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Background—The association of particulate matter (PM) with cardiovascular morbidity and mortality is well documented. PM-induced ischemia is considered a potential mechanism linking PM to adverse cardiovascular outcomes.

Methods and Results—In a repeated-measures study including 5979 observations on 48 patients 43 to 75 years of age, we investigated associations of ambient pollution with ST-segment level changes averaged over half-hour periods measured in the modified V_5 position by 24-hour Holter ECG monitoring. Each patient was observed up to 4 times within 1 year after a percutaneous intervention for myocardial infarction, acute coronary syndrome without infarction, or stable coronary artery disease without acute coronary syndrome. Elevation in fine particles ($PM_{2.5}$) and black carbon levels predicted depression of half-hour–averaged ST-segment levels. An interquartile increase in the previous 24-hour mean black carbon level was associated with a 1.50-fold increased risk of ST-segment depression ≥0.1 mm (95% CI, 1.19 to 1.89) and a −0.031-mm (95% CI, −0.042 to −0.019) decrease in half-hour–averaged ST-segment level (continuous outcome). Effects were greatest within the first month after hospitalization and for patients with myocardial infarction during hospitalization or with diabetes.

Conclusions—ST-segment depression is associated with increased exposure to $PM_{2.5}$ and black carbon in cardiac patients. The risk of pollution-associated ST-segment depression may be greatest in those with myocardial injury in the first month after the cardiac event. **(*Circulation*. 2008;118:1314-1320.)**

Key Words: air pollution ■ cardiovascular diseases ■ myocardial infarction ■ particulate matter ■ ST-segment depression

Traffic exposure has been documented as a trigger for myocardial infarction,[1] but electrophysiological evidence linking elevated ambient pollution to either myocardial injury or ischemia is limited. A recent chamber study of 20 men with prior myocardial infarction and stable coronary artery disease demonstrated increased ST-segment depression in response to exercise during concomitant controlled exposure to dilute diesel exhaust.[2] Associations of increased ambient particle mass with ST-segment depression have been demonstrated in 2 additional panel studies: 1 study of 45 nonhospitalized adults from Helsinki, Finland, with stable coronary heart disease[3] and another of 24 free-living elderly adults from Boston, Mass.[4] We hypothesized that pollution influenced ST-segment level in patients with documented coronary artery disease after hospitalization and percutaneous coronary intervention for either an acute coronary syndrome or chronic stable coronary artery disease with worsening symptoms. We further investigated whether myocardial injury increased vulnerability to pollution effects and whether patients were most at risk for pollution effects in the first month after hospitalization.

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Methods

Study Participants and Design

Before discharge, we recruited a panel of patients with documented coronary artery disease from the greater Boston area (within Route 495) who had undergone percutaneous coronary intervention for an acute coronary syndrome (acute myocardial infarction or unstable angina pectoris) or for worsening stable coronary artery disease. We excluded those with atrial fibrillation and left bundle-branch block because of the intent to evaluate heart rate variability and ST-segment depression as an outcome. Coronary artery bypass graft surgery within the last 3 months was an exclusion criterion because

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the nonspecific ST- and T-wave changes postoperatively would preclude accurate interpretation of new ST- and T-wave changes. Patients with psychiatric illness or drug abuse problems were excluded because of compliance and reliability issues. Active cigarette smoking was an exclusion criterion at entry to the study, and no participant reported current smoking at the time of recruitment. Although we did have 4 subjects who reported recidivist smoking, each reported smoking only at 1 visit, and only 1 reported >0 to 1 cigarettes per day at that visit (Table 1). The protocol included a home visit within 2 to 4 weeks after hospital discharge, followed by 3 additional follow-up visits at ≈3-month intervals. At the first visit, a baseline screening questionnaire regarding medications, pulmonary and cardiac symptoms, and smoking history was administered. Twenty-four–hour 3-lead Holter ECG monitoring (Marquette Seer Digital Recorder, Marquette Inc, Milwaukee, Wis) also was performed with electrodes in modified V_5 and aVF positions. For subsequent visits, participants were administered a brief questionnaire regarding cardiac and respiratory symptoms and medication use and then received 24-hour Holter monitoring. The study design was reviewed and approved by the human subjects committees of the Brigham and Women's Hospital and the Harvard School of Public Health. The authors had full access to and take full responsibility for the integrity of the data. All authors have read and agree to the manuscript as written.

Processing of Holter Recordings

As described in a previous study,[4] the digital Holter recordings were downloaded to a MARS Ultra 60 playback system (Marquette Inc) for analysis. ST segments were evaluated for the average value for each half-hour interval and for ischemic episode. Recordings were visually scanned by an experienced analyst to censor artifacts. Custom algorithms were created to calculate the average value referenced to the P-R isoelectric values for each segment. Each participant obtained ≈48 successful half-hour–averaged ST-segments per visit during 24-hour Holter monitoring period for further data analyses. Separately, each ischemic episode was evaluated by the use of real-time ECG strips examined by an experienced analyst and physician blinded to air pollution status. A table of J-point values, ST-segment values, ST-segment slope, and heart rate was printed for each candidate episode beginning 10 minutes before each episode and ending 10 minutes after the resolution of each episode. The ST-segment value 60 ms after the J point was used to define the ST-segment value. An episode of ischemia was defined as ≥1 mm horizontal or downsloping ST-segment depression compared with the resting baseline that lasted ≥1 minute and was separated by ≥5 minutes from other episodes.

Environmental Data

Ambient fine particulate matter ($PM_{2.5}$) and black carbon (BC) were collected at an ambient monitor site operated by the Harvard School of Public Health, which was a median distance of 17.6 km from participant homes. Hourly measurements of carbon monoxide (CO), ozone (O_3), nitrogen dioxide (NO_2), and sulfur dioxide (SO_2) were obtained from state monitoring sites in Boston, taking the mean of site values for each gas. There were 5 sites for NO_2 and SO_2 measurement; 4 sites for CO measurement; and 3 sites for O_3 measurement. Continuous $PM_{2.5}$ was measured with a tapered element oscillating microbalance (model 1400A, Rupprecht and Patashnick, Albany, NY). The tapered element oscillating microbalance sample filter is heated to 50°C, leading to season-specific temperature-related loss of semivolatile mass. Season-specific calibration factors were used to correct for the losses of mass.[5] The calibration factors were obtained by regressing continuous $PM_{2.5}$ concentrations averaged over 24-hour periods on the corresponding collocated integrated 24-hour Harvard Impactor (Air Diagnostics Environmental Inc, Harrison, Me) low-volume Teflon filter gravimetric measurements. BC was measured with a model AE-14 aethalometer (Magee Scientific Inc, Berkeley, Calif). Hourly temperature was obtained from the National Weather Service First Order Station at Logan Airport.

Table 1. Participant Characteristics

Characteristic	n (%)*
Sex	
Female	9 (19)
Male	39 (81)
Age, y	
Median	57
Range	43–75
Race	
Black	1 (2)
White	45 (94)
Asian and other	2 (4)
Discharge diagnosis	
Myocardial infarction	19 (40)
Unstable angina pectoris	19 (40)
Worsening stable coronary artery disease	10 (20)
Visits, n	
1	47 (37)
2	35 (27)
3	25 (20)
4	21 (16)
Total	128 (100)
Smoking	
Never	17 (35)
Former	27 (56)
Current	4 (8)
Medication use	
β-Blocker	45 (94)
Calcium channel blocker	8 (17)
Angiotensin-converting enzyme inhibitor	27 (56)
Statin	45 (94)
Aspirin	48 (100)
Ever had myocardial infarction	
Yes	29 (60)
No	19 (40)
Diabetes	
Yes	12 (25)
No	36 (75)
Ischemia episodes after hospitalization†	
Yes	13 (27)
No	35 (73)
ST-segment level, modified V_5 lead, mm	
Median‡	−0.11
Range	−3.65–2.85

*Percentages may not add up to 100 because of rounding.
†Thirteen participants with 38 episodes.
‡Based on 5979 observations of half-hour–averaged ST-segment levels on the 48 participants in analyses.

Statistical Analyses

We applied linear additive models[6] to analyze the association between half-hour–averaged ST-segment levels and air pollutants, including $PM_{2.5}$, BC, CO, O_3, NO_2, and SO_2, at previous 1- to 6-, 12-, 24-, 48-, 72-hour means in single-pollutant models. The moving

Table 2. Ambient Air Pollution and Temperature Levels During Holter Monitoring (5979 Valid Measurements)

	25th Percentile	50th Percentile	75th Percentile	Maximum
Ambient air pollution				
$PM_{2.5}$, $\mu g/m^3$				
12-h mean	6.18	8.91	13.18	37.13
24-h mean	6.38	9.20	13.31	40.38
BC, $\mu g/m^3$				
12-h mean	0.49	0.75	1.04	3.50
24-h mean	0.54	0.79	1.01	2.44
CO, ppm				
12-h mean	0.35	0.48	0.62	1.88
24-h mean	0.37	0.46	0.62	1.56
O_3, ppb				
12-h mean	12.69	20.78	29.23	83.60
24-h mean	14.32	21.28	28.62	71.84
NO_2, ppb				
12-h mean	17.30	21.40	25.77	46.04
24-h mean	18.02	21.40	24.94	44.45
SO_2, ppb				
12-h mean	3.09	4.43	6.40	29.39
24-h mean	3.29	4.55	6.43	23.72
Temperature, °C				
1-h mean	0.75	7.90	18.97	39.49

average was computed only if 75% of the data were present. Untransformed ST-segment levels were used for analyses because this outcome was normally distributed.[7] Each regression model included fixed effects for participant, day of the week, and visit order. The models also adjusted for several smooth terms as fit by penalized cubic regression splines to reflect possible nonlinear effects of several continuous covariates. These terms included visit date, hour of the day, and apparent temperature.[8] The smooth term hour of the day accounts for serial autocorrelation among measurements taken on the same day above that explained by the subject-specific intercepts in the model. Autocorrelation plots of the residuals were checked to see whether this term sufficiently accounted for autocorrelation in the data, and results suggested it did. Apparent temperature was calculated as follows: $-2.653+(0.994\times Ta)+(0.0153\times Td2)$, where Ta is the air temperature and Td is the dew point. To eliminate concurvity or correlation/collinearity between the penalized splines of date and apparent temperature, apparent temperature was regressed against date, with the residuals from this model included in all final models. All results are scaled to the interquartile increase in pollutant level for the appropriate cumulative average.

In secondary analyses, the additive mixed logistic regression models were used to estimate associations between the probability of ST-segment depression ≥0.1 mm and pollution. These analyses, which fall within the generalized additive mixed model[9] framework, contained the same terms as the linear models, except that the participant-specific terms were treated as random effects. Effect modifications by medical diagnosis, visit (the first visit versus the rest of the visits), and daytime (9 AM to 10 PM) versus nighttime (11 PM to 8 AM) were assessed in separate linear additive models and additive mixed logistic regression models by including interaction terms between air pollution effects and each potential effect modifier. We also evaluated the sensitivity of the results to the potential effects of dropout by estimating the effect modification by visit after excluding participants having only 1 visit. Finally, multipollutant and single-pollutant analyses were performed when less tightly correlated pollutants potentially representing different sources or components could be jointly entered into the model. All statistical analyses were performed with R statistical software version 2.4.1. Estimates of the effects of air pollutants were scaled to interquartile range (IQR), the difference between the 25th and the 75th percentile, in levels for the appropriate hour mean of air pollutants.

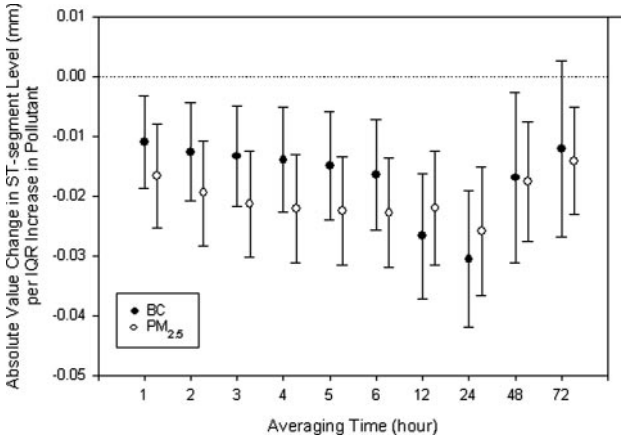

Figure 1. The effects of $PM_{2.5}$ and BC on half-hour–averaged ST-segment level estimated by single-pollutant models scaled to IQR increase in levels for individual hour mean. Error bars indicate 95% CIs.

Results

Forty-eight participants were recruited for the study, and 128 visits with 5979 half-hour observations were included in the analyses. Of the 48 participants, 35 (Table 1) had >1 visit. The median age of the population was 57 years; 81% of the participants were male. Nineteen (40%) of the participants had a discharge diagnosis of myocardial infarction; 13 (27%) had ischemic episodes during the 24-hour Holter periods after hospitalization; and 12 (25%) had diabetes. Most participants took β-blockers and aspirin (Table 1). Ambient air pollution and temperature levels are summarized in Table 2. The mean levels for US Environmental Protection Agency criteria pollutants at 24-hour averaging time were all below accepted or proposed National Air Quality Standards (Table 2).[10]

Associations of Particulate Air Pollutants With ST-Segment Depression

Ambient levels of particulate air pollutants rose early in the morning at 4 AM and were at their peak between 7 and 8 AM, whereas half-hour mean ST-segment levels fell in the morning at 5 AM and were at their lowest between 3 and 4 PM. Pearson correlations showed moderate correlations between $PM_{2.5}$ and BC ($r=0.56$) and low correlations between $PM_{2.5}$ and O_3 ($r=0.20$), SO_2 ($r=0.25$), or NO_2 ($r=0.38$) among all 2×2 combinations of the 6 air pollutants.

Increases in the mean 1- to 24-hour $PM_{2.5}$ and BC levels predicted depression of half-hour–averaged ST-segment levels (Figure 1). For ST-segment depression as a continuous outcome, the cumulative effect was strongest at 24 hours and waned after 48 hours (Figure 1). This association persisted with adjustment for elevation in half-hour–averaged heart rate, which itself was associated with a very small but significant ST-segment depression (estimated effect,

Table 3. Ambient Pollution as a Predictor of ST-Segment Level

Air Pollutant	Estimated ST-Segment Change for Continuous Outcome, mm*†		Estimated Relative Risk for ST-Segment Depression ≥0.1 mm*‡	
	12-Hour Mean (95% CI)	24-Hour Mean (95% CI)	12-Hour (95% CI)	24-Hour (95% CI)
Single-pollutant model				
$PM_{2.5}$, $\mu g/m^3$	−0.022 (−0.032–−0.012)	−0.026 (−0.037–−0.015)	1.02 (0.86–1.21)	1.22 (0.99–1.50)
BC, $\mu g/m^3$	−0.027 (−0.037–−0.016)	−0.031 (−0.042–−0.019)	1.13 (0.94–1.37)	1.50 (1.19–1.89)
CO, ppm	0.013 (0.003–0.024)	0.007 (−0.004–0.019)	0.70 (0.58–0.84)	0.84 (0.68–1.03)
O_3, ppb	0.001 (−0.012–0.014)	0.004 (−0.01–0.019)	0.88 (0.70–1.09)	0.59 (0.45–0.77)
NO_2, ppb	−0.01 (−0.022–0.002)	−0.029 (−0.041–−0.017)	1.06 (0.87–1.29)	1.51 (1.23–1.85)
SO_2, ppb	−0.032 (−0.042–−0.023)	−0.033 (−0.043–−0.023)	1.23 (1.08–1.41)	1.41 (1.18–1.69)
Two-pollutant models				
$PM_{2.5}+NO_2$				
$PM_{2.5}$, $\mu g/m^3$	−0.023 (−0.034–−0.012)	−0.017 (−0.029–−0.004)	0.99 (0.82–1.21)	1.00 (0.80–1.25)
NO_2, ppb	0.003 (−0.01–0.017)	−0.019 (−0.033–−0.006)	1.06 (0.85–1.34)	1.51 (1.19–1.92)
$PM_{2.5}+SO_2$				
$PM_{2.5}$, $\mu g/m^3$	−0.009 (−0.02–0.001)	−0.014 (−0.025–−0.002)	0.87 (0.71–1.05)	1.04 (0.83–1.30)
SO_2, ppb	−0.028 (−0.039–−0.018)	−0.028 (−0.039–−0.017)	1.30 (1.12–1.52)	1.39 (1.14–1.70)
$BC+SO_2$				
BC, $\mu g/m^3$	−0.013 (−0.024–−0.001)	−0.015 (−0.029–−0.002)	0.97 (0.78–1.21)	1.30 (1.01–1.68)
SO_2, ppb	−0.027 (−0.038–−0.017)	−0.026 (−0.038–−0.015)	1.24 (1.06–1.45)	1.28 (1.04–1.57)
$PM_{2.5}+BC$				
$PM_{2.5}$, $\mu g/m^3$	−0.011 (−0.023–0.001)	−0.012 (−0.026–0.003)	0.92 (0.74–1.14)	0.87 (0.65–1.17)
BC, $\mu g/m^3$	−0.019 (−0.032–−0.006)	−0.022 (−0.038, −0.006)	1.20 (0.94–1.52)	1.68 (1.22–2.32)

*All effect estimates are scaled to the interquartile increase in pollutant level for the appropriate cumulative average.

†All models adjusted for indicators for participant, day of the week, and order of the visit and smooth functions of visit date, hour of day, and hourly temperature.

‡All models included fixed effects for day of the week and order of the visit, random effects for participant, and smooth functions of visit date, hour of day, and hourly temperature.

−0.004 mm for an IQR increase in mean half-hour heart rate; 95% CI, −0.005 to −0.003). An interquartile increase in 12- to 24-hour $PM_{2.5}$ and BC predicted a small but significant decrease in the mean half-hour heart rate (eg, −1.03 bpm for 12-hour BC; 95% CI, −1.65 to −0.41).

Logistic regression analyses showed that increases in $PM_{2.5}$ and BC also were associated with an increased risk of ST-segment depression ≥0.1 mm (Table 3). Cumulative effects were greatest at 48 hours. The estimated risk increased 1.43-fold per IQR increase in the mean 48-hour $PM_{2.5}$ (95% CI, 1.19 to 1.74) and 1.72-fold per IQR increase in the mean 48-hour BC (95% CI, 1.28 to 2.31) (Figure 2).

Associations of Gaseous Air Pollutants With ST-Segment Depression

In single-pollutant models, elevation in the mean 12-hour and 24-hour NO_2 and SO_2 levels also predicted depression of half-hour–averaged ST-segment levels. No significant association of ST-segment depression was observed with CO and O_3. The effect of the traffic marker BC[11] predominated in models with both BC and $PM_{2.5}$ (Table 3). Findings were similar for $PM_{2.5}$ and NO_2, a somewhat less specific marker for traffic. In models with $PM_{2.5}$ and SO_2, effects were divided between the 2 pollutant measures, neither of which is specific to a particular source (see Discussion).[12,13]

Effect Modification by Medical Condition and Time Since Hospitalization

In models in which 12-hour and 24-hour average pollution predicted ST-segment level as a continuous outcome, we found the effect of $PM_{2.5}$ and BC to be modified by myocardial infarction discharge diagnosis, time since discharge (visit

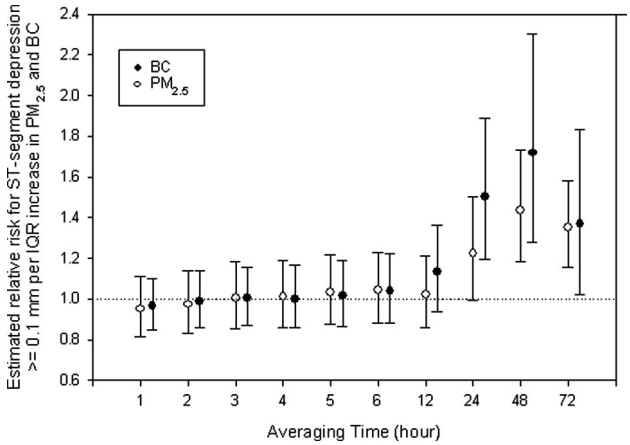

Figure 2. The effects of $PM_{2.5}$ and BC on half-hour–averaged ST-segment depression ≥0.1 mm below a subject-visit set point, as estimated by additive mixed logistic regression models, scaled to IQR increase in levels for individual hour mean. Error bars indicate 95% CIs.

Table 4. Effect Modification of Association of ST-Segment Level With Ambient Pollution*

	$PM_{2.5}$, $\mu g/m^3$		BC, $\mu g/m^3$	
	12-Hour Mean (95% CI)	24-Hour Mean (95% CI)	12-Hour Mean (95% CI)	24-Hour Mean (95% CI)
Myocardial infarction				
Yes	−0.042 (−0.057–−0.026)	−0.027 (−0.043–−0.012)	−0.041 (−0.055–−0.027)	−0.053 (−0.068–−0.038)
No	−0.012 (−0.023–0.00)	−0.025 (−0.038–0.011)	−0.011 (−0.025–0.004)	−0.004 (−0.020–0.012)
P for interaction	0.002	0.787	0.002†	<0.001
Visit				
Visit 1	−0.102 (−0.12–−0.085)	-0.127 (−0.148–−0.105)	−0.081 (−0.099–−0.064)	−0.111 (−0.132–−0.090)
Visits 2–4	0.006 (−0.005–0.017)	0.001 (−0.011–0.013)	−0.001 (−0.013–0.012)	−0.007 (−0.020–0.005)
P for interaction	<0.001	<0.001	<0.001	<0.001
Diabetes				
Yes	−0.097 (−0.119–−0.074)	−0.118 (−0.144–−0.091)	−0.034 (−0.061–−0.006)	−0.059 (−0.092–−0.026)
No	−0.009 (−0.019–0.002)	−0.013 (−0.024–−0.002)	−0.032 (−0.044–0.021)	−0.025 (−0.037–−0.013)
P for interaction	<0.001	<0.001	0.935	0.103
Diurnal pattern				
Daytime (9 AM–10 PM)	−0.032 (−0.043–−0.021)	−0.031 (−0.043–−0.020)	−0.028 (−0.039–−0.017)	−0.022 (−0.032–−0.011)
Nighttime (11 PM–8 AM)	−0.006 (−0.018–0.006)	−0.018 (−0.030–−0.005)	−0.022 (−0.036–0.007)	−0.020 (−0.032–−0.007)
P for interaction	<0.001	0.233	0.349	0.964

*All effect estimates are scaled to the interquartile increase in pollutant level for the appropriate cumulative average. All models adjusted for indicators for participant, day of the week, and order of the visit and smooth functions of visit date, hour of day, and hourly temperature.

number), diabetes diagnosis, and diurnal pattern (Table 4). Participants with myocardial infarction discharge diagnosis showed a change of −0.042 mm in ST segment associated with increased previous 12-hour mean $PM_{2.5}$, whereas participants without myocardial infarction discharge diagnosis showed a change of −0.012 mm in ST-segment level (*P* for interaction=0.002). We also found stronger effects of particulate pollution on participants at the first visit than at the rest of the visits (*P* for interaction <0.001). Participants with diabetes (42% of whom had ever had a myocardial infarction; 75% of whom had coronary artery disease diagnoses without current myocardial infarction at the time of enrollment) showed higher response to increased levels of particulate pollution than those without diabetes (*P* for interaction <0.001). Participants showed higher response to increased level of $PM_{2.5}$ effect during daytime. There was no effect modification by personal smoking or environmental tobacco smoke. Except for the comparison of daytime and nighttime, evidence for effect modification in the logistic models was not consistent between pollutants and between cumulative averages. Use of β-blocker, calcium channel blocker, statin, or angiotensin-converting enzyme inhibitor medications did not modify the effects of air pollution on ST-segment depression.

Discussion

Our study results suggest that patients may be most vulnerable to air pollution ischemic effects in the month after hospitalization for evaluation and treatment of coronary artery disease. Moreover, myocardial injury (infarction) during hospitalization may put patients at greater risk of posthospitalization pollution-associated ST-segment depression than acute coronary syndrome or worsening stable coronary disease without myocardial injury. Three other studies found a relationship between elevated ambient pollution and ST-segment depression in the elderly or in subjects with stable coronary artery disease but did not study patients in the immediate posthospitalization period.[2–4] Consistent with other studies suggesting that diabetes is a risk factor for air pollution–associated cardiac morbidity,[14] patients with diabetes also were at greater risk of developing pollution-related ST-segment depression than patients without diabetes.

Potential mechanisms through which ambient pollution may increase the risk of ischemia in vulnerable patients with coronary artery disease have been reviewed.[15,16] Mechanisms considered include impaired fibrinolytic activity and decreased myocardial oxygen supply related to either vasoconstriction or transient thrombus formation, possibly resulting from systemic or local inflammation,[17,18] oxidative stress,[19] endothelial dysfunction,[20,21] and/or autonomic dysfunction.[22] Patients with type 2 diabetes are known to have chronic endothelial vascular dysfunction, chronic systemic inflammation, oxidative stress, and chronic autonomic dysfunction,[23–25] all of which may increase the risk of acute pollution effects.

Although the Air Pollution and Health: A European Approach 2 (APHEA2) project suggested that SO_2 itself plays an independent role in triggering ischemia heart disease admissions,[26] at the low levels found in Boston, SO_2 is more likely to be a marker for exposure to pollution from a number of sources, including diesel exhaust, home heating fuel oil, and regional power plant emissions.[12,13] BC is a more specific surrogate for diesel and nondiesel traffic particle exposure that is either local or regionally transported,[11] and the multiple-pollutant model including $PM_{2.5}$ and BC suggested a strong traffic effect. We found no associations of either O_3 or CO on ST-segment level. CO, known to have ischemic effects on the risk of arrhythmia at high levels,[27] was likely

encountered at levels too low for measurable effects in this study, and given the local nature of CO levels that are above background, imprecision in exposure estimations also may have contributed to the null associations.[28] Ozone, which has well-documented and reproducible pulmonary effects,[29] has not been as reproducibly related to cardiac effects in large epidemiological studies, even in high-O_3-level cities like Mexico City.[30]

Although the half-hour pollution-associated decrements in ST-segment levels were small in continuous models, we also found pollution effects on the risk of ST-segment depression ≥0.1 mm. Palinkas and colleagues[31] found changes of similar magnitude measured during stress testing to be predictive of subsequent increased risk of adverse cardiac events among patients with chest pain syndromes. This finding supports the likelihood that the more subtle pollution-related ST-segment depression represents ischemia.

Our study has several limitations. The magnitude of ST-segment depression in these patients was generally small; averaging over half-hour periods likely combined periods of greater and lesser levels of ST-segment depression. It is unknown whether the small, but statistically significant, ST-segment values represent transient myocardial ischemia or transient inflammatory responses to exacerbations in air pollution. Compared with the effect modification results for the continuous outcome analyses, the results for the logistic analyses were less stable and less consistent, perhaps as a result of loss of information incurred by dichotomizing the primary end point. The use of central-site pollution measurements for these analyses may have resulted in some misclassification of exposure. This limitation may be more relevant for BC, which has more local traffic sources, than for $PM_{2.5}$.[32] Short-term exposures may be less well estimated than longer-term averaged exposures because they may be influenced more by brief local personal exposures that differ from exposures measured at the central site. That may account in part for the somewhat stronger associations with longer (24-hour) averaged exposures in the continuous models. It is also true that in the logistic models we cannot discount that the null findings at shorter lags may be due to exposure misclassification. Alternatively, with the logistic models, the evidence for an effect with longer or greater cumulative exposure may suggest that longer/greater cumulative exposure to pollution may be needed for a more extreme (although from a clinical point of view still modest) level of ST-segment depression. The sample size is relatively small, limiting the potential to evaluate interactions between participant characteristics and pollutant exposure. In addition, because of the selective nature of the population pool, the generalizability to other patient populations may be limited. However, there is no reason to believe that the internal comparisons within and between subjects are biased.

Our study suggests immediate and longer cumulative effects of air pollution on ST-segment depression. Although cumulative effects of $PM_{2.5}$ and BC on ST-segment level peaked at 6 to 48 hours, effects also were seen in relation to the prior 1- to 2-hour–averaged pollution levels, which is consistent with the findings of Peters et al[1] and Mills et al[2] that exposure to traffic can trigger myocardial infarction. However, it is possible that the longer-term summary air pollution for 6 to 48 hours simply is a more accurate measure of air pollution exposure than the single-hour measurement and thus correlates to end points better. The time course of effect may remain unclear, but at the least we can see rapid effects after exposure to air pollution.

Of the >1 million patients who suffer a myocardial infarction in the United States each year, one quarter to one third of survivors will die within 12 months, and a significant proportion will experience reinfarction or sudden death over the ensuing years.[33] The immediate post–myocardial infarction period has been well demonstrated to be a period of increased risk of recurrent events and electric instability.[34] In a double-blind, randomized, crossover study of 20 men with a history of myocardial infarction exposed to exercise plus either diesel exhaust or filtered air, diesel pollution was demonstrated to worsen the effects of vigorous exercise on the risk of ST-segment depression.[35,36] Our study suggests that these effects of air pollution on increased risk of ST-segment depression and ischemia may be heightened in the immediate period after an acute coronary event, when risk of ischemia might be reduced by reduction in pollution exposure, including exposure to traffic.

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CLINICAL PERSPECTIVE

Of the >1 million patients who suffer a myocardial infarction in the United States each year, one quarter to one third of survivors will die within 12 months, and a significant proportion will experience reinfarction or sudden death over the ensuing years. We evaluated the association of elevated air pollution with ST-segment depression in 48 patients followed up after hospitalization for myocardial infarction, acute coronary syndrome without infarction, or stable coronary artery disease without acute coronary syndrome. An interquartile increase in the previous 24-hour mean black carbon, a marker for traffic pollution, was associated with a 1.50-fold increased risk of ST-segment depression ≥0.1 mm (95% CI, 1.19 to 1.89) and a −0.031-mm (95% CI, −0.042 to −0.019) decrease in half-hour–averaged ST-segment level (continuous outcome). Effects were greatest within the first month after hospitalization and for patients with myocardial infarction during hospitalization or with diabetes. Our study suggests that the effects of air pollution on increased risk of ST-segment depression and ischemia or myocardial inflammation may be heightened in the immediate period after an acute coronary event. During this period, cardiac risk might be reduced by reduction in pollution exposure, including exposure to traffic.