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SCIENTIFIC INVESTIGATIONS

Nasal resistance and inflammation: mechanisms for obstructive sleep apnea from chronic rhinosinusitis

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Study Objectives: We have previously estimated that the prevalence of obstructive sleep apnea (OSA) among World Trade Center rescue and recovery workers is 75% and identified that having symptoms of chronic rhinosinusitis (CRS) is an independent risk factor for OSA in this population. Nasal inflammation and/or elevated awake nasal resistance that carried over into sleep could explain this association. To understand the mechanism(s) for the elevated risk of OSA observed in World Trade Center responders with CRS symptoms we examined if elevated awake supine nasal resistance was associated with OSA, CRS and/or nasal inflammatory biomarkers.

Methods: A total of 601 individuals (83% male, average age 53 years, body mass index = 29.9 ± 5.5 kg/m^2) enrolled in the World Trade Center Health Program and without significant snoring prior to September 11, 2001 underwent 2 nights of home sleep apnea testing, measurements of anterior rhinomanometry in the supine position, and nasal lavage.

Results: Awake supine nasal resistance was not associated with OSA; 74.8% and 74.4% of the participants with low and high nasal resistance respectively, had OSA. Patients with CRS had elevated nasal inflammatory markers (interleukin 6, interleukin 8, eosinophilic cationic protein, and neutrophil) but did not have high nasal resistance. Nasal inflammatory markers were not correlated with nasal resistance.

Conclusions: As awake nasal resistance did not explain the relationship of CRS to OSA in this large and well characterized dataset, our findings suggest that either "sleep" nasal resistance or other factors such as increased supraglottic inflammation, perhaps through impairing upper airway reflex mechanisms, or systemic inflammation are involved in the pathophysiology of OSA in the World Trade Center population.

Keywords: obstructive sleep apnea, chronic rhinosinusitis, nasal resistance, nasal inflammation, WTC dust exposure

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BRIEF SUMMARY

Current Knowledge/Study Rationale: There is conflicting evidence regarding the role of elevated nasal resistance as a pathophysiologic mechanism for obstructive sleep apnea (OSA). We previously identified chronic rhinosinusitis as a risk factor for OSA in World Trade Center dust exposed individuals and this study tests whether elevated nasal resistance and nasal inflammation are mechanisms for OSA.

Study Impact: We were unable to demonstrate that the high prevalence of OSA in World Trade Center dust exposed individuals is due to high awake nasal resistance. These findings are similar to prior studies in other populations and suggest limited clinical utility of anterior nasal resistance in the assessment of patients with OSA.

INTRODUCTION

A significant number of World Trade Center (WTC) dust-exposed responders and rescue workers report chronic nasal and upper airway symptoms following the WTC disaster.[1,2] In addition, sleep complaints are common and obstructive sleep apnea (OSA)[3] is in the top 5 certified conditions for medical coverage in the WTC Health Program (WTC HP). We previously estimated the prevalence of OSA at 75% in this population,[4,5] and reported that symptoms of chronic rhinosinusitis (CRS) are an independent risk factor for OSA after controlling for age, body mass index (BMI), sex, and other factors.[5] OSA is a chronic condition with recurrent episodes of partial or complete upper airway collapse during sleep. The main risk factors for OSA in the WTC[5–7] and general population are obesity, age, and male sex; OSA is highly prevalent in the general middle-aged adult population, with estimates ranging from 34–50% in males and 17–23% in females.[8–10]

Exposure via inhalation to toxic dust/fumes causing upper airway inflammation resulting in mucosal congestion is a

potential mechanism for development of compromised upper airway patency during sleep in the WTC population, as the effect of nasal obstruction and increased nasal resistance from such inflammation could lead to greater downstream upper airway collapsibility. There is increasing evidence of inflammation in both OSA and CRS with high serum/tissue levels of inflammatory markers such as C reactive protein, interleukin 1, interleukin 6 (IL6), interleukin 8 (IL8), and tumor necrosis factor-alpha.[11,12] In previous work, we have also shown elevated inflammatory biomarkers collected from the nasal cavities of participants with moderate to severe OSA.[13] This inflammation could cause increased upper airway/nasal resistance via local swelling and edema.[14] If CRS is a causative factor for OSA, elimination or reduction of CRS may play a role in preventing or treating OSA.

There is some evidence in the published literature suggesting chronic nasal obstruction/congestion as a risk factor for snoring and OSA.[15,16] The plausible biological pathways for high nasal resistance (as a measure of nasal obstruction) leading to OSA are (1) increased negative pressure required to maintain airflow resulting in upper airway collapse, (2) switch to oral breathing, (3) reduced nasal ventilatory reflex, and (4) reduced amounts of nitric oxide.[17] In fact, artificially inducing partial or complete nasal obstruction induces OSA in normal individuals.[18,19] However, with the exception of 2 studies,[20,21] most clinical and epidemiological adult populations have failed to show a relationship between nasal resistance and OSA severity.[15,16,22–24] In addition, some studies suggest that obesity may mask the independent effect of nasal obstruction in the pathophysiology of OSA.[23,25] Despite the preponderance of evidence against the impact of awake nasal resistance in OSA, reviews summarizing the role of nasal obstruction in OSA emphasize the need for additional data relating nasal resistance and OSA in large carefully characterized populations with objective measurements of both OSA and nasal resistance.

In order to examine the possible mechanisms linking the observed relationship between OSA and CRS, we measured (1) nasal resistance and (2) nasal inflammation in our study participants. We hypothesized that (1) awake nasal resistance (with carryover into sleep) and (2) inflammatory biomarkers from nasal cavities are elevated in participants with OSA.

We present analyses of data acquired in WTCSNORE from individuals enrolled in the WTC General Responders' Cohort at the WTC HP clinical centers of excellence at the Environmental and Occupational Health Sciences Institute of Rutgers Biomedical and Health Sciences, the New York University Grossman School of Medicine/Bellevue Hospital, and the Icahn School of Medicine at Mount Sinai.

METHODS

Additional detail on the methods has been previously published.[5,13,26] Preliminary findings have been presented as posters/abstracts at the American Thoracic Society International conferences.

The study protocol was approved by the institutional review boards of Rutgers Biomedical and Health Sciences (Pro2012002164), New York University School of Medicine (I12-02578), and the Icahn School of Medicine at Mount Sinai (HS#16-00511), and all individuals signed informed consent.

Study population and clinical evaluation

Between February 2013 and February 2017, we recruited 634 individuals without self-reported history of snoring or OSA before September 11, 2001 from a multidimensional interviewer-administered exposure and snoring questionnaire that was administered at the time of initial or baseline evaluation in the WTC HP clinical centers of excellence. All participants in the WTC General Responders' Cohort of the 3 WTC HP clinical centers of excellence, or previously seen and listed in the database were included. Exclusion criteria were as follows: (1) Gross skeletal alterations affecting the upper airway assessed by physician general impression (eg, micrognathia). (2) Unstable chronic medical conditions known to affect OSA (eg, CHF, stroke). (3) Pregnancy or intent to become pregnant within the period of the protocol. (4) Inability to sign informed consent form. (5) Being a habitual snorer or having a diagnosis of OSA before September 11, 2001. (6) Currently on treatment for OSA. Participants who had discontinued OSA treatment for > 1 year at time of enrollment were eligible for participation.

Demographic information, comorbid conditions, current medication use, self-reported nasal and sleep symptoms, nasal lavage and measurements of nasal resistance in the seated and supine position before and after decongestion with a 0.1% xylometazoline solution were obtained and 2-night home sleep testing (HST; Apnea Risk Evaluation System Unicorder) was performed.

Demographic information

Information collected following recruitment to the study included age, sex, and measured BMI, current and 3 years self-reported prior weight, current and past smoking, current regular or intermittent alcohol use, snoring, sleepiness, and sleep quality. Current medication use including nasal and oral corticosteroid use, and use of nasal or oral anti-inflammatories and decongestants.

Exposure assessment

Self-reported WTC exposure level was obtained from the WTC General Responders' Cohort Data Center, and classified as very high, high, intermediate, or low.[2]

Definition of CRS

As previously described,[5] a nasal symptom score was assigned to each individual based on current symptoms present for > 8 weeks. Presence of ≥ 3 symptoms (see supplemental material) was considered indicative of CRS.[27] CRS was also separately assessed using the 2012 European Position Paper on Rhinosinusitis and Nasal Polyps for epidemiological studies.[28]

Definition of OSA

As described in our previous publication[5] OSA was assessed by 2 nights of HST using the Apnea Risk Evaluation System (ARES Unicorder, Watermark Medical, West Palm Beach, FL). OSA was defined as apnea-hypopnea index (4% oxygen desaturation for hypopnea) (AHI4%) ≥ 5 events/h or respiratory

disturbance index (RDI) ≥ 15 events/h. Mild OSA was defined as AHI4% < 15 events/h when OSA is present, moderate as AHI4% between 15 and 30 events/h, and severe as AHI4% ≥ 30 events/h. Each index was a weighted average for the 2 nights based on the respective recording duration.

Objective assessment of nasal pathology

We assessed nasal resistance using the 4-phase rhinomanometer (RhinoLab GmbH, Rendsburg, Germany). It consists of simultaneous measurement of airflow through the nares and the differential pressure required for its generation. Parameters obtained include the unilateral effective and vertex resistances during inspiration, expiration and during the entire breath. "Effective Resistance (Reff)" describes the computerized measurement and calculation of 2000 effective flow and differential pressure measurements recorded for each averaged breath. Total nasal resistance (TNR) was calculated using Ohm's law modeling the 2 nostrils of the nose as parallel resistors using the following formula: TNR = Rright * Rleft/(Rright + Rleft) and is presented after logarithmic transformation as logTNR. Measurements were performed with individuals in the seated and supine position before and 10 minutes after decongestion with 0.1% xylometazoline solution) in a quiet room with a constant temperature, as temperature has been shown to affect nasal patency.[29,30] After each nasal resistance measurement, participants provided a self-reported perception rating of the degree of congestion through each nostril using a visual analog scale. The individual was asked to rate "how easy it was to breathe" on a scale of 1–10 with 1 being nasal airway completely blocked/congested and 10 being completely open. Visual assessment of nasal polyps, polypoid swelling and inferior turbinate edema in each nostril was performed by a study physician who examined the anterior nares with an otoscope speculum and light and coded these as present or absent.

Nasal inflammation

Nasal lavage samples were collected by trained personnel. A total of 8 mL of sterile saline was instilled, and returned nasal lavage was collected by passive draining into a sterile cup.[31] The returned fluid from both nostrils was pooled. The sample was immediately placed on ice and processed within 2 hours.

Measurement of inflammatory markers in nasal lavage fluid

Nasal lavage fluid was filtered through a 40-μm nylon mesh syringe filter to remove larger particles. The strainer was rinsed with a sputolysin solution (1:20 sputolysin/Dithiothreitol) and the filtrate was centrifuged at 500 g for 10 minutes at 4°C. The cell-free supernatants were aliquoted and stored at −80°C for later analyses of soluble markers. Cells from the pellet were resuspended in 1 mL of a buffered salt solution. If the resuspension appeared bloody, the red blood cells were lysed with a red blood cells lysis buffer. Cell counts were performed on a hemocytometer. The lower limit of detection for the cell concentration was 10,000 cells/mL. For the differential cell counts, cytocentrifuge slides were prepared, fixed, and stained with a Wright-Giemsa stain. On each slide, 200 cells were counted and proportions of epithelial cells, squamous cells, neutrophils, lymphocytes, eosinophils, and basophils were tallied. Cytokines (IL8 and IL6) were measured using high-sensitivity ELISA (BD Biosciences, Franklin Lakes, New Jersey; catalog #BDB550999 and catalog #BDB550799, respectively) and values were expressed in pg/mL. The limits of detection for the IL8 and IL6 assays were 0.8 pg/mL and 2.2 pg/mL, respectively.

Timeline of assessments

Nasal lavage was performed on the same day between pre and post decongestion nasal resistance measurements. In 96% of individuals HST was obtained within 3 months of nasal resistance measurements. The median number of days between HST and nasal resistance measurements was 9 days.

Statistical analysis

OSA and CRS were defined as dichotomous variables as in prior work.[5] Descriptive statistics were calculated and compared between individuals with vs without OSA (OSA+ vs OSA−), high vs low nasal resistance by median split (log(TNR) > 0.77 vs log(TNR) ≤ 0.77) and lowest vs highest quartiles and with vs without CRS (CRS+ vs CRS−) using 2-sample *t* test or Wilcoxon test, when normality assumption did not hold, for continuous variables, and χ^2 test for categorical variables. Correlation coefficients were calculated to describe the correlations between nasal resistance and sleep parameters (eg, AHI4% and RDI, etc). To evaluate the associations of inflammation markers (IL8, IL6, eosinophilic cationic protein, neutrophils) with CRS (+/−) and OSA (+/−), we performed linear regression analyses to compare the levels of inflammation markers between individuals with vs without CRS (CRS+ vs CRS−), and with or without an adjustment for age, BMI, and sex. Similar analysis was also repeated with vs without OSA (OSA+ vs OSA−). Logistic regression analyses with CRS (+/−) and OSA (+/−) were also used to estimate the odds ratios associated with inflammation markers, with or without an adjustment for age, BMI, and sex. Statistical significance was defined by $P < .05$. All statistical analyses were performed using SAS v9.4. SAS Institute Inc, Cary, NC, USA.

RESULTS

After excluding individuals without valid data for OSA, our study population consisted of 601 individuals (451 with OSA), and **Table 1** shows their demographic and clinical characteristics. Mean age is 53 years, with the male sex and overweight/obesity predominance of the WTC General Responders' Cohort. As previously reported, a very high prevalence of OSA (defined as AHI4% ≥ 5 events/h or RDI ≥ 15 events/h) was observed (75%, AHI4% = 15.5 ± 13.8 events/h; RDI = 30.6 ± 15.6 events/h), with predominance of mild OSA (46%, 5 < AHI4% < 15 events/h).[5] Individuals with OSA were more obese, more likely male, older, had more nasal edema and had more CRS symptoms than those without OSA. There were no differences in the proportion of individuals with nasal polyps/polypoid tissue between OSA+/− groups.

Nasal resistance (supine, pre-decongestion)

Contrary to our hypothesis, we did not see an association between OSA and TNR (**Figure 1**) as either a continuous variable

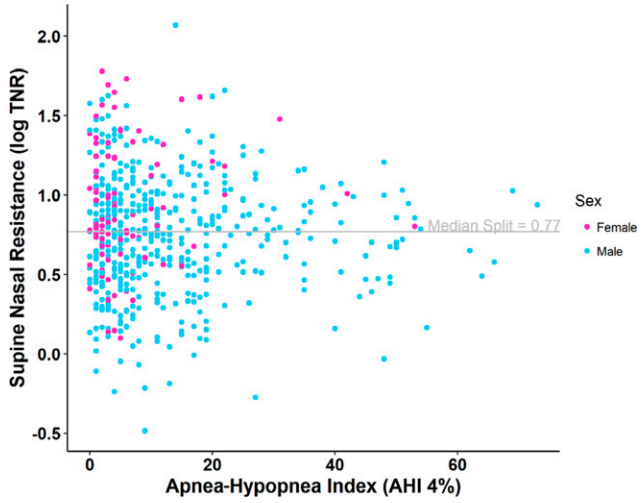
Table 1—Characteristics of the participants overall study, and comparisons between those with and without OSA.

	All (n = 601)	OSA+ (n = 451)	OSA− (n = 150)	*P*
Age (years)	52.8 ± 8.5	53.6 ± 8.3	50.2 ± 8.7	< .0001
Sex				< .0001
Male (%)	498 (83)	392 (87)	106 (71)	
Female (%)	103 (17)	59 (13)	44 (29)	
BMI (kg/m^2)	29.9 ± 5.5	30.7 ± 5.5	27.4 ± 4.7	< .0001
WTC exposure level (n = 525)				ns
Very high + high	94 (17.9)	72 (18.4)	22 (16.4)	
Intermediate	346 (65.9)	259 (66.2)	87 (64.9)	
Low	85 (16.2)	60 (15.3)	25 (18.7)	
Nasal symptom score (n = 586)	2.4 ± 2.2	2.5 ± 2.3	2.0 ± 2.1	.02
CRS+ WTC (≥ 3) (%)	255 (42.4)	204 (45.2)	51 (34)	.04
CRS+ EPOS (≥ 2) (%)	275 (45.8)	218 (48.3)	57 (38)	.03
Snoring (%) (n = 598)	302 (50.5)	254 (56.7)	48 (32.0)	< .0001
ESS (n = 596)	8.2 ± 4.8	8.3 ± 4.9	7.9 ± 4.5	ns
FOSQ (n = 545)	17.5 ± 2.6	17.4 ± 2.7	17.7 ± 2.4	ns
Nasal edema (%)	12.0	14.4	4.8	.003
Nasal polyps (%)	3.1	2.5	4.8	ns
Nasal polypoid swelling (%)	6.2	5.2	8.8	ns
Asthma (%)	16.5	17.5	13.3	ns

Values are presented as mean ± standard deviation or n (%). Additional details are in Sunderram et al.[5] BMI = body mass index, CRS = chronic rhinosinusitis, EPOS = European Position Paper on Rhinosinusitis and Nasal Polyps, ESS = Epworth Sleepiness Scale, FOSQ = Functional Outcomes of Sleep Questionnaire, ns = not statistically significant, OSA = obstructive sleep apnea, WTC = World Trade Center.

(correlation estimate for supine logTNR [95% Confidence Interval] for logAHI4% = 0.003 [−0.09, 0.1 *P* = .9] and logRDI = 0.02 [−0.08, 0.11], *P* = .7) or when comparing OSA+ vs OSA− individuals (supine logTNR in OSA+ vs OSA− = 0.77 ± 0.37 vs 0.80 ± 0.38, *P* = ns). **Table 2** compares individuals with high nasal resistance (logTNR > 0.77) vs low nasal resistance. The proportion of individuals with OSA and severity of OSA (AHI4%, RDI) was not different between high and low nasal resistance groups. Findings were unchanged when controlled for age, BMI, and sex (**Table S1** in the supplemental material) and for comorbidities and medications (**Table S2** in the supplemental material). Results were similar when the highest and lowest quartiles of nasal resistance were compared (**Table S7** and **Figure S1** in the supplemental material). Since nasal resistance can be influenced by sex, age, body position, and BMI, we performed analyses of the relationship between these factors and nasal resistance before and after the use of a nasal decongestant. Females showed significantly higher nasal resistance than males in both supine and sitting positions, before and after decongestant (**Figure 2**; **Table S3** in the supplemental material). Both males and females showed a significant increase in nasal resistance from sitting to supine position prior to decongestant. Decongestion decreased nasal resistance significantly within the same position and abrogated the nasal resistance increase with body position change from sitting to supine in both males and females (**Figure 2**). No correlation was found between BMI and nasal resistance (*r* = .023, *P* = NS) in either sex. We also assessed the relationship between AHI and the change in nasal resistance (supine to sitting position) using Pearson correlation. No significant relationships were observed in either males or females (data not shown).

Figure 1—Scatter plot of OSA severity by AHI 4% (x-axis) and supine nasal resistance log TNR (y-axis).



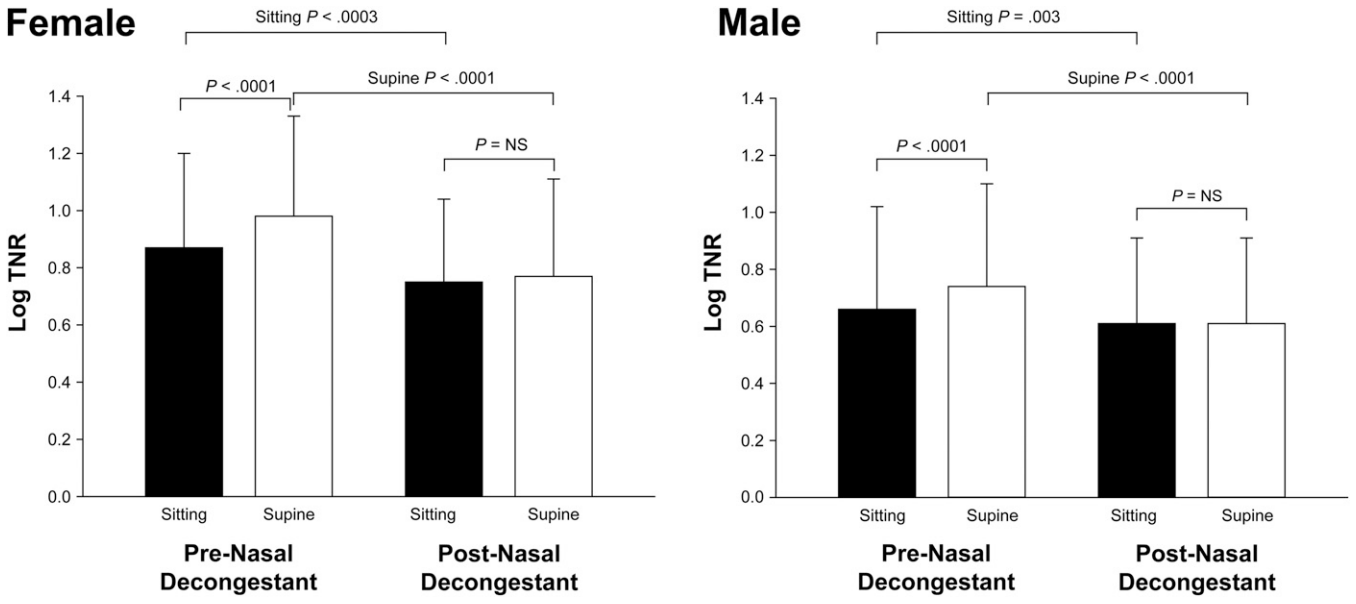
AHI4% = apnea-hypopnea index (hypopnea associated with 4% oxygen desaturation), OSA = obstructive sleep apnea, logTNR = logarithmic value of total nasal resistance.

Table 2—Comparison of individuals with high and low nasal resistance.

	High Nasal Resistance [logTNR > 0.77] (n = 278)	Low Nasal Resistance [logTNR ≤ 0.77] (n = 277)	*P*
Age (years)	52.2 ± 8	53.5 ± 9	.06
BMI (kg/m^2)	30.1 ± 5	29.7 ± 5	ns
% female	23%	12%	< .001
Snoring %	49.5%	52.2%	ns
ESS	8.0 ± 4.7	8.5 ± 4.9	ns
OSA %	74.8%	74.4%	ns
AHI4% events/h	12.2 ± 12.8	12.2 ± 13.4	ns
RDI events/h	25.6 ± 16.0	25.3 ± 16.9	ns
CRS score (n = 540)	2.47 ± 2.24	2.33 ± 2.2	ns
CRS+ WTC	44.3%	43.8%	ns
CRS+ EPOS	48%	46%	ns
Perception of congestion	5.8 ± 2.2	6.2 ± 2.1	.03
Nasal edema (%)	12.2	12.2	ns
Nasal polyps (%)	2.9	3.3	ns
Nasal polypoid swelling (%)	5.5	7.4	ns
Asthma (%)	18.3	14.4	ns

Only individuals with valid sleep study data, n = 555, 46 individuals were excluded as nasal resistance measurements could not be obtained. AHI4% = apnea-hypopnea index (hypopnea associated with 4% oxygen desaturation), BMI = body mass index, CRS = chronic rhinosinusitis, EPOS = European Position Paper on Rhinosinusitis and Nasal Polyps, ESS = Epworth Sleepiness Scale, logTNR = logarithmic value of total nasal resistance, ns = not statistically significant, OSA = obstructive sleep apnea, Perception of congestion = higher value indicates that nostrils are more open, RDI = respiratory disturbance index, WTC = World Trade Center.

Figure 2—Effect of position and decongestant on log TNR in females and males showing a significant increase in log TNR in the supine position and a significant decrease with decongestant in log TNR in both sexes, based on paired *t* test.



Note that the postdecongestant log TNR is not different with change in position in either sex. NS = not statistically significant, TNR = total nasal resistance.

We also did not find an association between CRS measures (either CRS scores or proportion of individuals with CRS), presence of nasal polyps and nasal edema and nasal resistance. (**Table 2**) A third of the participants had tried some nasal treatments and/or medications for their nasal symptoms; medication use was similar between high and low nasal resistance groups. (**Table S2**) Stratification by sex and multiple nasal resistance measures (sitting, supine, prepost decongestion) did not change results (data not shown).

Self-reported perception of nasal congestion

Self-reported perception of congestion (average of both nostrils) was greater in individuals with high nasal resistance (**Table 2**, $P = .03$). Similarly, when each nostril was examined independently, a significant correlation was observed between the perception of congestion and nasal resistance for that nostril (left $r = -.2$, $P < .0001$; right $-.27$, $P < .0001$). CRS+ individuals reported a higher self-reported perception of nasal congestion using the highest of left and right nostril congestion scores ($P < .0005$).

Nasal inflammation

Individuals with CRS (using both the WTC and the European Position Paper on Rhinosinusitis and Nasal Polyps definitions) demonstrated significantly greater levels of nasal inflammatory markers (IL6, IL8, eosinophilic cationic protein, and %eosinophils; **Table 3**, **Table S4a** in the supplemental material). This association was confirmed using a logistic regression model (unadjusted—model 0 and adjusted for age, BMI, and sex—model 1; **Table S4b**). Individuals with OSA had substantially elevated levels of IL8 and eosinophilic cationic protein that failed to reach statistical significance, compared to OSA negative individuals, after controlling for age, sex, and BMI (**Table 4** and **Table 5**). There was no correlation between nasal resistance and nasal inflammation markers (**Table S5** in the supplemental material) or change in nasal resistance (from sitting to supine and pre and post decongestion) and inflammation markers (**Table S6** in the supplemental material).

DISCUSSION

Our studies demonstrate that the associations between CRS and OSA[5] and between inflammation and OSA[13] that we previously observed in this WTC-exposed study population are not explained by *elevated nasal resistance*. Despite assessment of confounding factors such as medication use, nasal anatomy assessment and other comorbidities we also found no apparent relationship between nasal resistance and OSA, regardless of body position (sitting vs supine) and use of decongestant (data not shown). As expected, CRS was associated with elevated nasal inflammatory markers but we were unable to show an association between CRS or nasal inflammatory markers with nasal resistance.

Table 3—Inflammation and CRS.

	EPOS			WTC		
	CRS+ (n = 203)	CRS− (n = 250)	*P*	CRS+ (n = 192)	CRS− (n = 263)	*P*
Age (years)	52.4 ± 8.9	52.5 ± 8.4	ns	52.2 ± 8.7	52.7 ± 8.6	ns
Sex						
Male (%)	176 (87%)	210 (84%)	ns	165 (86)	222 (84)	ns
Female (%)	27 (13%)	40 (16%)		27 (14)	41 (16)	
BMI (kg/m^2)	30.2 ± 5.5	29.4 ± 5.4	.077	30.4 ± 5.6	29.4 ± 5.3	.046
Asthma	22.4%	11.5%	.001	23.9%	10.9%	< .001
Nasal steroids	18.1%	3.1%	< .001	19.8%	2.6%	< .001
%eosinophils (n = 422)*	0–28.5	0–9	.008	0–28.5	0–10	.03
logIL8 (n = 481)	7.9 ± 1.1	7.5 ± 1.2	.002	7.9 ± 1.2	7.6 ± 1.2	.010
logECP (n = 480)	2.4 ± 1.9	1.8 ± 2.0	.007	2.3 ± 2.0	1.9 ± 2.0	.032
logNeut (n = 475)	11.2 ± 1.7	10.9 ± 1.5	.052	11.1 ± 1.6	11.0 ± 1.6	.418
IL6 (n = 480)						
Q1	45 (22.2%)	65 (26.5%)	.018	47 (24.6%)	65 (25.1%)	.008
Q2	48 (23.6%)	64 (26.1%)		45 (23.6%)	66 (25.5%)	
Q3	45 (22.2%)	69 (28.2%)		37 (19.4%)	77 (29.7%)	
Q4	65 (32.0%)	47 (19.2%)		62 (32.5%)	51 (19.7%)	

CRS defined using EPOS and WTC definitions. Values presented as mean ± standard deviation or n (%). %eosiophils reported as min-max. For continuous variables, the *P* values were obtained from 2-sample *t* test or Wilcoxon Test when normality assumption did not hold. For categorical variables, the *P* values were obtained from χ^2 test. *Nonparametric test. BMI = body mass index, CRS = chronic rhinosinusitis, ECP = eosinophilic cationic protein, EPOS = European Position Paper on Rhinosinusitis and Nasal Polyps, IL6 = interleukin 6, IL8 = interleukin 8, log = logarithmic value, Neut = neutrophils, ns = not statistically significant, Q1, 2, 3, 4 = quartiles 1, 2, 3, 4, WTC = World Trade Center.

Table 4—Inflammation and OSA.

	OSA+ (n = 341)	OSA− (n = 114)	*P*
Age (years)	53.4 ± 8.1	49.8 ± 9.1	< .0001
Sex			
Male (%)	304 (89%)	84 (74%)	< .0001
Female (%)	37 (11%)	30 (26%)	
BMI (kg/m^2)	30.6 ± 5.4	27.7 ± 4.9	< .0001
logIL8 (n = 481)	7.8 ± 1.1	7.5 ± 1.2	< .05
logECP (n = 480)	2.2 ± 2.0	1.8 ± 2.1	.07
logNeut (n = 475)	11.1 ± 1.6	10.9 ± 1.7	ns
IL6 (n = 480)			
Q1	75 (22.3%)	36 (31.9%)	ns
Q2	85 (25.2%)	30 (26.5%)	
Q3	86 (25.5%)	26 (23.0%)	
Q4	91 (27.0%)	21 (18.6%)	

Values are presented as mean ± standard deviation or n (%). For continuous variables, the *P* values were obtained from 2-sample *t* test or Wilcoxon Test when normality assumption did not hold. For categorical variables, the *P* values were obtained from χ^2 test. Nasal lavage samples graded as unacceptable quality (eg, no reliable cells) were excluded from analysis. BMI = body mass index, ECP = eosinophilic cationic protein, IL6 = interleukin 6, IL8 = interleukin 8, log = logarithmic value, Neut = neutrophils, ns = not statistically significant, OSA = obstructive sleep apnea, Q1, 2, 3, 4 = quartiles 1, 2, 3, 4.

The nasal airway accounts for about half of total airway resistance with plausible mechanisms for OSA, and assessment of self-reported and objective nasal resistance in order to intervene (using decongestion or surgery) is recommended clinically. Our nasal resistance findings are consistent with the large epidemiologic study in middle aged adults (n = 991) by Young et al who demonstrated no relation between nasal obstruction measured by rhinometry and OSA severity but showed that reported symptoms of nasal congestion were an elevated risk for moderate to severe OSA.[16] Our findings also confirm previous literature in epidemiologic and sleep clinic populations showing an absence of a correlation between objectively measured nasal resistance and presence or severity of OSA.[16,22,24,32] Our data are in contrast to the study by Lofaso et al that showed that baseline nasal resistance was higher in OSA individuals than in non-OSA individuals.[21] One possible explanation for this difference was their use of posterior rhinomanometry as opposed to anterior rhinomanometry in our study to measure nasal resistance. In addition, previous randomized control studies of nasal decongestion[33] and nasal steroids[34] have shown that interventions to improve nasal patency have only small effects on OSA severity. Taken together, our data confirm Kohler et al's conclusion that nasal resistance may play only a limited role in the pathophysiology and management of OSA.[35] However, the limitation in most of these studies is that assessments were not made during sleep. Our findings are similar to results in the general population by Lange et al where nasal resistance obtained by acoustic rhinometry did not correlate with presence or absence of CRS.[36]

Table 5—Linear regression analysis: OSA and nasal inflammation.

Covariates	Inflammation Markers (log)	OSA+ Mean	OSA+ SE	OSA− Mean	OSA− SE	*P*
Model 0: none	IL8	7.78	0.06	7.50	0.11	.02
	ECP	2.25	0.11	1.77	0.19	.03
	Neut	11.08	0.09	10.86	0.16	ns
Model 1: age, BMI	IL8	7.77	0.06	7.54	0.11	.07
	ECP	2.27	0.11	1.72	0.19	.01
	Neut	11.06	0.09	10.91	0.16	ns
Model 2: age, BMI, sex	IL8	7.75	0.06	7.61	0.11	ns
	ECP	2.22	0.11	1.87	0.20	ns
	Neut	11.05	0.09	10.94	0.16	ns

Covariates	IL6 Quartiles	OR (OSA+ vs OSA−)	95% CI		*P*
Model 0: none	Q1	1.00			
	Q2	1.36	0.77	2.42	ns
	Q3	1.59	0.88	2.87	ns
	Q4	2.08	1.12	3.86	.02
Model 1: age, BMI, sex	Q1	1.0			
	Q2	0.98	0.52	1.83	ns
	Q3	1.34	0.70	2.56	ns
	Q4	1.68	0.87	3.27	ns

BMI = body mass index, CI = confidence interval, ECP = eosinophilic cationic protein, IL8 = interleukin 8, Neut = neutrophil, ns = not statistically significant, OSA = obstructive sleep apnea, SE = standard error, Q1, 2, 3, 4 = quartiles 1, 2, 3, 4.

Similarly Lund et al found no change in nasal resistance despite endoscopic surgery for CRS despite improvement in symptom scores and ciliary beat frequency.[37]

In contrast to adults, Sin et al showed higher anterior nasal resistance using 4-phase rhinomanometry in obese children with OSA compared to those without OSA.[38] This difference in finding is possibly due to the predominant pathophysiologic mechanism of OSA in children being anatomic as opposed to the multifactorial causes of OSA in adults.

Our data confirmed evidence of an inflammatory profile in individuals with CRS and a trend in OSA (some markers) similar to other studies with high serum levels of C reactive protein, interleukin 1, IL6, IL8, and tumor necrosis factor-alpha.[11,39] We had hypothesized that inflammation resulting in increased nasal resistance is a key link of CRS to OSA. Although measured nasal resistance was associated with the self-reported perception of nasal congestion, the differences between high and low nasal resistance groups is small and we did not detect any association of TNR with inflammation, CRS, or OSA. Dynamic changes in nasal resistance associated with factors such as nasal cycling could impact the measured resistance. It is also possible that nasal congestion symptoms could be a predictor of OSA independent of increased nasal resistance if inflammation of the collapsible upper airway segment occurs in parallel to the inflammation of the nose and sinuses. The resulting local swelling, upper airway edema and damage to the upper airway could directly predispose to upper airway collapse independent of nasal resistance and should be examined. Furthermore, reduced nasal pressure reflexes due to CRS may still contribute to OSA.

In our data, females demonstrated higher nasal resistance compared to males, as has been previously reported,[40] suggesting that factors other than vascular tone alone may be involved in the measurement. Sex hormones have been hypothesized to play a role in differences in nasal resistance between sexes and for the decreases in nasal patency during pregnancy.[41] The small number of females recruited for this study and the absence of information regarding their ovulatory cycle are a limitation of our data. In addition, the high prevalence of CRS and OSA in this specific population may limit the generalizability of the results, although we did not see differences in nasal resistance based on CRS case definition.[42]

Another limitation of our study was that measurements of nasal resistance were made during wakefulness. Elevated upper airway resistance resulting from a switch to mouth breathing[43] during sleep due to nasal congestion from CRS is a potential mechanism for OSA that we cannot rule out. While measurement of nasal resistance during sleep would have been ideal its measurement in large numbers of individuals without disturbing sleep is difficult. We hypothesized that if we were able to demonstrate an association between wake resistance and OSA it would have more clinical utility. In addition, Miljeteig et al[22] measured continuous nasal resistance during sleep and did not find a relationship with snoring. Internal validity of nasal resistance measurements in our study was confirmed by finding the expected increase from sitting to supine position and the expected decrease with use of a decongestant. In addition, the perception of nasal congestion reported by the individual at the time of testing was associated with nasal resistance.[44]

We used the median logTNR value of 0.77 as a cut-off for high vs low nasal resistance. As we did not include non-WTC participants in the current study, we are unable to comment on whether the nasal resistance values in this cohort are higher than a normal population. Using 4-phase anterior rhinomanometry, Vogt et al reported a mean logTNR = 0.66 (sitting) in a large dataset of Caucasian individuals[45] and recommended using 0.7–0.9 and > 0.9 (2 highest quintiles of logTNR) as representative of high nasal resistance in clinical practice. The mean logTNR value in our data is 0.77 (same as the median) and 59.3% of participants have values > 0.7 suggesting high nasal resistance using these published data, albeit in a demographically unmatched group.

Despite significant CRS the prevalence of nasal polyposis in our data was only 1.7%, which is similar to that reported in a recent OSA population.[46] We did not see differences in nasal resistance or OSA associated with this subset, although our findings are limited by the small sample size. The pathophysiology of OSA is complex[47] and our data suggest that the component due to nasal obstruction may be less important to the impact of CRS than other factors known to cause OSA, including disturbed/fragmented sleep and arousals from CRS.[48]

Finally, our findings may have been impacted by variability/stability of OSA, inflammation and nasal resistance measurements. Although we used 2 nights of data for OSA assessment other assessments were only performed at one time. Future studies could consider evaluation at multiple time points to ascertain the potential impact of the variability and reproducibility of these measurements. In the present study only standard OSA severity metrics (AHI4%, RDI) that were available from the HST were used and we are unable to explore differences in additional metrics such as frequency of inspiratory flow limitation breaths or severity of inspiratory flow limitation that may have been impacted by nasal resistance. Furthermore, modulation of upper airway collapsibility by nasal resistance may provide additional insights to the mechanism of OSA in this population and remains to be explored.

In conclusion, although we found evidence that symptoms of CRS and inflammatory markers were positively associated with OSA in a sample of the WTC cohort who reported no history of OSA or snoring prior to September 11, 2001, we found no evidence that increased nasal resistance accounts for that association in this WTC population. Although a role for nasal obstruction and nasal congestion has mechanistic plausibility and has been suggested as a significant pathophysiological mechanism for OSA, our findings do not support this hypothesis. Specifically, we were unable to demonstrate the clinical utility of anterior nasal resistance in the assessment of patients with OSA similar to previous reports in the literature. In our large dataset, nasal resistance did not differ in individuals with and without CRS or OSA, suggesting that other mechanisms need to be examined.

ABBREVIATIONS

AHI4%, apnea-hypopnea index (4% oxygen desaturation for hypopnea)
BMI, body mass index

CRS, chronic rhinosinusitis
ECP, eosinophilic cationic protein
HST, home sleep testing
IL6, interleukin 6
IL8, interleukin 8
log, logarithmic value
OSA, obstructive sleep apnea
RDI, respiratory disturbance index
TNR, total nasal resistance
WTC, World Trade Center
WTC HP, World Trade Center Health Program

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Table S1—Comparisons of subjects with high vs. low nasal resistance (logTNR=0.77 as the cutoff) using regression analysis with an adjustment of age, BMI and sex.

LOGISTIC REGRESSION ANALYSIS							
Variable	**Low Nasal Resistance (logTNR≤0.77)**		**High Nasal Resistance (logTNR>0.77)**		**Comparison/Association**		
	Proportion	**95% CI**	**Proportion**	**95% CI**	**OR**	**95% CI**	***P***
Sex* (male)	0.89	(0.85, 0.92)	0.77	(0.72, 0.82)	2.34	(1.46, 3.73)	.0004
Snoring	0.50	(0.44, 0.56)	0.52	(0.46, 0.58)	0.93	(0.65, 1.32)	.7
OSA	0.76	(0.70, 0.81)	0.79	(0.74, 0.84)	0.85	(0.56, 1.29)	.4
CRS+ WTC	0.45	(0.39, 0.51)	0.44	(0.38, 0.50)	1.04	(0.73, 1.47)	.8
CRS+ EPOS	0.46	(0.40, 0.52)	0.48	(0.42, 0.54)	0.90	(0.63, 1.26)	.5
Nasal edema	0.12	(0.08, 0.16)	0.12	(0.08, 0.16)	1.01	(0.59, 1.73)	.96
Nasal polyps	0.02	(0.01, 0.05)	0.02	(0.01, 0.05)	1.01	(0.37, 2.80)	.98
Nasal polypoid swelling	0.08	(0.05, 0.11)	0.05	(0.03, 0.08)	1.72	(0.84, 3.52)	.1
Asthma	0.14	(0.11, 0.19)	0.17	(0.13, 0.22)	0.84	(0.52, 1.34)	.5
LINEAR REGRESSION ANALYSIS							
Variable	**Low Nasal Resistance (logTNR≤0.77)**		**High Nasal Resistance (logTNR>0.77)**		**Comparison/Difference**		
	Mean	**95% CI**	**Mean**	**95% CI**	**Mean**	**95% CI**	***P***
ESS	8.67	(8.11, 9.23)	7.82	(7.26, 8.37)	0.85	(0.05, 1.65)	.04
logAHI4	2.09	(1.99, 2.20)	2.19	(2.09, 2.29)	0.09	(0.05, 0.24)	.2
logRDI	3.06	(2.98, 3.11)	3.13	(3.06, 3.20)	0.08	(0.01, 0.18)	.09
CRS Score	2.35	(2.08, 2.62)	2.45	(2.19, 2.71)	0.10	(0.28, 0.48)	.6
Perception of congestion	6.05	(5.79, 6.31)	5.76	(5.50, 6.02)	0.29	(-0.09, 0.66)	.1

ESS= Epworth Sleepiness Scale; logAHI4%=apnea-hypopnea index (hypopnea associated with 4% O_2 desaturation); logRDI= respiratory disturbance index; Perception of congestion= higher value indicates that nostrils are more open. *Adjusted for BMI and age only.

Sex and BMI effects

As nasal resistance is higher in women than men, the linear relationship between OSA severity (AHI4) and nasal resistance (supine pre-decongestion logTNR) was assessed in men and women separately using Pearson correlation coefficients. No significant linear relationships were observed (r = 0.01, 95% CI: −0.080, 0.10 in men and r = 0.10, 95% CI: −0.10, 0.30 in women). Further we assessed this relationship in men with BMI < 30 kg/m^2 versus ≥ 30 kg/m^2; Pearson correlation coefficient of AHI and nasal resistance showed no significant associations (r = 0.03, 95% CI: −0.095, 0.15 in men with BMI < 30 and r = −0.03, 95% CI: −0.17, 0.11 in men with BMI ≥ 30). Findings were similar (ie, no significant associations between AHI and nasal resistance) in women (r = 0.07, 95% CI: −0.19, 0.32 in women with BMI < 30 and r = 0.10, 95% CI: −0.24, 0.41 in women with BMI ≥ 30).

We also examined the association of OSA (+/−) vs. nasal resistance (high/low) in men and women separately using the median resistance value for each group as the cutoff for high vs low nasal resistance. (men cutoff: log–TNR=0.75 and women cutoff: log–TNR=0.88). A Chi square test showed no association between OSA+/− and nasal resistance in men and women (odds ratio (OR) for OSA = 1.23, 95% CI: 0.79,1.91, *P*-value = .37 in men, and OR = 1.92, 95% CI: 0.84,4.36, *P*-value = .12 in women). Similar analysis was performed to examine whether BMI < 30 vs. ≥ 30 was associated with nasal resistance using the median cutoff in men (0.75) and women (0.88). Chi square test showed that BMI was not significantly associated with nasal resistance in men nor in women (OR = 1.26, 95% CI: 0.87, 1.82, *P*-value = 0.22 in men, and OR= 1.78, 95% CI: 0.77, 4.11, *P*-value = 0.18 in women).

Table S2—Logistic regression analysis: Comorbidities, current medications and prior treatments tried for nasal symptoms adjusted for age, BMI and sex.

Comorbidity	**Low Nasal Resistance (logTNR≤0.77)**		**High Nasal Resistance (logTNR>0.77)**		**Comparisons/Association**		
	Proportion	**95% CI**	**Proportion**	**95% CI**	**OR**	**95% CI**	***P***
Adjustment disorder	0.03	(0.01, 0.05)	0.00	(0.00, 0.03)	7.23	(0.87, 59.93)	.07
Anxiety	0.12	(0.08, 0.16)	0.14	(0.10, 0.19)	0.81	(0.49, 1.33)	.4
Depression	0.12	(0.08, 0.16)	0.12	(0.09, 0.17)	0.93	(0.55, 1.57)	.8
GERD	0.31	(0.26, 0.37)	0.30	(0.25, 0.36)	1.06	(0.73, 1.53)	.8
OAD	0.21	(0.16, 0.26)	0.20	(0.15, 0.25)	1.07	(0.70, 1.64)	.7
PTSD	0.14	(0.10, 0.19)	0.11	(0.08, 0.16)	1.28	(0.77, 2.13)	.3
URD	0.42	(0.37, 0.49)	0.42	(0.36, 0.48)	1.02	(0.72, 1.45)	.9
CHF	0.01	(0.00, 0.04)	0.01	(0.00, 0.03)	1.93	(0.47, 7.90)	.4
HTN	0.24	(0.19, 0.30)	0.23	(0.18, 0.28)	1.1	(0.73, 1.66)	.6
STROKE	0.01	(0.00, 0.03)	0.01	(0.00, 0.03)	1.22	(0.30, 4.99)	.8
MI	0.01	(0.00, 0.04)	0.02	(0.01, 0.05)	0.67	(0.20, 2.29)	.5
DM	0.07	(0.05, 0.11)	0.05	(0.03, 0.08)	1.5	(0.78, 2.88)	.2
Medications	**Low Nasal Resistance (logTNR≤0.77)**		**High Nasal Resistance (logTNR>0.77)**		**Comparisons/Association**		
	Proportion	**95% CI**	**Proportion**	**95% CI**	**OR**	**95% CI**	***P***
Nasal steroids	0.09	(0.06, 0.13)	0.11	(0.07, 0.15)	0.84	(0.48, 1.47)	.5
Oral/Inhaled steroids	0.09	(0.06, 0.13)	0.11	(0.08, 0.15)	0.84	(0.48, 1.47)	.5
Antihistamines	0.06	(0.04, 0.10)	0.08	(0.05, 0.11)	0.82	(0.42, 1.60)	.6
Nasal washes	0.48	(0.41, 0.56)	0.63	(0.55, 0.70)	0.56	(0.34, 0.86)	.008
Neti pots	0.34	(0.27, 0.41)	0.32	(0.25, 0.39)	1.09	(0.69, 1.71)	.7

No differences were observed between high and low resistance groups.

GERD= gastroesophageal reflux disorder; OAD= obstructive airway disease; PTSD=post traumatic stress disorder; URD= upper respiratory disease; CHF= congestive heart failure; HTN=hypertension; MI= myocardial infarction; DM=diabetes mellitus.

Table S3—Total nasal resistance (TNR) (mean ± SD) in females and males while sitting and supine prior to and after nasal decongestant.

Variable	Females		Males	
	n	Mean	n	Mean
Sit_Pre_logTNR	102	0.87±0.33*	491	0.65±0.37
Supine_Pre_logTNR	103	0.96±0.38*	491	0.73±0.36
Sit_post_logTNR	99	0.75±0.30*	490	0.60±0.30
Supine_post_logTNR	97	0.75±0.33*	473	0.60±0.30

Resistance was statistically lower in males than females for all rows (*$P < .0001$), using two-sample paired t test. “Pre” indicates prior to decongestant, “Post” indicates after decongestant.

Table S4a—Linear regression analysis: Nasal inflammation and CRS.

Inflammation Markers (log)	Model 1: Unadjusted						
	CRS+		CRS−		Difference		
	Mean	95% CI	Mean	95% CI	Mean	95% CI	*P*
logIL8	7.91	(7.75, 8.07)	7.52	(7.37, 7.66)	0.39	(0.17, 0.60)	.000
logECP	2.39	(2.12, 2.66)	1.79	(1.55, 2.04)	0.60	(0.23, 0.97)	.002
logNeut	11.21	(10.99, 11.43)	10.89	(10.69, 11.09)	0.32	(0.03, 0.62)	.034
	Model 2: Adjusted for age, BMI and sex						
	CRS+		CRS−		Difference		
	Mean	95% CI	Mean	95% CI	Mean	95% CI	*P*
logIL8	7.89	(7.73, 8.05)	7.53	(7.39, 7.67)	0.36	(0.14, 0.57)	.001
logECP	2.37	(2.10, 2.64)	1.81	(1.57, 2.06)	0.56	(0.18, 0.93)	.003
logNeut	11.20	(10.97, 11.42)	10.90	(10.70, 11.10)	0.30	(0.00, 0.59)	.051

Similar results for CRS (WTC definition).

Logistic regression analysis for CRS and IL6 quartile groups.

Covariates	IL6 Quartiles	OR (CRS+ vs CRS−)	95% CI	*P*
Model 0: none	Q1	1.00		
	Q2	1.08	(0.64,1.85)	.769
	Q3	0.94	(0.55, 1.61)	.827
	Q4	2.00	(1.17, 3.41)	.011
Model 1: age, BMI, sex	Q1	1.0		
	Q2	1.03	(0.59, 1.77)	.930
	Q3	0.87	(0.50, 1.51)	.623
	Q4	1.90	(1.10, 3.25)	.021

Table S4b—Logistic regression analysis for CRS, OSA and each inflammation marker used as a predictor (per unit change for logarithm transformed IL8, ECP, Neut, and IL6 quartile groups).

Covariates	Inflammation Markers (log)	CRS+ vs CRS− (EPOS)		*P*	OSA+ vs OSA−		*P*
		OR	95% CI		OR	95% CI	
Model 0: none	IL8	1.34	(1.14, 1.59)	.001	1.24	(1.03, 1.49)	.025
	ECP	1.17	(1.06, 1.29)	.002	1.12	(1.01, 1.25)	.030
	Neut	1.14	(1.01, 1.28)	.035	1.07	(0.94 ,1.22)	ns
	IL6 Quartiles						
	Q1	1	-	-	1	-	-
	Q2	1.08	(0.64, 1.85)	ns	1.36	(0.77, 2.42)	ns
	Q3	0.94	(0.55,1.61)	ns	1.59	(0.88, 2.87)	ns
	Q4	2.00	(1.17, 3.41)	.011	2.08	(1.12, 3.86)	.021
Model 2: age, BMI, sex	IL8	1.33	(1.12, 1.58)	.001	1.09	(0.89, 1.34)	ns
	ECP	1.16	(1.05, 1.28)	.003	1.08	(0.97, 1.22)	ns
	Neut	1.13	(1.00, 1.27)	.052	1.04	(0.90,1.19)	ns
	IL6 Quartiles						
	Q1	1	-	-	1	-	-
	Q2	1.03	(0.59, 1.77)	ns	0.98	(0.52, 1.83)	ns
	Q3	0.87	(0.50, 1.51)	ns	1.34	(0.70, 2.56)	ns
	Q4	1.90	(1.10, 3.25)	.021	1.68	(0.87, 3.27)	ns

Results were similar for CRS by WTC definition.

Table S5—Nasal inflammation and nasal resistance.

Variable	With Variable	n	Correlation Estimate	95% CI		*P* value for H0:Rho=0
logIL6	Supine_Pre_logTNR	449	-0.05127	-0.143137	0.041464	.2779
logIL8	Supine_Pre_logTNR	450	-0.10089	-0.191540	-0.008528	.0321
logECP	Supine_Pre_logTNR	449	-0.05757	-0.149314	0.035161	.2230
logNeutC	Supine_Pre_logTNR	443	-0.05819	-0.150537	0.035171	.2212

Pearson correlation statistics (Fisher's z transformation) increased IL8 was negatively correlated with nasal resistance.

Table 6—Relationship between ~~AHI~~ and the change in nasal resistance (by position and decongestion) using Pearson correlation by sex.

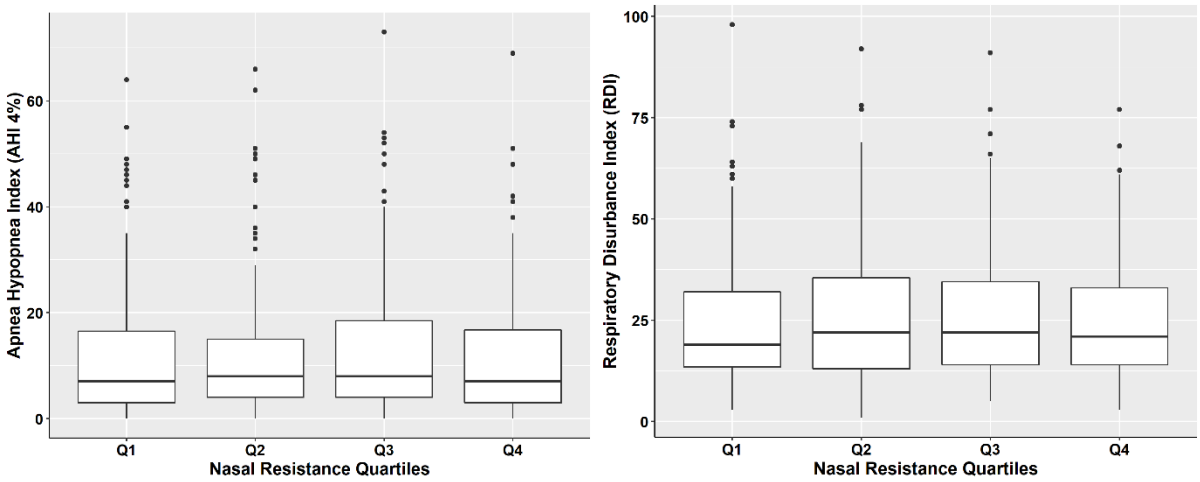
Variable logTNR	With Variable	n	Correlation Estimate	95% CI	*P*
Entire Sample					
Δ(Sit-Supine)Pre	logIL6	417	0.02	(-0.08, 0.11)	.732
Δ(Post-Pre)Sit	logIL6	414	-0.01	(-0.10, 0.09)	.903
Δ(Post-Pre)Supine	logIL6	402	0.01	(-0.09, 0.10)	.913
Δ(Sit-Supine)Pre	logIL8	417	0.04	(-0.05, 0.14)	.370
Δ(Post-Pre)Sit	logIL8	414	-0.04	(-0.14, 0.05)	.369
Δ(Post-Pre)Supine	logIL8	403	-0.02	(-0.12, 0.08)	.661
Δ(Sit-Supine)Pre	logECP	417	0.02	(-0.08, 0.11)	.713
Δ(Post-Pre)Sit	logECP	414	-0.03	(-0.13, 0.07)	.524
Δ(Post-Pre)Supine	logECP	402	-0.03	(-0.12, 0.07)	.616
Δ(Sit-Supine)Pre	logNeutC	414	0.00	(-0.10, 0.09)	.973
Δ(Post-Pre)Sit	logNeutC	412	-0.04	(-0.14, 0.06)	.409
Δ(Post-Pre)Supine	logNeutC	398	0.00	(-0.09, 0.10)	.930
Female					
Δ(Sit-Supine)Pre	logIL6	62	-0.04	(-0.28, 0.22)	.784
Δ(Post-Pre)Sit	logIL6	60	-0.01	(-0.26, 0.24)	.940
Δ(Post-Pre)Supine	logIL6	60	-0.15	(-0.39, 0.11)	.265
Δ(Sit-Supine)Pre	logIL8	62	0.01	(-0.24, 0.26)	.918
Δ(Post-Pre)Sit	logIL8	60	-0.07	(-0.32, 0.19)	.602
Δ(Post-Pre)Supine	logIL8	60	-0.07	(-0.32, 0.18)	.571
Δ(Sit-Supine)Pre	logECP	62	-0.08	(-0.33, 0.17)	.517
Δ(Post-Pre)Sit	logECP	60	0.02	(-0.24, 0.27)	.881
Δ(Post-Pre)Supine	logECP	60	-0.06	(-0.31, 0.20)	.640
Δ(Sit-Supine)Pre	logNeutC	62	0.05	(-0.20, 0.30)	.691
Δ(Post-Pre)Sit	logNeutC	60	-0.05	(-0.30, 0.21)	.720
Δ(Post-Pre)Supine	logNeutC	59	-0.05	(-0.30, 0.21)	.693
Male					
Δ(Sit-Supine)Pre	logIL6	355	0.02	(-0.08, 0.12)	.697
Δ(Post-Pre)Sit	logIL6	354	-0.01	(-0.11, 0.10)	.895
Δ(Post-Pre)Supine	logIL6	342	0.03	(-0.08, 0.13)	.602
Δ(Sit-Supine)Pre	logIL8	355	0.04	(-0.07, 0.14)	.466
Δ(Post-Pre)Sit	logIL8	354	-0.05	(-0.15, 0.06)	.375
Δ(Post-Pre)Supine	logIL8	343	-0.02	(-0.13, 0.08)	.675
Δ(Sit-Supine)Pre	logECP	355	0.02	(-0.08, 0.13)	.676
Δ(Post-Pre)Sit	logECP	354	-0.04	(-0.15, 0.06)	.408
Δ(Post-Pre)Supine	logECP	342	-0.03	(-0.13, 0.08)	.631
Δ(Sit-Supine)Pre	logNeutC	352	-0.01	(-0.12, 0.09)	.811
Δ(Post-Pre)Sit	logNeutC	352	-0.04	(-0.15, 0.06)	.427
Δ(Post-Pre)Supine	logNeutC	339	0.01	(-0.10, 0.12)	.860

Δ(Sit-Supine)Pre =(Sitting_Predecongestion_logTNR)-(Supine_Predecongestion_logTNR); ΔSit (Post-Pre)=(Sitting_Postdecongestion_logTNR)-(Sitting_Predecongestion_logTNR); Δ(Post-Pre)Supine=(supine_postdecongestion_logTNR)-(supine_predecongestion_logTNR).

Table S7—Comparison of subjects in the highest versus lowest quartiles of nasal resistance.

	Higest Nasal Resistance logTNR>1.0 (n=140)	**Lowest Quartile Nasal Resistance logTNR<0.54 (n=138)**	***P***
Age (years)	52.5±8.2	53.9±8.7	ns
BMI (kg/m^2)	30.0±5.6	29.9±5.6	ns
% female	27.1%	8.7%	< .001
Snoring %	55.7%	51.7%	ns
ESS	8.5±4.9	8.0±4.7	ns
OSA %	75%	74.6%	ns
AHI4% events/h	11.2±11.4	11.7±13.1	ns
RDI events/h	24.7±14.7	24.4±16.3	ns
CRS Score	2.58±2.2	2.43±2.3	ns
CRS+ WTC	46.8%	43.9%	ns
CRS+ EPOS	51.8%	43.9%	ns
Perception of congestion	5.3±2.3	6.1±2.1	< .001

Figure S1—Box plot of OSA severity (median, 25-75%) as measured by AHI4% on the left and RDI on the right, grouped by nasal resistance quartiles.



Nasal resistance quartiles = Log TNT Q1: -0.486 > 0.539; Q2: 0.540 > 0.770; Q3: 0.771 > 1.001; Q4: 1.002 > 2.069. There is no difference in OSA severity between groups (*P* = ns).