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## Correlation between subjective nasal patency and intranasal airflow distribution

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### Abstract

**Objectives.**—(1) Analyze the relationship between intranasal airflow distribution and subjective nasal patency in healthy and nasal airway obstruction (NAO) cohorts using computational fluid dynamics (CFD). (2) Determine whether intranasal airflow distribution is an important objective measure of airflow sensation that should be considered in future NAO virtual surgery planning.

**Study Design.**—Cross sectional.

**Setting.**—Academic tertiary medical center and academic dental clinic.

**Subjects and Methods.**—Three-dimensional models of nasal anatomy were created based on computed tomography scans of 15 NAO patients and 15 healthy subjects and used to run CFD simulations of nasal airflow and mucosal cooling. Subjective nasal patency was quantified with a visual analog scale (VAS) and the Nasal Obstruction Symptom Evaluation (NOSE). Regional distribution of nasal airflow (inferior, middle, and superior) was quantified in coronal cross-sections in the narrowest nasal cavity. The Pearson correlation coefficient was used to quantify the correlation between subjective scores and regional airflows.

**Results.**—Healthy subjects had significantly higher middle airflow than NAO patients. Subjective nasal patency had no correlation with inferior and superior airflows, but a high correlation with middle airflow ( $|r|=0.64$  and  $|r|=0.76$  for VAS and NOSE, respectively). Anterior septal deviations tended to shift airflow inferiorly, reducing middle airflow and reducing mucosal cooling in some NAO patients.

**Conclusion.**—Reduced middle airflow correlates with the sensation of nasal obstruction, possibly due to a reduction in mucosal cooling in this region. Further research is needed to elucidate the role of intranasal airflow distribution in the sensation of nasal airflow.

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IRB approval: This project was approved by the IRB committee at the Medical College of Wisconsin and informed consent was obtained from each patient.

## Keywords

Sensation of nasal airflow; nasal airway obstruction surgery; subjective nasal patency; computational fluid dynamics (CFD) simulations; virtual surgery planning

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## Introduction

Nasal airway obstruction (NAO) is one of the most common indications for otolaryngology referral<sup>1</sup> and carries an estimated economic burden upwards of \$5 billion annually.<sup>2</sup> Many studies have aimed to improve diagnosis of this condition to predict and optimize surgical outcomes. Despite these efforts, NAO remains a diagnostic challenge due to inconsistencies between subjective symptoms and clinical exam,<sup>3</sup> and the lack of reliable symptomatic correlation with objective assessment of nasal function by methods such as rhinomanometry, peak nasal inspiratory flow (PNIF), and acoustic rhinometry.<sup>4–10</sup>

Given that current objective methods do little to identify specific, clinically-significant anatomical sites of obstruction, the diagnosis of NAO, the decision to proceed with surgery, and the selection of structures to target is often based on surgeon intuition. The development of better objective methods to guide decision-making may help improve the success rate of NAO surgery, which has been deemed unsatisfactory by many otolaryngologists.<sup>11,12</sup> Short-term studies report surgical failure rates as high as 20–37%,<sup>13–17</sup> while long-term studies report even higher failure over time.<sup>7,11,18</sup> For example, in one study on long-term septoplasty outcomes, the proportion of patients stating “my symptoms are gone” was 53% six months postoperatively, but only 18% three to six years postoperatively.<sup>11</sup> In today’s setting of increasing focus on health care cost and utilization, accurate (and early) identification of NAO patients with a high likelihood of surgical benefit is more important than ever.<sup>19,20</sup>

Recent literature utilizing three-dimensional nasal airway modeling and computational fluid dynamics (CFD) have identified key objective variables of nasal airflow and mucosal cooling that reliably correlate with subjective nasal patency<sup>21–23</sup> and offer the potential for clinical application in virtual surgery planning. This body of literature proposes that while common tests such as rhinomanometry, PNIF, and acoustic rhinometry accurately measure nasal airflow resistance, perhaps mucosal cooling has the greatest clinical relevance to subjective patency.<sup>24,25</sup>

Zhao and Jiang<sup>26</sup> recently reported that subjective nasal patency scores had a higher correlation with airflow near the middle turbinate than with peak heat flux in 22 healthy subjects. Therefore, the purpose of this study is to apply CFD to quantify the intranasal airflow distribution in a cohort of healthy and NAO subjects aimed at (1) investigating whether intranasal airflow distribution is abnormal in NAO patients and (2) analyzing whether subjective nasal patency correlates with intranasal airflow distribution. Most importantly, if such a correlation exists, this knowledge may have potential for application in future virtual surgery planning for NAO corrective surgery.

## Methods

### Patient Selection

The research was performed under approval by the institutional review board at the Medical College of Wisconsin. Informed consent was obtained from each patient. This project is part of a larger study aimed at correlation of subjective and objective measures of nasal patency and their application to NAO virtual surgery.<sup>21,22,27–30</sup>

Twenty-seven NAO patients undergoing corrective surgery (septoplasty, turbinectomy and/or septorhinoplasty) were recruited between 2009 and 2013. Preoperative axial CT scans were obtained in 0.6-mm increments with in-plane resolution of 0.31mm. Included patients were at least 16 years-old and diagnosed with anatomic NAO (deviated septum, medically-resistant turbinate hypertrophy, or nasal valve dysfunction) (Table A1). Patients with nasal obstructive symptoms primarily due to rhinitis, sinusitis, or neoplastic or autoimmune processes (i.e., not due to anatomic obstruction) were excluded.

Fifty-two healthy subjects undergoing cone-beam CT (CBCT) scans at Marquette University School of Dentistry for indications unrelated to nasal etiology were recruited. CBCT scans were obtained in 0.5-mm increments with in-plane resolution of 0.5mm. Subjects were at least 18 years-old, denied symptoms of nasal obstruction, and were non-smokers for at least 3 months preceding their scan. Exclusion criteria were pregnancy, history of nasal surgery, severe nasal trauma, autoimmune disease, chronic sinusitis, severe allergies or other sinonasal disease. Subjects were included if NOSE score  $\geq 32$  based on the mean NOSE score (15) plus one standard deviation (17) of healthy individuals described in a recent literature review.<sup>28</sup>

The first 15 patients from each cohort were selected for evaluation, regardless of subjects' nasal cycle status.<sup>29</sup> Within the NAO cohort (ten male, five female), 13 identified as Caucasian, one as Hispanic, and one as "other" ethnicity. Within the healthy cohort (four male, 11 female), eight identified as Caucasian, three as Hispanic, three as Asian, one as African-American and one as "other" ethnicity.

### Creation of Three-Dimensional Models

Three-dimensional digital models of nasal passages (excluding paranasal sinuses) were created in Mimics 16.0 (Materialise Inc., Plymouth, Michigan). Models were exported in STL format and imported into ICEM-CFD 14.0 (ANSYS, Inc., Canonsburg, Pennsylvania), where planar nostrils and outlet surfaces were created and the geometry was meshed with approximately 4 million tetrahedral cells.

### Definition of Intranasal Regions for Airflow Distribution

Each nasal cavity was sectioned into 11 uniformly-spaced coronal sections. The most posterior extent of either nostril was designated as relative distance (D)=0.0 and the posterior-most edge of the septum as D=1.0 (Figure 1). Coronal sections were labeled according to their relative distance from the nostril, as defined by  $D=Z/L_{\text{septum}}$ , where Z is distance from the nostrils and  $L_{\text{septum}}$  is septum length.

To analyze regional airflow, the coronal sections at D=0.3, D=0.5, and D=0.7 were divided into three vertical segments designated as inferior, middle and superior regions independently for each nasal cavity using horizontal lines at the ventral lamella of each turbinate (Figure 2 and Figure A1). For clarity of presentation, the results for section D=0.7 are described below, while the results for sections D=0.3 and D=0.5 are presented in the Appendix. Section D=0.7 was selected for presentation because it includes the inferior, middle, and superior turbinates in nearly all subjects. The main conclusions of this manuscript were not dependent on the section selected for analysis (see Appendix).

### CFD Simulations

Our CFD modeling methods have been described in detail elsewhere.<sup>22,31</sup> Steady-state inspiratory laminar airflow simulations were conducted in Fluent 14.0 (ANSYS, Inc.) with the following boundary conditions: (1) air velocity set to zero at stationary walls, (2) pressure inlet at the nostrils with gauge pressure set to zero, and (3) an outlet pressure such that bilateral airflow was equal to 15L/min. The outlet pressure required to obtain 15 L/min of bilateral airflow was estimated by running preliminary simulations to quantify the relationship between outlet pressure and flowrate. Heat transfer simulation methods are described in detail in prior studies.<sup>21,31</sup>

### Assessment of Subjective Nasal Patency

All participants were administered the Nasal Obstruction Symptom Evaluation (NOSE) to assess disease-specific quality-of-life. This is a 5-item scale in which patients rate symptoms of nasal congestion, nasal blockage, difficulty breathing through nose, difficulty sleeping, and air hunger sensation on a 0 (not a problem) to 4 (severe problem) scale. The score is then multiplied by 5 to give a score from 0 to 100.

In addition, a unilateral visual analog scale (VAS) score was obtained. Patients were asked to cover one nostril and rate their ability to breathe on a 0 (no obstruction) to 10 (severe obstruction) scale. This was repeated for the contralateral nostril. The VAS score represented an assessment of subjective nasal patency at the time of administration, while the NOSE score reflected NAO symptoms during the preceding 30 days.

### Outcome Measures

CFD simulations provided the following measurements of previously-described objective measurements of nasal patency<sup>21,22</sup>: (1) unilateral nasal airflow, (2) unilateral nasal resistance, (3) total unilateral heat flux, (4) unilateral surface area where heat flux exceeds 50 W/m<sup>2</sup> (SAHF50). In addition, regional flow was quantified in inferior, middle and superior regions (Figure 2).

### Statistical Analysis

Wilcoxon signed-rank tests were used to test whether differences between the healthy and NAO cohorts were statistically significant at the level  $p < 0.05$ . The correlation coefficients between subjective and objective measures of nasal patency were computed using both the Pearson and Kendall's tau correlation coefficients, while trendlines were obtained using a least squares linear regression.

The manuscript focuses on correlations between subjective nasal patency and unilateral measures of nasal airflow in the narrowest nasal cavity based on previous reports that: (1) subjective nasal patency has a stronger correlation with unilateral rather than bilateral objective measures,<sup>5</sup> and (2) subjective nasal patency has a stronger correlation with unilateral measures in the most obstructed side than with measures in the least obstructed side.<sup>22</sup> The narrow side was defined as the cavity with lesser unilateral airflow in each individual. The correlation between subjective scores and intranasal airflow distribution in the non-narrow side was also investigated and the results are presented in the Appendix.

## Results

### Subjective Patency Scores

Subjective nasal patency scores were significantly different between NAO patients and healthy subjects measured by both NOSE ( $65 \pm 18$  vs.  $6 \pm 8$ , respectively,  $p < 0.0001$ ) and VAS ( $6.7 \pm 2.7$  vs.  $1.7 \pm 2.6$  on the narrow side with  $p < 0.001$ ,  $3.3 \pm 2.3$  vs.  $1.4 \pm 2.5$  on the non-narrow side with  $p < 0.01$ , respectively) (Figure 3). These data confirm a symptomatic distinction between cohorts as measured by NOSE and VAS scores.<sup>28</sup>

### Objective CFD Variables

Unilateral CFD variables were analyzed separately for narrow and non-narrow nasal cavities (Table 1). Unilateral nasal resistance was higher in NAO patients than in healthy subjects in the narrow cavity ( $0.75 \pm 1.4$  Pa.s/ml vs.  $0.10 \pm 0.04$  Pa.s/ml,  $p = 0.0006$ ). Consequently, average unilateral airflow ( $72 \pm 34$  ml/s vs.  $105 \pm 14$  ml/s,  $p = 0.0025$ ), average unilateral heat flux ( $114 \pm 54$  W/m<sup>2</sup> vs.  $167 \pm 27$  W/m<sup>2</sup>,  $p = 0.0055$ ), and average unilateral SAHF50 ( $30 \pm 13$  cm<sup>2</sup> vs.  $41 \pm 5$  cm<sup>2</sup>,  $p = 0.007$ ) were smaller in the narrow side of NAO patients as compared to healthy subjects.

The correlation between unilateral CFD variables and subjective patency scores was analyzed for the entire cohort of 30 individuals combined together. Before looking at regional airflows, the two variables with the strongest correlation with subjective scores were total unilateral airflow (NOSE:  $r = -0.55$ ,  $p = 0.0016$ ; VAS:  $r = -0.49$ ,  $p = 0.0056$ ) and unilateral SAHF50 (NOSE:  $r = -0.55$ ,  $p = 0.0016$ ; VAS:  $r = -0.51$ ,  $p = 0.0038$ ) (Table 2).

### Regional Airflow Distribution

Regional airflow distribution is graphically depicted in Figure 4. In the narrow cavity, only the average middle airflow differed significantly between cohorts, with NAO patients having less middle airflow than healthy individuals ( $31 \pm 18$  ml/s vs.  $68 \pm 10$  ml/s, respectively;  $p < 0.0001$ ) (Figure 4). Analysis of regional airflow as a percentage of total unilateral airflow revealed that the main flow pathway was the middle region in healthy individuals ( $66 \pm 9\%$  vs.  $23 \pm 7\%$  in the middle and inferior regions, respectively,  $p < 0.0001$ ). In contrast, similar percentages of inhaled air flowed through the middle and inferior regions in the narrow side of NAO patients ( $39 \pm 13\%$  middle region,  $50 \pm 18\%$  inferior region,  $p = 0.16$ ). This difference in airflow allocation between the two cohorts is further illustrated by the fact that middle flow exceeded inferior flow in the narrow cavity of all 15 healthy subjects, but in 7 of 15 NAO patients, inferior flow was greater than middle flow. Superior airflow in the narrow

side did not differ significantly between cohorts with  $11\pm 5\%$  and  $11\pm 10\%$  of inspired air reaching the superior region in healthy and NAO cohorts, respectively ( $p=0.23$ ).

### Subjective Patency vs. Regional Airflow

Subjective patency scores were plotted against narrow-side regional airflow (Figure 5). Narrow-side middle airflow demonstrated a strong correlation with both NOSE ( $r=-0.76$ ,  $p<0.0001$ ) and VAS scores ( $r=-0.64$ ,  $p=0.0002$ ), but inferior and superior airflows failed to correlate with subjective patency (Table 2 and Figure 5). The higher correlation of subjective patency with middle airflow is partially explained by a stronger correlation between total unilateral airflow and middle airflow ( $r=0.90$ ,  $p<0.0001$ ) than between total unilateral airflow and inferior or superior airflows ( $r=0.56$ ,  $p=0.001$ ; and  $r=0.49$ ,  $p=0.006$ , respectively) (Figure 6).

### Effect of Anatomic Obstruction on Airflow Distribution

We explored possible anatomical differences between NAO patients and healthy individuals that may explain the different airflow distributions in the two cohorts. First, several NAO patients (8 out of 15) had anterior septal deviations constricting the nasal valve region (Figures 7A, 7B). These airway constrictions were usually located at the superior margin of the nasal valve, thus redirecting the airstream and favoring more inferior airflow in NAO patients (Figures 7C). Second, there was a tendency for narrower nasal cavities to have less middle airflow ( $r=-0.76$ ,  $p<0.0001$ ) (Figure 8A). Finally, middle airflow also correlated with SAHF50 ( $r=0.46$ ,  $p=0.0002$ ) (Figure 8B), suggesting that there is less stimulation of cold receptors in patients with low middle airflow.

## Discussion

The mechanism responsible for nasal airflow sensation remains incompletely understood. Multiple *in vivo* studies found that subjective nasal patency does not correlate with nasal resistance measured via rhinomanometry or the airspace minimal cross-sectional area (MCA) measured via acoustic rhinometry.<sup>4,5,8-10</sup> This agrees with the concept that NAO patients present due to a subjective perception of decreased patency rather than an objective reduction in nasal resistance.<sup>32</sup> Certainly, resistance is a related entity, however it remains a distinctly different variable than subjective patency,<sup>9</sup> which recent literature suggests may be more related to mucosal cooling.<sup>24</sup>

The effect of mucosal cooling on nasal patency has been studied for over a century. In 1927, Fox<sup>33</sup> reported that volatile oils such as camphor, eucalyptus and menthol improved patency perception without changing nasal resistance, which was supported by subsequent research in the 1980s and 90s.<sup>34-36</sup> Further support to the mucosal cooling hypothesis comes from the observation that subjects report improved nasal patency when inspiring dry air (as compared to room air at the same temperature) due to evaporative mucosal cooling.<sup>6</sup>

Earlier studies suggested that airflow sensation occurs primarily at the nasal vestibule.<sup>37,38</sup> Jones and coauthors<sup>32</sup> reported that local anesthesia of the nasal vestibule produced a sensation of nasal obstruction. Clarke and Jones<sup>39</sup> measured intranasal sensation to air jets and reported that the nasal vestibule is more sensitive to these mechanical stimulations than

the posterior nose. Jones and colleagues<sup>40</sup> measured the intranasal distribution of thermoreceptors using a cold probe and reported a higher density of thermoreceptors in the nasal vestibule relative to the nasal cavum. These studies suggested that the density of mechanoreceptors and thermoreceptors was not uniform within the nasal cavity, leading some investigators to conclude that the nasal mucosa has a limited role in airflow sensation and that the skin-lined nasal vestibule is the primary site for airflow sensation.<sup>37</sup>

Recent studies confirm that the mucosa of the nasal cavity is not a homogenous tissue; rather it consists of a heterogeneous distribution of sensory receptors.<sup>41,42</sup> Frasnelli and colleagues used air puffs to determine that the mucosa of the anterior septum was more sensitive to CO<sub>2</sub> while the posterior septum was more sensitive to mechanical stimuli.<sup>42</sup> Meusel and collaborators measured trigeminal electrophysiological responses to several chemosensory stimuli, including menthol and CO<sub>2</sub>. While response to CO<sub>2</sub> displayed an anterior-posterior gradient, menthol stimulation was similar throughout the nasal cavity, suggesting that menthol-sensitive cold receptors are uniformly distributed throughout the nasal cavity. Recent advances in molecular biomarkers have led to identification of a transient receptor potential cation channel, subfamily M, member 8 (TRPM8) as a cold- and menthol-sensitive receptor, and inferior turbinate biopsies have confirmed its presence within nasal mucosa.<sup>43,44</sup> Altogether, these studies demonstrate that trigeminal somatosensory neurons enable the detection of a wide range of environmental stimuli within the nasal mucosa, including pressure, temperature, and chemical irritants.

Recent CFD studies have confirmed that mucosal cooling correlates with subjective nasal patency.<sup>21,22,26</sup> Kimbell and colleagues found a correlation ( $|r|=0.65$ ) between NOSE score and narrow side unilateral heat flux.<sup>22</sup> Zhao and colleagues also reported correlation ( $|r|=0.46$ ) between peak heat flux posterior to the nasal vestibule and average VAS score.<sup>26</sup> In a study by Sullivan and colleagues<sup>21</sup> looking at pre- and post-operative NAO patients, SAHF50 was determined to be the strongest predictor of nasal patency scores with a correlation of  $|r|=0.76$  and  $|r|=0.63$  for NOSE and VAS scores, respectively. These authors concluded that sensation of nasal patency was due to stimulation of cold receptors throughout the nasal mucosa (rather than at a single site where heat flux is maximum), which is consistent with the uniform distribution of TRPM8 receptors reported by Meusel and colleagues.<sup>41</sup>

Our study confirms the observation by Zhao and Jiang<sup>26</sup> that subjective nasal patency correlates with intranasal airflow distribution (Figure 5 and Table A2). We expanded on their findings, demonstrating that (1) NAO patients have a deficit in middle airflow in the narrow cavity as compared to healthy individuals (Figure 4 and Figure A2); (2) subjective nasal patency has a stronger correlation with middle airflow in the narrow cavity than with any other regional airflow (Figure 5 and Figures A3–A7); (3) total unilateral airflow better correlates with middle airflow than inferior or superior airflows (Figure 6); (4) the abnormal airflow distribution in the NAO cohort is partially due to anterior septal deviations shunting airflow away from the middle region (Figure 7); and (5) intranasal airflow distribution correlates with both nasal resistance and SAHF50, suggesting that patients with a high nasal resistance tend to have less middle airflow and less stimulation of cold receptors (Figure 8).

Limitations of our study include the fact that we did not control for the nasal cycle.<sup>29</sup> Both the NAO and healthy cohorts included some patients with asymmetric engorgement of the turbinates due to the nasal cycle. Our results (Figure 8) reveal that nasal cavities with high resistance tend to have less middle airflow, which suggests that intranasal airflow distribution may change during the nasal cycle. Future studies are needed to test this prediction. Another limitation of our study is that NAO symptoms can be caused by multiple anatomic deformities. We did not characterize airflow patterns by anatomic deformity (e.g., deviated septum vs. hypertrophied inferior turbinate). While future studies may consider characterizing airflow patterns by anatomic deformity, multiple anatomic deformities are often found concomitantly in the same patient (Table A1). Thus, we believe there is value in identifying CFD variables that correlate with subjective nasal patency in all-comers with NAO complaints. Finally, another limitation is that the two cohorts were not paired for demographics and an inter-cohort gender discrepancy was noted; however prior studies have indicated that no significant gender difference exists in nasal resistance measurements.<sup>45-47</sup>

In summary, in a cohort of 15 healthy individuals and 15 NAO patients, we found that NAO patients had a deficit in airflow around the middle turbinate in the narrow cavity, which was strongly correlated with the perception of nasal obstruction. It is unclear whether this implies that mucosal cooling in the region surrounding the middle turbinate is especially important for the sensation of nasal airflow. To the best of our knowledge, menthol-sensitive cold receptors have a uniform distribution on the nasal mucosa.<sup>41</sup> However, the high correlation of middle airflow with subjective nasal patency raises an intriguing possibility that the 3-dimensional pattern of cold-receptor stimulation may be important for nasal airflow perception. Further research is required to confirm or refute this hypothesis.

## Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

## Acknowledgements

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## APPENDIX

### Effect of coronal section selected for analysis

Intranasal airflow distribution was studied in three coronal sections, namely at relative distances from nostrils  $D=0.3$ ,  $D=0.5$ , and  $D=0.7$ . (The relative distance from nostrils  $D$  is defined in Figure 1.) Each section was divided into inferior, middle, and superior regions using horizontal lines through the ventral lamella of the inferior and middle turbinates (Figure A1). This systematic approach was applied to all sections in all patients, except that section  $D=0.3$  did not always include the inferior and/or middle turbinates (e.g., see Patient 2



in Figure A1). In these patients, the coordinates used to split section D=0.5 were also used to split section D=0.3.

In all three coronal sections, NAO patients had less airflow through the middle region than healthy individuals in the narrow side (Figure A2). Also, middle airflow in the narrow side correlated with both NOSE and VAS scores irrespective of the coronal section selected for analysis (Table A2 and Figures A3 and A4). Inferior and superior airflows measured in the narrow side did not correlate with subjective patency scores in any cross-section (Table A2).

Altogether, these results strongly suggest that the following conclusions do not depend on the cross-section selected for analysis:

- (1) NAO patients have a deficit in middle airflow in the narrow side when compared to healthy individuals (Figure A2);
- (2) Subjective nasal patency scores correlate with airflow in the middle region of the narrow side (Table A2 and Figures A3 and A4).

### **Narrow vs. non-narrow cavity**

Our analysis of correlations between subjective and objective measures of nasal patency focused on unilateral measures in the narrowest nasal cavity (Table 2). The finding that inferior flow in the non-narrow side was significantly higher in NAO patients than in healthy subjects (Figure A2) raises the possibility that airflow in the non-narrow side could also contribute to the perception of nasal airflow. To consider this possibility, we also investigated the correlation between subjective scores and regional airflows in the non-narrow side.

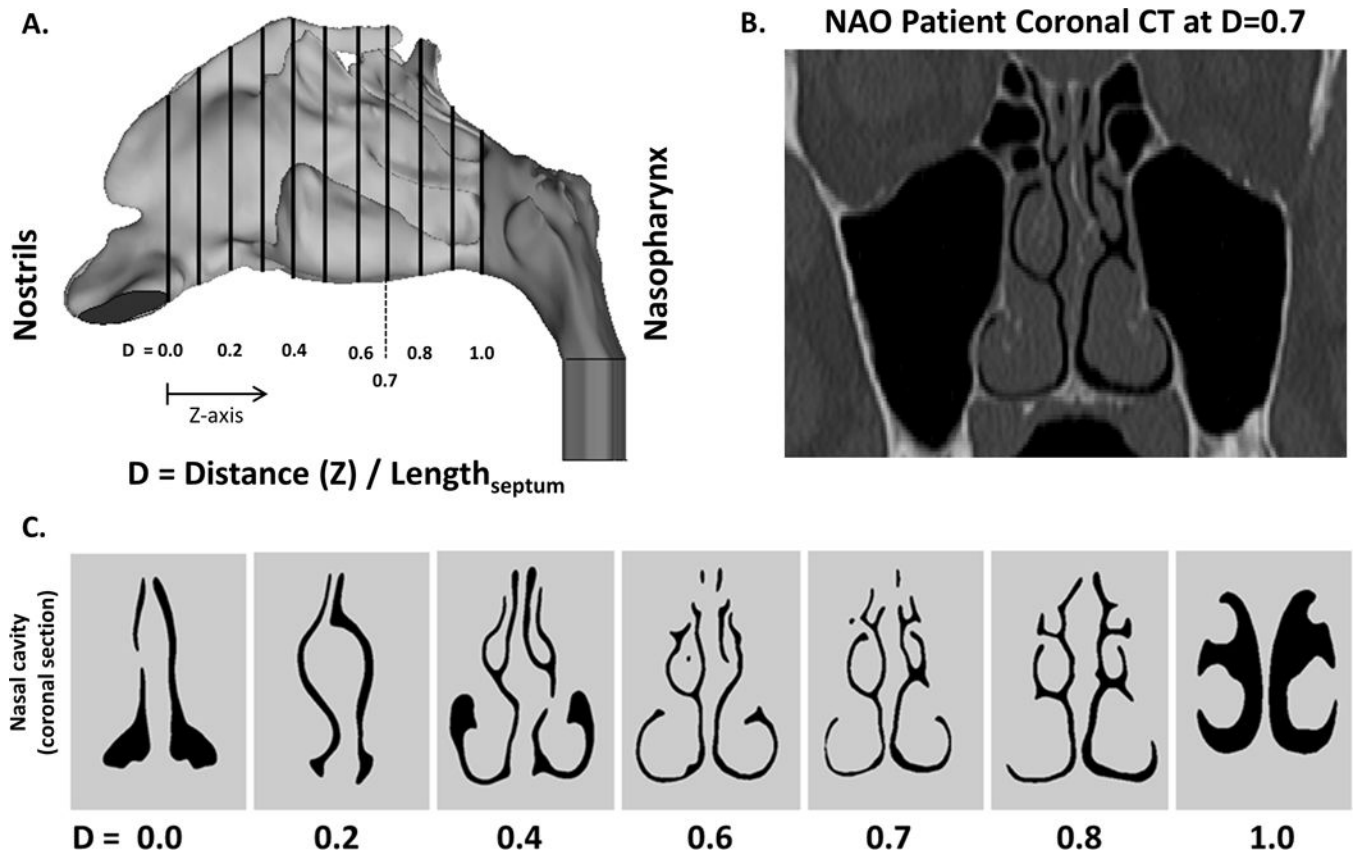
A statistically significant correlation was found between the NOSE score and inferior flow in the non-narrow side at section D = 0.7 (Table A2 and Figure A5). However, at sections D=0.3 and D=0.5, the correlation between NOSE and inferior flow in the non-narrow side was not statistically significant (Table A2). Furthermore, VAS score did not correlate with inferior flow in the non-narrow side in any of the 3 coronal sections studied (Table A2 and Figure A6). Therefore, the correlation between subjective scores and inferior flow in the non-narrow side was inconsistent. In contrast, the correlation between subjective scores and middle flow in the narrow side was statistically significant for both NOSE and VAS scores in all 3 coronal sections studied (Table A2).

Based on these findings, we believe that the key physiologic measurement responsible for the sensation of nasal obstruction in NAO patients is the airflow limitation in the narrow side. This is further supported by an analysis of the correlation between NOSE and VAS in our sample of 15 NAO patients and 15 healthy subjects. The NOSE survey is a bilateral measurement of NAO symptoms, while a unilateral VAS was used in this study. NOSE had a stronger correlation with VAS in the narrow side ( $r = 0.76$ ,  $CI = 0.55$  to  $0.88$ ,  $p < 0.0001$ ) than with VAS in the non-narrow side ( $r = 0.40$ ,  $CI = 0.05$  to  $0.66$ ,  $p = 0.03$ ) (Figure A7). This suggests that the sensation of nasal obstruction, as assessed by the NOSE survey, is more related to airflow in the narrow side than to airflow in the non-narrow side.

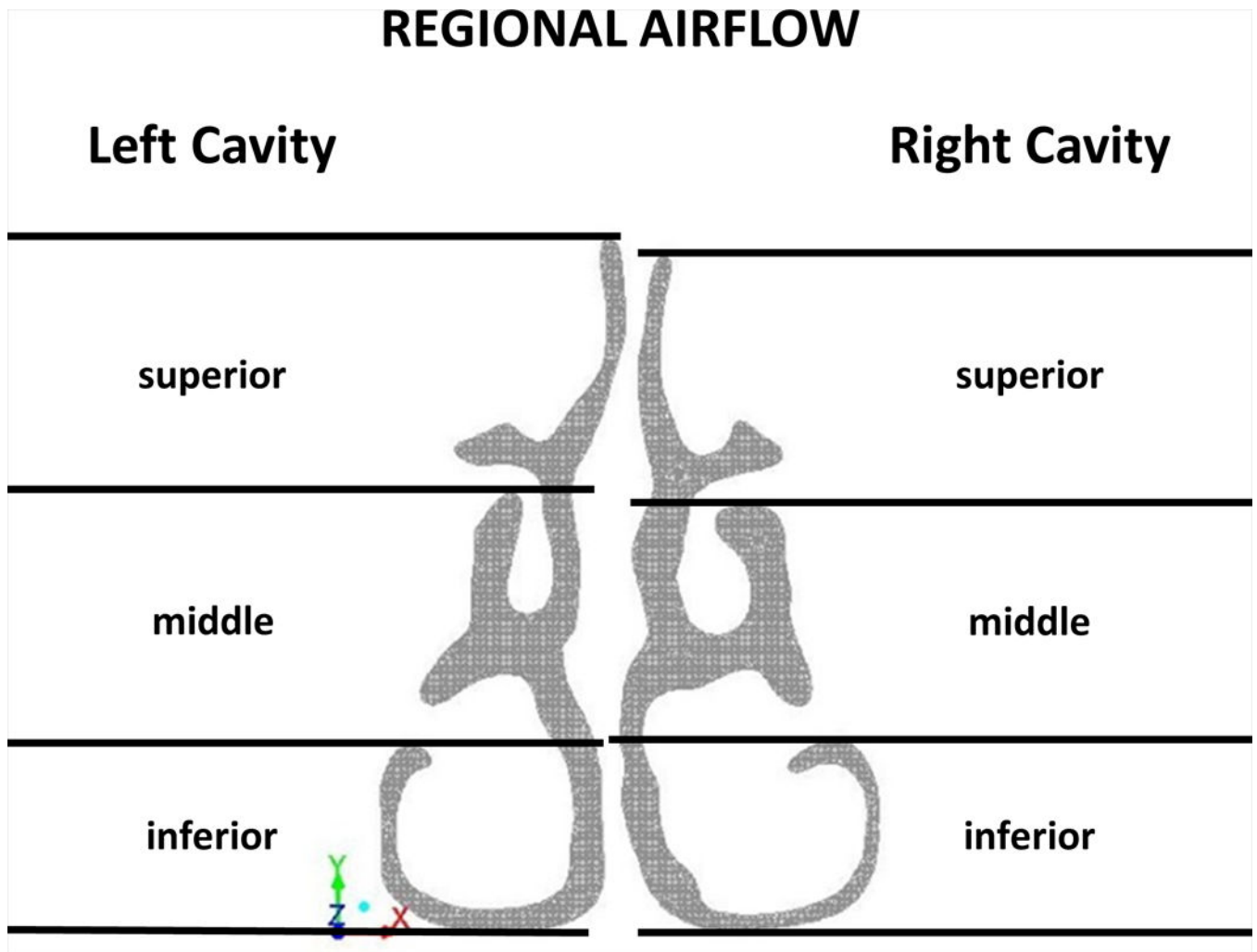
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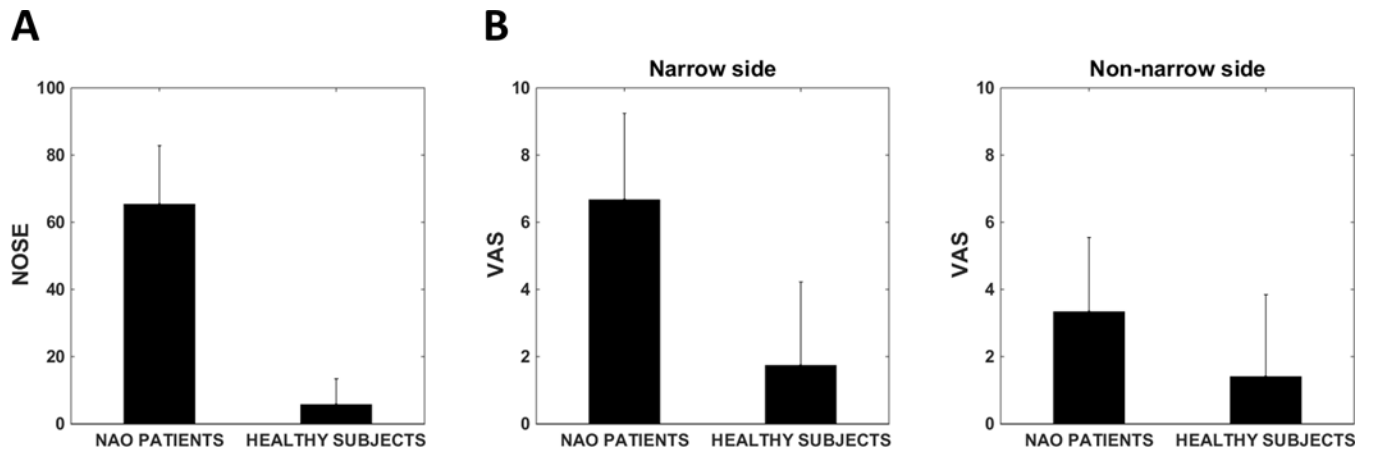
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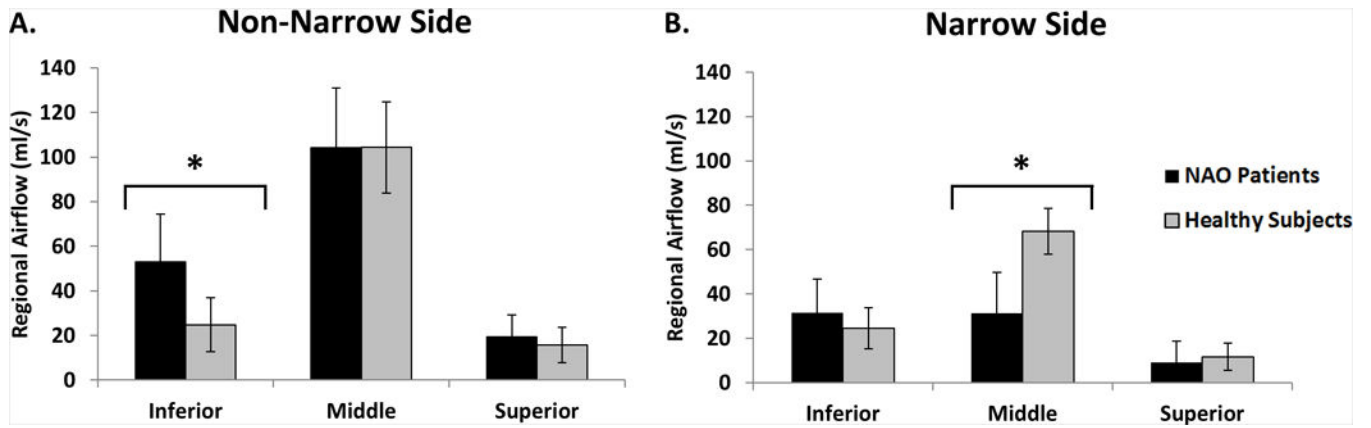
**Figure 1:**  
 (A) CFD nasal airway (sagittal view) demonstrating 11 equally-spaced coronal cross-sections. (B) Coronal CT of NAO patient at D=0.7. (C) Coronal cross-sections of nasal cavity at corresponding relative distance (D).



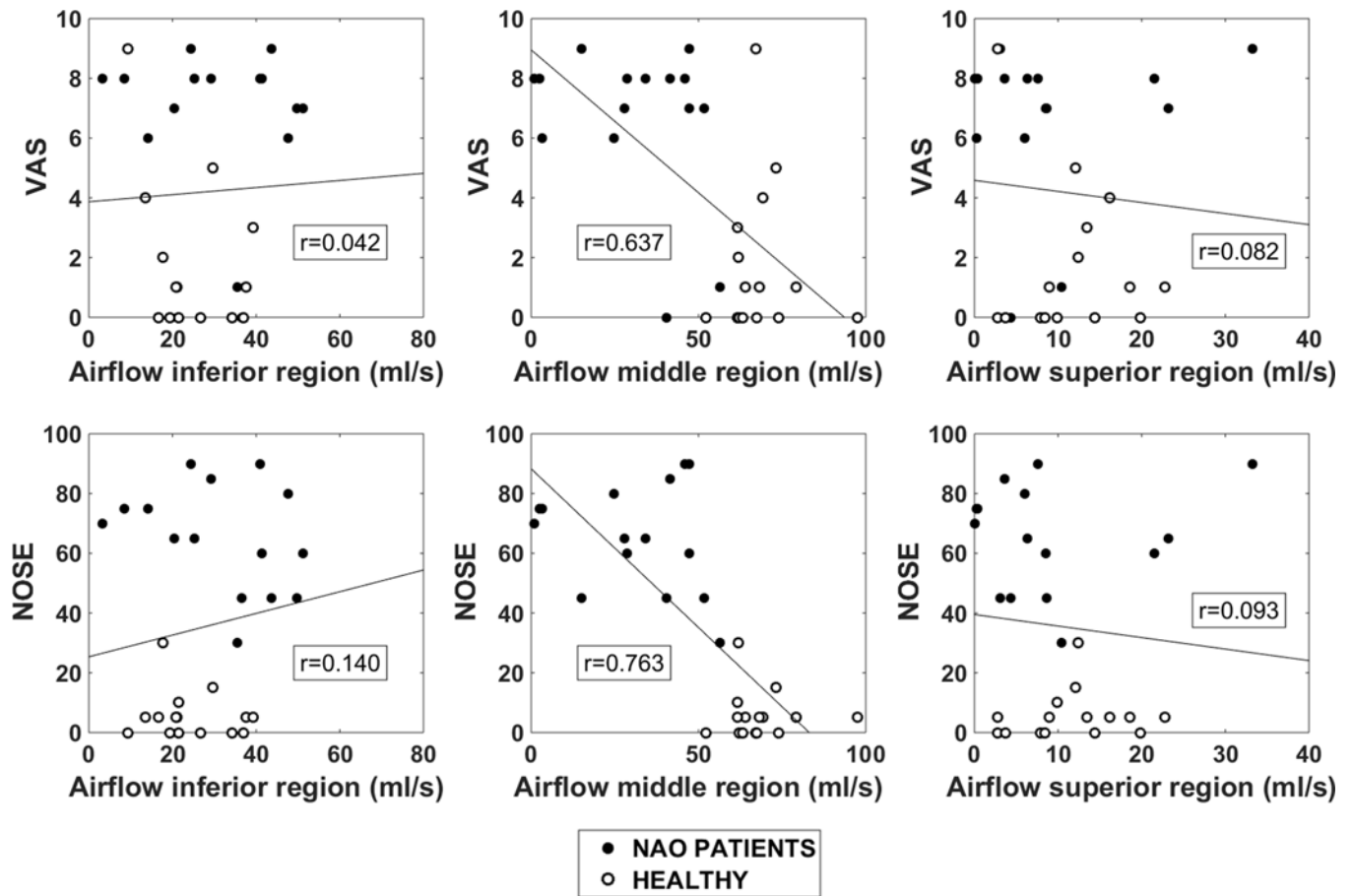
**Figure 2:**  
Each nasal cavity was vertically divided into inferior, middle and superior regions at relative distance  $D=0.7$ .



**Figure 3:** (A) NOSE scores in NAO and healthy cohorts. (B) VAS scores in NAO and healthy cohorts (narrow side). (C) VAS scores in NAO and healthy cohorts (non-narrow side). Error bars:  $\pm 1$  standard deviation.

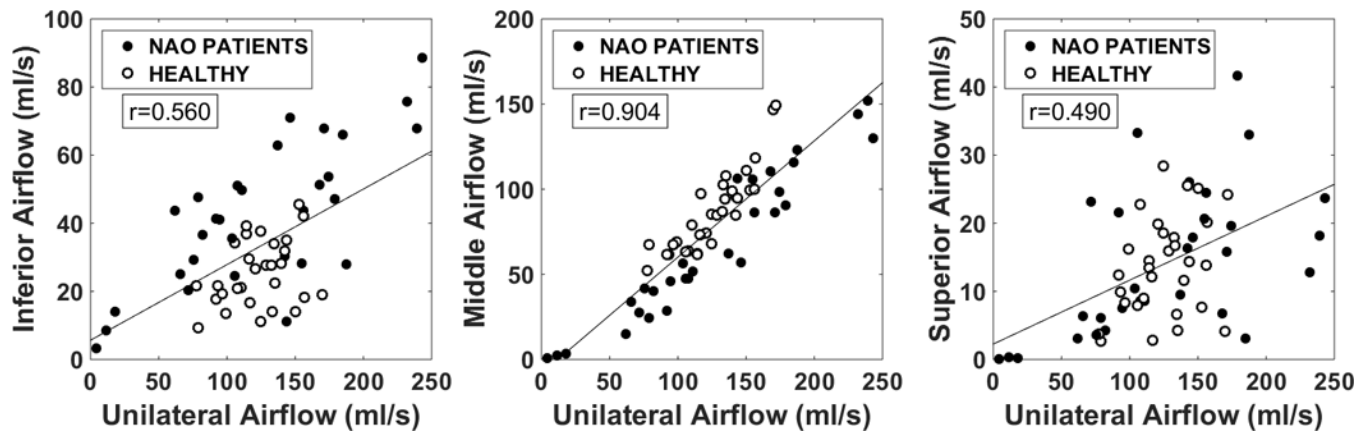


**Figure 4:** Regional airflow distribution in NAO and healthy cohorts, (A) Non-narrow and (B) narrow sides. Asterisk (\*) denotes statistically significant differences. Error bars:  $\pm 1$  standard deviation.

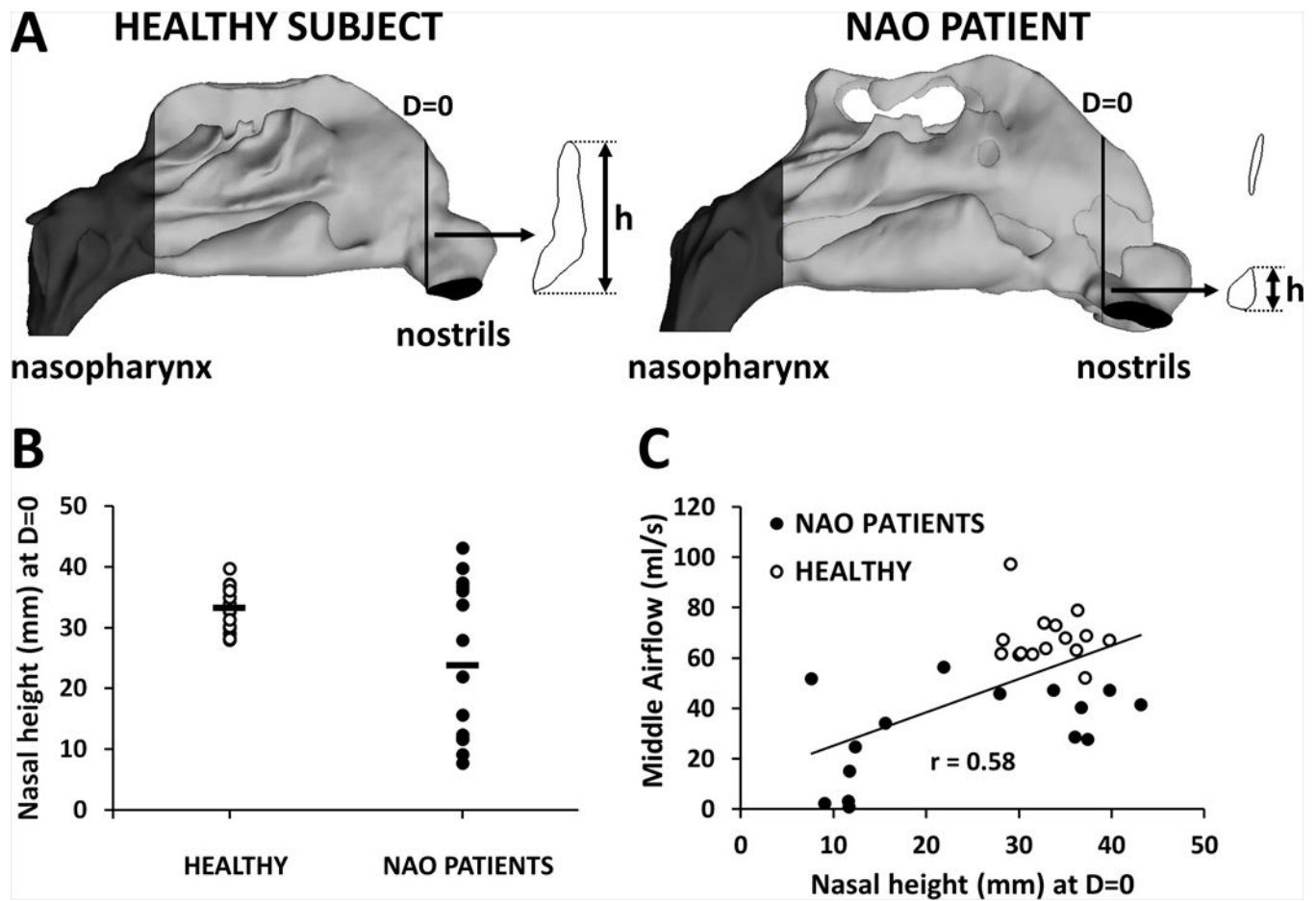


**Figure 5:** Unilateral VAS (top) and NOSE (bottom) scores plotted against regional airflow (inferior, middle, superior) in the narrow side.



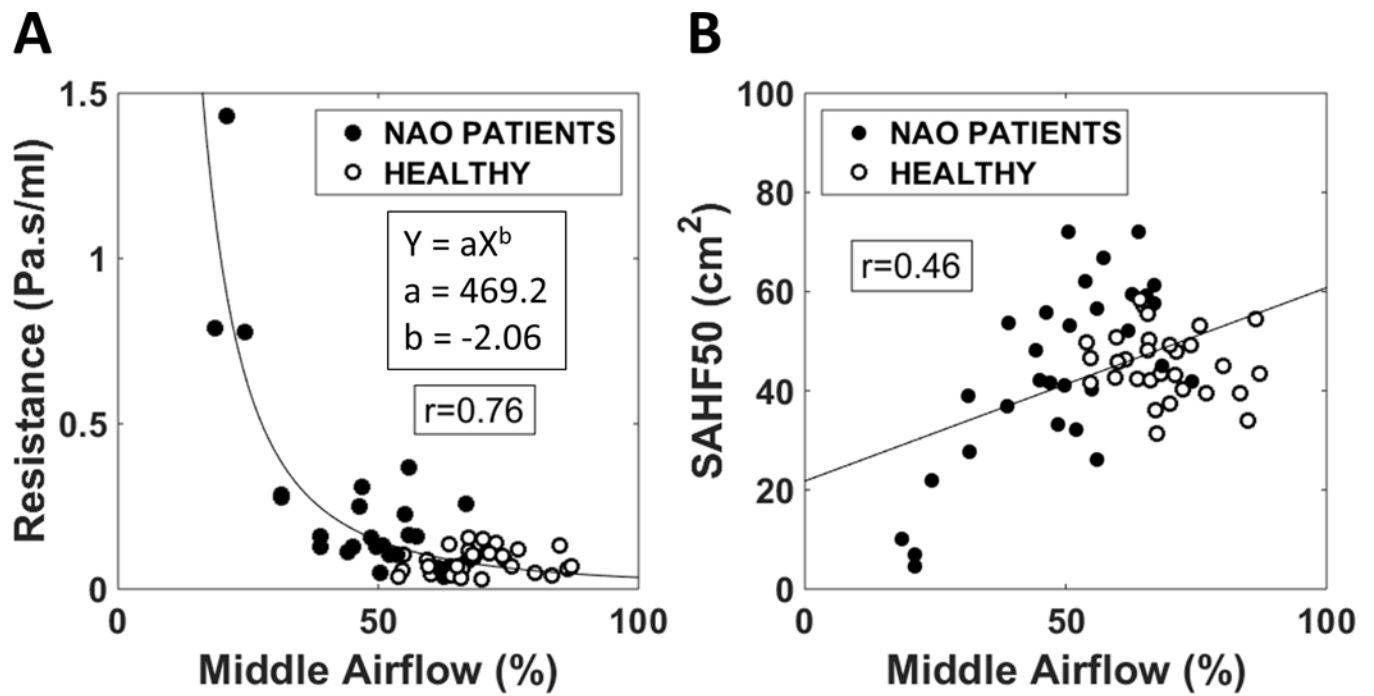


**Figure 6:**  
Unilateral regional airflow vs total unilateral airflow in NAO and healthy cohorts. Both narrow and non-narrow sides included (30 subjects, 60 nasal cavities).



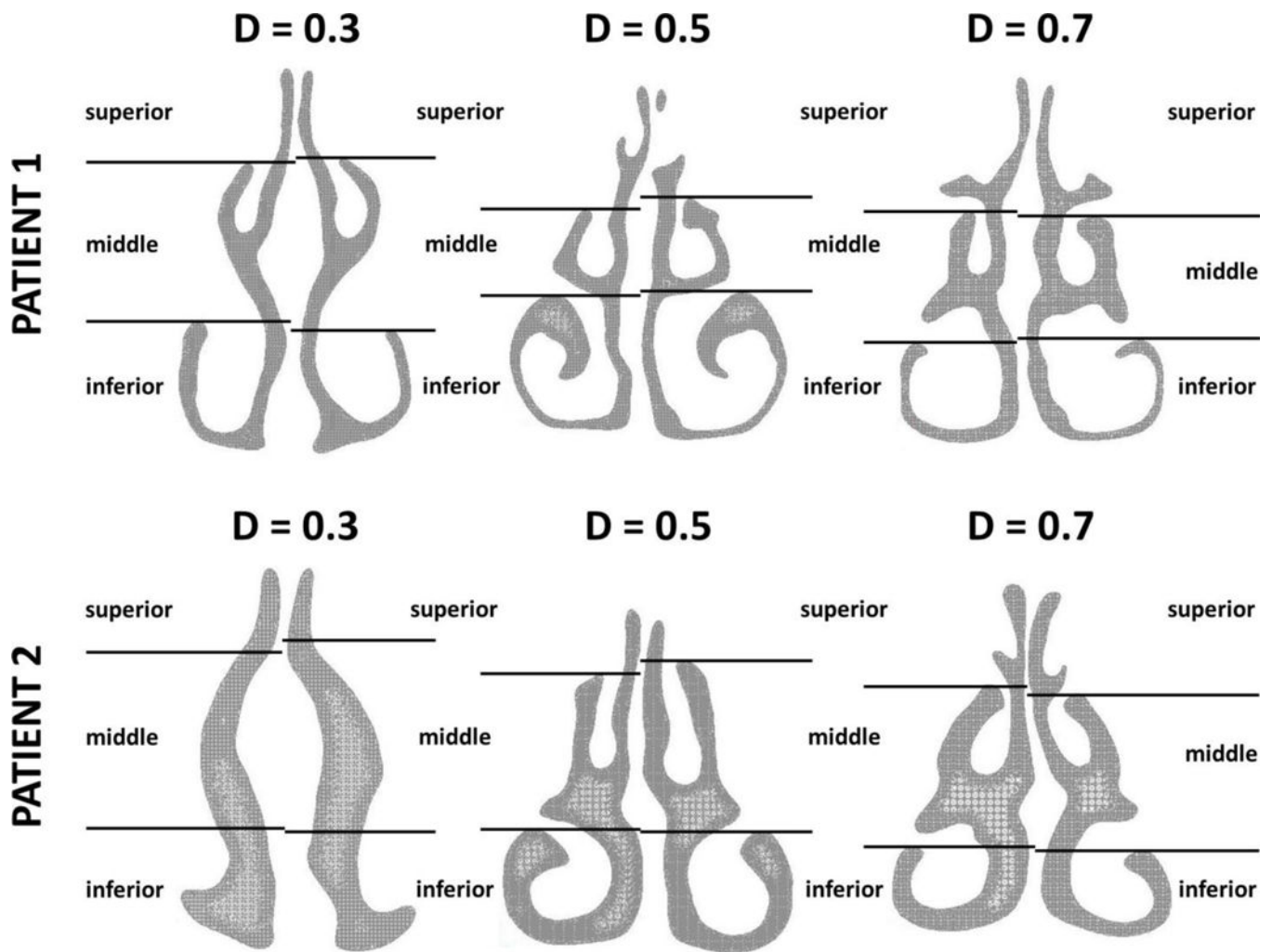
**Figure 7:**

(A,B) Several patients in the NAO cohort had anterior septal deviations, which reduced the nasal height ( $h$ ) measured at  $D=0$  in the narrow side. (C) Middle airflow was lower in NAO patients with a small nasal height at  $D=0$ .



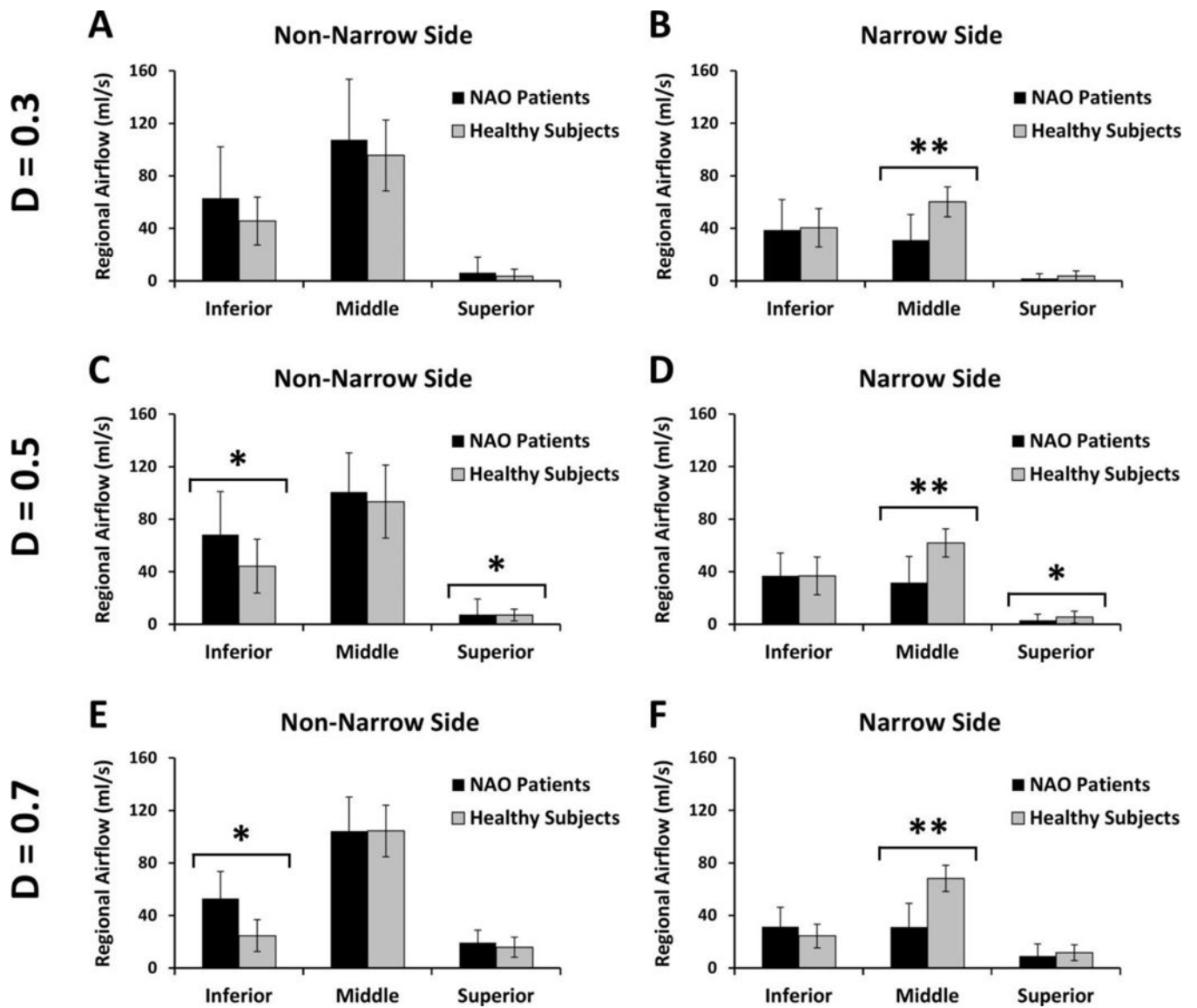
**Figure 8:**

The percentage of unilateral airflow passing through the middle region correlated with (A) the unilateral nasal resistance and (B) the surface area where heat flux exceeds 50 W/m<sup>2</sup> (SAHF50).



**Figure A1 –.**

Definition of inferior, middle, and superior regions in three coronal sections of the nasal cavity ( $D=0.3$ ,  $D=0.5$ , and  $D=0.7$ , where  $D$  is the relative distance from nostrils, see Figure 1.) Each section was divided into inferior, middle, and superior regions using horizontal lines through the ventral lamella of the inferior and middle turbinates. This systematic approach was applied to all sections in all patients, except that section  $D=0.3$  did not always include the inferior and/or middle turbinates. In these patients (such as Patient 2 in this figure), the coordinates used to split section  $D=0.5$  were also used to split section  $D=0.3$ .



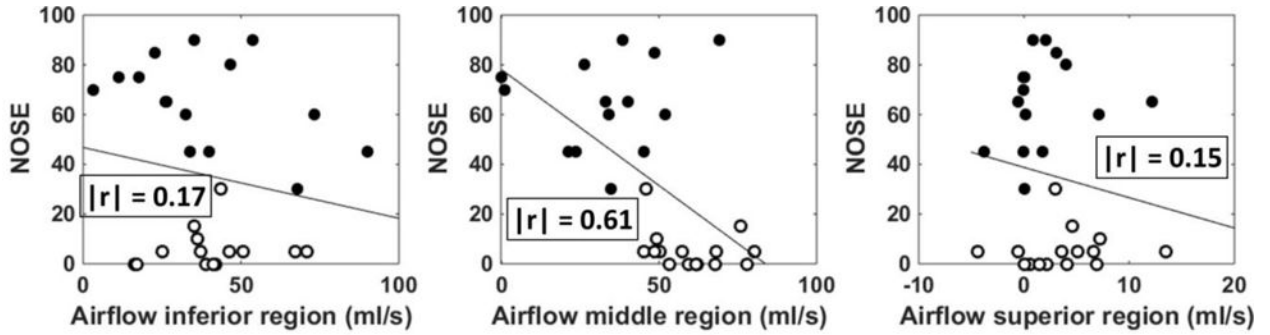
**Figure A2 –.**

Regional airflow distribution in NAO and healthy cohorts. (A,B) Coronal section D=0.3.

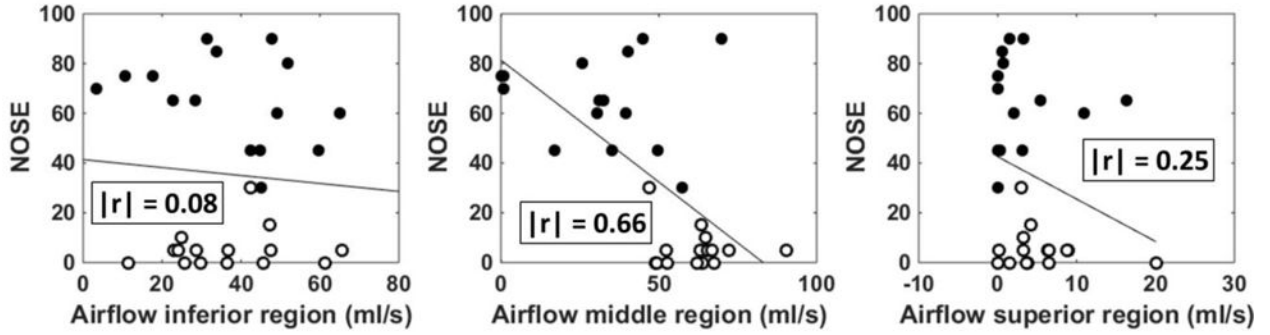
(C,D) Coronal section D=0.5. (E,F) Coronal section D=0.7. Single asterisk (\*) denotes

statistically significant differences at level  $p < 0.05$ . Double asterisk (\*\*) denotes statistically significant differences at level  $p < 0.0002$ .

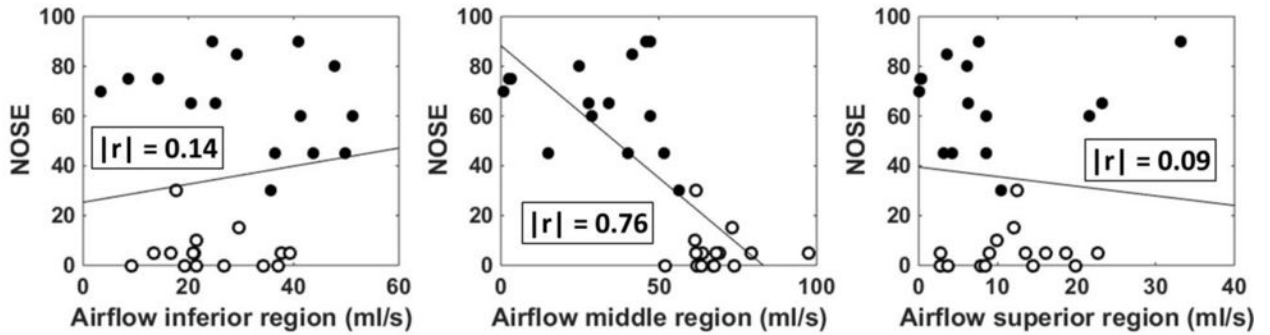
**D = 0.3**



**D = 0.5**

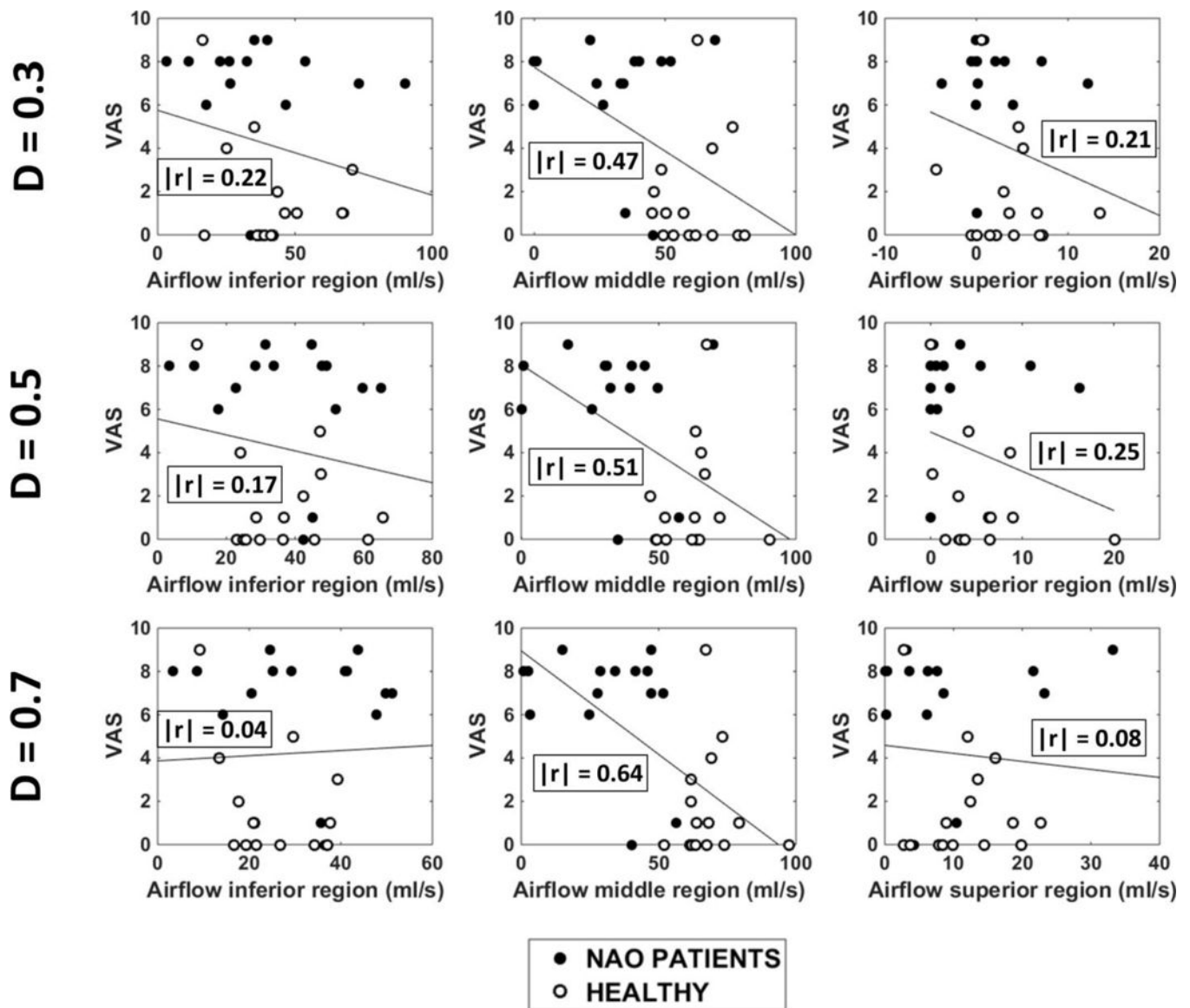


**D = 0.7**



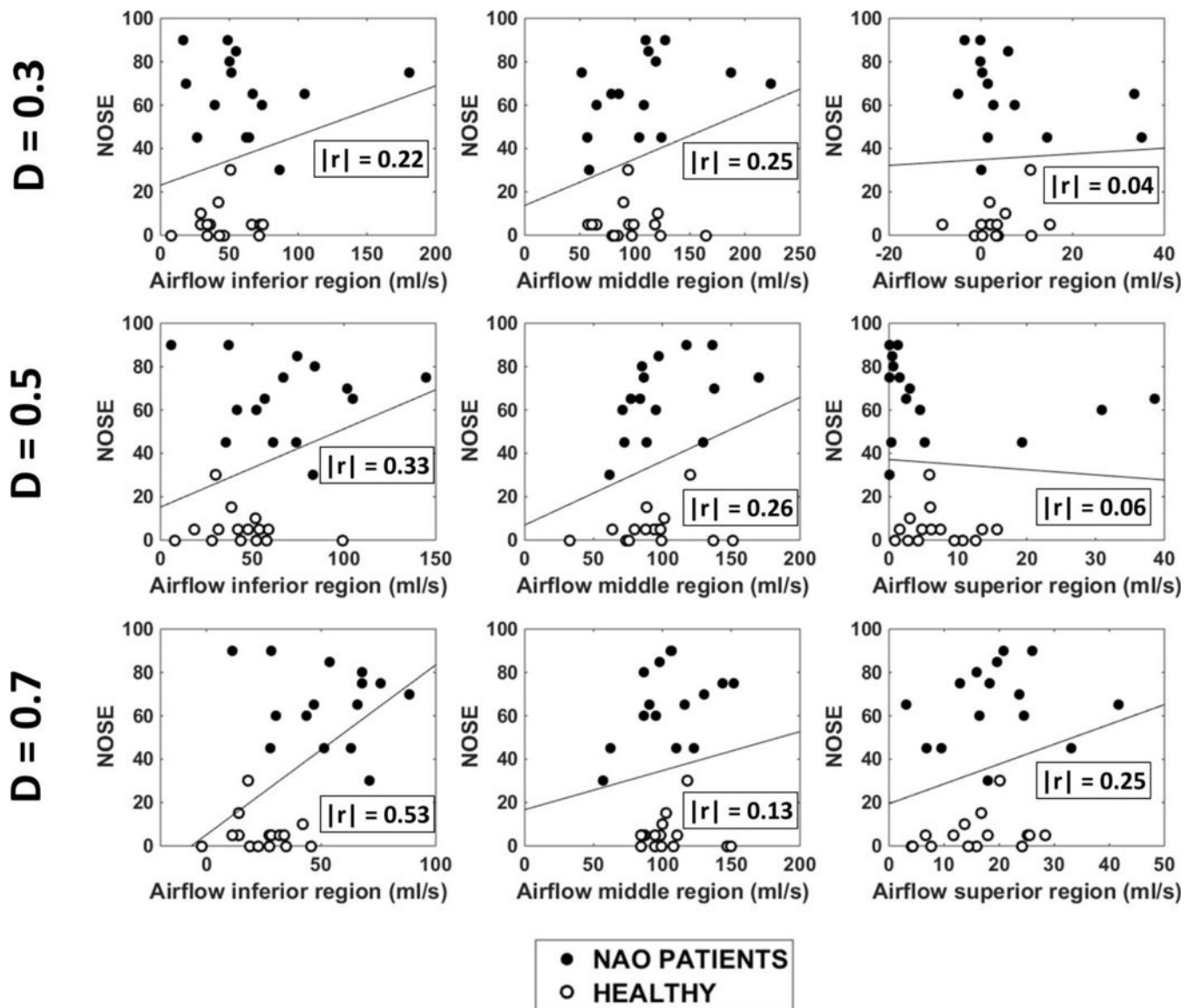
● NAO PATIENTS  
○ HEALTHY

**Figure A3 –.**  
NOSE scores plotted against regional airflow (inferior, middle, and superior) measured unilaterally in the narrow cavity of 15 NAO patients and 15 healthy individuals in three coronal sections (D=0.3, D=0.5, and D=0.7). Abbreviations: D = relative distance from nostrils (see Figure 1); r = Pearson correlation coefficient.



**Figure A4 –.**

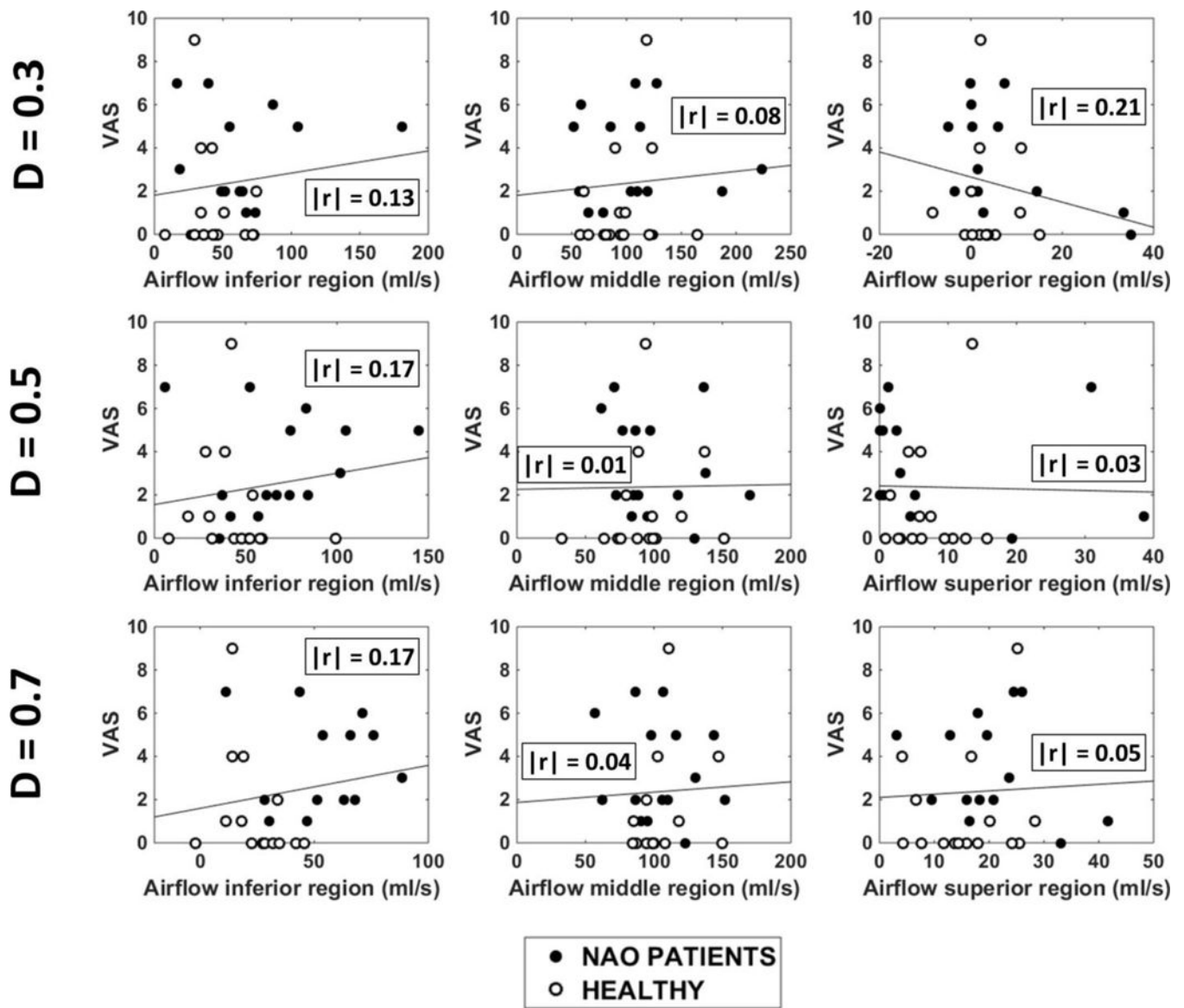
Unilateral VAS scores plotted against regional airflow (inferior, middle, and superior) measured unilaterally in the narrow cavity of 15 NAO patients and 15 healthy individuals in three coronal sections (D=0.3, D=0.5, and D=0.7). Abbreviations: D = relative distance from nostrils (see Figure 1); r = Pearson correlation coefficient.



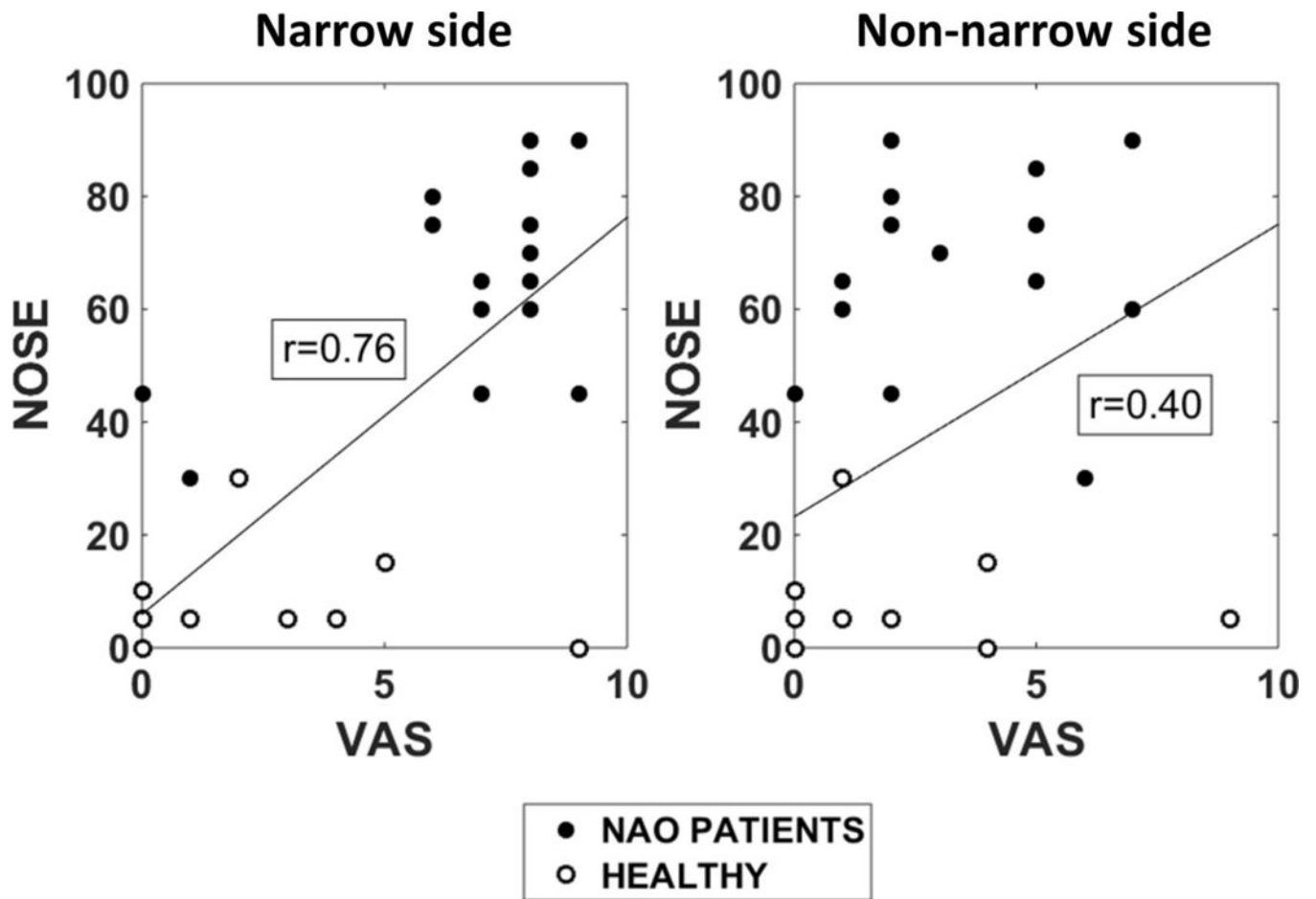
**Figure A5 –.**

NOSE scores plotted against regional airflow (inferior, middle, and superior) measured unilaterally in the non-narrow cavity of 15 NAO patients and 15 healthy individuals in three coronal sections (D=0.3, D=0.5, and D=0.7). Abbreviations: D = relative distance from nostrils (see Figure 1); r = Pearson correlation coefficient.





**Figure A6 --.**  
Unilateral VAS scores plotted against regional airflow (inferior, middle, and superior) measured unilaterally in the non-narrow cavity of 15 NAO patients and 15 healthy individuals in three coronal sections (D=0.3, D=0.5, and D=0.7). Abbreviations: D = relative distance from nostrils (see Figure 1); r = Pearson correlation coefficient.



**Figure A7 –.**

The NOSE score has a stronger correlation with the unilateral VAS score in the narrow side (Pearson  $r = 0.76$ ) than with the unilateral VAS in the non-narrow side (Pearson  $r = 0.40$ ). In each subject, the narrow side was defined as the nasal cavity with lesser unilateral airflow based on the CFD simulations.

**Table 1:**

Unilateral CFD variables previously described as correlating with subjective nasal patency are shown with comparison of mean values between NAO patients and healthy subjects.

CFD Variables (mean $\pm$ standard deviation)	Narrow side			Non-narrow side		
	NAO	Healthy	<i>P</i> value	NAO	Healthy	<i>P</i> value
Unilateral Airflow (ml/s)	72 $\pm$ 34	105 $\pm$ 14	0.0025	177 $\pm$ 34	145 $\pm$ 14	0.0025
Unilateral Resistance (Pa.s/ml)	0.75 $\pm$ 1.45	0.097 $\pm$ 0.040	0.0006	0.12 $\pm$ 0.07	0.07 $\pm$ 0.03	0.031
Unilateral Heat Flux (W/m <sup>2</sup> )	114 $\pm$ 54	167 $\pm$ 27	0.0055	230 $\pm$ 35	212 $\pm$ 15	0.12
Surface area where heat flux > 50 W/m <sup>2</sup> (cm <sup>2</sup> )	30 $\pm$ 13	41 $\pm$ 5	0.007	58 $\pm$ 8	50 $\pm$ 5	0.0048

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**Table 2:**

Pearson and Kendall's tau correlation coefficients, 95% confidence intervals (CI), and *P* values between CFD variables and subjective nasal patency (NOSE and VAS scores), narrow side only.

Subjective scores vs objective variable (Narrow side)	Pearson correlation			Kendall's tau correlation		
	r	95% CI	P Value	rho	95% CI	P Value
<b>NOSE</b>						
Unilateral Airflow (ml/s)	-0.55	-0.24 to -0.76	0.0016	-0.35	-0.14 to -0.56	0.001
Unilateral Resistance (Pa.s/ml)	-	-	N.S.	0.40	0.21 to 0.58	<0.0001
Unilateral Heat Flux (W/m <sup>2</sup> )	-0.48	-0.14 to -0.72	0.0075	-	-	N.S.
SAHF50 (cm <sup>2</sup> )	-0.55	-0.24 to -0.76	0.0016	-0.38	-0.14 to -0.62	0.0016
Inferior region airflow (ml/s)	-	-	N.S.	-	-	N.S.
Middle region airflow (ml/s)	-0.76	-0.56 to -0.88	<0.0001	-0.54	-0.38 to -0.69	<0.0001
Superior region airflow (ml/s)	-	-	N.S.	-	-	N.S.
<b>VAS</b>						
Unilateral Airflow (ml/s)	-0.49	-0.16 to -0.73	0.0056	-0.32	-0.12 to -0.53	0.0018
Unilateral Resistance (Pa.s/ml)	-	-	N.S.	0.41	0.22 to 0.61	<0.0001
Unilateral Heat Flux (W/m <sup>2</sup> )	-0.43	-0.09 to -0.69	0.0166	-	-	N.S.
SAHF50(cm <sup>2</sup> )	-0.51	-0.19 to -0.74	0.0038	-0.37	-0.17 to -0.58	0.0004
Inferior region airflow (ml/s)	-	-	N.S.	-	-	N.S.
Middle region airflow (ml/s)	-0.64	-0.36 to -0.81	0.0002	-0.38	-0.19 to -0.58	0.0002
Superior region airflow (ml/s)	-	-	N.S.	-	-	N.S.

Abbreviations: N.S. = Not significant; SAHF50 = Surface area where heat flux > 50 W/m<sup>2</sup>.

**Table A1 –**

Diagnosis, predominant side of obstruction, and surgical procedure in the cohort of 15 nasal airway obstruction (NAO) patients.

Subject (Gender)	Diagnosis	Predominant Side of Obstruction	Surgical Procedure
1 (Male)	Deviated Nasal Septum	Bilateral	Septorhinoplasty
2 (Female)	Deviated Nasal Septum Right inferior turbinate hypertrophy	Left	Septoplasty Right inferior turbinectomy
3 (Male)	Deviated Nasal Septum	Left	Septoplasty
4 (Male)	Deviated Nasal Septum	Left	Septoplasty
5 (Male)	Deviated Nasal Septum Left inferior turbinate hypertrophy	Bilateral	Septoplasty Left inferior turbinectomy
6 (Male)	Deviated Nasal Septum	Right	Septoplasty (with slight lateralization of inferior turbinates)
7 (Male)	Deviated Nasal Septum External Nasal Deformity	Left	Septorhinoplasty
8 (Female)	Deviated Nasal Septum External Nasal Deformity Inferior Turbinate Hypertrophy	Right	Septorhinoplasty Turbinectomy
9 (Male)	Deviated Nasal Septum External Nasal Deformity	Right	Septorhinoplasty
10 (Male)	Deviated Nasal Septum Bilateral Vestibular Stenosis	Bilateral	Repair of bilateral vestibular stenosis Septoplasty
11 (Female)	Deviated Nasal Septum Bilateral Vestibular Stenosis Bilateral Inferior Turbinate Hypertrophy	Right	Septoplasty Repair of bilateral vestibular stenosis with butterfly onlay graft Bilateral turbinectomy
12 (Female)	Deviated Nasal Septum	Right	Septoplasty
13 (Male)	Deviated Nasal Septum Bilateral Vestibular Stenosis	Bilateral	Repair of bilateral vestibular stenosis Septoplasty
14 (Male)	Deviated Nasal Septum	Right	Septoplasty
15 (Female)	Deviated Nasal Septum Bilateral Vestibular Stenosis	Bilateral	Septoplasty Repair of bilateral vestibular stenosis with septal cartilage butterfly onlay graft

**Table A2 –**

Pearson correlation coefficients (r), 95% confidence intervals, and P values between subjective nasal patency scores (NOSE and VAS) and regional airflow (inferior, middle, superior) measured either in the narrow side or in the non-narrow side at sections D=0.3, D=0.5, and D=0.7. N.S. = Not significant at level  $p < 0.05$ .

<b>NARROW SIDE</b>						
	NOSE			VAS		
	r	95% CI	P value	r	95% CI	P value
Section D = 0.3						
Inferior airflow (ml/s)	N.S.	-	-	N.S.	-	-
Middle airflow (ml/s)	-0.61	-0.80 to -0.32	< 0.001	-0.47	-0.71 to -0.13	0.009
Superior airflow (ml/s)	N.S.	-	-	N.S.	-	-
Section D = 0.5						
Inferior airflow (ml/s)	N.S.	-	-	N.S.	-	-
Middle airflow (ml/s)	-0.66	-0.82 to -0.39	< 0.001	-0.51	-0.74 to -0.19	0.004
Superior airflow (ml/s)	N.S.	-	-	N.S.	-	-
Section D = 0.7						
Inferior airflow (ml/s)	N.S.	-	-	N.S.	-	-
Middle airflow (ml/s)	-0.76	-0.88 to -0.56	< 0.001	-0.64	-0.81 to -0.36	< 0.001
Superior airflow (ml/s)	N.S.	-	-	N.S.	-	-
<b>NON-NARROW SIDE</b>						
	NOSE			VAS		
	r	95% CI	P value	r	95% CI	P value
Section D = 0.3						
Inferior airflow (ml/s)	N.S.	-	-	N.S.	-	-
Middle airflow (ml/s)	N.S.	-	-	N.S.	-	-
Superior airflow (ml/s)	N.S.	-	-	N.S.	-	-
Section D = 0.5						
Inferior airflow (ml/s)	N.S.	-	-	N.S.	-	-
Middle airflow (ml/s)	N.S.	-	-	N.S.	-	-
Superior airflow (ml/s)	N.S.	-	-	N.S.	-	-
Section D = 0.7						
Inferior airflow (ml/s)	0.53	0.21 to 0.75	0.003	N.S.	-	-
Middle airflow (ml/s)	N.S.	-	-	N.S.	-	-
Superior airflow (ml/s)	N.S.	-	-	N.S.	-	-