Air Pollution and Hospital Admissions for Ischemic Heart Disease in Persons with Congestive Heart Failure or Arrhythmia

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We examined whether ischemic heart disease (IHD) hospital admissions were associated with air pollutants in those with and without secondary diagnoses of arrhythmia (ARR) or congestive heart failure (CHF). We assessed the occurrence of increased vulnerability among persons with these conditions to daily variations in ozone, carbon monoxide, nitrogen dioxide, or particulate matter ≤ 10 μm in aerodynamic diameter (PM_{10}). The study population consisted of members of a large health maintenance organization residing in the South Coast Air Basin of California from 1988 to 1995. After adjustment for day of week, study year, and smoothing splines for day of study, temperature, and relative humidity, CO and NO_2 were both associated with admissions with the greatest effects for CO. A 1-ppm increase in 8-hr average CO was associated with a 3.60% [95% confidence interval (CI), 1.62–5.63%] increase in same-day IHD admissions in persons with a secondary diagnosis of CHF, a 2.99% (95% CI, 1.80–4.19%) increase in persons with a secondary diagnosis of ARR, and a 1.62% (95% CI, 0.65–2.59%) increase in IHD admissions in persons without either secondary diagnosis. Air pollution was most strongly associated with myocardial infarction hospital admissions. The vulnerability of the secondary CHF subgroup may be due to a greater prevalence of myocardial infarction primary diagnoses and not the modifying effect of CHF. This study suggests that people with IHD and accompanying CHF and/or ARR constitute a sensitive subgroup in relation to the effects of criteria ambient air pollutants associated with motor vehicle combustion. *Key words:* **air pollution, arrhythmia, carbon monoxide, congestive heart failure, hospital admissions, ischemic heart disease, nitrogen dioxide.** *Environ Health Perspect* **110:1247–1252 (2002). [Online 29 October 2002]**
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Over the past 15 years, epidemiologic studies consistently have demonstrated an association between ambient levels of ambient air pollutants and daily cardiovascular mortality, hospital admissions, and emergency room visits. Associations often have been observed at levels below the National Ambient Air Quality Standards (NAAQS) for various pollutants (Burnett et al. 1999; Linn et al. 2000; Mar et al. 2000; Moolgavkar 2000; Morris and Naumova 1998; Morris et al. 1995; Poloniecki et al. 1997; Schwartz 1997, 1999; Schwartz and Morris 1995). Particle air pollutants, in particular, have been associated with cardiac outcomes (Samet et al. 2000; Schwartz 1999; Schwartz and Morris 1995; Zanobetti et al. 2000), but gaseous pollutants such as carbon monoxide (Morris et al. 1995), nitrogen dioxide (Linn et al. 2000; Moolgavkar 2000; Poloniecki et al. 1997), and ozone (Burnett et al. 1999; Goldberg et al. 2001; Wong et al. 1999) also have been associated. Toxicologic studies in diseased animals and monitoring studies in humans indicate that preexisting heart or respiratory disease might be related to the association of respirable particulate matter and cardiac outcomes (Godleski 2000; Gold et al. 2001; Gordon and Riebman 2000; Pope et al. 1999b; Watkinson et al. 1998). Recent epidemiologic studies also have shown that persons with preexisting cardiopulmonary conditions are at increased risk for adverse cardiac health events (Kwon et al. 2001; Zanobetti et al. 2000) associated with ambient particulate matter. The present study investigates the modifying effect of secondary diagnoses of arrhythmia (sARR) and congestive heart failure (sCHF) on the relationship between hospital admissions for ischemic heart disease (IHD) and ambient air pollutants among members of a large health maintenance organization who reside in Southern California.

Methods

Subjects. This study included residents who were Southern California Kaiser Permanente (SCKP) members at any point from 1988 to 1995 and who lived within 20 km of one of five particle air pollution monitors used in a 1995 intensive particulate matter monitoring data collection. The study area included the most densely populated areas of the South Coast Air Basin (SoCAB), which includes the city of Los Angeles, and contained an annual average of 1,515,776 members over the 8-year study period (70.3% of SCKP membership). The air basin is known both for summertime photochemical smog and relatively high wintertime NO_2 and particulate matter concentrations. The study area extended from the Pacific coast of California east to the Riverside/San Bernadino metropolitan areas, and from the San Fernando Valley to the north to Newport Beach to the south.

Outcomes. Daily hospital admissions for IHD [*International Classification of Diseases*, Revision 9 (ICD-9) codes 410–414] alone (no secondary diagnosis; sNO) or with accompanying diagnoses of sCHF (ICD-9 code 428) and/or sARR (ICD-9 codes 426 and 427) were the main outcomes studied. Discharge diagnoses were used to classify each admission.

Almost half of those with sCHF also had sARR. To evaluate the effect of each secondary diagnosis, admissions among those with either secondary condition were divided into three mutually exclusive groups: those with either an sARR or sCHF diagnosis, and those with both secondary diagnoses. ICD-9 codes 410 [myocardial infarction (MI)] and 411 (other acute and subacute forms of IHD) were the primary diagnoses in 71.6% of admissions. These two diagnoses were not evenly distributed among sCHF, sARR, and sNO admission groups. Therefore, these specific admission diagnoses were also studied.

Air pollutants/exposure assignment. Routine monitoring data for criteria air pollutants from 1988 to 1995 in the SoCAB were acquired from the South Coast Air Quality Management District (SCAQMD). Hourly concentration data for O_3, NO_2, and CO were obtained from a network of 25–35 monitoring stations in the SoCAB. Daily mass concentrations of particles with aerodynamic diameters ≤ 10 μm (PM_{10}) were measured at 20 sites every 6 days. Hourly meteorologic data for temperature and relative humidity were acquired from a network of 15 monitoring stations in the region [from the National Climatic Data Institute (Asheville, NC) and SCAQMD] (Figure 1).

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This analysis uses daily maximum 8-hr average O_3 (ultraviolet photometry) and CO concentrations (nondispersive infrared photometry) and 24-hr average NO_2 (gas-phase chemoluminescence) and PM_{10} concentrations (gravimetric analysis with a size-selective inlet sampler).

To assign daily exposure for each pollutant, the air basin was divided into 10 km × 10 km grids. Each Kaiser Permanente member in the study area was assigned to a grid based on the centroid of his or her residential ZIP code on 1 January of each year. The study area included 84 grids with SCKP members. Daily pollutant exposures were interpolated to grid centroids from up to three monitors weighted by the inverse of distance to the grid centroid. Each grid was assigned to one of seven meteorologic subregions based on temperature and humidity patterns in January and July over the 8-year period. A recent article that presented a conceptual model of exposure measurement error in time-series studies of air pollution showed that measurement error was reduced when exposures were weighted by baseline risk levels (Zeger et al. 2000). For IHD admissions, persons ≥ 60 years of age have been suggested to be at greatest risk. Therefore, the annual population of members ≥ 60 years of age residing in each grid was used for risk-weighting daily exposures.

Analysis. Poisson regression with allowance for overdispersion was used to model the relationships between daily health outcomes and daily concentrations of ambient air pollutants. Separate base models were developed for each diagnostic subgroup within each region because temporal patterns of outcomes differed across the regions. Generalized additive models (S-Plus; Insightful; Seattle, WA), with air pollutants omitted, were developed with cubic B-spline–smoothed terms for study day, temperature, and relative humidity. Fixed effects terms for year and day of week also were evaluated. Each model included an offset term, the log of the number of members residing in the region on 1 January of each year, so that effects could be interpreted as relative rates. The base model was selected on the basis of Akaike's information criterion. After selection of the base model, each pollutant was regressed against daily admission counts in each of the seven regions. Because there was no evidence of heterogeneity where effect estimates were statistically significant, effect estimates were pooled based on inverse variance weights. Pollutants lagged from 0 to 5 days, and 2–5-day moving averages were tested.

Single pollutant analyses were repeated for all pollutants restricted to days on which PM_{10} was measured. Analyses also were restricted to April through October of each year, the months in which O_3 concentrations were elevated. Base models were developed for the ozone season to account for the differences in periodicity and trend in the outcome series. To examine potential effect modification by age group, admissions in those ≥ 40 years of age were divided into two age groups, 40–59 years and ≥ 60 years. Finally, analyses with the mutually exclusive diagnostic groups were conducted to help elucidate the modifying effect of each cardiac condition.

Results

Over the 8-year period, there were 54,863 IHD admissions among SCKP members in the study area. In 34.5% (n = 18,935) and 14.1% (n = 7,754) of admissions, there was a diagnosis of sARR and/or sCHF, respectively. Admissions were most frequent in those without either secondary diagnosis (sNO; n = 31,760). The mean number of daily admissions in each region was 1.6, 0.93, and 0.38 for the sNO, sARR, and sCHF subgroups, respectively. About one-half of those with a diagnosis of sCHF also had a diagnosis of sARR (n = 3,766) (Table 1). Specific IHD admission diagnoses were not evenly distributed among the diagnostic subgroups. Persons with sCHF were more likely to have a primary diagnosis of MI (61.9%) than were those with a diagnosis of sARR (37.8%) or with sNO (28.8%). The annual rate of IHD admissions was 10-fold greater in the older age stratum (29.9/1,000 vs. 2.5/1,000). However, the distribution of specific IHD diagnoses was similar in each age stratum (Table 2).

IHD admission counts among people with sARR diagnoses rose from 1988 to 1992 and then declined. IHD admissions with sCHF diagnoses increased in winter and decreased in summer, whereas admissions in those with sNO diagnoses had little seasonality but increased over the 8-year period. Admissions were most likely to occur on

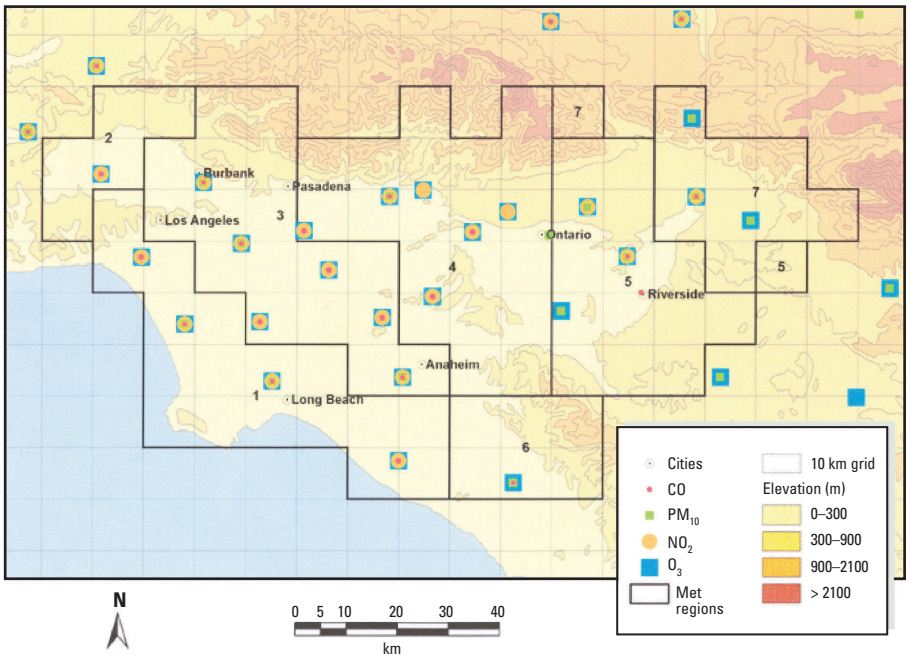

Figure 1. Map of the study area with the locations of meteorologic (Met) regions and stationary air pollution monitors.

Table 1. Distribution of events and rates for each outcome among IHD hospital admissions.

Diagnoses	Mean admissions per region-day (range)	Percent region-days with 0 admissions	Total admissions	Average annual rate/1,000
Main secondary outcomes				
sNO	1.6 (0.14–3.3)	34.8	31,760	2.62
sARR	0.93 (0.12–2.0)	50.4	18,935	1.56
sCHF	0.38 (0.03–0.87)	71.7	7,754	0.64
Mutually exclusive secondary outcomes				
sARR, not sCHF	0.74 (0.10–1.7)	56.4	15,169	1.25
sCHF, not sARR	0.20 (0.06–0.45)	83.3	3,988	0.33
sARR and sCHF	0.18 (0.02–0.35)	84.3	3,766	0.31
Specific primary admission diagnoses				
Acute MI	0.96 (0.28–2.12)	48.0	19,690	1.62
Other acute forms of IHD	0.95 (0.11–2.05)	49.7	19,460	1.60
Angina pectoris	0.26 (0.01–0.58)	79.0	5,327	0.79
Other forms of chronic IHD	0.50 (0.07–1.06)	69.4	10,199	0.69

Mondays and least likely to occur on Saturdays. Regions 1 and 3 contained 59.9% of the population and contributed more than one-half of the admissions for each subgroup. Only 11.7% of the study population lived in regions 2, 6, and 7. Admission rates were highest in region 2 and lowest in region 4 for each outcome (data not shown).

Table 3 shows the mean, median, interquartile range, and range for each weather and pollutant variable. Annual PM_{10} and daily O_3 concentrations frequently exceeded NAAQS. Annual PM_{10} concentrations were > 50 μg/m^3 25% of the time. Eight-hour average O_3 levels were > 80 ppb on 16.5% of region-days. In contrast, daily CO and annual NO_2 concentrations rarely, if ever, surpassed federal guidelines (0.09% and 0.00%, respectively). Concentrations for all air pollutants declined over the study period.

Pollutant concentrations varied by region, which reflects regional differences in motor vehicle traffic, land use, and climate. O_3 concentrations were higher in the eastern regions where temperatures were higher in summer. CO and NO_2 concentrations were greatest in regions 3 and 4, partly because of motor vehicle traffic in those regions (SCAQMD 1997), and PM_{10} concentrations were highest in region 5. CO and O_3 had the largest spatial variation and NO_2 had the least as measured by a comparison of mean concentrations from 1988 to 1995 (data not shown).

Partial correlations between pollutants are presented in Table 4. PM_{10} was modestly associated with CO (r = 0.15–0.40) and NO_2 (r = 0.36–0.60) in all regions. NO_2 was highly correlated with CO (0.64–0.86). NO_2 was positively associated with O_3 in all but region 6 (r = –0.16 to 0.42). PM_{10} was most correlated with O_3 in region 2 (r = 0.57), CO in region 5, and NO_2 in region 7 (r = 0.60). Partial correlations of O_3 and CO varied in both sign and magnitude across the regions but were generally low.

Table 5 presents the results of single pollutant models based on same-day concentrations. PM_{10} was not significantly related to admissions at any of the lags and moving averages tested. O_3 coefficients were all negative and generally nonsignificant. CO and NO_2 were both related to admissions in each subgroup across a range of lags and moving averages, with strongest effects found for a 0-day lag or 2-day moving average; effects were no longer evident with days lagged 4 days or more and 5-day moving averages. A 1-ppm increase in 8-hr average CO was associated with a 3.60% increase [95% confidence interval (CI), 1.62–5.63] in daily hospitalizations for sCHF and a 2.99% change (95% CI, 1.80–4.19) in those with a diagnosis of sARR. By contrast, in the group with sNO diagnosis, hospital admissions increased only 1.6% with a 1-ppm increase in CO. A 10-ppb increase in NO_2 was associated with a 2.3% change in sCHF, a 1.8% change in sARR, and a 1.3% change in sNO admissions. Two pollutant models with CO and NO_2 would have been unstable because of their high correlation in some regions and so were not evaluated.

Associations were reduced in magnitude and were nonsignificant for CO and NO_2 on days on which PM_{10} was measured (21% of region-days). O_3 coefficients remained nonsignificant. Because there might not have been sufficient days of analysis to detect PM_{10} associations, given the number of daily admissions in this population, PM_{10} was not included in other sensitivity analyses.

O_3 coefficients remained nonsignificant even when the analysis was restricted to months in which O_3 was elevated (April through October). However, CO and NO_2 associations were generally reduced in magnitude and were nonsignificant possibly because of the large loss of days and/or loss of temporal variability in CO and NO_2 concentrations during the O_3 season.

When the analysis was restricted to persons ≥ 60 years of age, CO and NO_2 relationships with sARR and sCHF admissions were similar to the main analysis, whereas effects with the sNO subgroup were greater (Table 6). A 10-ppb increase in NO_2 was associated with a 2.4% (95% CI, 1.02–3.71) increase in admissions. When comparing the three subgroups, the percentage increase in admissions with CO was still greatest among those with sCHF. A 1-ppm increase in 8-hr average CO concentrations was associated with a 2.9% increase in sCHF admissions (95% CI, 0.79–5.1). In the younger age group, CO effects were slightly greater in the sARR subgroup (3.06%; 95% CI, 0.56–5.61%) and much greater in persons with sCHF (8.02%; 95% CI, 2.95–13.3%) relative to the older age group. Air pollutants were not associated with sNO admissions in the 40–59-year age group.

Effects on sCHF admissions were not due to associated ARR. The effects of CO and NO_2 were similar when admissions in those with ARR were removed from the analysis. Effect sizes among those with both secondary conditions were not greater than those for having sCHF or sARR alone (Table 7). Based on mutually exclusive diagnostic groups, the same rank order in magnitude of effects was observed, with the strongest effects in those with diagnoses of sCHF without sARR and the smallest effects in the sNO subgroup.

Although the magnitude of effect for a 1-ppm increase in CO was greater than that for a 10-ppb NO_2 increase, an increase in NO_2 of 10 ppb or more occurred almost twice as often (15.0% of region-days) as a 1-ppm CO increase (8.3% of region-days). Increases equal to or greater than the span of the interquartile range occurred about half as often for both of these pollutants (Table 8).

Table 2. Distribution of IHD primary diagnoses by secondary diagnosis and age group.

Primary diagnosis	ICD-9 code	Secondary diagnosis (%)			Age group (%)	
		sARR	sCHF	sNO	40–59 years	≥ 60 years
Acute MI	410	37.8	61.9	28.8	34.5	36.6
Other acute and subacute forms of IHD	411	33.5	21.9	39.9	35.8	35.6
Angina pectoris	413	8.5	4.4	11.6	10.1	9.5
Other forms of chronic IHD	414	20.1	11.8	19.6	19.5	18.3

Table 3. Distribution of air pollutants and weather variables.

Pollutant	*n*	Mean ± SD	Median	IQR	Range
8-Hr average CO (ppm)	20,454	2.07 ± 1.29	1.70	1.14–2.61	0.30–11.8
24-Hr average NO_2 (ppb)	20,447	37.2 ± 15.7	34.8	25.6–45.8	3.68–138
8-Hr average O_3 (ppb)	20,454	50.3 ± 30.1	43.2	27.6–67.2	0.00–206
PM_{10} (μg/m_3)	4,311	43.7 ± 27.7	40.6	24.0–58.4	0.22–251
Minimum temperature (°F)	20,454	53.8 ± 8.41	54.4	47.8–60.4	15.8–77.2
24-Hr average relative humidity (%)	20,440	54.1 ± 13.8	56.1	45.2–63.4	11.9–89.5

Abbreviations: IQR, interquartile range; *n*, number of region-days of measurements.

Table 4. Partial correlations for each pollutant pair.[a]

Pollutant pair	Region						
	1	2	3	4	5	6	7
CO/NO_2	0.83	0.65	0.84	0.72	0.80	0.86	0.64
CO/O_3	0.06	–0.30	0.13	–0.20	0.28	–0.37	–0.23
CO/PM_{10}	0.28	0.15	0.36	0.27	0.40	0.33	0.28
O_3/NO_2	0.27	0.25	0.42	0.34	0.54	–0.16	0.34
O_3/PM_{10}	0.20	0.57	0.30	0.33	0.43	0.20	0.48
NO_2/PM_{10}	0.36	0.53	0.46	0.50	0.53	0.42	0.60

[a]Correlation remaining after adjustment for day of week, year, and smoothing splines of study day, minimum temperature, and average relative humidity using the base model for ischemic heart disease admissions.

Discussion

Numerous studies have demonstrated an association between ambient air pollutants and hospital admissions for cardiovascular diseases. Few studies have investigated the subsets of such patients who might be at particular risk for hospital admission. This study demonstrates that, among persons admitted to the hospital with a primary diagnosis of IHD, the presence of sCHF or sARR substantially increases the risk of hospitalization associated with air pollution, with greatest susceptibility among those with a diagnosis of sCHF.

CO and NO_2, at concentrations well below NAAQS, were associated with admissions in each diagnostic subgroup of IHD admissions. The greatest effects were found for both pollutants with same-day and 2-day moving average concentrations. Because ambient concentrations of these two pollutants were highly correlated, the independent contribution of each could not be evaluated in two pollutant models. O_3 was not associated with admissions in any subgroup, even when the analysis was restricted to months when ambient O_3 concentrations were at their highest levels. Although PM_{10} was not associated with IHD admissions, it was only measured every 6 days. When analyses were restricted to the days on which PM_{10} was measured, none of the pollutants were associated with admissions. Because there might have been an insufficient number of monitoring days for particulate air pollution (an average of 615 noncontiguous days for each series), a PM_{10} association cannot be ruled out. CO and NO_2 were probably not surrogates of PM_{10} exposure, however, because PM_{10} was less correlated with CO and NO_2 than the two pollutants were with one another.

Almost one-half of persons with sCHF admissions also had a diagnosis of sARR. However, larger effects in the sCHF subgroup were not due to associated sARR diagnoses; sCHF effects were similar when persons who also had diagnoses of sARR were removed from the analysis. In addition, persons with both secondary diagnoses were not at increased risk relative to persons with either sCHF or sARR.

Two primary diagnoses accounted for 72% of all admissions, MI and "other acute IHD." Persons with a diagnosis of sCHF were about twice as likely to have a primary diagnosis of MI than were persons from the other two subgroups. Effect estimates were 71% greater for MI than for other acute IHD. Therefore, the vulnerability of the sCHF subgroup may be due to the greater prevalence of the MI diagnosis and not the modifying effect of CHF.

The greater effect estimates among the sCHF and sARR subgroups could reflect solely the independent associations between air pollution and CHF and ARR. There are two arguments against this explanation. First, effects, although smaller, were present among persons with sNO diagnoses. Second, in earlier studies, hospital admissions for CHF and ARR were not more strongly associated with CO or NO_2 than MI, angina, or the group of IHD admissions (Linn et al. 2000; Poloniecki et al. 1997).

Levy et al. (2001) used a case–crossover design to examine the association of particle air pollution with out-of-hospital cardiac arrest. Patients with a history of cardiac disease, including ARR, CHF, or prior MI, were excluded. In this relatively healthy population, none of the air pollutants was associated with subsequent MI. Presumably their cases were healthier than any of the subgroups in this study, including the sNO subgroup, because only cases of first MI were included. More than half of their study population was younger than 61 years. In this study, air pollution was not significantly related to admissions in persons younger than 60 years without ARR or CHF.

Zanobetti et al. (2000) examined the modifying effect of secondary diagnoses and prior cardiorespiratory hospitalizations in associations between PM_{10} and cardiorespiratory admissions. No other pollutants were investigated. Associations of daily PM_{10} and cardiovascular hospitalizations were modified by previous hospital admissions for conduction disorders or dysrhythmias. Prior admission for CHF and MI did not increase risk of a subsequent PM-associated cardiovascular hospitalization.

CO has been associated with primary admissions for CHF, IHD, and ARR in several studies (Burnett et al. 1997; Morris and Naumova 1998; Morris et al. 1995; Schwartz and Morris 1995). Increases in daily NO_2 concentrations have also been associated with increased admissions for specific cardiac conditions (Burnett et al. 1999; Linn et al. 2000; Ye et al. 2001). In most of these studies, same-day or 1-day lagged concentrations had the strongest association with admissions. CO at the monitor is poorly correlated with personal exposure relative to other criteria air pollutants in cross-sectional studies (Akland et al. 1985).

The lack of association of particles with IHD admissions in this study is in contrast to several other epidemiologic studies (Burnett et al. 1995; Linn et al. 2000; Lippmann et al. 2000). However, particulate matter was not associated with admissions in London (Atkinson et al. 1999) or Birmingham (UK) (Wordley et al. 1997).

Recently, mechanisms have been proposed to explain observed associations of particle air pollution with cardiovascular morbidity and mortality. One hypothesis is that particles trigger the production of inflammatory mediators, which in turn affects procoagulants (e.g., fibrinogen, factor VII) and viscosity

Table 5. Percentage increase (95% CI) in IHD hospital admissions with increasing concentrations of air pollutants,[a] 0–2-day lags, and 2–4-day moving averages.

Type of admission/pollutant	Lags			Moving averages		
	0-day	1-day	2-day	2-day	3-day	4-day
sARR admissions						
CO (ppm)	2.99 (1.80–4.19)*	1.51 (0.37–2.66)*	1.26 (0.15–2.38)*	2.66 (1.40–3.94)*	2.59 (1.27–3.92)*	2.25 (0.90–3.63)*
NO_2 (ppb)	1.81 (0.78–2.85)*	0.84 (−0.18–1.87)	0.61 (−0.41–1.64)	1.43 (0.32–2.55)*	1.50 (0.31–2.70)*	1.35 (0.09–2.62)*
O_3 (ppb)	−0.43 (−1.07–0.21)	−0.40 (−1.04–0.25)	−0.80 (−1.44–−0.15)*	−0.47 (−1.14–0.21)	−0.67 (−1.37–0.03)	−0.91 (−1.63–−0.18)
PM_{10} (μg/m^3)	0.59 (−0.71–1.91)	0.46 (−0.86–1.80)	−0.04 (−1.37–1.31)			
sCHF admissions						
CO (ppm)	3.60 (1.62–5.63)*	3.34 (1.48–5.22)*	1.90 (0.11–3.72)*	4.23 (2.13–6.37)*	4.14 (1.96–6.37)*	4.07 (1.81–6.38)*
NO_2 (ppb)	2.32 (0.69–3.98)*	2.13 (0.52–3.77)*	0.90 (−0.70–2.52)	2.63 (0.87–4.41)*	2.47 (0.59–4.39)*	2.24 (0.26–4.22)*
O_3 (ppb)	−0.08 (1.25–1.10)	−0.30 (−1.50–0.93)	−0.10 (−1.31–1.13)	−0.22 (−1.50–1.07)	−0.24 (−1.61–1.14)	−0.60 (−2.03–0.85)
PM_{10} (μg/m^3)	−0.62 (−1.77–0.55)	−0.45 (−1.60–0.71)	−0.36 (−1.52–0.82)			
sNO admissions						
CO (ppm)	1.62 (0.65–2.59)*	1.45 (0.54–2.37)*	0.92 (0.04–1.82)*	1.83 (0.80–2.86)*	1.79 (0.72–2.87)*	1.82 (0.71–2.94)*
NO_2 (ppb)	1.30 (0.51–2.10)*	1.43 (0.65–2.22)*	0.75 (−0.03–1.53)	1.63 (0.77–2.49)*	1.35 (0.43–2.27)*	1.30 (0.30–2.31)*
O_3 (ppb)	−0.61 (−1.23–0.02)	−0.21 (−0.76–0.34)	−0.25 (−0.80–0.30)	−0.40 (−0.97–0.18)	−0.40 (−1.00–0.21)	−0.62 (−1.26–0.02)
PM_{10} (μg/m^3)	−0.25 (−1.23–0.75)	0.04 (−0.97–1.06)	0.18 (−0.82–1.20)			

[a]Percentage increase in admissions with a 1 ppm increase in CO, a 10 ppb increase in NO_2 or O_3 or a 10 μg/m^3 increase in PM_{10}; for example, a 1-ppm increase in same-day CO is associated with a 2.99% increase in IHD admissions in persons with a sARR. For each lag, pollutant coefficients from seven regions were pooled weighted by the inverse of the standard error. Before pooling, estimates were adjusted for day of week, year, and region-specific cubic B-spline smooths of study day, temperature, and relative humidity.
*Statistically significant association ($p < 0.05$).

(Seaton et al. 1995). Similarly, particles have been hypothesized to affect autonomic function of the heart (Peters et al. 2000a). Both hypotheses are supported by several studies in animals and humans (Creason et al. 2001; Liao et al. 1999; Peters et al. 1997, 2000a, 2000b; Pope et al. 1999a, 1999b; Schwartz 2001; Watkinson et al. 1998).

Although these hypotheses were developed to explain cardiovascular morbidity and mortality associated with particulate air pollution, similar mechanisms might be true for both CO and NO_2. In controlled human exposure studies using broncheoalveolar lavage, acute NO_2 exposures as dilute as 1 mg/m^3 were associated with increased production of inflammatory mediators (Jeffrey 1999). Both NO_2 and CO have been associated with increased concentrations of inflammatory markers in human exposure and epidemiologic studies. In London office workers, NO_2 and CO levels on the day before were associated with increased fibrinogen concentrations (Pekkanen et al. 2000). Plasma viscosity was increased during an air pollution episode in Germany in which levels of sulfur dioxide and total suspended particles were elevated. However, in that study, CO concentrations were also positively associated with plasma viscosity over the whole study period (CO did not increase appreciably during the air pollution episode) (Peters et al. 1997). Based on data from the Third National Health and Nutrition Examination Survey (NHANES III), a representative sample of the U.S. adult population, NO_2 was associated with increased platelet counts and fibrinogen but not increased white blood cells, whereas PM_{10} was associated with all three outcomes (Schwartz 2001).

Particles have been associated with decreased heart rate variability and slightly increased heart rate in two small studies (Gold et al. 2001; Pope et al. 1999b). CO and NO_2 were not associated with increased heart rate and decreased heart rate variability, however (Gold et al. 2001). Peters et al. (2000a) examined the relationship of air pollution to cardiac ARR incidence among 100 cardiac patients with implanted defribillators. Particles, O_3, CO, SO_2, and NO_2 were studied. Only NO_2 (lagged 1 day or a 5-day moving average) was associated with ARRs that triggered the defibrillator in these patients.

Carboxyhemoglobin (COHb) levels of 2% (produced in 10% of the population in response to 8-hr average 9-ppm CO concentrations) were associated with shorter time to exercise-induced angina and shorter ST intervals among 62 nonsmoking volunteers with IHD (Allred et al. 1989). CO also has been shown to impair myoglobin's oxygen transport and storage capacity. The resulting reduction in oxygen in the myocardial circulation could increase the likelihood of angina and MI. Allred et al. (1989) hypothesized that CO-associated decreases in pO_2 (partial pressure of O_2) might raise the risk of ventricular fibrillation in patients with preexisting ischemia. However, CO was not associated with increased ectopic beats at COHb of 3% or 5% (Maynard and Waller 1999).

The known increase in wall tension in CHF and its associated effects on epicardial circulation certainly also could place persons with CHF at greater risk for air pollution associated acute MI.

Conclusions

This is the first epidemiologic study showing that people with IHD and accompanying CHF and/or ARR constitute a sensitive subgroup in relation to the effects of criteria air pollutants associated with motor vehicle combustion. Persons with a diagnosis of sCHF were at greatest risk. There was insufficient power to determine whether a higher proportion of MI diagnoses in those groups explained the added risk of these comorbid conditions. This study should be repeated in an area with sufficient events to analyze MI admissions in persons with and without diagnoses for sCHF or sARR. Although an effect of PM_{10} could not be ruled out, same-day and 2-day moving average concentrations of CO and NO_2 were consistently associated with admissions in each subgroup. The major source of ambient CO and NO_2 in the study area is motor vehicles. Therefore, either or both pollutants might be surrogates for the pollution mix associated with motor vehicle combustion.

Table 6. Percentage increase (95% CI) in IHD hospital admissions with increasing concentrations of air pollutants[a]: comparison of effects in two age strata.

Pollutants	Age (years)	Secondary diagnosis		
		sARR	sCHF	sNO
8-Hr average CO (ppm)	40–59	3.06 (0.558–5.61)*	8.02 (2.95–13.3)*	0.9s (−0.65–2.50)
24-Hr average NO_2 (ppb)		2.96 (0.799–5.16)*	4.71 (0.702–8.87)*	0.46 (−0.81–1.74)
8-Hr average CO (ppm)	≥ 60	2.99 (1.64–4.37)*	2.93 (0.788–5.13)*	1.94 (0.675–3.22)*
24-Hr average NO_2 (ppb)		1.56 (0.377–2.75)*	2.06 (0.276–4.27)*	2.36 (1.02–3.71)*

[a]Percentage increase in admissions with a 1 ppm increase in CO, a 10 ppb increase in NO_2 or O_3 or a 10 μg/m^3 increase in PM_{10}.*Statistically significant association ($p < 0.05$).

Table 7. Percentage increase (95% CI) in IHD hospital admissions with increasing concentration of air pollutants[a]: comparison of effects with mutually exclusive secondary outcomes.

Pollutants	Secondary diagnosis			
	sARR but not sCHF	sCHF but not sARR	Both sCHF and sARR	sNO
8-Hr average CO (ppm)	2.77 (1.44–4.11)*	4.28 (1.55–7.10)*	3.00 (0.20–5.87)*	1.62 (0.65–2.59)*
24-Hr average NO_2 (ppb)	1.92 (0.77–3.09)*	3.34 (1.08–5.64)*	1.39 (−0.91–3.75)	1.30 (0.51–2.10)*
8-Hr average O_3 (ppb)	−0.21 (−0.92–0.51)	0.47 (−1.13–2.11)	−0.46 (−2.13–1.24)	−0.61 (−1.23–0.02)

[a]Percentage increase in admissions with a 1 ppm increase in CO, a 10 ppb increase in NO_2 or O_3 or a 10 μg/m^3 increase in PM_{10}. *Statistically significant association ($p < 0.05$).

Table 8. Percentage increase (95% CI) in hospital admissions with increasing concentrations of air pollutants[a]: comparison of effects with specific IHD primary diagnoses.

Pollutant	All IHD admissions (ICD-9 410–414)	MI (ICD-9 410)	Other acute IHD (ICD-9 411)
8-Hr average CO (ppm)	2.20 (1.56–2.83)*	3.48 (2.42–1.55)*	2.04 (0.80–3.29)*
24-Hr average NO_2 (ppb)	1.68 (1.08–2.28)*	2.04 (1.05–3.02)*	1.75 (0.72–2.78)*
8-Hr average O_3 (ppb)	−0.41 (−0.745–−0.072)	−0.92 (−1.48–−0.35)	−0.12 (−0.77–0.54)
24-Hr average PM_{10} (μg/m^3)	0.19 (−0.576–0.955)	−0.10 (−1.33–1.12)	0.36 (−0.87–1.60)

[a]Percentage increase in admissions with a 1 ppm increase in CO, a 10 ppb increase in NO_2 or O_3 or a 10 μg/m^3 increase in PM_{10}. *Statistically significant association ($p < 0.05$).

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