**Triggering of Transmural Infarctions, but Not Nontransmural Infarctions, by Ambient Fine Particles**

**David Q. Rich,1,2 Howard M. Kipen,2,3 Junfeng Zhang,1,2 Leena Kamat,1 Alan C. Wilson,3 and John B. Kostis,3**

*for the Myocardial Infarction Data Acquisition System Study Group (MIDAS 12)*

1School of Public Health, University of Medicine and Dentistry of New Jersey, Piscataway, New Jersey, USA; 2Environmental and Occupational Health Sciences Institute, Robert Wood Johnson Medical School and Rutgers University, Piscataway, New Jersey, USA; 3Robert Wood Johnson Medical School, University of Medicine and Dentistry of New Jersey, Piscataway, New Jersey, USA

**BACKGROUND:** Previous studies have reported increased risk of myocardial infarction (MI) after increases in ambient particulate matter (PM) air pollution concentrations in the hours and days before MI onset.

**OBJECTIVES:** We hypothesized that acute increases in fine PM with aerodynamic diameter ≤ 2.5 µm (PM$_{2.5}$) may be associated with increased risk of MI and that chronic obstructive pulmonary disease (COPD) and diabetes may increase susceptibility to PM$_{2.5}$. We also explored whether both transmural and nontransmural infarctions are acutely associated with ambient PM$_{2.5}$ concentrations.

**METHODS:** We studied all hospital admissions from 2004 through 2006 for first acute MI of adult residents of New Jersey who lived within 10 km of a PM$_{2.5}$ monitoring site (n = 5,864), as well as ambient measurements of PM$_{2.5}$, nitrogen dioxide, sulfur dioxide, carbon monoxide, and ozone.

**RESULTS:** Using a time-stratified case-crossover design and conditional logistic regression showed that each interquartile-range increase in PM$_{2.5}$ concentration (10.8 µg/m$^3$) in the 24 hr before arriving at the emergency department for MI was not associated with an increased risk of MI overall but was associated with an increased risk of a transmural infarction. We found no association between the same increase in PM$_{2.5}$ and risk of a nontransmural infarction. Further, subjects with COPD appeared to be particularly susceptible, but those with diabetes were not.

**CONCLUSIONS:** This PM$_{2.5}$–transmural infarction association is consistent with earlier studies of PM and MI. The lack of association with nontransmural infarction suggests that future studies that investigate the triggering of MI by ambient PM$_{2.5}$ concentrations should be stratified by infarction type.

**KEYWORDS:** air pollution, epidemiology, myocardial infarction. 

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Most previous studies (D’Ippoliti et al. 2003; Peters et al. 2001, 2005; Pope et al. 2006; Zanobetti and Schwartz 2005), but not all (Sullivan et al. 2005), that have investigated the triggering of myocardial infarction (MI) by particulate matter (PM) air pollution concentrations in the hours and days before MI onset have reported an association. Other studies have reported increased mortality due to MI or increased mortality or cardiovascular admissions among MI survivors associated with increases in PM over the previous few days (Braga et al. 2001; von Klot et al. 2005; Zanobetti and Schwartz 2007). Several studies have investigated whether certain subgroups are particularly susceptible and have reported increased cardiovascular effects among those with diabetes (Dubowsky et al. 2006; Goldberg et al. 2001; Liu et al. 2007; O’Neill et al. 2005; Zanobetti and Schwartz 2002) and among patients with chronic obstructive pulmonary disease (COPD) (Naess et al. 2007; Zanobetti and Schwartz 2005; Zanobetti et al. 2000). However, Zanobetti and Schwartz (2005) reported increased susceptibility among patients with COPD but not among persons with diabetes.

Numerous researchers have reported that the percentage of infarctions that are nontransmural has been increasing (Goff et al. 2000; Hellermann et al. 2003; Kostis et al. 2007; Myerson et al. 2009; Roger et al. 2006, 2010; Rogers et al. 2008). More recently, Shao (2008) noted a similar secular trend in clinical presentation of MI to emergency departments (EDs) in New Jersey. In short, 72% of persons admitted to hospitals in New Jersey from 1990 through 1999 had transmural infarctions, and only 28% had had nontransmural infarctions. Since then, however, this pattern has reversed. From 2002 through 2004, most of the admissions for MI were for nontransmural infarctions (63%), with only 37% for transmural infarctions (Shao 2008). These changes may be due in part to improvements in preventive pharmacotherapies (statins, beta blockers, aspirin), interventional procedures [angioplasty, coronary artery bypass graft (CABG)], more sensitive diagnostic tests (troponins), and treatment of the MI upon ED arrival (reperfusion therapy, increased use of antplatelet agents). It has not been reported whether PM with aerodynamic diameter ≤ 2.5 µm (PM$_{2.5}$) triggers all infarctions, whether PM–MI associations differ in magnitude, or whether these associations are restricted to PM–transmural or PM–nontransmural infarctions alone. Such investigations may provide insight into the mechanisms by which PM may trigger cardiovascular events.

Using the same data as Shao (2008), we attempted to replicate, in New Jersey, previous MI–PM$_{2.5}$ studies that were conducted in other US and European cities. We hypothesized that increases in mean PM$_{2.5}$ concentration on the same day and a few days before ED arrival for MI may be associated with increased risk of MI and that these effect estimates would be greater for persons with diabetes and those with COPD than for individuals without these conditions. Further, we explored whether there were differences in risks associated with increases in ambient PM$_{2.5}$ concentration between transmural and nontransmural infarctions.

**Materials and Methods**

**Study population and outcome definition.** Using the Myocardial Infarction Data Acquisition System (MIDAS), a statewide surveillance system in New Jersey that combines hospital discharge data and death certificate registration data (Kostis et al. 1994, 2001), we extracted all records with a primary diagnosis of acute MI (International Classification of Diseases, version 9 (ICD-9), codes 410.01, 410.11, 410.21, 410.31, 410.41, 410.51, 410.61, 410.71, 410.81, and 410.91) for patients who were admitted between 1 January 2004 and 31 December 2006, were ≥ 18 years of age, were residents of New Jersey at the time of their MI, and who were without a previous diagnosis of MI (ICD-9 code 412). Because the “1” in the fifth digit of the ICD-9 code (e.g., 410.01) indicates a first MI for the subject, we also used this designation to exclude those persons who had had a previous MI. Those who were not admitted into the hospital (e.g., patient declined admission,

Address corresponding D.Q. Rich, University of Rochester School of Medicine and Dentistry, Department of Community and Preventive Medicine, 601 Elmwood Ave., PO Box 644, Rochester, NY 14642. Telephone: (585)276-4119. Fax: (585) 461-4532. E-mail: David_Rich@URMC.Rochester.edu

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patient died before admission) were not included in this data set. We classified patients with an MI coded as 410.7 (subendocardial infarction) as having a nontransmural infarction, and those with codes 410.0 (infarction of anterolateral wall), 410.1 (infarction of other anterior wall), 410.2 (infarction of inferolateral wall), 410.3 (infarction of inferoposterior wall), 410.4 (infarction of other inferior wall), 410.5 (infarction of other lateral wall), and 410.6 (true posterior wall infarction) as having transmural infarctions.

From these extracted data, we also retained the following variables: date and hour of ED admission; ZIP code of residence; age; sex; race; variables indicating the presence or absence of other comorbid conditions (based on ICD-9 codes)—congestive heart failure (ICD-9 code 428.0), arrhythmia (ICD-9 codes 426.0, 426.10, 426.12, 426.2, 426.3, 426.4, 426.5, 426.6, 426.89, 426.9, and 427), hypertension (ICD-9 codes 401–405), diabetes (ICD-9 code 250), COPD (ICD-9 codes 490–496), and history of ischemic heart disease (ICD-9 codes 410–414); and variables indicating in-hospital and postinfarction procedures (based on ICD-9 code)—angioplasty, CABG, and catheterization.

This study and the original MIDAS study were approved by the University of Medicine and Dentistry of New Jersey—New Brunswick Institutional Review Board. MIDAS was also approved by the New Jersey Department of Health and Senior Services Institutional Review Board.

**Air pollution.** Using ambient pollutant measurements from the New Jersey Department of Environmental Protection and from U.S. Environmental Protection Agency (EPA) Web sites (U.S. EPA 2008), we used hourly concentrations of PM$_{2.5}$ (7 monitoring stations), nitrogen dioxide (NO$_2$; 9 stations), sulfur dioxide (SO$_2$; 14 stations), carbon monoxide (CO; 13 stations), and ozone (O$_3$; 15 stations) for the study period 1 January 2004 to 31 December 2006. For each patient, we calculated the distance between each PM$_{2.5}$ monitor (in operation at the time of the MI) and the patient’s residence and assigned PM$_{2.5}$ measurements from the closest monitor to their residence. Those patients who lived >10 km from a PM$_{2.5}$ monitoring station were excluded from PM$_{2.5}$ analyses. We calculated mean PM$_{2.5}$ concentrations for each successive 24-hr period before ED arrival for the MI (e.g., mean of hours 0–23 before ED arrival; 24–47 mean of hours before ED arrival, etc.). If >6 hr (>25%) of a 24-hr period of PM$_{2.5}$ concentrations were missing, we set the mean for this 24-hr period of PM$_{2.5}$ concentration to missing. We used these mean concentrations in all analyses. We repeated this monitor matching and mean concentration calculation process for each of the other pollutants.

**Weather.** Hourly temperature and dew point measurements were made at the Newark, Caldwell, Somerset, and Trenton, New Jersey, airports during the study period. We used the airport monitor closest to each patient’s residence to provide the weather observations for that patient during the study period. After calculating 24-hr mean temperature and dew point, in the same manner as for the pollutant concentrations, we calculated 24-hr mean apparent temperature (Steadman 1979; Zanobetti and Schwartz 2005) as a measure of each patient’s perceived air temperature given the humidity and used these values in all analyses.

**Study design.** We used a time-stratified case-crossover design (Levy et al. 2001; Maclure 1991) that has previously been used in studies of ambient air pollution and MI (D’ippoliti et al. 2003; Pope et al. 2006; Sullivan et al. 2005; Zanobetti and

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**Table 1.** Frequency and percentage of characteristics of study population (cases matched to PM$_{2.5}$ monitors at ≤10 km distance): MIDAS study 2004–2006.

| Characteristic | Total MI (n = 5,864) | Nontransmural MI (n = 3,822) | Transmural MI (n = 1,942) |
|----------------|----------------------|-----------------------------|----------------------------|
| Age (years)    |                      |                             |                            |
| 18–44          | 376 (6)              | 214 (6)                     | 162 (9)                    |
| 45–54          | 842 (14)             | 454 (12)                    | 388 (20)                   |
| 55–64          | 1,245 (21)           | 736 (19)                    | 509 (26)                   |
| 65–74          | 1,187 (20)           | 790 (21)                    | 397 (20)                   |
| 75–84          | 1,431 (25)           | 1,027 (27)                  | 404 (18)                   |
| ≥85            | 783 (14)             | 595 (15)                    | 188 (8)                    |
| Sex            |                      |                             |                            |
| Male           | 3,296 (56)           | 2,048 (54)                  | 948 (36)                   |
| Female         | 2,568 (44)           | 1,774 (46)                  | 583 (37)                   |
| Race           |                      |                             |                            |
| White          | 4,027 (69)           | 2,625 (69)                  | 1,402 (69)                 |
| Black          | 901 (15)             | 623 (16)                    | 278 (12)                   |
| Other          | 936 (16)             | 574 (15)                    | 362 (19)                   |
| Year           |                      |                             |                            |
| 2004           | 1,634 (28)           | 1,066 (28)                  | 568 (29)                   |
| 2005           | 1,523 (26)           | 994 (26)                    | 529 (25)                   |
| 2006           | 2,707 (46)           | 1,762 (46)                  | 715 (46)                   |
| Comorbidity    |                      |                             |                            |
| Hypertension   | 3,658 (62)           | 2,506 (66)                  | 884 (65)                   |
| Diabetes mellitus | 1,761 (30)    | 1,207 (32)                  | 454 (27)                   |
| Type 1 diabetes | 126 (2)            | 103 (3)                     | 22 (1)                     |
| Type 2 diabetes | 1,625 (28)         | 1,104 (29)                  | 401 (26)                   |
| COPD           | 839 (14)             | 608 (16)                    | 164 (10)                   |
| Pneumonia      | 445 (8)              | 350 (9)                     | 60 (4)                     |
| Heart disease  | 5,100 (87)           | 3,733 (88)                  | 1,326 (85)                 |
| Ischemic heart disease | 3,603 (61)   | 2,285 (60)                  | 1,362 (67)                 |
| Congestive heart failure | 1,878 (32) | 1,427 (37)                  | 299 (19)                   |
| Atrial fibrillation | 971 (17)        | 722 (19)                    | 174 (11)                   |
| Arrhythmia     | 1,793 (31)           | 1,177 (31)                  | 466 (30)                   |
| Ventricular tachycardia | 332 (6)       | 173 (5)                     | 129 (8)                    |
| In-hospital procedure | 786 (13)    | 393 (10)                    | 350 (22)                   |
| Angioplasty    | 288 (5)              | 202 (5)                     | 84 (4)                     |
| CABG           | 3,178 (54)           | 1,908 (50)                  | 1,028 (66)                 |

**Table 2.** Distribution of daily mean PM$_{2.5}$ concentrations at each monitoring station used.

| Monitoring station | No. (%) of subjects matched to this monitor | Start and end dates of monitor during study period | No. of nonmissing days | PM$_{2.5}$ concentration (µg/m$^3$) |
|--------------------|--------------------------------------------|-----------------------------------------------|-----------------------|-------------------------------------|
| Camden Lab         | 1,473 (25)                                 | January 2004–December 2006                     | 986                   | Minimum: 0.5 25th: 6.7 Median: 11.1 Maximum: 17.0 (52.2) |
| Elizabeth Lab      | 2,009 (34)                                 | January 2004–December 2006                     | 1,062                 | 0 7.1 12.2 18.8 61.0                |
| Rahway             | 407 (7)                                    | January 2004–December 2006                     | 246                   | 5.1 9.0 12.3 18.3 48.8              |
Next, we examined whether the risk of MI associated with an IQR increase in mean PM$_{2.5}$ concentration in the 24 hr before ED arrival was different for patients with transmural versus nontransmural infarctions. We reran the same model described above for patients with transmural infarctions only, and then for patients with nontransmural infarctions only. To examine potential effect modification by other factors, including COPD, diabetes, age (< 65 years, ≥ 65 years), sex, race (white, black, other), and season (winter = December, January, February; summer = June, July, August), we used an interaction term (e.g., COPD × PM$_{2.5}$) in the main model.

Sensitivity analyses. To assess the stability of our PM$_{2.5}$ relative risk estimates after adjusting for gaseous pollutant concentrations, we created two-pollutant models (PM$_{2.5}$ + NO$_2$, PM$_{2.5}$ + CO, PM$_{2.5}$ + SO$_2$, PM$_{2.5}$ + O$_3$) using mean pollutant concentrations from the 24 hr before ED arrival. We also evaluated whether any association between ED arrival for MI and the mean PM$_{2.5}$ concentration in the previous 24 hr was independent of concentrations from previous 24-hr periods. We reran the same conditional logistic regression model described above, including all seven lagged PM$_{2.5}$ concentrations (i.e., the mean PM$_{2.5}$ concentrations from the 24 hr before ED arrival for MI, and the mean concentrations from the previous six lagged 24-hr periods).

All data sets included in the analyses were constructed using SAS software (version 9.1.3; SAS Institute Inc., Cary, NC), and all analyses were conducted using R (version 2.6.1; R Foundation for Statistical Computing, Vienna, Austria). The authors had full access to the data and take responsibility for its integrity.

Results
During the study period, a total of 37,791 patients were admitted to nonfederal New Jersey hospitals for a first acute MI; of these, 5,864 lived within 10 km of a PM$_{2.5}$ monitoring site and had PM$_{2.5}$ data available for analysis (i.e., PM$_{2.5}$ data available for at least 18 of the 24 hr before ED arrival for the index MI). Study patients were predominantly older (59% > 65 years of age), white (69%), and male (56%). Sixty-two percent had hypertension, 61% had a history of ischemic heart disease, and 30% had diabetes (Table 1). Those who were excluded from our analysis were similar to persons who were included in age (61% > 65 years of age), sex (57% male), and comorbidities (e.g., 59% with hypertension), but they were slightly more likely to be white (82%). Subjects included in the analysis who experienced a nontransmural infarction were generally older and were more likely to have had cardiorespiratory comorbidities than those who experienced a transmural infarction. Compared with the subjects who had a nontransmural infarction, those who had a transmural infarction were more likely to have had an angioplasty and/or catheterization postinfarction but less likely to have had CABG (Table 1). Of note, there were seven monitors that made PM$_{2.5}$ measurements in 2006 but only three in 2004 and 2005, which resulted in a larger number of patients living within 10 km of a PM$_{2.5}$ monitoring site and thus available for analysis in 2006 (Table 2).

Of the seven monitors that were continuously measuring PM$_{2.5}$ during the study period, patients were most often assigned to the Elizabeth Lab (32%), Camden Lab (26%), and New Brunswick (18%) monitors. The distribution of mean daily PM$_{2.5}$ concentrations at each of these seven monitors is shown in Table 2. When combining all the monitors, PM$_{2.5}$ concentrations had a median of 11.7 μg/m$^3$, 5th and 95th percentiles of 3.6 and 31.5 μg/m$^3$, respectively; and 25th and 75th percentiles of 7.4 and 18.3 μg/m$^3$, respectively (IQR = 10.8 μg/m$^3$). We scaled all of our effect estimates presented below by this IQR. Table 3 shows Pearson correlation coefficients for individual pollutants and apparent temperature.

Next, we separately estimated the risk of ED admission for MI associated with each IQR increase in the mean PM$_{2.5}$ concentration in the previous 24 hr, and lagged 24-hr periods (hours 24–47, 48–71, 72–95, 96–119, 120–143, and 144–167), adjusting for apparent temperature during that same lag period. Each 10.8-μg/m$^3$ increase in the mean PM$_{2.5}$ concentration in the 24 hr before ED arrival was not associated with an increased risk of MI (Table 4). Similarly, we found no associations between ED admission for overall MI and any of the lagged PM$_{2.5}$ concentrations. However, when we then restricted our analysis to transmural infarctions only we found a significantly increased risk associated with each 10.8-μg/m$^3$ increase in PM$_{2.5}$ concentration in the previous...
24 hr (OR = 1.10; 95% CI, 1.01–1.20). When examining lagged PM$_{2.5}$ concentrations, the relative risk estimates were mostly > 1.0, but none was statistically significant. In contrast, when we restricted our analysis to nontransmural infarctions, we found no increased risks associated with any lagged PM$_{2.5}$ concentrations (Table 4).

Because we found an association with transmural infarctions only, we restricted all further analyses to this infarction type and evaluated whether several factors modified this association. Patients with preexisting COPD and those <65 years of age had substantially larger risks of transmural infarction associated with each $10.8\mu g/m^3$ increase in PM$_{2.5}$ concentration in the previous 24 hr than did patients without preexisting COPD and those ≥65 years of age (Table 5). We found no difference in PM$_{2.5}$ relative risk estimates by race, sex, season, or whether subjects had diabetes (Table 5).

We then included mean PM$_{2.5}$ and NO$_2$ concentrations from the 24 hr before ED arrival simultaneously in a model ($n = 1,262$ patients with transmural infarctions with both PM$_{2.5}$ and NO$_2$ mean concentrations). The PM$_{2.5}$ relative risk estimate in this two-pollutant model was not substantially different from the single-pollutant model on the same $n = 1,262$ patients (Table 6). This was also true when adjusting for CO, SO$_2$, and O$_3$. IQR increases in CO, SO$_2$, and O$_3$ were not associated with significantly increased risks of transmural infarctions in any single- or two-pollutant model (Table 6). Next, when including all seven lagged PM$_{2.5}$ concentrations in the same model, the risk associated with the 24-hr moving-average PM$_{2.5}$ concentration was larger and still statistically significant (OR = 1.15; 95% CI, 1.04–1.28). All the PM$_{2.5}$ concentration relative risk estimates for the other lag periods were smaller than the 24-hr moving-average relative risk estimate, and none was statistically significant (data not shown).

**Discussion**

Using a large multiyear (2004–2006) statewide data set of hospital admissions for first MI, we found no association between admission for MI overall and PM$_{2.5}$ concentrations in the previous week. However, when we restricted the analysis to patients with transmural infarctions, we found a significant 10% increase in the risk of a transmural infarction associated with the mean PM$_{2.5}$ concentration in the 24 hr before ED arrival. This association persisted with adjustment for gaseous pollutant concentrations in the prior 24 hr and with adjustment for PM$_{2.5}$ concentrations during each of the previous six 24-hr periods. Further, patients with COPD, but not diabetes, were particularly susceptible to acute increases in ambient PM$_{2.5}$ concentrations. We found no association with this same PM$_{2.5}$ concentration and nontransmural infarctions.

Our findings are consistent with previous studies (D’Ippoliti et al. 2003; Peters et al. 2001; Peters et al. 2005; Pope et al. 2006; Zanobetti and Schwartz 2005) in indicating an acute association between PM and MI onset, although the method of estimating MI onset time (day of hospital admission for MI, time of symptom onset estimated by patient, etc.), lags of pollutant concentrations examined (lag days 0–6, 0–6 lagged 24-hr periods before ED arrival for MI), and specific particle sizes examined (PM$_{10}$, PM$_{2.5}$) are not uniform. Previous studies reported PM associations with all MIs, not just transmural infarctions (D’Ippoliti et al. 2003; Peters et al. 2001; Peters et al. 2005; Pope et al. 2006; Zanobetti and Schwartz 2005). However, these studies drew data from earlier time periods (e.g., Peters et al. 2001, Boston, Massachusetts, 1995–1996; Peters et al. 2005, Augsburg, Germany, 1999–2001; D’Ippoliti et al. 2003, Rome, Italy, 1995–1997; Zanobetti and Schwartz 2005, 21 U.S. cities, 1985–1999) when most infarctions were likely transmural. Therefore, their reports of increased relative risk of MI are consistent with our finding of increased relative risk of transmural infarctions only. Thus, our study adds to the body of knowledge that relates increased risk of MI with increases in PM in the previous hours and days, but ours is the first to report that associations are restricted to transmural infarctions.

Pathophysiologic pathways proposed as mechanisms underlying previously reported PM/MI associations include systemic inflammation, endothelial dysfunction, disturbance of autonomic tone, and enhanced coagulation/thrombosis (Brook et al. 2004). Our finding of an acute (within 24 hr) association between PM and transmural infarctions, but not nontransmural infarctions, suggests another mechanism or pathway, perhaps related to those listed above, by which particles may trigger an MI. In a recent study, Bartoli et al. (2009) reported decreased myocardial blood flow in canines associated with concentrated air particles exposure, but not with filtered air exposure, after experimental occlusion of the coronary artery. Cardiac work was not

**Table 4.** Estimated risk of ED admission for MI (95% CI) associated with each $10.8\mu g/m^3$ increase in moving average PM$_{2.5}$ concentration, by infarction type.

| Lag period | No. of admissions | OR (95% CI) |
|------------|------------------|-------------|
| All infarctions |                |             |
| 0–23       | 5,864            | 1.02 (0.98–1.07) |
| 24–47      | 5,838            | 1.01 (0.97–1.06) |
| 48–71      | 5,821            | 0.99 (0.95–1.04) |
| 72–95      | 5,784            | 1.01 (0.97–1.05) |
| 96–119     | 5,795            | 1.02 (0.98–1.07) |
| 120–143    | 5,786            | 1.00 (0.96–1.05) |
| 144–167    | 5,770            | 1.00 (0.96–1.04) |
| Transmural infarctions |          |             |
| 0–23       | 1,563            | 1.10 (1.01–1.20) |
| 24–47      | 1,560            | 1.02 (0.93–1.11) |
| 48–71      | 1,548            | 1.04 (0.96–1.13) |
| 72–95      | 1,544            | 1.03 (0.95–1.12) |
| 96–119     | 1,554            | 1.05 (0.97–1.13) |
| 120–143    | 1,558            | 1.04 (0.97–1.13) |
| 144–167    | 1,551            | 0.97 (0.90–1.05) |
| Nontransmural infarctions |        |             |
| 0–23       | 3,822            | 0.99 (0.94–1.05) |
| 24–47      | 3,803            | 1.00 (0.94–1.05) |
| 48–71      | 3,805            | 0.96 (0.91–1.01) |
| 72–95      | 3,771            | 0.98 (0.93–1.04) |
| 96–119     | 3,773            | 1.01 (0.96–1.06) |
| 120–143    | 3,766            | 0.99 (0.94–1.04) |
| 144–167    | 3,758            | 1.00 (0.95–1.05) |

Each estimate of the risk of MI associated with each IQR increase in lagged PM$_{2.5}$ concentration was modeled separately, adjusting for apparent temperature during that same lag period.

**Table 5.** Risk of ED admission for transmural infarction (and 95% CI) associated with each $10.8\mu g/m^3$ increase in the mean PM$_{2.5}$ concentration in the previous 24 hr.

| Characteristic | No. of infarctions | OR (95% CI) | p-Value for interaction |
|---------------|--------------------|-------------|-------------------------|
| COPD          |                    |             |                         |
| Yes           | 164                | 1.32 (1.05–1.66) | 0.10                     |
| No            | 1,399              | 1.07 (0.98–1.18) |                         |
| Diabetes      |                    |             |                         |
| Yes           | 423                | 1.06 (0.90–1.23) | 0.54                     |
| No            | 1,140              | 1.11 (1.01–1.23) |                         |
| Age (years)   |                    |             |                         |
| < 65          | 867                | 1.18 (1.05–1.31) | 0.05                     |
| ≥ 65          | 696                | 1.01 (0.89–1.14) |                         |
| Sex           |                    |             |                         |
| Male          | 980                | 1.12 (1.01–1.24) | 0.54                     |
| Female        | 583                | 1.07 (0.94–1.21) |                         |
| Race          |                    |             |                         |
| White         | 1,079              | 1.11 (1.01–1.23) |                         |
| Black         | 180                | 1.14 (0.93–1.41) | 0.79*                    |
| Other         | 304                | 1.02 (0.84–1.23) | 0.40*                    |
| Season        |                    |             |                         |
| Winter        | 345                | 1.08 (0.90–1.30) | 0.90                     |
| Summer        | 404                | 1.03 (0.94–1.26) |                         |

Each estimate of the risk of MI associated with each IQR increase in lagged PM$_{2.5}$ concentration was modeled separately, adjusting for apparent temperature during that same lag period.

*Comparing black with white. **Comparing other with white.
increased by PM in this dog model, and data suggested that blood flow reductions were due to increased coronary vascular resistance, perhaps related to more limited recruitment of collateral vessels. Thus, particle inhalation, by reducing compensatory mechanisms, may transform limited (nontransmural) injury into more extensive (transmural) infarction. This finding is consistent with other research in which PM has been associated with increased rates of ST-segment depression in humans (Gold et al. 2005; Peckanan et al. 2002) or in canine model markers of ischemia (Wелlеniус et al. 2003). There is also increasing support in the literature for the prothrombotic effects of air pollutants that indicates the possibility that limitations in revascularization after a primary plaque-related thrombotic event could be due to enhanced thrombosis in general (Delfino et al. 2009; Jacobs et al. 2010; Lucking et al. 2008). A recent study that examined the association between PM and acute coronary events demonstrated greater relative risk in those individuals with angiographically documented previous coronary disease (Pope et al. 2006). Future analyses using data from MDAS will include examining differences in susceptibility to PM by prior disease events, including MI.

Ambient PM has previously been associated with increased hospital admissions for COPD and asthma (Chen et al. 2004; Dominici et al. 2006; Medina-Ramón et al. 2006; Peel et al. 2005; Zanobetti and Schwartz 2003). COPD is associated with a greater propensity to hypoxia, reduced pulmonary reserve, and a generally heightened inflammatory state, which all may predispose to transmural infarcts.

Although several researchers have reported acute associations between PM and cardiovascular outcomes in panels of patients with diabetes or have reported greater changes in vascular outcomes in panels of patients with acute associations between PM and cardio pulmonary reserve, and a generally heightened inflammatory state, which all may predispose to transmural infarcts.

Table 6. Risk of transmural infarction (and 95% CI) associated with each IQR increase in mean pollutant concentration in the previous 24 hr.

| Pollutant | Model type       | No. of infarctions | OR (95% CI)       |
|-----------|------------------|--------------------|------------------|
| PM<sub>2.5</sub> | Single pollutant | 1,262              | 1.10 (1.00–1.21) |
| NO<sub>2</sub>    | Single pollutant | 1,103              | 1.11 (0.97–1.25) |
| NO<sub>x</sub>    | Two pollutant    | 1,103              | 1.09 (0.96–1.22) |
| PM<sub>2.5</sub> | Single pollutant | 1,183              | 1.00 (0.98–1.19) |
| CO              | Single pollutant | 1,02               | 1.02 (0.93–1.12) |
| PM<sub>2.5</sub> | Two pollutant   | 1,02               | 1.02 (0.98–1.22) |
| PM<sub>2.5</sub> | Two pollutant   | 0.97               | 0.97 (0.87–1.08) |
| NO<sub>2</sub>    | Single pollutant | 1,238              | 1.00 (0.98–1.18) |
| SO<sub>2</sub>    | Single pollutant | 1,12               | 1.02 (0.93–1.11) |
| PM<sub>2.5</sub> | Two pollutant   | 1,10               | 1.10 (0.98–1.24) |
| PM<sub>2.5</sub> | Two pollutant   | 0.96               | 0.96 (0.86–1.08) |
| PM<sub>2.5</sub> | Single pollutant | 1,003              | 1.00 (0.97–1.21) |
| O<sub>3</sub>      | Single pollutant | 0.95               | 0.80 (0.81–1.12) |
| PM<sub>2.5</sub> | Two pollutant   | 1.00               | 1.00 (0.97–1.21) |
| O<sub>3</sub>      | Two pollutant   | 0.95               | 0.95 (0.81–1.11) |

Table 6. Risk of transmural infarction (and 95% CI) associated with each IQR increase in mean pollutant concentration in the previous 24 hr.

IQR = 10.8 μg/m³ for PM<sub>2.5</sub>, 16 ppb for NO<sub>2</sub>, 0.35 ppm for CO, 4.1 ppb for SO<sub>2</sub>, and 18 ppb for O<sub>3</sub>.

Third, linking MI to hourly and daily air pollution fluctuations requires minimizing misclassification of the estimate of MI onset time, so as to minimize bias. Although four previous studies (Peters et al. 2001; Peters et al. 2005; Pope et al. 2006; Sullivan J. et al. 2005) have used patients’ self-reported time of pain and symptom onset, this was not practical for our study, which relied on an administrative data set without personal interviews. Previous studies have reported median and mean delay times from symptom onset to ED arrival of 2.3–4.7 hr (Goldberg et al. 2002), with 44% of MI patients in Massachusetts arriving within 2 hr, and 78% arriving within < 6 hr (Goldberg et al. 2000). Thus, because there is often a delay of several hours from symptom onset to ED arrival, use of ED arrival time instead of hour of symptom onset results in greater exposure misclassification and bias toward the null. Further, in our analysis, the mean PM<sub>2.5</sub> concentrations in the 6, 12, and 24 hr before ED arrival were highly correlated (r-values = 0.83–0.95).

Therefore, we did not examine associations with ambient PM<sub>2.5</sub> concentrations < 24 hr before ED arrival, but instead focused on associations between infarctions and the ambient air pollution concentration in the 24 hr before ED arrival for that MI. Our finding of an association between increased 24-hr mean PM<sub>2.5</sub> concentrations and transmural infarction needs to be replicated in a study that better estimates MI symptom onset time. This study would also allow a more proper investigation of the risk of a transmural infarction associated with PM<sub>2.5</sub> concentrations < 24 hr before MI symptom onset than is possible in our analysis.

Fourth, because all of the 24 hr used to calculate the mean PM<sub>2.5</sub> concentration in the 24 hr before ED arrival may not have been before the onset of MI symptoms, this again was a source of nondifferential exposure misclassification that may have resulted in underestimation of the relative risk. As reported by Lokken et al. (2009), this error in estimation of symptom onset time and the resulting relative risk–rate underestimation may be substantial in studies of acute cardiovascular and cerebrovascular events and short-term increases in PM. When comparing relative risk estimates based on symptom onset of stroke versus those based on hospital presentation for stroke, they observed an approximately 40% underestimation of the relative risk of stroke when using time of hospital presentation (Lokken et al. 2009).

Last, we assigned PM<sub>2.5</sub> concentrations to all patients who lived < 10 km from a PM<sub>2.5</sub> monitor, regardless of how close they lived to the monitor or how much time they spent at locations other than their residence. Because this error is not likely differential with respect to symptom onset, our findings of an association between PM<sub>2.5</sub> and transmural MI may thus be considered to be an underestimate of the true risk association for PM<sub>2.5</sub> and transmural MI.
to when a patient had the MI, it likely resulted in nondifferential exposure misclassification and underestimates of relative risk. In the two pollutant analyses adjusting for gaseous pollutant concentrations, gaseous pollutants may have greater degrees of spatial variability than does PM2.5 within this 10-km radius, resulting in residual confounding.

Conclusions

We found increased risk of transmural infarctions, but not transmural infarctions, associated with each 10.8 µg/m³ increase in mean PM2.5 concentration in the 24 hr before ED arrival. Further, patients with COPD, but not those with diabetes, appeared particularly susceptible to effects of ambient particles. If our findings are confirmed, future investigations of PM and MI triggering should stratify by type of MI, with particular emphasis on transmural infarctions. Future work should also investigate mechanistic explanations for these findings.

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