indicated. Complications denotes the occurrence of any respiratory complication that is not directly attributable to the invasiveness of the procedure. These complications are described in Table 2. Statistically significant results are indicated in bold.

^a Fisher exact test was used to calculate p-values unless the contingency table >2 × 2, then a Chi-squared test was used to compute p-value.

^b Odds ratio cannot be calculated off of a 3 × 2 table.

Table 4. Non-categorical patient, clinical, and anesthetic characteristics.

Variable	Min.	Mean	Max	P-value ^a
Age (years)				0.94
No Complications	18	63.8	91	
Complications	20	63.2	86	
Weight (kg)				0.31
No Complications	32	78.8	163	
Complications	40	84.6	189	
Total Procedure Duration (minutes)				0.00009
No Complications	20	88.7	391	
Complications	36	111.8	681	
Procedure End to Extubation (minutes)				0.039
No Complications	0	11.9	77	
Complications	3	14.2	45	
Procedure End to OR exit (minutes)				0.78
TIVA	0	18.9	98	
Gas	0	19.1	142	
Procedure End to OR exit (minutes)				0.0016
No Complications	0	18.4	98	
Complications	7	23.1	142	
Fentanyl (mcg)				0.64
No Complications	0	124.3	500	
Complications	0	138	750	
Number of Stations Sampled				0.084
No Complications	1	2.69	7	
Complications	1	3	7	
Number of TBNA Needle Passes				0.52
No Complications	1	4.1	10	
Complications	1	4.3	9	

Non-Categorical data are presented with Minimum (Min.), 1st Quartile (Qu.), Median, Mean, 3rd Quartile (Qu.), and Maximum (Max). Units are indicated where appropriate, Statistically significant results are indicated in bold.

^a Mann–Whitney U Test (Wilcoxon Rank Sum Test with continuity correction) was used to calculate p-values.

the incidence of respiratory complications, especially those not directly attributable to the invasiveness of the procedure itself. In this study, we have retrospectively assessed 586 patients at a single institution in order to determine what factors, if any, influence the occurrence of perioperative respiratory complications under GA during EBUS-TBNA including pre-existing patient characteristics and anesthetic factors.

In the bivariate analysis, our findings show that home oxygen use, pre-existing respiratory disease, ASA score, and intra-operative albuterol use are all associated with the occurrence of respiratory complications. The resultant patient characteristics are not unexpected, as supplemental oxygen therapy is a mainstay of treatment for seriously ill patients and

Table 6. Multivariable linear regression of longer post-extubation OR exit times on individual variables.

Outcomes and Covariates	p-value	Estimate
Outcome: Longer OR Exit Times		
Weight (kg)	0.029	0.052
Fentanyl (mcg)	0.028	0.013
Ketamine	0.0018	9.09

Statistically significant results are indicated in bold.

those with advanced respiratory disease.^{29–31} However, no individual anesthetic factors assessed were found to be associated with the occurrence of respiratory complications. Of note, the changes in respiratory physiology inherent to GA can contribute to the development of respiratory complications in vulnerable patients with poor baseline lung function, who are already at higher risk for a procedural respiratory complication.^{32–34} Our results are notably different from Eapen et al., who showed that transbronchial biopsy was the only risk factor for complications during EBUS-TBNA, and from Dhooria et al., who demonstrated a broad range of complications but established no outlined risk factors.^{10,12,35}

Our study found no significant association with TIVA versus volatile inhalation anesthesia during EBUS-TBNA and the incidence of respiratory complications. This result is inconclusive, especially when considering the results of other studies. Lai et al. demonstrated prolonged emergence and extubation among patients who received inhalational anesthetics versus propofol-based TIVA.³⁶ In contrast, a systematic literature review by Gupta et al. illustrated that emergence and early recovery is faster among patients receiving desflurane or sevoflurane compared to propofol.³⁷ Furthermore, propofol in combination with sevoflurane has been demonstrated to lead to shorter awakening and extubation times compared to pure volatile inhalational agents alone.³⁸ Given our result, more research must be done with regards to specific anesthetic management and its effects on emergence and extubation during EBUS-TBNA to elucidate any association.

Interestingly, our study demonstrated that higher fentanyl and ketamine doses are associated with longer OR exit times. With regards to fentanyl, this

Table 5. Multivariable logistic regression of respiratory complications on individual variables.

Outcomes and Covariates	OR	CI (2.5%–97.5%)	p-value
Outcome: Any Respiratory Complication			
Total Procedure Duration (minutes)	0.016	1.008–1.024	<0.0001
Albuterol Use Intraoperatively	1.83	1.007–3.226	0.041

Statistically significant results are indicated in bold.

result is consistent with some established findings. For example, patients undergoing coronary artery bypass grafting surgery who received fentanyl intraoperatively in place of shorter acting opiates required a longer period of mechanical ventilation.³⁹ However, other researchers observed that short acting opiates are not more advantageous than fentanyl as part of an intraoperative regimen.^{40,41} Lin et al. noted improved emergence when intraoperative fentanyl is used compared to tramadol among neurosurgical patients.⁴² With regards to ketamine, only two studies have assessed its efficacy and safety during EBUS-TBNA procedures. As an anesthetic agent in EBUS-TBNA, ketamine has been shown to be safe, efficacious, and effective.^{19,22} In this study, we demonstrate that ketamine is associated with prolonged time to OR exit in EBUS-TBNA patients, providing new insight into its role in the perioperative management in this cohort of patients. However, given the small fraction of patients in this study that received ketamine, this result requires further future analysis.

Our study also reflects a particularly high complication rate of 13.5%, especially when compared to other published studies. Notably, one of the largest EBUS-TBNA research efforts, the AQUIRE study, is significant for only 19 patient complications among 1317 patients. These complications included sustained hypoxemia defined as an oxygen saturation <90% for >1 min, which is much more liberal than our definition of SpO₂ <90% for >5 min. However, we do not view our higher complication rate to be inaccurate. The AQUIRE registry methods involved manual extraction of data from procedural notes, versus our utilization of an electronic medical recording system automatically recording oxygen saturations every minute, to track all hypoxemic events intraoperatively. Electronic scanning has previously been shown to be significantly more sensitive than voluntary reporting for intraoperative hypoxemia, as demonstrated by Sanborn et al. who showed that only 2 of their 54 prolonged desaturation events were reported voluntarily.⁴³ Thus, our higher complication rate likely reflects better ascertainment of complications.

This study is limited in several regards. First, this is a single site study with all EBUS-TBNA procedures performed by a small group of physicians. While our study had a relatively large sample size, further research should be conducted to incorporate data from a multi-center registry or data warehouse in order to enhance its overall power and standardize complication guidelines for greater consistency. Second, as a retrospective study, we are dependent on the observations and recordkeeping of others for

appropriate assessment, and potentially subjected to both selection and information bias. Third, our complications represent only those that occurred in the perioperative period as follow up after discharge was not conducted. Fourth, selection of anesthetic agents is not a random process and implicit to this is an inherent bias. In this study, we do not address the inherent selection biases on the part of the anesthesia practitioners. In future studies, prospective randomization would decrease this apparent bias. Lastly, although patient characteristics are comparable between those with and without respiratory complications, we cannot rule out the possibility that practice evolution and trends or initiatives at our institution may have confounded our results.

In summary, we conducted a novel retrospective analysis of patients undergoing EBUS-TBNA to investigate how patient characteristics and various aspects of GA influence the occurrence of respiratory complications intraoperatively. Each case was evaluated for respiratory complications that could not be attributed to the invasiveness of the procedure itself. Here, we have identified variables that influence the occurrence of respiratory complications and prolonged OR exit times. As such, we have contributed to the dialogue regarding general anesthetic techniques for EBUS-TBNA and identified particular patient elements that influence the occurrence of respiratory complications. These findings may be most helpful to individuals developing a program to risk-stratify patients through a pre-procedural checklist or to provide an additional layer of perioperative guidance to anesthesia providers.

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Conflicts of interest

None related to this work.

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