Functional relevance of Computational Fluid Dynamics in the field of nasal obstruction: a literature review

Running title: Functional relevance of CFD

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INTRODUCTION

Nasal airway obstruction (NAO) is a common symptom affecting the quality of life of patients (1). It may involve different etiologies including septal deviations (SD), nasal valve collapse (NVC), or inferior turbinal hypertrophy (ITH) (2). The clinical evaluation of NAO can be subjective, by self-questionnaires (NOSE, SNOT 22) and Visual Analog Scale (VAS), or reported by different tests such as rhinomanometry or Peak Nasal Inspiratory Flow (PNIF) (3) (4)(5).

Computational fluid dynamics (CFD) consists in studying fluid movements, or its effect, by numerical resolution of equations governing this fluid. It can be applied to nasal anatomy: over the past 10 years, there have been many studies focusing on CFD in nasal airway (6)(7). CFD can accurately model the airflow and its conditioning in the nasal cavities and calculate new variables, unknown in the world of medicine, such as Heat Flux (HF) or Wall Shear Stress (WSS) (8). 3D reconstruction tools can help the clinician better understand nasal anatomy, and CFD data to better analyze NAO genesis (9). The final goal is to guide surgical procedures. However, these data are not often correlated with patients perceptions or measurements carried out in clinical routine (10). The correlation between clinical evaluation of nasal breathing and CFD is essential to improve the interpretation of the latter. There is a lack in literature of comparative study analyzing the different results obtained, as Leite et al. reports in his recent literature review. (11)(12)

We conducted a literature review of CFD studies regarding the nasal airway, focusing on articles comparing clinical data to CFD. The goal is to provide what are the most reliable CFD measures: this study investigates the correlation between CFD and NAO.

METHODS

The selected studies were obtained from the database of the US National Library of Medicine (PubMed) online database, MEDLINE (Ovid), Google scholar, and Cochrane Library using a combination of MeSH terms (nose, paranasal sinus, fluid dynamics, rhinology) and no MeSH terms (CFD, nasal airway, nasal airflow, numerical, nasal symtoms). Studies that do not incorporate objective or subjective clinical assessment were excluded.

RESULTS

Articles selection

Table 1 reports all selected studies and the ways they assess clinical evaluation. Of the 258 articles selected, 47 dealt with nasal airway and corresponded to our topic. Thirteen of these 47 articles were found to be revevant, including with clinical measurements (**Figure 1**). This review sums up the correlation between clinical assessment of NAO and CFD results. We did not apply a time-out filter for the research.

Nasal Airway obstruction: Clinical Assessment

Clinical assessment of NAO can be performed by many tools. Regarding subjective assessment, most authors use the NOSE questionnaire and / or the VAS scale (10) (14). NOSE questionnaire is a disease-specific quality-of-life instrument for NAO that has been validated in literature (15). NOSE is a graduated 20-point scale, which may be multiplied by 5 to give a final total out of 100. A score of 100 indicates complete nasal obstruction. A NOSE score under 25 is considered normal; a score between 25 and 50 denotes low nasal obstruction and a score above 50 severe nasal obstruction. Others use the SNOT 22 questionnaire, or more specific questionnaires as in the Empty Nose Syndrome (ENS) with the ENS6Q questionnaire (16)(17).

Regarding the paraclinical evaluation, the most used tool remains the rhinomanometry which measures pressure and flow during normal inspiration and expiration through the nose. (4). Acoustic rhinomatry is a measurement of cross sectional area and length of the nose and the nasal cavity through acoustic reflections. It can be correlated to minimal cross section area (MCAs) and is also used by some authors for functional assessment, although it is actually a morphological examination (18). We did not found any study involving PNIF.

CFD Calculations

The main data measured by CFD are as follows:

- Airflow (AF) (uni- or bilateral, in mL/s), and Airflow partitioning (%) corresponding to the balance between obstructed and non-obstructed nasal fossa.
- Nasal resistance (CFD-NR) to uni- or bilateral inspiration and expiration, (Pa/(mL/s)): Nasal resistance ($\Delta P/QV$) is defined as the ratio of the drop in transnasal pressure ΔP (nostrils to nasopharynx or to the end of the septum) to the volumetric airflow rate.
- Total Heat flux (HF) (W/m2), which is the rate of heat transfer across a surface per unit time and area and measures heat loss from the nasal mucosa to the inspired air; Surface Area where Heat Flux > 50 W/m^2 (SAHF50); or Peak Heat Flux defined as the value above which only 1 cm2 of mucosa is exposed to.
- Total Pressure (Pa) and pressure drop
- Air velocity (m/s) and Maximal velocity (Vmax)
- Wall shear stress (WSS) (Pa), which is a friction force generated when moving air contacts the nasal walls
- Streamlines, allowing airway visualization

The decision to analyze all or part of these data depends on the purpose and design of the study. Some data may be concerned only with airflow (velocity, pressure), and some only with air conditioning.

Correlation between CFD and clinical assessment

Airflow (AF)

Casey et al. Found a strong correlation between unilateral nasal AF and NOSE (r=-0.55, p=0.0016) or VAS (r=-0.45, p=0.0056) (19). It is the same for Gaberino et al., but only after correction of the nasal cycle: without correction of the latter, AF was correlated with NOSE (p = 0.048), but not with VAS (20). Kimbell also reports a moderate correlation between NOSE and AF (21).

In patients improved after surgery for NAO, several studies found improvement of AF in the narrow side, and a deterioration of AF in the non-narrow side after surgery (21–23).

CFD-calculated Nasal Resistances (CFD-NR)

Nasal resistances are among the most analyzed data in the literature concerning NAO. By analyzing two groups of patients (NAO and non-NAO), Casey et al. found a statistically significant difference (p = 0.0006) in CFD-NR measurements (19). However, in his study on 30 patients, there was no correlation between CFD-NR and the NOSE or VAS. It is the same for Gaberino et al. who need to correct the nasal cycle to obtain a correlation between CFD-NR with the clinical data. Thus, and only after correction of the nasal cycle, CFD-NR were correlated with NOSE and VAS (r = 0.55, p = 0.005 and r = -0.58, p = 0.003 respectively) (20). Kimbell found that CFD-NR were moderately correlated with NOSE and strongly with VAS, similar results for Rhee et al. (21,23,24). In contrast, Zhao et al. found no correlation between CFD-NR and VAS

(25). Concerning the non-narrow side, it is possible to find an increase in postoperative resistance (26).

Regarding objective measurements, nasal resistances obtained with rhinomanometry and CDF-NR are correlated with no significative differences ($p>0.05$ and $r=0.41$, $p<0.05$) (25,27).

Total Heat Flux (HF), SAHF50, Peak Heat Flux

HF analysis have now a major place in CFD in the field of NAO. NOSE et VAS were strongly correlated with total unilateral HF ($r=-0.48$, $p= 0.0075$ and $r=0.43$, $p=0.0166$ respectively), and with SAHF50 ($r=-0.55$, $p=0.0016$ and $r=-0.51$, $p=0.0038$ respectively) in Casey's study. The correlation between HF and NOSE was moderate (19). Sullivan et al. also found that HF and SAHF50 was strongly correlated with NOSE ($r=0.76$, $p<0.01$) and VAS ($r=0.5$, $p<0.05$) (28).

Gaberino et al. found a statistical significative difference between pre and post-operative analyze for HF ($p=0.027$); after correction of the nasal cycle, NOSE was correlated to HF and SAHF50 but VAS was only correlated to HF (20).

For Zhao et al., only the peak nasal mucosal heat loss posterior to the nasal valve was correlated to clinical impairment ($r=-0.46$, $p<0.01$) (25).

Pressure

Hildebrandt et al. shows a diminution of pressure drop in the nasal valve area after surgery for NAO **(Figure 3a)** (26). It highlights that the nasal valve is a key-zone for NAO. When comparing 3 symptomatic versus asymptomatic patients, Kim et al. also found a pressure drop more important in patients with NAO ($p<0.05$) (22). **(Figure 3b)**

Maximum Velocity (Vmax)

For Kim et al. Vmax was higher in patients with SD ($p=0.05$) (22). Vmax could also be correlated to clinical impairment: when the SD is caudal, Vmax and symptoms are higher than in posterior SD (29).

Wall Shear Stress (WSS)

WSS in nasal valve area was higher in patients with SD ($p=0.05$)(22). In patients with ENS, WSS is lower in the inferior region, due to absence of inferior turbinate (30,31).

Streamlines

Regarding nasal airway, patients with NAO have less air in the middle pathway (31 +- 18 mL/s vs 68 +- 10 mL/s, $p<0.001$). It was strongly correlated with NOSE ($r=-0.76$, $p<0.001$) and VAS scores ($r=0.9$, $p<0.0001$) (19).

In a more specific population with ENS patients, there's a surprising modification in airflow when inferior turbinate is missing : we observe a frank diminution of airflow in the inferior region and an augmentation of the latter in middle region ($p<0.05$) (31).

Nasal geometry

No differences were obtained by acoustic rhinometry and by 3D measurement (all $p > 0.05$) (27).

DISCUSSION

Synopsis of new findings

One of the difficulties regarding outcomes of esthetic and/or functional surgery is the objectivity of the evaluations carried out and their correlation with the patient's perception. (32). While self-evaluation using quality of life questionnaires remains the gold standard, results of objective tests such as rhinomanometry remain controversial (33). The development and improvement of CFD processes should allow for reliable and correlated assessments of patient-reported outcomes. The advantage of CFD lies not only in airflow analysis but also in its conditioning: e.g. in heat flux measurements that could be influental in the etiopathogeny of NAO (34). This is very innovative as these data are not measurable by conventional investigations.

Functional relevance of CFD

The study of CDF-NR and AF is easy because these physical data have been used for a long time in rhinology. These are values that are commonly used by clinicians.

Regarding the comparison between patient perceptions and nasal resistances, authors agree that unilateral evaluation is more reliable than bilateral evaluation (23)(35) (37). Thus, it is necessary to focus on narrow-side and non narrow-side rather than total AF or total resistance (20). While in most studies there is a significant improvement after surgery on the narrow-side, contralateral deterioration is often found, probably because of medialization of the nasal septum. However, these patients do not have a functional complaint (26). It therefore appears that the balance of airflow partitioning is important to consider in the functional complaint. Airflow partitioning is easily evaluable with CFD.

In the field of nasal resistances, we find globally similar results between clinical nasal resistances and CFD-NR. Some studies have already shown the correlation between clinical measures of nasal resistances and CFD-NR (27) (25) (37). However, these studies focus on a small number of subjects or on a healthy population. More studies need to be done about it. The study of correlations between CFD-NR with patient perception finds heterogeneous results. Kimbell reports a moderate correlation between CFD-NR and NOSE or VAS (22,24). Gaberino et al. found that only AF and NOSE are correlated before correction of the nasal cycle in their population, results similar in other studies (20)(19,25). Many reasons can explain these discordant results. Firstly, the sensation of NAO is not only due to the increase of nasal resistances. This is why clinical measurements such as rhinomanometry are themselves discussed. Indeed, several studies have shown that rhinomanometry is not always correlated with clinical impairment, and more complex factors intervene in the perception of NAO. (38)(39). Secondly, it is necessary to pay attention to the nasal cycle in CFD study, which can be a confounding factor (40)(41)(20). If a significant difference in the volume of the inferior turbinates is noted on CTscans, it is necessary to make a correction thanks to virtual surgery, or to take it into account in the interpretation of the results. (20). Third, tissue compliance is currently not considered in CFD studies, working on rigid walls. It is recognized that NAO problems due to nasal valve may be static or dynamic (42)(43). Dynamic problems can be highlighted by an examination called rhinoresisometry (44). If static (architectural) problems are well explored in CFD, simulating a NVC appearing during breathing would require modeling deformable walls according to the airflow.

We did not find major difference between NOSE and VAS, their degree of correlation varying according to the studies. We recommend to use both, as well as more specific questionnaires like the ENS6Q for the ENS. In addition, we did not find any CFD study with PNIF as an objective measurement of NAO.

Recent studies show the major interest that seems to represent HF in rhinology. (19,20,30,31,45). For a long time, a link has been found between perception of cold and NAO perception (46). The new CFD tools allow a fine analysis of this thermal condition. In the studies reviewed, all data agree to give a major place to HF in the genesis of NAO perception. Different versions of HF can be used (Total HF, SAHF50, Peak HF), each of which has shown a statistically significant correlation with patients' perceptions (**Figure 2**) (28). It suggests that NAO is related to a lack of cooling effect rather than high nasal resistance. Perhaps the truth lies in a combination of both (34).

Nasal valve area is a key-zone in the sensation of NAO (47). It is also difficult to treat surgically, hence the major interest of understanding its pathophysiology (48)(49). Pre- and postoperative analyzes of patients with NVC or high and anterior SD show a link between a sudden total pressure drop and NAO perception (**Figure 3a, b**) (26)(22). In this area velocities are often the highest: Liu finds that the caudal septal deviations responsible for NVC are both correlated with higher velocities and NAO perception (29). The study of pressures and velocities is easy and must be systematically undertaken when performing CFD.

Regarding WSS, it is in nasal valve area we find the most important friction areas (22). But the study of WSS also brings a lot in the analysis of patients with an ENS. Indeed, in this specific population, ENS6Q questionnaire was correlated with WSS: the absence of friction around the inferior turbinate causes the paradoxical NAO perception (50)(31). However, while presented results seem interesting, there is still a lack of data to interpret the WSS as well as possible. It will be necessary to correlate WSS and patient perception, before and after surgery.

Concerning the airway, several authors report a strong correlation between the patient's obstruction and the path taken by the air inside the nasal cavity. Patients with a decreased flow at the middle meatus appear more uncomfortable in case of SD (19).

Contrariwise, when the inferior turbinate is missing, there is an increase of the flow in the middle meatus (15,20). Changing the passage of air through the nasal cavity, even without deterioration of nasal resistance, changes the perception of patients. It is likely that this impairment is multifactorial: thanks to CFD, it appears that mucosal cooling effect, HF and humidity exchanges are related to the symptoms brought by the patients (11). As such, we did not find study involving humidity exchange and NAO evaluation.

Li et al. and Lu et al. compare acoustic rhinometry with MCAs and found no significant difference (27,30,31). This confirms that acoustic rhinotry is a reliable morphological examination. On the other hand, although often presented as functional, we think that it is an anatomical examination. It is therefore difficult to make correlations between subjective perceptions and cross section areas.

Limits

Performing comparisons between clinical data and CFD remains difficult. To do this, authors have several possibilities: they can either compare healthy to pathological subjects (for example a patient population with SD and NAO vs a population without SD and NAO), or compare the same patient before and after surgery. Then, they compare clinical tests with CFD. It remains difficult to carry out such studies on large populations of subjects, for many reasons. First of all, the realization of postoperative CT scan is not always justified, and it is necessary to obtain the approval of the local Ethics Committee, as CTscans exposes the patient to additional radiation. Moreover, the calculation and implementation times are still long and often require the presence of a computer engineer, programs available at the moment not being "user-frendly" for a surgeon. New software seems to be easier to use but we do not have the experience (51).

Of the studies reviewed, two do not include validated assessment of NAO but simply report a clinical difference between the groups of patients (22,26). However, given the number of studies, we have incorporated all those that report the patient's perception. Moreover, because of the small number of patients included, sometimes correlations seem to be emerging but without satisfactory statistical test. It is therefore necessary to conduct other studies on a larger number of patients.

Other data remains to be integrated to make the simulations more and more precise: in the future, we have to be able to perform more often inspiratory and expiratory simulations, following a normal breathing (and not a constant incoming airflow), to allow a deformation of nasal walls which have a major importance regarding NVC, to integrate new data such as hygrometry or to vary the temperature of the nasal mucosa according to inspiration or expiration. This will allow more reliable extrapolation of CFD results.

CONCLUSION

The multiplication of CFD studies in the nose helps to better understand NAO. The clinical interpretation of previously unknown data, such as WSS or HF, opens up new horizons in the understanding of this symptom. Further studies on larger cohorts of patients need to be undertaken. However, we must be keep in mind that NAO may include a notion of subjectivity, non “CFDable”.

Tables

Article	Clinical assessment of NAO	
	Subjective	Objective
Casey et al. 2017 (19)	NOSE / VAS	/
Gaberino et al. 2017 (20)	NOSE / VAS	/
Hildebrandt et al. 2013 (26)	*Improvement after surgery*	/
Kim et al. 2014 (22)	*Patients with NAO vs healthy subjects*	/
Kimbell et al. 2012 (23)	NOSE / VAS	/
Kimbell et al. 2013 (21)	NOSE / VAS	/
Li, Farag, Leach et al. 2017 (30)	NOSE / SNOT-22 / ENS6Q	Rhinomanometry / Acoustic rhinometry
Li, Farag, Maza et al. 2017 (31)	NOSE / SNOT-22 / ENS6Q	/
Liu et al. 2012 (29)	VAS	/
Lu et al. 2014 (27)	/	Rhinomanometry / Acoustic rhinometry
Rhee et al. 2012 (9)	NOSE / VAS	/
Sullivan et al. 2013 (28)	NOSE / VAS	/
Zhao et al. 2013 (25)	VAS	Rhinomanometry

Table 1. Clinical assessment of NAO according to studies.

Authors	Type of obstruction	NOSE	VAS	Patients with NAO (compared to patients without NAO)	Before / after surgery comparison
Casey et al. 2017	**SD, ITH, NVC**	**Unilateral nasal AF *** Unilat nasal CFD-NR (NS) **Total HF *** **SAHF50 *** **Less air in middle pathway ***	**Unilateral nasal AF *** Unilat nasal CFD-NR (NS) **Total HF *** **SAHF50 *** **Less air in middle pathway ***	**Unilateral nasal AF *** **CFD-NR *** **Total HF*** **SAHF50 ***	
Gaberino et al. 2017 (after correction of nasal cycle)	**SD, ITH**	**Unilat nasal AF *** **Unilat nasal CDF-NR *** **Total HF *** **SAHF50 ***	**Unilat nasal AF *** **Unilat nasal CDF-NR *** **Total HF *** SAHF50 (NS)		**CFD-NR *** **Unilateral nasal AF *** **Total HF *** SAHF50 (NS)
Hildebrandt et al. 2013 (no statistical tests)	SD, ITH			↓ Airflow ↑ Pressure drop ↑ CDF-NR	
Kim et al. 2014	SD			**↑ Pressure drop *** **↑ Vmax *** **↑ WSS in nasal valva area ***	
Kimbell et al. 2012	SD, ITH, NVC	CDF-NR: moderate correlation (no value)	CDF-NR: strong correlation (no value)		
Kimbell et al. 2013	SD, ITH, NVC	Moderate correlation for unilat nasal AF, CFD-NR, Total HF (-0.70 0.48, -0.65, -0.51 respectively).	Moderate correlation for Unilat nasal AF, CFD-NR, Total HF (0.52, -0.42, 0.46 respectively)		**Unilat nasal AF *** **CFD-NR *** **Total HF *** **WSS ***

Li, Farag, Leach et al. 2017	ENS			**↑ Unilat nasal AF *** **↓ AF in inferior region *** **↓ WSS in inferior region ***	
Li, Farag, Maza et al. 2017	ENS			**↓ CFD-NR *** **↓ WSS *** **↑ Cross Sectional Area *** **↑ AF in middle region ***	
Liu et al. 2012	SD		CFD-NR (no value) V max (no value)		
Rhee et al. 2012	SD, ITH, NVC	Unilat nasal AF (no statistical test) CFD-NR (no statistical test)	Unilat nasal AF (no statistical test) CFD-NR (no statistical test)	↓ Unilat Nasal AF ↑ CFD-NR	
Sullivan et al. 2013	SD, ITH, NVC	**Heat transfert rate across entire obstructed cavity *** **Heat transfer rate across vestibule in obstructed side *** **SAHF50 *** **Peak HF ***	**Heat transfert rate across entire obstructed cavity *** **Heat transfer rate across vestibule in obstructed side *** **SAHF50 *** Peak HF (NS)		**Total HF ***
Zhao et al. 2013	SD		**Peak HF (nasal vestibule) *** CFD-NR (NS) Total HF (NS)		

Table 2. The table reports all CFD-calculated values. Comparison between CFD and:- NOSE and VAS scores; - Symptomatic and non symptomatic patients; - Pre vs post operative situations. All results are presented for the most obstructed side. SD = Septal Deviation. ITH = Inferior Turbinate Hypertrophy. NVC = Nasal Valve Collapse. Bold and * indicates a statistically significant correlation or difference ($p<0.05$). NS = Non significative test. If empty, not analyzed.

Figures

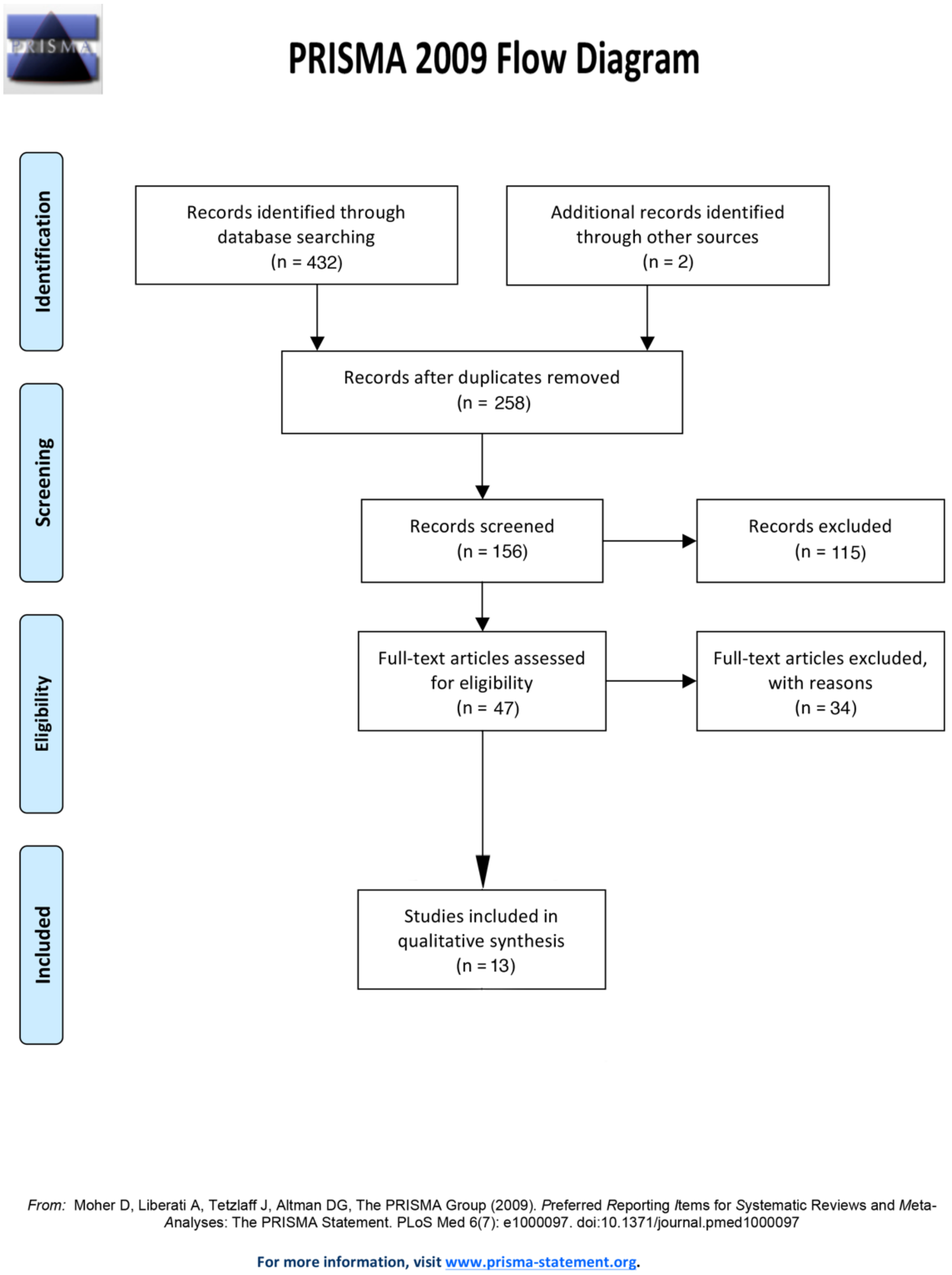

Figure 1. PRISMA Flow Diagram.

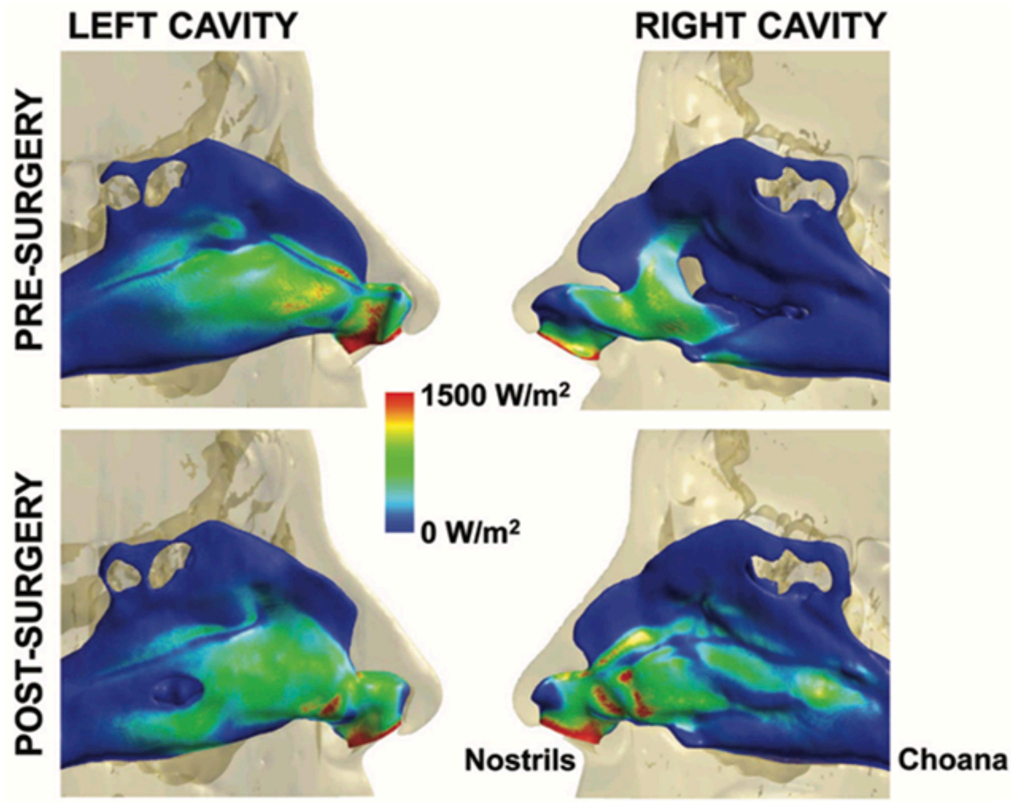

Figure 2. Spatial distributions of Heat Fluxes on the nasal septum of a patient with nasal obstruction. Heat fluxes are increased on the right cavity after surgery (most obstructed side). Retrieved from Sullivan et al. (28)

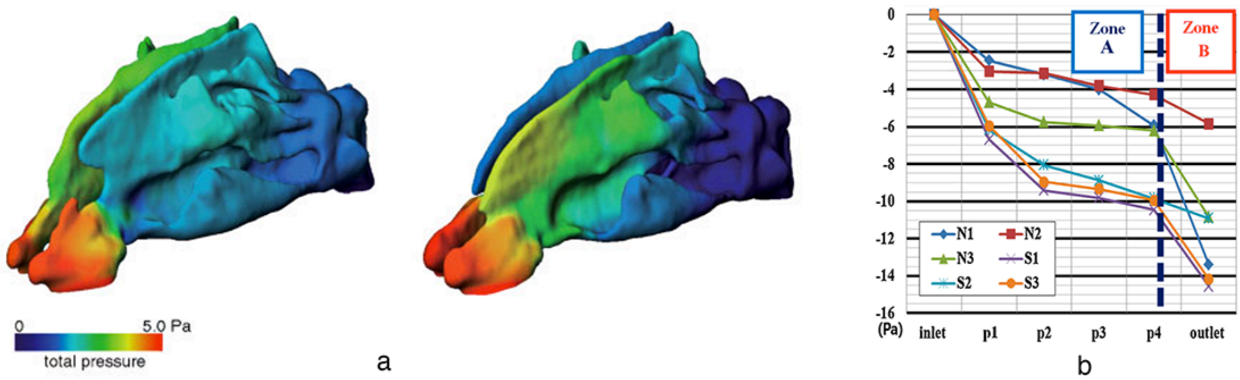

Figure 3. Evolution of total pressure during inspiration.

Figure 3a. shows the distributions of the relative total pressure during inspiration of the symptomatic patient, before (left) and after (right) surgery, retrieved from Hildebrandt et al. (26)

Figure 3b. show the pressure drop along the nasal fossa. p1 corresponds to the nasal valve area. Retrieved from Kim et al. (23)

REFERENCES

1. Rhee JS, Book DT, Burzynski M, Smith TL. Quality of life assessment in nasal airway obstruction. The Laryngoscope. 2003 Jul;113(7):1118–22.

2. Frank-Ito DO, Kimbell JS, Laud P, Garcia GJ, Rhee JS. Predicting postsurgery nasal physiology with computational modeling: current challenges and limitations. Otolaryngol Head Neck Surg. 2014 Nov;151(5):751-9.

3. Rhee JS, Sullivan CD, Frank DO, Kimbell JS, Garcia GJM. A Systematic Review of Patient-Reported Nasal Obstruction Scores: Defining Normative and Symptomatic Ranges in Surgical Patients. JAMA Facial Plast Surg. 2014 May 1;16(3):219.

4. Vogt K, Wernecke K-D, Behrbohm H, Gubisch W, Argale M. Four-phase rhinomanometry: a multicentric retrospective analysis of 36,563 clinical measurements. Eur Arch Oto-Rhino-Laryngol Off J Eur Fed Oto-Rhino-Laryngol Soc EUFOS Affil Ger Soc Oto-Rhino-Laryngol - Head Neck Surg. 2016 May;273(5):1185–98.

5. Pendolino AL, Nardello E, Lund VJ, Maculan P, Scarpa B, Martini A, et al. Comparison between unilateral PNIF and rhinomanometry in the evaluation of nasal cycle. Rhinology. 2018 Jun 1;56(2):122–6.

6. Burgos MA, Sanmiguel-Rojas E, Rodríguez R, Esteban-Ortega F4. A CFD approach to understand nasoseptal perforations.Eur Arch Otorhinolaryngol. 2018 Sep;275(9):2265-2272.

7. Chen XB, Lee HP, Chong VF, Wang de Y. Numerical simulation of the effects of inferior turbinate surgery on nasal airway heating capacity. Am J Rhinol Allergy. 2010 Sep-Oct;24(5)

8. Dayal A, Rhee JS, Garcia GJ. Impact of Middle versus Inferior Total Turbinectomy on Nasal Aerodynamics. Otolaryngol Head Neck Surg. 2016 Sep;155(3):518-25

9. Kimbell JS, Frank DO, Laud P, Garcia GJ, Rhee JS. Changes in nasal airflow and heat transfer correlate with symptom improvement after surgery for nasal obstruction. J Biomech. 2013 Oct 18;46(15):2634-43.

10. Rhee JS, Cannon DE, Frank DO, Kimbell JS. Role of virtual surgery in preoperative planning: assessing the individual components of functional nasal airway surgery. Arch Facial Plast Surg. 2012 Sep-Oct;14(5):354-9.

11. Otto BA, Li C, Farag AA, Bush B, Krebs JP, Hutcheson RD, Kim K, Deshpande B, Zhao K. Computational fluid dynamics evaluation of posterior septectomy as a viable treatment option for large septal perforations. Int Forum Allergy Rhinol. 2017 Jul;7(7):718-725.

12. Leite SHP, Jain R, Douglas RG. The clinical implications of computerised fluid dynamic modelling in rhinology. Rhinology. 2018

13. Shadfar S, Shockley WW, Fleischman GM, Dugar AR, McKinney KA, Frank-Ito DO, Kimbell JS. Characterization of postoperative changes in nasal airflow using a cadaveric computational fluid dynamics model: supporting the internal nasal valve.JAMA Facial Plast Surg. 2014 Sep-Oct;16(5):319-27.

14. Floyd EM, Ho S, Patel P, Rosenfeld RM, Gordin E. Systematic Review and Meta-analysis of Studies Evaluating Functional Rhinoplasty Outcomes with the NOSE Score. Otolaryngol--Head Neck Surg Off J Am Acad Otolaryngol-Head Neck Surg. 2017;156(5):809–15.

15. Hsu HC, Tan CD, Chang CW, Chu CW, Chiu YC, Pan CJ, et al. Evaluation of nasal patency by visual analogue scale/nasal obstruction symptom evaluation questionnaires and anterior active rhinomanometry after septoplasty: a retrospective one-year follow-up cohort study. Clin Otolaryngol Off J ENT-UK Off J Neth Soc Oto-Rhino-Laryngol Cervico-Facial Surg. 2017 Feb;42(1):53–9.

16. Stewart MG, Witsell DL, Smith TL, Weaver EM, Yueh B, Hannley MT. Development and

validation of the Nasal Obstruction Symptom Evaluation (NOSE) scale. Otolaryngol--Head Neck Surg Off J Am Acad Otolaryngol-Head Neck Surg. 2004 Feb;130(2):157–63.

17. Erskine SE, Hopkins C, Clark A, Anari S, Kumar N, Robertson A, et al. SNOT-22 in a control population. Clin Otolaryngol Off J ENT-UK Off J Neth Soc Oto-Rhino-Laryngol Cervico-Facial Surg. 2017 Feb;42(1):81–5.

18. Velasquez N, Thamboo A, Habib A-RR, Huang Z, Nayak JV. The Empty Nose Syndrome 6-Item Questionnaire (ENS6Q): a validated 6-item questionnaire as a diagnostic aid for empty nose syndrome patients. Int Forum Allergy Rhinol. 2017;7(1):64–71.

19. Geißler K, Guntinas-Lichius O. [Rhinomanometry and acoustic rhinometry]. Laryngorhinootologie. 2015 Jan;94(1):8–9.

20. Casey_Correlation between Subjective Nasal Patency and Intranasal Airflow Distribution.pdf.

21. Gaberino C, Rhee JS, Garcia GJ. Estimates of nasal airflow at the nasal cycle mid-point improve the correlation between objective and subjective measures of nasal patency. Respir Physiol Neurobiol. 2017 Apr;238:23-32.

22. Kimbell JS, Frank DO, Laud P, Garcia GJ, Rhee JS. Changes in nasal airflow and heat transfer correlate with symptom improvement after surgery for nasal obstruction. J Biomech. 2013 Oct 18;46(15):2634-43.

23. Kim SK, Heo GE, Seo A, Na Y, Chung SK. Correlation between nasal airflow characteristics and clinical relevance of nasal septal deviation to nasal airway obstruction. Respir Physiol Neurobiol. 2014 Feb 1;192:95-101.

24. Kimbell JS, Garcia GJ, Frank DO, Cannon DE, Pawar SS, Rhee JS. Computed nasal resistance compared with patient-reported symptoms in surgically treated nasal airway passages: a preliminary report. Am J Rhinol Allergy. 2012 May-Jun;26(3):e94-8.

25. Rhee JS. Role of Virtual Surgery in Preoperative Planning: Assessing the Individual Components of Functional Nasal Airway Surgery. Arch Facial Plast Surg. 2012 Sep 1;14(5):354.

26. Zhao K, Jiang J, Blacker K, Lyman B, Dalton P, Cowart BJ, Pribitkin EA. Regional peak mucosal cooling predicts the perception of nasal patency. Laryngoscope. 2014 Mar;124(3):589-95.

27. Hildebrandt T, Goubergrits L, Heppt WJ, Bessler S, Zachow S. Evaluation of the intranasal flow field through computational fluid dynamics. Facial Plast Surg. 2013 Apr;29(2):93-8.

28. Lu J, Han D, Zhang L. Accuracy evaluation of a numerical simulation model of nasal airflow. Acta Otolaryngol. 2014 May;134(5):513-9.

29. Sullivan CD, Garcia GJ, Frank-Ito DO, Kimbell JS, Rhee JS. Perception of better nasal patency correlates with increased mucosal cooling after surgery for nasal obstruction. Otolaryngol Head Neck Surg. 2014 Jan;150(1):139-47.

30. Liu T, Han D, Wang J, Tan J, Zang H, Wang T, Li Y, Cui S. Effects of septal deviation on the airflow characteristics: using computational fluid dynamics models. Acta Otolaryngol. 2012 Mar;132(3):290-8.

31. Li C, Farag AA, Leach J, Deshpande B, Jacobowitz A, Kim K, Otto BA, Zhao K. Computational fluid dynamics and trigeminal sensory examinations of empty nose syndrome patients. Laryngoscope. 2017 Jun;127(6):E176-E184.

32. Li C, Farag AA, Maza G, McGhee S, Ciccone MA, Deshpande B, Pribitkin EA, Otto BA, Zhao K. Investigation of the abnormal nasal aerodynamics and trigeminal functions among empty nose syndrome patients. Int Forum Allergy Rhinol. 2018 Mar;8(3):444-452.

33. Barone M, Cogliandro A, Di Stefano N, Tambone V, Persichetti P. A systematic review of patient-reported outcome measures after rhinoplasty. Eur Arch Oto-Rhino-Laryngol Off J

Eur Fed Oto-Rhino-Laryngol Soc EUFOS Affil Ger Soc Oto-Rhino-Laryngol - Head Neck Surg. 2017 Apr;274(4):1807–11.

34. Pawar SS, Garcia GJM, Kimbell JS, Rhee JS. Objective measures in aesthetic and functional nasal surgery: perspectives on nasal form and function. Facial Plast Surg FPS. 2010 Aug;26(4):320–7.

35. . Zhao Zhao K, Blacker K, Luo Y, et al. Perceiving nasal patency through mucosal cooling rather than air temperature or nasal resistance. PLoS One 2011; 6(10):e24618.

36. Roithmann R, Cole P, Chapnik J, Barreto SM, Szalai JP, Zamel N. Acoustic rhinometry, rhinomanometry, and the sensation of nasal patency: a correlative study. J Otolaryngol. 1994 Dec;23(6):454–8.

37. Naito K, Komori M, Kondo Y, Takeuchi M, Iwata S. The effect of L-menthol stimulation of the major palatine nerve on subjective and objective nasal patency. Auris Nasus Larynx. 1997 Apr;24(2):159–62.

38. Zachow S, Muigg P, Hildebrandt T, Doleisch H, Hege H-C. Visual Exploration of Nasal Airflow. IEEE Trans Vis Comput Graph. 2009 Nov;15(6):1407–14.

39. Chandra RK, Patadia MO, Raviv J. Diagnosis of nasal airway obstruction. Otolaryngol Clin North Am. 2009 Apr;42(2):207–25, vii.

40. Umihanic S, Brkic F, Osmic M, Umihanic S, Imamovic S, Kamenjakovic S, et al. The Discrepancy Between Subjective and Objective Findings After Septoplasty. Med Arch Sarajevo Bosnia Herzeg. 2016 Oct;70(5):336–8.

41. Kahana-Zweig R, Geva-Sagiv M, Weissbrod A, Secundo L, Soroker N, Sobel N. Measuring and Characterizing the Human Nasal Cycle. PloS One. 2016;11(10):e0162918.

42. Patel RG, Garcia GJM, Frank-Ito DO, Kimbell JS, Rhee JS. Simulating the Nasal Cycle with Computational Fluid Dynamics. Otolaryngol-Head Neck Surg. 2015 Feb;152(2):353–60.

43. Bloching MB. Disorders of the nasal valve area. GMS Curr Top Otorhinolaryngol Head Neck Surg. 2007;6:Doc07.

44. Aksoy F, Veyseller B, Yildirim YS, Acar H, Demirhan H, Ozturan O. Role of nasal muscles in nasal valve collapse. Otolaryngol--Head Neck Surg Off J Am Acad Otolaryngol-Head Neck Surg. 2010 Mar;142(3):365–9.

45. Temmel AF, Toth J, Marks B, Jäger S, Berger U, Reiser K, et al. Rhinoresistometry versus rhinomanometry--an evaluation. Wien Klin Wochenschr. 1998 Sep 18;110(17):612–5.

46. Inthavong K, Ma J, Shang Y, Dong J, Chetty ASR, Tu J, et al. Geometry and airflow dynamics analysis in the nasal cavity during inhalation. Clin Biomech Bristol Avon. 2017 Oct 7;

47. Lindemann J, Tsakiropoulou E, Scheithauer MO, Konstantinidis I, Wiesmiller KM. Impact of menthol inhalation on nasal mucosal temperature and nasal patency. Am J Rhinol. 2008 Aug;22(4):402–5.

48. Barrett DM, Casanueva FJ, Cook TA. Management of the Nasal Valve. Facial Plast Surg Clin N Am. 2016 Aug;24(3):219–34.

49. Nyte CP. Hyaluronic acid spreader-graft injection for internal nasal valve collapse. Ear Nose Throat J. 2007 May;86(5):272–3.

50. Xavier R, Azeredo-Lopes S, Papoila A. Spreader grafts: functional or just aesthetical? Rhinology. 2015 Dec;53(4):332–9.

51. Balakin BV, Farbu E, Kosinski P. Aerodynamic evaluation of the empty nose syndrome by means of computational fluid dynamics. Comput Methods Biomech Biomed Engin. 2017 Nov;20(14):1554-1561.

52. Burgos MA, Sanmiguel-Rojas E, del Pino C, Sevilla-García MA, Esteban-Ortega F. New CFD tools to evaluate nasal airflow. Eur Arch Otorhinolaryngol. 2017 Aug;274(8):3121–8.