Evaluation of gastroesophageal reflux disease and hiatal hernia as risk factors for lobectomy complications

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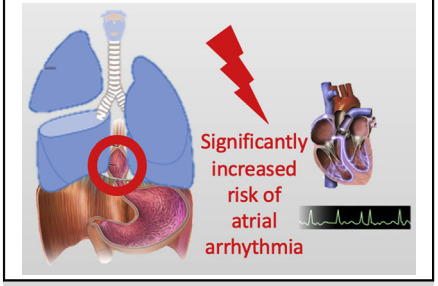
ABSTRACT

Objective: Up to 40% of lobectomies are complicated by adverse events. Gastroesophageal reflux disease (GERD) and hiatal hernia have been associated with morbidity across a range of clinical scenarios, yet their relation to recovery from pulmonary resection is understudied. We evaluated GERD and hiatal hernia as predictors of complications after lobectomy for lung cancer.

Methods: Lobectomy patients at Yale-New Haven Hospital between January 2014 and April 2021 were evaluated for predictors of 30-day postoperative complications, pneumonia, atrial arrhythmia, readmission, and mortality. Multivariable regression models included sociodemographic characteristics, body mass index, surgical approach, cardiopulmonary comorbidities, hiatal hernia, GERD, and preoperative acid-suppressive therapy as predictors.

Results: Overall, 824 patients underwent lobectomy, including 50.5% with a hiatal hernia and 38.7% with GERD. The median age was 68 [interquartile range, 61-74] years, and the majority were female (58.4%). At least 1 postoperative complication developed in 39.6% of patients, including atrial arrhythmia (11.7%) and pneumonia (4.1%). Male sex (odds ratio [OR], 1.51; 95% confidence interval [CI], 1.11-2.06, $P = .01$), age ≥70 years (OR, 1.55; 95% CI, 1.13-2.11, $P = .01$), hiatal hernia (OR, 1.40; 95% CI, 1.03-1.90, $P = .03$), and intraoperative packed red blood cells (OR, 4.80; 95% CI, 1.51-15.20, $P = .01$) were significant risk factors for developing at least 1 postoperative complication. Hiatal hernia was also a significant predictor of atrial arrhythmia (OR, 1.64; 95% CI, 1.02-2.62, $P = .04$) but was not associated with other adverse events.

Conclusions: Our findings indicate that hiatal hernia may be a novel risk factor for complications, especially atrial arrhythmia, following lobectomy that should be considered in the preoperative evaluation of lung cancer patients. (JTCVS Open 2022;11:327-45)



Hiatal hernia may significantly increase the risk of postlobectomy atrial arrhythmia.

CENTRAL MESSAGE

Hiatal hernia may be a novel risk factor for complications, especially atrial arrhythmia, after lobectomy for lung cancer that should be considered during preoperative risk stratification.

PERSPECTIVE

Within our single institution, hiatal hernia but not GERD was a risk factor for postoperative complications, especially atrial arrhythmia, after lobectomy. Considering hiatal hernia during preoperative risk stratification may enhance shared decision-making for pulmonary lobectomy, and if validated, potentially inform surveillance and prophylaxis strategies for atrial fibrillation in the future.

Lung cancer can be a particularly aggressive malignancy, accounting for 158,000 cancer-related deaths each year in the United States alone.[1] Surgical management via pulmonary lobectomy has traditionally been associated with the greatest cure rates for early-stage non–small cell lung cancer, yet the complication rate (approximately 40%) is greater than for many other oncologic procedures.[2,3] As a result, there is a great

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Abbreviations and Acronyms

BMI = body mass index
CI = confidence interval
CT = computed tomography
GERD = gastroesophageal reflux disease
OR = odds ratio
RBC = red blood cell

need to understand the risk factors for different types of surgical complications associated with lobectomy for lung cancer.

Many factors have been associated with complication rates after lobectomy. For example, the surgical approach (thoracotomy vs minimally invasive) as well as hospital and surgeon attributes, such as annual procedural volumes, have been correlated with postoperative adverse event rates.[2,3] Several patient characteristics also have been associated with lobectomy complication rates. For example, patient sex, advanced age, and tobacco smoking, all predict greater rates of complications after pulmonary resection for lung cancer.[4-6] Risk stratification based on patient attributes may not only improve shared decision-making and patient selection but also may expose opportunities to mitigate risk.

Gastroesophageal reflux disease (GERD), which affects an estimated 44.1% of the adult population in North America, has been increasingly linked to pulmonary and cardiac disease.[7] For example, GERD has been associated with pneumonia, emphysema, graft dysfunction following lung transplantation, and atrial arrhythmia in the general population.[8-11] Furthermore, hiatal hernias, a common cause of GERD, can be large enough to impact cardiorespiratory function independent of GERD.[12-14] Given the potential for GERD and hiatal hernia to impact respiratory and cardiac function, it is possible that these conditions could impact the recovery from pulmonary surgery to treat lung cancer. However, the relationships between GERD, hiatal hernia, and complications after surgical management for lung cancer have not been fully explored.

We hypothesized that patients with GERD or hiatal hernia were at increased risk for complications, and specifically cardiopulmonary complications, after lobectomy for lung cancer. We examined 30-day lobectomy outcomes within our single institution experience to clarify the relationship between GERD and hiatal hernia with adverse events among patients recovering from lobectomy for lung cancer.

METHODS

Data Source

This study was a retrospective cohort study of patients undergoing lobectomy at Yale-New Haven Hospital. A research database was created and populated via direct chart review, as well as data-sharing from our prospectively maintained institutional database for participation in the Society of Thoracic Surgeons General Thoracic Surgery Database. The Yale School of Medicine institutional review board approved this study with consent waived because patient data were deidentified (protocol ID: 1103008160; most recent approval date March 5, 2020).

Patient Cohort

All patients undergoing lobectomy for lung cancer at Yale-New Haven Hospital from January 2014 to April 2021 were eligible for the study. Patients without available cross-sectional imaging (computed tomography [CT] or CT/positron emission tomography scanning) before lobectomy were excluded (13 patients, 1.6%).

Covariates

Covariates were determined by review of the patient's medical record and, when applicable, defined in accordance with the Society of Thoracic Surgeons General Thoracic Surgical Database.[15] The following data elements were assessed: patient sex, age (<70 years old vs ≥70 years old),[16] race (White vs not White), body mass index (BMI; <25 vs 25-29.9 vs ≥30), lobectomy laterality (left vs right), pulmonary lobe involved (upper, middle, lower), smoking status (current smoker: yes vs no), preoperative chemotherapy within 6 months of lobectomy, previous radiation therapy, surgical approach (minimally invasive, ie, thoracoscopic or robotic-assisted, vs open), forced expiratory volume in 1 second percent of predicted (≤80% vs >80%),[17] and the receipt of intraoperative red blood cells (RBCs). Information on select comorbidities was collected if documented before the day of lobectomy: asthma, previous history of pneumonia, diabetes, hypertension, coronary artery disease, hiatal hernia, and GERD. Preoperative acid-suppressive therapy was similarly determined using the electronic medical record and defined as either a proton pump inhibitor or H2-blocker. Hiatal hernia and GERD were considered independent variables, as there was imperfect overlap between the 2 diagnoses.

Every patient had a minimum of 1 CT scan reviewed, which had to be obtained within the 6 months before operative resection and include at least a 5-mm thickness series. When available within this time frame, an additional CT scan of the chest or abdomen or a CT scan acquired in concordance with CT/positron emission tomography scan was assessed, including scans with oral contrast for other indications. Axial and coronal images with mediastinal window settings were evaluated solely for the presence of a hiatal hernia by a single radiologist (M.D.C.), without previous knowledge of diagnosis. The presence of hiatal hernia was determined by evaluation of the esophagus in relation to the diaphragm, using standard anatomical definitions (any criterion sufficient for diagnosis)[18-20]: (1) lower esophageal ring ≥1 to 2 cm above the level of the diaphragmatic hiatus; (2) esophageal hiatus widened to 3 to 4 cm (upper limit of normal: 1.5 cm); and (3) stomach folds or oral contrast pooling above the level of the gastroesophageal junction.

We do not routinely administer oral contrast for lung cancer screening or preoperative CT scans. However, a considerable proportion of our patients have a nodule and ultimately a cancer diagnosed as an incidental finding on a CT scan performed for an unrelated reason. A subset of these scans for unrelated reasons includes oral contrast administration.

Outcomes

Dependent variables included 30-day surgical complications, postoperative pneumonia, postoperative atrial arrhythmia, hospital readmission, and mortality, which were defined in accordance with the Society of Thoracic Surgeons General Thoracic Surgical Database and abstracted from the medical record by trained registrars.[15] Any of the following were considered major complications: pneumonia, acute respiratory distress syndrome, bronchopleural fistula, pulmonary embolism, mechanical ventilation for >48 hours, respiratory failure, tracheostomy, myocardial infarction, and nonspecified other event requiring the operating room with anesthesia.[21]

TABLE 1. Lobectomy patient characteristics

Covariate	n (%)
Sex	
Female	481 (58.4)
Male	343 (41.6)
Age, y	
<70	462 (56.1)
≥70	362 (43.9)
Race	
White	711 (86.3)
Not White	113 (13.7)
BMI	
<25	276 (33.5)
25-29.9	288 (35.0)
≥30	260 (31.5)
Laterality	
Left	310 (37.6)
Right	514 (62.4)
Lobe	
Upper	495 (60.1)
Middle	73 (8.8)
Lower	256 (31.1)
Active smoker	
No	627 (76.1)
Yes	197 (23.9)
Preoperative chemotherapy	
No	767 (93.1)
Yes	57 (6.9)
Previous radiation therapy	
No	779 (94.5)
Yes	45 (5.5)
Minimally invasive vs open	
Minimally invasive	699 (84.8)
Open	125 (15.2)
FEV1 % predicted	
>80	528 (64.1)
≤80	273 (33.1)
Missing	23 (2.8)
Asthma	
No	673 (81.7)
Yes	151 (18.3)
Past pneumonia	
No	694 (84.2)
Yes	130 (15.8)
Diabetes	
No	685 (83.1)
Yes	139 (16.9)
Hypertension	
No	317 (38.5)
Yes	507 (61.5)
Coronary artery disease	
No	695 (84.3)
Yes	129 (15.7)
Hiatal hernia	
No	408 (49.5)
Yes	416 (50.5)
GERD	
No	505 (61.3)
Yes	319 (38.7)
Preoperative acid-suppressive therapy	
No	554 (67.2)
Yes	270 (32.8)
Intraoperative RBCs	
No	803 (97.5)
Yes	21 (2.5)
Tumor size	
<2 cm	382 (46.3)
2-2.9 cm	209 (25.4)
3-4.9 cm	162 (19.7)
5-6.9 cm	50 (6.1)
≥7 cm	21 (2.5)
Clinical N stage	
N0	739 (89.7)
N1	59 (7.2)
N2	25 (3.0)
N3	1 (0.1)

BMI, Body mass index; *FEV1*, forced expiratory volume in 1 second; *GERD*, gastroesophageal reflux disease; *RBCs*, red blood cells.

Statistical Analysis

Categorical variables were compared using the Pearson χ^2 tests or the Fisher exact test, as appropriate. Multivariable logistic regression analyses were performed to identify predictors of the 30-day postoperative outcomes of interest (complications, pneumonia, atrial arrhythmia, readmission, and mortality) and were adjusted for by patient sex, age, race, BMI, tumor laterality, tumor lobe, active smoking status, preoperative chemotherapy in the 6 months before lobectomy, previous radiation therapy, surgical approach, forced expiratory volume in 1 second percentage of predicted, asthma, past pneumonia, diabetes, hypertension, coronary artery disease, hiatal hernia, GERD, preoperative acid-suppressive therapy, and intraoperative RBCs. All tests were 2-sided. Data were analyzed using SAS, version 9.4 (SAS Institute Inc) and Stata, version 16.1 (StataCorp LLC).

RESULTS

Patient Population

Overall, 824 patients underwent lobectomy, including 416 (50.5%) patients with a preoperative hiatal hernia, and 319 (38.7%) with GERD. The overlap between hiatal hernia and GERD was inconsistent, with 45.4% of hernia patients having documented GERD and 59.2% of GERD patients having a hiatal hernia. A total of 270 (32.8%) patients were documented as taking preoperative acid-suppressive therapy before lobectomy. The median age was 68 [interquartile range, 61-74] years, 481 (58.4%) patients were female, and 197 (23.9%) patients reported actively smoking at the time of lobectomy. Additional patient characteristics are listed in Table 1.

30-Day Postoperative Complication Rates

At least 1 complication occurred in 39.6% of patients, including major complications (see the Methods) in 7.3% (Table 2). Among the most common complications were atrial arrhythmia (11.7%) and pneumonia (4.1%). In general, patients who developed adverse events were more likely to be male, ≥70 years old, undergo upper lobectomy, undergo open surgery, have a hiatal hernia, and receive packed RBCs intraoperatively (Table 3).

Predictors of at Least One 30-Day Postoperative Complication

Multivariable logistic regression analyses were performed to determine predictors of at least 1 complication following lobectomy (Table 3). Male sex (odds ratio [OR], 1.51, 95% confidence interval [CI], 1.11-2.06, $P = .01$), age ≥70 years (OR, 1.55; 95% CI, 1.13-2.11, $P = .01$), hiatal hernia (OR, 1.40; 95% CI, 1.03-1.90, $P = .03$), and intraoperative RBCs (OR, 4.80; 95% CI, 1.51-15.20, $P = .01$) were significant risk factors. Interestingly, chemotherapy in the 6 months before lobectomy appeared to be protective (OR, 0.47; 95% CI, 0.24-0.93, $P = .03$).

Predictors of 30-Day Postoperative Cardiopulmonary Complications

We performed a more focused evaluation of cardiopulmonary complications, as these could be supported by the anatomic and physiologic changes associated with hiatal hernia and GERD (Figure 1). For postoperative pneumonia, active smoking (OR, 2.24; 95% CI, 1.01-4.96, $P = .048$), chemotherapy in the 6 months before lobectomy (OR, 4.16; 95% CI, 1.28-13.48, $P = .02$), and receiving intraoperative RBCs (OR, 3.87; 95% CI, 1.01-14.78, $P = .048$) were identified as significant risk factors (Table E1). Hiatal hernia and GERD were not significantly associated with the risk of postoperative pneumonia. BMI ≥30 appeared to be protective (OR, 0.23; 95% CI, 0.06-0.87, $P = .03$). For postoperative atrial arrhythmia, male sex (OR, 2.18; 95% CI, 1.35-3.52, $P = .001$), age ≥70 years (OR, 1.84; 95% CI, 1.13-2.98, $P = .01$), previous radiation therapy (OR, 3.14; 95% CI, 1.26-7.77, $P = .01$), open surgery (OR, 2.17; 95% CI, 1.18-3.97, $P = .01$), asthma (OR, 1.92; 95% CI, 1.08-3.40, $P = .03$), hiatal hernia (OR, 1.64; 95% CI, 1.02-2.62, $P = .04$), and receiving intraoperative RBCs (OR, 3.10; 95% CI, 1.10-8.70, $P = .03$) were identified as risk factors (Figure 2, Table E2).

Predictors of 30-Day Postoperative Readmission and Mortality

None of the assessed factors were significantly associated with 30-day readmission on adjusted analysis (Table E3). The risk of 30-day mortality was significantly elevated in patients who had asthma (OR, 7.61; 95% CI, 1.45-39.99, $P = .02$) and underwent open surgery (OR, 8.25; 95% CI, 1.39-49.06, $P = .02$) (Table E4). Neither GERD nor hiatal hernia were predictors of readmission or mortality.

TABLE 2. Complications after lobectomy for lung cancer

	n (%)*
At least 1 complication†	326 (39.6)
Major complication‡	60 (7.3)
Pulmonary complications	
Pneumonia	34 (4.1)
Pleural effusion	18 (2.2)
Pneumothorax	22 (2.7)
Atelectasis	16 (1.9)
ARDS	4 (0.5)
Bronchopleural fistula	1 (0.1)
Pulmonary embolism	6 (0.7)
Respiratory failure	19 (2.3)
Other pulmonary complications§	119 (14.4)
Cardiovascular complications	
Atrial arrhythmia	96 (11.7)
Ventricular arrhythmia	2 (0.2)
Myocardial infarction	1 (0.1)
Other cardiovascular complications‖	15 (1.8)
Noncardiopulmonary complications	
Ileus	8 (1.0)
Urinary tract infection	34 (4.1)
Empyema	5 (0.6)
Sepsis	1 (0.1)
Other complications¶	152 (18.4)

ARDS, Acute respiratory distress syndrome. *Column is not additive because complications are not mutually exclusive. †Patients who developed any complication. ‡At least 1 of the following: pneumonia, ARDS, bronchopleural fistula, pulmonary embolism, mechanical ventilation for >48 hours, respiratory failure, tracheostomy, myocardial infarction, or nonspecified other event requiring the operating room with anesthesia. §At least 1 of the following: postoperative air leak >5 days, initial mechanical ventilation support for > 48 hours, tracheostomy, nonspecified other pulmonary complications. ‖At least 1 of the following: deep venous thrombosis, nonspecified other cardiovascular complication. ¶At least 1 of the following: unanticipated postoperative invasive procedure, *Clostridium difficile* infection, other gastrointestinal complication, transfusion, urinary retention, discharged with Foley, surgical-site infection, nonspecified infection requiring antibiotics, new central neurologic event, laryngeal nerve paresis, delirium tremens, nonspecified other neurologic complication, renal failure, chylothorax, nonspecified other event requiring the operating room with anesthesia, or unexpected intensive care unit admission.

Distribution of Preoperative Acid-Suppressive Therapy and Complications by Hiatal Hernia and GERD Status

The prevalence of preoperative acid-suppressive therapy differed by hiatal hernia and GERD status. Preoperative acid-suppressive therapy was more prevalent among patients with GERD only (65.4%) or with both GERD and hiatal hernia (67.2%) than in patients who only had a hiatal hernia (14.5%) or neither GERD nor hiatal hernia (9.0%). Patients with only GERD had the lowest frequency of any postoperative complication (31.5%) and atrial arrhythmia (7.7%), whereas patients with only hiatal hernia

TABLE 3. Characteristics of lobectomy patients with or without postoperative complications following lobectomy and multivariable logistic regression for any postoperative complications

	Any postoperative complication		Multivariable logistic regression	
Covariate	**n (%)**	***P* value**	**Odds ratio (95% CI)**	***P* value**
Sex				
Female	169 (35.1)	.002	Ref	
Male	157 (45.8)		1.51 (1.11-2.06)	.01
Age, y				
<70	158 (34.2)	<.001	Ref	
≥70	168 (46.4)		1.55 (1.13-2.11)	.01
Race				
White	282 (39.7)	.88	Ref	
Not White	44 (38.9)		0.96 (0.22-1.48)	.84
BMI				
<25	114 (41.3)	.25	Ref	
25-29.9	120 (41.7)		0.90 (0.62-1.30)	.64
≥30	92 (35.4)		0.70 (0.47-1.04)	.08
Laterality				
Left	123 (39.7)	.96	Ref	
Right	203 (39.5)		1.02 (0.75-1.39)	.91
Lobe				
Upper	213 (43.0)	.01	Ref	
Middle	19 (26.0)		0.55 (0.31-0.99)	.11
Lower	94 (36.7)		0.78 (0.56-1.08)	.81
Active smoker				
No	244 (38.9)	.50	Ref	
Yes	82 (41.6)		1.08 (0.75-1.54)	.69
Preoperative chemotherapy				
No	306 (39.9)	.47	Ref	
Yes	20 (35.1)		0.47 (0.24-0.93)	.03
Previous radiation therapy				
No	304 (39.0)	.19	Ref	
Yes	22 (48.9)		1.76 (0.87-3.55)	.12
Minimally invasive vs open				
Minimally invasive	263 (37.6)	.01	Ref	
Open	63 (50.4)		1.51 (0.97-2.35)	.07
FEV1 % predicted				
>80	201 (38.1)	.50	Ref	
≤80	115 (42.1)		1.03 (0.75-1.42)	.57
Missing	10 (43.5)		1.44 (0.59-3.53)	.44
Asthma				
No	263 (39.1)	.55	Ref	
Yes	63 (41.7)		1.34 (0.90-1.97)	.15
Past pneumonia				
No	265 (38.2)	.06	Ref	
Yes	61 (46.9)		1.23 (0.82-1.83)	.31
Diabetes				
No	268 (39.1)	.57	Ref	
Yes	58 (41.7)		1.07 (0.71-1.62)	.75
Hypertension				
No	115 (36.3)	.13	Ref	
Yes	211 (41.6)		1.15 (0.83-1.60)	.40

(Continued)

TABLE 3. Continued

Any postoperative complication			Multivariable logistic regression	
Covariate	**n (%)**	***P* value**	**Odds ratio (95% CI)**	***P* value**
Coronary artery disease				
No	268 (38.6)	.17	Ref	
Yes	58 (45.0)		1.02 (0.66-1.56)	.94
Hiatal hernia				
No	146 (35.8)	.03	Ref	
Yes	180 (43.3)		1.40 (1.03-1.90)	.03
GERD				
No	216 (42.8)	.02	Ref	
Yes	110 (34.5)		0.76 (0.52-1.10)	.16
Preoperative acid-suppressive therapy				
No	228 (41.2)	.18	Ref	
Yes	98 (36.3)		0.91 (0.62-1.34)	.64
Intraoperative RBCs				
No	309 (38.5)	<.001	Ref	
Yes	17 (80.9)		4.80 (1.51-15.20)	.01

CI, Confidence interval; *Ref*, reference; *BMI*, body mass index; *FEV1*, forced expiratory volume in 1 second; *GERD*, gastroesophageal reflux disease; *RBCs*, red blood cells.

had the greatest (48.9% and 17.2%, respectively; Table E5). For patients with hiatal hernia, GERD, or both, the rates of any complication were consistently lower for patients receiving preoperative acid-suppressive therapy compared with patients who were not receiving preoperative acid-suppressive therapy. However, there was no clear trend in pneumonia or atrial arrhythmia rates for patients with hiatal hernia, GERD, or both based on preoperative acid-suppressive therapy status (Table E6).

COMMENT

Our objective was to evaluate GERD and hiatal hernia as risk factors for complications after lobectomy for lung cancer. This is the first study to identify hiatal hernia as an independent risk factor for postlobectomy complications, in particular for atrial arrhythmia. Atrial fibrillation remains one of the most common complications after pulmonary resection and has been associated with increased short-term morbidity, mortality, and decreased long-term survival.[6,22] Previous studies have described an association between hiatal hernia and atrial fibrillation in the general hospital population and among patients scheduled for cardiac ablation.[14,23] While the mechanism is unknown, hiatal hernia has been hypothesized to cause atrial fibrillation through direct mechanical or reflux-induced inflammatory irritation of the left atria.[11,14] Mechanical irritation, potentially enhanced by intraoperative manipulation and lobectomy-associated anatomical changes, may partially explain our findings.[24] We observed that patients with only hiatal hernia—a population that may include a subset of patients with occult and untreated reflux—had lower rates of preoperative acid-suppressive therapy but a greater prevalence of developing at least 1 complication, as well as pneumonia and atrial arrhythmia, than patients with both GERD and hiatal hernia. We considered the possibility that preoperative acid-suppressive therapy was having a protective effect, however, were not able to confirm this in multivariable analyses. This evaluation may have been confounded by our standard to administer postoperative acid-suppressive therapy for ulcer prophylaxis regardless of GERD status. In other studies, long-term acid-suppressive therapy has actually been associated with increased complications such as pneumonia, possibly due to alterations in the pH or the microbiome of refluxed material.[25,26] Interestingly, the prevalence of hiatal hernia in our study population was 50.5%, which is more than twice the estimated prevalence of 15% to 20% in the general population.[27] This is likely the result of our diagnostic approach of having a dedicated radiologist specifically focusing on anatomy at the hiatus, which would increase sensitivity, or potentially shared risk factors for the development of lung cancer and esophagitis (eg, age, smoking/chronic obstructive pulmonary disease).[28,29]

GERD, in contrast, did not increase the risk for any complication following lobectomy in our study. Although reflux has been associated with atrial fibrillation[30] and pneumonia[8] in the general population, information about the implications of GERD in patients with lung cancer undergoing lobectomy is sparse. Our findings are in line with another study in which GERD was not a risk factor for unfavorable disposition or mortality following lobectomy.[31]

The incomplete overlap between hiatal hernia and GERD, which also has been demonstrated by other investigators,[32,33] could indicate differences in pathophysiology and risk profile. A large population-based study, for example, attempted to elucidate the interplay between

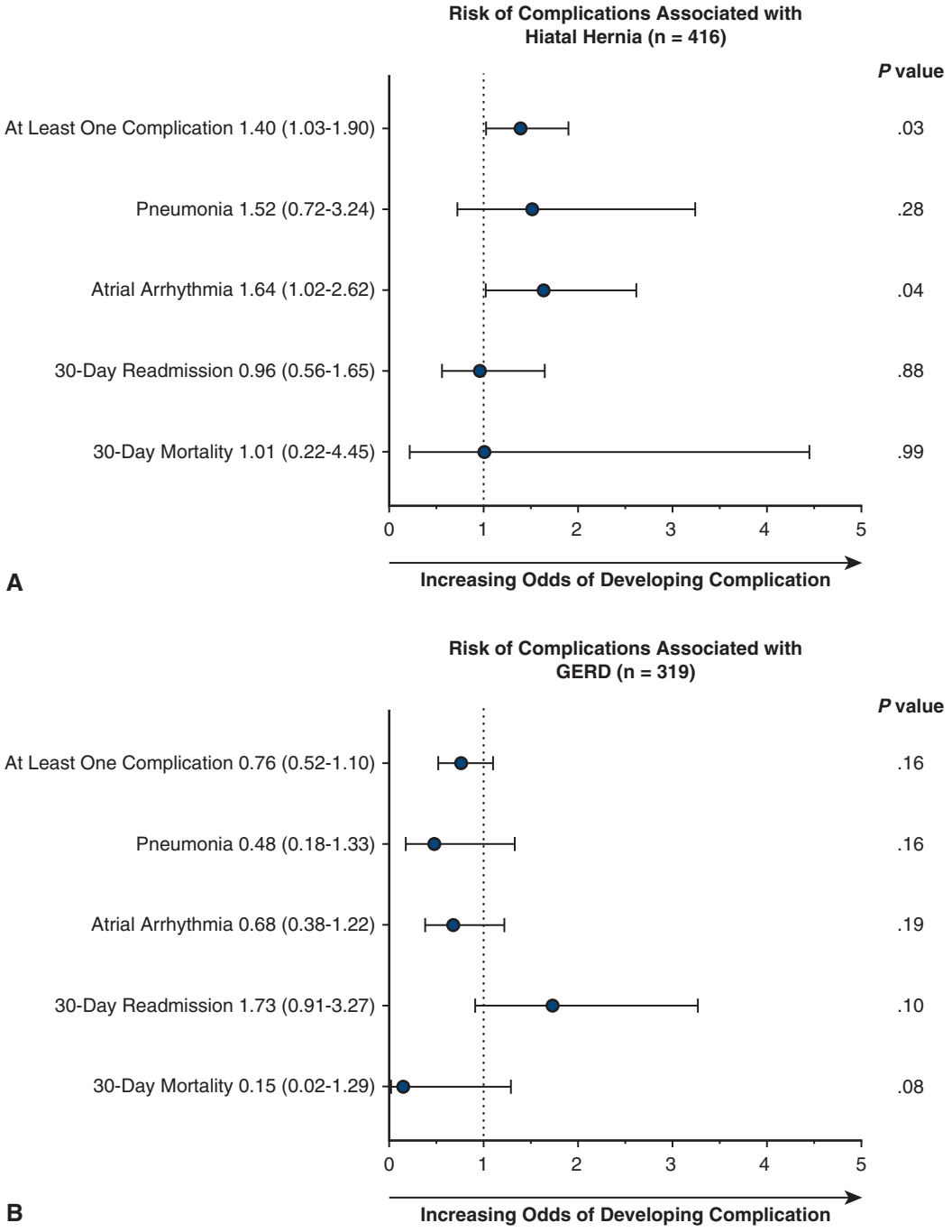

FIGURE 1. Likelihood of developing postoperative complications within 30 days after lobectomy for lung cancer in the presence of (A) hiatal hernia or (B) GERD. Odds ratios were obtained in separate logistic regression models for every complication, which, besides hiatal hernia and GERD, were also adjusted for sex, age, race, BMI, tumor laterality, lobe involved, smoking status, preoperative chemotherapy, previous radiation, surgical approach (minimally invasive vs open), FEV1% predicted, asthma, history of pneumonia, diabetes, hypertension, coronary artery disease, preoperative acid-suppressive therapy, and intraoperative transfusion (see Table 3 and Tables E1-E4). *GERD*, Gastroesophageal reflux disease.

GERD and esophagitis. Similar to our findings, GERD alone was not associated with atrial fibrillation. However, in the presence of esophagitis, for which hiatal hernia is a strong risk factor, the risk of atrial fibrillation significantly increased.[34] Given the high complication rates among patients with hiatal hernia only in our study, it is possible that this group included a subpopulation with undiagnosed reflux esophagitis.

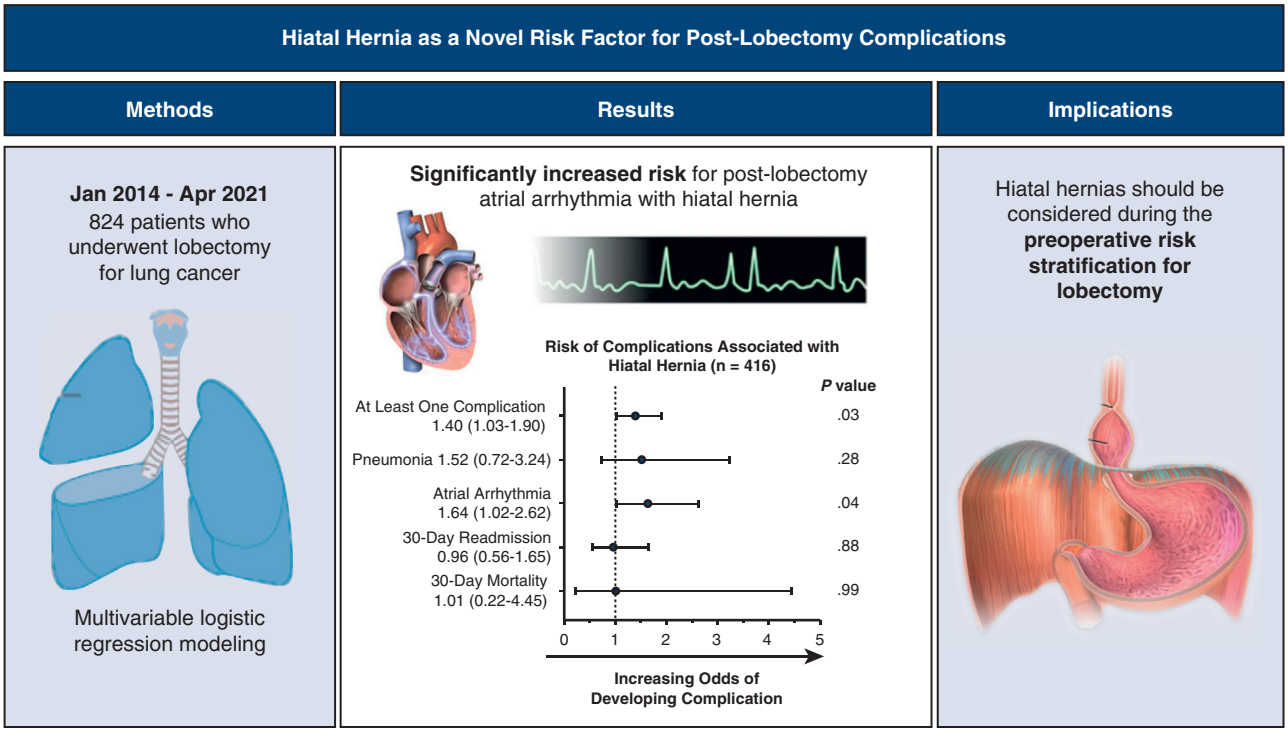

FIGURE 2. Graphical abstract summarizing the study methods, results, and implications.

Several other risk factors for postlobectomy complications were identified. Open surgery, for example, was associated with an increased risk of atrial fibrillation and approached significance as a risk factor for at least one complication. While surgical approach has been clearly correlated with postoperative complications in the literature, the evidence for atrial fibrillation is mixed.[2,35,36] Moreover, we identified an association between neoadjuvant chemotherapy within 6 months before lobectomy and postoperative pneumonia, which is partially congruent with the findings of previous studies.[16,17] Interestingly, neoadjuvant chemotherapy within 6 months before lobectomy appeared to be protective against any complication for our study sample, but this represented a small subgroup that may have been influenced by health related selection effects such as a higher threshold for medical clearance and optimization before surgery. We also identified an association between previous radiation therapy and postoperative atrial arrhythmia. Although radiation therapy has been implicated as a risk factor for atrial fibrillation and other arrhythmias in cancer patients, presumably through injury and fibrosis of the cardiac conduction system,[37] other studies failed to find an association.[6,38]

The median BMI was very similar among patients with and without hiatal hernia and GERD diagnosis. However, a BMI $\geq$30 was associated with a decreased risk of postoperative pneumonia, which may be a reflection of greater nutritional reserves aiding during the postoperative recovery period. In fact, there is considerable disagreement within the literature about the effect of obesity on pneumonia following lung cancer surgery, as some studies also found a protective effect of obesity or higher BMI,[39-41] whereas other studies have found obesity to be a risk factor.[4,42,43]

Limitations

Our study has several limitations. As a single institution series of just more than 800 cases, it is possible that important associations between hiatal hernia, GERD, and postoperative complications were missed because of power. For example, our power to detect the observed difference in pneumonia rate associated with hiatal hernia was only 18.6%. The gold standard for diagnosis of hiatal hernia is esophagogastroduodenoscopy or barium-swallow esophagram rather than CT,[44] but the former are not routinely collected before lobectomy and thus cannot be used for patient risk stratification. Hiatal hernia diagnosis can be subjective and may, therefore, vary highly across radiologist reviews.[45] In an attempt to be consistent, a single radiologist evaluated all patient scans based on previously published criteria to classify hiatal hernias.[18-20] However, a radiologist overreading existing CT scans looking solely for hiatal hernia may have increased the observed prevalence of hiatal hernia in our patient population compared with standard radiology reads. However, we recognize that there may be nuanced implications based

on relative size of hernia and morphology that were not able to be characterized because CT scans provide only a "snapshot" of hiatal hernias, most of which are sliding hernias and whose maximal dimensions are not accurately measured by CT. Moreover, comorbidities like GERD may be inconsistently documented in the medical record, and proper diagnosis and treatment are likely influenced by socioeconomic factors affecting access to care such as income or geographic proximity to medical facilities. Our institution's standard to administer postoperative acid-suppressive therapy for ulcer prophylaxis regardless of GERD status and postoperative calcium channel blockers for atrial fibrillation prophylaxis may have affected the postoperative complication rates and confounded our analyses, particularly between GERD and postoperative complications. However, our study sample's 30-day postoperative pneumonia and atrial arrhythmia complication rates closely approximated previously reported rates of postlobectomy pneumonia[4,5,21,46,47] and atrial arrhythmia.[22,47-49] Finally, a considerable proportion of GERD is asymptomatic, but the GERD prevalence in our study approximates recent estimates of GERD in the US population.[7]

CONCLUSIONS

Hiatal hernia was identified as a novel risk factor for complications after pulmonary lobectomy, particularly for atrial arrhythmia. The increased risk should be considered in the perioperative consultation with lobectomy patients and potentially be considered as patients are risk stratified for prophylaxis. Further study to more completely characterize the relationship of hiatal hernia and GERD with surgical outcomes in lung cancer is warranted.

Conflict of Interest Statement

D.J.B. is a member of the Commission on Cancer and receives nonfinancial support from Epic science, which performs assays for free, but this work is not directly tied to or supported by either. All other authors reported no conflicts of interest.

The *Journal* policy requires editors and reviewers to disclose conflicts of interest and to decline handling or reviewing manuscripts for which they may have a conflict of interest. The editors and reviewers of this article have no conflicts of interest.

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Key Words: lung cancer, lobectomy, hiatal hernia, GERD, postoperative complications, atrial arrhythmia

TABLE E1. Characteristics of lobectomy patients with or without postoperative pneumonia following lobectomy and multivariable logistic regression for postoperative pneumonia

	Any postoperative pneumonia		Multivariable logistic regression	
Covariate	**n (%)**	***P* value**	**Odds ratio (95% CI)**	***P* value**
Sex				
Female	14 (2.9)	.04	Ref	
Male	20 (5.8)		1.96 (0.92-4.17)	.08
Age, y				
<70	17 (3.7)	.47	Ref	
≥70	17 (4.7)		1.22 (0.56-2.62)	.62
Race				
White	28 (3.9)	.50	Ref	
Not White	6 (5.3)		1.34 (0.49-3.64)	.57
BMI				
<25	15 (5.4)	<.001	Ref	
25-29.9	16 (5.6)		0.87 (0.39-1.97)	.16
≥30	3 (1.1)		0.23 (0.06-0.87)	.03
Laterality				
Left	11 (3.5)	.52	Ref	
Right	23 (4.5)		1.28 (0.58-2.82)	.54
Lobe				
Upper	25 (5.1)	.01	Ref	
Middle	1 (1.4)		0.35 (0.04-2.81)	.40
Lower	8 (3.1)		0.73 (0.31-1.74)	.74
Active smoker				
No	20 (3.2)	.02	Ref	
Yes	14 (7.1)		2.24 (1.01-4.96)	.048
Preoperative chemotherapy				
No	28 (3.7)	.01	Ref	
Yes	6 (10.5)		4.16 (1.28-13.48)	.02
Previous radiation therapy				
No	32 (4.1)	.28	Ref	
Yes	2 (4.4)		0.38 (0.06-2.33)	.30
Minimally invasive vs open				
Minimally Invasive	26 (3.7)	.17	Ref	
Open	8 (6.4)		0.96 (0.36-2.56)	.93
FEV1 % predicted				
>80	19 (3.6)	.50	Ref	
≤80	14 (5.1)		1.13 (0.53-2.43)	.96
Missing	1 (4.3)		1.36 (0.16-11.88)	.82
Asthma				
No	29 (4.3)	.58	Ref	
Yes	5 (3.3)		0.79 (0.28-2.26)	.66
Past pneumonia				
No	25 (3.6)	.08	Ref	
Yes	9 (6.9)		1.76 (0.75-4.13)	.20
Diabetes				
No	29 (4.2)	.73	Ref	
Yes	5 (3.6)		0.93 (0.31-2.75)	.89
Hypertension				
No	11 (3.5)	.45	Ref	
Yes	23 (4.5)		1.35 (0.59-3.09)	.48

(Continued)

TABLE E1. Continued

	Any postoperative pneumonia		Multivariable logistic regression	
Covariate	**n (%)**	***P* value**	**Odds ratio (95% CI)**	***P* value**
Coronary artery disease				
No	26 (3.7)	.20	Ref	
Yes	8 (6.2)		1.30 (0.51-3.36)	.58
Hiatal hernia				
No	14 (3.4)	.32	Ref	
Yes	20 (4.8)		1.52 (0.72-3.24)	.28
GERD				
No	25 (5.0)	.13	Ref	
Yes	9 (2.8)		0.48 (0.18-1.33)	.16
Preoperative acid-suppressive therapy				
No	23 (4.1)	.96	Ref	
Yes	11 (4.1)		1.68 (0.64-4.42)	.29
Intraoperative RBCs				
No	309 (38.5)	.01	Ref	
Yes	4 (19.0)		3.87 (1.01-14.78)	.048

CI, Confidence interval; *Ref*, reference; *BMI*, body mass index; *FEV1*, forced expiratory volume in 1 second; *GERD*, gastroesophageal reflux disease; *RBCs*, red blood cells.

TABLE E2. Characteristics of lobectomy patients with or without postoperative atrial arrhythmia following lobectomy and multivariable logistic regression for postoperative atrial arrhythmia

	Postoperative atrial arrhythmia		Multivariable logistic regression	
Covariate	n (%)	*P* value	Odds ratio (95% CI)	*P* value
Sex				
Female	42 (8.7)	.002	Ref	
Male	54 (15.7)		2.18 (1.35-3.52)	.001
Age, y				
<70	42 (9.1)	.01	Ref	
≥70	54 (14.9)		1.84 (1.13-2.98)	.01
Race				
White	87 (12.2)	.19	Ref	
Not White	9 (8.0)		0.60 (0.28-1.27)	.18
BMI				
<25	28 (10.1)	.60	Ref	
25-29.9	37 (12.8)		1.21 (0.68-2.13)	.62
≥30	31 (11.9)		1.15 (0.61-2.15)	.87
Laterality				
Left	28 (9.0)	.07	Ref	
Right	68 (13.2)		1.49 (0.90-2.45)	.12
Lobe				
Upper	58 (11.7)	.98	Ref	
Middle	8 (11.0)		1.20 (0.51-2.81)	.76
Lower	30 (11.7)		1.10 (0.66-1.83)	.98
Active smoker				
No	76 (12.1)	.45	Ref	
Yes	20 (10.2)		0.97 (0.54-1.72)	.91
Preoperative chemotherapy				
No	89 (11.6)	.88	Ref	
Yes	7 (12.3)		0.48 (0.17-1.38)	.17
Previous radiation therapy				
No	85 (10.9)	.01	Ref	
Yes	11 (24.4)		3.14 (1.26-7.77)	.01
Minimally invasive vs open				
Minimally invasive	71 (10.2)	.002	Ref	
Open	25 (20.0)		2.17 (1.18-3.97)	.01
FEV1 % predicted				
>80	64 (12.1)	.01	Ref	
≤80	32 (11.7)		0.82 (0.50-1.34)	.96
Missing	0 (0.0)		<.001 (<.001 to >999.99)	.96
Asthma				
No	75 (11.1)	.34	Ref	
Yes	21 (13.9)		1.92 (1.08-3.40)	.03
Past pneumonia				
No	80 (11.5)	.80	Ref	
Yes	16 (12.3)		0.82 (0.45-1.52)	.54
Diabetes				
No	82 (12.0)	.52	Ref	
Yes	14 (10.1)		0.73 (0.38-1.42)	.35
Hypertension				
No	35 (11.0)	.67	Ref	
Yes	61 (12.0)		1.01 (0.61-1.66)	.97

(Continued)

TABLE E2. Continued

	Postoperative atrial arrhythmia		Multivariable logistic regression	
Covariate	**n (%)**	***P* value**	**Odds ratio (95% CI)**	***P* value**
Coronary artery disease				
No	80 (11.5)	.77	Ref	
Yes	16 (12.4)		0.70 (0.37-1.34)	.29
Hiatal hernia				
No	38 (9.3)	.04	Ref	
Yes	58 (13.9)		1.64 (1.02-2.62)	.04
GERD				
No	67 (13.3)	.07	Ref	
Yes	29 (9.1)		0.68 (0.38-1.22)	.19
Preoperative acid-suppressive therapy				
No	67 (12.1)	.57	Ref	
Yes	29 (10.7)		0.98 (0.55-1.76)	.95
Intraoperative RBCs				
No	88 (11.0)	<.001	Ref	
Yes	8 (38.1)		3.10 (1.10-8.70)	.03

CI, Confidence interval; *Ref*, reference; *BMI*, body mass index; *FEV1*, forced expiratory volume in 1 second; *GERD*, gastroesophageal reflux disease; *RBCs*, red blood cells.

TABLE E3. Characteristics of lobectomy patients with or without 30-day readmission following lobectomy and multivariable logistic regression for 30-day readmission

	30-day readmission		Multivariable logistic regression	
Covariate	n (%)	*P* value	Odds ratio (95% CI)	*P* value
Sex				
Female	37 (7.8)	.92	Ref	
Male	27 (7.9)		0.91 (0.52-1.62)	.76
Age, y				
<70	32 (7.0)	.31	Ref	
≥70	32 (8.9)		1.26 (0.73-2.19)	.41
Race				
White	57 (8.1)	.52	Ref	
Not White	7 (6.3)		0.83 (0.35-1.93)	.66
BMI				
<25	21 (7.7)	.55	Ref	
25-29.9	26 (9.1)		1.23 (0.65-2.33)	.27
≥30	17 (6.6)		0.82 (0.40-1.70)	.34
Laterality				
Left	19 (6.2)	.17	Ref	
Right	45 (8.8)		1.49 (0.83-2.67)	.18
Lobe				
Upper	44 (8.9)	.01	Ref	
Middle	5 (6.8)		0.65 (0.23-1.80)	.65
Lower	15 (6.0)		0.67 (0.36-1.26)	.63
Active smoker				
No	53 (8.5)	.19	Ref	
Yes	11 (5.6)		0.64 (0.32-1.30)	.22
Preoperative chemotherapy				
No	57 (7.5)	.08	Ref	
Yes	7 (12.5)		1.00 (0.36-2.80)	1.00
Previous radiation therapy				
No	57 (7.4)	.03	Ref	
Yes	7 (12.5)		2.32 (0.83-6.50)	.11
Minimally invasive vs open				
Minimally invasive	51 (7.3)	.20	Ref	
Open	13 (10.7)		1.15 (0.54-2.46)	.72
FEV1 % predicted				
>80	40 (7.6)	.03	Ref	
≤80	22 (8.1)		1.07 (0.60-1.89)	.97
Missing	2 (8.7)		1.09 (0.24-5.05)	.94
Asthma				
No	53 (7.9)	.86	Ref	
Yes	11 (7.5)		1.04 (0.51-2.11)	.91
Past pneumonia				
No	54 (7.8)	.99	Ref	
Yes	10 (7.9)		0.97 (0.47-2.01)	.93
Diabetes				
No	51 (7.5)	.43	Ref	
Yes	13 (9.5)		1.56 (0.77-3.17)	.22
Hypertension				
No	28 (8.9)	.37	Ref	
Yes	36 (7.2)		0.71 (0.40-1.27)	.25

(Continued)

TABLE E3. Continued

	30-day readmission		Multivariable logistic regression	
Covariate	**n (%)**	***P* value**	**Odds ratio (95% CI)**	***P* value**
Coronary artery disease				
No	52 (7.5)	.46	Ref	
Yes	12 (9.4)		1.16 (0.56-2.42)	.68
Hiatal hernia				
No	31 (7.7)	.87	Ref	
Yes	33 (8.0)		0.96 (0.56, 1.65)	.88
GERD				
No	35 (7.0)	.27	Ref	
Yes	29 (9.1)		1.73 (0.91-3.27)	.10
Preoperative acid-suppressive therapy				
No	43 (7.8)	.98	Ref	
Yes	21 (7.9)		1.46 (0.74-2.88)	.27
Intraoperative RBCs				
No	60 (7.5)	.04	Ref	
Yes	4 (21.1)		2.44 (0.69-8.63)	.17

CI, Confidence interval; *Ref*, reference; *BMI*, body mass index; *FEV1*, forced expiratory volume in 1 second; *GERD*, gastroesophageal reflux disease; *RBCs*, red blood cells.

TABLE E4. Characteristics of lobectomy patients with or without postoperative 30-day mortality following lobectomy and multivariable logistic regression for 30-day mortality

	30-day mortality		Multivariable logistic Regression	
Covariate	**n (%)**	***P* value**	**Odds ratio (95% CI)**	***P* value**
Sex				
Female	5 (1.1)	.22	Ref	
Male	5 (1.5)		1.81 (0.43-7.61)	.42
Age, y				
<70	4 (0.9)	.15	Ref	
≥70	6 (1.7)		2.13 (0.46-9.84)	.33
Race				
White	8 (1.2)	.26	Ref	
Not White	2 (1.8)		1.77 (0.29-10.65)	.53
BMI				
<25	6 (2.2)	.02		
25-29.9	2 (0.7)		0.21 (0.03-1.36)	.61
≥30	2 (0.8)		0.11 (0.01-1.08)	.18
Laterality				
Left	3 (1.0)	.24	Ref	
Right	7 (1.4)		2.28 (0.43-12.04)	.33
Lobe				
Upper	5 (1.0)	.08	Ref	
Middle	1 (1.4)		1.88 (0.15-23.48)	.82
Lower	4 (1.6)		2.02 (0.42-9.69)	.66
Active smoker				
No	8 (1.3)	.29	Ref	
Yes	2 (1.0)		0.45 (0.07-3.08)	.42
Preoperative chemotherapy				
No	8 (1.1)	.13	Ref	
Yes	2 (3.5)		0.94 (0.09-9.54)	.96
Previous radiation therapy				
No	9 (1.2)	.33	Ref	
Yes	1 (2.3)		1.11 (0.06-19.03)	.94
Minimally invasive vs open				
Minimally invasive	5 (0.7)	.01	Ref	
Open	5 (4.0)		8.25 (1.39-49.06)	.02
FEV1 % predicted				
>80	6 (1.2)	.06	Ref	
≤80	3 (1.2)		0.60 (0.12-2.88)	.42
Missing	1 (4.3)		1.69 (0.08-36.45)	.61
Asthma				
No	6 (0.9)	.07	Ref	
Yes	4 (2.7)		7.61 (1.45-39.99)	.02
Past pneumonia				
No	7 (1.0)	.14	Ref	
Yes	3 (2.4)		1.52 (0.33-7.06)	.59
Diabetes				
No	7 (1.1)	.16	Ref	
Yes	3 (2.2)		6.31 (0.85-47.08)	.07
Hypertension				
No	4 (1.3)	.25	Ref	
Yes	6 (1.2)		0.66 (0.13-3.28)	.61

(Continued)

TABLE E4. Continued

	30-day mortality		Multivariable logistic Regression	
Covariate	**n (%)**	***P* value**	**Odds ratio (95% CI)**	***P* value**
Coronary artery disease				
No	8 (1.2)	.28	Ref	
Yes	2 (1.6)		1.43 (0.22-9.30)	.71
Hiatal Hernia				
No	5 (1.3)	.25	Ref	
Yes	5 (1.2)		1.01 (0.23-4.45)	.99
GERD				
No	8 (1.6)	.13	Ref	
Yes	2 (0.6)		0.15 (0.02-1.29)	.08
Preoperative acid-suppressive Therapy				
No	7 (1.3)	.26	Ref	
Yes	3 (1.1)		2.08 (0.30-14.32)	.46
Intraoperative RBCs				
No	8 (1.0)	.02	Ref	
Yes	2 (10.0)		6.19 (0.86-44.54)	.07

CI, Confidence interval; *Ref*, reference; *BMI*, body mass index; *FEV1*, forced expiratory volume in 1 second; *GERD*, gastroesophageal reflux disease; *RBCs*, red blood cells.

TABLE E5. Distribution of BMI, preoperative acid-suppressive therapy, and complications by hiatal hernia and GERD status

	BMI	Preoperative acid-suppressive therapy		Any complication		Pneumonia		Atrial arrhythmia	
	Median (IQR)	**No, n (%)**	**Yes, n (%)**	**No, n (%)**	**Yes, n (%)**	**No, n (%)**	**Yes n (%)**	**No, n (%)**	**Yes, n (%)**
Neither*	26.6 (23.1, 30.6)	253 (91.0)	25 (9.0)	173 (62.2)	105 (37.8)	266 (95.7)	12 (4.3)	250 (89.9)	28 (10.1)
Hiatal hernia only†	27.5 (24.8, 31.4)	194 (85.5)	33 (14.5)	116 (51.1)	111 (48.9)	214 (94.3)	13 (5.7)	188 (82.8)	39 (17.2)
GERD only‡	26.8 (22.6, 31.9)	45 (34.6)	85 (65.4)	89 (68.5)	41 (31.5)	128 (98.5)	2 (1.5)	120 (92.3)	10 (7.7)
Both§	27.7 (24.4, 31.9)	62 (32.8)	127 (67.2)	120 (63.5)	69 (36.5)	182 (96.3)	7 (3.7)	170 (89.9)	19 (10.1)

BMI, Body mass index; *IQR*, interquartile range; *GERD*, gastroesophageal reflux disease. *Neither hiatal hernia nor GERD. †Hiatal hernia but no GERD. ‡GERD but no hiatal hernia. §Both hiatal hernia and GERD.

TABLE E6. Complication rates relative to preoperative acid-suppressive therapy status for patients divided by hiatal hernia and GERD status

	Any complication rate (%)		Pneumonia rate (%)		Atrial arrhythmia rate (%)	
	Preoperative acid-suppressive therapy		Preoperative acid-suppressive therapy		Preoperative acid-suppressive therapy	
	No	Yes	No	Yes	No	Yes
Neither*	36	52	4	12	9	16
Hiatal hernia only†	49	45	6	3	17	18
GERD only‡	36	29	0	2	11	6
Both§	39	35	3	4	8	11

GERD, Gastroesophageal reflux disease. *Neither hiatal hernia nor GERD. †Hiatal hernia but no GERD. ‡GERD but no hiatal hernia. §Both hiatal hernia and GERD.