

The association of air pollutants and allergic and nonallergic rhinitis in chronic rhinosinusitis

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Background: There has been little investigation regarding air quality and rhinitis in the pathophysiology of upper airway disease. In this study, we assessed the impact of inhalant pollutants (particulate matter 2.5 [PM_{2.5}] and black carbon [BC]) on allergic rhinitis and chronic rhinosinusitis (CRS) disease severity.

Methods: CRS patients with nasal polyps (CRSwNP) and without polyps (CRSsNP) were identified. Spatial modeling from pollutant monitoring sites was used to estimate exposures for patients meeting the inclusion criteria (total, n = 125; CRSsNP, n = 67; CRSwNP, n = 58). Skin-prick, intradermal dilutional, and in-vitro testing methods were utilized to determine aeroallergen sensitization. Disease severity indicators were measured by modified Lund-Mackay score (LMS), the 22-item Sino-Nasal Outcome Test (SNOT-22), systemic steroid therapy, and number of functional endoscopic sinus surgeries (FESS).

Results: Thirty-six percent (n = 45) of patients who described rhinitis symptoms demonstrated no reactivity to aeroallergen testing. Sixty-four percent (n = 80) tested positive for at least 1 allergen, with no differences found between CRSsNP and CRSwNP (62.1% vs 67.2%). There were significant differences in air pollutants between patients

testing negative and positive for allergies (nonallergic vs allergic: PM_{2.5}, 11.32 vs 11.07 $\mu\text{g}/\text{m}^3$, $p = 0.030$; BC, 0.81 vs 0.76 absorbance, $p = 0.044$). Nonallergic CRSwNP demonstrated higher PM_{2.5} compared with allergic counterparts (11.48 vs 11.09 $\mu\text{g}/\text{m}^3$, $p = 0.032$). A similar pattern was observed with BC (0.82 vs 0.75 absorbance, $p = 0.017$). In CRSsNP, BC correlated significantly with SNOT-22 ($r = 0.55$, $p = 0.042$).

Conclusion: Our results suggest that small inhalant pollutants may contribute to nonallergic symptomatology in patients with and without nasal polyps. Regardless of allergy status, BC may play a role in CRS symptom severity. © 2018 ARS-AAOA, LLC.

Key Words:

air pollutants; allergens; asthma; environmental exposure; nasal polyps; particulate matter; quality of life; rhinitis; risk factors; sinusitis

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Allergic rhinitis (AR) is the fifth most common chronic disease in the United States, affecting up to 30%

of American adults, and accounts for 50% of rhinitis overall.¹⁻³ In the setting of negative allergy testing, patients are often diagnosed with nonallergic rhinitis (NAR). Given its poorly understood pathophysiology and limited treatment options, NAR can be frustrating to manage both for providers and patients.⁴

There is often overlap of rhinitis with chronic rhinosinusitis (CRS) disease presentation.⁵ CRS with nasal polyposis (CRSwNP) and without nasal polyposis (CRSsNP) is driven by chronic inflammation with manifestations

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beyond rhinitis symptoms and clinical findings alone.^{6,7} The exact role of AR in CRS development, severity, and postsurgical outcomes is controversial.^{8–10} The relationship between NAR and CRS is even less well understood. Studies have shown that air pollutants (AP) induce nasal inflammation, suggesting a possible role of nonallergen exposures in NAR-mediated inflammation.^{11,12}

A tremendous body of literature has shown that AP exposure can negatively impact cardiovascular, neurologic, and respiratory health.^{13–15} However, investigations examining the contribution of AP to sinonasal disease pathology have been limited. PM_{2.5} consists of fine inhalable particles measuring $\leq 2.5 \mu\text{m}$ in diameter.¹⁶ Black carbon (BC), which denotes the light-absorbing components of aerosols that contain 2 forms of elemental carbon, is a major component of particulate matter (PM) and is directly emitted into the atmosphere in the form of PM_{2.5}.^{17,18} In this study, we examine the relationship between AP exposures and AR and disease severity in CRS patients.

Patients and methods

Study design

The protocol for this study was reviewed and approved by the institutional review board of the University of Pittsburgh, Pittsburgh, PA. Adults aged ≥ 18 years of age, diagnosed with CRSwNP and CRSsNP, who described rhinitis symptoms and had subsequent allergy testing, were identified over a 2-year period (2013–2015). Exclusion criteria included relocation within 5 years or absence of computed tomography (CT) imaging within 3 years of the pre- and poststudy period. Aeroallergen sensitivity was assessed by testing results from either skin-prick testing (SPT), intradermal dilutional testing (IDT), or in-vitro blood testing. Data from 14 common inhalant allergens were collected, including *Dermatophagoides farinae* (European dust mite), *Dermatophagoides pteronyssinus* (North American dust mite), American cockroach, *Alternaria*, *Epicoccum*, *Helminthosporium*, cat, dog, Bermuda grass, Timothy grass, oak, maple, tree of Heaven, and ragweed. Mites, molds, animals, and cockroach were categorized as perennial allergens, and grasses, trees, and weeds were classified as seasonal allergens. Allergens were grouped as high or low reactors according to test results: (1) SPT (wheal, in millimeters)—high reactor (≥ 9), low reactor (5–8), nonreactive (≤ 4); IDT (endpoint)—high reactor (4–6), low reactor (1–3), nonreactive (0); and in-vitro (class)—high reactor (4–6), low reactor (1–3), nonreactive (0).

Patients included in the study had at least 1 visit encounter with 1 of 2 otolaryngology providers, and there were no differences found between participants by provider ($p > 0.05$). Analysis of CT imaging was performed by 3 investigators independently (L.J.M., J.A.M., and S.E.L.) using the Zinreich staging system (modification of Lund-Mackay, herein referred to as LMS) to quantify disease inflammation (interrater reliability, 92.6%; $p < 0.05$).²¹ Scores on the

22-item Sino-Nasal Outcome Test (SNOT-22) were collected and analyzed for each patient.

Ambient air quality sampling and exposure assignment

A spatial model generated from a Pittsburgh-area air pollution monitoring campaign, as described by Tunno et al, was used to estimate patients' exposures to PM_{2.5} and BC.¹⁹ Air pollution was monitored at 37 sites during summer 2012 and winter 2013. Data were merged from both seasons and used to develop hybrid land-use regression (LUR) models, which included a dispersion covariate developed from AERMOD PM_{2.5} industrial emissions.²⁰ Patients' addresses were geocoded in a geographic information system (GIS) using a composite address locator, and mean predicted pollutant concentrations were calculated within 300 meters of patient residences. Residential pollutant exposure estimates were then temporally adjusted to estimate chronic exposures from 2009 to 2013 using data from an Environmental Protection Agency (EPA) regulatory monitor.

Statistical analysis

Comparisons on demographic and clinical categorical variables were performed using χ^2 tests. For small cell counts, Fisher's exact test was used. Before analysis, the distributions of PM_{2.5} and BC particulates and all continuous clinical measures were examined for non-normality, skewness, multimodality, and outliers. Outliers were identified and corrected. Excessively skewed distributions were log-transformed. Comparisons between groups on continuous measures were conducted using 2-sample independent t tests with Satterthwaite correction for unequal variances as indicated. For continuous measure distributions considered overly skewed and/or non-normally distributed, the Wilcoxon rank sum test was used when analyzing them using the original scale. A certain percentage of patients were not prescribed steroids. To accommodate this aspect, for comparisons between groups in their overall cumulative steroid dose, a 2-part hurdle model with a log-normal distribution was used.²¹ Subanalyses comparing the dose among patients who were prescribed steroids were also conducted using the more typical methods described earlier. Bivariate associations of PM_{2.5} or BC with continuous clinical measures were tested using Pearson correlation coefficients followed by linear regression to adjust for potential confounders of age and sex. A 2-tailed p value of < 0.05 was considered statistically significant. All statistical calculations were performed using SAS version 9.3 for Windows (SAS Institute, Cary, NC).

Results

Clinical and demographic characteristics

One-hundred twenty-five patients were included in the study. Clinicodemographic characteristics are depicted in

TABLE 1. Clinicodemographic characteristics of study cohorts*

	Overall (N = 125)	CRSsNP (N = 58)	CRSwNP (N = 67)
Sex			
Male	60 (48.0)	24 (41.4)	36 (53.7)
Female	65 (52.0)	34 (58.6)	31 (46.3)
Asthma			
No	60 (48.0)	32 (55.2)	28 (41.8)
Yes	65 (52.0)	26 (44.8)	39 (58.2)
Allergy testing result			
Negative	45 (36.0)	22 (37.9)	23 (34.3)
Positive	80 (64.0)	36 (62.1)	44 (65.7)
Allergy testing technique			
SPT	39 (31.2)	16 (27.6)	23 (34.3)
IDT	8 (6.4)	2 (3.4)	6 (9.0)
In vitro	78 (62.4)	40 (69.0)	38 (56.7)
Steroids^a			
No	33 (26.4)	21 (36.2)	12 (17.9)
Yes	92 (73.6)	37 (63.8)	55 (82.1)
FESS^b			
None	86 (68.8)	33 (56.9)	53 (79.1)
Primary	25 (20.0)	18 (31.0)	7 (10.4)
Revision (≥ 2)	14 (11.2)	7 (12.1)	7 (10.4)
Tobacco history			
Never	71 (56.8)	34 (58.6)	37 (55.2)
Former	12 (9.6)	2 (3.4)	10 (14.9)
Current	42 (33.6)	22 (37.9)	20 (29.9)
Age [mean (SD)]	48 (15.6)	47 (15.7)	49 (15.5)
SNOT-22 [mean (SD)]	38 (24.1)	42 (16.8)	37 (26.0)
LMS [mean (SD)]	21 (14.4)	14 (11.2)	26 (14.8)

*Data expressed as number (%), unless noted otherwise. Italics represent comparison groups for which differences were statistically significant.

^aCRSwNP vs CRSsNP: steroids, $p = 0.021$.

^bCRSwNP vs CRSsNP: FESS, $p = 0.012$.

CRSsNP = chronic rhinosinusitis without nasal polyposis; CRSwNP = chronic rhinosinusitis with nasal polyposis; FESS = functional endoscopic sinus surgery; IDT = intradermal dilutional testing; LMS = Lund-Mackay score; SD = standard deviation; SNOT-22 = 22-item Sino-Nasal Outcome Test; SPT = skin-prick testing.

Table 1. Eleven CRSwNP patients (16.0%) who presented with asthma were identified as having aspirin-exacerbated respiratory disease (AERD). Among the CRSwNP patients, there was a statistically significant difference in the presence of concomitant asthma disease in those who tested positive for allergies compared with those who tested negative (66.7% vs 40.9%, $p = 0.045$). There were no differences

in clinical and demographic characteristics among CRSsNP patients with and without asthma.

Allergy testing results

Overall, 45 patients (36.0%) who described rhinitis symptoms at presentation demonstrated no reactivity to aeroallergens upon subsequent testing. Allergy testing results among those who tested positive by CRS phenotype are shown in Figure 1. Of 80 patients who tested positive, 65 (81.2%) demonstrated reactivity to ≤ 6 allergens. Of 15 patients (18.8%) who tested positive to ≥ 7 allergens, those with polyposis comprised the majority ($n = 10$), with 3 of these patients testing positive for 11–14 allergens. Allergens were grouped as high or low reactors according to allergy testing-specific results. Of 161 positive test results, 119 (74.0%) were low reactor allergens. Overall, perennial allergen positivity ($n = 89$, 55.0%) was more common compared with seasonal allergens ($n = 72$, 45.0%) (Figure 2).

Reactivity (high vs low) and temporality (perennial vs seasonal) of inhalant allergens by CRS phenotype are represented in Figure 3. There were no significant differences found between allergen group results for CRSsNP vs CRSwNP. Among CRSsNP patients, those with asthma demonstrated a trend toward higher mean number of positive low reactor perennial allergens compared with those without asthma ($p = 0.053$). In contrast, CRSsNP patients without asthma demonstrated a significantly higher mean number of positive high reactor seasonal allergens compared with those with asthma ($p = 0.042$).

Air pollutant exposures among allergic and nonallergic patients

The geographic distribution of AP is illustrated in Figure 4A. There were significant differences in AP levels between allergy-negative and -positive patients (Fig. 4B and C; differences were also significant by log-transformed data, results not shown). $PM_{2.5}$ concentration measured, on average, $11.32 \mu\text{g}/\text{m}^3$ in nonallergic patients, compared with $11.07 \mu\text{g}/\text{m}^3$ in allergic patients ($p = 0.030$; Fig. 4B). BC was, on average, 0.81 absorbance (abs) among allergy-negative patients, compared with 0.76 abs among allergy-positive patients ($p = 0.044$; Fig. 4C). Mean $PM_{2.5}$ and BC were not significantly different between patients with or without asthma.

Figure 5 portrays AP differences by CRS phenotype among allergy groups. Nonallergic CRSwNP patients demonstrated statistically significantly higher mean average $PM_{2.5}$ than their allergy-positive counterparts (11.48 vs $11.09 \mu\text{g}/\text{m}^3$, $p = 0.032$). A similar pattern was observed for BC (0.82 vs 0.75 abs, $p = 0.017$). Nonallergic polyp patients were also found to have a significant difference in $PM_{2.5}$ compared with allergic non-polyp patients (11.48 vs $11.04 \mu\text{g}/\text{m}^3$, $p = 0.023$). A similar, but not statistically significant trend was observed in BC levels.

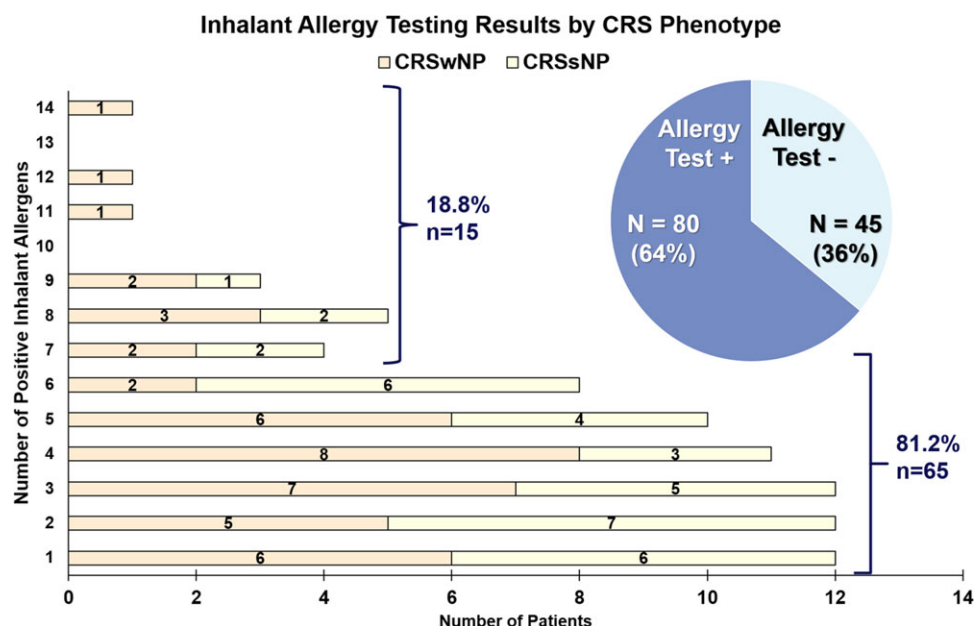


FIGURE 1. Inhalant allergy testing results by CRS phenotype. Data from 14 common inhalant allergens were collected. Horizontal axis represents number of patients who underwent allergy testing by either SPT, IDT, or in-vitro blood testing and tested positive for at least 1 aeroallergen. Vertical axis represents cumulative number of positive test results per patient. Results are shown by CRS phenotype (CRSsNP vs CRSwNP). Overall, 45 (36.0%) patients who described rhinitis symptoms at presentation demonstrated no reactivity to aeroallergens upon subsequent testing (inset). Of the 80 patients who tested positive, 65 (81.2%) demonstrated reactivity to ≤ 6 allergens. Of the patients who tested positive to ≥ 7 allergens ($n = 15$, 18.8%), those with polyposis comprised the majority ($n = 10$). CRS = chronic rhinosinusitis; CRSsNP = chronic rhinosinusitis without nasal polyposis; CRSwNP = chronic rhinosinusitis with nasal polyposis; IDT = intradermal dilutional testing; SPT = skin-prick testing.

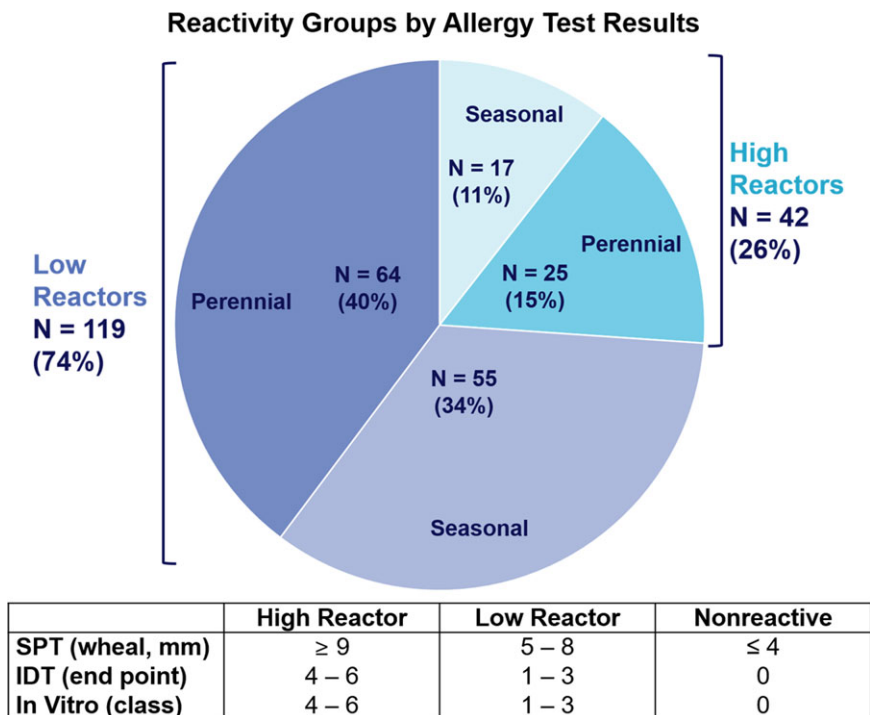


FIGURE 2. Reactivity groups by allergy test results. Allergens were grouped as high or low reactors according to allergy testing-specific results. Of 161 positive allergen test results, the majority ($n = 119$, 74.0%) were low reactor allergens. Overall, perennial allergens ($n = 89$, 55.3%) were more common compared with seasonal allergens ($n = 72$, 44.7%).

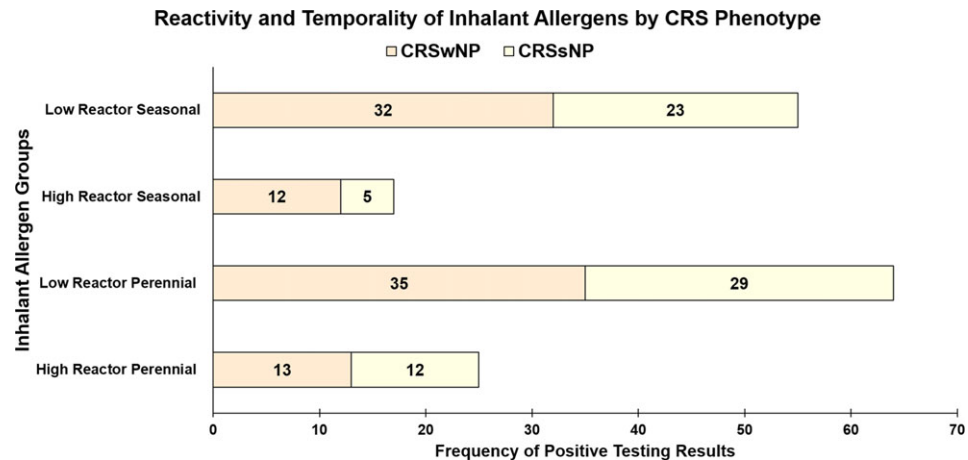


FIGURE 3. Reactivity and temporality of inhalant allergens by CRS phenotype. Horizontal axis represents cumulative frequency of positive test results. Vertical axis represents aeroallergen groups by reactivity (high vs low reactor) and temporality (perennial vs seasonal). There were no significant differences found between allergen group results between CRSwNP and CRSsNP. CRS = chronic rhinosinusitis; CRSsNP = chronic rhinosinusitis without nasal polyposis; CRSwNP = chronic rhinosinusitis with nasal polyposis.

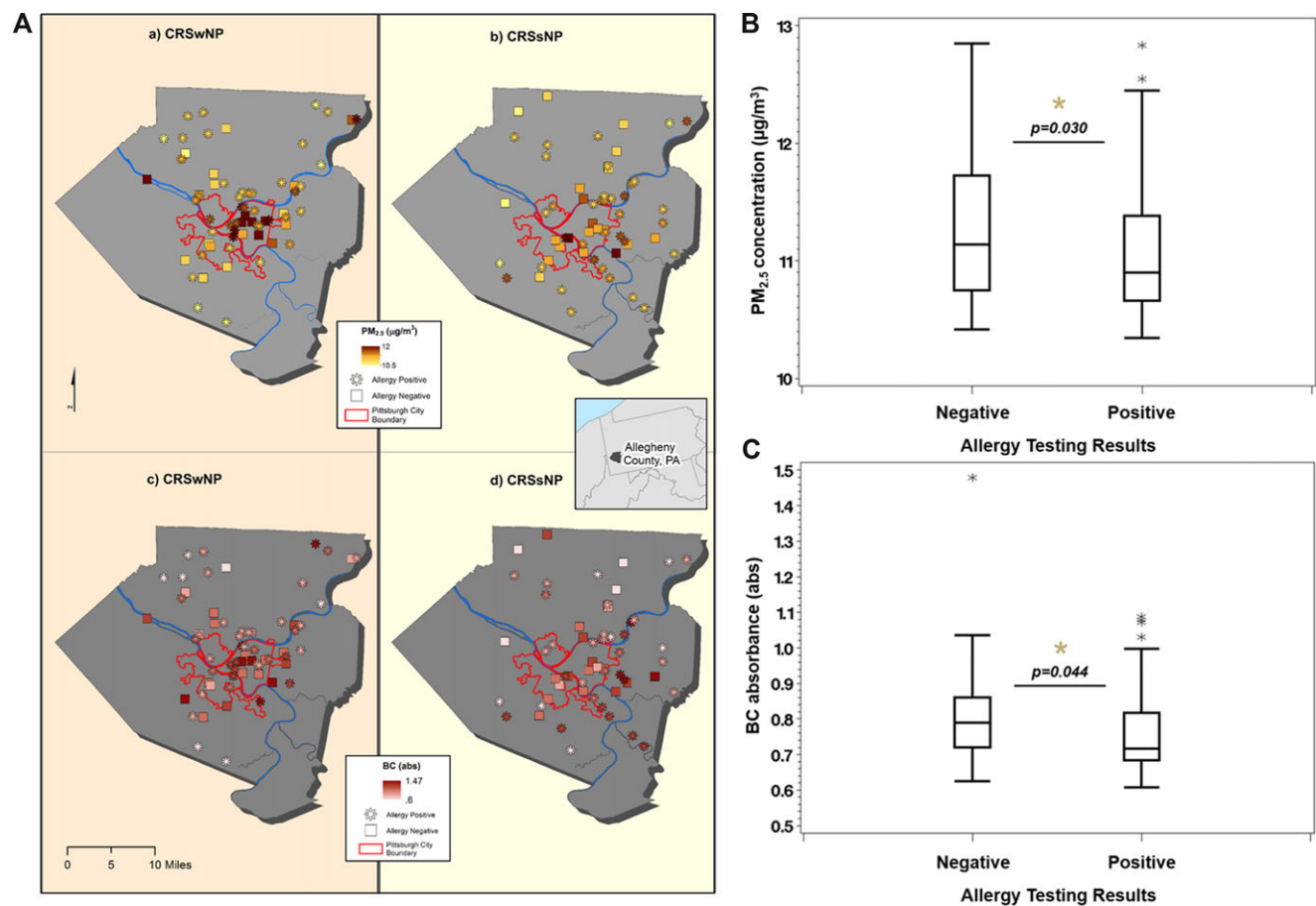


FIGURE 4. (A) Spatial distribution of air pollutants (top panels: PM_{2.5} concentration [µg/m³]; bottom panels: BC absorbance [abs]) by disease phenotype (left panels: CRSwNP; right panels: CRSsNP). Allegheny County, PA, is represented in gray; the Pittsburgh city boundary is marked in red. Confluence of Allegheny, Monongahela, and Ohio Rivers is depicted in blue. Symbols represent individual patient residences by allergy status (asterisk = allergy positive; square = allergy negative). (B, C) Air pollutants by allergy testing results. Boxplots of (B) PM_{2.5} concentration (µg/m³) and (C) BC absorbance (abs) by negative and positive allergy testing results. Significance values are demonstrated for differences between group means. BC = black carbon; CRSsNP = chronic rhinosinusitis without nasal polyposis; CRSwNP = chronic rhinosinusitis with nasal polyposis; PM_{2.5} = particulate matter 2.5.

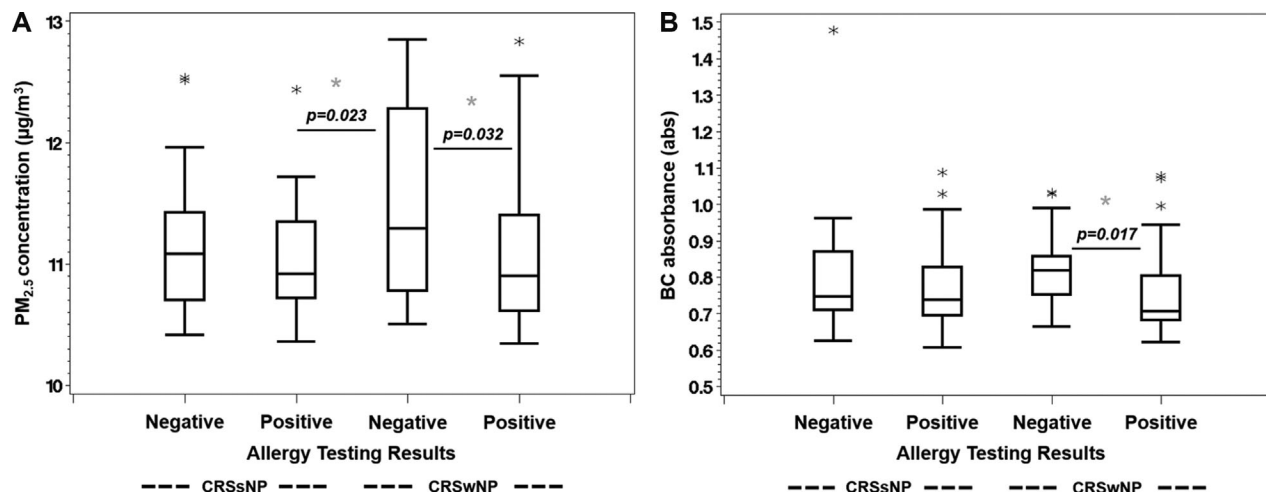


FIGURE 5. Air pollutants by allergy testing results and CRS phenotype. Boxplots of (A) PM_{2.5} concentration ($\mu\text{g}/\text{m}^3$) and (B) BC absorbance (abs) by negative and positive allergy testing results according to CRS phenotype (CRSsNP vs CRSwNP). Significance values are demonstrated for differences between group means. BC = black carbon; CRS = chronic rhinosinusitis; CRSsNP = chronic rhinosinusitis without nasal polyposis; CRSwNP = chronic rhinosinusitis with nasal polyposis; PM_{2.5} = particulate matter 2.5.

Association of disease severity indicators with aeroallergen sensitization and air pollutant exposures

Among patients who tested negative for aeroallergens, there was a significant difference in SNOT-22 scores with CRSsNP demonstrating, on average, higher symptom scores than CRSwNP (45 vs 28, $p = 0.042$). Objective inflammation by LMS, however, was significantly higher, on average, in CRSwNP (30 vs 14, $p < 0.001$), as were steroid doses (2155 vs 541 mg, $p = 0.003$). A similar difference in LMS by CRS phenotype was found among patients who tested positive for inhalant allergens (24 vs 14, $p < 0.001$). There were no differences in clinicodemographic characteristics or disease severity indicators among CRS phenotypes with and without asthma.

There was a trend toward elevated PM_{2.5} and BC among females compared with males, although these differences were not statistically significant (PM_{2.5}, 11.32 vs 11.08 $\mu\text{g}/\text{m}^3$; BC, 0.80 vs 0.76 abs). Female patients were more likely to present without polyposis and demonstrate negative results on allergy testing compared with males ($p = 0.020$). There was a trend toward higher rates of steroid use in females, although these differences were not statistically significant (90.3% vs 75%). Overall, females demonstrated a statistically significant difference in symptomatology scores with mean SNOT-22 scores averaging 45 as compared with 33 in males ($p = 0.039$). There were no differences in LMS between sexes.

There were no significant differences in SNOT-22, LMS, or steroid doses between nonallergic and allergic patients. Regardless of allergy status in CRSsNP, BC correlated strongly with symptom severity scores as measured by SNOT-22 ($r = 0.55$, $p = 0.042$). Log-transformed BC values also demonstrated a similarly substantial correlation with SNOT-22 ($r = 0.56$, $p = 0.039$). Adjusting for age and

sex as potential confounders in a linear regression model predicting SNOT-22 did not modify the BC association. Both age and sex were strongly nonsignificant ($p = 0.500$ and 0.480, respectively). In CRSsNP patients, no significant bivariate associations were identified between AP and disease severity variables.

Discussion

Although the effects of environmental exposure to tobacco smoke and aeroallergens have been investigated in upper airway disease, less is known about the role of AP exposure.^{22,23} In this study we have examined the relationship between AP exposures in CRS with and without polyps among patients with concomitant rhinitis symptoms. We found significant differences in AP levels between allergy-negative and -positive patients with higher average PM_{2.5} and BC in patients with negative allergy testing. There was a significant difference in symptom severity among patients with negative allergy testing, with CRSsNP patients demonstrating higher average SNOT-22 scores than CRSwNP patients. BC specifically appeared to play a significant role in these patients.

Interestingly, nonallergic CRSwNP patients demonstrated the highest exposure levels to PM_{2.5} and BC. Among CRSwNP patients who received steroid treatment, a statistically significant difference in dose was found, with higher doses associated with negative allergy testing. These results suggest that AP may contribute to NAR symptomatology, highlighting the role of environmental factors in differential disease expression.

Despite an overall improvement in regional air quality, Pittsburgh and Allegheny County have been noncompliant with federal standards for over 2 decades, with PM_{2.5} levels exceeding both average annual and daily National Ambient Air Quality Standards.^{19,24} In a recent systematic

review and meta-analysis examining traffic-related air pollution (TRAP) exposure and the risk of developing childhood asthma, a statistically significant association was seen with PM_{2.5} exposure with an overall risk estimate of 1.03 per 1 $\mu\text{g}/\text{m}^3$ PM_{2.5}.²⁵ Another study showed that a 10 $\mu\text{g}/\text{m}^3$ increase in PM_{2.5} was associated with a 1.2-fold increase in the odds of a severe asthma exacerbation and a 1.08-fold increase in medication use in children with asthma.²⁶ Although TRAP has been associated with childhood asthma, similar average exposures to BC and ultra-fine particles between asthmatic and nonasthmatic children have been demonstrated.²⁷ In a study of adults with active asthma, even at levels as low as 4.00-7.06 $\mu\text{g}/\text{m}^3$, each 1 $\mu\text{g}/\text{m}^3$ increase in PM_{2.5} was associated with an increase in asthma symptoms.²⁸ These results suggest that ambient pollutants may differentially impact inflammatory disease severity and expression, regardless of absolute levels.

Unlike PM_{2.5}, there are no established standards for which BC is considered harmful to public health. Environmental toxins have been linked to epigenetic modifications, including DNA methylation and histone alterations, which may be inherited transgenerationally and influence genome function.²⁹ Repetitive element hypomethylation has been associated with malignancy, oxidative stress, atherosclerosis, and cardiovascular disease.³⁰⁻³³ In a study of 1097 serum DNA samples, BC exposure at levels ranging from 0.79 to 1.35 was associated with decreased DNA methylation in long interspersed nuclear elements (LINE-1).³⁴ In a 2012 systematic review, the World Health Organization reported that the estimated health effects from short- and long-term BC exposure may be much higher compared with PM. However, due to the lack of in-vivo and in-vitro studies, the potential mechanisms of toxicity and levels at which the health consequences of BC may be independent of PM effects remain areas of further investigation.¹⁷

AR is an atopic disease that may be associated with CRS, but data regarding this association are inconclusive. One study found positive SPT in 64% of CRS patients compared with <30% of the city's general population.⁸ Another study reported sinusitis in 67.5% of AR patients compared with 33.4% of healthy controls.⁹ However, another recent study did not find an association between LMS and in-vitro allergy results despite reporting an increase in LMS in patients with asthma, a history of anaphylaxis, and nasal polyps.¹⁰ In previous reports that demonstrated a relationship between AR and CRS, sensitization to perennial allergens was more common than to seasonal allergens.³⁵⁻³⁷ In our study, perennial sensitivities were most common with higher rates of low vs high reactors. There were no significant differences found between allergen group results between CRSsNP and CRSwNP. Although an association between allergic sensitization (and AR specifically) and asthma is widely accepted, its role in CRS is still unknown.

Although all patients in this study reported rhinitis symptoms, over one third (36.0%) tested negative for inhalant allergies, suggesting a diagnosis of NAR. NAR is a poorly understood disorder in which patients present with chronic

nasal symptoms, but an allergic trigger seems unlikely or allergy testing is negative. Several NAR subsets have been described with known infectious, pharmacologic, and hormonal etiologies, but idiopathic nonallergic rhinitis accounts for about two thirds of NAR.^{38,39} Similar to AR and CRS, the association between NAR and CRS is debated, but studies have reported that both may impact CRS symptomatology.^{5,40} Localized atopy, in which nasal production of immunoglobulin E (IgE) occurs without positive allergy testing, and "mixed rhinitis," in which patients are diagnosed with AR but report nonallergic triggers, muddle the dichotomy between NAR and AR, indicating there may be greater complexity or overlap in disease expression.^{41,42}

Because this study was retrospective in nature it is subject to recall or misclassification biases. Overlapping disease characteristics between rhinitis and sinonasal inflammation among CRS phenotypes may mask statistically significant associations between exposures and disease severity measures. Negative allergy testing does not completely exclude a diagnosis of AR given varying sensitivities and specificities of testing assays. Our study was limited to data regarding 14 commonly tested aeroallergens and may miss sensitivities associated with allergens that were not included. We recognize that different exposure assignment methods (including spatial, seasonal, or temporal changes) may differ in accuracy and precision of exposure estimates, which may influence estimated health impacts of different pollutants.

Socioeconomic factors may also influence the association between exposures and health outcomes not examined in this study. We acknowledge that the study findings represent *potential* associations between air pollutant exposures and disease expression. This investigation was limited to a single health system within 1 county (93.5% of the Allegheny County population is at the high school graduate level or higher, with 87.0% of individuals above the poverty level), which may produce less variability in socioeconomic cohort characteristics compared with statewide, multi-institutional, or national studies.^{43,44} Nevertheless, we recognize that the pollutant and associated symptomatology differences identified in this investigation may represent surrogate factors for social determinants of health which were not examined (income and social status, education level, access and use of health services, use of health services, and social support networks). To address these limitations, further investigations are required, ideally in a prospective fashion, comparing sinonasal disease subgroups with a control population.

Conclusion

Our results suggest that small inhalant pollutants may contribute to nonallergic symptomatology in CRS patients. Regardless of allergy status, our findings propose that air pollutants may play a role in CRSsNP symptom severity. This study is the first to evaluate objectively the influence of AP exposures in rhinitis disease expression among CRS phenotypes. Our findings may partly explain persistent

rhinitis symptoms in allergy test-negative patients, which are often labeled with a diagnosis of chronic rhinitis. Through this pilot study, our findings highlight the potential role of environmental factors in differential disease expression and provide insight into potentially underlying etiologies of chronic rhinitis. 

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