Case–Control Study of Lung Function in World Trade Center Health Registry Area Residents and Workers

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Rationale: **Residents and area workers who inhaled dust and fumes from the World Trade Center disaster reported lower respiratory symptoms in two World Trade Center Health Registry surveys (2003–2004 and 2006–2007), but lung function data were lacking.**

Objectives: **To examine the relationship between persistent respiratory symptoms and pulmonary function in a nested case–control study of exposed adult residents and area workers 7–8 years after September 11, 2001.**

Methods: **Registrants reporting post September 11th onset of a lower respiratory symptom in the first survey and the same symptom in the second survey were solicited as potential cases. Registrants without lower respiratory symptoms in either Registry survey were solicited as potential control subjects. Final case–control status was determined by lower respiratory symptoms at a third interview (the study), when spirometry and impulse oscillometry were also performed.**

Measurements and Main Results: **We identified 180 cases and 473 control subjects. Cases were more likely than control subjects to have abnormal spirometry (19% vs. 11%; $P < 0.05$), and impulse oscillometry measurements of elevated airway resistance (R_5; 68% vs. 27%; $P < 0.0001$) and frequency dependence of resistance (R_{5-20}; 36% vs. 7%; $P < 0.0001$). When spirometry was normal, cases were more likely than control subjects to have elevated R_5 and R_{5-20} (62% vs. 25% and 27% vs. 6%, respectively; both $P < 0.0001$). Associations between symptoms and oscillometry held when factors significant in bivariate comparisons (body mass index, spirometry, and exposures) were analyzed using logistic regression.**

Conclusions: **This study links persistent respiratory symptoms and oscillometric abnormalities in World Trade Center–exposed residents and area workers. Elevated R_5 and R_{5-20} in cases despite normal spirometry suggested distal airway dysfunction as a mechanism for symptoms.**

Keywords: distal airways; oscillometry; spirometry; disaster

AT A GLANCE COMMENTARY

Scientific Knowledge on the Subject

World Trade Center–exposed residents and area workers have experienced ongoing lower respiratory symptoms, but spirometry measurements incompletely explain these findings, indicating a need for additional lung function studies.

What This Study Adds to the Field

The case–control design allowed demonstration of an association between lower respiratory symptoms and impulse oscillometry measurements of elevated airway resistance and frequency dependence of resistance. The presence of these findings despite normal spirometry suggested that regional distal airways dysfunction contributes to lower respiratory symptoms.

The attack on the World Trade Center (WTC) exposed 409,000 rescue and recovery workers, area workers, and residents to toxins, dust, and smoke that persisted after September 11, 2001 (9/11) (1, 2). Persistent cough, wheeze, dyspnea, and asthma have been documented both acutely and up to 7 years later (3–13). WTC exposures significantly associated with respiratory symptoms in residents and area workers included dust cloud interaction, dust in the home or workplace, and duration of dust and odors in the home (11, 14). Positive, graded links between these exposures and reported upper and lower respiratory symptoms (LRS) and asthma have been documented up to 6 years after 9/11 (14–16).

Abnormal screening spirometry has been demonstrated in approximately 25% of subjects in studies of WTC disaster–exposed populations with LRS (5, 16–18), supporting a link between symptoms and functional impairment. However, spirometry results in most subjects were within population norms. Spirometry remained normal in most exposed firefighters after 9/11, although the group mean showed significant longitudinal decrements in forced expiratory volume in one second (FEV_1) (19). Therefore, the utility of spirometry in explaining LRS in WTC-exposed groups has been limited.

Spirometry may not detect abnormalities in the distal airways (20, 21) potentially damaged by environmental exposures. This "silent zone of the lung" has a large aggregate cross-sectional area, and contributes minimally to total resistance (21, 22). However, in obstructive airway diseases, the predominant reduction may occur distally (23–25). Impulse oscillometry (IOS) assesses airway resistance and frequency dependence of resistance (FDR). FDR provides a measure of nonuniformity of airflow distribution, which may reflect regional functional abnormalities in the distal airways (26–28). FDR correlates with frequency dependence of compliance measured by esophageal manometry, an established test of distal airway function (29–31).

Elevated airway resistance measured by IOS was demonstrated in ironworkers from the WTC site, but was predominantly in smokers and not associated with symptoms (4). An

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association between airway resistance measured by IOS and either WTC exposure or LRS was not found in a study of New York State (NYS) rescue workers (32). However, elevated airway resistance on IOS was demonstrated in symptomatic WTC-exposed residents and workers despite normal spirometry (33).

The WTC Health Registry comprises individuals exposed to the disaster on 9/11 and its aftermath (2). A case-control study of residents and area workers, nested within the Registry, was conducted to determine whether those with persisting, post-9/11 onset LRS (the cases) had greater exposure to the disaster than asymptomatic registrants (the control subjects) (34). In the current study, we investigated whether these cases were more likely to have physiologic indicators of airway injury by spirometry and oscillometry when compared with control subjects; and whether cases, especially those with normal spirometry, were more likely to demonstrate IOS findings consistent with distal airways abnormalities.

Some of the results of this study have been previously reported in the form of an abstract presented to the 2010 annual meeting of the American Thoracic Society (35).

METHODS

The study population comprised Lower Manhattan adult residents and area workers who had responded to the first (2003–2004) and second Registry surveys (2006–2007). Potential cases and control subjects underwent a third evaluation, the case–control interview, including a questionnaire, spirometry, and IOS. Cases were defined as reporting post-9/11 onset LRS (persistent cough, shortness of breath, or wheezing) in the first Registry survey and a LRS or use of a physician-prescribed inhaler at two subsequent points: the second Registry survey and the case–control interview. Control subjects did not report LRS during these timeframes in these three surveys. Registrants were excluded from this study if, at the time of recruitment for the case–control interview, they (*1*) lived more than 50 miles from New York City; (*2*) ever smoked cigarettes ($\geqslant$ 100 cigarettes lifetime); (*3*) reported a history of respiratory or cardiopulmonary disease before 9/11; (*4*) were pregnant; or (*5*) were taking a β-adrenergic blocking medicine at the time of interview, because it may induce bronchospasm.

All participants provided written informed consent. The Institutional Review Boards of the New York City Department of Health and Mental Hygiene and New York University Medical Center, New York, New York, approved the protocol.

Recruitment and Data Collection

All of the limited pool of 140 residents and 59 resident and area workers who met the case criteria were recruited (Figure 1). To increase statistical power, all 479 residents and 151 resident and area workers who met the control criteria were recruited. Because the Registry comprises larger numbers of eligible area worker cases and control subjects, random samples of these were prepared.

A computer-assisted, nurse-administered symptom and exposure questionnaire, height, weight, and blood pressure measurements, spirometry, and IOS were performed during a single visit to a community field site. Acute WTC disaster exposures involved contact with the dust cloud created by the towers' collapse. Chronic factors were based on prolonged exposures in the home or work site including extent of dust, cleaning, smelling smoke, and time spent at home or work. Principal components analyses were used to create composite exposure scales based on responses to detailed questions about participants' experiences on 9/11 and the months that followed (34). Symptom questions were modified from validated questionnaires (36–38). Additional details of subject selection and recruitment are provided in the online supplement.

Spirometry

Spirometry (Masterscreen IOS; Viasys Healthcare, Yorba Linda, CA) was performed in accordance with American Thoracic Society/European Respiratory Society standards (39). FEV_1, FVC, and FEV_1/FVC were referenced to published predictive equations (40–42). Spirometry patterns were classified as normal (FEV_1/FVC and FVC $\geqslant$ 5th percentile); obstructive spirometry (FEV_1/FVC < 5th percentile); or restrictive spirometry (FVC < 5th percentile with normal FEV_1/FVC).

Oscillometry

Testing and data selection procedures are provided in the online supplement. Measurements included airway resistance assessed at an oscillating frequency of 5 Hz (R_5) and FDR calculated as the difference between resistance at 5 and 20 Hz ($R_{5–20}$) (28). Published values were used for upper limits of normal for R_5 (3.96 cm H_2O/L/s) and $R_{5–20}$ (0.76 cm H_2O/L/s) (4, 31, 33).

Statistical Analyses

Analyses used SAS version 9.2 (SAS Institute, Cary, NC). The chi-square test was used to determine group differences on categorical variables; the Wilcoxon two-sample test was chosen for group differences on nonnormally distributed R_5 and $R_{5–20}$ values. Stratification and multiple logistic regression were used to ascertain the independent associations between case status and elevated airway resistance or FDR while controlling for confounders including body mass index (BMI). Two-tailed tests were used in all analyses. A maximum P value of 0.05 was chosen for statistical significance.

RESULTS

Participation

Participants were interviewed between March 2008 and June 2010, an average of 20 months after the second Registry survey (range, 6−42 mo) and 7.1 years (78−105 mo) after 9/11. Of 1,384 registrants solicited, 785 were studied, including 274 (59%) eligible cases and 511 (56%) eligible control subjects (Figure 1). Participants and nonparticipants did not vary significantly by case–control status, resident or worker group, sex, age, race and ethnicity, marital status, income, or mode of recruitment into the first Registry survey (data not shown). Participation was significantly lower among the relatively few registrants with less than a high school education (35% of 46 eligible subjects).

Of the 274 potential cases interviewed (i.e., symptomatic on the two prior surveys), 180 (65.7%) reported experiencing a LRS or using an inhaler during the 4 weeks before interview and were accepted as cases. Of the 511 potential control subjects (i.e., with no symptoms on the two prior surveys), 473 (92.6%) reported absence of any of these LRS during the 4 weeks before the interview and were accepted as control subjects.

Case Symptoms

By definition, cases reported a new post-9/11 onset LRS by the date of the first Registry survey, and more than half (53%) reported onset within a year after 9/11. For the four weeks before the case–control interview, cases reported cough (62.8%), dyspnea (56.7%), or wheeze (47.2%). Half the cases (52%) reported having only one LRS (most commonly persistent cough), 25% reported having two symptoms, and 22% reported all three; 2% reported being asymptomatic but used an inhaled or oral medicine for a breathing problem. Nearly two-thirds (63.9%) of cases reported that the LRS occurred on average at least twice a week during the 4 weeks before interview. Cases were more likely than control subjects to report nasal congestion (66% vs. 17%) or sinus congestion (52% vs. 11%) (P < 0.0001 for both). A third (63 of the 180 cases) reported at least one of the following post-9/11 physician diagnoses: asthma (52 cases), chronic bronchitis (22), chronic obstructive pulmonary disease (4), or emphysema (2).

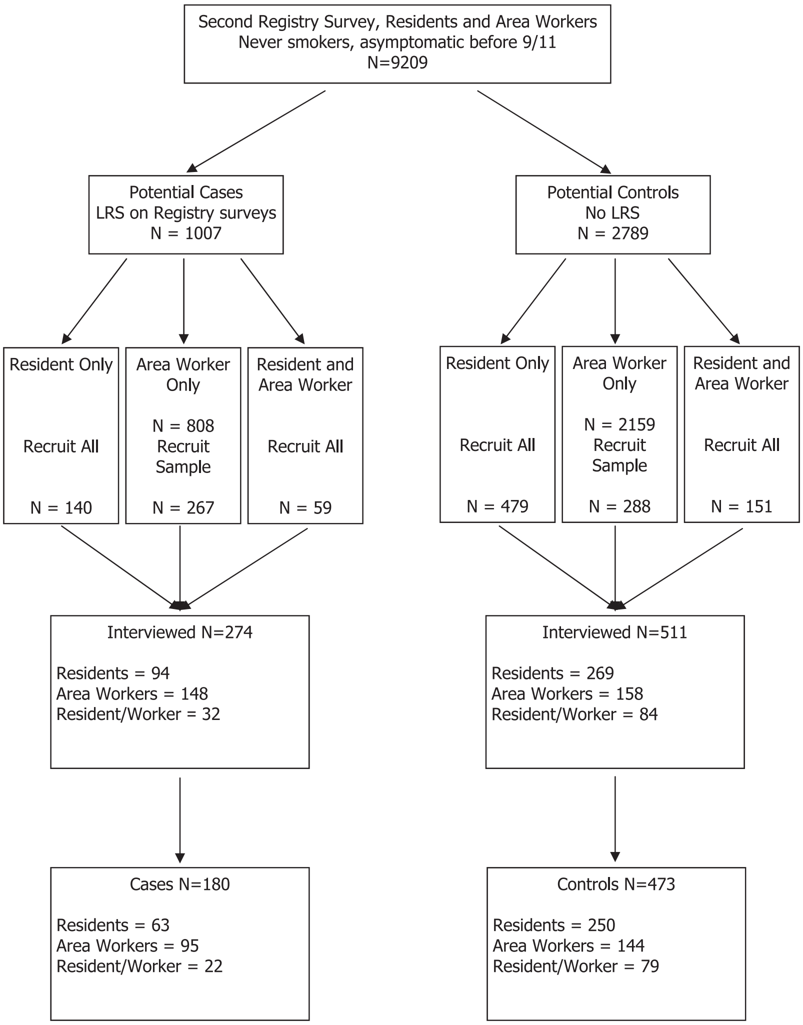

Figure 1. Case–control recruitment flow diagram. Of 25,140 Lower Manhattan residents and area workers who responded to both Registry surveys, 9,209 were never-smokers who denied a history of lower respiratory symptoms (LRS) or cardiopulmonary disease before September 11, 2001. "Potential cases" (1,007) reported LRS on the first survey and LRS or inhaler use on the second survey. "Potential controls" (2,789) reported no LRS or inhaler use. All eligible resident and resident and area worker cases and control subjects, and a sample of worker cases and control subjects, totaling 1,384, were solicited. Of these, 785 were interviewed and tested. Final criteria were met by 180 cases and 473 control subjects.

Demographic and WTC Disaster Exposure Characteristics

Cases were more likely than control subjects to be female, a racial ethnic group other than white non-Hispanic or Asian non-Hispanic, 40 years or older, overweight or obese (BMI $\geq$ 25), and have less than a college education (Table 1).

Using composite measures of acute and chronic exposure to the disaster, crude odds ratios were significantly higher for cases versus control subjects except for time at home or work (Table 2). Odds ratios adjusted for demographic variables and the other exposure factors remained significantly higher on dust cloud density and on two of the composite measures of chronic exposures, dust and smoke at the home or workplace. Adjusted odds ratios for time at home or workplace and cleaning of home or workplace were not found to be significant. Because of participants' lack of knowledge or recall of some exposures, most notably cleaning of their home or office, adjusted odds ratios could be calculated on only 55.6% of the overall 653 participants. Although only those who responded on all demographic and exposure factors were included in the multivariable analysis, those included were not significantly different from those not included in terms of demographics or case status (data not shown).

Occupational or avocational exposure to pulmonary toxins, such as organic solvents, vehicle emissions, or asbestos, was rarely reported by either cases or control subjects.

Pulmonary Function Test Results

Spirometry results were of acceptable quality in 96.0% (627 of 653) of subjects, and IOS results were acceptable in 91.7% (599 of 653).

Cases had a significantly lower median percent of predicted FEV_1 and FVC compared with control subjects ($P < 0.0001$ for both) (Table 3). FEV_1/FVC did not differ significantly. A higher proportion of cases than control subjects had an abnormal spirometry pattern (18.7% vs. 10.8%; $P < 0.05$). The rates of obstructive and restrictive spirometry patterns for cases were 10.2% and 8.4%, respectively, and cases were more likely than control subjects to have a restrictive pattern (8.4% vs. 3.9%; $P < 0.05$).

IOS measurements of airway resistance (R_5) and FDR ($R_{5–20}$) were significantly higher in cases than in control subjects. In cases, the median R_5 was 4.69 cm H_2O/L/s (95% confidence interval [CI], 4.42–4.89) compared with 3.24 in control subjects (95% CI, 3.14–3.36); similarly, median $R_{5–20}$ in cases was 0.54 cm H_2O/L/s (95% CI, 0.45–0.68) compared with 0.052 (95% CI, 0.012–0.11) in control subjects ($P < 0.0001$ for both comparisons). As shown in Table 4, 67.5% of cases had elevated R_5 versus 27.1% of control subjects, and 35.6% of cases had elevated $R_{5–20}$ versus 6.6% of control subjects ($P < 0.0001$ for both comparisons). When spirometry was normal, cases demonstrated elevated R_5 and elevated $R_{5–20}$ significantly more often than did

TABLE 1. DEMOGRAPHIC MEASURES BY CASE–CONTROL STATUS ($N = 653$)

	Cases		Control Subjects		
	N	%	N	%	*P* Value*
Total	180	27.6	473	72.4	
Sex					
Male	59	32.8	241	51.0	Reference
Female	121	67.2	232	49.0	**<0.0001**
Age at interview					
21–39	30	16.7	144	30.4	Reference
40–59	107	59.4	266	56.2	**<0.01**
⩾60	43	23.9	63	13.3	**<0.0001**
Race					
White non-Hispanic	91	50.6	362	76.5	Reference
Black non-Hispanic	32	17.8	22	4.7	**<0.0001**
Hispanic	32	17.8	22	4.7	**<0.0001**
Asian non-Hispanic	13	7.2	63	13.3	0.65
Other	12	6.7	4	0.8	**<0.0001**
Education level, 2003–2004					
< High school graduate	5	2.8	9	1.9	0.20
High school graduate	29	16.1	25	5.3	**<0.0001**
Some college	40	22.2	44	9.3	**<0.0001**
⩾ College graduate	106	58.9	393	83.4	Reference
Body mass index					
Underweight/normal (<25)	44	24.4	273	58.1	Reference
Overweight (25–29)	58	32.2	135	28.7	**<0.0001**
Obese (⩾30)	78	43.3	62	13.2	**<0.0001**

* *P* values compare a given level with the reference category. Bold type indicates $P < 0.05$.

control subjects: 61.7% versus 24.5% and 26.7% versus 5.9%, respectively ($P < 0.0001$ for both). Of the 74 cases with normal spirometry and elevated R_5, 30 (41%) also had elevated $R_{5–20}$. The increased rates of elevated R_5 and elevated $R_{5–20}$ in cases compared with control subjects were not explained by the presence of upper respiratory symptoms. For example, nasal or sinus congestion was not associated with abnormal R_5 or $R_{5–20}$ among cases or control subjects (data not shown).

Because obesity is known to affect airway function, we examined the effect of BMI on the relationship between LRS and IOS results (Figures 2 and 3). Median R_5 increased with increasing BMI for both cases and control subjects (Figure 2), but cases still demonstrated higher median R_5 than control subjects within each BMI group ($P < 0.05$ by Wilcoxon two-sample test). Similarly, in Figure 3, $R_{5–20}$ increased with increasing BMI for both cases and control subjects, but cases had significantly higher $R_{5–20}$ than control subjects within each BMI category ($P < 0.01$). In the absence of obesity, control subjects were likely to have normal airway resistance and FDR: 79% of non-obese control subjects had a normal R_5 value, and 98% of non-obese control subjects had a normal $R_{5–20}$.

Associations between case status and elevated R_5 or $R_{5–20}$ were assessed via logistic regression (Table 5) controlling for variables that were significant in bivariate analyses: spirometry, BMI, age group, sex, race and ethnicity, education, and composite exposure factors (Tables 1 and 2). Odds ratios for increasing R_5 or increasing $R_{5–20}$ in the multivariable model remained significant, although decreased in magnitude, 1.68 (95% CI, 1.21–2.35) and 2.59 (95% CI, 1.21–5.56). Among the exposure factors, dust cloud density, smoke at home or work, and dust at home or work were the strongest predictors of case status. The obese BMI category, sex, age group, non-Hispanic black or Hispanic race and ethnicity, and education level also remained significant in the model but abnormal spirometry did not. Therefore, LRS were significantly associated with oscillometry but not spirometry measurements. When the relationship between each exposure factor and IOS outcome was assessed in an additional logistic regression model controlling for demographics, BMI, and case status, none of the six exposure factors was associated with either R_5 or $R_{5–20}$ (data not shown). Therefore, both exposure factors and IOS outcomes were associated with persistent LRS, but exposure was not associated with R_5 or $R_{5–20}$ in the absence of symptoms.

DISCUSSION

This case–control study of WTC-exposed residents and area workers demonstrated that subjective LRS were associated with objective measures of airway dysfunction and degree of exposure to WTC dust. Whereas spirometry results were not associated with LRS in a multivariable model, elevated airway resistance (increased R_5) and FDR (increased $R_{5–20}$) on IOS were more likely in exposed cases with persistent LRS than in less exposed, asymptomatic control subjects. Although most cases had normal spirometry, most of these normal spirometry cases had elevated airway resistance, indicating that IOS provided additional information about airway function. Many of these subjects with elevated airway resistance also had FDR, compatible with regional distal airways dysfunction as a contributing mechanism for LRS. Lastly, airway injury was evident only in exposed subjects who developed persistent LRS.

Our study used IOS to assess airway resistance and FDR, which has been shown to be a marker of nonuniform distribution of airflow in the distal airways (27, 28). We noted an increased degree and higher prevalence of FDR in cases compared with control subjects suggesting that LRS may reflect dysfunction in the distal airways. Recent literature supports the clinical relevance of distal airway function measurement (43). In smokers with obstructive spirometry (reduced FEV_1/FVC), distal airway

TABLE 2. ODDS RATIO ESTIMATES FOR CASE STATUS BASED ON WORLD TRADE CENTER DISASTER EXPOSURES ($n = 653$)

	N Cases/N Control Subjects*	Crude Odds Ratio (*95% confidence interval*)	Adjusted Odds Ratio†‡ (*95% confidence interval*)
Acute exposures			
Dust cloud density	158/412	2.15 (1.76–2.62)	1.95 (1.38–2.77)
Time in dust cloud	158/412	1.32 (1.11–1.58)	1.02 (0.76–1.39)
Chronic exposures			
Dust at home or work	146/376	1.79 (1.48–2.17)	2.25 (1.50–3.37)
Smoke at home or work	146/376	1.22 (1.01–1.49)	2.25 (1.35–3.76)
Time spent at home or work	146/376	0.79 (0.66–0.94)	1.06 (0.73–1.54)
Cleaning of home or work	122/357	1.67 (1.36–2.05)	1.00 (0.68–1.47)

* Number of participants who answered the specific exposure questions.
† Adjusted for age, sex, race or ethnicity, education, BMI, and listed exposures.
‡ N = 363 (97 cases and 266 control subjects) with responses for all exposure and demographics questions above.

TABLE 3. SPIROMETRY RESULTS, CASES VERSUS CONTROL SUBJECTS ($n = 627$)

Spirometry parameters	Cases ($n = 166$)*		Control Subjects ($n = 461$)*		
	Median	Quartiles	Median	Quartiles	*P* Value†
FEV_1 (% pred)	94.7	[85.3, 104.9]	100	[91.7, 107.1]	<**0.0001**‡
FVC (% pred)	95.8	[87.4, 104.9]	101.3	[93.1, 107.9]	<**0.0001**‡
FEV_1/FVC (%)	78.7	[73.8, 82.2]	79.3	[74.9, 83.2]	0.10‡
Spirometry pattern	N	(%)	N	(%)	
Normal	135	(81.3)	411	(89.2)	<**0.05**§
Obstructive‖	17	(10.2)	32	(6.9)	0.13¶
Restrictive	14	(8.4)	18	(3.9)	<**0.05**#

*14 cases and 12 control subjects with unsatisfactory spirometry results were excluded.
† Bold type indicates $P < 0.05$.
‡ Wilcoxon two-sample test.
§ Overall chi-square for spirometry.
‖ Includes one case and two control subjects with both obstructive and restrictive patterns.
¶ Chi-square, obstructive versus normal.
# Chi-square, restrictive versus normal.

TABLE 4. OSCILLOMETRY RESULTS, CASES VERSUS CONTROL SUBJECTS ($n = 599$)

	Cases ($n = 160$)		Control Subjects ($n = 439$)		Total ($n = 599$)		
	n	(%)	n	(%)	n	(%)	*P* Value*
All participants†	160		439		599		
$R_5 > 3.96$‡	108	(67.5)	119	(27.1)	227	(37.9)	<**0.0001**
$R_{5-20} > 0.76$‡	57	(35.6)	29	(6.6)	86	(14.4)	<**0.0001**
Normal spirometry‖	120		387		507		
$R_5 > 3.96$‡	74	(61.7)	95	(24.5)	169	(33.4)	<**0.0001**
$R_{5-20} > 0.76$‡	32	(26.7)	23	(5.9)	55	(10.9)	<**0.0001**

* Bold type indicates $P < 0.05$ by chi-square.
† 20 cases and 34 control subjects with unsatisfactory quality oscillometry results were excluded.
‡ cm H_2O/L/s.
‖ Either spirometry or oscillometry was not of acceptable quality for 31 cases and 42 control subjects.

dysfunction was highly predictive of further decline in FEV_1 (44). Lastly, other studies have demonstrated that distal airway dysfunction is associated with an accelerated decline in FEV_1 (45, 46).

This study is consistent with reports that only a minority of symptomatic WTC-exposed subjects demonstrate spirometric abnormalities, predominantly reduced FVC with normal FEV_1/FVC (5, 8). Although reduced FVC often indicates a restrictive pattern, our finding of increased airway resistance suggests a functional airway abnormality, supported by reports of bronchial hyperreactivity and demonstration of bronchial wall thickening and air trapping on computed tomography (16, 18, 47).

In the setting of normal spirometry, oscillometric evaluation of distal airway function has provided information not apparent on spirometry in several clinical settings. In coal workers, oscillometry detected abnormalities not found on spirometry, plethysmography, and pulmonary diffusion testing (48). In school-aged children, oscillometric abnormalities were highly correlated with both atopy and exercise-induced bronchospasm (49). In subjects with chronic obstructive pulmonary disease, oscillometric measurements correlated with symptoms and quality of life independent of spirometry and imaging (50). Our data are in accord with these studies. Future longitudinal studies will determine whether our findings progress to overt airflow obstruction. The likelihood of distal airway abnormalities also indicates a potential target for treatment (24).

A minority of our cases had both normal spirometry and normal oscillometry results. In these cases, neither test may have been sufficiently sensitive to detect functional abnormality, or other pathophysiologic processes may have been responsible for these symptoms.

We found an association between IOS abnormalities and LRS in contrast to a study of NYS rescue workers (32). Our cases may have had greater acute exposure to the disaster on 9/11 (73% reported being in the dust cloud, whereas most NYS workers arrived after 9/11), and all our cases had LRS during the 4 weeks before testing compared with 37% of NYS cases.

We excluded registrants who ever smoked cigarettes to eliminate a known but extraneous cause of reduced pulmonary function, and we adjusted for obesity, which is potentially a confounder (32, 51). Increased R_5 and R_{5-20} were associated with obesity, and obesity attenuated the relationship between these parameters and LRS. However, an association between IOS parameters and LRS independent of obesity was demonstrated both by analysis stratified by BMI category and by multivariable logistic regression analysis, which included BMI and IOS.

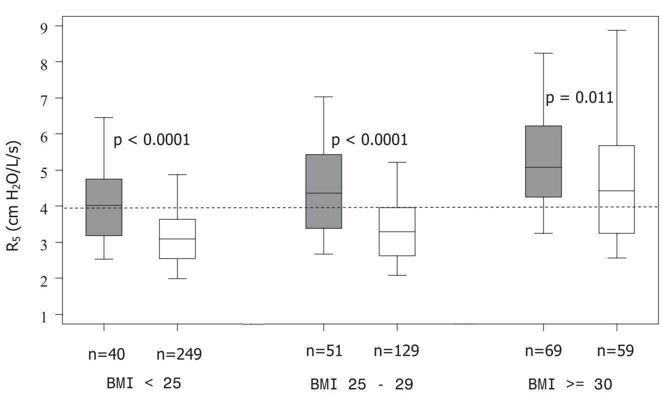

Figure 2. Pulmonary resistance (R_5) by body mass index (BMI) status, cases versus control subjects. ($n = 597$) Case boxes are shaded, control boxes are clear. Boxes represent 25th, 50th, and 75th percentiles for R_5 distribution. Whiskers represent 5th and 95th percentiles. The dotted line at 3.96 cm H_2O/L/s represents the maximum normal value for R_5. R_5 for cases is significantly different from control subjects for each BMI category.

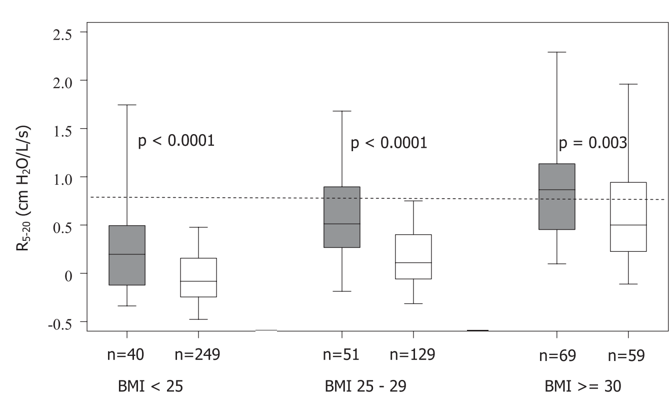

Figure 3. Frequency dependence of resistance (R_{5-20}) by body mass index (BMI) status, cases versus control subjects. ($n = 597$) Case boxes are shaded, control boxes are clear. Boxes represent 25th, 50th, and 75th percentiles for R_{5-20} distribution. Whiskers represent 5th and 95th percentiles. The dotted line at 0.76 cm H_2O/L/s represents the maximum normal value for R_{5-20}. R_{5-20} for cases is significantly different from control subjects for each BMI category.

TABLE 5. CRUDE AND ADJUSTED ODDS RATIOS FOR ASSOCIATIONS BETWEEN CASE STATUS AND OSCILLOMETRY, ($n = 326$)*

Factor (Respondents)	Risk Group	Crude Odds Ratio† (*95% CI*)	Adjusted Odds Ratio† (*95% CI*) Model 1	Adjusted Odds Ratio† (*95% CI*) Model 2
Sex (653)	Female	**2.13 (1.49–3.05)**	1.77 (0.69–4.57)	**3.42 (1.44–8.12)**
	Male	Reference	Reference	Reference
Age group (653)	⩾60 yr	**3.28 (1.89–5.69)**	**6.63 (1.66–26.46)**	**5.74 (1.45–22.77)**
	40–59 yr	**1.93 (1.23–3.04)**	**5.08 (1.62–15.94)**	**4.65 (1.51–14.28)**
	18–39 yr	Reference	Reference	Reference
Race and ethnicity (653)	Hispanic, black, other	**6.47 (4.25–9.85)**	**3.34 (1.24–9.05)**	**2.80 (1.05–7.48)**
	White, Asian	Reference	Reference	Reference
Education (651)	⩽ High school	**2.99 (1.80–4.99)**	**10.79 (3.01–38.69)**	**8.69 (2.50–30.23)**
	At least some college	Reference	Reference	Reference
Body mass index (650)	⩾30 (obese)	**7.81 (4.92–12.38)**	**3.58 (1.23–10.46)**	**4.35 (1.50–12.57)**
	25–29 (overweight)	**2.67 (1.71–4.15)**	2.02 (0.73–5.62)	2.55 (0.96–6.80)
	<25 (normal/underweight)	Reference	Reference	Reference
Dust cloud density (570)	Continuous variable	**2.15 (1.76–2.62)**	**1.76 (1.18–2.63)**	**1.83 (1.24–2.70)**
Time in dust cloud (570)	Continuous variable	**1.32 (1.11–1.58)**	1.00 (0.73–1.36)	0.95 (0.70–1.30)
Dust at home or work (522)	Continuous variable	**1.79 (1.48–2.17)**	**2.02 (1.30–3.15)**	**1.98 (1.28–3.06)**
Smoke at home or work (481)	Continuous variable	**1.22 (1.01–1.49)**	**2.45 (1.29–4.64)**	**2.56 (1.34–4.88)**
Time at home or work (522)	Continuous variable	**0.79 (0.66–0.94)**	1.12 (0.73–1.72)	1.13 (0.74–1.73)
Cleaning home or work (479)	Continuous variable	**1.67 (1.36–2.05)**	1.29 (0.82–2.00)	1.19 (0.77–1.82)
Spirometry status (627)	Abnormal	**1.85 (1.14–3.01)**	1.22 (0.41–3.67)	1.19 (0.38–3.72)
	Normal	Reference	Reference	Reference
R_5 (599)	Continuous variable	**1.91 (1.64–2.21)**	**1.68 (1.21–2.35)**	
$R_{5–20}$ (599)	Continuous variable	**7.27 (4.70–11.26)**		**2.59 (1.21–5.56)**

Model 1: case status = R_5 controlling for age, sex, race or ethnicity, education, body mass index, spirometry, and exposures. Model 2: case status = $R_{5\text{-}20}$ controlling for age, sex, race or ethnicity, education, body mass index, spirometry, and exposures.

* Data unavailable for 101 cases and 226 control subjects because of unacceptable lung test results or missing responses on questionnaires.

† Bold type indicates $P < 0.05$.

A potential limitation to our study is that we classified IOS measurements as abnormal based on limited normal population data. However, values for airway resistance and FDR in nonobese control subjects were generally below the published upper limit of normal, supporting the limits chosen (79% had a normal R_5 value and 98% had a normal $R_{5–20}$). In addition, we found similarly significant results when we analyzed cases versus control subjects based on the distribution about the median. Another possible limitation is that we conducted spirometry and oscillometry during only a single visit. Day to day variation may have reduced the accuracy of individual lung function measurement, but introduction of a specific bias is unlikely.

Our study is subject to selection and recall biases that affect the Registry in which it is nested (2, 11). Exposed people may have been more likely to recall symptoms, symptomatic people may have been more likely to recall exposures, and both may have been more likely to enroll in the Registry. In the first Registry survey, 17.4% of the estimated 409,000 exposed population were interviewed; 68% of these were interviewed in the second survey, from which our potential cases and control subjects were chosen. Selection bias may decrease the generalizability of findings from Registry surveys to the overall exposed population. Selection bias within our case–control study was minimized by vigorous recruitment with enrollment of 57% of eligibles. Participants were similar demographically to residents and area workers who were eligible but did not participate. Responses to detailed questions in our study interview correlated strongly and significantly with responses to prior Registry surveys, suggesting that additional recall bias was minimal. Furthermore, IOS measurement is effort independent, and cases and control subjects did not know their pulmonary function test results before interview. Therefore, selection or recall biases do not apply to these results, and do not affect the association between these measurements and LRS.

In summary, WTC dust and smoke exposure in these residents and area workers is associated with persistent LRS. This study links these symptoms to lung function abnormalities. IOS captured abnormalities beyond those identified by spirometry. The association between post-9/11 onset, repeatedly reported LRS years after exposure, and current lung function abnormalities suggests persistent airway disease. The presence of FDR is compatible with distal airways dysfunction as a contributing mechanism for these symptoms. This analysis highlights the value of assessing distal airway function when evaluating individuals with persistent respiratory symptoms and normal spirometry.

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