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Associations between arrhythmia episodes and temporally and spatially resolved black carbon and particulate matter in elderly patients

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Abstract

Objectives—Ambient air pollution has been associated with sudden deaths, some of which are likely due to ventricular arrhythmias. Defibrillator discharge studies have examined the

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association of air pollution with arrhythmias in sensitive populations. No studies have assessed this association using residence-specific estimates of air pollution exposure.

Methods—In the Normative Aging Study, we investigated the association between temporally- and spatially-resolved black carbon (BC) and PM_{2.5} and arrhythmia episodes (bigeminy, trigeminy or couplets episodes) measured as ventricular ectopy (VE) by 4-min electrocardiogram (ECG) monitoring in repeated measures of 701 subjects, during the years 2000 to 2010.

We used a binomial distribution (having or not a VE episode) in a mixed effect model with a random intercept for subject, controlling for seasonality, temperature, day of the week, medication use, smoking, having diabetes, BMI and age. We also examined whether these associations were modified by genotype or phenotype.

Results—We found significant increases in VE with both pollutants and lags; for the estimated concentration averaged over the three days prior to the health assessment we found increases in the odds of having VE with an OR of 1.52 (95% CI: 1.19–1.94) for an IQR (0.30 µg/m³) increase in BC and an OR of 1.39 (95% CI: 1.12–1.71) for an IQR (5.63 µg/m³) increase in PM_{2.5}. We also found higher effects in subjects with the GSTT1 and GSTM1 variants and in obese (P-values<0.05).

Conclusion—Increased levels of short-term traffic related pollutants may increase the risk of ventricular arrhythmia in elderly subjects.

Keywords

arrhythmia episodes; spatially-resolved black carbon and particulate matter; traffic pollution; elderly

INTRODUCTION

Air pollution has been consistently associated with cardiovascular morbidity, mortality [1] and premature death [2,3], but the underlying mechanisms are not well understood.

In relation to more specific cardiac events, there is evidence that air pollution may contribute through a wide range of pathways, and several biological mechanisms by which air pollution can elicit cardiovascular morbidity and mortality have been identified, including oxidative stress[4], autonomic dysfunction [5–9], and systemic inflammation [10–12].

Several studies have observed associations between air pollution and cardiac arrhythmias, based on data from implantable cardioverter-defibrillator (ICDs). These devices, which restore a normal heart rhythm, allow the continuous monitoring of patients and the documentation of type and time of ventricular arrhythmias. These studies have found the associations of air pollution with arrhythmias [13–16] in sensitive populations, although results have been mixed. However, less is known for the general population. Further, none of these existing studies have used exposure estimates that are specific to the location of each study participant. Ljungman and co-authors [17] found that patients with implantable cardioverter defibrillators also showed evidence of rapid effects of air pollution on the risk of life-threatening ventricular arrhythmias. Among cardiovascular health indicators,

irregularities in myocardial repolarization may be especially important because they can lead to the development of cardiac arrhythmias.

Another study [18] examined the effects of air pollutants on repeated measurements of QT interval (QTc), an electrocardiographic marker of ventricular repolarization, in 580 men from the Veterans Affairs Normative Aging Study (NAS). The authors found an association between QTc and BC measurements from the Harvard supersite. Similarly, in a repeated-measures study of patients with coronary artery disease [19], we found associations between ambient and indoor black carbon and a report of being in traffic with risk of increase in T-Wave Alternans (TWA), a marker of cardiac electrical instability. In Boston, traffic-related pollutants were also related to the promotion of ST segment depression among elderly subjects [20].

These findings suggest a possible biological pathway linking acute effects of air pollution on increased risk of ventricular repolarization, cardiovascular arrhythmias, and cardiac death.

Short-term exposure studies have mostly used stationary monitors to estimate exposure; however, specific components of traffic-related air pollution vary substantially within cities, and traffic variables may contribute to this variation [21–23]. This suggests that spatio-temporal prediction of BC levels within the Boston-area could substantially improve exposure assessment. An important tool for studying within-city variation in air pollution is the development of geographically-based exposure models; however previous studies have been limited by the lack of high resolution daily exposure data.

Black carbon (BC) is a traffic-related particle and a common surrogate for traffic particles in general, weighted towards diesel particles. We have developed a spatio-temporal land use regression model for traffic particles based on BC in the greater Boston metropolitan area [24]. Predictions from this model have been merged to the geocoded address of each subject of the Normative Aging Study cohort and have been used to study the effect of traffic pollution with, markers of inflammatory and endothelial response [25], blood pressure [26] and other outcomes. This model for BC has been now updated and revised to include data from 125 monitoring stations recording BC levels at some point between January 1999 and August 2011.

Growing evidence also suggests that traffic-related components of PM pollution contribute significantly to particle-related cardiovascular effects. For example, a recent chamber study examined the short-term effects of PM_{2.5} on blood pressure and found that effects were much stronger for the samples collected from a high-traffic area [27].

We have recently presented a new method [28] of assessing temporally-and spatially-resolved PM_{2.5} exposures for epidemiological studies. This approach is an extension of existing land use models to include satellite based physical aerosol optical depth (AOD) measurements [24,29]. We have applied these predictions to study the association between PM_{2.5} exposure and hospital admissions among elderly across New England, as well as with geocoded birth weight in MA.[30,31]

In this study we hypothesized that increases in estimated BC concentrations and estimated PM_{2.5} concentrations may be associated with increases in ventricular arrhythmias.

We therefore investigated the association between black carbon, and PM_{2.5} and arrhythmia episodes measured as ventricular ectopy among participants of the Veterans Affairs (VA) Normative Aging Study (NAS) residing in the greater Boston area. We also examined whether participant characteristics (obesity, diabetes, statin use, genetic susceptibility) might modify this association.

METHODS

Our study population consisted of a cohort of elderly men recruited to the Normative Aging Study (NAS), an ongoing longitudinal study of aging established by the Veterans Administration in 1963 from community-dwelling men from the Greater Boston area aged 21 to 80 years at the time of entry, who were free of any known chronic medical conditions and were asked to return for onsite physical examinations and questionnaires every 3–5 years. Study participants provided written informed consent and the study protocol was approved by the Institutional Review Boards of all participating institutions.[32]

Eligibility for this study required continued participation as of the time when heart rate variability measurements began in the year 2000. Drop out has been less than 1% per year in the cohort, and is predominantly when subjects move out of the study area, or mortality. The study population is a self-selected group of people who continued to participate in this ongoing study. Since 1963, every 3 to 5 years, participants have undergone routine physical examinations, laboratory tests, collection of medical history information, and completion of questionnaires on smoking history, educational level, food intake, and other factors that may influence health. Diabetes was defined as either a physician diagnosis of diabetes, use of any diabetes medication, or fasting glucose >126 mg/dL, and obesity was defined as a BMI of at least 30. Self-reported data on diabetes status and statin use were updated at each study visit and confirmed by a physician interview. In addition, BMI and obesity were updated based on height and weight measurements at each visit. Thus, this data reflect changes in disease status and medication use over time.

Beginning in November 2000, ECG measurements were also obtained during each participant's regularly scheduled visit.

ECG measurement and analysis

After a 5-minute rest, with the subject seated, the ECG was recorded for 5–10 min with a two-channel (five lead) ECG monitor (Trillium 3000; Forest Medical, Inc., East Syracuse, NY) using a sampling rate of 256 Hz per channel. A detailed description of the protocol is provided elsewhere [6,33]. Briefly, with a PC-based software beats were automatically labeled and assigned tentative annotations, and then an experienced scanner reviewed the results to correct for any mislabeled beats or artifacts, and the best 4-consecutive-minute intervals were used for the analysis. The normal or supraventricular beats were recorded; 153 measurements were excluded because of ECG recordings that have recording time < 3.5 minutes, or insufficient T wave amplitude.

In this study we examined arrhythmia episodes measured as ventricular ectopy (VE). We defined ventricular ectopy as having bigeminy, trigeminy or couplets episodes. We then created an indicator variable for having (=1) or not having (=0) episodes.

We examined 1448 observations of subjects who had either one (n = 701), two (n = 451), three (n = 217), or four (n=79) ECG measurements.

Air pollution and meteorology

PM_{2.5} (particulate air matter with aerodynamic diameter less than 2.5 mm) and Black Carbon (BC) concentrations were continuously measured at the stationary ambient monitoring site at the Harvard University Countway Library, which is located < 1 km from the clinical laboratory where subjects were examined.

Hourly outdoor black carbon concentrations were also obtained from 2 sites operated by the Massachusetts Department of Environmental Protection.

We obtained measurements from specific monitoring campaigns from two sources: beginning in 1999, hourly outdoor and indoor black carbon concentrations were measured inside and outside of 30 residential homes, using aethelometers over 48 hour intervals as part of a NIEHS funded study of air pollution and heart rate variability (APAHVRV) conducted at Harvard School of Public Health. Secondly, outdoor 24 hour averages of elemental carbon concentration were obtained from an EPA funded multi-pollutant exposures study of sensitive individuals during winter and summer of 2000 for seven-day periods in 23 locations. A third source was rotating monitoring sites located at the homes of 50 people, sampling for 1 month each in the hot and cold season, with addresses chosen to fill in locations undersampled or not sampled in the previous monitoring campaigns.

Finally reflectance data was obtained from PM_{2.5} filters from six monitors located geographically around the Boston area (1 in the city, 1 slightly north of the city, 2 north and west of the city, and 2 south and east of the city. These data were obtained daily.

Hourly meteorological measurements, such as mean temperature (°F), dew point temperature (°C) were obtained from the National Weather Service First Order Station at Logan Airport in East Boston.

BC Exposure Prediction—We estimated BC exposures using a validated spatiotemporal land-use regression model that provides daily estimates of BC concentrations throughout the greater Boston, Massachusetts, area; details of this model have been published previously [24]. We used an updated and revised version of the aforementioned model, with data from 125 monitoring stations that collected data during the period of January 1999 to August 2011, with a total of 14,238 daily averages from 125 monitoring stations.

We used measurements from continuous ambient monitors as well as specific monitoring campaigns as described above. Briefly, daily average BC estimates from 125 monitoring sites were used to develop a BC prediction model, where the majority of sites measured BC continuously using aethelometers and other sites collected particles on a filter over 24 hours and measured elemental carbon (EC) using reflectance analysis. Predictors in the final

model included measures of land use for each address (cumulative traffic density within 100 meters, land cover within 1 km radius, and distance to coast), GIS location (latitude, longitude), daily meteorological factors (apparent temperature, wind speed, and height of the planetary boundary layer) and other characteristics (day of week, day of season), as well as interaction terms of land use measures and daily meteorological factors (e.g. interaction between the height of the planetary boundary layer and an indicator of the values above the median value of land cover within 1 km radius). The Boston central-site monitor was also included as a predictor to reflect average pollutant concentrations over the entire region on each day. Predicted daily concentrations showed a >3-fold range of variation in exposure across measurement sites (adjusted $R^2 = 0.83$). Out-of-sample cross-validation at 32 monitoring sites showed an average correlation of 0.73 between predicted and observed daily BC levels. As opposed to evaluating the predictive ability of the model for all monitors, which included both residential and urban, non-residential locations, we selected as our test set a subset of monitors that were sited in residential locations. This validation approach provides a better estimate of the predictive performance of the exposure model at study subject residences, as opposed to a more general metric that encompasses locations in which no subjects are located.

This predictive performance of the model at any given held out (out-of-sample) location is being compared to the predictive performance when one uses the central-site monitor as the value for that given location. The direct comparison of the correlations between the predictions from these two exposure measures and the actual monitored value at any location is directly comparable, since the central site reading is effectively an out-of-sample prediction because the data from that monitor is not being used when one uses the central site reading as a surrogate. We used the 24-hour average estimates of BC exposure at the geocoded residence of each participant as a surrogate for individual exposure to traffic-related air pollution, and average these predicted values to obtain 2, 3, and 4 day moving averages of exposure.

PM_{2.5} Exposure Prediction—We generated daily predictions of PM_{2.5} concentration levels across New England for 2000–2008 at a 10×10 km spatial resolution, using satellite derived AOD measurements. Full details of the modeling framework have been previously published [28,30]. In brief, we used day-specific calibrations of AOD data, using ground PM_{2.5} measurements from 78 monitoring sites in the EPA (Environmental Protection Agency) and IMPROVE (Interagency Monitoring of Protected Visual Environments) monitoring network. The model included also land use regression and meteorological variables (temperature, wind speed, visibility, elevation, distance to major roads, percent of open space, point emissions and area emissions). To estimate PM_{2.5} concentrations in each grid cell on each day, we started by calibrating the AOD-PM_{2.5} relationship for each day using grid cells with both monitors and AOD values using mixed models with random slopes for day and nested regions. The first stage calibrations resulted in high out-of-sample R^2 (mean out-of-sample $R^2 = 0.85$). We then used a second model to address days when AOD measures are not available (due to cloud coverage, snow etc...), fitting a model with a smooth function of latitude and longitude and a random intercept for each cell that takes advantage of the association of grid cells AOD values with PM_{2.5} monitoring located

elsewhere, and the association with available AOD values in neighboring grid cells, which provided a mean out-of-sample $R^2 = 0.81$. $PM_{2.5}$ exposure data were generated by our prediction models at a 10×10 km spatial resolution. This data was matched to the NAS subject's addresses using ArcGIS and SAS based on spatial location and date. For both BC and $PM_{2.5}$ we computed averages of 2, 3 and 4 previous days as our exposure metrics.

Genotyping

Participants' blood was collected at each visit—Multiplex PCR assays were designed using the Sequenom Spectro DESIGNER software. Assays were genotyped using the Sequenom MassArray MALDI-TOF mass spectrometer with semi-automated primer design and implementation of the very short extension method. Assays that failed to multiplex were genotyped using the TaqMan 5' exonuclease (ABI PRISM 7900 Sequence Detector).

To reduce multiple comparisons by investigations of multiple gene deletions and polymorphisms, and based on previous literature we selected only two gene deletions [glutathione S-transferase mu-1 (GSTM1) and glutathione S-transferase theta-1 (GSTT1)] that were related to the genetic susceptibility of a participant to oxidative stress. The gene deletions were categorized as 1=no deletion, and 0=deletion.

Statistical Analyses

We used mixed effects models to examine the associations between ambient pollution and ventricular ectopy (VE). The VE episodes were dichotomized as present or absent and we therefore applied mixed logistic regression models to account for correlation among measurements on the same subject across different medical visits. This is a standard approach for analyzing longitudinal data with repeated measures on the same subject [34]. We adjusted for a priori chosen known or plausible confounders including specific personal and temporal characteristics. We included in all models random subject-specific intercepts and fixed effects for body mass index (BMI, as a continuous variable), age, cumulative cigarette smoking in pack-years, use of medication such as ACE inhibitors, β -Blockers, Calcium Blockers, statins, and having diabetes (yes/no), and an indicator variable for alcohol consumption defined as 2 or more drink per day. We adjusted for socioeconomic status (SES) at the individual level with average income and years of education (defined as less than 12 years, 12–16 years, over 16 years), and at the neighborhood level with poverty level for each address as measured by percent below poverty level of each census block group in the 1999 census, and percent of population over 25 years of age without a high school diploma as measured by the 1999 census.

We also adjusted for the 24-hour means of temperature, for seasonality using sine and cosine terms, and a linear variable for year to capture long-term changes in both outcome and exposure.

Healthier men are more likely to come back to subsequent visits, therefore we used inverse probability weighting (IPW) to correct for a potential survival bias. [35] The probability at first visit was 1; we then calculated the probability of having a second, third of subsequent

visit using logistic regressions given all relevant factors at the previous visit: age, body mass index, smoking status and pack-years, hypertension, cholesterol, diabetes. We then used the inverse of the predicted probabilities as the weights in the models.

In the models used to examine effect modification we included an interaction term that allowed associations between the pollutants and the outcomes to vary among subgroups. Diabetes, obesity, and statin use, were treated as time-varying covariates, where the status was updated at each visit to reflect changes since the last visit. We also examined effect modification by gene variants GSTM1 and GSTT1. Interaction terms were added to the model one at a time.

Air pollution was examined for the previous 24 hours, and for the moving averages of 2, 3 and 4 previous days.

As sensitivity analysis we included in the model ozone which activates C-fibers and could thereby influence ventricular rhythm; we also examined whether the results changed without using the IPW.

The results are reported as odds ratios per an IQR increase in the pollutants. The analyses were performed with statistical software R 2.15.1.

RESULTS

In Table 1 we present characteristics of the patients, health and environmental variables among the NAS population during 2000–2010. The age range of the study subjects was 57–100 years, and 189 (26.9%) of them were obese, as defined by a body mass index ≥ 30 at the first visit. 701 subjects had one clinic visit, 451 had two visits, 217 had three visits, and 79 had four visits, with a total of 1448 observations.

Table 2 shows the results of the association between ventricular ectopy and air pollution. We found increases in the odds of having ventricular ectopic beats, with an OR of 1.32 (95% CI: 1.06–1.65) for an IQR ($0.39 \mu\text{g}/\text{m}^3$) increase in the same day of BC. The OR associated with an IQR ($0.30 \mu\text{g}/\text{m}^3$) increase in the 3 days average of BC was 1.52 (95% CI: 1.19–1.94).

The association between having ventricular ectopic beats and estimated $\text{PM}_{2.5}$ was positive and significant.

We found increases in the odds of having ventricular ectopic beats with an OR of 1.26 (95% CI: 1.05–1.52) for an IQR ($6.89 \mu\text{g}/\text{m}^3$) increase in the same day of $\text{PM}_{2.5}$, and an OR of 1.39 (95% CI: 1.12–1.71) for an IQR ($5.63 \mu\text{g}/\text{m}^3$) increase in the 3 days average of $\text{PM}_{2.5}$.

We then examined effect modification by obesity, statin use, having diabetes and gene variants (figure 1). We didn't find any evidence of modification by personal characteristics and BC, but we found significantly higher effects in obese in the association between estimated $\text{PM}_{2.5}$ and having ventricular ectopic beats with an OR of 1.17 (95% CI: 0.95–1.43) in non-obese and an OR of 1.80 (95% CI: 1.24–2.63) in obese for an IQR ($6.89 \mu\text{g}/\text{m}^3$) increase in the same day of $\text{PM}_{2.5}$. Subjects having the deletion of GSTM1 and for subjects without the deletion of GSTT1 had also significantly higher effects (figure 1).

When we included ozone in the model this was not significant; when included with each of the other pollutants, ozone was not significant and didn't change the effects of PM_{2.5} or BC. The results without adjusting for the IPW are consistent but less strong.

DISCUSSION

We found a significant association between having ventricular arrhythmias and both BC concentrations estimated at each participant's home, and temporally-and spatially-resolved PM_{2.5} concentrations, in a cohort of elderly men. Our interactions with obesity (only for BC), statin, and diabetes were not significant indicating no effect modification by this individual characteristics, while we found that GSTM1 and GSTT1 significantly modify the association.

This study therefore provides evidence that the traffic-related pollution markers are associated with ventricular arrhythmias.

Our results further suggest that individuals with gene variants related to oxidative stress may be at higher risk from air pollution.

Our findings are consistent with previous studies based on data from implantable cardioverter-defibrillator (ICDs), which have found the associations of air pollution with arrhythmias [13–17] in sensitive populations. In this study in which we examined a more general population, and we focused on a more accurate exposure defined by estimates of spatially resolved BC and PM_{2.5}, we found a stronger association with ventricular arrhythmias compared to the previously published studies.

Consistent with these findings, ambient traffic-related pollutants' concentrations have been associated in several Boston-area studies of intermediate cardiovascular indicators, including heart rate variability [5,7,8], ST-segment depression [20,36], QT interval (QTc), an electrocardiographic marker of ventricular repolarization [18], and T-wave alternans [19].

Black carbon (BC) is a traffic-related particle and a common surrogate for traffic particles in general, weighted towards diesel particles. We have developed a spatio-temporal land use regression model for traffic particles based on BC in the greater Boston metropolitan area. [24]. In the same NAS cohort of elderly men and using the same BC predictions at each home address, we have previously reported associations with several outcomes: markers of inflammatory and endothelial response [25], blood pressure [26].

Our observed associations can be explained by plausible pathophysiological mechanisms. Toxicity of traffic particles may have a direct effect on the blood, cardiovascular system, and lung receptors [37,38].

Deposition in the airways and lung alveoli may trigger proinflammatory signaling via a reactive oxygen species (ROS)-dependent mechanism [39,40]. For example, Ghelfi and coworkers have shown that blocking the TRPV1 receptor in the lung prevents particle induced disturbances in cardiac rhythm [41]. Diesel particles have also been shown to increase oxidative stress in endothelial tissue [42,43], inducing the production of heme

oxygenase-1, a rapid response part of the body's defense system against oxidative stress. The viability of cell cultures of microvascular endothelial cells was impaired by diesel particles with an accompanying large increase in induction of heme oxygenase-1[43].

Moreover, traffic particles may also cross the pulmonary epithelium and may be able to reach the heart via the vasculature [44,45], where they may induce oxidative stress and proinflammatory changes in the vasculature and myocardial substrate [38]. The generated proinflammatory cytokines and ROS may subsequently affect a variety of health measures, including autonomic cardiac control [38].

We didn't find effect modification by obesity, diabetes or statin use for BC and only by obesity for PM_{2.5}; this is contrary of what has been previously found for other endpoints [6,7].

Genetic polymorphisms of the GSTs are common, the GSTM1 gene is deleted in approximately half of the white population (the polymorphic "null" genotype), and lack of the GSTM1 protein have been shown to modify the response to air pollutants; for example GST deficiency was associated with significant HRV alterations in the general population [46].

In the NAS cohort GSTM1 deletion has been associated with the high-frequency (HF) component of heart rate variability[9], and larger effects of black carbon on sVCAM were seen in subjects who were GSTM1 null [10]. Baja and co-authors found a stronger association between QTc and BC among participants who had higher oxidative stress gene scores. Therefore this is agreement with our results of a higher risk of having ventricular episodes due to BC in subject GSTM1-null. Ren and co-authors [47] found that the GSTT1 modified effects of black carbon on total plasma homocysteine, with a higher effect in subjects with the deletion, and no effect modification by GSTM1. A case-control study looking at the relation between occupational exposure to vehicular exhaust and oxidative stress (OS) in traffic police, found a significant increase in urinary 8-hydroxydeoxyguanosine (8-OHdG) levels in null GSTM1 ($p < 0.01$) genotypes, but the genotype frequencies GSTT1 genes did not vary in both exposed and control groups.[48] Similar results were found by Ren and co-authors in the NAS population.[49] On the other hand, survival of patients with malignant glioma was reduced in subjects with the GSTM1 deletion, but longer in subjects without the GSTT1 deletion. [50] Glutathione S-Transferases (GSTs) are the most important family of phase II isoenzymes known to detoxify a variety of electrophilic compounds, including carcinogens, and environmental toxins. Individuals with the deletion of GSTM1 or GSTT1 have been shown to reduce GST activity and thus may be unable to eliminate toxins as efficiently when they expose to oxidative pollutants [50] A recent review and meta-analysis also found that null genotypes of GSTM1/GSTT1 were associated with increased risk of diabetes.[51] Differential findings among studies of effect modification by GSTM1 and GSTT1 variation might be attributable to several issues such as differences in exposure, outcome and population, measurement errors in exposure or phenotype, or chance. Further research is needed in order to understand the biological mechanisms.

One limitation of this study is that these results cannot be generalized to other populations without further research as our study population consisted entirely of elderly men, 97% of whom were Caucasian. Additionally, the study population is a self-selected group of people who continued to participate in an ongoing study for many years and may not be representative of all elderly men in the USA. In particular, there may be survivor bias if the subjects who continue to participate are healthier than other older people, which would bias effect estimates towards the null, so the true effect in the general population may be stronger.

Another limitation is that we do not have the exposure during travel as that would have required personal monitoring, which was not available for a large cohort with measurements over a decade.

In conclusion, these results add support for the hypothesis that traffic related pollution alters autonomic control in a manner conducive to increased arrhythmia, and that oxidative stress plays a role in this process.

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What this paper adds

- Defibrillator discharge studies have examined the association of air pollution with arrhythmias in sensitive populations.
- None of these existing studies used exposure estimates that are specific to the location of each study participant.
- This is the first study to examine the association between arrhythmias and residence-specific estimates of air pollution exposure.
- We found a clear association between arrhythmias and increased levels of traffic related pollutants and these associations are higher compared to previously published studies.
- Moreover individuals with gene variants related to oxidative stress may be at higher risk from air pollution.

Figure 1.

Odds Ratio (OR) and 95% Confidence Interval per an interquartile (IQR) increase in each pollutant. Effect modification by statin, diabetes, obesity and GSTM1 and GSTT1 genes. The symbol * indicates a significant interaction.

Table 1

Characteristics of the VA Normative Aging Study subjects at baseline and across all visits and distributions of the weather and outcome variables

Variable	Baseline				All visits			
	N	Mean	sd		N	Mean	sd	
Ventricular episodes (VE)	701	4.98	17.93		1448	6.77	22.19	
Age (years)	701	73.33	6.70		1448	75.31	6.77	
Body mass index (BMI, kg/m ²)	701	28.23	4.05		1448	28.14	4.24	
Pack-years of cigarettes smoked	701	21.76	25.91		1448	20.53	24.64	
Temperature (°F)	696	53.47	16.13		1443	53.32	16.29	
BC Same Day (µg/m ³)	596	0.62	0.36		1190	0.56	0.33	
BC 2 days average (µg/m ³)	593	0.59	0.33		1187	0.53	0.30	
BC 3 days average (µg/m ³)	592	0.54	0.29		1186	0.48	0.27	
PM2.5 Same Day (µg/m ³)	616	12.34	7.00		1247	11.18	6.51	
PM2.5 2 days average (µg/m ³)	618	12.20	6.22		1251	11.09	5.68	
PM2.5 3 days average (µg/m ³)	618	11.88	5.43		1252	10.83	4.99	

	N	(%)	N	(%)
VE 0/1	69	9.84	177	12.22
Statin user	289	41.23	737	50.9
Beta-blocker	259	36.95	583	40.26
ace	227	32.38	525	36.26
ca	122	17.4	312	21.55
Diabetes	135	19.3	305	21.3
Obese (BMI≥30)	189	26.96	390	26.93
Take two or more drinks a day	130	18.5	262	18.1
GSTM1 (no deletion)	303	46.76	649	47.58
GSTT1 (no deletion)	483	80.23	1027	79.8

Table 2

Odds ratios and 95% confidence intervals (CI) of the association between ventricular arrhythmia episodes and air pollution

VE	%	95%CI		IQR
BC				
Same Day	1.32	1.06	1.65	0.39
2 days average	1.47	1.16	1.87	0.35
3 days average	1.52	1.19	1.94	0.30
PM2.5				
Same Day	1.26	1.05	1.52	6.89
2 days average	1.26	1.02	1.54	6.21
4 days average	1.39	1.12	1.71	5.63