doi: 10.30934/kusbed.1439344 **e-ISSN:** 2149-8571

Kocaeli Üniversitesi Sağlık Bilimleri Dergisi

Özgün Araştırma / Original Article

http://dergipark.org.tr/kusbed

COMPUTED TOMOGRAPHIC ANALYSIS OF THE RELATIONSHIP BETWEEN FRONTAL RECESS CELLS AND ISOLATED FRONTAL SINUSITIS

Atılay Yaylacı[1*], Hasan Mervan Değer[1]

[1]Kocaeli University, Faculty of Medicine, Department of Otorhinolaryngology Head and Neck Surgery, Kocaeli University, Kocaeli, Turkey

ORCID iD: Atılay Yaylacı: 0000-0002-7842-0342; Hasan Mervan Değer: 0000-0002-7415-5465

***Sorumlu Yazar / Corresponding Author:** Atılay Yaylacı, **e-posta / e-mail:** dratilay@yahoo.com

Geliş Tarihi / Received: 19.02.2024 **Kabul Tarihi / Accepted:** 26.06.2024 **Yayım Tarihi / Published:** 04.09.2024

Abstract

Objective: The relationship between frontal recess (FR) cells and frontal sinusitis is a topic of controversy. Numerous studies have explored this connection, but the majority have encompassed patients with frontal sinusitis in combination with chronic rhinosinusitis, with or without polyps. For a stronger causal link, it's crucial to focus on isolated frontal sinusitis (IFS), though primary IFS is exceptionally rare. This study aims to investigate the role of FR cells in the development of IFS.

Methods: Two reviewers examined FR cells in triplanar computed tomography scans of 22 patients with 25 sides of IFS and 50 patients with healthy sinuses. The prevalence of each cell type was determined using the International Frontal Sinus Anatomy Classification (IFAC), and logistic regression analysis was used to determine whether any FR cells were associated with IFS.

Results: Our results showed that supraorbital ethmoid cells (SOEC) (p <0.001) and supra agger frontal cells (p =0.038) were significantly more prevalent in the IFS group than in the control group. Logistic regression analysis revealed that the presence of SOEC was associated with a 4.79-fold greater risk of IFS (95% CI, 1.30–17.65, p =0.018).

Conclusion: The FR cells may play a role in the development of frontal sinusitis. Among the IFAC cell types, SOEC appears to be associated with IFS.

Keywords: *Frontal sinusitis, frontal cells, international frontal sinus anatomy classification, supraorbital ethmoid cell, computed tomography.*

Introduction

The pathophysiology of frontal sinusitis is well known to be associated with disturbances of its drainage through the frontal recess (FR), which is an inverted cone-shaped space with the superior narrow end at the internal frontal ostium.[1] The FR contains various cells that determine the outflow tract of the frontal sinus.[2] Several studies have investigated the occurrence of FR cells and their relationship with frontal sinusitis, but the results have been conflicting. The majority of these studies[3-7] included patients with frontal sinusitis associated with chronic sinusitis, with or without polyps. Nevertheless, to better establish the causal role of FR cells in the development of frontal sinusitis, it is crucial to explore cases of isolated frontal sinusitis (IFS). This is essential because the inflammatory component of chronic rhinosinusitis may exert a greater influence on the development of frontal sinusitis than the anatomical configuration of the FR. Primary IFS is an exceptionally rare condition in clinical practice. Instead, IFS is more commonly encountered as a secondary manifestation, often arising due to scarring or neo-osteogenesis of the frontal ostium following endoscopic sinus surgery or as a result of neoplastic lesions obstructing the frontal drainage system.

Previous research differed not just in the characteristics of their samples but also in the methodologies used to classify FR cells. The International Frontal Sinus Anatomy Classification (IFAC) [2] is a recently developed classification system that enables the accurate classification of FR cells. IFAC is a user-friendly and anatomically relevant method that provides detailed information about the impact of FR cells on frontal drainage. It has been demonstrated to be a reliable tool for identifying FR cells.[8, 9] While a limited number of studies have utilized the IFAC system to explore the connection between FR cells and frontal sinusitis, only one study has employed this system to investigate this possible link in patients with IFS.[10] Therefore, the main objective of this study is to investigate the association between different FR cells classified by the IFAC system and the development of IFS.

Methods

A retrospective analysis of paranasal sinus computed tomography (CT) images from a radiology database at a tertiary hospital was carried out, covering the period from January 2018 to December 2022. The objective was to identify patients exhibiting primary IFS on paranasal sinus CT images. Frontal sinusitis was defined as complete opacification or mucosal thickness greater than 3 mm involving the entire frontal sinus on CT examination.[5] In this study, IFS was defined as CT imaging opacification limited to the frontal sinuses, while the other sinuses did not display any mucosal thickening greater than 3mm. In cases of complete opacification of the frontal sinus, magnetic resonance images were used to rule out pathologies other than inflammatory diseases. The inclusion criteria were as follows: (1) patients older than 16 years old who had CT scans with fine-cut axial image acquisition (0.5 mm); (2) CT examination showing frontal sinus opacification confined to the frontal sinuses. Patients who had a fungus ball, osteoma, fibrous dysplasia, or neoplasm in the frontal sinus were excluded from this study. The exclusion criteria encompassed patients with a history of previous nasal surgery or maxillofacial trauma. Furthermore, CT images exhibiting excessive motion, beam-hardening artifacts, or distorted FR anatomy due to a mucocele were also excluded. To establish a control group, patients who underwent preoperative CT examinations for pituitary surgery and had healthy paranasal sinuses in CT images were identified, matching their age and gender with the IFS group in a 2:1 control-to-case ratio.

We retrieved the patients' scans from our radiology database, which were stored in Digital Imaging and Communications in Medicine (DICOM) format. Image reconstructions in the axial, coronal, and sagittal planes were analyzed using the Picture Archive and Communication System (PACS) (Sectra, Linköping, Sweden). Two rhinologists (the authors) independently assessed each FR on a CT scan for the presence of IFAC cells as well as potential confounding factors such as nasal septal deviation and concha bullosa. The type of FR cell was determined according to the criteria defined by the IFAC.[2] These cells included the agger nasi cell (ANC), supra agger cell (SAC), supra agger frontal cell (SAFC), supra bulla cell (SBC), supra bulla frontal cell (SBFC), supraorbital ethmoid cell (SOEC), and frontal septal cell (FSC). Only the affected side of patients in the IFS group and the corresponding side of patients in the control group were evaluated. Any disagreements among observers were settled through consensus.

The current study was conducted in accordance with the principles outlined in the Helsinki Declaration of 1975, as revised in 2013, and received approval from the local ethics committee of our institution (KU-GOKAEK-2023/42). The need for patient consent was waived by the local ethical committee because our study is retrospective and uses existing data or records from patients who have already been discharged.

Statistical Analysis

The statistical analyses in this study were conducted using IBM SPSS for Windows, version 20.0 (SPSS, Chicago, IL, USA). Qualitative data were described using counts and percentages, while quantitative data were presented as the mean standard deviation (SD). To examine relationships between categorical variables, a chi-square test was used. Furthermore, univariate and multivariate logistic regression analyses were conducted to identify FR cells associated with frontal sinusitis. Results with a *p*-value less than 0.05 were considered statistically significant.

Results

During the specified time frame, a total of 36 patients were diagnosed with IFS. Fourteen of these patients were excluded based on the exclusion criteria, resulting in 22 eligible patients for this study. Among these, three patients had bilateral IFS, contributing to a total of 25 sides with primary IFS, all of which were included in the "IFS group". The IFS group consisted of 16 men (73%) and 6 women (27%), with a mean age of 36 years (SD: 14; range: 16–58 years). Fifteen of the IFS cases were on the right side, and ten were on the left side. Among these patients, 9 out of 22 displayed rhinosinusitis complications. These complications included frontal mucocele (n = 2), superior subperiosteal abscess (n = 2), epidural abscess (n = 2), periorbital cellulitis (n = 1), Pott's abscess (n = 1), and brain abscess (n = 1).

In the IFS group, IFAC cell prevalences were as follows: ANC (72%), SOEC (60%), SAC (20%), SAFC (20%), SBC (16%), FSC (12%), and SBFC (8%). The control group exhibited the following distribution of percentages: ANC

(92%), SBC (58%), SAC (20%), SOEC (14%), FSC (10%), SBFC (6%), and SAFC (4%). The prevalence of various IFAC cells in both groups is shown in Table 1. The prevalence of SOEC (p <0.001) and SAFC (p =0.038) was significantly higher in the IFS group than in the control group, while the prevalence of ANC (p =0.035) and SBC (p =0.001) was higher in the control group than the IFC group. In the IFS group, nasal septal deviation was observed in 6 patients (24%) and concha bullosa on the affected side was found in 3 patients (12%), whereas these values were 13 (26%) and 8 (16%) in the control group, respectively. There was no statistically significant difference between the groups in the occurrence of nasal septal deviation or concha bullosa (p >0.05 for all).

In the logistic regression analysis investigating the impact of different IFAC cells on the development of IFS, the univariate analysis showed a statistically significant association between the presence of SOEC (OR = 9.21, 95% CI: 2.98–28.54, p <.001) and SAFC (OR = 6.00, 95% CI: 1.07–33.53, p =.041) with the outcome, while SBC (OR = 0.14, 95% CI: 0.04–0.46, p =.001) and ANC (OR = 0.22, 95% CI: 0.06–0.86, p =0.029) showed a negative association (Table 2). However, in the multivariate analysis, adjusted for ANC, SAFC, and SBC, only the presence of SOECs remained statistically significant with the development of IFS (OR = 4.79, 95% CI: 1.30–17.65, p =0.018). It is worth noting that out of the 15 frontal recesses occupied by SOECs, 13 had at least one other FR cell present, while in the two remaining recesses, SOEC was the only cell present. Furthermore, only three of the 22 individuals with unilateral IFS had SOEC in the contralateral FR. An example of a case with SOEC and frontal sinusitis is illustrated in Figure 1.

Table 1: Prevalences of IFAC cells in the IFS group and the control group

	IFS Group (25 cases) n (%)	**Control Group (50 cases) n (%)**	***p* value***
ANC	18 (72)	46 (92)	**0.035**
SAC	5 (20)	10 (20)	1.00
SAFC	5 (20)	2 (4)	**0.038**
SBC	4 (16)	29 (58)	**0.001**
SBFC	2 (8)	3 (6)	1.00
SOEC	15 (60)	7 (14)	<**0.001**
FSC	3 (12)	5 (10)	1.00

IFAC, International Frontal Sinus Anatomy Classification; IFS, isolated frontal sinusitis; n, number of frontal recesses; ANC, agger nasi cell; SAC, supra agger cell; SAFC, supra agger frontal cell; SBC, supra bulla cell; SBFC, supra bulla frontal cell; SOEC, supraorbital ethmoid cell; FSC, frontal septal cell.
*Chi-square test
Boldface values indicate statistical significance.

Table 2: Association between the IFAC cells and IFS

	IFS Group (25 cases) n (%)	**Control Group (50 cases) n (%)**	**Univariate Analysis***			**Multivariate Analysis***		
			OR	**95% CI**	***p* value**	**OR**	**95% CI**	***p* value**
ANC	18 (72)	46 (92)	0.22	0.06–0.86	**0.029**	0.37	0.06–2.23	0.280
SAC	5 (20)	10 (20)	1.00	0.30–3.32	1.00			
SAFC	5 (20)	2 (4)	6.00	1.07–33.53	**0.041**	2.61	0.28–24.78	0.404
SBC	4 (16)	29 (58)	0.14	0.04–0.46	**0.001**	0.29	0.07–1.18	0.083
SBFC	2 (8)	3 (6)	1.36	0.21–8.73	0.744			
SOEC	15 (60)	7 (14)	9.21	2.98–28.54	**<0.001**	4.79	1.30–17.65	**0.018**
FSC	3 (12)	5 (10)	1.23	0.27–5.61	.0792			

IFAC, International Frontal Sinus Anatomy Classification; IFS, isolated frontal sinusitis; n, number of frontal recesses; OR, odds ratio; CI, confidence interval; ANC, agger nasi cell; SAC, supra agger cell; SAFC, supra agger frontal cell; SBC, supra bulla cell; SBFC, supra bulla frontal cell; SOEC, supraorbital ethmoid cell; FSC, frontal septal cell.
*Logistic regression analysis
Boldface values indicate statistical significance.

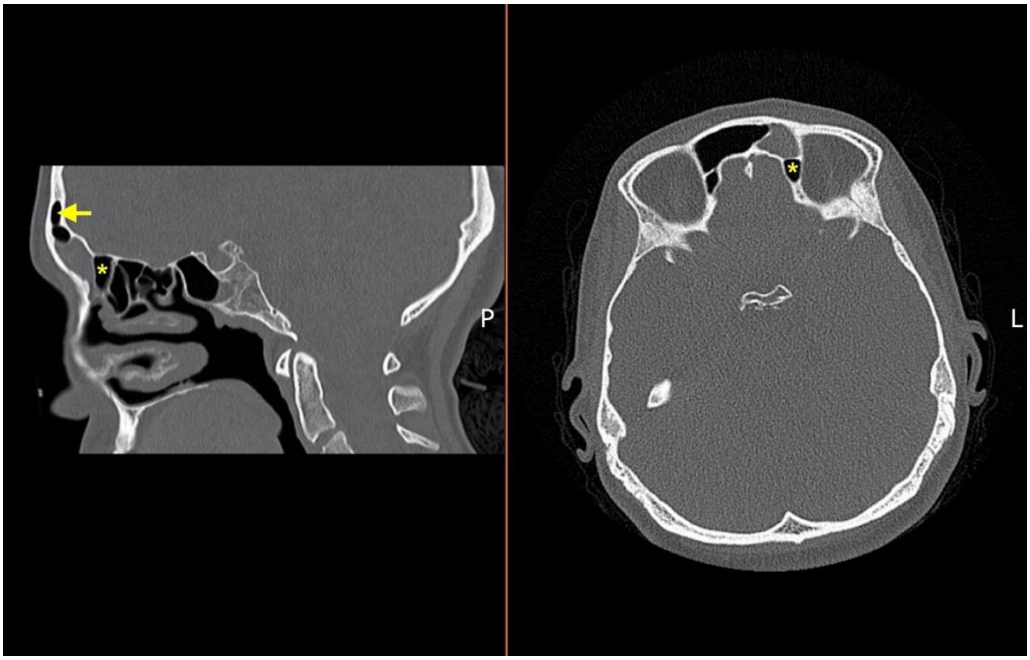

Figure 1: Computed tomography images of a patient with isolated frontal sinusitis on the left side. The posterior wall of the frontal sinus drainage pathway is formed by a supraorbital ethmoid cell (asterisk). Note that the right frontal sinus extends into the left side (arrow). *P*, posterior; *L*, left.

Discussion

We conducted an analysis utilizing multiplanar CT images of the paranasal sinuses to investigate the potential relationship between FR cells and the development of isolated frontal sinusitis. Our study focused on evaluating the prevalence of various IFAC cells in patients diagnosed with primary IFS and comparing them to individuals with healthy paranasal sinuses. After analyzing the prevalence of IFAC cells in cases with IFS, we found that ANC was the most common cell, present in 72% of cases. SOEC was the second most frequent, found in 60% of cases, while SAC and SAFC were equally present in 20% of cases. SBC and FSC were observed in 16% and 12% of cases, respectively, and SBFC was found in only 8% of cases. In a similar study by Pham et al.[10], comparing 10 CTs with IFS to those without sinusitis in Vietnamese patients, the researchers found that all of the IFS cases contained ANC, while SAC was present in 60% of cases, SBC in 50%, SBFC in 40%, SAFC in 20%, FSC in 20%, and SOEC in 10%. Excluding the ANC, which had a higher prevalence in both studies, our analysis revealed that SOEC was the second most frequently occurring FR cell. In contrast, Pham et al.'s study found SAC to hold that position.

In our evaluation, we identified a significant association between SOECs and the development of IFS. The IFS cases demonstrated a significantly higher overall prevalence of SOEC compared to healthy control cases (60% versus 14%), and the presence of an SOEC was found to be associated with an approximately five-fold greater risk of developing IFS, as determined through logistic regression analysis. The association between SOEC and IFS may be elucidated by the findings of previous studies. Lien et al.[5] found a significant correlation between SOECs and a narrow antero-posterior diameter of the frontal ostium and frontal recess. Furthermore, Lee et al.[11] observed that large SOECs were associated with relatively small frontal sinuses or pneumatization from the contralateral frontal sinus. However, we believe that both the extent of SOEC pneumatization and the specific configuration of other FR cells relative to this cell are crucial factors influencing the frontal drainage pathway. Although our study group consists of patients with IFS, it is likely that an acute rhinosinusitis affecting the osteomeatal complex or frontal recess was present at the onset. Even if the osteomeatal complex disease resolves, the frontal sinus disease may persist due to the narrowed frontal recess caused by FR cells, potentially leading to complications. We think that for patients with IFS associated with SOEC, maintaining a low threshold for surgical intervention may be preferable over attempting to resolve the sinusitis with prolonged medical therapy.

Contrary to our result, a positive association was reported between the presence of SAC and IFS in the study of Pham et al.[10] Although SACs do not pneumatize into the frontal sinus, they noted that the presence of SACs and other adjacent cells along the frontal sinus drainage pathway can narrow the frontal recess. The disparity in findings between our study and the study of Pham et al. can likely be attributed to several factors,including the limited sample sizes in both studies, ethnic variations, and differences in patient demographics.

Several CT-based studies have investigated the association between FR cells and non-isolated frontal sinusitis using various FR cell classification systems. Meyer et al.[3] observed a significant difference in the prevalence of types III and IV frontal cells in patients with frontal sinusitis using Bent et al.'s criteria [12] to classify FR cells. However, using the same criteria, two studies [4,6] found no significant difference in the prevalence of frontal sinusitis in the presence or absence of any of the FR cells. Kubota et al.[1] used criteria established by Lee et al.[11] and found that the presence of frontal bullar cells had a significant association with frontal sinusitis. Applying the same criteria, Lien et al.[5] found that the presence of SOECs had the highest odds of indicating frontal sinusitis, followed by the presence of SBCs, frontal bullar cells, and recessus terminalis. Kemal et al.[7] investigated the link between FR cell types and the development of IFS in a cohort of 20 patients, encompassing 28 sides with IFS. They used both criteria established by Lee et al.[11] and IFAC to identify FR cells. The study found that FR cells did not have a significant relationship with the occurrence of IFS. While the study used the phrase “isolated frontal sinusitis”, it should be noted that despite not having nasal polyposis, a significant percentage of participants also had sinusitis in other sinuses.

The IFAC group defines SOEC as "an anterior ethmoid cell that pneumatizes around, anterior to, or posterior to the anterior ethmoidal artery over the roof of the orbit, often forming part of the posterior wall of an extensively pneumatized frontal sinus." They classified SOEC as posterior cells, pushing the drainage pathway anteriorly.[2] From a surgical perspective, SOEC presents a surgical challenge during frontal sinusotomy due to its close proximity to the anterior skull base. Furthermore, when there is an SOEC, the anterior ethmoid artery usually lies below the skull base, within the septation that extends from the cell's posterior aspect.[13,14] Consequently, the surgical approach in these cases demands meticulous preoperative assessment and strategic planning to mitigate the potential risk of harm to these adjacent structures. This caution is especially imperative considering the frequent occurrence of sinusitis complications, which can further complicate the surgery for these patients.

The current study has several limitations that must be acknowledged. Firstly, the rhinologists who assessed the CT scans were not blinded to the patient groups, which may have introduced bias in the analysis. Secondly, although two independent observers analyzed the CT data and the results were compared and reviewed, there is always an inherent subjectivity involved in the interpretation of the results. Thirdly, while the study assessed the presence of potential confounding anatomical factors such as nasal septal deviation and concha bullosa, other factors such as smoking, allergies, and immune status that could affect the development of IFS were not considered in the analysis. However, the lack of mucosal inflammation in the other sinuses aside from the frontal sinus suggests that these systemic factors were not significant contributors to the condition. Lastly, while our findings imply a correlation between SOEC and IFS, it's important to note that causality cannot be definitively established. The relationship between FR cells and frontal sinusitis is complex and likely involves several variables beyond the mere presence or absence of individual cells. Our final limitation is the small sample size, which may limit the generalizability of the findings. Notwithstanding these limitations, the data presented in our study provides valuable insights into the role of FR cells in the development of IFS.

Conclusion

Our study suggests that anatomic variations in the FR may contribute to the development of frontal sinusitis. Specifically, among the FR cell types defined by IFAC, SOEC appears to be the most likely cause of IFS. Additional studies with larger sample sizs and prospective designs are needed to confirm these results and fully comprehend the potential mechanisms underlying this association.

Acknowledgements

I am grateful to Assistant Professor Sibel Balcı for assisting us in the statistical analysis.

Conflict of Interest

The authors have no financial relationships or conflicts of interest to disclose.

Compliance of Ethical Statement

Ethical approval was granted by the Ethics Committee of the Kocaeli University Faculty of Medicine (2023/no:42).

Financial Support

No funding was received for conducting this study.

Author Contributions

A.Y.: Study design, data collection, data analysis, and manuscript preparation; H.M.D.: Data collection, and data analysis.

References

1. Kubota K, Takeno S, Hirakawa K. Frontal recess anatomy in Japanese subjects and its effect on the development of frontal sinusitis: computed tomography analysis. *J of Otolaryngol - Head & Neck Surg*. 2015;44:21. doi:10.1186/s40463-015-0074-6.
2. Wormald PJ, Hoseman W, Callejas C, et al. The International Frontal Sinus Anatomy Classification (IFAC) and Classification of the Extent of Endoscopic Frontal Sinus Surgery (EFSS). *Int Forum Allergy Rhinol*. 2016;6(7):677-696. doi:10.1002/alr.21738.
3. Meyer TK, Kocak M, Smith MM, Smith TL. Coronal computed tomography analysis of frontal cells. *Am J Rhinol*. 2003;17(3):163-168. doi:10.1177/194589240301700310.
4. DelGaudio JM, Hudgins PA, Venkatraman G, Beningfield A. Multiplanar computed tomographic analysis of frontal recess cells: effect on frontal isthmus size and frontal sinusitis. *Arch Otolaryngol Head Neck Surg*. 2005;131(3):230-235. doi: 10.1001/archotol. 131.3.230.
5. Lien CF, Weng HH, Chang YC, Lin YC, Wang WH. Computed tomographic analysis of frontal recess anatomy and its effect on the development of frontal sinusitis. *Laryngoscope*. 2010;120(12):2521-2527. doi:10.1002/lary.20977.
6. Eweiss AZ, Khalil HS. The prevalence of frontal cells and their relation to frontal sinusitis: a radiological study of the frontal recess area. *ISRN Otolaryngol*. 2013;24:1-4. doi:10.1155/2013/687582.
7. Kemal Ö, Tahir E, Sayıt AT, Cengiz E, Ünal R. Frontal recess anatomy and frontal sinusitis association from the perspectives of different classification systems. *B-ENT*. 2021;17:7-12. doi:10.5152/B-ENT.2021.20318.
8. Choby G, Thamboo A, Won TB, Kim J, Shih LC, Hwang PH. Computed tomography analysis of frontal cell prevalence according to the International Frontal Sinus Anatomy Classification. *Int Forum Allergy Rhinol*. 2018;8(7):825-830. doi:10.1002/alr.22105.
9. Villarreal R, Wrobel BB, Macias-Valle LF, et al. International assessment of inter- and intrarater reliability of the International Frontal Sinus Anatomy Classification system. *Int Forum Allergy Rhinol*. 2019;9(1):39-45. doi:10.1002/alr.22200.
10. Pham HK, Tran TT, Nguyen TV, Thai TT. Multiplanar Computed Tomographic Analysis of Frontal Cells According to International Frontal Sinus Anatomy Classification and Their Relation to Frontal Sinusitis. *Rep Medical Imaging*. 2021;14:1-7. doi:10.2147/RMI.S291339.
11. Lee WT, Kuhn FA, Citardi MJ. 3D computed tomographic analysis of frontal recess anatomy in patients without frontal sinusitis. *Otolaryngol Head Neck Surg*. 2004;131(3):164-173. doi:10.1016/j.otohns.2004.04.012.
12. Bent JP, Cuilty-Siller C, Kuhn FA. The Frontal Cell as a Cause of Frontal Sinus Obstruction. *Am J Rhinol*. 1994;8(4):185-192. doi:10.2500/105065894781874278.
13. Simmen D, Raghavan U, Briner HR, et al. The surgeon's view of the anterior ethmoid artery. *Clin Otolaryngol*. 2006;31(3):187-191. doi:10.1111/j.1365-2273.2006.01191.x.
14. Jang DW, Lachanas VA, White LC, Kountakis SE. Supraorbital ethmoid cell: a consistent landmark for endoscopic identification of the anterior ethmoidal artery. *Otolaryngol Head Neck Surg*. 2014;151(6):1073-1077. doi:10.1177/0194599814551124.