

# Increased risk of Eustachian tube disorders in patients with sleep-disordered breathing

Meng-Shih Chou, MD<sup>a</sup>, Wen-Dien Chang, PhD<sup>b</sup>, Che-Chen Lin, MD<sup>c,d</sup>, Yu-Fen Li, PhD<sup>e</sup>, Yung-An Tsou, MD, PhD<sup>a,f,g,\*</sup>

## Abstract

Sleep-disordered breathing (SDB) and Eustachian tube disorders (ETDs) share the same risk factors. The specific aim of this study was to determine the correlation between these 2 conditions and to determine whether treatments for SDB reduce the risk of ETD.

This is a retrospective and large population-based cohort study. According to Taiwan's National Health Insurance Research Database, out of 1,000,000 insured patients, 24,251 patients were newly diagnosed with SDB from year 2000 through 2009. The control group for this study comprised 96,827 patients without SDB who were randomly selected from the same database at a ratio of 1:4, frequency matched for sex, age, and index year of SDB. The incidence of developing ETD was compared between these 2 groups; the main covariates were demographic data, interventions, and medical comorbidities.

There was an increased risk of developing ETD among the SDB cohort compared with the control group (hazard ratio = 1.51, 95% confidence interval = 1.41–1.63). Compared with SDB patients who did not receive treatment, those who received the treatment, that is, pharyngeal or nasal surgery, CPAP, or multiple modalities (both surgery and CPAP), had a significantly reduced risk of developing ETD.

This study showed that patients with SDB are at an increased risk of developing ETD and other comorbidities. The risk of developing ETD can be reduced by implementing prompt treatment for SDB. Multidisciplinary evaluation including ETD should be conducted in the management of patients presenting with SDB.

**Abbreviations:** ATH = adenotonsillar hypertrophy, AR = allergic rhinitis, CIs = confidence intervals, CPAP = continuous positive airway pressure, ENT = ear, nose, and throat department, ETD = eustachian tube disorders, GERD = gastroesophageal reflux disease, HR = hazard ratio, LAUP = laser-assisted uvulopalatoplasty, LHID = Longitudinal Health Insurance Database, HIRD = National Health Insurance Research Database, NHRs = hazard ratios, OM = otitis media, OSA = obstructive sleep apnea, SDB = sleep-disordered breathing, T&A = tonsillectomy, adenoidectomy, adenotonsillectomy, UPPP = uvulopalatopharyngoplasty.

**Keywords:** Eustachian tube disorders, hazard ratio, incidence, sleep-disordered breathing

## 1. Introduction

Sleep-disordered breathing (SDB) is a common disease in adults, with a prevalence of 24% in males and 9% in females aged 30 to 60 years.<sup>[1]</sup> The spectrum of SDB ranges from simple primary snoring to severe obstructive sleep apnea (OSA) in the clinic studies, and SDB patients revealed OSA is evident in 56% in males and 11% in females.<sup>[1,2]</sup> SDB is associated with an

increased risk of cardiovascular disease,<sup>[3,4]</sup> and it is considered a chronic disease that requires long-term multidisciplinary management according to the American Academy of Sleep Medicine.<sup>[5]</sup> The risk factors for SDB are diabetes mellitus, obesity, cardiovascular disease, and smoking.<sup>[6]</sup> Conservative treatments include weight loss, modification of the patient's sleep position, and continuous positive airway pressure (CPAP), with CPAP being the most recommended and the standard treatment modality.<sup>[7]</sup> Common surgical interventions that have been used include tracheostomy, uvulopalatopharyngoplasty (UPPP), tonsillectomy, adenoidectomy, adenotonsillectomy (T&A), laser-assisted uvulopalatoplasty (LAUP), and maxillomandibular advancement.<sup>[8]</sup> Although a recent systemic review found limited evidence to support the use of surgery in SDB,<sup>[9]</sup> some studies have demonstrated the benefits of surgical management in well-selected surgical candidates.<sup>[10,11]</sup>

Although otitis media (OM) is generally considered a disease that occurs mostly in infants and children, its incidence rate in adults is also significant. The incidence rate of active OM in adults is approximately 1.5%,<sup>[12]</sup> although a much higher prevalence has been reported for clinical practices of most otolaryngologists.<sup>[13]</sup> Eustachian tube disorders (ETDs) play the most relevant role in the development of OM,<sup>[13]</sup> with 1 animal study finding that ETD was the sole cause and was sufficient for the development of persistent OM.<sup>[14]</sup> The goal of treatment for either ETD or OM is improving aeration of the middle ear, improving hearing and vestibular function, and preventing cholesteatoma formation.<sup>[15]</sup> The primary management of ETD involves reversing the precipitating factors such as nasal

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MSC and WDC contributed equally to be first authors.

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<sup>a</sup> Department of Otolaryngology-Head and Neck Surgery, <sup>b</sup> Department of Sports Medicine, <sup>c</sup> Management Office for Health Data, <sup>d</sup> Department of Public Health,

<sup>e</sup> Institute of Biostatistics, <sup>f</sup> Graduate Institute of Clinical Medical Science,

<sup>g</sup> Department of Audiology and Speech-Language Pathology, Asia University,

Taichung, Taiwan.

\* Correspondence: Yung-An Tsou, Graduate Institute of Clinical Medical Science,

Departments of Otorhinolaryngology, Audiology and Speech-Language

Pathology, China Medical University and Hospital, No. 91, Hsueh-Shih Road,

Taichung City 40402, Taiwan (R.O.C) (e-mail: d22052121@gmail.com).

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allergy or sinusitis. For patients with recurrent and persistent OM who are resistant to medical treatment, surgical interventions such as the placement of a tympanostomy tube, temporary myringotomy, or adenoidectomy are the next best step. In children, if the patient requires a reinsertion of a tympanostomy tube, concurrent adenoidectomy is recommended.<sup>[16]</sup>

SDB and ETD share similar risk factors, which include adenotonsillar hypertrophy (ATH), smoking, and obesity. Gozal et al<sup>[17]</sup> reported that there were correlations among habitual snoring, recurrent OM, and tympanostomy tube placement in school children aged between 5 and 7 years. Tauman et al<sup>[18]</sup> reported that children who underwent isolated tympanostomy tube insertion have a higher risk of developing snoring and require subsequent T&A. Robison et al<sup>[19]</sup> recently found the prevalence of ETD to be significantly higher among infants with OSA, and also concluded that surgical interventions can effectively reduce the need for further tympanostomy tube placement. However, such a correlation is not yet confirmed in an adult population with SDB. Furthermore, physicians often neglect ear problems; instead, they place too much emphasis on the symptoms of SDB and the results of polysomnography, which may in some cases result in them overlooking preexisting ear diseases. Therefore, the aim of this study was to assess the correlation between SDB and ETD and whether treatment of SDB can reduce the risk of ETD across all age groups.

## 2. Methods

### 2.1. Database

A universal single-payer health insurance was established in Taiwan in 1996, which has covered approximately 99% of the country's population since 1998. The National Health Research Institutes established the National Health Insurance Research Database (NHIRD) that contains all of the available data on insurance reimbursement claims. All personal information is encrypted with surrogate identification codes before being released to the public so as to protect the patients' privacy. This study was approved by the Ethics Review Board of the China Medical University (approval CMU-REC-101-012).

This study used the Longitudinal Health Insurance Database (LHID), which contains the annual claims data of 1 million individuals randomly selected from the NHIRD during the period from 1996 through 2000. All disease history was recorded from outpatient and inpatient files, and the diagnosis of diseases was defined by the International Classification of Disease, Ninth Revision, Clinical Modification (ICD-9-CM).

### 2.2. Study population

A population-based retrospective cohort study was conducted. The SDB cohort comprised patients who had been newly diagnosed with SDB (ICD-9-CM 780.51, 780.53, 780.57, and 780.59) from year 2000 through 2009 and aged over 18 years. The index date of the SDB cohort was set as the SDB diagnosis date. The SDB cohort was categorized according to their age (divided into 5-year bins), sex, and index year of SDB, for the random selection of fourfold frequency-matched non-SDB individuals in the LHID. The index date of individuals in the control cohort was assigned as the same year as their matched SDB patients along with a randomly generated month and day. Both of the cohorts excluded individuals with head and neck

cancer (ICD-9-CM 140-149 from the catastrophic illness registry file), and those with ETD before the index date. The event of interest in the study was the development of ETD during the study period (ever coded as ICD-9-CM 381.1 and 381.5–381.9, or ever received one or more treatments with a tympanostomy tube, myringotomy, or tympanocentesis). Data collection from a patient was considered complete at insurance withdrawal (including death), occurrence of event of interest, or until December 31, 2010.

To investigate the benefit of SDB treatment in relation to ETD risk, the SDB cohort was subdivided according to treatment status (i.e., with or without). The types of treatment included pharyngeal or nasal surgery, CPAP, or multiple modalities (both surgery and CPAP). The types of nasal surgery comprised septoplasty, submucosal turbinoplasty, septomeatoplasty, and laser turbinoplasty. The pharyngeal surgical procedures of T&A, UPPP, and LAUP were included.

The possible confounders were rhinosinusitis (ICD-9 471 and 473), AR (ICD-9 477), gastroesophageal reflux disease (GERD; ICD-9 530.11 and 530.81), ATH (ICD-9 474), and the number of clinic visits to an ear, nose, and throat department (ENT). Obesity and smoking were 2 of the most critical risk factors for developing either ETD or SDB. "Triple H" [hypertension (ICD-9 401–405), hyperlipidemia (ICD-9 272), and hyperglycemia (ICD-9 250)] was used as a substitute confounder for obesity, because obesity is not available in the LHID. The analysis was stratified according to gender for assessing whether smoking is a confounder because female smokers are less common than male smokers in Taiwan.

### 2.3. Statistical analysis

The distribution of demographic factors and comorbidities in the SDB and control cohorts are reported as total numbers and proportions for categorical variables, and mean standard deviation values for continuous variables. The Chi-square test for categorical variables and *t* test for continuous variables were used to test for differences between the 2 cohorts. The incidence of developing ETD is quantified per 10,000 person-years. The incidence curve was estimated with the Kaplan–Meier method. The difference between the incidence curves among the study subcohorts was tested with the log-rank test. Hazard ratios (HRs) and 95% confidence intervals (95% CIs) were calculated with the Cox proportional hazards model.

All data analyses were performed with SAS 9.3 (SAS Institute, Cary, NC), and the incidence curve was drawn with R software (R Foundation for Statistical Computing, Vienna, Austria). All statistical tests were 2-sided, with the significance level set at  $P < .05$ .

## 3. Results

There were no significant differences between the SDB ( $n = 24,251$ ) and control ( $n = 96,827$ ) cohorts in mean age (47.2 years) and sex ratio (35.6% males; Table 1), as per the experimental design. The mean durations of follow-up were 4.34 and 4.38 years for the SDB and control cohorts, respectively. The proportions of patients with various comorbidities, including rhinosinusitis, AR, GERD, ATH, and triple H, were significantly higher in the SDB cohort than in the control cohort ( $P < .05$ ).

The incidence of ETD in the SDB cohort was 101.4 per 10,000 person-years, nearly 1.7-fold higher than that in the control cohort (58.9 per 10,000 person-years; Table 2). The cumulative

**Table 1**  
**Baseline demographic status and comorbidity between control and SDB cohort.**

Variable	Comparison cohort n=96,827 (%)	SDB cohort		P*	
		All n=24,251 (%)	SDB with treatment n=1652 (%)		SDB without treatment n=22,599 (%)
Age, y (SD)	47.2 (15.2)	47.2 (15.2)	46.4 (15.6)	47.2 (15.1)	.94
19–44	46,035 (46.0)	11,553 (46.2)	843 (51.0)	10,710 (47.4)	.97
45–64	36,836 (36.8)	9209 (36.8)	580 (35.1)	8629 (38.2)	
≥65	13,956 (14.0)	3489 (14.0)	229 (13.9)	3260 (14.4)	
Sex					.96
Female	59,852 (61.8)	14,995 (61.8)	432 (26.2)	14,563 (64.4)	
Male	36,975 (38.2)	9256 (38.2)	1220 (73.9)	8036 (35.6)	
ENT clinic visits					<.0001
<5	73,003 (75.4)	14,995 (61.8)	533 (32.3)	14,462 (64.0)	
5–9	11,388 (11.8)	3821 (15.8)	408 (24.7)	3413 (15.1)	
≥10	12,436 (12.8)	5435 (22.4)	711 (43.0)	4724 (20.9)	
Comorbidity					
Rhinosinusitis	2004 (2.07)	1074 (4.43)	127 (7.69)	947 (4.19)	<.0001
Allergic rhinitis	11,941 (12.3)	5962 (24.6)	582 (35.2)	5380 (23.8)	<.0001
GERD	1244 (1.28)	718 (2.96)	69 (4.18)	649 (2.87)	<.0001
ATH	644 (0.67)	541 (2.23)	127 (7.69)	414 (1.83)	<.0001
Triple H	27,837 (28.8)	9094 (37.5)	788 (47.7)	8306 (36.8)	<.0001

ATH=adenotonsillar hypertrophy, ENT=ear, nose, and throat department, GERD=gastroesophageal reflux disease, SD=standard deviation, SDB=sleep-disordered breathing, triple H=hypertension, hyperglycemia, and hyperlipidemia.

\* t test.

incidence was significantly higher for the SDB cohort than for the control cohort ( $P < .0001$ ; Fig. 1). After adjustment for age, sex, ENT clinic visits, rhinosinusitis, AR, GERD, ATH, and triple H, the risk of ETD was 1.51-fold higher in the SDB cohort than in the control cohort (95% CI=1.41–1.63). When the data were stratified according to different demographic factors (other than age and sex), SDB was still found to be significantly associated with an increased risk of ETD (Table 2).

Detailed analyses of the risk of developing ETD stratified according to comorbidities in the SDB and control cohorts were conducted (Table 3). Overall, with the exception of those with rhinosinusitis and ATH, the risk of ETD was significantly higher in SDB cohort than in the control cohort. Even without any comorbidity, the SDB cohort still exhibited a 1.61-fold higher risk of ETD (95% CI=1.44–1.80). Furthermore, compared with the

control cohort, the SDB cohort had 1.58-fold and 1.40-fold increased risks of ETD when stratified according to without and with triple H, respectively.

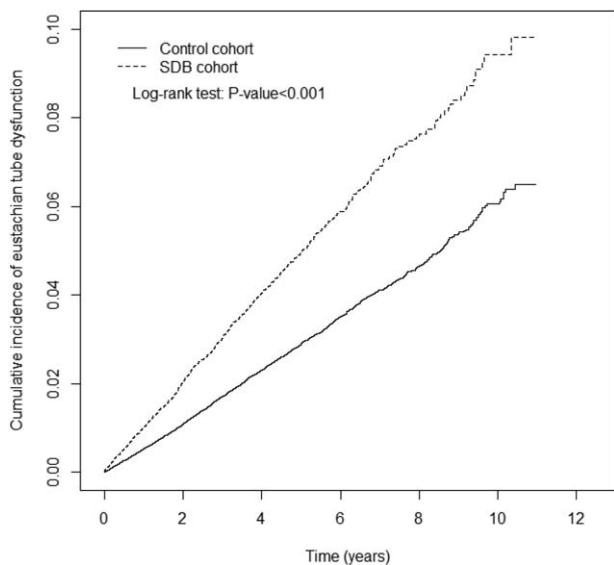
The risk of ETD was 1.54-fold higher in the SDB cohort than in the controls (95% CI=1.43–1.66); however, the ETD risk was not different between the control and SDB with treatment subcohort (HR=1.14, 95% CI=0.90–1.46; Table 4). In addition, there were significant differences in the cumulative incidence of ETD among the controls, SDB without treatment, and SDB with treatment ( $P < .0001$ ; Fig. 2) and the  $P$  values were <.001, <.001, and 0.12 for SDB with treatment versus comparisons, SDB without treatment versus comparisons, and SDB without treatment versus SDB with treatment, respectively; of note, the risk of ETD might be lower in the SDB patients with treatment than in those without treatment (HR=0.83, 95% CI=0.65–1.05).

**Table 2**  
**Incidence of ETD between Control and SDB cohort stratified by baseline characteristics.**

Variable	Comparison cohort		SDB cohort		Adjusted HR* (95% CI)
	Event	Rate	Event	Rate	
All	2504	58.9	1071	101.4	1.51 (1.41–1.63)
Age group					
19–44	1228	61.5	527	106.0	1.55 (1.39–1.72)
45–64	973	59.1	430	105.9	1.56 (1.39–1.76)
≥65	303	49.5	114	74.4	1.27 (1.02–1.58)
Sex					
Female	1688	64.8	690	106.9	1.50 (1.37–1.64)
Male	816	49.5	381	92.8	1.52 (1.34–1.73)
ENT clinic visits					
<5	1566	51.8	585	99.1	1.69 (1.53–1.86)
5–9	427	77.7	186	106.2	1.30 (1.09–1.55)
≥10	511	75.1	300	103.3	1.29 (1.12–1.49)

ATH=adenotonsillar hypertrophy, CI=confidence interval, ETD=eustachian tube disorders, ENT=ear, nose, and throat department, GERD=gastroesophageal reflux disease, HR=hazard ratio, SDB=sleep-disordered breathing.

\* Model was measured by Cox proportional hazards regression and adjusted for age, sex, ENT visits, rhinosinusitis, allergic rhinitis, GERD, ATH, and triple H. Rate is incidence rate per 10,000 person-years.



**Figure 1.** Cumulative incidence of ETD by SDB status. The cumulative incidence curve for SDB cohort was significantly higher than the control cohort ( $P < .0001$ ).

**4. Discussion**

There has been some controversy regarding the correlation between SDB and ETD; the findings of this large population-based cohort study clearly demonstrate an increased risk of developing ETD among SDB patients. To reduce any possible selection bias and clarify the effects of SDB on ETD, patients with head and neck cancer and those diagnosed with ETD before the index date were excluded from the study population. In addition, because SDB and ETD are common diseases that are mostly diagnosed by ENT physicians, one may assume that the greater the number of clinic

visits by individual patients to ENT doctors, the greater the likelihood of encountering ETD patients. Hence, the number of ENT clinic visits was included in possible cofounders along with ATH, rhinosinusitis, AR, and GERD in statistical analyses. The results of these analyses demonstrate that the risk of ETD in the SDB cohort was higher than in the control cohort (HR = 1.51, 95% CI = 1.41–1.63). After adjustment for confounding factors, the present study demonstrated that the risk of developing ETD remained significantly elevated.<sup>[20]</sup> Males and females with SDB had similar risk of developing ETD, consistent with previous study that did not find a gender predilection for ETD.<sup>[19]</sup>

Whether treating for SDB could reduce the ETD or not is summarized in Table 1. In our study, we found that the SDB treated group had higher ENT clinics visits than nontreated group. SDB group also had higher clinics demands than control group. This is because there were higher comorbidities in SDB group such as rhinosinusitis, allergic rhinitis, GERD, ATH, and Triple H. That causes the higher clinic utilization rate than control group and nontreated SDB group. Besides, in Table 2, there was higher ETD occurrence in SDB group no matter in gender and age variables. However, the treated SDB group had lesser ETD occurrence rate than the nontreated SDB group. Therefore, higher demand for ENT clinic visits helps solving the comorbidities of SDB and offered various treatments for SDB that really help patients to have a decreased ETD occurrence rate.

It is widely accepted that SDB is associated with increased comorbidities, such as hypertension, hyperlipidemia, and hyperglycemia.<sup>[21,22]</sup> In addition to triple H, the present study further showed an increased prevalence of rhinosinusitis, AR, GERD, and ATH in the SDB cohort. The effect of these possible confounders on the development of ETD was analyzed using Cox proportional hazards regression models stratified according to comorbidity. This analysis revealed that the risk of developing ETD was significantly higher in the SDB cohort, even without any confounders. Furthermore, only those SDB patients with ATH or

**Table 3**  
Incidence of ETD between Control and SDB cohort stratified by comorbidities.

Variable	Comparison cohort		SDB cohort		Adjusted HR <sup>†</sup> (95% CI)
	Event	Rate	Event	Rate	
Without any comorbidity*	1386	51.6	417	87.5	1.61 (1.44–1.80)
Rhinosinusitis					
No	2398	57.5	992	98.0	1.52 (1.41–1.64)
Yes	106	129.6	79	180.7	1.32 (0.98–1.77)
Allergic rhinitis					
No	2022	53.5	731	89.9	1.57 (1.44–1.71)
Yes	482	102.1	340	139.8	1.36 (1.18–1.57)
GERD					
No	2474	58.7	1027	99.3	1.49 (1.39–1.61)
Yes	30	82.2	44	202.2	2.52 (1.56–4.05)
ATH					
No	2477	58.6	1033	100.2	1.52 (1.41–1.63)
Yes	27	103.8	38	152.5	1.44 (0.86–2.41)
Triple H					
No	1727	56.8	657	100.8	1.58 (1.44–1.73)
Yes	777	64.1	414	102.3	1.40 (1.24–1.58)

Rate is incidence rate per 10,000 person-years.

ATH = adenotonsillar hypertrophy, CI = confidence interval, ETD = eustachian tube disorders, ENT = ear, nose, and throat department, GERD = gastroesophageal reflux disease, HR = hazard ratio, SDB = sleep-disordered breathing.

\* Model was adjusted for age and sex.

† Model was measured by Cox proportional hazards regression and adjusted for age, sex, ENT visits, rhinosinusitis, allergic rhinitis, GERD, ATH, and triple H.



**Table 4****Incidence of ETD between Control and SDB cohort with or without treatment.**

Variable	Event	Rate	Model 1 HR (95% CI)	Model 2 HR (95% CI)
Comparison cohort	2504	58.9	Reference	
SDB with treatment	70	84.4	1.14 (0.90–1.46)	0.83 (0.65–1.05)
SDB without treatment	1001	102.9	1.54 (1.43–1.66)*	reference
			<i>P</i> for trend <.0001	

Rate is incidence rate per 10,000 person-years.

ATH = adenotonsillar hypertrophy, CI = confidence interval, ETD = Eustachian tube disorders, ENT = ear, nose, and throat department, GERD = gastroesophageal reflux disease, HR = hazard ratio, SDB = sleep-disordered breathing.

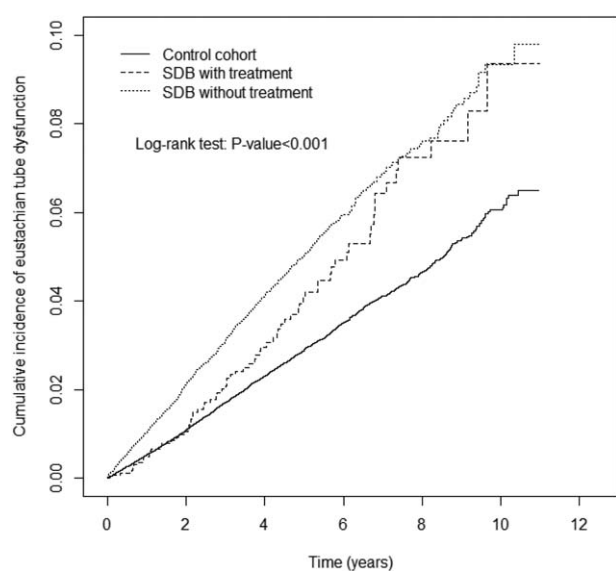
\* Both of model 1 and model 2 were measured by multivariate Cox proportional hazards regression analysis and adjusted for age, sex, ENT visits, triple H, rhinosinusitis, allergic rhinitis, GERD, and ATH.

rhinosinusitis had a risk of ETD that was similar to that in the control cohort. This suggests that compared with SDB, either ATH or rhinosinusitis is a stronger confounding factor with respect to ETD. Consistent with previous studies, enlarged lymphadenoid tissues and accumulation of purulent discharge within the nasopharyngeal region are strongly associated with the pathophysiologic mechanism of developing ETD.<sup>[23,24]</sup>

Because the risk of ETD was found to be increased in patients with SDB, we hypothesized that treatment of SDB could reduce the risk of ETD. The results of this study show that there is a significant higher risk of ETD in nontreated SDB group (HR = 1.54, 95% CI = 1.43–1.66). In addition, the trend of decreased ETD was noted in treated SDB group (HR = 0.83, 95% CI = 0.65–1.05). The possible benefits from SDB surgery may be not only reducing the obstructive pressure of the Eustachian tube but also increasing the normal physiological function of this structure. Yasan et al<sup>[24]</sup> concluded that adenoid enlargement not only occluded the nasopharyngeal opening of the Eustachian tube but also impaired mucociliary clearance through fibrotic changes in the neighboring adenoid tissue. Some studies have found improved nasal mucociliary clearance after septoplasty and turbinoplasty.<sup>[25,26]</sup> Z-palatopharyngoplasty, a surgical procedure for SDB that is a modification of the classical UPPP, can lower middle-ear pressure.<sup>[27]</sup> Taken together, the effective-

ness of SDB surgery in decreasing the risk of ETD could be attributed to improved mucociliary function and ameliorated anatomic deficit. Although CPAP treatment is effective in treating patients with SDB, the treatment is associated with adverse events such as rhinorrhea, nasal congestion, epistaxis, otalgia, and mouth dryness.<sup>[28]</sup> In addition, the ability of CPAP to alter middle-ear pressure and induce ETD remains a matter of debate. Aksoy et al<sup>[29]</sup> reported that Eustachian tube function was not influenced by 6 months of CPAP. CPAP possibly reduces the risk of ETD by inducing a sustained reduction of soft-tissue edema and inflammation in the upper airways.<sup>[30]</sup> However, Sivri et al<sup>[31]</sup> found that the middle-ear pressure was significantly increased after 6 months of CPAP treatment. Further large-scale studies should be conducted to achieve consensus in this matter.

This study was subject to several limitations. First, although the results demonstrate a strong correlation between SDB and ETD, the possibility that the cohort included patients with latent confounding diseases for ETD that were not diagnosed in the LHID cannot be totally excluded despite the application of meticulous exclusions and adjustments. Second, the selection of ETD events could have been biased by those who had a temporal requirement for the procedures mentioned in this study, or else a diagnosis of ETD that was not coded postoperatively. These limitations could result in overestimated effects of SDB on ETD. Third, the obesity and smoking data are not included in the LHID. To address the lack of obesity data, triple H was set as a substitute confounder for obesity; the results showed comparable risks of developing ETD regardless of the presence or absence of triple H. Although the model could not be adjusted for smoking habit, the results of gender-stratified analyses showed similar incidence rate of ETD between the genders. Because smoking is rare among females in Taiwan, this finding implies that the effects of SDB may not be confounded by smoking. Fourth, the ethnicity of the population in this study was homogeneously Han-Chinese<sup>[32,33]</sup>; hence, it may not be appropriate to generalize the results to other ethnicities. Further research involving patients from different ethnicities are warranted to confirm these findings. Finally, it was not possible to objectively assess the audiologic and polysomnography data in this study; therefore, it was not possible to determine the severity of the patients' SDB or to quantify the actual benefit of SDB treatments on their hearing and middle-ear pressure.



**Figure 2.** Cumulative incidence of ETD in the SDB cohort with or without treatment. The SDB patients receiving prompt treatments were associated with a significantly decreased cumulative incidence of developing ETD ( $P < .0001$ ).

## 5. Conclusion

After adjustment for confounding factors, including hypertension, hyperglycemia, hyperlipidemia, rhinosinusitis, AR, ATH, GERD, and the number of ENT clinic visits, the risk of developing ETD is higher among patients with SDB. The

treatment, that is, pharyngeal or nasal surgery, CPAP, or multiple modalities (both surgery and CPAP) for SDB might reduce the risk of ETD. Further investigation is necessary to assess the clinical relevance of the severity of SDB with respect to the development of ETD and to quantify the alteration of middle-ear pressure after SDB treatment. It is also necessary to determine the most effective intervention strategies for managing both diseases simultaneously. Multidisciplinary evaluation, including ETD, should be conducted in the management of patients presenting with SDB. Early detection and prompt intervention for SDB might reduce the risk of developing ETD and help to prevent further middle-ear injury.

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