Original Article

Inhaled medications for chronic obstructive pulmonary disease predict surgical complications and survival in stage I non-small cell lung cancer

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Background: Lung function is routinely assessed prior to surgical resection for non-small cell lung cancer (NSCLC). Further assessment of chronic obstructive pulmonary disease (COPD) using inhaled COPD medications to determine disease severity, a readily available metric of disease burden, may predict postoperative outcomes and overall survival (OS) in lung cancer patients undergoing surgery.

Methods: We retrospectively evaluated clinical stage I NSCLC patients receiving surgical treatment within the Veterans Health Administration from 2006–2016 to determine the relationship between number and type of inhaled COPD medications (short- and long-acting beta2-agonists, muscarinic antagonists, or corticosteroids prescribed within 1 year before surgery) and postoperative outcomes including OS using multivariable models. We also assessed the relationship between inhaled COPD medications, disease severity [measured by forced expiratory volume in 1 second (FEV1)], and diagnosis of COPD.

Results: Among 9,741 veterans undergoing surgery for clinical stage I NSCLC, patients with COPD were more likely to be prescribed inhaled medications than those without COPD [odds ratio (OR) =5.367, 95% confidence interval (CI): 4.886–5.896]. Increased severity of COPD was associated with increased number of prescribed inhaled COPD medications (P<0.0001). The number of inhaled COPD medications was associated with prolonged hospital stay [adjusted OR (aOR) =1.119, 95% CI: 1.076–1.165), more major complications (aOR =1.117, 95% CI: 1.074–1.163), increased 90-day mortality (aOR =1.088, 95% CI: 1.013–1.170), and decreased OS [adjusted hazard ratio (aHR) =1.061, 95% CI: 1.042–1.080]. In patients with FEV1 ≥80% predicted, greater number of prescribed inhaled COPD medications was associated with increased 30-day mortality (aOR =1.265, 95% CI: 1.062–1.505), prolonged hospital stay (aOR =1.130, 95% CI: 1.051–1.216), more major complications (aOR =1.147, 95% CI: 1.064–1.235), and decreased OS

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(aHR =1.058, 95% CI: 1.022–1.095). When adjusting for other drug classes and covariables, short-acting beta2-agonists were associated with increased 90-day mortality (aOR =1.527, 95% CI: 1.120–2.083) and decreased OS (aHR =1.087, 95% CI: 1.005–1.177).

Conclusions: In patients with early-stage NSCLC, inhaled COPD medications prescribed prior to surgery were associated with both short- and long-term outcomes, including in patients with FEV1 ≥80% predicted. Routine assessment of COPD medications may be a simple method to quantify operative risk in early-stage NSCLC patients.

Keywords: Pulmonary; chronic obstructive pulmonary disease (COPD); medications; lung cancer; thoracic

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Introduction

Non-small cell lung cancer (NSCLC) remains the leading cause of cancer-related mortality in the United States (1). Reported 5-year survival rates for patients with pathological stage I disease range from 55% to 72% (2). The percentage of patients diagnosed with stage I lung cancer is increasing, which may be attributed to national lung cancer screening efforts and a higher detection of incidental lung nodules (3). Surgical resection is the preferred treatment for functionally fit patients with early-stage NSCLC and adequate pulmonary function (4). However, patients with NSCLC frequently have comorbid chronic obstructive pulmonary disease (COPD) as tobacco use is a known risk factor for both disease processes (5,6). Coexisting COPD is associated with worse survival in patients with early-stage NSCLC, particularly those with squamous cell histology (7-9).

Clinical studies including pulmonary function testing (PFT), cardiopulmonary exercise testing, nuclear perfusion scanning, and 6-minute walk tests can be used to guide patient selection and the assessment of surgical risk for lung resection (10-14). However, the presence of severe COPD increases the risk of postoperative complications and reduces the extent of lung that can be safely resected in patients with lung cancer (15). Patients with COPD undergoing surgical resection of NSCLC require comprehensive preoperative optimization with attention to smoking cessation, pulmonary rehabilitation, and optimal medical therapy (14). Despite efforts aimed at preoperative optimization, surgical risk prediction in this select patient population remains challenging. In prior studies, symptom assessment and quality of life-based scoring did not predict postoperative outcomes in patients with COPD undergoing pulmonary resection for NSCLC (16). Currently, the utility of COPD medications in predicting surgical risk and postoperative outcomes for patients with comorbid early-stage NSCLC requiring resection remains unknown. Lawson *et al.* previously reported that intense COPD medication regimens (triple inhaler therapy, prescribed oral corticosteroids, or oxygen therapy) were associated with an increased risk of hospitalization and death in patients with heart failure (17). Prior studies have also demonstrated that

Highlight box

Key findings

- In a large cohort of veterans undergoing surgery for early-stage non-small cell lung cancer (NSCLC), the number and type of preoperatively prescribed inhaled medications for chronic obstructive pulmonary disease (COPD) was associated with several short- and long-term postoperative outcomes including prolonged hospital length of stay (LOS), major complications, and overall survival (OS).

What is known and what is new?

- It is known that COPD disproportionately impacts lung cancer outcomes.
- Our analysis demonstrates that the number of inhaled COPD medications prescribed prior to surgery is associated with prolonged hospital LOS, more major complications, and decreased OS even in patients with preserved lung function [forced expiratory volume in 1 second (FEV1) ≥80% predicted] on preoperative testing.

What is the implication, and what should change now?

- Assessment of inhaled medications for COPD may help predict outcomes in patients undergoing surgery for early-stage NSCLC beyond FEV1. To minimize the risk of adverse events, medication optimization should be included as part of the comprehensive preoperative evaluation for patients with COPD undergoing surgery for early-stage NSCLC.

perioperative inhaled pharmacologic treatment for COPD in patients undergoing surgery for lung cancer is associated with improved postoperative lung function, longer overall survival (OS), and lower recurrence rates (18-21). It remains unknown if the number and type of preoperative inhaled COPD medications is associated with COPD disease severity, postoperative outcomes, and survival in lung cancer patients undergoing surgical treatment.

The Veterans Health Administration (VHA) is the largest integrated healthcare system in the United States and provides exceptional care to veterans with early-stage NSCLC (22,23). Our group previously demonstrated that a cohort of veterans undergoing surgery for clinical stage I NSCLC had significantly reduced 30-day mortality and increased median OS than the civilian population in a propensity score-matched analysis (23). The VHA, which diagnoses approximately 7,400 new lung cancers each year and provides equitable access to healthcare resources, provides a valuable clinical setting to understand the role of inhaled COPD medications in surgical risk prediction for patients with NSCLC undergoing resection (24). In this current study, we analyze a VHA dataset of patients with clinical stage I NSCLC who underwent surgical treatment from 2006 to 2016 to determine the relationship between the number and type of inhaled COPD agents [short-acting beta2-agonists (SABA) and long-acting beta2-agonists (LABA), muscarinic antagonists, or corticosteroids prescribed within 1 year before surgery] and various postoperative outcomes including length of stay, readmissions, 30-day mortality, and OS. We present this article in accordance with the STROBE reporting checklist (available at https://jtd.amegroups.com/article/view/10.21037/jtd-23-1273/rc).

Methods

Data source and patient population

In this retrospective cohort study, veterans diagnosed with clinical stage I NSCLC who underwent definitive surgical treatment through the VHA between October 2006 and September 2016 were uniquely and extensively compiled. Data elements for this study were queried using the VHA Informatics and Computing Infrastructure (VINCI) system, which collates clinical and administrative data from multiple platforms in the Corporate Data Warehouse (CDW), including Oncology Raw and Veterans Affairs Surgical Quality Improvement Program (25). Veterans diagnosed with NSCLC were identified using International Classification of Diseases (ICD) for Oncology, Third Edition codes. Surgical treatments were confirmed using either ICD-9, ICD-10, or Current Procedural Terminology codes. Inclusion criteria were all adults diagnosed with clinical stage I (tumors ≤5 cm, node-negative disease) NSCLC, as defined by the American Joint Committee on Cancer (7th edition), who underwent surgery (26). We excluded patients who received neoadjuvant therapy, those who presented with recurrent disease from a previously diagnosed cancer, and patients with an unavailable date of diagnosis. A dedicated team of researchers also performed manual medical record review—augmented with natural language processing techniques—across 24 months to ensure maximal data capture.

This study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). Our research protocol was approved by the St. Louis VHA's Research and Development Committee (No. 1214632, issued 08/02/2019) and Institutional Review Board, which also waived the requirement for signed informed consent given the deidentified nature of the analyses.

Medications

Patient prescriptions were obtained using the CDW Pharmacy Outpatient database, which provides access to specific drug information including date issued, date filled, number of refills prescribed, as well as medication administration route, dosing, and frequency. Details of all prescriptions filled by veterans from 1-year prior to surgery up to 14 days prior to surgery were collected. Inhaled medications for COPD were classified into categories by pharmacologic mechanism and duration of action from the Global Initiative for Chronic Obstructive Lung Disease (GOLD) guidelines including SABAs, LABAs, short-acting muscarinic antagonists (SAMAs), long-acting muscarinic antagonists (LAMAs), and inhaled corticosteroids (ICSs) (27).

Covariates

We extracted several covariates for our analyses including sex, race, and age, body mass index (BMI), smoking status at time of surgery, comorbidities, and others. Comorbidities were measured using the composite Charlson-Deyo score using ICD 9/10 codes to assess specific comorbidities over a period from 5 years prior to 1 month after surgery (28). Smoking status was defined using the algorithm described in our prior studies (29,30). The GOLD guidelines use

forced expiratory volume in 1 second (FEV1) to measure the severity of airflow limitation in COPD (27). FEV1 was obtained from the most recently available PFT result prior to surgery. Patients with COPD with recorded spirometry values were stratified into three groups according to disease severity: (I) mild, FEV1 ≥80% predicted; (II) moderate, FEV1 50–79% predicted; and (III) severe, FEV1 <50% predicted. The area deprivation index, a measure of socioeconomic deprivation that incorporates several poverty, education, housing, and employment indicators from the United States census, was calculated for each patient based on residential zip code (31). Distance to each VHA was calculated from the center of the patients' residential zip codes to the treatment facility.

Oncologic surgery-related covariates including tumor size, grade, histology (e.g., adenocarcinoma, squamous cell, other), year of operation, hospital case load (defined as the volume of lung cancer cases treated in a specific VHA facility in the year prior to surgery), surgical approach [video-assisted thoracoscopic surgery (VATS) or thoracotomy], type of operation (lobectomy, segmentectomy, wedge resection, or pneumonectomy), number of lymph nodes assessed (at least one N1 and three N2 nodal stations based on prior guidelines), and final pathologic stage were extracted for each patient (32).

Outcomes

The primary outcome of this study was OS, defined as the time between date of surgery and all-cause death. OS was assessed using the VHA Vital Status Files and was censored at the end of the study follow-up period (May 1, 2020) (33). We also assessed the following secondary outcomes: 30-day mortality, 90-day mortality, 30-day readmission, prolonged hospital length of stay (defined as 14 days or greater), presence of a major complication, and disease-free survival. Consistent with definitions from the Society of Thoracic Surgery, a major complication was defined as pneumonia, empyema, myocardial infarction, respiratory failure, renal failure, or stroke within 30 days after surgery (34). Disease-free survival was defined as the time between the date of surgery and cancer recurrence and was coded using a combination of clinical documentation and billing codes suggestive of recurrence, as previously described by our group (29).

Statistical analysis

Descriptive statistics were presented for the cohort using means (standard deviations) for continuous variables and frequencies (proportions) for categorical variables. OS was assessed using multivariable Cox proportional hazards model and displayed using the Kaplan-Meier method. Disease-free survival was assessed with a multivariable competing risk model (Fine and Gray sub-distribution hazard function) with recurrence as the outcome and death as a competing event. Given the highly curated nature of this data set, missing data points were minimal and were displayed using unknown categories. All statistical tests were two-sided. P values less than 0.05 were considered statistically significant. All analyses were performed in SAS version 9.3 (SAS Institute Inc., Cary, NC, USA).

Results

Study population

There were 9,741 total veterans receiving surgery for clinical stage I NSCLC included in this analysis. The median age was 67.0 [interquartile range (IQR), 62.3–73.0] years. Most patients were males (n=9,383, 96.3%) of White race (n=8,060, 82.7%) and were smoking at the time of diagnosis (n=5,697, 58.5%). Additional characteristics of the study cohort are detailed in Table S1. Among 9,741 veterans, 53.8% (n=5,243) were not prescribed any inhaled COPD medications. Meanwhile, 9.9% (n=961) of patients were prescribed one medication, 15.5% (n=1,510) two medications, 8.7% (n=846) three medications, 9.8% (n=956) four medications, and 2.3% (n=225) five medications. COPD was diagnosed based on ICD codes in 63.2% of patients (n=6,154). In the study cohort, 6,907 (70.9%) veterans underwent lobectomy, 155 (1.6%) underwent pneumonectomy, 540 (5.5%) underwent segmentectomy, and 2,139 (22%) underwent wedge resection. Major postoperative complications occurred in 1,281 (14.2%) patients. The rates of 30-day postoperative mortality and readmission were 2.2% (n=196) and 7.6% (n=685), respectively. The median length of hospital stay was 7 (IQR, 5–10) days, and the rate of prolonged hospital stay in the study cohort was 15.6% (n=1,332). Deaths occurred in 5,760 patients (59.1%) over a median follow-up of 6.1 (IQR, 2.5–11.4) years. For mortality, 3,853 cases (66.9%) had an ICD diagnosis of COPD.

Number of inhaled COPD medications and COPD diagnosis and severity of airflow limitation

Inhaled agents for COPD were prescribed to 60.3%

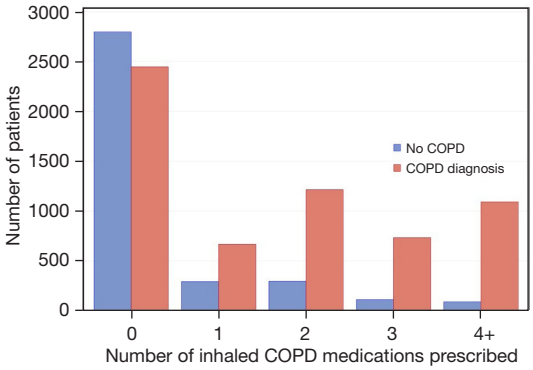

Figure 1 Relationship between the number of inhaled prescription medications for COPD and diagnosis of COPD. COPD, chronic obstructive pulmonary disease.

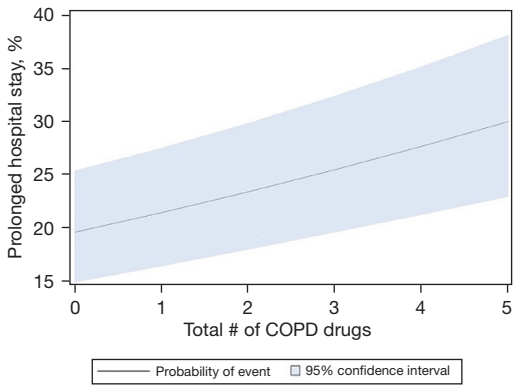

Figure 2 Association between the number of prescribed inhaled COPD medications and prolonged hospital length of stay (defined as fourteen days or greater). COPD, chronic obstructive pulmonary disease.

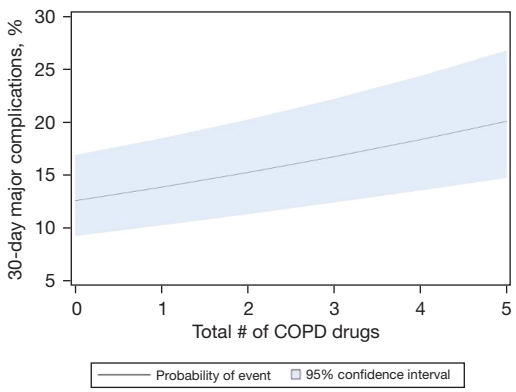

Figure 3 Association between the number of prescribed inhaled COPD medications and 30-day major complications. COPD, chronic obstructive pulmonary disease.

(n=3,708) of patients with an ICD code for COPD, compared to 22.0% (n=790) of patients without an ICD code for COPD (*Figure 1*). Patients with a diagnosis of COPD were more likely to be prescribed inhaled agents compared to those without COPD [odds ratio (OR) =5.367, 95% confidence interval (CI): 4.886–5.896]. PFT results was available for 9,243 (94.9%) patients. Of patients with an FEV1 <80% prior to surgery (n=4,873), 28.2% (n=1,373) did not have an ICD diagnosis of COPD. In univariate analysis, increased severity of COPD based on FEV1 from PFT was associated with increased number of prescribed inhaled COPD medications (P<0.0001). In comparison to patients with an FEV1 ≥80% predicted, those with an FEV1 50–79% predicted were prescribed an additional 0.73 inhaled medications and those with an FEV1 <50% predicted were prescribed an additional 1.67 inhaled medications (both P<0.0001).

Number of prescribed inhaled COPD medications and postoperative outcomes

The number of inhaled COPD medications was associated with worse short-term outcomes including prolonged hospital stay [adjusted OR (aOR) =1.119, 95% CI: 1.076–1.165] and major postoperative complications [aOR =1.117, 95% CI: 1.074–1.163) (*Figures 2,3*). As demonstrated in *Table 1*, there was no significant association between the number of inhaled prescription COPD medications and 30-day mortality (aOR =1.097, 95% CI: 0.996–1.208) or 30-day readmission (aOR =1.016, 95% CI: 0.963–1.071). In this cohort, a higher number of inhaled COPD medications was associated with increased 90-day mortality (aOR =1.088, 95% CI: 1.013–1.170) and decreased OS [adjusted hazard ratio (aHR) =1.061, 95% CI: 1.042–1.080] (*Figure 4*). There was no significant association with disease-free survival (aHR =1.020, 95% CI: 0.992–1.050).

While our primary multivariable analysis adjusted for the type of operation and surgical approach used, we also examined the relationship between the number of prescription medications and outcomes based on the operation type received. The detailed results of this analysis are listed in Table S2. The results of the primary and secondary outcomes were mostly consistent among subgroups despite different operation types being performed. A higher number of medications was associated with worse OS in patients undergoing open lobectomy, VATS lobectomy, and VATS sublobar (segmentectomy or wedge) resection.

Table 1 Probability of adverse postoperative outcomes, after adjusting for covariates, stratified by the number of prescribed inhaled COPD medications

Short-term outcome	Total number of inhaled COPD drugs	Probability of adverse outcome compared to average evaluated patient, %	Lower 95% confidence interval, %	Upper 95% confidence interval, %
30-day mortality	0	0.68	0.25	1.80
	1	0.74	0.28	1.95
	2	0.82	0.31	2.14
	3	0.89	0.33	2.37
	4	0.98	0.36	2.65
	5	1.07	0.38	2.98
30-day readmission	0	7.10	4.73	10.52
	1	7.20	4.81	10.63
	2	7.30	4.87	10.81
	3	7.41	4.89	11.06
	4	7.51	4.89	11.38
	5	7.62	4.86	11.75
Prolonged hospital stay	0	19.60	14.87	25.39
	1	21.44	16.40	27.52
	2	23.40	17.98	29.86
	3	25.48	19.60	32.42
	4	27.68	21.25	35.18
	5	29.99	22.94	38.14
30-day major complications	0	12.64	9.30	16.95
	1	13.91	10.31	18.52
	2	15.30	11.36	20.28
	3	16.79	12.46	22.24
	4	18.40	13.60	24.41
	5	20.12	14.78	26.80

COPD, chronic obstructive pulmonary disease.

Number of prescription inhaled medications and postoperative outcomes stratified by FEV1

In a subset of patients with FEV1 ≥80% predicted, a greater number of inhaled COPD medications was associated with increased 30-day mortality (aOR =1.265, 95% CI: 1.062–1.505), increased 90-day mortality (aOR =1.166, 95% CI: 1.019–1.333), prolonged hospital stay (aOR =1.130, 95% CI: 1.051–1.216), more major complications (aOR =1.147, 95% CI: 1.064–1.235), and decreased OS (aHR =1.058, 95% CI: 1.022–1.095). However, there was no association between number of medications and 30-day readmission (aOR =0.965, 95% CI: 0.871–1.068) or disease-free survival (aHR =1.025, 95% CI: 0.973–1.080).

In a subset of patients with FEV1 50–79% predicted, a greater number of inhaled COPD medications was associated with prolonged hospital stay (aOR =1.108, 95% CI: 1.047–1.173), major postoperative complications (aOR =1.066, 95% CI: 1.009–1.127), and decreased OS (aHR =1.035, 95% CI: 1.009–1.062). However, there was no significant association between number of medications and 30-day mortality (aOR =1.027, 95% CI: 0.906–1.164),

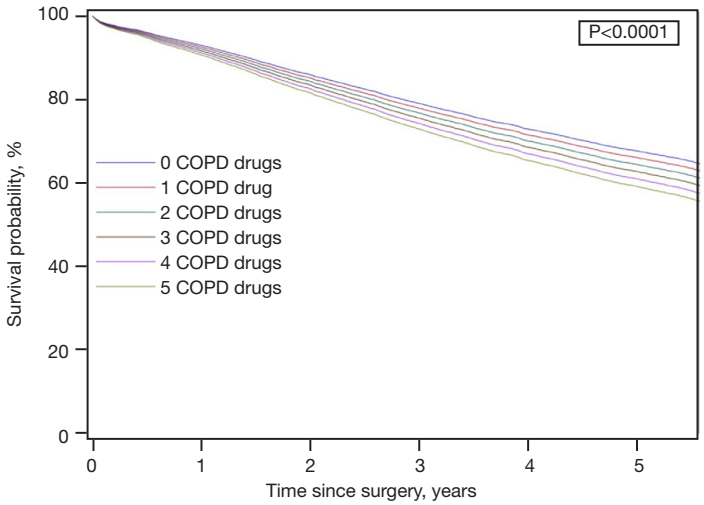

Figure 4 Adjusted Kaplan-Meier survival analysis stratified by the number of prescribed inhaled COPD medications. COPD, chronic obstructive pulmonary disease.

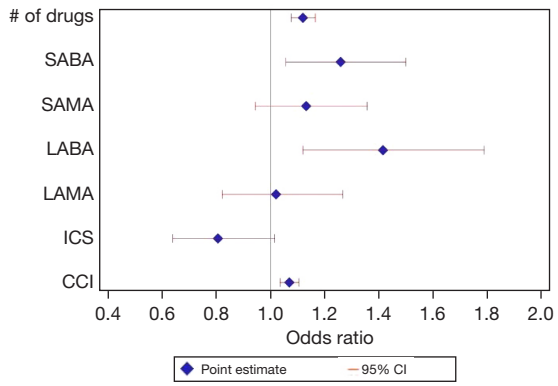

Figure 5 Relationship between the number and type of prescribed inhaled COPD medications and prolonged hospital stay (defined as fourteen days or greater). SABA, short-acting beta2-agonists; SAMA, short-acting muscarinic antagonists; LABA, long-acting beta2-agonists; LAMA, long-acting muscarinic antagonists; ICS, inhaled corticosteroids; CCI, Charlson comorbidity index; COPD, chronic obstructive pulmonary disease.

90-day mortality (aOR =1.054, 95% CI: 0.955–1.164), 30-day readmission (AOR =1.024, 95% CI: 0.949–1.105), or disease-free survival (aHR =1.010, 95% CI: 0.970–1.051).

In a subset of patients with FEV1 <50% predicted, the number of prescribed inhaled COPD medications was not associated with 30-day mortality (aOR =0.988, 95% CI: 0.737–1.324), 90-day mortality (aOR =0.832, 95% CI: 0.663–1.043), 30-day readmission (aOR =1.007, 95% CI: 0.830–1.221), prolonged hospital stay (aOR =0.945, 95% CI: 0.814–1.098), major complication rate (aOR =1.091, 95% CI: 0.936–1.272), OS (aHR =0.991, 95% CI: 0.927–1.059), or disease-free survival (aHR =1.043, 95% CI: 0.925–1.176).

Types of inhaled COPD medications and postoperative outcomes

When controlling for other drug classes and other covariables, treatment with SABAs, SAMAs, LABAs, LAMAs, or ICSs was not associated with 30-day mortality, 30-day readmission, or disease-free survival (all P>0.05). As demonstrated in *Figure 5*, use of SABAs or LABAs was associated with prolonged hospital stay (aOR =1.258 and 1.414, respectively, both P<0.05). Only LABA use was associated with a higher rate of major postoperative complications (aOR =1.303, 95% CI: 1.029–1.650) (*Figure 6*). Among inhaled COPD medications, only SABAs were associated with increased 90-day mortality (aOR =1.527, 95% CI: 1.120–2.083) and decreased OS (aHR =1.087, 95% CI: 1.005–1.177).

Discussion

Robust comorbidity assessment is a central tenet of the preoperative evaluation for early-stage lung cancer resection. While modern electron health records have increased the availability of documented comorbidities, these data entries are often incomplete, limiting the applicability of

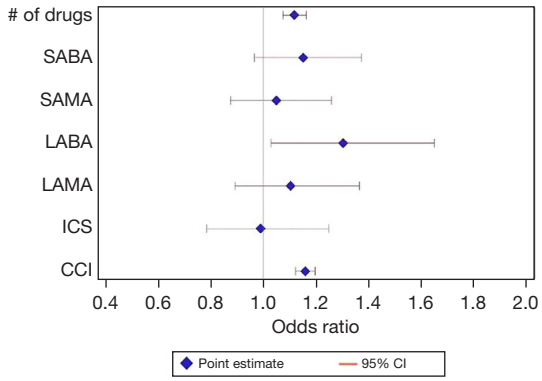

Figure 6 Relationship between the number and type of prescribed inhaled COPD medications and 30-day major complications. SABA, short-acting beta2-agonists; SAMA, short-acting muscarinic antagonists; LABA, long-acting beta2-agonists; LAMA, long-acting muscarinic antagonists; ICS, inhaled corticosteroids; CCI, Charlson comorbidity index; COPD, chronic obstructive pulmonary disease.

comorbidity indices for risk-stratifying surgical patients (35). Conversely, prescription medications could be a potentially more accurate and up-to-date comorbidity measure that provides a simpler mechanism for operative risk stratification for NSCLC. We comprehensively evaluated the relationship between the number and type of preoperatively prescribed inhaled COPD medications and outcomes in patients with lung cancer undergoing resection.

In a large cohort of 9,741 veterans undergoing surgery for clinical stage I NSCLC, we found that increased number of preoperatively prescribed inhaled medications for COPD was associated with several short- and long-term postoperative outcomes including prolonged hospital length of stay, more major complications, and decreased OS. Increased severity of COPD based on inhaled medicines is likely associated with impairments in functional status, pulmonary function, and higher rates of coexisting comorbidities in patients with severe COPD. Furthermore, our analysis demonstrated that the number of inhaled COPD medications prescribed prior to surgery adversely affected 30-day mortality, hospital length of stay, major complication rate, and OS even in patients with preserved lung function (FEV1 ≥80% predicted) on preoperative PFT. This notable finding suggests that preoperative assessment of inhaled COPD medications, in addition to FEV1 testing, may aid in predicting short- and long-term outcomes in patients undergoing surgery for early-stage NSCLC.

This current study provides insight into the potential benefits of medication optimization for COPD prior to elective lung cancer resection. Based on our findings, routine assessment of each patient's medications prior to elective NSCLC resection may help identify those patients at risk for adverse outcomes. In our study population, a higher number of prescribed inhaled COPD medications and SABA usage were associated with increased 90-day mortality and decreased OS. While it is relatively intuitive that the number of prescribed inhaled agents is representative of a patient's COPD severity, we hypothesize that the significant association between increased mortality and SABA usage could be due to poor overall disease control among patients prescribed multiple drugs from this specific class. The number of inhaled COPD medications, especially SABAs, could be used by thoracic surgeons as a simple marker of elevated risk for poor postoperative outcomes following resection of early-stage NSCLC. Combined with PFT and smoking cessation efforts, review of the number and type of inhaled COPD medications for each patient may allow surgeons to determine if additional work-up is necessary prior to surgery, including six-minute walk tests, referral to a pulmonologist, or enrollment in a prehabilitation program. Efforts to medically optimize COPD patients with uncontrolled symptoms or not receiving evidence-based COPD treatments may aid in preventing short- and long-term complications from lung cancer surgery.

There are some limitations to this study. First, our study population consists of United States veterans who were primarily men. Further research is warranted to validate if our findings translate to the population outside of the VHA, including women. Second, the number of inhaled COPD medications was calculated only from VHA prescriptions that were filled by the patient prior to surgery. This number did not include prescriptions that may have originated from outside of the VHA system. Additionally, we were unable to evaluate adherence to medications given the retrospective nature of this study. Lastly, it is worth noting that hospital readmission within 30 days was not associated with the number or type of inhaled COPD medications, likely due to the relatively high number of patients (15.6%) in the study population who experienced a prolonged hospital stay.

Despite these limitations, we believe there to be several strengths to this study. Most notably, it presents data from a nationally representative and comprehensive dataset which allows access to an exhaustive list of treatment-related covariates with high accuracy and a low number of missing

data points. Additionally, VHA patients have more equitable access to care compared to privately insured patients, including medicines, surgeries, inpatient and outpatient visits, and rehabilitation services available to veterans with low or no copayments (36-38). As such, VHA patients have low rates of cost-related medication nonadherence and assessment of prescriptions is considered reliable in this population (39).

While not included in this analysis, it is important to note that the association between prescription medications and OS may be present in other disease states as well. Our group is exploring these associations in prostate cancer and multiple myeloma. Additionally, future research should investigate the utility of prescription medications as a comorbidity measure through direct comparison to other routinely used comorbidity indices, such as the Charlson comorbidity index.

Conclusions

In veterans who had surgery for clinical stage I NSCLC, prescriptions for inhaled COPD medications were associated with both short- and long-term outcomes including prolonged hospital length of stay, major complications, and decreased OS, particularly in patients with normal lung function (FEV ≥80%). The number and type of medications for COPD are relatively easy to identify in modern electronic medical records and routine assessment of this information may be a simple method to quantify operative risk prior to elective oncologic lung resection. To minimize the risk of adverse events, medication optimization should be included as part of the comprehensive preoperative assessment for patients with COPD undergoing surgery for early-stage NSCLC.

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Footnote

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