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Pre-Hospital Use of Inhaled Corticosteroids and Point Prevalence of Pneumonia at the time of Hospital Admission: Secondary Analysis of a Multicenter Cohort Study

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Abstract

Objective—To address clinical concern regarding the use of inhaled corticosteroids (ICS) and its risk for pneumonia, particularly among patients with COPD and asthma, we hypothesized that this risk may be partially confounded. No study has looked at the risk of ICS and the risk of developing pneumonia in the broader population of patients requiring hospitalization.

Patients and Methods—A multi-centered prospective cohort of patients admitted to the hospital between March 1st and August 31st, 2009 with pneumonia or another risk factor for acute respiratory distress syndrome (ARDS) was analyzed to determine the risk for pneumonia requiring hospitalization among patients taking ICS. The adjusted risk (odds ratio, OR) for developing pneumonia due to ICS was determined in a multiple logistic regression model.

Results—Of the 5584 patients in the cohort, 495 (9%) were taking ICS and 1234 (22%) had pneumonia requiring hospitalization. In univariate analyses, pneumonia occurred in 45% of patients on ICS versus 20% in those who were not (OR 3.28, 95% CI 2.71-3.96, $p<0.001$). After adjusting in the logistic regression model, pre-hospital ICS use was not significantly associated with pneumonia in the whole cohort (OR 1.20, 95% CI 0.93-1.53, $p=0.162$), among the subset of 589 patients with COPD (OR 1.40, 95% CI 0.95-2.09, $p=0.093$), the 440 patients with asthma (OR 1.07, 95% CI 0.61-1.87, $p=0.81$), nor among the remaining 4629 patients without COPD or asthma (OR 1.32, 95% CI 0.88-1.97, $p=0.179$).

Conclusion—When adjusted for multiple confounding variables, ICS use was not significantly associated with increased risk for pneumonia requiring admission in our cohort.

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Introduction

Inhaled corticosteroids (ICS) are potent anti-inflammatory medications frequently used in the treatment of asthma¹ and chronic obstructive pulmonary disease (COPD).² There is clinical controversy regarding a possible increased risk of pneumonia in patients chronically taking ICS. Initially, the safety evaluation in the TORCH (Toward a Revolution in COPD Health) trial demonstrated an excess of pneumonia in patients receiving fluticasone.³ This incidence of excess pneumonia was also demonstrated in a meta-analysis of clinical trials of ICS in COPD.⁴ In contrast, another meta-analysis of individual patient data restricted to clinical trials of budesonide in patients with COPD did not find an excess of pneumonia.⁵ O'Byrne et al. observed no excess of pneumonia reported as an adverse event with ICS use in patients with asthma.⁶

Most of the previous studies on the topic were limited with narrow inclusion of potential confounders in the analyses. Also, previous trials assessed an overall risk of pneumonia for the whole duration of the trials, which may have predisposed these to multiple additional confounding factors. The confounders of particular importance are those occurring during the hospitalization (e.g. health-care associated pneumonia), which might have influenced the diagnosis of pneumonia more so than the mere history of ICS use prior to hospitalization. Moreover, many previous studies did not have radiographic data to support the diagnosis of pneumonia. Additionally, the degree of the severity of pneumonia also has not always been clear in these studies, in particular whether they required acute hospitalization or not. To better address these issues, we evaluated the point prevalence of pneumonia requiring hospitalization, in a broad spectrum of patients from the large LIPS (Lung Injury Prediction Score) cohort, adjusting for demographics, chronic comorbidities and concurrent medications.

Patients and Methods

This is a secondary analysis of the previously published LIPS cohort,⁷ consisting of patients admitted to the hospital with pneumonia or another risk factor for ARDS. The cohort included 5584 patients enrolled from 20 centers prospectively and from two centers retrospectively from March 1st through August 31st, 2009. The study protocol was approved by institutional review board at each participating location. The ancillary study was commenced to test our hypothesis that patients who were receiving ICS (ICS group) prior to admission had similar point prevalence of pneumonia at the time of hospital admission as did the patients who were not receiving ICS (non-ICS group). It was approved by the U.S. Critical Illness and Injury Trials Group/LIPS ancillary committee.

Study Population

The details of the primary study population were described previously.⁷ Briefly, the inclusion criteria were: adult patients with at least one major risk factor for ARDS, including pneumonia, aspiration, sepsis, shock, pancreatitis, high-risk trauma, or major cardiac and lung surgery. Exclusion criteria were: ARDS at the time of admission, transfer from an outside hospital, death in the emergency department, comfort or hospice care, or hospital

readmission during the study period. In this secondary study, we divided all patients into 2 groups based on pre-hospital use of ICS, as determined at the time of admission.

Predictor Variables

Demographic and clinical information were obtained at the time of hospital admission or preoperatively at the time of surgery. The main predictor variable of this secondary study was use of ICS prior to hospital admission, as documented in the admission medical record. The medication lists were obtained from the patients or family members at the time of hospital admission, but the details of medication doses, duration or compliance were not ascertained. However, we assembled a comprehensive multivariate logistic regression model that included demographics (age, sex, race, admission source, body mass index, alcohol and tobacco use), chronic comorbidities (diabetes mellitus, cirrhosis, chronic hemodialysis, class IV congestive heart failure, interstitial lung disease, metastatic solid cancer, lymphoma, leukemia, chest radiation, sleep apnea, gastroesophageal reflux disease, COPD and asthma), and concurrent medications (systemic steroid, ACE inhibitor, angiotensin receptor blocker, statin, aspirin, amiodarone, oral hypoglycemic, insulin, inhaled beta agonist, proton pump inhibitor, histamine 2 receptor blocker and chemotherapy).⁷

Outcome Variables

The main outcome was the diagnosis of pneumonia on admission among all patients receiving ICS versus those not receiving ICS. At the time of data collection, the presence of pneumonia was considered according to the 2005 International Sepsis Forum Consensus Conference on Definitions of Infection in the Intensive Care Unit.⁸ Given the timing of our evaluation (within six hours of hospital admission) the microbiologic proof was not required and a practical CDC definition⁹ was applied: Chest radiographs showing new or progressive infiltrate, consolidation, cavitations or pleural effusion and new onset purulent sputum and/or change in its character.

Statistical Analysis

We first performed univariate analyses to determine the unadjusted associations of the pre-hospital use of ICS (and other predictor variables) with the diagnosis of pneumonia at the time of hospital admission. Statistical significance was tested for by the Mann Whitney test or the Fisher's exact test, as appropriate. We then assembled the multivariate logistic regression model by including demographics, chronic comorbidities and concurrent medications (as detailed above) and assessed the model's ability to discern significant association of ICS with pneumonia in the whole cohort. Similarly, we assessed the adjusted risk for pneumonia from ICS in the following clinically determined three diagnostic subgroups: COPD, asthma, and non-COPD/asthma. Frequency distributions are presented as percentages, means with standard deviations, or medians with interquartile (1st, 3rd) range, where appropriate. Risk assessments are reported as Odds Ratios (OR) with 95% confidence intervals (CI). A p-value of less than 0.05 was considered statistically significant. All statistical analyses were performed using JMP 9.0.1 statistical software and SAS 9.1.3 (SAS Institute Inc., Cary, NC).

Results

There were 5584 patients in the original LIPS cohort, of which 495 (9%) were taking ICS at the time of the hospital admission. As previously reported,⁷ the median age of the entire cohort was 57 (43, 70), and the majority was Caucasian (63%) and male (57%). The median severity of illness reflected by the APACHE-II score was 9 (5, 14), and LIPS was 2.5 (1.5, 4.5).

A total of 1234 (22%) patients were diagnosed with pneumonia on admission; 222 in ICS group, compared to 1012 in non-ICS group, for unadjusted point prevalence of pneumonia of 45% and 20%, respectively (OR 3.28, 95% CI 2.71-3.96, $p<0.001$). The patients with and without pneumonia were 63 (50, 77) and 55 (41, 68) years old, respectively. The median age of patients in ICS and non-ICS group was 64 (51, 75) and 56 (42, 70) years old. There was no difference in age between those with and without pneumonia among ICS users. Other baseline characteristics including demographics, comorbidities and concurrent medications are displayed in Table 1.

After adjusting for pertinent variables including demographics, chronic comorbidities and concurrent medications in the logistic regression model, the association between ICS use and pneumonia requiring hospitalization was not statistically significant, OR 1.2, 95% CI 0.93-1.53 (Table 2). There were 589 patients with COPD and 440 patients with asthma in these two subgroups, of which 226 (38%) and 151 (34%) patients were taking ICS at the time of hospital admission, respectively. The remaining 4629 patients comprised the non-COPD/asthma subgroup, of which 156 (3.4%) patients were on ICS. Similar to the whole cohort, multivariate analyses of these three subgroups of patients showed no significant associations (Table 2), although the point risk estimate was higher for COPD than for asthma or non-COPD/asthma subgroups. In order to further explore interesting non-COPD/asthma subgroup, we performed a post-hoc propensity analysis of the patients in ICS group by including all clinical variables from the Table 1, except COPD and asthma. We then compared by Wilcoxon signed rank test propensities to be on ICS between 2 subgroups, COPD/asthma and non-COPD/asthma, respectively. There was a significant difference in propensity to be on ICS between these two groups ($p<0.0001$, Table 3), suggesting that these patients differed significantly by other clinical characteristics included in the model independent of the diagnosis of COPD and asthma.

Discussion

Although univariate analyses initially suggested a multifold increased risk for pneumonia with ICS use, after adjusting for multiple confounders, pre-hospital ICS use did not independently associate with an increased risk for pneumonia that requires hospitalization. Although the risk estimate was highest for the subgroup of patients with COPD compared to asthma and non-COPD/asthma patients, this did not reach statistical significance. Yet, based on our study, we cannot rule out clinically important association but results do suggest that once adjusted for important confounders, the estimated risk is significantly decreased. This is the first study to our knowledge which evaluated for pneumonia requiring hospitalization among a broader spectrum of patients receiving ICS, including but not limited to COPD and

asthma. In addition, we developed a comprehensive multivariate model to eliminate multiple confounders, which have limited the interpretation of prior studies.

Several recent studies in patients with COPD reported increased rates of nonfatal pneumonia among patients treated with fluticasone.^{3,10-15} A Canadian nested case-control study in a cohort of patients with COPD¹⁶ suggested that an increased risk of pneumonia with any ICS treatment might be as high as 70%. These conclusions are supported by a number of metaanalyses in patients with COPD.^{4,17,18} The underlying mechanism(s) for this increase in risk is not completely clear. Several studies suggested that the proposed mechanism could be due to an increase in immunosuppressive effects of ICS by achieving locally high concentrations in the lung.¹⁹⁻²¹ This, in turn could diminish the ability of the innate immune system to defend against primary bacterial infections or post viral super infections. This hypothesis is supported by a recent multicenter trial demonstrating that ICS use reduces lung specific but not generalized biomarkers of systemic inflammation in patients with COPD.²² However, the risk for pneumonia may not apply to all inhaled corticosteroids, and differences in deposition, clearance, potency, and pharmacodynamics may be important in determining whether there will be an increased risk for pneumonia.^{23,24} For example, budesonide did not increase the risk for pneumonia in COPD patients.^{5,15,25,26} The lack of an association between budesonide use and increased risks of pneumonia in COPD could be due to more rapid clearance of budesonide from airways compared to fluticasone.²⁷ In contrast, the risk of developing community-acquired pneumonia (CAP) does not appear to be significantly increased among asthmatic patients on ICS.^{6,28,29} It is probable that in asthma, as primarily an inflammatory airway disease with “reversible” airflow obstruction, ICS more efficiently reduces airway inflammation, segmental atelectasis, and mucoid impaction, as compared to patients with COPD, which then reduces the risk of pneumonia.³⁰

Interestingly, despite above discussed reports of an increased risk of pneumonia in selected patients, this risk was not associated with worse outcomes, including higher pneumonia-related mortality. In two large retrospective observational studies in patients with COPD hospitalized for CAP, the hospital mortality³¹, as well as 30-day and 90-day mortality³² rates were lower in previous users of ICS compared to non-ICS users, after adjusting for potential confounders. In addition, patients with ICS less frequently required mechanical ventilation and vasopressors.³² Recently, Sellares and colleagues³³ demonstrated the protective effect of ICS in patients with and without COPD and Liapikou and colleagues supported that previous use of ICS before the development of CAP had a lower incidence of parapneumonic effusion.³⁴ In another study, Singanayagam observed that prior ICS use was not associated with different clinical outcomes in COPD patients hospitalized with CAP.³⁵

Despite somewhat inconsistent and controversial results in previous studies, it is conceivable that the observed risk of pneumonia pertains mostly to older patients with more severe COPD, chronically taking ICS, especially fluticasone. Major limitations of previous studies include the lack of adjustment for important confounders. Moreover, these previous studies were largely focused on pneumonia events documented as adverse events. However, the diagnostic accuracy of this endpoint was uncertain since many events were not validated with established criteria for pneumonia³⁶, and furthermore, the clinical impact based on severity (i.e. requiring hospitalization) has not always been clarified. Evidence suggests that

the diagnosis of pneumonia, based on clinical symptoms and signs alone, is unreliable.³⁷ Since the clinical presentation of COPD exacerbation and pneumonia may overlap considerably, without radiographic confirmation an adverse event could potentially be misclassified as pneumonia rather than exacerbation (and vice versa). This raises doubts over whether a true increase in pneumonia has been observed in these trials, or it is due to reported overlap between pneumonia and COPD.³⁸⁻⁴⁰ In a large Spanish study of 1336 patients with confirmed CAP, ICS was not associated with CAP after adjustment on multivariate analysis.⁴¹ The specific advantage of this study, similarly to ours, was that all patients had radiologically confirmed pneumonia, thus eliminating the possibility of significant overlap with COPD exacerbations. Additionally, we honed our interest to patients with more clinically pertinent pneumonia that required hospitalization.

Our results fit well into the existing body of literature. This pertains to the higher observed estimates of risk in the COPD subgroup, compared to asthma, and overall there was no significant increase in the risk for pneumonia from ICS after adjustment for pertinent potential confounders. The novel report of a subgroup of patients taking ICS prior to hospitalization without known diagnoses of COPD or asthma deserves further comments. Given that there are no indications for ICS use outside COPD or asthma, the logically imposed question is: Who are these patients that received ICS and did not have COPD or asthma? In attempt to answer this question, we propose that a proportion of these patients may have had subclinical or early COPD and/or asthma, which had not been diagnosed at the time when ICS were prescribed, or perhaps patients were not aware of the diagnosis. However, propensity analysis (Table 3) suggests that this group's propensity for ICS differed significantly from the group with known COPD/asthma independently of that diagnosis. We suspect that a large proportion of these patients were taking ICS for a short period of time, having received ICS as the result of persistence of respiratory symptoms. It is quite possible, though it remains speculative, that some of the patients who were prescribed ICS by their physicians were already reporting persistent respiratory problems that could have been signs of early pneumonia. In such case, ICS use would be merely associated with pneumonia, rather than causative. Indeed, in a previous study it was demonstrated that the clinical path prior to pneumonia diagnosis in patients with COPD can be markedly different.¹² While some patients have short duration of symptoms, others are hospitalized after a protracted symptomatic period. The latter groups of patients were mainly receiving ICS.¹² Therefore, clinicians prescribing ICS to patients with worsening respiratory symptoms should be alerted to the possibility of pneumonia rather than focusing only on bronchospasm or asthma.

There are certain limitations of our study that ought to be further discussed. Its observational design may have introduced significant selection bias. Our study was limited to the LIPS cohort of patients admitted to the hospital with at least one risk factor for ARDS, but notably every patient with pneumonia would have been captured. We did not collect data on ICS use in patients without risk factors for ARDS. However, had we done that, it would likely further reduce estimated effects as we included all patients with pneumonia and without fully established ARDS on admission. While we feel confident that we did not miss patients diagnosed with pneumonia within 6 hours of hospital admission, other patients may have had pneumonia only apparent later on in the hospital course. However, as mentioned earlier,

the later development of pneumonia, during the hospitalization, introduces additional “noise” and many confounding factors would need to be addressed as to the nosocomial basis for developing pneumonia rather than from ICS. Despite limitations, our results fit well with previously published studies. To further support this, we report increased risk of pneumonia on admission in our cohort of patients taking proton pump inhibitors (OR 1.25, 95% CI 1.05-1.48, $p=0.011$) when adjusted in the same multivariate logistic regression, which also fits well with previous reports.⁴²⁻⁴⁴ Furthermore, we did not have details on the type of ICS, dose, duration and compliance with outpatient therapy, or COPD severity. These data would certainly improve the quality of our analysis. As the data were obtained in the multicenter cohort study, a potential for variability in diagnostic ascertainment of pneumonia needs to be considered as well. However, the participating sites were mostly academic centers, experienced in data collection and all the investigators completed a formal training and followed a study operation manual for data collection. The major strength of our study is comprehensive adjustment for extensive list of potential confounders, particularly comorbidities and concomitant medications, as well as description of risk in a novel subgroup of patients taking ICS without known COPD or asthma. The additional strengths are large sample size and prospective data collection.

Conclusion

When adjusted for demographics, chronic comorbidities and concurrent medications, ICS were not independently associated with pneumonia requiring hospitalization in the broader population of patients at risk for ARDS, including those with COPD and asthma. This supports our hypothesis that the risk for pneumonia seen in other reports may have been, at least in part, due to important confounding factors.

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Abbreviations

ARDS	Acute respiratory distress syndrome
BMI	Body Mass Index
CAP	Community acquired pneumonia

CHF	Congestive Heart Failure
CI	Confidence Interval
COPD	Chronic Obstructive Pulmonary Disease
GERD	Gastroesophageal Reflux Disease
ICS	Inhaled Corticosteroid(s)
LIPS	Lung injury prediction score
OR	Odds Ratio

Table 1
Baseline cohort characteristics and unadjusted associations with prevalent pneumonia and ICS use at the time of hospital admission

Clinical variable	Total	Pneumonia	No Pneumonia	OR (95 CI)	p-value	ICS	Non-ICS	OR (95 CI)	p-value
Age median (1st, 3rd quartile)	57 (43, 70)	63 (50, 77)	55 (41, 68)	NA	<0.001	64 (51, 75)	56 (42, 70)	NA	<0.001
Male (%)	3155 (57)	647 (21)	2508 (79)	0.81 (0.71-0.92)	0.001	221 (7)	2934 (93)	05.59 (0.49-0.71)	<0.001
Caucasian (%)	3419 (63)	742 (22)	2677 (78)	0.97 (0.85-1.11)	0.655	344 (10)	3075 (90)	1.48 (1.21-1.82)	<0.001
Admission from home (%)	4447 (81)	941 (21)	3506 (79)	0.78 (0.67-0.91)	0.002	395 (9)	4052 (91)	1.03 (0.81-1.31)	0.800
Alcohol (%)	489 (8.8)	93 (19)	396 (81)	0.81 (0.64-1.03)	0.081	26 (5)	463 (95)	0.55 (0.37-0.83)	0.002
Active smoking (%)	1337 (24)	301 (23)	1036 (77)	1.03 (0.89-1.20)	0.676	112 (8)	1225 (92)	0.92 (0.74-1.15)	0.469
BMI >30 (%)	1408 (25)	237 (17)	1171 (83)	0.65 (0.55-0.75)	<0.001	156 (11)	1252 (89)	1.41 (1.15-1.72)	<0.001
Diabetes mellitus (%)	1295 (24)	338 (26)	957 (74)	1.34 (1.16-1.54)	<0.001	142 (11)	1153 (89)	1.37 (1.12-1.69)	0.003
Cirrhosis (%)	124 (2.2)	17 (14)	107 (86)	0.55 (0.33-0.93)	0.016	8 (6)	116 (94)	0.70 (0.34-1.45)	0.317
Chronic hemodialysis (%)	219 (3.9)	65 (30)	154 (70)	1.52 (1.13- 2.04)	0.008	20 (9)	199 (91)	1.03 (0.65-1.65)	0.887
CHF class IV (%)	183 (3.3)	65 (36)	118 (64)	1.99 (1.46-2.72)	<0.001	32 (17)	151 (83)	2.26 (1.53-3.35)	<0.001

Clinical variable	Total	Pneumonia	No Pneumonia	OR (95 CI)	p-value	ICS	Non-ICS	OR (95 CI)	p-value
COPD (%)	589 (11)	254 (43)	335 (57)	3.11 (2.60–3.71)	<0.001	226 (38)	363 (62)	10.94 (8.9–13.45)	<0.001
Asthma (%)	440 (8)	151 (34)	289 (66)	1.96 (1.59–2.41)	<0.001	149 (34)	291 (66)	7.10 (5.67–8.9)	<0.001
Interstitial lung disease (%)	50 (1)	35 (70)	15 (30)	8.44 (4.59–15.50)	<0.001	13 (26)	37 (74)	3.68 (1.94–6.98)	<0.001
Lymphoma (%)	89 (1.6)	29 (33)	60 (67)	1.72 (1.10–2.69)	0.022	10 (11)	79 (89)	1.31 (0.67–2.54)	0.444
Leukemia (%)	58 (1)	22 (38)	36 (62)	2.18 (1.27–3.71)	0.006	8 (14)	50 (86)	1.66 (0.78–3.51)	0.215
Metastatic solid cancer (%)	290 (5.2)	94 (32)	196 (68)	1.75 (1.35–2.25)	<0.001	23 (8)	267 (92)	0.88 (0.57–1.36)	0.560
Chest radiation (%)	71 (1.3)	29 (41)	42 (59)	2.47 (1.53–3.98)	<0.001	15 (21)	56 (79)	2.81 (1.58–5.00)	0.002
Sleep apnea (%)	252 (4.5)	67 (27)	185 (73)	1.29 (0.97–1.72)	0.085	54 (21)	198 (79)	3.02 (2.20–4.15)	<0.001
GERD (%)	700 (13)	173 (25)	527 (75)	1.18 (0.98–1.42)	0.078	129 (18)	571 (82)	2.79 (2.24–3.47)	<0.001
Pneumonia (%)	1234 (22)	NA	NA	NA	NA	222 (18)	1012 (82)	3.28 (2.71–3.96)	<0.001
Inhaled steroid (%)	495 (9)	222 (45)	273 (55)	3.28 (2.71–3.96)	<0.001	NA	NA	NA	NA
Systemic steroid (%)	458 (8)	175 (38)	283 (62)	2.37 (1.94–2.90)	<0.001	94 (21)	364 (79)	3.04 (2.37–3.90)	<0.001

Clinical variable	Total	Pneumonia	No Pneumonia	OR (95 CI)	p-value	ICS	Non-ICS	OR (95 CI)	p-value
ACE inhibitor (%)	1125 (20)	270 (24)	855 (76)	1.14 (0.98-1.34)	0.088	129 (11)	996 (89)	1.45 (1.17-1.79)	0.001
Angiotensin receptor blocker (%)	307 (6)	92 (30)	215 (70)	1.55 (1.20-2.00)	0.001	54 (18)	253 (82)	2.34 (1.72-3.19)	<0.001
Statin (%)	1411 (25)	366 (26)	1045 (74)	1.33 (1.16-1.53)	<0.001	194 (14)	1217 (86)	2.05 (1.69-2.48)	<0.001
Aspirin (%)	1511 (27)	393 (26)	1118 (74)	1.35 (1.18-1.55)	<0.001	172 (11)	1339 (89)	1.49 (1.23-1.81)	<0.001
Amiodarone (%)	49 (1)	14 (29)	35 (71)	1.41 (0.76-2.64)	0.288	7 (14)	42 (86)	1.72 (0.77-3.86)	0.214
Oral hypoglycemic (%)	624 (11)	153 (25)	471 (75)	1.17 (0.96-1.42)	0.126	78 (13)	546 (87)	1.56 (1.20-2.01)	0.001
Insulin (%)	559 (10)	155 (28)	404 (72)	1.40 (1.15-1.71)	0.001	66 (12)	493 (88)	1.43 (1.09-1.89)	0.013
Inhaled beta agonist (%)	763 (14)	364 (48)	399 (52)	4.14 (3.53-4.86)	<0.001	347 (45)	416 (55)	26.34 (21.2-32.72)	<0.001
Proton pump inhibitor (%)	1281 (23)	378 (30)	903 (70)	1.69 (1.46-1.94)	<0.001	222 (17)	1059 (83)	3.09 (2.56-3.74)	<0.001
H2 blocker (%)	295 (5.3)	69 (23)	226 (77)	1.08 (0.82-1.43)	0.585	32 (11)	263 (89)	1.27 (0.87-1.85)	0.232
Chemotherapy (%)	173 (3.1)	67 (39)	106 (61)	2.30 (1.68-3.14)	<0.001	18 (10)	155 (90)	1.20 (0.73-1.97)	0.480

ICS: Inhaled Corticosteroid, BMI: Body Mass Index, CHF: Congestive Heart Failure, COPD: Chronic Obstructive Pulmonary Disease, GERD: Gastroesophageal Reflux Disease

Table 2
Adjusted prevalence of pneumonia in the whole cohort and the diagnostic subgroups

Group	ICS Group	Non-ICS Group	OR (95% CI)	p-value
Whole cohort	495	5089	1.20 (0.93-1.53)	0.162
COPD	226	363	1.40 (0.95-2.09)	0.093
Asthma	151	289	1.07 (0.61-1.87)	0.81
Non-COPD/Asthma	156	4473	1.32 (0.88-1.97)	0.179

ICS: Inhaled Corticosteroid, COPD: Chronic Obstructive Pulmonary Disease

Table 3

Post-hoc propensity analysis of the patients on ICS.

ICS propensity	COPD/asthma	Non-COPD/asthma	p-value*
Median (1 st , 3 rd quartile)	0.427 (0.257, 0.594)	0.263 (0.043, 0.480)	<0.0001

* Wilcoxon signed rank test