Association of ambient air pollution with risk of out of hospital cardiac arrest in the United States

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Abstract

Objective: We assessed the association of acute exposure to ambient air particulate matter < 2.5 μm ($PM_{2.5}$) and Ozone with risk of out of hospital cardiac arrest (OHCA).

Methods: We used data from the Cardiac Arrest Registry to Enhance Survival (CARES), a prospective multicenter registry of patients with OHCA in the U.S. Environmental data was obtained from publicly available data and linked with each patient. A case-crossover design was used to estimate association of acute exposure to ambient air $PM_{2.5}$ and Ozone with risk of OHCA. Case day was defined as the day of the OHCA, and control days were same days of the week from preceding two weeks.

Results: Of 187,047 patients with OHCA, mean age was 61.5 ± 19.9 years, 59.7 % were males and 47.1 % were of White race. Mean daily $PM_{2.5}$ concentration on case day was 9.2 ± 4.9 μg/m³ and mean averaged 8-hour Ozone concentration was 36.9 ± 12.1 ppb. Each 5 μg/m³ increase in $PM_{2.5}$ concentration (*case day vs. control day*) was not associated with risk of OHCA (OR 0.99 [95 % CI 0.998, 1.017] p = 0.72). In contrast, there was an association of exposure to Ozone with risk of OHCA with every 12 ppb increase in Ozone associated with a higher risk for OHCA on case day (OR 1.011 [95 % CI 1.003, 1.019] p = 0.01).

Conclusion: In the U.S., higher exposure to Ozone was associated with increased risk of OHCA.

1. Introduction

Out of hospital cardiac arrest (OHCA) is a growing public health issue with an annual incidence in the U.S. of about 89 per 100,000 people [1]. Although rates of survival have improved over the years, survival remains low with only ~15 % of the patients surviving to

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hospital discharge [2]. Several studies have shown an association between acute exposure to particulate matter < 2.5 μm ($PM_{2.5}$) and other air pollutants with OHCA risk [3,4]. However, these reports have been from smaller geographically homogenous cohorts. The geographical and environmental factors associated with OHCA risk in a more heterogenous population, such as the U.S., may be different. Moreover, air pollutant levels in the U.S. are much lower than other countries [5] and the relationship between acute exposure to air pollutants at these levels and OHCA risk is not completely understood. To examine the association between acute exposure to $PM_{2.5}$ and Ozone with the risk of OHCA in the U.S., we leveraged data from a national OHCA registry and linked it to publicly available data on air quality from the U.S. Environment Protection Agency (EPA).

2. Methods

The study was approved by Saint Luke's Mid America Heart Institute, which waived the requirement for informed consent because the analyses included only deidentified data.

2.1. Study population

Cardiac Arrest Registry to Enhance Survival (CARES) is a prospective multicenter registry of patients with OHCA in the U.S. [6]. It was established by the Centers of Disease Control and Emory University for public health surveillance and continuous quality improvement. It collects OHCA related data from three sources, 911 dispatch centers, Emergency Medical Services (EMS) providers, and receiving hospitals. CARES had a catchment area of over 150 million residents in the U.S. in 40 states. Patient-level data include demographics (age, sex, and race/ethnicity), location of cardiac arrest, initial cardiac arrest rhythm, and whether the arrest was witnessed. Additionally, information as to whether bystander cardiopulmonary resuscitation or defibrillation with an automated external defibrillator was administered prior to EMS arrival and cardiac arrest etiology (presumed cardiac, respiratory, drug overdose and other) is collected, as well as times to EMS arrival and duration of EMS treatment. For this study., we used OHCA data from CARES during 2013–2016.

2.2. Study design

The primary outcome was the occurrence of OHCA. We estimated the association between short term exposure to $PM_{2.5}$ and Ozone with risk of OHCA using a case-crossover design [7]. The day of the OHCA was defined as "case day". We compared air pollutant levels on the case day with control days, which were defined as the same day of the week from the preceding two weeks. To understand the effect of exposure to air pollutants on days leading up to the OHCA event, we also examined the association between air pollutant levels 1 day and 2 days before OHCA event with risk of OHCA.

2.3. Environmental data

Daily ambient air levels of $PM_{2.5}$ and Ozone were estimated from validated air pollution models that combine monitoring data from the EPA, satellite-based measurements and other data sets [8,9]. Daily 24-hour $PM_{2.5}$ (in micro gram/cubic meter [μg/m^3]) and 8-hour maximum Ozone (in parts per billion [ppb]) concentrations at each 1-km by 1-km grid in the U.S. were estimated. Ambient air temperatures were retrieved from the North American

Regional Reanalysis data, and estimated daily mean values were determined for each 32-km by 32-km grid in the U.S. For each OHCA event, 24-hour $PM_{2.5}$, 8-hour maximum Ozone, and daily temperature levels for case and control days were based on zip code of the OHCA.

2.4. Statistical analysis

A time stratified conditional case crossover design was used to estimate the association between exposure to $PM_{2.5}$ and Ozone on case day with risk of OHCA. The regression model included both air pollutants as covariates with additional adjustment for temperature. Hence, we adjusted for $PM_{2.5}$ levels when examining association with Ozone and *vice versa*. Patient-level factors (age, sex, and race/ethnicity) were not included in the model given the case-crossover design, as these factors do not change over the two-week period within each individual. Results are presented as odds ratios (OR) and 95 % confidence interval (CI) per +5 $\mu g/m^3$ for $PM_{2.5}$ and per +12 ppb for Ozone (approximately 1 standard deviation for each). Nonlinearity was evaluated using restricted cubic splines but was not significant in either instance ($p > 0.15$ for all), so results are presented as linear effects. Several sub-group analyses were defined *a priori* based on age (as a continuous variable), sex, race (White/African American/Hispanic) and first monitored rhythm (shockable/non-shockable). An interaction between these variables and association of exposure to air pollutants with risk of OHCA was assessed. All analyses were performed in R-software version 4.0 (R foundation).

3. Results

Between January 1, 2013 and December 31, 2016, there were 193,343 OHCAs in the CARES registry. Of these, environmental data were not available for 6296 events. The final study cohort comprised 187,047 OHCA events. Mean age was 61.5 ± 19.9 years, 59.7 % were males and 47.1 % were of White race (Table 1). Mean daily $PM_{2.5}$ concentration on case day was 9.2 ± 4.9 $\mu g/m^3$ and mean averaged 8-hour Ozone concentration was 36.9 ± 12.1 ppb.

Each 5 $\mu g/m^3$ increase in $PM_{2.5}$ concentration (*case day vs. control days*) was not associated with risk of OHCA (OR 0.99 [95 % CI 0.998, 1.017] $p = 0.72$). However, every 12 ppb increase in Ozone (*case day vs. control days*) was associated with a higher risk for OHCA (OR 1.011 [95 % CI 1.003, 1.019] $p = 0.01$). Fig. 1 illustrates the dose-response curve for change in $PM_{2.5}$ and Ozone exposure and risk of OHCA. Table 2 details the association of $PM_{2.5}$ and Ozone levels 1 and 2 days before case day with risk of OHCA. We found no association, between change in $PM_{2.5}$ and Ozone levels (compared to control days).

Additionally, there was no interaction between age, sex, race and initial rhythm with the association of exposure to $PM_{2.5}$ and Ozone with risk of OHCA (p-value >0.06 for all). Fig. 2 illustrates these pre-specified sub-group analyses.

4.   Discussion

In a large U.S. registry, we found that exposure to higher levels of ambient air Ozone on day of OHCA but not $PM_{2.5}$ was associated with a higher risk of OHCA. Importantly, this relationship was observed at levels within the EPA's accepted threshold.

There are several pathophysiological mechanisms that could explain the higher risk of OHCA with acute exposure to Ozone. These include oxidative stress, endothelial dysfunction, and activation of thrombotic pathways [10]. Our null results with $PM_{2.5}$, could be due low concentrations of $PM_{2.5}$ in the U.S., as compared to other countries, where acute exposure has been shown to be associated with increased cardiovascular mortality and morbidity [10]. For example, in an analysis from Japan, mean $PM_{2.5}$ concentration on the day of OHCA was 13.9 μg/m^3 *vs.* 9.2 ± 4.9 μg/m^3 in this study [3]. Moreover, the association between higher exposure to $PM_{2.5}$ and OHCA risk has not been consistent [11,12].

4.1.   Limitations

This study could have biases, that are inherent to a retrospective analysis. However, adherence to EPA methodology to estimate exposure and use of a large national OHCA registry are strengths. Moreover, our estimates of exposure were based of ambient air levels. There could have been heterogeneity in the amount of time patients in our study spent outdoors, and this could also have affected our results. In addition, it is known that in the U.S. racial/ethnic disparities exist for exposure to ambient air pollution exist [13]. While we did not explore these disparities in our analysis, understanding the racial/ethnic disparities in exposure to ambient air pollutants and risk of OHCA remains an important area for future work. Finally, we only examined associations of $PM_{2.5}$ and Ozone with OHCA risk. Assessing risk of OHCA with acute exposure to other ambient air pollutants in the U.S. is a potential area for further research.

5.   Conclusions

We found a significant relationship between higher exposure to Ozone and risk of OHCA in the U.S., at levels within the EPA's accepted threshold. As ambient air pollution is a modifiable risk factor, our results highlight the importance of understanding dose-response relationship of Ozone with risk of OHCA to inform policy on monitoring ambient air levels in the U.S.

Funding disclosure

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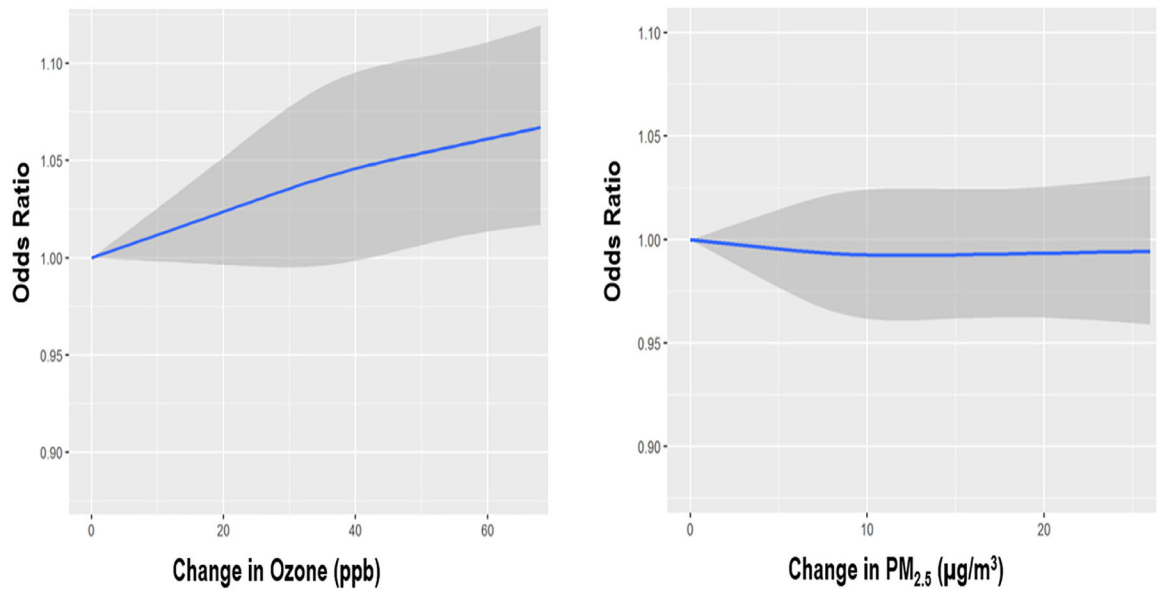
Fig. 1.
Dose-response relationship between PM$_{2.5}$ and Ozone levels from control day to case day and risk of OHCA on a continuous scale. (Results are adjusted for temperature.)
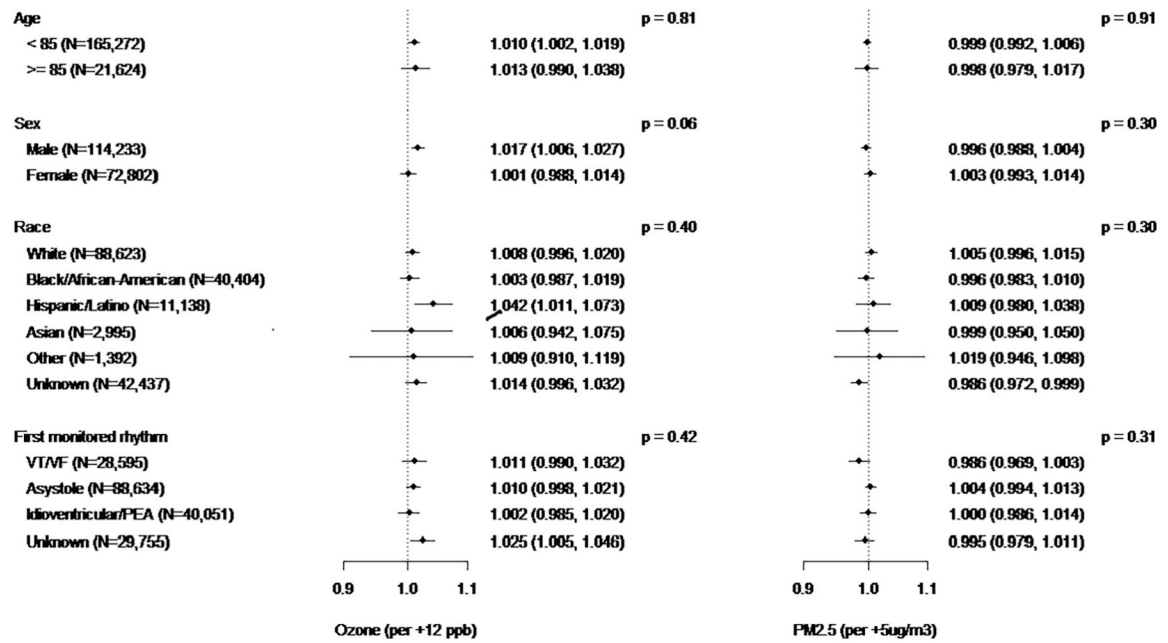
Fig. 2.
Subgroup analyses for association between $PM_{2.5}$ and Ozone levels and risk of OHCA
(Results are adjusted for temperature.)

Table 1

Baseline characteristics of the study population.

Air pollutant levels	
PM$_{2.5}$ level on case day (μg/m^3) (mean ± SD)	9.2 ± 4.9
Ozone level on case day (ppb) (mean ± SD)	36.9 ± 12.1
Patient factor	**Study cohort**
Age (yeas) [mean ± SD]	61.5 ± 19.9
Male sex n (%)	59.7 %
Race n (%)	
White	47.1 %
African American	21.8 %
Hispanic	6.1 %
Initial rhythm type n (%)	
Shockable	17.7 %
Non-shockable	82.3 %
Presumed cardiac arrest etiology n (%)	84.5 %
Outcomes (n, %)	
Alive to hospital admission	26.6 %
Alive at hospital discharge	11.2%
Neurologically intact survival to discharge	8.9 %

Table 2

Association between PM2.5 and Ozone levels at 1 and 2 days before OHCA and OHCA risk.

	PM$_{2.5}$ per 5 μg/m^3	Ozone per 12 ppb
1 day before OHCA	1.000 (0.991–1.009) p = 0.96	1.008 (0.997, 1.020) p = 0.15
2 days before OHCA	1.001 (0.991–1.011) p = 0.84	1.004 (0.992, 1.017) p = 0.50