Endoscopic sinus surgery improves Eustachian tube function in patients with chronic rhinosinusitis: a multicenter prospective study*

Xiaoxin Chen^{1,2,#}, Hua Dang^{1,#}, Qiujian Chen^{1,#}, Zhangxiong Chen^{3,#}, Yun Ma¹, Rhinology 59: 6, 560 - 566, 2021 Xiang Liu¹, Peiliang Lin¹, Hua Zou¹, Hao Xiong^{1,2}

¹ Department of Otolaryngology, Sun Yat-sen Memorial Hospital, Sun Yat-sen University, Guangzhou, Guangdong, China ² Institute of Hearing and Speech-Language Science, Sun Yat-sen University, Guangzhou, Guangdong, China ³ Dazhu County People's Hospital, Dazhou, Sichuan, China

https://doi.org/10.4193/Rhin21.209

*Received for publication: June 11, 2021 Accepted: August 17, 2021

* These authors contributed equally

Abstract

Background: Patients with chronic rhinosinusitis (CRS) often have Eustachian tube dysfunction (ETD) symptoms. This study aimed to prospectively investigate the effect of endoscopic sinus surgery (ESS) on improvement of Eustachian tube function in CRS patients with ETD from a Chinese population and determine factors associated with improvement.

Methods: A prospective study was performed in CRS patients with ETD who underwent ESS from 3 tertiary medical centers in south China. The Eustachian tube Dysfunction Questionnaire 7 (ETDQ-7), Sinonasal Outcome Test 22 (SNOT-22), tympanograms, endoscopic findings and Valsalva maneuver were recorded and analyzed preoperatively and postoperatively at 8-12 weeks.

Results: A total of 70 CRS patients with ETD were included in this study. The ETDQ-7 score and the ability of positive Valsalva maneuver in CRS patients were significantly improved postoperatively at 8-12 weeks. The number of patients with type A tympanogram was increased postoperatively. Reduced Eustachian tube mucosal inflammation was also observed postoperatively. In addition, ESS appeared to reverse slight tympanic membrane atelectasis after 8-12 weeks. Moreover, improvement in tympanogram was presented in more than half of CRS patients with concomitant otitis media with effusion postoperatively at 8-12 weeks. Univariate and multivariate analysis revealed failure of normalization of ETDQ-7 postoperatively was associated with concomitant allergic rhinitis and higher preoperative SNOT-22 score.

Conclusions: This study confirms Eustachian tube function is often improved after ESS in CRS patients with ETD. Concomitant allergic rhinitis and higher preoperative SNOT-22 score are associated with failure of normalization of ETD symptoms.

Key words: chronic rhinosinusitis, Eustachian tube dysfunction, endoscopic sinus surgery, ETDQ-7, tympanic membrane

Introduction

Eustachian tube dysfunction (ETD) is one of the most common ear diseases with a prevalence of around 1% in adults ^(1, 2). The major symptoms of ETD include ear pressure, aural fullness, hearing loss, otalgia, and tinnitus, which significantly impacts quality of life. Although the pathogenesis of ETD is not fully elucidated, the co-occurrence of ETD and chronic rhinosinusitis (CRS) has been well documented, suggesting these two disorders potentially have shared mechanism (3-5). This view was further strengthened by recent research demonstrating that ETD symptoms were often improved after endoscopic sinus surgery (ESS) ⁽⁶⁻⁹⁾. However, diagnosis of ETD in these studies was only based on a score of the Eustachian tube Dysfunction Questionnaire 7 (ETDQ-7), a valid patient-reported instrument ⁽¹⁰⁾. Notably, a high score of ETDQ-7 may be also presented in non-middle ear diseases, such as endolymphatic hydrops and temporomandibular joint dysfunction (9, 11, 12). Thus, patients with these disorders might be misdiagnosed as ETD in the previous

studies. Moreover, the effect of ESS on Eustachian tube mucosal inflammation and tympanic membrane morphology has not been mentioned ever.

This study aimed to determine whether ESS have a substantial impact on improvement of Eustachian tube function in CRS patients with ETD by relatively rigorous definition. Besides, the change of Eustachian tube mucosal inflammation and tympanic membrane morphology after ESS was evaluated. We also sought to investigate factors associated with improvement of Eustachian tube function.

Materials and methods

Patient selection and data collection

A prospective study was performed at 3 tertiary medical centers, including 2 hospital campuses (the North Hospital and the South Hospital) of Sun Yat-sen memorial Hospital of Sun Yat-sen University and Dazhu County People's Hospital from December 2019 to December 2020. Consecutive CRS patients over 17 years old who were admitted for ESS were initially assessed and those who met criteria for diagnosis of ETD were recruited in the present study. CRS were diagnosed based on clinical symptoms, nasal endoscopy and sinus computed tomography (CT) scan. All included patients were refractory to conservative treatment (topical and oral steroids, oral antibiotics, and nasal irrigation) for at least 12 weeks. ETD was strictly diagnosed based on a combination of patient-reported symptoms (ETDQ-7 score) and objective tests, including tympanogram and tubomanometry (TMM) (13). In the present study, patients met one of the following two criteria were considered to have ETD: 1) ETDQ-7 score \geq 14.5 plus abnormal tympanogram (type B or type C)(14); 2) ETDQ-7 score \geq 14.5 plus Eustachian tube score (ETS) \leq 5 in presence of type A tympanogram. ETS contains 3 TMM results and 2 subjective estimations regarding the ability to perform positive Valsalva and Toynbee maneuver, which is a valid and reliable instrument for evaluation of ETD ^(15, 16). Positive Valsalva and Toynbee maneuver were defined as hearing clicking sound when forcibly exhaling or swallowing with the nose and mouth occluded. Patients were excluded if they had diseases which would confound ETD symptoms, including Meniere's disease, low-frequency sensorineural hearing loss, patulous Eustachian tube, chronic suppurative otitis media, acute upper respiratory infection and temporomandibular joint dysfunction. All patients underwent a complete history and routine physical examination, and sinus CT scan preoperatively. Otoscopy, nasal endoscopy, tympanometry, TMM, ETDQ-7, Sinonasal Outcome

Test 22 (SNOT-22) and positive Valsalva maneuver were recorded preoperatively and postoperatively at 8-12 weeks. Eustachian tube mucosal inflammation was graded as normal, mild, moderate, and severe based on nasal endoscopy findings as previously reported (Supplementary Figure 1) ⁽¹⁴⁾]. All patients were asked to continue medical therapy such as glucocorticoids Table 1. Baseline patient characteristics.

Characteristics	% (N) or Mean ± SD or Median
Age (years)	45.31 ± 15.70
Sex (male)	77.1% (54/70)
Course of disease (years)	3.00
Side(left)	45.7% (32/70)
Nasal polyposis	72.9% (51/70)
Nasal septal deviation	34.3% (24/70)
Allergic rhinitis	35.7% (25/70)
OSAHS	10.0% (7/70)
Asthma	4.3% (3/70)
Laryngopharyngeal reflux	10.0% (7/70)
Nasal surgery history	24.3% (17/70)
Topical nasal steroids therapy history	55.7% (39/70)
Smoking	10.0% (7/70)
Alcohol	4.3% (3/70)
Lund-Kennedy score	5.09 ± 1.24
Lund-Mackay CT score	7.69 ± 2.97
SNOT-22 score	30.04 ± 7.67
VAS score of nasal obstruction	7.39 ± 2.47
ETDQ-7 score	20.13 ± 6.18
ETS score	3.15 ± 1.75
Peripheral blood eosinophils percentage	2.35
Eosinophils CRS	30.2% (16/53)
lgE (IU/mL)	197.60 ± 318.79
Inspiratory resistance (kPa·s)/L	0.232 ± 0.302
Exhalation resistance (kPa·s)/ L	0.312 ± 0.654
Positive Valsalva maneuver	14.3% (60/70)
Tympanogram type	
Туре А	64.3% (45/70)
Туре В	17.1% (12/70)
Type C	18.6% (13/70)
Retracted tympanic membrane	
Normal	38.6% (27/70)
Class I	47.1% (33/70)
Class II	11.4% (8/70)
Class III	2.9% (2/70)
Eustachian tube mucosal inflammation	
Normal	14.3% (10/70)
Mild	44.3% (31/70)
Moderate	31.4% (22/70)
Severe	10.0% (7/70)

CRS: chronic rhinosinusitis; ETD: Eustachian tube dysfunction; OSAHS: obstructive sleep apnea-hypopnea syndrome; CT: computed tomography of the paranasal sinuses; SNOT-22: Sinonasal Outcome Test 22; VAS: visual analogue scale; ETDQ-7: Eustachian Tube Dysfunction Questionnaire-7; ETS: Eustachian tube score.



Figure 1. ETDQ-7 score preoperatively and after endoscopic sinus surgery. Data was presented as individual points. ** P < 0.01. N = 70. ETDQ-7: Eustachian Tube Dysfunction Questionnaire-7; op: operation; wk: week.

sprays and saline irrigation following ESS. All surgical procedures were conducted by one of the senior authors (H.D., Q.C., Z.C., and H.Z.). Improvement of Eustachian tube function was defined as a reduction in ETDQ-7 score by greater than 3.5, the minimal clinically important difference (MICD) (8, 9). ETDQ-7 score < 14.5 was considered normalization of ETD symptoms. This research protocol was approved by the ethical review board of Sun Yatsen memorial Hospital of Sun Yat-sen University (Ethics approval number: SYSEC-KY-KS-2020-109).

Statistical analysis

The results were analyzed by SPSS 25.0. (Chicago, IL, USA). T test was used to compare means. Chi square test was utilized to compare categorical variables. All significant variables were placed in a multiple logistic regression model with P < 0.15 being placed in a backward stepwise regression model. P < 0.05 was considered to be statistically significant. The nomogram model was developed by R programming language (Version 4.0.0) and the area under the curve (AUC) was calculated.

Results

Data were initially collected on 254 patients, with 84 (33%) patients met criteria for diagnosis of ETD. Fourteen patients were lost to follow-up. Finally, 70 patients were included in this study and the baseline characteristics were shown in Table 1. Consistent with previous studies, ETDQ-7 score in CRS patients with ETD statistically decreased exceeding the MCID postoperatively at 8-12 weeks (20.13 \pm 6.18 VS 8.63 \pm 3.62, P = 0.002, Figure 1). In addition, 85.7% of patients reached a normalization of ETDQ-7 score at this follow-up time point, which indicated they



Figure 2. Tympanogram preoperatively and after endoscopic sinus surgery. * P < 0.05. N = 70. ns: no statistically significant; op: operation; wk: week.

were totally free of ETD symptoms. Meanwhile, the proportion of positive Valsalva maneuver increased remarkably from 14.3% preoperatively to 75.7% at 8-12 weeks (P < 0.001, Supplementary Figure 2). Improvement in tympanogram was associated with reduced ETDQ-7 score. Type A tympanogram was presented in 64.3% of patients preoperatively, which increased to 80.0% at 8-12 weeks postoperatively (P < 0.05, Figure 2). Furthermore, long-term improvement of ETDQ-7 score (Supplementary Figure 3), positive Valsalva maneuver (Supplementary Figure 4A) and tympanogram (Supplementary Figure 4B) were observed in 33 patients who were followed up for 24-36 weeks. Otitis media with effusion (OME) is the most common sequela of persist ETD. In the present study, 12 patients were diagnosed with OME based on otoscopic finding and tympanogram. Our results revealed that ETDQ-7 score of these patients significantly reduced at 8-12 weeks postoperatively (P < 0.001, Supplementary Figure 5A). Meanwhile, 58.3% of type B tympanogram preoperatively changed to type A or type C after ESS (P < 0.05, Supplementary Figure 5B). These results suggested that at least a certain subset of CRS patients with OME could benefit from ESS alone.

Reduced ETD symptoms are correlated with improvement of Eustachian tube mucosal inflammation ⁽¹⁴⁾. The rate of non-inflammatory Eustachian tube mucosa was 14.3% preoperatively and increased to 42.9% at 8-12 weeks, while moderate inflammation was attenuated (31.4% VS 12.9%, P < 0.05, Figure 3A). These findings indicated ESS is capable to ameliorate Eustachian tube mucosal inflammation.

The morphology of tympanic membrane reflects, at least partly, the pressure of middle ear ⁽¹⁷⁾. In the present study, normal tympanic membrane was presented in 38.6% of patients and others showed atelectasis to some extent according to the classification criteria of middle ear atelectasis ⁽¹⁸⁾. After ESS, the proportion of normal tympanic membrane significantly increased to 68.4%



Figure 3. Eustachian tube mucosal inflammation and tympanic membrane morphology preoperatively and after endoscopic sinus surgery. (A) Normal, mild, moderate, and severe Eustachian tube mucosal inflammation. (B) Normal, class 1, class 2, and class 3 tympanic membrane atelectasis. * P < 0.05. N = 70. ns: no statistically significant; op: operation; wk: week.

(P < 0.05, Figure 3B). The rate of slight (Class 1) tympanic membrane atelectasis showed a tendency of reduction, however the difference did not reach statistical significance. Our data demonstrate ESS has a positive role in improvement of morphology of tympanic membrane.

According to ETDQ-7 normalization standard, 53 patients were divided into ETDQ-7 normalization group and non-normalization group after ESS. Through univariate analysis, allergic rhinitis was determined to be associated with failure of ETDQ-7 normalization postoperatively (OR = 9.579, P = 0.024, Supplementary Table 1). On multivariate analysis, SNOT-22 \geq 40 was independently associated with failure of ETDQ-7 normalization postoperatively (OR = 10.951, P = 0.047, 95% CI: 1.029-116.535, Table 2). These results are in line with prior reports ^(8, 9).

Nomograms are based on multi-factor regression analysis, using multiple clinical or biological indicators to predict a certain clinical outcome or the probability of a certain clinical event based on the value of multiple variables. Medical nomograms are often applied on predicting a clinical outcome of cancers. Here we used nomogram to establish a model to predict the probability of ETDQ-7 normalization after ESS. There are three steps to utilize it. One is assigning a score to each stage of a certain factor, and then cumulating the scores to obtain the total score, and finally the total score for all the variables is matched to a scale of outcome ⁽¹⁹⁾. In our study, ROC curve was used to determine the cutoff of the probability of ETDQ-7 normalization (Figure 4A). Probability > 0.6 could predict ETDQ-7 normalization, and the accuracy was 81.7%, the sensitivity was 95.6% and the specificity was 62.5% (95% CI: 0.6164-1). In the univariate analysis and binary logistic regression analysis, preoperative SNOT-22 score was the most dangerous factor for failure of ETDQ-7 normalization, followed by allergic rhinitis, while nasal septal deviation and inferior turbinate surgery were not significantly risk factors. Based on these 4 factors, a nomogram model was established (Figure 4B).

Discussion

In the current multicenter prospective study, we found the incidence of ETD was 33% in CRS patients who were admitted for ESS, which is relatively lower than that reported in prior studies ^(4, 8, 9, 20). We speculated that the discrepancy is most likely due to the strict criteria for diagnosis of ETD in our study. Nevertheless,

Table 2. Multivariate binary logistic regression for ETDQ-7 normalization.

Variable	P value	OR	95% Cl	
			Lower	Upper
Allergic rhinitis	0.066	8.470	0.867	82.718
SNOT-22 score	0.047	10.951	1.029	116.535
Nasal septal deviation	0.215	3.838	0.458	32.182
Inferior turbinate surgery	0.584	1.794	0.221	14.537

OR: odds ratio; CI: confidence interval; SNOT-22: Sinonasal Outcome Test 22.





patients with intermittent dilatory ETD or baro-challengeinduced ETD might be included, which explains the reason why more than 60% of patients had type A tympanogram at baseline in the present study ⁽¹¹⁾.

Our results showed ETDQ-7 score, the ability of positive Valsalva maneuver, and tympanogram was significantly improved in most of CRS patients 8-12 weeks after ESS. Moreover, persisted improvement of ETDQ-7 score was observed postoperatively at 24-36 weeks in up to 50% of patients. These findings are consistent with previous studies ⁽⁶⁻⁹⁾. Although the correlation between CRS and ETD remains to be fully elucidated, nasal obstruction and mucosal inflammation caused by CRS are considered two major factors leading to ETD (21, 22). Removal of irreversible inflammatory tissues and restore nasal drainage pathway might contribute to improvement of Eustachian tube function by ESS. Additionally, we identified for the first time the effect of ESS on Eustachian tube mucosal inflammation. The number of CRS patients who exhibited normal mucosal inflammation score was significantly increased, whereas the proportion of mucosal inflammation at different degrees reduced postoperatively at 8-12 weeks. The pathophysiology linking of ETD and mucosal inflammation has been previously reported ^(14, 23). Massive sinus purulent secretions in CRS flows towards the Eustachian tube orifice adjacent to nasopharynx, causes mucosal inflammation and edema, and consequently results in obstruction of the Eustachian tube orifice (24). The causal relationship between mucosal inflammation and ETD is also evidenced by the fact that balloon

dilation of the Eustachian tube treats ETD successfully, at least partly, through reducing Eustachian tube mucosal inflammation (14, 25).

Long-lasting ETD is supposed to cause several pathologies of tympanic membrane, including atelectasis and retraction. There is no report regarding morphologic change of tympanic membrane following ESS previously. Here we demonstrated more than 60% of CRS patients showed tympanic membrane atelectasis at varying degrees preoperatively. The proportion of normal morphology of tympanic membrane increased postoperatively at 8-12 weeks. Further analysis revealed that the majority of recovered tympanic membrane came from slight atelectasis, while ESS failed to reverse more severe atelectasis. The morphology of tympanic membrane is determined by Eustachian tube function and middle ear mucosa status. Persistent negative pressure induced by long-lasting ETD comprises gas exchange function of middle ear mucosa, both of which would cause loss of the lamina propria and leads to atrophy of the tympanic membrane eventually. In such a case, tympanic membrane atelectasis due to loss of support of the lamina propria will persist even Eustachian tube function has been improved ^(26, 27). This could explain why severe tympanic membrane atelectasis cannot be reversed after ESS in most of cases.

Our study demonstrated that concomitant allergic rhinitis and higher preoperative SNOT-22 score were negative factors associated with normalization of ETDQ-7 score after ESS. Accumulating evidence has supported an association between allergic rhinitis and ETD ^(28, 29). Moreover, our previous study also indicates allergic rhinitis patients with severe nasal obstruction have a high risk of ETD and successful treatment of allergic rhinitis by nasal glucocorticoids and oral antihistamines is correlated with reduced ETD symptoms ⁽³⁰⁾. Concurrent pharmacological treatment of allergic rhinitis would facilitate improvement of Eustachian tube function further in this subset of CRS patients. Previous studies have demonstrated a strong link between SNOT-22 and ETDQ-7 normalization ^(8, 9), consistent with our findings, which indicates a high preoperative disease burden would definitely influence ETD outcome.

This study has several limitations. There is currently no consensus statement on precise diagnosis of ETD. To be noted, a recent study has revealed that type A tympanogram may be presented in less severe cases of ETD, suggesting the threshold for traditionally normal tympanogram should be redefined ⁽³¹⁾. Future research needs to update conventional criteria or develop novel objective tests, which is more sensitive for detection of ETD. Then, the interpretation and value of our study is limited by a relatively small numbers of participants and short duration of follow-up. Therefore, the observed correlation among CRS, ESS, and ETD needs further verification, which requires future research with a larger sample size and longer follow-up. Furthermore, medications such as glucocorticoids and saline irrigation were used postoperatively, we thereby cannot exclude the possibility that beneficial effects of these non-surgical interventions may play a role on improvement of Eustachian tube function. Lastly, there was no control group (patients who did not undergo ESS) in the present study, which may affect

the judgement on efficacy of ESS. Thus, a future study including non-surgical control group would precisely elucidate the crucial role of ESS in treatment of ETD in CRS patients.

Conclusion

ETD has a high prevalence in CRS patients. ESS not only improves the symptoms of ETD, but also has a positive impact on Eustachian tube mucosal inflammation and tympanic membrane morphology. Concomitant allergic rhinitis and higher preoperative SNOT-22 score have negative associations with normalization of ETD symptoms.

Acknowledgements

This work was supported by the National Natural Science Foundation of China (81873699) and Guangdong Basic and Applied Basic Research Foundation (2021A1515012346).

Authorship contribution

Study idea and design: XC, HZ, HX; data collection and analysis: XC, HD, QC, ZC, YM, XL, PL; manuscript preparation: XC, HZ, HX; final approval: all authors.

Conflict of interest

The authors claim that there are no conflicts of interest.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

References

- Browning GG, Gatehouse S. The prevalence of middle ear disease in the adult British population. Clin. Otolaryngol. Allied Sci. 1992; 17: 317-321.
- Vila PM, Thomas T, Liu C, Poe D, Shin JJ. The Burden and Epidemiology of Eustachian Tube Dysfunction in Adults. Otolaryngol. Head Neck Surg. 2017; 156: 278-284.
- Marino MJ, Ling LC, Yao WC, Luong A, Citardi MJ. Eustachian tube dysfunction symptoms in patients treated in a tertiary rhinology clinic. Int Forum Allergy Rhinol 2017; 7: 1135-1139.
- Tangbumrungtham N, Patel VS, Thamboo A, Patel ZM, Nayak JV, Ma Y, Choby G, Hwang PH. The prevalence of Eustachian tube dysfunction symptoms in patients with chronic rhinosinusitis. Int Forum Allergy Rhinol 2018; 8: 620-623.
- Juszczak H, Aubin-Pouliot A, Sharon JD, Loftus PA. Sinonasal risk factors for eustachian tube dysfunction: Cross-sectional findings from NHANES 2011-2012. Int Forum Allergy Rhinol 2019; 9: 466-472.
- 6. Maniakas A, Desrosiers M, Asmar MH, Al

Falasi M, Endam LM, Hopkins C, Philpott C, Erskine S, Smith R, Kilty S. Eustachian tube symptoms are frequent in chronic rhinosinusitis and respond well to endoscopic sinus surgery. Rhinology 2018; 56: 118-121.

- Bowles PFD, Agrawal S, Salam MA. Eustachian Tube dysfunction in chronic rhinosinusitis: pre and post-operative results following endoscopic sinus surgery, a prospective study. Rhinology 2019; 57: 73-77.
- Chang MT, Hosseini DK, Song SH, Nayak JV, Patel ZM, Lee JY, Hwang PH. The Effect of Endoscopic Sinus Surgery on Eustachian Tube Dysfunction Symptoms. Otolaryngol. Head Neck Surg. 2020; 163: 603-610.
- Higgins TS, Cappello ZJ, Wu AW, Ting JY, Sindwani R. Predictors of eustachian tube dysfunction improvement and normalization after endoscopic sinus surgery. Laryngoscope 2020; 130: E721-E726.
- Teixeira MS, Swarts JD, Alper CM. Accuracy of the ETDQ-7 for Identifying Persons with Eustachian Tube Dysfunction. Otolaryngol. Head Neck Surg. 2018; 158: 83-89.
- 11. Schilder AG, Bhutta MF, Butler CC, Holy C, Levine LH, Kvaerner KJ, Norman G, Pennings

RJ, Poe D, Silvola JT, Sudhoff H, Lund VJ. Eustachian tube dysfunction: consensus statement on definition, types, clinical presentation and diagnosis. Clin. Otolaryngol. 2015; 40: 407-411.

- Bachinger D, Eckhard AH, Roosli C, Veraguth D, Huber A, Dalbert A. Endolymphatic hydrops mimicking obstructive Eustachian tube dysfunction: preliminary experience and literature review. Eur. Arch. Otorhinolaryngol. 2021; 278: 561-565.
- Schroder S, Lehmann M, Korbmacher D, Sauzet O, Sudhoff H, Ebmeyer J. Evaluation of tubomanometry as a routine diagnostic tool for chronic obstructive Eustachian tube dysfunction. Clin. Otolaryngol. 2015; 40: 691-697.
- Poe D, Anand V, Dean M, Roberts WH, Stolovitzky JP, Hoffmann K, Nachlas NE, Light JP, Widick MH, Sugrue JP, Elliott CL, Rosenberg SI, Guillory P, Brown N, Syms CA, 3rd, Hilton CW, McElveen JT, Jr., Singh A, Weiss RL, Jr., Arriaga MA, Leopold JP. Balloon dilation of the eustachian tube for dilatory dysfunction: A randomized controlled trial. Laryngoscope 2018; 128: 1200-1206.

- Schroder S, Lehmann M, Sauzet O, Ebmeyer J, Sudhoff H. A novel diagnostic tool for chronic obstructive eustachian tube dysfunction-the eustachian tube score. Laryngoscope 2015; 125: 703-708.
- Ockermann T, Reineke U, Upile T, Ebmeyer J, Sudhoff HH. Balloon dilatation eustachian tuboplasty: a clinical study. Laryngoscope 2010; 120: 1411-1416.
- Redaelli de Zinis LO, Nassif N, Zanetti D. Long-term results and prognostic factors of underlay myringoplasty in pars tensa atelectasis in children. JAMA otolaryngology-- head & neck surgery 2015; 141: 34-39.
- Sade J, Berco E. Atelectasis and secretory otitis media. Ann. Otol. Rhinol. Laryngol. 1976; 85: 66-72.
- Balachandran VP, Gonen M, Smith JJ, DeMatteo RP. Nomograms in oncology: more than meets the eye. Lancet Oncol. 2015; 16: e173-180.
- Wu AW, Walgama ES, Higgins TS, Borrelli M, Vardanyan N, Hopp S, Shamsian A, Hopp ML. Eustachian Tube Quality of Life and Severity of Disease in Patients With Chronic Rhinosinusitis. Am J Rhinol Allergy 2020; 34: 532-536.
- 21. Stoikes NF, Dutton JM. The effect of endoscopic sinus surgery on symptoms of eustachian tube dysfunction. Am. J. Rhinol. 2005; 19: 199-202.
- Stammberger H. An endoscopic study of tubal function and the diseased ethmoid sinus. Arch. Otorhinolaryngol. 1986; 243:

254-259.

- 23. Kivekas I, Poyhonen L, Aarnisalo A, Rautiainen M, Poe D. Eustachian Tube Mucosal Inflammation Scale Validation Based on Digital Video Images. Otol. Neurotol. 2015; 36: 1748-1752.
- 24. Grimmer JF, Poe DS. Update on eustachian tube dysfunction and the patulous eustachian tube. Curr. Opin. Otolaryngol. Head Neck Surg. 2005; 13: 277-282.
- Anand V, Poe D, Dean M, et al. Balloon Dilation of the Eustachian Tube: 12-Month Follow-up of the Randomized Controlled Trial Treatment Group. Otolaryngol. Head Neck Surg. 2019; 160: 687-694.
- Sharp JF, Robinson JM. Treatment of tympanic membrane retraction pockets by excision. A prospective study. J. Laryngol. Otol. 1992; 106: 882-886.
- Kalra VK, Yadav SPS, Verma M, Singh B, Goel A. Treatment of Tympanic Membrane Retraction Pockets by Excision and Cartilage Tympanoplasty: A Prospective Study. Indian J Otolaryngol Head Neck Surg. 2018; 70: 392-394.
- 28. Juszczak HM, Loftus PA. Role of Allergy in Eustachian Tube Dysfunction. Curr Allergy Asthma Rep 2020; 20: 54.
- Lazo-Saenz JG, Galvan-Aguilera AA, Martinez-Ordaz VA, Velasco-Rodriguez VM, Nieves-Renteria A, Rincon-Castaneda C. Eustachian tube dysfunction in allergic rhinitis. Otolaryngol. Head Neck Surg. 2005; 132: 626-629.

- Ma Y, Liang M, Tian P, Liu X, Dang H, Chen Q, Zou H, Zheng Y. Eustachian tube dysfunction in patients with house dust mite-allergic rhinitis. Clin Transl Allergy 2020; 10: 30.
- 31. Parsel SM, Unis GD, Souza SS, Bartley H, Bergeron JM, Master AN, McCoul ED. Interpretation of Normal and Abnormal Tympanogram Findings in Eustachian Tube Dysfunction. Otolaryngol. Head Neck Surg. 2021; 164: 1272-1279.

Hao Xiong and Hua Zou Department of Otolaryngology Sun Yat-sen Memorial Hospital Institute of Hearing and Speech-Language Science Sun Yat-sen University 107 West Yan Jiang Road Guangzhou 510120 China

Tel: +86-20-81332566 Fax: +86-20-81332115 E-mail: xiongh7@mail.sysu.edu.cn zouhua@mail.sysu.edu.cn

SUPPLEMENTARY MATERIAL



Supplementary Figure 1. Eustachian tube mucosal inflammation rating scale. (A) Normal. (B) Mild edema or erythema. (C) Moderate inflammation compromise of dilation. (D) Severe inflammation, inability to dilate lumen open.



Supplementary Figure 2. Positive Valsalva maneuver preoperatively and after endoscopic sinus surgery. *** P < 0.001. N = 70. op: operation; wk: week.



Supplementary Figure 3. ETDQ-7 score preoperatively and after endoscopic sinus surgery at 8-12 weeks and 24-36 weeks. Data was presented as means \pm SD. *** P < 0.001. N = 33. ETDQ-7: Eustachian tube dysfunction questionnaire-7; ns: no statistically significant; op: operation; wk: week.



Supplementary Figure 4. Positive Valsalva maneuver and tympanogram preoperatively and after endoscopic sinus surgery at 8-12 weeks and 24-36 weeks. *** P < 0.001. N = 33. ns: no statistically significant; op: operation; wk: week.



Supplementary Figure 5. ETDQ-7 score and tympanogram preoperatively and after endoscopic sinus surgery in CRS patients with OME. ETDQ-7 score (A) and tympanogram (B) at baseline and postoperatively at 8-12 weeks in OME. *P < 0.05, ***P < 0.001. N = 12. OME: otitis media with effusion; ETDQ-7: Eustachian tube dysfunction questionnaire-7; op: operation; wk: week.

S Table 1. Univariate binary logistic regression for ETDQ-7 normalization (N = 53).

Variable % (N)	ETDQ-7 normalization	Failure of ETDQ-7 nor- malization	OR	P value
Age (years)				
> 60	85.7% (6/7)	14.3% (1/7)	0.929	1.000
≤ 60	84.8% (39/46)	14.8% (7/46)		
Sex				
Male	83.3% (35/42)	16.7% (7/42)	2.000	0.879
Female	90.9% (10/11)	9.1% (1/11)		
Course of disease (years)				
> 5	84.0% (21/25)	16.0% (4/25)	1.143	1.000
≤ 5	85.7% (24/28)	14.3% (4/28)		
Nasal polyposis				
Yes	87.2% (34/39)	12.8% (5/39)	0.539	0.736
No	78.6% (11/14)	21.4% (3/14)		
Nasal septal deviation				
Yes	73.3% (11/15)	26.7% (4/15)	3.091	0.139
No	89.5% (34/38)	10.5% (4/38)		
Allergic rhinitis				
Yes	73.1% (19/26)	26.9% (7/26)	9.579	0.024
No	96.3% (26/27)	3.7% (1/27)		
OSAHS				
Yes	85.7% (6/7)	14.3% (1/7)	0.929	1.000
No	84.8% (39/46)	15.2% (7/46)		
Asthma				
Yes	100.0% (3/3)	0(0/3)	-	1.000
No	84.0% (42/50)	16.0% (8/50)		
Laryngopharyngeal reflux				
Yes	100.0% (7/7)	0(0/7)	-	0.528
No	82.6% (38/46)	17.4% (8/46)		

Chen et al.

Variable % (N)	ETDQ-7 normalization	Failure of ETDQ-7 nor- malization	OR	P value
Nasal surgery history				
Yes	85.7% (12/14)	14.3% (2/14)	0.917	1.000
No	84.6% (33/39)	15.4% (6/39)		
Topical nasal steroids thera	ipy history			
Yes	88.2% (15/19)	11.8% (4/19)	0.500	0.436
No	78.9% (30/34)	21.1% (4/34)		
Diabetes				
Yes	75.0% (3/4)	25.0% (1/4)	2.000	0.491
No	85.7% (42/49)	14.3% (7/49)		
Hypertension				
Yes	80.0% (4/5)	20.0% (1/5)	1.464	0.574
No	85.4% (41/48)	14.6% (7/48)		
Hyperlipidemia				
Yes	83.3% (10/12)	16.7% (2/12)	1.167	1.000
No	85.4% (35/41)	14.6% (6/41)		
Alcohol				
Yes	100.0% (8/8)	0(0/8)	-	0.448
No	82.2% (37/45)	17.8% (8/45)		
Smoking				
Yes	85.7% (6/7)	14.3% (1/7)	0.929	1.000
No	84.8% (39/46)	15.2% (7/46)		
Peripheral blood eosinoph				
≥ 5%	77.8% (7/9)	22.2% (2/9)	1.810	0.885
< 5%	86.4% (38/44)	13.6% (6/44)		
IgE (IU/mL)				
≥ 100	78.9% (15/19)	21.1% (4/19)	1.733	0.694
< 100	86.7% (26/30)	13.3% (4/30)		
Eustachian tube mucosal ir				
Normal-Mild	84.2% (16/19)	15.8% (3/19)	1.088	1.000
Moderate-Severe	25.3% (29/34)	14.7% (5/34)		
Lund-Kennedy score				
≥ 5	90.9% (20/22)	9.1% (2/22)	0.417	0.445
< 5	80.6% (25/31)	19.4% (6/31)		
Lund-Mackay CT score				
≥ 4	85.1% (40/47)	14.9% (7/47)	0.875	1.000
< 4	83.3% (5/6)	16.7 % (1/6)		
SNOT-22 score				
≥ 40	50.0% (3/6)	50.0% (3/6)	8.400	0.054
< 40	89.4% (42/47)	10.6% (5/47)		
VAS score of nasal obstruct				
≥7	84.2% (13/15)	15.8% (2/15)	1.219	1.000
<7	86.7% (32/38)	13.3% (6/38)		
Inspiratory resistance (kPa-				
≥ 0.6	60.0% (3/5)	40.0% (2/5)	4.667	0.159
< 0.6	87.5% (42/48)	12.5% (6/48)		0.135
- 0.0	07.07.0 (12/10)			

Exhalation resistance (kPa·s)/L ≥ 0.6 83.3% (5/6) 16.7% (1/6) 1.143 1.000 < 0.6 85.1% (40/47) 14.9% (7/47) Uncinate resection <
< 0.6 85.1% (40/47) 14.9% (7/47) Uncinate resection Yes 88.9% (32/36) 11.1% (4/36) 0.406 0.443 No 76.5% (13/17) 23.5% (4/17)
Uncinate resection Yes 88.9% (32/36) 11.1% (4/36) 0.406 0.443 No 76.5% (13/17) 23.5% (4/17) 23.5% (4/17) 10.406 0.443
Yes 88.9% (32/36) 11.1% (4/36) 0.406 0.443 No 76.5% (13/17) 23.5% (4/17)
No 76.5% (13/17) 23.5% (4/17)
Maxillary antrostomy
Yes 86.3% (44/51) 13.7% (7/51) 0.159 0.282
No 50.0% (1/2) 50.0% (1/2)
Anterior ethmoidectomy
Yes 84.0% (42/50) 16.0% (8/50) - 1.000
No 100% (3/3) 0(0/3)
Posterior ethmoidectomy
Yes 88.6% (31/35) 11.4% (4/35) 0.452 0.526
No 77.8% (14/18) 22.2% (4/18)
Frontal sinusotomy
Yes 86.2% (25/29) 13.8% (4/29) 0.800 1.000
No 83.3% (20/24) 16.7% (4/24)
Sphenoidotomy
Yes 88.0% (22/25) 12.0% (3/25) 0.627 0.708
No 82.1% (23/28) 17.9% (5/28)
Septoplasty
Yes 76.5% (13/17) 23.5% (4/17) 2.462 0.443
No 88.9% (32/36) 11.1% (4/36)
Inferior turbinate surgery
Yes 76.9% (20/26) 23.1% (6/26) 3.750 0.142
No 92.6% (25/27) 7.4% (2/27)
Middle turbinate resection
Yes 90.9% (10/11) 9.1% (1/11) 0.500 0.879
No 83.3% (35/42) 16.7% (7/42)
Topical nasal steroids therapy post-operation
Yes 85.4% (41/48) 14.6% (7/48) 0.683 0.574
No 80.0% (4/5) 20.0% (1/5)
Antibiotic therapy over 2-week
Yes 73.3% (11/15) 26.7% (4/15) 3.091 0.202
No 89.5% (34/38) 10.5% (4/38)

OSAHS: obstructive sleep apnea-hypopnea syndrome; CT: computed tomography of the paranasal sinuses; SNOT-22: 22-item sino-nasal outcome test; VAS: visual analogue scale.