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Inhaled Corticosteroids and the Risk of Nontuberculous Mycobacterial Infection in Chronic Airway Disease: A Nationwide Population-Based Study

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Abstract

Background: Chronic airway diseases, such as asthma and chronic obstructive pulmonary disease (COPD), are increasingly being treated with inhaled corticosteroid (ICS). However, ICSs carry potential infection risks, particularly nontuberculous mycobacteria (NTM). This study investigated the association between ICS use and NTM infection risk using national insurance data, particularly for individuals with chronic airway diseases.

Methods: We conducted a nationwide population-based study using data from the National Health Insurance Service-National Sample Cohort in South Korea from 2002 to 2019. The cohort included 57,553 patients diagnosed with COPD or asthma. To assess the risk of NTM infection, we used Cox proportional hazards models and propensity score-based inverse probability of treatment weighting (IPTW) to ensure a balanced analysis of covariates.

Results: Of the 57,553 patients (mean age 56.0 years, 43.2% male), 16.5% used ICS and 83.5% did not. We identified 63 NTM infection cases, including nine among ICS users and 54 among non-users. Before and after IPTW, ICS use was associated with a higher risk of NTM infection (adjusted hazard ratio [HR], 4.01; 95% confidence interval [CI], 1.48 to 15.58). Higher risks were significant for patients ≥65 years (adjusted HR, 6.40; 95% CI, 1.28 to 31.94), females (adjusted HR, 10.91; 95% CI, 2.24 to 53.20), never-smokers (adjusted HR, 6.31; 95% CI, 1.49 to 26.64), systemic steroid users (adjusted HR, 50.19; 95% CI, 8.07 to 312.19), and those with higher comorbidity scores (adjusted HR, 6.64; 95% CI, 1.19 to 37.03).

Conclusion: ICS use in patients with chronic airway diseases might increase the risk of NTM infection, particularly in older females, never-smokers, and systemic steroid users.

Keywords: Chronic Airway Diseases; Infection; Asthma; Chronic Obstructive Pulmonary Disease; Epidemiology

Introduction

Chronic airway diseases, including asthma and chronic obstructive pulmonary disease (COPD), are characterized by airway inflammation and limitation[1,2]. Although inhaled corticosteroid (ICS) effectively manage these conditions by reducing inflammation and improving lung function[3-5], concerns regarding their safety have emerged[6,7]. ICS use can potentially cause local (e.g., oral thrush and hoarseness) and systemic (e.g., adrenal

suppression and bone density reduction) side effects[7,8]. In particular, prolonged or high-dose use of ICS may suppress the immune system, potentially elevating the risk of infections in the airways and lungs by various pathogens including bacteria, viruses, fungi, and particularly nontuberculous mycobacteria (NTM)[9-14].

NTM, prevalent in the environment, are known to cause significant pulmonary infections, especially in patients with preexisting lung conditions or compromised immune systems[15]. Their increasing global incidence and prevalence have raised significant public health concerns and pose a substantial medical burden[16,17]. Recent studies have suggested a potential association between ICS use and the incidence of NTM infections[18-24]. A meta-analysis of four studies found that ICS may elevate the risk of NTM-lung disease, particularly at higher daily doses[18]. Similarly, a Korean study using a national claims database observed no overall increased risk of NTM infection in ICS users among patients with COPD, but a higher risk for those on medium and high doses[22], supporting a potential dose-dependent association. However, the current evidence remains inconclusive and is often limited by small-scale studies or restricted generalizability, with a notable absence of research that includes all forms of obstructive airway diseases, particularly studies analyzing the impact of various covariates. Therefore, this comprehensive nationwide population-based study aimed to assess the association between ICS use and the risk of NTM infection in patients with chronic airway disease.

Materials and Methods

1. Data source

We used the National Health Insurance Service-National Sample Cohort (NHIS-NSC, version 2.2), an updated dataset derived from the National Health Insurance (NHI) database, originally collated in 2006. This cohort, representing approximately 2.2% of the South Korean population as of 2002[25] is a valuable resource for public health researchers and policymakers. The NHIS-NSC database was assembled using both retrospective (2002–2005) and prospective (2007–2019) data-collection methods. The database contains data pertaining to newly born individuals and excludes the data of deceased or emigrated individuals during these periods. Other comprehensive information, such as insurance eligibility, medical histories, healthcare provider details, and extensive health examination records, is also included.

2. Study population

Based on the classification of the Korean Standard Classification of Diseases (KCD), our study screened patients diagnosed with COPD (codes J42–44, excluding J430 [emphysema]) or asthma (codes J45–J56). Patients with a sole diagnosis of emphysema were excluded because airway obstruction solely due to this condition could not be confirmed. The inclusion criteria required patients to have had over two medical consultations within a year after their initial diagnosis and to have used respiratory medications at least twice in that same year. Respiratory medications included ICS, long-acting muscarinic antagonists (LAMA), ICS/long-acting beta-agonists (LABA), short-acting beta-agonists (SABA), xanthine, leukotriene receptor antagonists (LTRA), and systemic steroids.

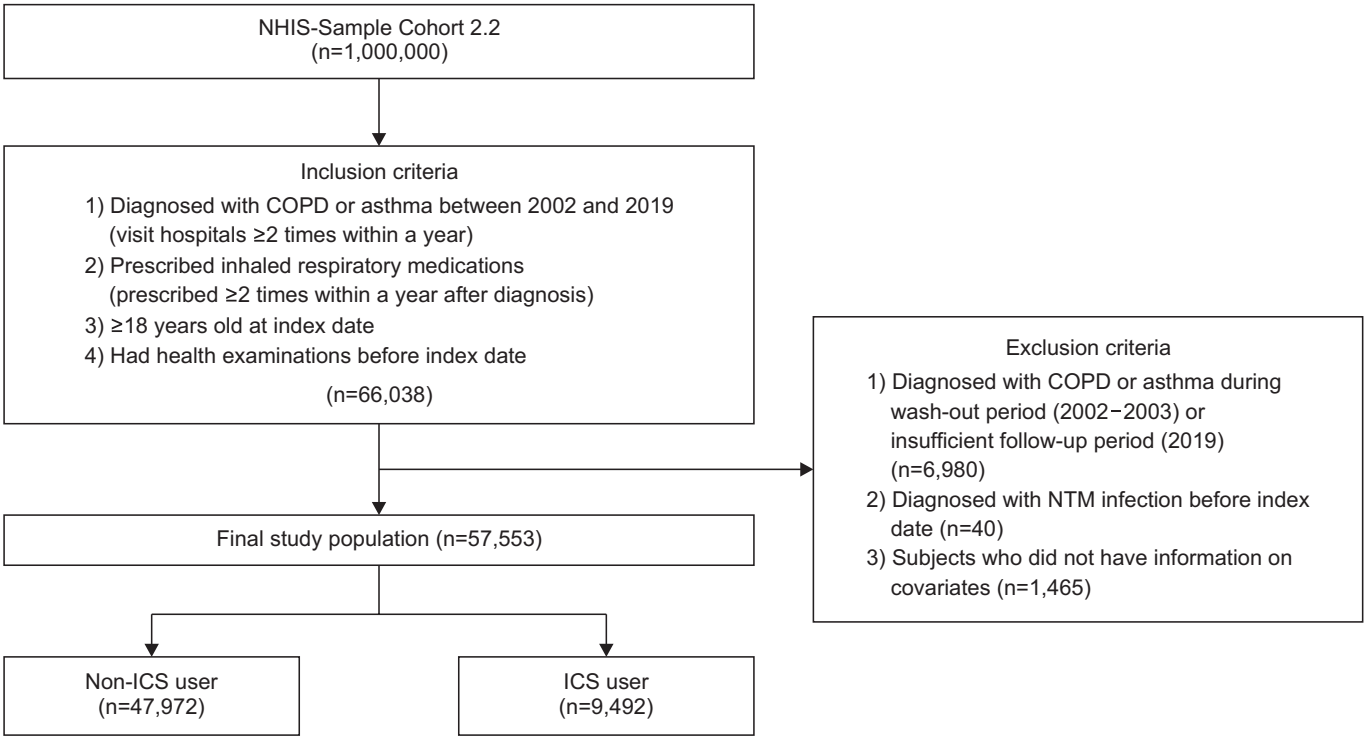
Our analysis involved a subset of the NHIS-NSC comprising 100,000 participants. Initially, we identified 66,038 individuals aged >18 years diagnosed with COPD or asthma who underwent health screening to obtain the major covariates from 2002 to 2019 (Figure 1). The exclusion criteria was: diagnosis of COPD or asthma during the washout period (2002 or 2003), or with less than 1 year of follow-up after the 2019 diagnosis (n=6,980), prior diagnosis of NTM infection before the index date (n=40), and missing major covariates (n=1,465). After these exclusions, the final cohort consisted of 57,553 patients. The Institutional Review Board of Soonchunhyang University Seoul Hospital approved the study protocol (2023-06-008). The requirement for informed consent was waived due to the anonymized nature of the NHIS-NSC dataset.

3. Exposure and outcome assessment

We assessed exposure by analyzing treatment claims recorded in the NHI system. Participants were categorized based on their use of ICS, leading to the formation of two distinct groups: 'ICS users' and 'non-ICS users.' To standardize the potency across various steroid formulations, we converted ICS doses to 50-mg fluticasone equivalents using equivalency ratios of 80 mg for budesonide, 32 mg for ciclesonide, and 100 mg for beclomethasone. The mean daily dose was determined by dividing the total medication quantity dispensed over the follow-up period by the prescription duration, aiding in the analysis of dose-dependent associations.

In this study, the index date was defined as the date of the first ICS prescription for ICS users; for non-ICS users, it was the date of the first prescription of other respiratory medications. Covariates were documented as the index date and monitored until the development of NTM infection, death, or conclusion of the study

Figure 1. Patient enrolment. NHIS: National Health Insurance Service; COPD: chronic obstructive pulmonary disease; ICS: inhaled corticosteroid; NTM: nontuberculous mycobacteria.



period in December 2019. Our primary study outcome was the identification of NTM infection cases, defined as those with either one hospitalization or two outpatient visits under KCD code A31.

4. Statistical analysis

We evaluated the baseline characteristics of ICS and non-ICS users using Wilcoxon rank-sum and chi-squared tests. For balanced differences propensity score-based inverse probability of treatment weighting (IPTW)[26] was employed. Covariates affecting NTM infection risk were included to determine treatment likelihood, with a post-IPTW standardized mean difference (SMD) below 0.10, signifying a balanced group. The NTM infection risk was assessed using Cox proportional hazards models to derive both unadjusted and adjusted (post-IPTW) hazard ratios (HRs) with 95% confidence intervals (CIs). Landmark analyses at 6 months, 1 year, and 2 years were conducted to minimize bias from early diagnosis and to assess the impact of ICS on NTM infection.

For continuous dose-dependent analysis, the HR was calculated per 100 μg/day increase. Categorically, doses were grouped into high (1,000 μg/day), medium (500–999 μg/day), and low (<500 μg/day) categories. Furthermore, our study employed subgroup analyses to identify ICS user groups at elevated NTM infection risk. This involved assessing variables, including sex, age, smoking habits, existing airway conditions (asthma or COPD), overall systemic steroid usage, and Charlson comorbidity index (CCI) scores. All statistical analyses were performed using SAS Enterprise Guide version 8.3 (SAS Institute Inc., Cary, NC, USA) and R Studio version 4.3.0 (RStudio Inc., Boston, MA, USA), with a significance threshold of $p<0.05$.

Results

1. Baseline demographics

Among the 57,553 participants, the average age was 56.0 years, with 43.2% male and 69.1% non-smokers. Of these, 9,520 (16.5%) were ICS users, whereas the remaining 48,033 (83.5%) did not use ICS (Table 1). Before IPTW matching, ICS users were generally older, had a lower proportion of never-smokers, and had a higher body mass index than non-users. They also demonstrated a higher rate of medical aid use and several comorbid conditions, including COPD and asthma, diabetes mellitus, dyslipidemia, hypertension, ischemic heart disease, arrhythmia, renal failure, malignancy, and increased CCI. In terms of medication, ICS users received more prescriptions for LAMA, SABA, and

Table 1. Baseline demographics before and after IPTW

Characteristic	ICS users	Non-ICS users	p-value	SMD before IPTW	SMD after IPTW
No. of patients	9,520 (16.5)	48,033 (83.5)			
Age, yr	59.3±15.5	55.3±14.8	<0.001	0.260	0.063
Male sex	4,108 (43.2)	20,251 (42.2)	0.073	−0.010	−0.012
Smoking status			<0.001		
Never	6,041 (63.5)	33,754 (70.3)		−0.068	−0.003
Former	1,639 (17.2)	5,561 (11.6)		0.056	0.006
Current	1,840 (19.3)	8,718 (18.2)		0.012	−0.003
BMI, kg/m^2	24.3±3.7	24.0±14.7	<0.001	0.026	0.016
Year of diagnosis			<0.001		
2002–2008	2,677 (28.1)	11,691 (24.3)		0.038	−0.042
2009–2011	1,386 (14.6)	11,071 (23.1)		−0.085	−0.011
2012–2014	1,436 (15.1)	12,462 (25.9)		−0.109	0.009
2015–2018	4,021 (42.2)	12,809 (26.7)		0.156	0.045
Income			<0.001		
Medical aid	7,453 (4.8)	281 (0.6)		0.042	0.000
Low	453 (4.8)	281 (0.6)		0.042	0.000
Middle	2,050 (21.5)	10,577 (22.0)		−0.005	0.000
High	3,193 (33.5)	17,683 (36.8)		−0.033	−0.004
Comorbidity					
COPD	572 (6.0)	5,495 (11.4)	<0.001	−0.054	0.010
Asthma	6,831 (71.8)	36,180 (75.3)	<0.001	−0.036	−0.009
Both COPD and asthma	2,117 (22.2)	6,358 (13.2)	<0.001	0.090	−0.001
Diabetes mellitus	1,367 (14.4)	5,540 (11.5)	<0.001	0.028	0.007
Dyslipidemia	2,238 (23.5)	7,166 (14.9)	<0.001	0.086	0.010
Hypertension	3,136 (32.9)	13,107 (27.3)	<0.001	0.057	0.008
Ischemic heart disease	805 (8.5)	2,583 (5.4)	<0.001	0.031	0.003
Arrhythmia	314 (3.3)	921 (1.9)	<0.001	0.014	0.001
Infection	18 (0.19)	25 (0.05)	<0.001	0.001	−0.000
Fungal infection	2 (0.02)	7 (0.01)	0.646	0.000	−0.000
IPA	2 (0.02)	7 (0.01)	0.646	NC	NC
Renal failure	133 (1.4)	226 (0.5)	<0.001	NC	NC
Malignancy	569 (6.0)	1,760 (3.7)	<0.001	NC	NC
CCI score ≥2	4,115 (43.2)	18,791 (39.1)	<0.001	0.041	0.008
Medication					
ICS only	4,381 (46.0)	-		NA	NA
ICS/LABA	6,878 (72.3)	-		NA	NA
LABA only	2,249 (23.6)	20,021 (41.7)	<0.001	−0.181	−0.009
LABA/LAMA	152 (1.6)	164 (0.3)	<0.001	0.013	0.001
LAMA only	1,644 (17.3)	1,390 (2.9)	<0.001	0.144	0.002
SABA	5,112 (53.7)	16,702 (34.8)	<0.001	0.189	0.030
Xanthine	4,280 (45.0)	26,996 (56.2)	<0.001	−0.113	−0.002
LTRA	6,562 (68.9)	28,899 (60.2)	<0.001	0.088	0.021
Systemic steroid	2,774 (29.1)	22,825 (47.5)	<0.001	−0.184	−0.027

Values are presented as mean±standard deviation or number (%). Among the variables, items included in the other variables were not separately calculated for the IPTW.
IPTW: inverse probability of treatment weighting; ICS: inhaled corticosteroid; SMD: standardized mean difference; BMI: body mass index; COPD: chronic obstructive pulmonary disease; IPA: invasive pulmonary aspergillosis; NC: not calculated; CCI: Charlson comorbidity index; NA: not applicable; LABA: long-acting beta-agonist; LAMA: long-acting muscarinic antagonist; SABA: short-acting beta-agonist; LTRA: leukotriene receptor antagonist.

LTRA but fewer prescriptions for LABA, xanthines, and systemic steroids compared with non-ICS users. During a median follow-up period of 4.8 years (interquartile range, 1.5 to 14.8), 6.5% (n=622) of ICS users and 8.8% (n=5,047) of non-ICS users died. After IPTW matching, the covariates were well balanced with all SMDs below 0.1, indicating a balance between the groups (Figure 2).

2. Association between ICS and NTM infection risk

We identified 63 NTM infection cases, including nine among ICS users and 54 among non-users. Prior to IPTW matching, ICS use was associated with a higher risk of NTM infection (unadjusted HR, 3.38; 95% CI, 1.52 to 7.54; p=0.00) (Table 2), and remained significant after IPTW matching (adjusted HR, 4.01; 95% CI, 7.48 to 15.58; p=0.045). This trend was consistent across landmark analyses at 6 months (adjusted HR, 5.36; 95% CI, 1.23 to 23.43; p=0.026), 1 year (adjusted HR, 6.63; 95% CI, 1.47 to 27.91; p=0.014), and 2 years (adjusted HR, 14.04; 95% CI, 3.25 to 60.64; p<0.001).

In our study, the association between NTM infection risk and continuous ICS dosage was not significant in either pre- or post-IPTW analyses. However, when categorized into three daily ICS dosage levels (<500 μg/day),

Figure 2. Covariate balance before and after inverse probability of treatment weighting treatment. Dot plot displaying the covariate balance before and after adjustment. The Y-axis lists the covariates, and the X-axis shows the standardized mean differences. Red dots represent unadjusted values, and blue dots represent adjusted values post-propensity score matching, with dots closer to the vertical zero line indicating a better balance between groups. BMI: body mass index; COPD: chronic obstructive pulmonary disease; CCI: Charlson comorbidity index; LABA: long-acting beta-agonist; LAMA: long-acting muscarinic antagonist; SABA: short-acting beta-agonist; LTRA: leukotriene receptor antagonist.

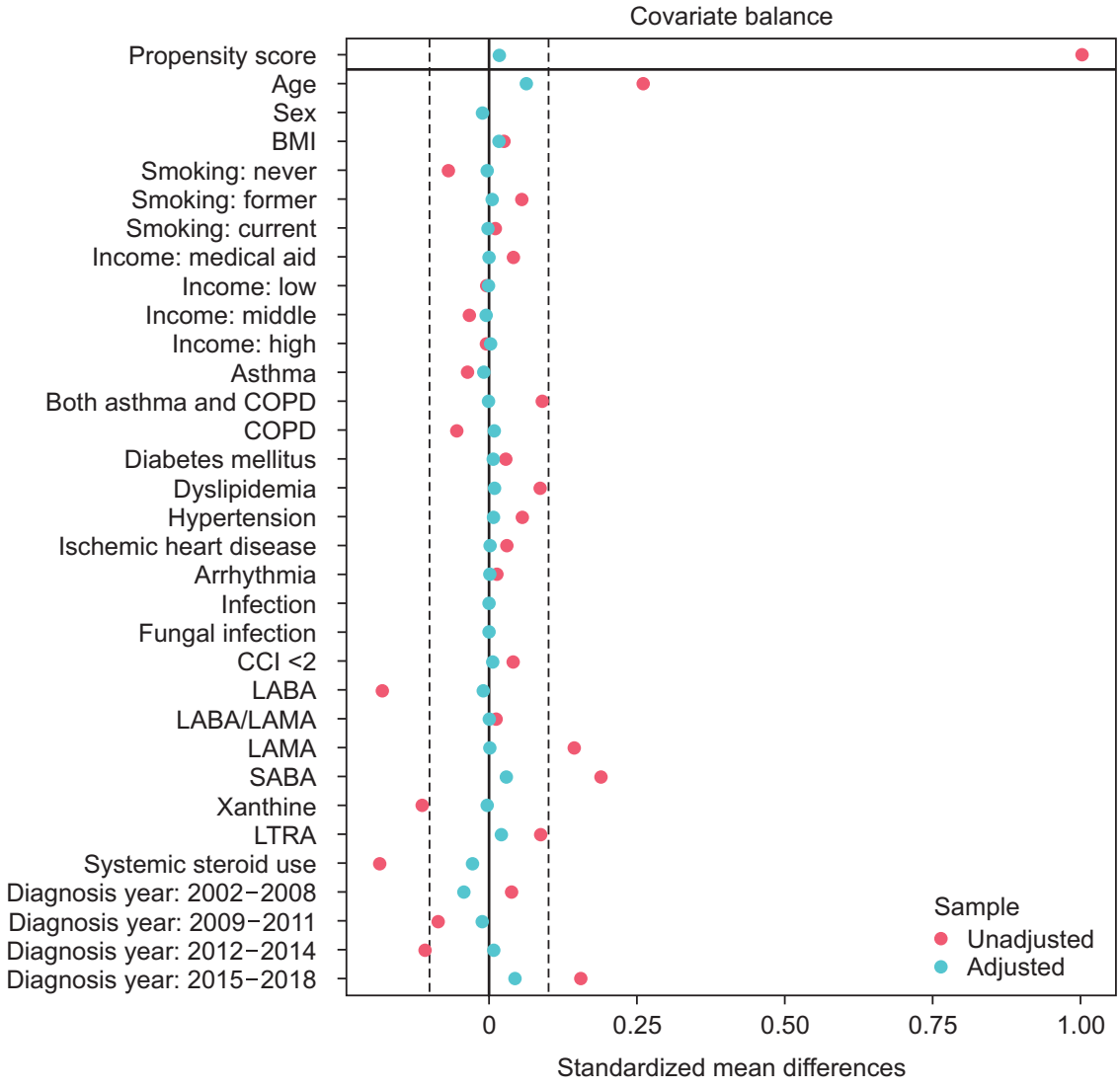


Table 2. Cox proportional analysis for the risk of NTM infection according to ICS use

Variable	Unadjusted HR (95% CI)	p-value	Adjusted HR (95% CI)	p-value
ICS uses	3.38 (1.52–7.54)	0.003	4.01 (1.48–15.58)	0.045
Landmark analysis				
6-month	3.19 (1.23–8.3)	0.017	5.36 (1.23–23.43)	0.026
1-year	3.67 (1.03–426.14)	0.015	6.63 (1.47–29.91)	0.014
2-year	5.99 (1.76–20.39)	0.004	14.04 (3.25–60.64)	<0.001
Categorical dose, μg/day				
Non-ICS	Reference		Reference	
1,000	NA*		NA*	
500–999	3.14 (0.72–13.57)	0.126	0.85 (0.17–4.19)	0.840
<500	3.78 (1.58–9.04)	0.003	5.23 (1.29–21.13)	0.020
ICS ingredient				
Non-ICS	Reference		Reference	
Fluticasone	2.74 (0.93–8.08)	0.068	6.03 (1.31–27.79)	0.021
Beclomethasone	5.60 (1.30–24.15)	0.021	2.62 (0.54–12.79)	0.233
Budesonide	1.32 (0.31–5.72)	0.710	0.35 (0.07–1.70)	0.191
Ciclesonide	8.51 (1.14–63.68)	0.037	2.54 (0.33–19.35)	0.370

*Not applicable because no events occurred.
NTM: nontuberculous mycobacteria; ICS: inhaled corticosteroid; HR: hazard ratio; CI: confidence interval; NA: not applicable.

low-dose daily ICS use showed a significant association with NTM infection risk compared with non-ICS users, both pre-IPTW (unadjusted HR, 3.78; 95% CI, 1.58 to 9.04; p=0.003) and post-IPTW (adjusted HR, 5.23; 95% CI, 1.29 to 21.13; p=0.020). In terms of specific ICS ingredients, post-IPTW adjustment revealed that the use of fluticasone was significantly associated with increased NTM infection risk (adjusted HR, 6.03; 95% CI, 1.31 to 27.79; p=0.021). In terms of specific ICS ingredients, post-IPTW adjustment revealed a significant association between the use of fluticasone and an increased NTM infection risk (adjusted HR, 6.03; 95% CI, 1.31 to 27.79; p=0.021).

3. Subgroup analysis

The use of ICS in patients aged ≥65 years was associated with an increased risk of NTM infection (adjusted HR, 6.40; 95% CI, 1.28 to 31.94; p=0.024), and this association was not significant in patients aged <65 years (Table 3). In sex-stratified analysis, ICS use increased the risk of NTM infection in females (adjusted HR, 10.91; 95% CI, 2.24 to 53.20; p=0.003), but not in males. For never-smokers, ICS use was significantly associated with an increased risk of NTM infection (adjusted HR, 6.31; 95% CI, 1.49 to 26.64; p=0.012). Concurrent use of systemic steroids was also significantly linked to a higher risk of NTM infection (adjusted HR, 50.19; 95% CI, 8.07 to 312.19; p<0.001), a finding that was not significant in non-systemic steroid users. Additionally, patients with higher CCI (≥2) scores exhibited an increased NTM infection risk (adjusted HR, 6.64; 95% CI, 1.19 to 37.03; p=0.031), but not in the lower CCI group. No significant associations were observed in the other subgroups.

Discussion

This study investigated the association between ICS use and NTM infection incidence among patients with chronic airway diseases, including COPD and asthma, using a large representative cohort from the Korean NHIS-NSC database. Our findings indicate a significant association between ICS use and an increased risk of NTM infection, particularly among specific subgroups. This trend remained consistent even after adjusting for potential confounders by using IPTW matching and landmark analysis, highlighting the robustness of the results.

The increased risk of NTM infection among ICS users, as evidenced by our analyses, aligns with existing

Table 3. Subgroup analysis for the risk of NTM infection according to ICS use

Variable	Number	Event	Adjusted HR (95% CI)	p-value
Age, yr				
≥65	16,834	31	6.40 (1.28–31.94)	0.024
<65	40,719	32	1.42 (0.40–5.07)	0.591
Sex				
Male	24,359	34	0.52 (0.15–1.76)	0.289
Female	33,194	29	10.91 (2.24–53.20)	0.003
Smoking				
Never	39,795	44	6.31 (1.49–26.64)	0.012
Ever	17,758	19	0.50 (0.08–2.90)	0.437
Underlying airway disease				
Asthma	43,011	32	3.55 (0.77–16.30)	0.104
COPD	6,067	15	7.37 (0.85–64.25)	0.071
Both	8,475	16	0.48 (0.05–4.49)	0.517
Systemic steroid				
Use (cumulative PD dose ≥250 mg)	25,599	26	50.19 (8.07–312.19)	<0.001
None (cumulative PD dose <250 mg)	31,954	37	0.78 (0.28–2.19)	0.636
CCI				
≥2	34,647	35	1.42 (0.45–4.49)	0.552
<2	22,906	28	6.64 (1.19–37.03)	0.031

NTM: nontuberculous mycobacteria; ICS: inhaled corticosteroids; HR: hazard ratio; CI: confidence interval; COPD: chronic obstructive pulmonary disease; PD: prednisolone; CCI: Charlson comorbidity index.

studies[18-24]. A nested case-control study using a Canadian claims database from 2001 to 2013 found that the current use of ICS in patients with obstructive lung disease, including asthma, COPD, and asthma-COPD overlap syndrome, was associated with an increased risk of NTM infection (adjusted odds ratio [OR], 1.86; 95% CI, 1.60 to 2.15)[21]. A Danish population-based case-control study also reported that both current (adjusted OR, 24.3; 95% CI, 11.9 to 49.7) and former (adjusted OR, 8.8; 95% CI, 2.9 to 26.8) ICS users have an increased risk of NTM infection compared with those without chronic respiratory disease, with a notably higher risk observed in current ICS users with COPD (OR, 29.1; 95% CI, 13.3 to 63.8)[20]. In a meta-analysis of four studies and that of their own study, Shu et al.[18] found that patients prescribed ICS within a year before NTM infection had a 2-fold increased risk of developing NTM infection compared to non-ICS users (pooled OR, 2.02; 95% CI, 1.41 to 2.90). While varying in research design and target populations, these studies have consistently reported an association between ICS use and NTM infection[18-22]. This population-based analysis, based on extensive NHI data, confirmed the association between ICS use and the development of NTM infection in a combined cohort of patients with chronic airway diseases, including asthma and COPD.

On the other hand, previous studies suggested the dose-dependent association between ICS use and NTM infection[19-22], but our study did not find a clear dose-dependent association. A Korean NHIS study indicated that while overall ICS use did not significantly increase the risk of NTM infection in COPD patients, medium (500–999 μg) (HR, 1.229; 95% CI, 1.008 to 1.499), and high (≥1,000 μg) (HR, 1.637; 95% CI, 1.241 to 2.160) daily doses of ICS were associated with a greater risk[22]. A meta-analysis encompassing four studies also showed that, compared to no ICS exposure, moderate (pooled OR, 1.85; 95% CI, 1.30 to 2.64) and high doses (pooled OR, 3.49; 95% CI, 1.92 to 6.36) of ICS were significantly associated with higher NTM infection risk, whereas low-dose ICS was not (pooled OR, 1.61; 95% CI, 0.91 to 2.86)[21]. The absence of a clear dose-dependent relationship in our study could be partly due to statistical reasons, such as the low incidence of NTM infection in our NHI sample cohort and the limited number of patients in higher dose catego-

ries. Furthermore, our inability to calculate cumulative doses and reliance on average daily doses for determining dose-dependent relationships may have also contributed to this outcome.

The underlying reason for the association between ICS use and the increased incidence of NTM infection may involve various mechanisms. ICS use has been shown to diminish the function of alveolar macrophages, the key components of the innate immune defense against pathogens[27]. This impairment can reduce the ability of the lungs to clear mycobacteria, leading to an increased susceptibility to NTM infection[28]. In addition, ICS use can induce dysbiosis in the lung microbiome[29,30], leading to an increase in NTM infection[31]. Furthermore, the long-term use of ICS may lead to a systemic immunosuppressive effect[32], further diminishing the host's ability to effectively combat NTM infections. Consequently, this combination of diminished local and systemic immune responses, coupled with altered lung microbiota, markedly increases the possibility of developing NTM infection in individuals treated with ICS.

In our study, the risk of NTM infection occurrence varied across subgroups, which predominantly aligned with the risk factors identified in previous research on the development of NTM infection. Notably, older individuals, females, and non-smokers showed higher susceptibility, which is consistent with previous studies[33,34]. The increased risk of concurrent systemic steroid use suggests a synergistic effect that increases the risk of NTM infection, supporting the findings of earlier research[24,34]. In our study, we observed a substantial increase in the risk of NTM infection among users of systemic steroids, whereas this risk was not elevated in the group using only ICS. These findings suggested that the heightened risk of NTM infection in ICS users might be predominantly associated with the use of systemic steroids rather than with the ICS themselves. Moreover, elevated CCI scores and older age, indicative of greater comorbidity, were associated with a higher risk of NTM infection, likely due to a weakened immune state or poor overall health[35]. However, the limited number of NTM infection cases in our study restricts the interpretability of these results, necessitating caution when drawing conclusions from the subgroup analysis. Future large-scale research is essential to offer more conclusive evidence of NTM infection risk in populations treated with ICS.

This retrospective observational study has several limitations. First, its design precluded the establishment of causality and left potential confounding factors, particularly other NTM infection risk factors. To partially address this limitation, we implemented IPTW analysis with various covariates, including detailed health examination data. However, we were unable to adjust for the primary risk factor of NTM infection, particularly bronchiectasis. Second, reliance on claims data carries the risk of misclassifying NTM infection or chronic airway disease diagnoses. To mitigate this, we defined chronic airway disease using two medical visits and respiratory medication prescriptions at the index date, and NTM infection diagnosis through both inpatient and outpatient data. Third, the use of an NHI sample cohort might have led to a selection bias. Nevertheless, this cohort mirrored the broader Korean population, with the added benefit of examination data provided by the government free of charge, enhancing its relevance and representativeness. Finally, this study's focus on Korean demographics may limit its broader applicability, emphasizing the need for research across diverse populations. Nevertheless, our study benefits from the use of a comprehensive national insurance database and statistical methods to explore the association between ICS use and NTM infection risk.

In conclusion, our study indicates a potential association between ICS use and an increased risk of developing NTM infection. Considering widespread use of ICS in chronic respiratory disease management, a reassessment of its role, with particular attention paid to NTM infection risk, is advisable. Future comprehensive prospective clinical studies are required to elucidate this relationship.

Authors' Contributions

Conceptualization: Yoon HY. Methodology: Yoon EC, Yoon HY. Formal analysis: Lee H. Data curation: Lee H. Software: Lee H. Validation: Yoon EC, Yoon HY. Investigation: Yoon EC, Yoon HY. Writing - original draft preparation: all authors. Writing - review and editing: all authors. Approval of final manuscript: all authors.

Conflicts of Interest

Hee-Young Yoon is an early career editorial board member of the journal, but she was not involved in the peer reviewer selection, evaluation, or decision process of this article. No other potential conflicts of interest relevant to this article were reported.

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