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Ambient air pollution and emergency department visits and hospitalisation for cardiac arrest: a population-based case–crossover study in Reykjavik, Iceland

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ABSTRACT

Objectives To assess the association between traffic-related ambient air pollution and emergency hospital visits for cardiac arrest.

Design Case–crossover design was used with a lag time to 4 days.

Setting The Reykjavik capital area and the study population was the inhabitants 18 years and older identified by encrypted personal identification numbers and zip codes.

Participants and exposure Cases were those with emergency visits to Landspitali University Hospital during the period 2006–2017 and who were given the primary discharge diagnosis of cardiac arrest according to the International Classification of Diseases 10th edition (ICD-10) code I46. The pollutants were nitrogen dioxide (NO_2), particulate matter with aerodynamic diameter less than 10 µm (PM_{10}), particulate matter with aerodynamic diameter less than 2.5 µm ($PM_{2.5}$) and sulfur dioxide (SO_2) with adjustment for hydrogen sulfide (H_2S), temperature and relative humidity.

Main outcome measure OR and 95% CIs per 10 µg/m^3 increase in concentration of pollutants.

Results The 24-hour mean NO_2 was 20.7 µg/m^3, mean PM_{10} was 20.5 µg/m^3, mean $PM_{2.5}$ was 12.5 µg/m^3 and mean SO_2 was 2.5 µg/m^3. PM_{10} level was positively associated with the number of emergency hospital visits (n=453) for cardiac arrest. Each 10 µg/m^3 increase in PM_{10} was associated with increased risk of cardiac arrest (ICD-10: I46), OR 1.096 (95% CI 1.033 to 1.162) on lag 2, OR 1.118 (95% CI 1.031 to 1.212) on lag 0–2, OR 1.150 (95% CI 1.050 to 1.261) on lag 0–3 and OR 1.168 (95% CI 1.054 to 1.295) on lag 0–4. Significant associations were shown between exposure to PM_{10} on lag 2 and lag 0–2 and increased risk of cardiac arrest in the age, gender and season strata.

Conclusions A new endpoint was used for the first time in this study: cardiac arrest (ICD-10 code: I46) according to hospital discharge registry. Short-term increase in PM_{10} concentrations was associated with cardiac arrest. Future ecological studies of this type and their related discussions should perhaps concentrate more on precisely defined endpoints.

STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ The study is population based, relies on comprehensive population registries and includes information on daily concentrations of the pollutants, which cover more than 75% of the days in the study period.
⇒ The methodology allows within-subject comparison while adjusting for various time trends such as seasonality and day of week.
⇒ The concentration of the pollutants was derived from one monitoring station and not from individual exposure measurements.
⇒ The population is small; therefore, the total number of cases was low, resulting in low statistical power.

INTRODUCTION

Epidemiological studies have found increased risk of cardiovascular morbidity and mortality in association with particulate matter (PM) in air pollution,[1 2] and the overall evidence is considered to support the existence of a causal relationship between PM exposure and cardiovascular morbidity, primarily due to fine particles.[2] Both short-term and long-term PM air pollution contributes to cardiovascular morbidity and mortality.[1 2] Urban ambient air pollution is a complex mixture of gases, particles and liquid, and in an attempt to monitor air quality, certain pollutants are traditionally measured. However, adverse cardiovascular health impacts of exposure to a combination of air pollutants are not completely understood at present. A recent multilocation analysis found that a short-term increase in nitrogen dioxide (NO_2) on the previous day was associated with an increased risk of daily total, cardiovascular and respiratory mortality.[3] In a systemic review and meta-analysis of short-term exposure to NO_2 and ischaemic heart diseases, the authors

concluded that the relationship was likely causal,[4] but uncertainties remained due to possible confounding in the epidemiological studies and lack of evidence from mechanistic studies. Several epidemiological studies have found that NO_2 and PM are associated with cardiovascular diseases (CVDs), and the endpoints studied have included not only mortality from CVD,[3] but also discharge diagnosis at hospitals and emergency departments for a wide range of CVDs: ischaemic heart disease, myocardial infarction and different cardiac dysrhythmias.[5–10] In a large US study,[9] acute myocardial infarction and multiple other cardiovascular outcomes, like cardiac dysrhythmia and heart failure, were found to be associated with particulate air pollution; however, in that analysis, it was only possible to consider potential confounding by ozone (O_3), not by other pollutants. In a case–crossover study in China, an association was found between PM, NO_2 and carbon monoxide, and the number of hospital admissions for cardiac arrhythmia.[10] In another case–crossover study in the UK,[8] the risk of emergency hospital admissions for CVD, arrhythmias, atrial fibrillation and heart failure was associated with an increased concentration of NO_2; however, cardiac arrest was not included as an outcome in the study. Cardiac arrest was mentioned in the aforementioned Chinese study[10] but was not analysed separately.

There are several studies on the association between air pollution and out-of-hospital cardiac arrest (OHCA).[11–15] The risk of OHCA was associated with a short-term increase in exposure to PM, sometimes PM with aerodynamic diameter less than 2.5 µm ($PM_{2.5}$), or ultrafine PM,[11–14] and sometimes PM with aerodynamic diameter less than 10 µm (PM_{10}),[15] with various associations with O_3, other gaseous pollutants and high temperature. The collection of cases in the OHCA studies uses special registers as a source, regarding Utstein definition[16 17] with the original purpose to provide a structured framework to evaluate emergency medical service. The main criteria in the definition of the cases in the OHCA studies are: (1) the cardiovascular collapse has occurred outside a hospital and (2) the event has elicited a resuscitation attempt. Neither of these conditions is required for the physician given diagnosis of cardiac arrest according to the International Classification of Diseases 10th edition (ICD-10) code I46 registered as discharge diagnosis at hospitals or emergency departments.

The comprehensive population and health registries in Iceland make this an optimal setting to study the association between relatively low daily exposure to air pollution and different heart-related conditions.[7 18 19] The aims of the present study were to explore the association between traffic-related pollutants, NO_2, PM_{10}, $PM_{2.5}$ and sulfur dioxide (SO_2), in the Reykjavik capital area and urgent hospital and emergency department visits for cardiac arrest, ICD-10 code I46, as the primary discharge diagnosis; and to simultaneously adjust for meteorological variables and geothermal-originated pollutants.

METHODS

Study base

The Reykjavik capital area is in the southwestern part of Iceland. Traffic emission is the main source of air pollution in the city. Other sources of air pollution include two geothermal power plants: Hellisheidi, located 26 km east-southeast of the city, and Nesjavellir, located 33 km east of the city. Ambient hydrogen sulfide (H_2S) emissions originate from the plants. Reykjavik's capital area spreads over 247.5 km^2 and in 2017, the inhabitants numbered 217 000, equivalent to approximately two-thirds of the total Icelandic population.[20] The study base included the residents of the Reykjavik capital area, which consists of seven municipalities (Gardabaer, Hafnarfjordur, Kjosarhreppur, Kopavogur, Mosfellsbaer, Reykjavik and Seltjarnarnes) identified by 24 zip codes.

Health data

Hospital discharge data were obtained from 1 January 2006 to 31 December 2017 from computerised records in SAGA (register of hospital-treated patients in Iceland) for certain heart diseases; the procedures have been described in a previous publication.[7] The study included adult inhabitants (≥18 years) of the Reykjavik capital area, identified by zip code. We analysed data on urgent visits to the emergency department and urgent admissions to inpatient wards of Landspitali University Hospital (LUH). The study was confined to new admissions, meaning that no visits by appointment were included. LUH is operated by the Icelandic government and is the only acute care hospital serving the population of the Reykjavik capital area, making this study population based. In Iceland, the national health insurance scheme is covered by taxes and is available to all residents. For ambulatory visits, patients pay a small fee that amounts to approximately US$10–US$15, but seniors are exempt from payment. Admission to the hospital ward is free of charge. Every inhabitant of Iceland receives a personal identification number at birth (or at immigration), and the identification numbers are widely used in Icelandic society and population registries, including the SAGA register. We received the identification numbers in encrypted form, which enabled us to identify repeated visits to LUH. Readmissions to LUH within 10 days with the same ICD-10 primary discharge diagnosis were excluded. From the SAGA register, we received the following details: admission date, encrypted identification number, unique number of the admission, age, gender and primary discharge diagnosis for certain codes according to the ICD-10. In this study, both admission to the emergency department and formal admission to the hospital are included, so there is no requirement that a patient stayed overnight. The diagnoses are registered at discharge from the hospital, transfer to another hospital and death in the hospital. In a previous study,[7] the outcomes were heart diseases ICD-10 codes: I20–I25, I44–I50, ischaemic heart diseases ICD-10 codes: I20–I25, cardiac arrhythmias and heart failure ICD-10 codes: I44–I50 and atrial fibrillation ICD-10 I48.[7] In the present study, the outcome analysed was cardiac arrest ICD-10 code I46. Emergency department

visits and urgent hospital admissions were combined and are called emergency hospital visits.

Air pollutants and meteorological data

Information on pollution was obtained from Grensas monitor station (GRE), operated by the governmental institution Environment Agency of Iceland. GRE is in the centre of the Reykjavik capital area near one of the busiest road intersections in the city. Other stations in the city were not permanently located or were not continuously monitoring throughout the study period and were therefore not used in the study. However, to test whether GRE was reflective of the total capital area, Pearson's correlation was calculated for GRE measurements and measurements from another station located in Dalsmari, Kopavogur municipality, for the period 2014–2017. Results of Pearson's correlation coefficients between these two measurement stations were for PM_{10} 0.44, for NO_2 0.78, for SO_2 0.98 and for H_2S 0.84. $PM_{2.5}$ was not measured in Dalsmari.

Pollutants measured at GRE were NO_2, PM_{10}, $PM_{2.5}$, SO_2 and H_2S, all measured in µg/m^3. The meteorological data were obtained from the governmental institution Icelandic Meteorological Office and included temperature (°C) and relative humidity (RH). PM_{10} and $PM_{2.5}$ were measured with an Andersen EMS IR Thermo (model FH62 I-R), NO_2 with Horiba device (model APNA 360E), and SO_2 and H_2S with the Horiba model APOA 360E. Every 6–12 months, the devices are calibrated. Exposure data included 12 years or 4383 days. Daily averages (midnight to midnight the following day) were calculated from hourly concentrations if at least 75% of 1-hour data existed. Missing daily averages for NO_2, PM_{10}, $PM_{2.5}$, SO_2 and H_2S were 383 days (8.7%), 165 days (3.8%), 923 days (21.1%), 200 days (4.6%) and 284 days (6.5%), respectively. Data gaps were seen and can be attributed to inactive measurement devices due to unknown causes, with the exception of 52 days of missing H_2S measurements at the beginning of the study period, as H_2S measurements at GRE started at the end of February 2006. For temperature and RH, 6 days (0.1%) and 6 days (0.1%) were missing, respectively. Minor gaps in the curves were fitted by linear interpolation.

Descriptive statistics were calculated and shown as daily concentration levels in µg/m^3 of the pollutants, as well as Spearman's correlation coefficient between pollutants and meteorological factors.

Table 1 Descriptive statistics of emergency hospital visits for cardiac arrest (ICD-10: I46) to Landspitali University Hospital, according to subgroups, 1 January 2006–31 December 2017

Discharge diagnosis (ICD-10)	No of visits (%)	No of patients
Cardiac arrest (I46)	453 (100)	447
Females	125 (28)	123
Males	328 (72)	324
Older (≥71 years)	192 (42)	190
Younger (<71 years)	261 (58)	257
Older females	57	56
Younger females	68	67
Older males	135	134
Younger males	193	190
Winter	236 (52)	236
Summer	217 (48)	214
Cardiac arrest (I46)	5	5
Cardiac arrest with successful resuscitation (I46.0)	194	192
Sudden cardiac death, so described (I46.1)	23	23
Cardiac arrest, unspecified (I46.9)	231	229
Emergency department visits, only	313	312

Winter: 1 November–30 April.
Summer: 1 May–31 October.
ICD-10, International Classification of Diseases 10th edition.

Patient and public involvement

No patient was involved.

Analysis

Short-term associations between daily exposure to air pollutants and emergent hospital visits for cardiac arrest (ICD-10 code: I46) were assessed using bidirectional time-stratified case–crossover design. The study period was divided into monthly strata, and exposure during case periods (24 hours) was compared with exposure during control periods, which were matched as the same weekdays within the same month (three to four control periods per case period).[21 22] The matches control for measured or unmeasured personal confounding characteristics that do not vary over the relatively short time, such as gender, age and genetic factors. We did several calculations: single-pollutant models were calculated in conditional logistic regression, multivariate models containing all traffic-related pollutants, H_2S and the meteorological variables. Separate analyses were done for subgroups according to gender, age (≥71 and <71 years), gender and age combined, winter (1 November–30 April) and summer (1 May–31 October). It was possible to divide the diagnostic category I46 according to decimals into cardiac arrest with successful resuscitation (I46.0) and other categories without indication of successful resuscitation (I46, I46.1 and I46.9). These two subcategories were also analysed separately as there are indications that the latter category concerns mortality. The risk estimates were expressed as OR, and 95% CIs were calculated for every 10 µg/m^3 increase of pollutants (24-hour concentrations).

As the possible response period of discharge diagnosis of cardiac arrest after exposure to air pollutants is not known, we conducted the analyses with lag exposures for 0–4 days. Lag 0 was the average concentration on the day of the admission, lag 1 was the average concentration on the

day before admission and so on for the higher numbers of lags. Different lag structures were applied. Single-day lag structure (lag 0 to lag 4) and multiple-day lag structure (lag 0–1, lag 0–2, lag 0–3 and lag 0–4, moving average of pollutant concentration) were employed in the analyses to explore the temporal association between pollutants and cardiac arrest. The results of the multivariate models with all lag structures are presented in the article, and other results are shown as online supplemental data.

Although readmissions within 10 days with the same primary discharge diagnosis were excluded, it is still possible that some patients first went to the emergency department and were subsequently admitted that same day to in-hospital wards where they might have received a different diagnosis than they were given at the emergency department. To test whether this could distort the main result of the association between increased pollutant concentration and emergency hospital visits, a sensitivity analysis was done, in which data were restricted to emergency department visits only.

Statistical analysis was done with R V.4.0.3 (https://www.r-project.org/). Statistical tests used in this study were all two tailed and we considered results statistically significant for p<0.05.

RESULTS

The basic characteristics of cardiac arrest according to subcategories are shown in table 1. The total number of visits with primary discharge diagnosis cardiac arrest (ICD-10 code: I46) was 453, and repeated visits were extremely rare. The distribution of the 453 visits was even over the 4383-day study period. One visit per day was most common, but there were several days with up to two visits, which was the highest number of visits per day; thus, most days were without visits with cardiac arrest. The median age at the time of visits was 71 years. Descriptive statistics and Spearman's correlation coefficients of traffic-related pollutants, H_2S and meteorological variables are presented in table 2. Missing daily average was highest for $PM_{2.5}$ but did not exceed 25% of the days of the study period. The concentrations of PM_{10} and $PM_{2.5}$ were correlated, PM did not correlate with the gaseous pollutants and correlations among gaseous pollutants were moderate.

In the single-pollutant analyses, positive associations were observed for exposure to PM_{10} at lag 2 and lag 0–2, and unstratified emergency hospital visits for cardiac arrest (ICD-10 codes: I46); the increased risks of cardiac arrest were OR 1.077 (95% CI 1.020 to 1.137) and OR 1.097 (95% CI 1.016 to 1.184), respectively, per 10 µg/m^3 increase of PM_{10}, as shown in online supplemental table A. A positive association was observed between exposure to NO_2 at lag 4 and the increased risk of cardiac arrest; the increased risk was OR 1.081 (95% CI 1.002 to 1.166) per 10 µg/m^3 increase of NO_2, as shown in online supplemental table A.

In examining the daily lag exposure to PM_{10} and unstratified emergency hospital visits for cardiac arrest, positive

Table 2 Descriptive statistics of 24-hour concentration levels (µg/m^3) of pollutants and meteorological data in the Reykjavík capital area during the study period, 2006–2017, and Spearman's correlation between daily concentrations of pollutants

	PM_{10}	$PM_{2.5}$	NO_2	SO_2	H_2S	Temperature (°C)	RH (%)
24-hour availability n (%)	4218 (96.2)	3460 (78.9)	4000 (91.3)	4183 (95.4)	4099 (93.5)	4377 (99.9)	4377 (99.9)
Mean (SD)	20.5 (19.7)	12.5 (21.8)	20.7 (15.0)	2.51 (13.8)	2.98 (5.2)	5.5 (4.9)	74.9 (10.6)
Summer* mean (SD)	17.4 (14.9)	10.8 (16.2)	16.2 (9.9)	2.48 (14.1)	2.08 (3.1)	9.1 (3.2)	74.6 (9.8)
Winter† mean (SD)	23.6 (23.2)	14.2 (26.1)	25.3 (17.6)	2.54 (13.5)	3.90 (6.6)	1.9 (3.4)	75.1 (11.3)
Range	2.4–381	0–423	0–119	0–409	0–96	−10.5 to 17.7	37–97
Median	15.1	7.0	16.6	1.1	1.2	5.6	77.0
IQR	11.6	8.2	15.8	1.2	2.7	7.9	15.0
Spearman's correlation							
PM_{10}	1.00						
$PM_{2.5}$	0.76	1.00					
NO_2	0.09	0.00	1.00				
SO_2	0.08	0.08	0.50	1.00			
H_2S	−0.08	−0.11	0.31	0.39	1.00		
Temperature (°C)	−0.16	−0.08	−0.44	−0.17	−0.23	1.00	
RH (%)	−0.30	−0.56	0.09	−0.03	0.04	0.12	1.00

*1 May–31 October.
†1 November–30 April.
H_2S, hydrogen sulfide; NO_2, nitrogen dioxide; PM_{10}, particulate matter with aerodynamic diameter less than 10 µm; $PM_{2.5}$, particulate matter with aerodynamic diameter less than 2.5 µm; RH, relative humidity; SO_2, sulfur dioxide.

Table 3 Number of visits (n), ORs and 95% CIs for the daily emergency hospital visits for cardiac arrest (ICD-10 code: I46) in Reykjavik capital area associated with 10 µg/m^3 increase in NO_2, PM_{10}, $PM_{2.5}$, SO_2 and H_2S, adjusted for each pollutant, temperature and relative humidity, unstratified at lag 0 to lag 4, lag 0–1, lag 0–2, lag 0–3 and lag 0–4

Categories/ visits (n)	Lag	NO_2 OR (95% CI)	PM_{10} OR (95% CI)	$PM_{2.5}$ OR (95% CI)	SO_2 OR (95% CI)	H_2S OR (95% CI)
All (453)	0	0.989 (0.904 to 1.083)	1.017 (0.957 to 1.082)	0.990 (0.930 to 1.053)	1.084 (1.002 to 1.173)	1.187 (0.972 to 1.449)
	1	1.003 (0.916 to 1.099)	1.041 (0.987 to 1.097)	0.994 (0.936 to 1.055)	0.983 (0.873 to 1.107)	1.056 (0.829 to 1.344)
	2	0.972 (0.885 to 1.068)	1.096 (1.033 to 1.162)	0.993 (0.935 to 1.054)	0.999 (0.935 to 1.067)	1.118 (0.892 to 1.402)
	3	1.052 (0.963 to 1.150)	1.038 (0.988 to 1.090)	1.022 (0.968 to 1.079)	0.991 (0.916 to 1.074)	1.191 (0.980 to 1.449)
	4	1.096 (1.008 to 1.192)	1.029 (0.963 to 1.099)	1.054 (0.992 to 1.020)	1.003 (0.940 to 1.070)	0.915 (0.714 to 1.171)
	0–1	0.982 (0.876 to 1.101)	1.049 (0.978 to 1.124)	0.988 (0.922 to 1.059)	1.084 (0.971 to 1.211)	1.214 (0.923 to 1.597)
	0–2	0.957 (0.838 to 1.093)	1.118 (1.031 to 1.212)	0.989 (0.918 to 1.066)	1.070 (0.945 to 1.212)	1.301 (0.936 to 1.810)
	0–3	0.981 (0.846 to 1.137)	1.150 (1.050 to 1.261)	0.998 (0.921 to 1.081)	1.061 (0.922 to 1.221)	1.423 (1.007 to 2.011)
	0–4	1.039 (0.889 to 1.215)	1.168 (1.054 to 1.295)	1.019 (0.934 to 1.112)	1.057 (0.588 to 1.928)	1.313 (0.897 to 1.921)

H_2S, hydrogen sulfide; ICD-10, International Classification of Diseases 10th edition; NO_2, nitrogen dioxide; PM_{10}, particulate matter with aerodynamic diameter less than 10 µm; $PM_{2.5}$, particulate matter with aerodynamic diameter less than 2.5 µm; SO_2, sulfur dioxide.

associations were observed in the multivariate model; the increased risks of cardiac arrest were OR 1.096 (95% CI 1.033 to 1.162) for lag 2, OR 1.118 (95% CI 1.031 to 1.212) for lag 0–2, OR 1.150 (95% CI 1.050 to 1.261) for lag 0–3 and OR 1.168 (95% CI 1.054 to 1.295) for lag 0–4 per 10 µg/m^3 increase of PM_{10} (table 3). Significant associations were shown for exposure to NO_2 at lag 4 and for SO_2 at lag 0, and unstratified emergency hospital visits for cardiac arrest; the increased risks were OR 1.096 (95% CI 1.008 to 1.192) and OR 1.084 (95% CI 1.002 to 1.173) per 10 µg/m^3 increase of NO_2 and SO_2, respectively (table 3).

In the multivariate model, significant associations were shown between exposure to PM_{10} at lag 2 and at lag 0–2, lag 0–3 and lag 0–4, and increased risks of cardiac arrest (ICD-10 code I46), in the age, gender, age and gender combined, and season strata, that is, in all the strata except in the stratum of young females as shown in online supplemental tables B and C. In figure 1, OR and 95% CI of cardiac arrest per 10 µg/m^3 increase of PM_{10} concentrations in multipollutant models are shown at lag 0 to lag 4 for different strata and unstratified.

In the single-pollutant analyses, positive associations were observed for exposure to PM_{10} at lag 0–3 and lag 0–4, and emergency hospital visits for cardiac arrest with successful resuscitation (ICD-10 codes: I46.0); the increased risks of cardiac arrest were OR 1.161 (95% CI 1.014 to 1.329) and OR 1.177 (95% CI 1.013 to 1.368), respectively, per 10 µg/m^3 increase of PM_{10}, as shown in online supplemental table D. A positive association was observed for exposure to $PM_{2.5}$ at lag 3 and lag 4, and the increased risk of cardiac arrest with successful resuscitation; the increased risk was OR 1.090 (95% CI 1.008 to 1.178) and OR 1.101 (95% CI 1.006 to 1.204), per 10 µg/m^3 increase of $PM_{2.5}$, respectively, as shown in online supplemental table D. A positive association was observed for exposure to PM_{10} at lag 2, and the increased risk of cardiac arrest without indication of successful resuscitation (ICD-10 codes: I46, I46.1 and I46.9); the increased risk was OR 1.079 (95% CI 1.008 to 1.155), as shown in online supplemental table D.

In the multivariate model, a positive association was observed between exposure to PM_{10} and emergency hospital visits for cardiac arrest with successful resuscitation (ICD-10 code: I46.0); the increased risks of cardiac arrest were OR 1.104 (95% CI 1.002 to 1.216) at lag 2, OR 1.153 (95% CI 1.021 to 1.301) at lag 0–2, OR 1.202 (95% CI 1.039 to 1.392) at lag 0–3 and OR 1.209 (95% CI 1.027 to 1.422) at lag 0–4, per 10 µg/m^3 increase of PM_{10}, as shown in table 4. A positive association was observed between exposure to $PM_{2.5}$ and the increased risk of cardiac arrest with successful resuscitation; the increased risk was OR 1.088 (95% CI 1.001 to 1.182) at lag 3 and OR 1.104 (95% CI 1.006 to 1.21) at lag 4, per 10 µg/m^3 increase of $PM_{2.5}$, as shown in table 4. A positive association was observed between exposure to PM_{10} and the increased risk of cardiac arrest without indication of successful resuscitation (ICD-10 codes: I46, I46.1 and I46.9); the increased risk was OR 1.090 (95% CI 1.013 to 1.173) at lag 2, as shown in table 4. In figure 2, OR and 95% CI of cardiac arrest per 10 µg/m^3 increase of PM_{10} concentrations in multipollutant models are shown at lag 0 to lag 4 when stratified on season and whether there is an indication of successful resuscitation or not.

In the sensitivity analysis of the association between daily exposure to PM_{10} and emergency hospital visits for cardiac arrest (ICD-10 code: I46), when restricting the calculation to emergency department visits only (353 visits), the results did not change substantially: in the unstratified analysis, the increased risk of cardiac arrest was OR 1.099 (95% CI 1.028 to 1.175) at lag 2 per 10 µg/m^3 increase of PM_{10}.

DISCUSSION

Our study examined the association between ambient air pollution and emergency hospitalisation and emergency

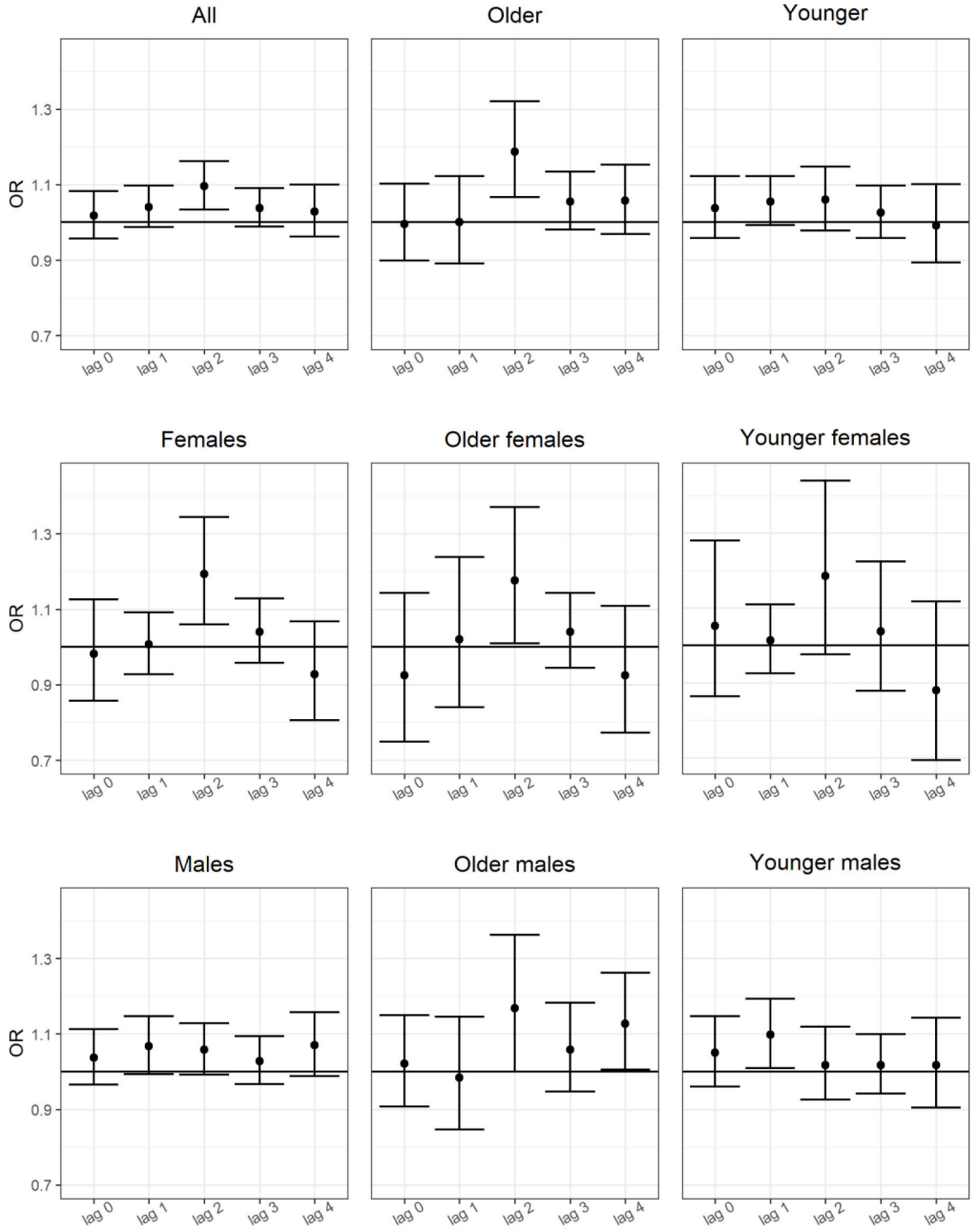

Figure 1 The OR and bars showing 95% CIs of cardiac arrest (ICD-10 code: I46) per 10 µg/m^3 increase in PM_{10} concentrations in multiple pollutant models at lag 0 to lag 4 for unstratified material and different strata. ICD-10, International Classification of Diseases 10th edition; PM_{10}, particulate matter with aerodynamic diameter less than 10 µm.

department visits where the primary discharge diagnosis was cardiac arrest (ICD-10 code: I46). To our knowledge, that single outcome has not been used in previous studies of a similar type. The main results of this study were the association between increased PM_{10} and cardiac arrest at lag 2, lag 0–2, lag 0–3 and lag 0–4, so the 24-hour concentrations of PM_{10} seem to be clearly separated from the event registered at the hospital and happened before the admittance. The effects seemed high in most subcategories, in both seasons and among those who were successfully resuscitated.

Cardiac arrest is a life-threatening event and may be the most serious outcome of CVD. The decimal following the code I46 indicates whether the patients were successfully

Table 4 Number of visits (n), OR and 95% CIs for the daily emergency hospital visits for cardiac arrest with successful resuscitation (ICD-10 code: I46.0) and other cardiac arrest categories grouped together (ICD-10 codes: I46, I46.1 and I46.9) in Reykjavik capital area associated with 10 μg/m^3 increase in NO_2, PM_{10}, $PM_{2.5}$, SO_2 and H_2S, adjusted for each pollutant, temperature and relative humidity, at lag 0 to lag 4, lag 0–1, lag 0–2, lag 0–3 and lag 0–4

Categories/ visits (n)	Lag	NO_2 OR (95% CI)	PM_{10} OR (95% CI)	$PM_{2.5}$ OR (95% CI)	SO_2 OR (95% CI)	H_2S OR (95% CI)
I46.0 (194)	0	0.988 (0.856 to 1.139)	1.057 (0.967 to 1.156)	0.983 (0.875 to 1.105)	1.386 (0.758 to 2.534)	1.008 (0.735 to 1.383)
	1	1.012 (0.881 to 1.163)	1.053 (0.982 to 1.129)	0.999 (0.894 to 1.115)	0.845 (0.471 to 1.515)	1.055 (0.707 to 1.577)
	2	0.953 (0.826 to 1.100)	1.104 (1.002 to 1.216)	1.037 (0.957 to 1.125)	1.078 (0.893 to 1.301)	1.177 (0.797 to 1.737)
	3	1.072 (0.937 to 1.227)	1.035 (0.941 to 1.138)	1.088 (1.001 to 1.182)	0.995 (0.910 to 1.089)	1.141 (0.794 to 1.642)
	4	1.194 (1.023 to 1.393)	1.040 (0.936 to 1.157)	1.104 (1.006 to 1.211)	0.292 (0.084 to 1.010)	1.313 (0.847 to 2.036)
	0–1	0.992 (0.832 to 1.183)	1.083 (0.985 to 1.190)	0.987 (0.870 to 1.121)	1.167 (0.932 to 1.462)	1.050 (0.663 to 1.664)
	0–2	0.952 (0.774 to 1.171)	1.153 (1.021 to 1.301)	1.017 (0.899 to 1.150)	1.196 (0.941 to 1.520)	1.203 (0.680 to 2.129)
	0–3	0.986 (0.781 to 1.246)	1.202 (1.039 to 1.392)	1.058 (0.936 to 1.197)	1.120 (0.879 to 1.426)	1.323 (0.693 to 2.527)
	0–4	1.047 (0.818 to 1.340)	1.209 (1.027 to 1.422)	1.093 (0.957 to 1.248)	1.015 (0.785 to 1.314)	1.421 (0.702 to 2.877)
I46, I46.1, I46.9 (259)	0	0.983 (0.875 to 1.105)	0.991 (0.909 to 1.081)	0.992 (0.921 to 1.068)	1.055 (0.964 to 1.155)	1.327 (1.012 to 1.739)
	1	0.998 (0.882 to 1.130)	1.024 (0.940 to 1.116)	0.991 (0.923 to 1.065)	0.996 (0.876 to 1.132)	1.055 (0.778 to 1.430)
	2	0.985 (0.869 to 1.116)	1.090 (1.013 to 1.173)	0.945 (0.861 to 1.036)	0.987 (0.914 to 1.067)	1.123 (0.843 to 1.497)
	3	1.041 (0.923 to 1.176)	1.027 (0.968 to 1.089)	0.960 (0.876 to 1.052)	0.993 (0.829 to 1.190)	1.191 (0.943 to 1.505)
	4	1.082 (0.975 to 1.201)	1.030 (0.945 to 1.121)	1.012 (0.929 to 1.102)	1.056 (0.968 to 1.152)	0.781 (0.564 to 1.082)
	0–1	0.972 (0.835 to 1.130)	1.011 (0.908 to 1.126)	0.987 (0.908 to 1.072)	1.051 (0.927 to 1.190)	1.312 (0.928 to 1.856)
	0–2	0.958 (0.803 to 1.142)	1.093 (0.976 to 1.223)	0.968 (0.879 to 1.066)	1.030 (0.895 to 1.185)	1.386 (0.922 to 2.084)
	0–3	0.968 (0.796 to 1.177)	1.108 (0.982 to 1.250)	0.951 (0.852 to 1.062)	1.033 (0.869 to 1.227)	1.485 (0.984 to 2.240)
	0–4	1.019 (0.830 to 1.252)	1.126 (0.983 to 1.290)	0.963 (0.852 to 1.087)	1.079 (0.905 to 1.286)	1.283 (0.813 to 2.027)

H_2S, hydrogen sulfide; ICD-10, International Classification of Diseases 10th edition; NO_2, nitrogen dioxide; PM_{10}, particulate matter with aerodynamic diameter less than 10 μm; $PM_{2.5}$, particulate matter with aerodynamic diameter less than 2.5 μm; SO_2, sulfur dioxide.

resuscitated or not. Patients categorised as I46 comprise those who have survived and those who have died, and in the present study, these are in nearly equal proportion. The associations between pollutants and mortality and hospital admission are commonly analysed separately.[8] The primary discharge diagnosis cardiac arrest (ICD-10 code: I46) has in previous studies been included within all CVDs, or large subgroups such as cardiac dysrhythmias, and the endpoint closest to this entity may be OHCA. However, there is a difference between patients with the diagnosis of cardiac arrest (ICD-10 code: I46) at hospitals and persons included in studies on OHCA. OHCA has often been the subject of air pollution studies. In a review of 67 studies on OHCA,[23] OHCA was associated with high mortality, with a global average survival rate of 7%, but in the present study, 42.8% of the registered cases with the ICD-10 code I46, cardiac arrest, were successfully resuscitated, a considerable difference in survival rates. The definition of OHCA is: (1) the cardiovascular collapse has occurred outside a hospital and (2) the event has elicited a resuscitation attempt, and these conditions are not required for cardiac arrest according to ICD-10 code I46, when this diagnosis is used at hospitals or emergency departments. In addition, the Utstein definition recommends registration of several time points and intervals important for the research and quality assurance related to the resuscitation, but such time elements are not required in the hospital discharge registries based on the ICD-10. Some studies have shown that the risks of OHCA were associated with a short-term increase in exposure to PM, sometimes $PM_{2.5}$, or ultrafine PM,[11–14] and sometimes PM_{10},[15] with various associations with O_3, other gaseous pollutants and high temperature. An OHCA study conducted in Stockholm, Sweden demonstrated a significant exposure–response association between OHCA risk and O_3, but no association for $PM_{2.5}$ or NO_2,[24] while another OHCA study in Lombardy, Italy showed, with a different methodology, that the concentrations of all the pollutants in the study were significantly higher in days with high incidence of OHCA except for O_3.[25] In these OHCA studies,[11–15 24 25] no difference is made between those who survive the event and those who do not survive. In the previously mentioned UK study[8] on the association between air pollution and hospital admission for different cardiovascular events, exposure to NO_2 was significant, while in the same publication, some of the mortality outcomes were associated with exposure to $PM_{2.5}$ but not to NO_2,[8] indicating the possibility of different pathogenetic pathways for the outcomes, as has been discussed briefly in the case of NO_2,[4] and in the comprehensive review of the causal role of particulate material.[2] The category cardiac arrest in the ICD-10

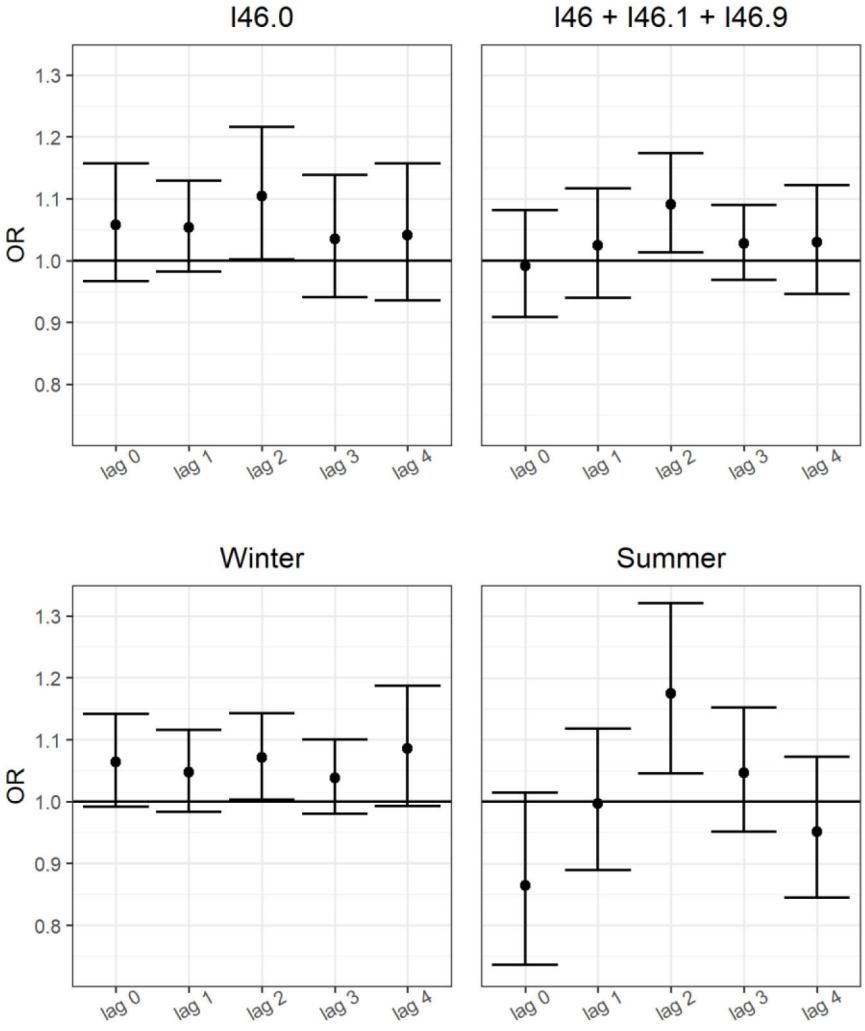

Figure 2 The OR and bars showing 95% CIs of cardiac arrest with successful resuscitation (ICD-10 code: I46.0) and other cardiac arrest categories grouped together (ICD-10 codes: I46, I46.1 and I46.9), as well as cardiac arrest (ICD-10 code: I46) stratified to winter and summer, per 10 µg/m^3 increase in PM_{10} concentrations in multiple pollutant models at lag 0 to lag 4. ICD-10, International Classification of Diseases 10th edition; PM_{10}, particulate matter with aerodynamic diameter less than 10 µm.

coding system represents a small group compared with other CVD diagnoses and seems to be concealed within the larger summary group of cardiac arrhythmias[10] or omitted from the analysis.[8] In this respect, our recent study on the same dataset is not an exception: increased risk of cardiac arrhythmias (ICD-10 codes: I44–I50) was associated with an increase in NO_2 exposure,[7] a finding that hides the association between cardiac arrest (ICD-10 code: I46) and exposure to PM_{10} as demonstrated in the present study.

Among the strengths of this study is that it is population based, as the hospital and emergency department data were obtained from the only emergency healthcare institution, the LUH, serving the population in the catchment area of the Reykjavik capital. The design of the study is also a strength, as the bidirectional time-stratified case–crossover approach virtually excludes confounding of individual characteristics and the matching adjusted for weekly pattern and time trends. Another strength of the study is its use of the encrypted identification number of each patient in the register of hospital-treated patients, which ensures the correct counting and identification of the cases and their admissions. Furthermore, it is noteworthy that visits of the cases receiving the primary discharge diagnosis of cardiac arrest (453 cases) were evenly distributed over the study period (4383 days), so the distribution diminished the risk of overlapping the sets of case and control days.

That said, there are few limitations. First, the concentration of the pollutants was derived from one monitoring station in the Reykjavik capital area, and not from individual exposure measurements. The results from these measurements did, however, correlate well with measurements from another monitoring station located in the capital area during 3 years of the study period. Another limitation is that only the primary discharge diagnosis was included in the study, meaning that the cases may have underlying diseases that could modify the result.

Furthermore, the quality of the routine discharge diagnosis at the LUH has not been investigated in a separate study for accuracy or reliability, which is a weakness our study shares with the many studies based on hospital

records. The primary discharge diagnosis of cardiac arrest (ICD-10 code: I46) set at emergency admission to the hospital and emergency department does not indicate whether the causes were cardiac or trauma related, and there may be doubt as to where the patient developed the cardiac arrest, that is, whether the event initially occurred outside or inside the hospital. The study population consisted of patients aged 18 years and older, which limits the generalisability of the results to those under 18 years.

The present study concentrates on traffic-related pollutants; however, emissions from the volcanic eruptions occurring in Iceland during the study period may have confounded the results. The Eyjafjallajökull eruption in 2010 was found to have minor health effect on the local population, but not the population in the Reykjavik capital area.[26] The Holuhraun eruption in 2014–2015 emitted a massive amount of SO_2 and mature volcanic plume, and the exposure to these was associated with an increase in the dispensing of asthma medication and an increase in healthcare utilisation for respiratory diseases in the Reykjavik capital area during 4 months in the year 2014.[27 28] The present study was not designed to catch the possible effect of these emissions on the cardiovascular health of the population of the Reykjavik capital area, and its role remains unknown in that respect.

We made several stratifications to explore the possible association between air pollutants and emergency hospital visits for cardiac arrest in this study. Because of this, some concerns may emerge about multiple comparisons; however, this has been dealt with in the literature.[29]

Conclusions

This study was, to our knowledge, the first to use the new endpoint of cardiac arrest (ICD-10 code: I46) according to the hospital discharge registry. This outcome has in previous epidemiological studies been included in larger groups of CVDs, and its special status may have been overshadowed by the more common diagnosis of CVDs. Our results indicate a positive association between short-term increase in PM_{10} and emergency hospital visits for cardiac arrest in the Reykjavik capital area, known for having low levels of traffic-related pollution. The effects were found in most subgroups, and were highest among the elderly, in the winter season and among those who were successfully resuscitated. Future ecological studies of this type should perhaps concentrate more on precisely defined endpoints; however, doing so will not replace the obvious lack of exact individual exposure measurements for each of the cases.

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Contributors SH, RGF and VR designed the study. SH, RGF, BTE and VR planned the analysis. SH, GG and VR collected the data. SH, RGF and BTE analysed the data. VR wrote the first draft. SH, RGF, BTE, OSG, GG and VR read the manuscript, interpreted the conclusion and agreed on the final version. VR is responsible for the over all content.

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Patient consent for publication Not required.

Ethics approval This study involves human participants and was approved by the National Bioethics Committee (ref. no. VSNb2018120011/03.01), the Data Protection Authority (ref. no. 10-050) and the Scientific Committee of LUH. Informed consent was not required as this is a register-based study; the ethical and scientific committees approved the study and access to data.

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Data availability statement Data may be obtained from a third party and are not publicly available. The hospital data contain sensitive individual-level information which is not publicly available. It can be made available to researchers after obtaining approval of a formal application to the National Bioethics Committee and the Scientific Committee of LUH. The dataset of air pollution used and analysed during the current study is available from the corresponding author on reasonable request.

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