Increased Adult Otitis Media with Effusion (OME) in Gastroesophageal Reflux Disease (GERD)

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Introduction

The relationship between otitis media with effusion (OME) and gastroesophageal reflux disease (GERD) remains clinically equivocal, particularly in adults. A recent study demonstrated that GERD was associated with a higher risk of adult OME. However, multiple comorbidities predisposed to adult OME, namely craniofacial anomaly, atopy, HIV, adenoid hypertrophy, obstructive sleep apnea, and patients with head and neck malignancies who received radiotherapy, were not excluded in previous studies. Furthermore, the treatment effects on the risk of adult OME were not determined. Therefore, we conduct a population-based study to investigate the real-world risk of OME in adult patients with GERD by excluding potential confounders in advance and evaluate the effect of various GERD treatment strategies and duration of treatment on the risk of adult OME. This study hypothesized that GERD is associated with an increased risk of adult OME, and adequate treatment of OME may exhibit a reduced risk of OME in adult patients with GERD.

Methods

This study analyzed data from the Longitudinal Health Insurance Database 2005, containing the information of 2 million randomly selected individuals in Taiwan. The inclusion criteria for the GERD cohort was adult patients with at least 3 outpatient or one inpatient diagnoses of GERD with at least one of the following procedures: esophageal 24-hour pH monitoring, upper gastrointestinal endoscopy, nasopharyngolaryngoscopy and medications for GERD (H_2 receptor blocker or proton pump inhibitor (PPI) over 28 days) during this period. Patients were excluded if they were <18 years old or had a history of GERD, OME, or diseases that might cause OME before the index date, including head and neck malignancies, chronic rhinosinusitis, allergic rhinitis or chronic rhinitis, asthma, adenotonsillitis, eustachian tube dysfunction, HIV infection, sarcoidosis, cleft palate or OSA.

The study outcome was a diagnosis of OME. The Kaplan–Meier method was used to determine the cumulative incidence rates of OME in the GERD and non-GERD cohorts, and a log-rank test was used to analyze the differences between the cohorts. In addition, Cox proportional hazards models were used to calculate each cohort's 18-year hazard ratios (HRs).

We performed subgroup analysis based on GERD treatment to determine the effect of interventions on the risk of OME. We defined medical treatment as ≥ 4 months of GERD medication use. The GERD medications used by the patients were H2-receptor antagonists and Proton pump inhibitors. Surgical treatment for GERD was fundoplication or related procedures. Moreover, effect of combined therapy on the risk of OME was assessed.

Figure 1. The flowchart of the study design.

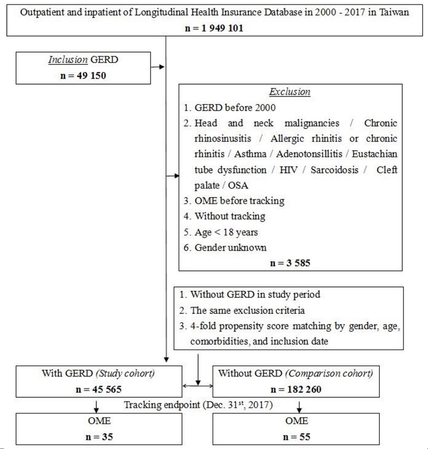

Figure 2. Kaplan-Meier method for cumulative risk of otitis media with effusion aged 18 and over stratified by GERD with log-rank test.

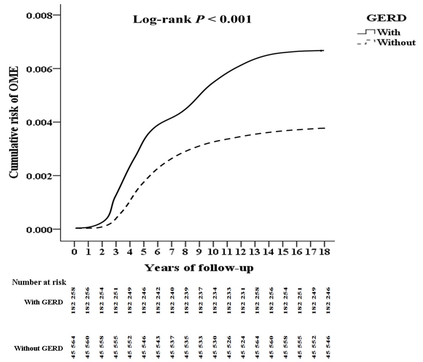

Table 1. Subgroup analyses of effects of medical and surgical treatment on the risk of adult OME between the GERD and non-GERD cohorts by using Cox regression and Bonferroni correction for multiple comparisons.

GERD subgroupz	Adjusted HR	95% CI	*P*	Adjusted HR	95% CI	*P*
Without GERD	Reference					
With GERD	2.38	1.64–3.45	< .001			
With GERD, without treatment	3.36	2.32–4.87	< .001	Reference		
With GERD, with treatment	1.66	1.14–2.40	< .001	0.49	0.38–0.82	< .001
With GERD, treatment < 4 months	1.97	1.36–2.82	< .001	0.59	0.46–0.93	< .001
With GERD, treatment ≥ 4 months	1.37	0.99–1.97	.057	0.41	0.31–0.67	< .001
With GERD, fundoplication only	1.54	1.07–2.23	.001	0.46	0.31–0.78	< .001
With GERD, H_2 blocker alone	1.86	1.28–2.69	< .001	0.55	0.43–0.91	< .001
With GERD, PPIs alone	1.61	1.11–2.33	< .001	0.48	0.30–0.70	< .001
With GERD, combined therapy	1.19	0.82–1.73	.178	0.35	0.15–0.54	< .001

Results

Of the 1,949,101 patients with inpatient or outpatient care records in the LHID2005 claims data from 2000-2017 (Figure 1), we enrolled 45,565 adult patients with GERD who met the inclusion criteria; and 182,260 (1:4 propensity score–matched individuals without GERD. No significant differences in sex, age, and comorbidities were found between the GERD and non-GERD cohorts after propensity score matching. The average follow-up periods were 10.94 and 11.15 years for the GERD and non-GERD cohorts, respectively.

A total of 90 patients-35 and 55 from the GERD and non-GERD cohorts, respectively-were diagnosed with OME during the follow-up period (Figure 1).

The adjusted HR (aHR) was 2.38 (95% CI, 1.64-3.45) after adjusting for demographic characteristics and comorbidities. A log-rank test of P < .001 demonstrated a significant difference between the GERD and non-GERD cohorts (Figure 2).

Subgroup analysis revealed that GERD with treatment for ≥ 4 months was associated with a reduced risk of OME (aHR, 0.379; 95% CI, 0.178-0.567). In addition, treatment with fundoplication, H_2 blockers, proton pump inhibitors, or combined therapy reduces the risk of OME (aHR, 0.459; 95% CI, 0.306-0.784, 0.552; 95% CI, 0.432-0.909, 0.478; 95% CI, 0.297-0.697 and 0.354; 95% CI, 0.152-0.542, respectively (Table 1).

Discussion

The study underlines a significant association between GERD and OME in adults. Historically, the link between these two conditions, especially in adults, has been ambiguous. The findings of this research, conducted on a large cohort from the Longitudinal Health Insurance Database in Taiwan, give valuable insights into this association.

A significant result emerging from the study is the stark difference in the incidence rates of OME among GERD and non-GERD patients. The aHR of 2.38 in GERD patients relative to the non-GERD group suggests that adults with GERD are over two times more likely to develop OME. This observation confirms the speculation that GERD might be a significant risk factor for developing OME in adults.

However, the silver lining in these findings lies in the impact of GERD treatment. The study shows that prolonged treatment (≥ 4 months) is associated with a reduced risk of OME, reflected in the aHR of 0.379. This suggests that managing GERD addresses the symptoms of acid reflux and could potentially curtail the risk of developing OME.

Furthermore, the treatments – fundoplication, H_2 blockers, PPIs, and combined therapy – demonstrates consistent risk reduction across the board. Combined therapy emerges as the most potent in diminishing OME risk, with an aHR of 0.354. PPIs, often a primary line of treatment for GERD, also seem to be effective, as indicated by the aHR of 0.478. Such data is pivotal for clinicians in making informed decisions about GERD management, considering the ancillary benefits concerning OME prevention.

However, while the association is clear, the underlying mechanisms linking GERD and OME remain undetermined. The reflux of stomach acid may cause inflammatory changes in the Eustachian tube and middle ear, leading to OME. Conclusively, this study underscores the importance of recognizing and effectively managing GERD to potentially reduce the incidence of secondary conditions like OME in adults. Future research delving deeper into the mechanistic pathways is imperative for a comprehensive understanding.

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Key Points

GERD is independently associated with an increased risk of OME in adult patients.
Treatment strategies including H_2 blockers, PPIs, surgeries, or combined therapy for GERD effectively reduced the risk of OME in adult patients with GERD.
Further studies were necessary to clarify the mechanism of the development of OME in adult patients with GERD.