LINKING CHRONIC OTITIS MEDIA AND NASAL OBSTRUCTION: A CFD APPROACH

RUNNING TITLE
CFD analysis of nasal cavity in patients with COM

KEYWORDS
Chronic otitis media. Middle Ear Cholesteatoma. Computational Fluid Dynamics. CFD tools. Nasal Obstruction. Deviated Nasal Septum. Dimensionless Estimators.

ABSTRACT
OBJECTIVES: To investigate a possible relationship between altered nasal flow and chronic otitis media (COM) using computational fluid dynamics (CFD).
DESIGN: Retrospective cohort sample of CT scans from patients with COM and controls without COM to compare the results of various nasal airflow parameters determined by CFD between a group of patients with COM (N=60) and a control group of subjects without any evidence of ear disease (N=81).
MAIN OUTCOME MEASURES: The CT were subjected to various procedures to carry out CFD studies, determining the resistance to nasal flow, the proportion of flow through the right and left nasal cavity, and two nondimentional estimators. The results of CFD studies between patients with COM and controls were compared.
RESULTS AND CONCLUSIONS: Whereas only 12.3% of the controls had CFD alteration (10 out of 81), 43.3% of the patients suffering COM displayed alterations of our nondimentional parameters $R-\phi$ (26 out of 60). According to our results, the incidence of alterations in nasal airflow by studying with CFD is significantly higher in patients with COM than in controls
IMPLICATIONS: To our knowledge, this is the first paper linking nasal cavity and COM using a CFD approach. Our results support the hypothesis that nasal flow alterations could be implicated in the etiopathogenesis of the COM.

KEY POINTS

- Computational Fluid Dynamics (CFD) has become a useful tool for diagnosis of nasal conditions.
- The relationship between middle ear and nose is well known for the otolaryngologists, however the exact mechanism remains elusive.
- Patients with chronic otitis media (COM) have frequently alterations in CFD parameters when compared with controls.
- CFD analysis supports the hypothesis that nasal flow alterations could be implicated in the etiopathogenesis of the COM.
- CFD opens a promising line of investigation between nasal problems and Eustachian Tube dysfunction.

ETHICAL CONSIDERATIONS: No ethical approval was required. No conflicts of interest exist, nor financial disclosure reported.

INTRODUCTION

The middle ear is an air cavity excavated in the temporal bone, embryologically derived from the first pharyngeal pouch,[1] constituting an appendix of the upper respiratory tract. The close anatomical relationship of the middle ear with the nasopharynx, mediated by the Eustachian tube, it also gives the middle ear a great functional dependence of the upper respiratory tract.[2] Many causes of tubal dysfunction of nasal and/or nasopharyngeal origin have been described[3] and it is well known for the clinicians that Eustachian tube dysfunction has a role in chronic otitis media with effusion (COME), adhesive OM, retraction pockets, and cholesteatoma pathogenesis.[2]

However, the relationship between the nose conditions and COM is controversial. While some authors have found a significant correlation between the incidence of nasal pathology and COM,[4–7] others do not find such a correlation.[8–11] Regardless of the role of alterations of the nose and/or nasopharynx on the middle ear, the intimate knowledge of this relationship would be of great interest for the treatment of patients with COM and concomitant nasal and/or nasopharyngeal alterations, a very common situation in the clinical practice. However, despite some study that sheds some light on this aspect,[11] no specific guidelines have been defined for the management of patients with COM and associated nasal and/or nasopharyngeal alterations.

As far as we know, no studies have been published on the relationship between nasal conditions and chronic otitis media (COM) from the perspective of computational fluid dynamics (CFD). CFD allows to analyze and solve different problems about the flow of fluids,[12] constituting a basic discipline of research and development in practically all branches of science, including medicine. CFD has been proposed to study the flow in the nasal cavities for more than 25 years. However, only in recent years new software products have started to be available for the ENT specialist to use the techniques of CFD and the nasal virtual surgery in their own clinical practice.[13,14]

The parameters commonly used in CFD to analyze the air flow inside the nose are pressure and pressure gradient, velocity, nasal resistance, wall shear stress, air flow through the right and left nasal cavity, the exchange of heat and humidity and, in case of nasal septum perforation, the exchange of air flow between one and another nasal cavity. These are dimensional parameters and compare the flow between both nasal cavities of a given patient, but generally they do not allow drawing conclusions about the normality or not of such registers. In a previous paper,[15] the authors presented two nondimentional estimators, based on data obtained from CFD analysis and geometric measures, which allow distinguishing between healthy and diseased nasal cavities. The first mathematical estimator ϕ is a function of geometric features and potential asymmetries between nasal passages, while the second estimator R represents in fluid mechanics terms the total nasal resistance that corresponds to the atmosphere-choana drop pressure. Later studies[15,16] suggest that this parameter allows guiding the surgery in a quantitative way, objectifying through virtual surgery the results of different alternatives, so that the surgeon can decide which is best suited to his patient and achieving success with a high probability.

OBJECTIVE

The aim of this research is to conduct CFD studies of the nose in a group of patients with COM and a control group of subjects without evidence of ear pathology, comparing the results of the parameters ϕ and R, to determine the incidence of alterations of such parameters in patients with COM and investigate the possible relationship between otitis and alterations in nasal airflow.

PATIENTS AND METHODS

This retrospective study was carried out with patients coming from the Otolaryngology Departments from Virgen del Rocío Hospital in Seville and Morales Meseguer Hospital in Murcia, between January 2014 and April 2019.

Control group: This group included CT scans of patients with parotid tumors performed in the Department of Radiology of the Virgen del Rocío Hospital. Inclusion criteria were to be adult, and to have a complete nasal scan allowing the CFD analysis. Eighty-one CT were collected, of which 38 were male and 43 female, with a mean age of 39.2 ± 13.2 years (range, 19-68 years), including all of them in the CFD analysis.

Group with COM: The CT scans were obtained from the databases of both Otolaryngology Departments, after reviewing the studies of 406 patients with COM (Cholesteatomatous chronic otitis media undergoing mastoidectomy) and CT, of which only 60 CT allowed the study by CFD, since in most cases the geometry of the nasal cavity was incomplete and/or the computed tomography was of poor quality. These CT corresponded to 28 men and 32 women, with a mean age of 38.7 ± 12.6 years (range 20-67 years).

Statistical analyses were performed with R-3.6.3 (R Foundation for Statistical Computing, Vienna, Austria). Continuous variables were expressed as mean ± standard deviation, categorical variables as frequency and percent. Pearson's Chi-square test was used to evaluate the strength of association between abnormal cavities and COM. Statistical significance was set at $p<0.05$.

COMPUTATIONAL FLUID DYNAMICS (CFD)

Computational fluid dynamics (CFD) is very useful to assess nasal airways.[17] Common parameters used to analyze air flow within a nasal cavity such as temperature, stress wall, velocity… are dimensional parameters. This kind of parameters usually do not allow to get objective conclusions about real air flow and compare flow between both nasal cavities. In previous papers the authors had introduced the use of nondimentional parameters[15] based on quantities obtained from CFD analysis and geometric quantities. Those parameters allow to distinguish between healthy or diseased nasal cavities, and had been used in a number of studies.[16,18] Both parameters $R-\phi$ were also used in the present work to investigate from an objective approach the relationship between chronic otitis media and nasal obstruction.

The software chosen for all flow simulations using CFD techniques was Flowgy© (www.flowgy.com). Flowgy© is a software available for personal computers with the Linux operating system.[19] It has been developed at the Polytechnic University of Cartagena (Murcia - Spain) with the collaboration of different hospitals and national and international universities. It is the result of the evolution of three other well-known softwares and whose results have been previously published by the authors of this study (MeComLand©, DigBody© and NoseLand©).[13,14,16,18] The three steps necessary for resolving the flow inside a nasal cavity, Nasal Cavity Segmentation, Mesh Generation, and Solving and Post Processing, are described elsewhere.[13,14,16,20–23]

Airflow from 60 patients suffering COM and 81 from control groups was analyzed using Flowgy©. Using the CFD results and geometries from every nasal cavity the values for the parameters $R-\phi$ were calculated. Table 1 and Table 2 show the results for CFD simulations and geometry data from the 60 patients with COM and 81 from control group respectively.

The first non-dimensional parameter R represents the total nasal resistance or bilateral resistance, and is computed from the unilateral resistance of the two passages $R_R \, y \, R_L$, as follows:

$$\frac{1}{R}=\frac{1}{R_R}+\frac{1}{R_L} \Rightarrow R=\left(\frac{1}{R_R}+\frac{1}{R_L}\right)^{-1},$$

$$R_R=\frac{\Delta P/Q_R}{\frac{1}{2}\rho Q_R/A_R^2}, R_L=\frac{\Delta P/Q_L}{\frac{1}{2}\rho Q_L/A_L^2},$$

where ΔP is the drop pressure between the atmosphere and the choana, $Q_R \, y \, Q_L$ are the flow rates in the right and left nostrils, $A_R \, y \, A_L$ are the areas of each nostril, and $\rho \approx 1.2\, kg/m^3$ is the density of the atmospheric air.

The second non-dimensional parameter ϕ provides a measure of nasal flow asymmetry. Normally, high asymmetries of nasal flow are associated with diseased nostrils. This parameter is defined as:

$$\phi=\frac{1+\left(\frac{A_R+A_L}{2A_C}-1\right)^2}{(1-\varepsilon p)\,q\eta+\varepsilon p},$$

A more detailed description of these parameters can be found in the reference.[15]

In most cases, this parameter will take values of the order of 1 in nostrils with low asymmetry (typical of healthy nostrils), and high values in nostrils with high asymmetries (typical of diseased nostrils).

RESULTS

Data form the patients and control groups were included in tables 1 and 2.

The Figure 2 represents the values of the estimator R versus the estimator ϕ, for both sets of nasal cavities corresponding to patients with chronic otitis media (red circles) and the control group (green circles). As can be seen, most of the parameters calculated for the 81 CT in the control group (88%) are within the central rectangle, suggesting that they do not have nasal obstruction. However, the parameters calculated in the group of 61 CT of patients with COM show a high dispersion, with 43.3% of the cases being outside the rectangle. If a case is inside the rectangle the probability to get a healthy cavity is higher than 99%,[15] and this will be considered as an abnormal CFD case.

Patients with chronic otitis media presented abnormal CFD results when compared with controls, and this association is strongly significant. Therefore, in our sample, alterations in the results of nasal flow determined by CFD are much more frequent in patients with COM than in the control group, p <0.0001 (Table 3).

DISCUSSION

The close anatomical and functional relationship of the middle ear to the respiratory tract through the Eustachian tube determines a great dependence on the nasal cavity and nasopharynx[2]. However, although pathological findings in the nose or the nasopharynx are often said to be responsible for inadequate tubal function, this relationship is not clearly established and studies and evidence are scarce and contradictory. Different studies[24,25] suggest that in case of septal deviation, the development of the cavities of the middle ear is minor on the affected side. However, through studies with acoustic rhinometry and rhinomanometry, Güçlü et al.[26] determined that patients with COM have significantly higher nasal resistances than controls, but they did not find a clear correlation between the side of the nasal cavity and that of the affected ear.

Watson et al.[6] determined by anterior active rhinomanometry that in a sample of 15 patients with COM the nasal resistance on the side of the affected ear was significantly greater than in controls. But, using the same technique, Arsla et al.[8] did not find significant differences in nasal airway resistance between the chronic otitis media sides and unaffected sides between 102 patients with unilateral COM and 40 individuals without any ear or nasal pathologies controls. And Toros et al.[10] did not observe correlation between the ear with COM and the side of nasal obstruction by acoustic rhinometric in a sample of 55 patient with COM. Studying 114 patients with COM, Ural et al.[5] suggested that septal deviation occurred more frequently on the same side of ear pathology in patients with tubotympanic chronic suppurative otitis media, but not in patients with atticoantral chronic suppurative otitis media. In our country, Suarez et al.[7] found in a sample of 5.414 children that the prevalence of secretory otitis was significantly related to infections of the upper respiratory tract and nasal obstruction.

Harju et al.[3] noted that patients with hypertrophic turbinate have more tubal symptoms than controls, and Damar et al.[4] found that the incidence of septal deviation, hypertrophic turbinate and/or concha bullosa determined by CT was significantly higher in patients with COM (177 patients) than in healthy subjects (50). On the contrary, on a large-scale Korean epidemiological basis, Heo et al.[9] did not found any relationship between the prevalence of chronic otitis media and septal deviation.

As far as we know, this is the first study that tries to shed light to determine the relationship between nasal and COM conditions from a CFD perspective. To obtain the reported results in this article, it was required to find 115 CT scans of subjects (60 from the COM group and 81 from the control group) that were suitable for a computational fluid mechanics (CFD) analysis. The task was especially tedious in recruiting CT into the COM group, as most studies did not include the nasal cavity, making the CFD study impracticable, forcing us to review more than 400 TCs to eventually get 60. To the authors' knowledge, there are no papers in which the results obtained with this kind of analysis and with such a high number of subjects are presented.

The high dispersion of the COM patients (Figure 2) clearly indicates that, although from a computational point of view these patients cannot be strictly catalogued either as healthy or as diseased, it can be suspected that patients with COM present differences with those from the control group and that these differences are related to nasal obstruction, alterations and the flow and/or resistance, and indeed they deserve a further and deeper analysis in the future.

It can be seen how the results of mastoidectomy patients of the COM group are scattered throughout the Cartesian coordinate system in the Figure 2. Abnormal values of R or ϕ are found in approximately equal percentage, so either parameter can lead - or be related- to COM. Although the results are scattered, it is interesting to mention two groups of patients. The first group of patients with significantly low values of resistance that allows the hypothesis to be made that high air velocities in the nasal cavity led to low pressures at the entrance of the Eustachian tube and may play an important role in causing its dysfunction. The second group worth to be mentioned are patients with normal resistances but with slightly elevated asymmetry values, causing a pressure difference in the entrances of both Eustachian tubes high enough to cause their dysfunction. It is quite tempting to propose Eustachian tube collapse in the first group whereas in the second could be asymmetry in a role which also needs further analysis.

If further studies confirm the relationship between COM and nasal air flow alterations, it is pending to determine the mechanism by which nasal flow alterations induce COM, thus the airflow current lines and pressures in nasopharynx would need to be studied in more detail.

CONCLUSIONS

According to our results, the incidence of alterations in nasal airflow determined by

CFD is significantly higher in patients with COM than controls. Based on this finding, it is quite tempting to suggest a role for the nose in the origin of primary acquired cholesteatoma inside the chronic middle ear pathology.

IMPLICATIONS

To our knowledge, this is the first paper linking nasal cavity and COM using a CFD approach. Our results support the hypothesis that nasal flow alterations could be implicated in the etiopathogenesis of the COM. Likewise, in the treatment of the COM, our findings suggest that management of nasal conditions should be considered.

DATA AVAILABILITY STATEMENT

The data generated and analyzed during the study are available from the corresponding author on reasonable request.

References

(1) Langman, J.; Sadler, T. W. *Langman's Medical Embryology*, Edición: 9th Revised edition.; Lippincott Williams and Wilkins: Philadelphia, Pa, 2003.

(2) Licameli, G. R. The Eustachian Tube. Update on Anatomy, Development, and Function. *Otolaryngol. Clin. North Am.* **2002**, *35* (4), 803–809.

(3) Harju, T.; Kivekäs, I.; Numminen, J.; Rautiainen, M. Eustachian Tube Dysfunction-Related Symptoms in Chronic Nasal Obstruction Caused by Inferior Turbinate Enlargement. *Ann. Otol. Rhinol. Laryngol.* **2017**, *126* (12), 798–803. https://doi.org/10.1177/0003489417735538.

(4) Damar, M.; Dinç, A. E.; Erdem, D.; Bişkin, S.; Eliçora, S. Ş.; Kumbul, Y. Ç. The Role of the Nasal and Paranasal Sinus Pathologies on the Development of Chronic Otitis Media and Its Subtypes: A Computed Tomography Study. *Niger J Clin Pract* **2017**, *20* (9), 1156–1160. https://doi.org/10.4103/njcp.njcp_124_16.

(5) Ural, A.; Minovi, A.; Çobanoğlu, B. Upper Airway Obstructions and Chronic Otitis Media: A Clinical Study. *Am J Otolaryngol* **2014**, *35* (3), 329–331. https://doi.org/10.1016/j.amjoto.2014.01.012.

(6) Watson, C. Chronic Otitis Media: The Significance of Nasal Obstruction. *Clin Otolaryngol Allied Sci* **1990**, *15* (5), 435–438.

(7) Suarez Nieto, C.; Malluguiza Calvo, R.; Barthe Garcia, P. Aetiological Factors in Chronic Secretory Otitis in Relation to Age. *Clin Otolaryngol Allied Sci* **1983**, *8* (3), 171–174. https://doi.org/10.1111/j.1365-2273.1983.tb01422.x.

(8) Arslan, F.; Binar, M.; Aydin, U. Assessment of Nasal Functions and Their Relationship with Cholesteatoma Formation in Patients with Unilateral Chronic Otitis Media. *J Laryngol Otol* **2018**, *132* (11), 974–977. https://doi.org/10.1017/S0022215118001767.

(9) Heo, K. W.; Kim, M. J.; Lee, J. H. Impact of Nasal Conditions on Chronic Otitis Media: A Cross-Sectional Study in Koreans. *Acta Otolaryngol* **2018**, *138* (2), 116–121. https://doi.org/10.1080/00016489.2017.1385848.

(10) Toros, S. Z.; Karaca, C. T.; Onder, S.; Caypinar, B.; Sahin-Yilmaz, A.; Oysu, C.

Nasal Obstruction and Unilateral Chronic Otitis Media: Evaluation by Acoustic Rhinometry. *Ann. Otol. Rhinol. Laryngol.* **2013**, *122* (12), 734–736. https://doi.org/10.1177/000348941312201202.
(11) Maier, W.; Krebs, A. [Is surgery of the inner nose indicated before tympanoplasty? Effects of nasal obstruction and reconstruction on the eustachian tube]. *Laryngorhinootologie* **1998**, *77* (12), 682–688. https://doi.org/10.1055/s-2007-997224.
(12) Computational Fluid Dynamics. *Wikipedia*; 2019.
(13) Burgos, M. A.; Sanmiguel-Rojas, E.; del Pino, C.; Sevilla-García, M. A.; Esteban-Ortega, F. New CFD Tools to Evaluate Nasal Airflow. *European Archives of Oto-Rhino-Laryngology* **2017**, *274* (8), 3121–3128. https://doi.org/10.1007/s00405-017-4611-y.
(14) Burgos, M. A.; Sanmiguel-Rojas, E.; Singh, N.; Esteban-Ortega, F. DigBody: A New 3D Modeling Tool for Nasal Virtual Surgery. *Computers in Biology and Medicine* **2018**, *98*, 118–125. https://doi.org/10.1016/j.compbiomed.2018.05.016.
(15) Sanmiguel-Rojas, E.; Burgos, M.; Del Pino, C.; Sevilla-García, M.; Esteban-Ortega, F. Robust Non-Dimensional Estimators to Assess the Nasal Airflow in Health and Disease. *International journal for numerical methods in biomedical engineering. DOI:10.1002/cnm.2906 (2017)* **2017**.
(16) Sanmiguel−Rojas, E.; Burgos, M. A.; Esteban−Ortega, F. Nasal Surgery Handled by CFD Tools. *International Journal for Numerical Methods in Biomedical Engineering* **2018**, *0* (ja), e3126. https://doi.org/10.1002/cnm.3126.
(17) Martonen, T. B.; Quan, L.; Zhang, Z.; Musante, C. J. Flow Simulation in the Human Upper Respiratory Tract. *Cell Biochem. Biophys.* **2002**, *37* (1), 27–36. https://doi.org/10.1385/CBB:37:1:27.
(18) Burgos, M. A.; Sanmiguel-Rojas, E.; Rodríguez, R.; Esteban-Ortega, F. A CFD Approach to Understand Nasoseptal Perforations. *Eur Arch Otorhinolaryngol* **2018**, 1–8. https://doi.org/10.1007/s00405-018-5073-6.
(19) Linux.org https://www.linux.org/ (accessed May 27, 2019).
(20) ITK - Segmentation & Registration Toolkit. https://itk.org https://itk.org/.
(21) Burgos, M. A.; Sanmiguel-Rojas, E.; Martín-Alcántara, A.; Hidalgo-Martínez, M. Effects of the Ambient Temperature on the Airflow across a Caucasian Nasal Cavity. *International Journal for Numerical Methods in Biomedical Engineering* **2013**, *30* (3), 430–445. https://doi.org/10.1002/cnm.2616.
(22) Taylor, D. J.; Doorly, D. J.; Schroter, R. C. Inflow Boundary Profile Prescription for Numerical Simulation of Nasal Airflow. *Journal of The Royal Society Interface* **2010**, *7* (44), 515–527. https://doi.org/10.1098/rsif.2009.0306.
(23) Kim, S. K.; Na, Y.; Kim, J.-I.; Chung, S.-K. Patient Specific CFD Models of Nasal Airflow: Overview of Methods and Challenges. *J Biomech* **2013**, *46* (2), 299–306. https://doi.org/10.1016/j.jbiomech.2012.11.022.
(24) Gencer, Z. K.; Özkiriş, M.; Okur, A.; Karaçavus, S.; Saydam, L. The Possible Associations of Septal Deviation on Mastoid Pneumatization and Chronic Otitis. *Otol. Neurotol.* **2013**, *34* (6), 1052–1057. https://doi.org/10.1097/MAO.0b013e3182908d7e.
(25) Sistani, S. S.; Dashipour, A.; Jafari, L.; Ghahderijani, B. H. The Possible Associations of Nasal Septal Deviation with Mastoid Pneumatization and Chronic Otitis. *Open Access Maced J Med Sci* **2019**, *7* (15), 2452–2456. https://doi.org/10.3889/oamjms.2019.670.
(26) Güçlü, O.; Sahin, E. M.; Tekin, K.; Dereköy, F. S. Evaluation of Nasal Airways by Objective Methods in Chronic Otitis Media. *Eur Arch Otorhinolaryngol* **2013**,

270 (4), 1263–1266. https://doi.org/10.1007/s00405-012-2122-4.