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Can air pollution trigger an onset of atrial fibrillation: a population-based study

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Abstract Atrial fibrillation (AF) is the most prevalent cardiac arrhythmia and a major risk factor for ischemic stroke. Previous data showed an effect of nitric dioxide, carbon monoxide, ozone, and particulate matter (PM) smaller than 2.5 μm in diameter on atrial fibrillation development. This study aims to evaluate the effect of air pollution on the new AF onset requiring hospitalization. A case-crossover analysis was performed on a population of patients hospitalized in a large tertiary teaching hospital between 2006 and 2010 with first life occurrence of atrial fibrillation; 1458 patients were admitted to the hospital with new-onset AF. AF onset was associated with an interquartile range elevation of carbon monoxide concentrations during the winter season (odds ratio 1.15, p=0.040) and sulfur dioxide concentrations during the fall season (odds ratio 1.21, p=0.028). An interquartile range elevation in nitric dioxide concentration was associated with AF onset only among patients younger than 65 years of age (odds ratio 1.08, p=0.025). Patients with diabetes mellitus or chronic obstructive pulmonary disorder had higher susceptibility for carbon monoxide-associated AF development. Short-term exposure to carbon monoxide, nitric dioxide, and sulfur dioxide was associated with AF onset, suggesting that these pollutants, originating primarily from traffic, might trigger new AF. This knowledge is essential for understanding a pathophysiology of the disease onset and for the development of recommendations for susceptible patients.

Keywords Atrial fibrillation · Traffic · Air pollution · Carbon monoxide

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Background

Approximately 4 % of US adults over 60 years of age have been diagnosed with atrial fibrillation (AF) (Go et al. 2001). Moreover, AF is a major contributor to heart failure incidence (Roy et al. 2009) and is associated with increased medical costs and all cause mortality (Benjamin et al. 1995). Despite the fact that a large proportion of AF cases are asymptomatic and intermittent, these episodes increase the risk of ischemic stroke (Healey et al. 2012).

Numerous studies have shown an association between air pollution and cardiovascular morbidity and mortality (Liao et al. 2011; Lepeule et al. 2012; Chen et al. 2013; Madrigano et al. 2013). Studies focusing on AF as the main outcome of interest usually identify AF by either hospitalization diagnosis or implantable cardioverter defibrillator (ICD) recorded episodes. Although the validity of hospitalization-based definition of AF has been demonstrated (Smith et al. 2010), this approach can result in misclassification of AF as a primary admission diagnosis rather than comorbidity (Powell et al.

2001). Studies utilizing ICD records are more accurate in defining the AF, but are usually of a limited sample size and lack generalizability. For instance, Rich et al. identified only 29 subjects with confirmed paroxysmal atrial fibrillation (PAF) episodes among approximately 200 Boston-area patients with ICD (Rich et al. 2005).

Ambient air pollution may trigger AF onset in several ways (Link et al. 2013). Particulate matter (PM) chemical components can *directly* influence the way in which potassium, calcium, and magnesium are transported by channel proteins that maintain the transmembrane voltage, a critical mechanism for the proper generation and conduction of action potentials in the atrial myocardium (Whitsel and Avery 2010). In addition, PM particles may induce the inflammatory response and oxidative stress, in which case an air pollution exposure may lead to a structural remodeling of the atria, increasing the risk for AF episodes (Aviles et al. 2003). Finally, air pollution exposure can *indirectly* trigger cardiac arrhythmias, as a result of a pulmonary disease exacerbation (Bunch et al. 2011).

This study aimed to examine the association between AF onset and daily measurements of air pollution in Southern Israel. To reduce a possibility of a misclassification in AF diagnosis in the recurrent hospitalizations, the study population was limited to the first-time documented life event leading to AF hospitalization.

Methods

Ambient exposure definition

Air pollution and meteorological data were obtained from the Israeli Environmental Protection Agency's monitoring station located in the largest city in the Negev area. This is the only monitoring station in the area, which measured all pollutants simultaneously through the entire exposure period. Daily records (at intervals of 20 min) of air pollutants and meteorological variables were obtained for the period of 2006–2010, including particulate matter smaller than 10 μm in diameter (PM_{10},), nitrogen dioxide (NO_2), sulfate dioxide (SO_2), ozone (O_3), carbon monoxide (CO), air temperature (°C), and relative humidity (%).

Seasons were defined according to Alpert et al. (2004) using an approach developed for the studied geographical region: winter (Dec 7–Mar 30) and summer (May 31–Sep 22) each lasting for about 4 months (3 months and 23 days), and the autumn (Sep 23–Dec 6) and spring (Mar 31–May 30) each lasting only for 2 months (75 and 61 days, respectively).

Negev population is particularly vulnerable to air pollution as it resides in the largest global dust belt and thus subjected to frequent natural pollution of dust storms (Krasnov et al. 2014) aside from anthropogenic pollution. In addition, the Negev population is ethnically diverse and comprises two groups: urban Jews and Bedouin Arabs. The Bedouin-Arab population is predominantly rural; approximately 40 % of them reside in temporary housing, with increased exposure to dust among other environmental hazards.

All patients hospitalized in Soroka University Medical Center (SUMC) during the years 2006–2010, with the first occurrence of atrial fibrillation as a primary admission diagnosis (ICD-9 427.3), were identified. Only new AF onset hospitalizations were included. Patients with previous documented AF episodes were excluded. SUMC is the only medical center in this area serving a population of 630,800 as a primary hospital and nearly 1 million people as a tertiary hospital. Computerized in- and outpatient medical records were fully available for the entire population. This unique setup of the medical system ensures completeness of the clinical data in a population level. Subjects residing within 20 km from the monitoring site were considered eligible for the study.

For each subject, the following comorbidities were identified: diabetes (ICD-9:250), hypertension (ICD-9: 401), chronic obstructive pulmonary disorder (COPD; ICD-9: 490 (unspecified bronchitis), 491 (chronic bronchitis), 492 (emphysema), and 496 (chronic airways obstruction)), ischemic heart disease (ICD-9: 411 (intermediate coronary syndrome), 413 (others and unspecified angina pectoris), 414 (chronic ischemic heart disease, unspecified)), and acute myocardial infarction (ICD-9:410). Sociodemographic information was obtained from SUMC's computerized registries.

The study protocol was approved by the SUMC Institutional Review Board (IRB).

Statistical analysis

Results are presented as mean±SD for continuous, normally distributed variables; as median and range for non-normally distributed variables; and as percentages for categorical data. Analyses were performed using SAS version 9.2 and R statistical package, version 2.15.1. We analyzed the association of air pollution and the onset of AF using a case-crossover design. We sampled only cases of AF and compared environmental exposures of each case on the day of the event (hazard period) with the environmental exposures on other reference days (control periods). This design provides an optimal match on all measured or unmeasured subject characteristics that do not vary over time. Hospitalization dates were defined as case days. To assure an adequate control for long-term trends and seasonality, control periods were matched by the same weekday within the same month (Janes et al. 2005). We performed single pollutant conditional logistic regression models, including the 24-h average concentration of each pollutant (PM_{10}, NO_2, CO, SO_2, and O_3). Models were adjusted for daily

Table 1 Characteristics and health status of the study population

Characteristics	Patients (N=1458)
Age, years	
Mean±SD	69±13.4
Female gender, *n* (%)	791 (54.46)
Health status	
Diabetes, *n* (%)	419 (28.74)
Hypertension, *n* (%)	840 (57.71)
Ischemic heart disease, *n* (%)	422 (28.94)
Chronic obstructive pulmonary disease, *n* (%)	74 (5.08)

average of relative humidity and air temperature at the same day.

Possible interactions were examined using stratified analyses by ethnicity and by the following chronic conditions: diabetes mellitus (DM), ischemic heart disease (IHD), and chronic obstructive pulmonary disease (COPD). We choose stratified analyses to control for possible interactions of the characteristic with meteorological variables as well (Zanobetti and Schwartz 2005).

To evaluate the differences between patients excluded from the study to those residing within 20 km from the urban monitoring site, and therefore represented in the study, sociodemographic characteristics and comorbidities of the two populations were compared.

The effect estimates are presented as odd ratios (OR) with 95 % confidence intervals (CI). ORs were calculated for an interquartile range (IQR) elevation of 24-h average pollutant concentration.

Results

Among the Negev residents eligible for study, 1458 patients were admitted to SUMC with first-time diagnosed AF during 2006–2010. Table 1 shows baseline characteristics of the study population. The patients were 69 years old on average. About half of them were women, and 75.4 % had at least one chronic condition (DM, HTN, IHD, or COPD).

The summary statistics of the daily 24-h average pollutant concentrations as well as daily meteorological variables are presented in Table 2. The climate in the Negev desert is hot and dry, featured by a negligible amount of rainfall through the entire year. The IQR of the 24-h average air temperature ranged between 11.6 and 15.4 °C in winter and between 25.1 and 27 °C in summer. During the study period, maximal daily air temperature reached 42.4 °C. Air pollutants IQR during the study period were as follows: CO 139.46 μg/m^3, NO_2 11.1 ppb, SO_2 2.6 ppb, O_3 25.2 ppb, and PM_{10} 23.9 μg/m^3. CO and NO_2 mean concentrations were higher during the cold seasons, while the O_3 highest mean concentration was presented in the summer and spring seasons. PM_{10} reached maximal daily average value of 894 μg/m^3 during a dust storm.

We observed statistically significant positive associations between IQR increase of CO daily average concentrations and AF onset during the winter season (OR=1.15, p=0.040). An IQR elevation in SO_2 daily average concentration was associated with AF onset hospitalizations only during the fall season (OR=1.21, p=0.028). No associations were found with PM_{10}, O_3 or NO_2 (Table 3). No delayed effects were observed.

Table 2 Summary statistics for daily air pollutant and weather data, by season (2006–2010)

	Summer (May 31–Sep 22)	Autumn (Sep 23–Dec 6)	Winter (Dec 7–Mar 30)	Spring (Mar 31–May 30)
Daily pollutant level Mean±SD *median [IQR]				
PM_{10} (μg/m^3)*	36.1 (30.1–45.9)	36.6 (26.0–54.5)	33.9 (23.0–56.3)	35.2 (2.9–54.2)
NO_2 (ppb)	13.5±5.2	23.4±10	22.9±11.7	15.4±6.2
CO (μg/m^3)	1072±93	1112.5±137	1145.7±171	1098±127
SO_2 (ppb)	4.21±1.9	5.26±2.6	5.5±2.0	5.47±2.12
O_3 (ppb)	82.0±11	60.6±12	60.8±14.4	85.2±12
Temperature (°C)				
IQR	25.07–27	17.55–23.3	11.64–15.37	17.54–22.46
MAX	33.5	31.3	27.7	30.8
Relative humidity (%)				
IQR	61–70.4	50.4–72.5	51–77.3	48.45–68.6
MAX	82.4	92.2	99.9	90.3
Rain (mm)				
IQR	0	0	0	0
MAX	0.9	0.9	1.6	0.02

The asterisk (*) indicates that the variable was not normally distributed and therefore presented as median[IQR] and not as mean ±SD.

SD standard deviation, *IQR* interquartile range, *ppm* parts per million, *ppb* parts per billion, *μg/m^3* microgram per cubic meter

Table 3 Odd ratios for AF onset associated an interquartile range (IQR) increase of the average pollutants concentrations

Average value of pollutant	Interquartile range (IQR)	Adjusted odd ratios per IQR elevation [95 % CI]	*p* value
CO (μg/m^3)			
All available data	139.46 μg/m^3	1.04 (0.96–1.13)	0.238
Winter season		1.15 (1.00–1.33)	0.040*
Spring season		0.92 (0.74–1.14)	0.453
Summer season		1.10 (0.86–1.40)	0.421
Fall season		0.84 (0.64–1.11)	0.230
NO_2 (ppb)			
All available data	11.1 ppb	1.03 (0.95–1.12)	0.387
Winter season		1.05 (0.94–1.17)	0.307
Spring season		1.10 (0.81–1.49)	0.515
Summer season		1.13 (0.81–1.57)	0.456
Fall season		0.96 (0.80–1.15)	0.661
SO_2 (ppb)			
All available data	2.6 ppb	1.04 (0.95–1.13)	0.354
Winter season		1.03 (0.88–1.21)	0.648
Spring season		1.05 (0.86–1.29)	0.570
Summer season		0.87 (0.72–1.05)	0.168
Fall season		1.21 (1.02–1.44)	0.028*
O_3 (ppb)			
All available data	25.2 ppb	0.95 (0.82–1.09)	0.498
Winter season		0.93 (0.73–1.19)	0.608
Spring season		0.89 (0.63–1.26)	0.535
Summer season		0.95 (0.71–1.26)	0.748
Fall season		1.00 (0.71–1.42)	0.969
PM_{10} (μg/m^3)			
All available data	23.9 μg/m^3	0.99 (0.97–1.02)	0.807
Winter season		0.98 (0.94–1.01)	0.306
Spring season		1.02 (0.97–1.08)	0.264
Summer season		1.01 (0.86–1.20)	0.824
Fall season		1.02 (0.85–1.22)	0.815

Odd ratios are presented for all available data and for stratified analyses by seasons for the associations of each pollutant with AF onset. Each model is adjusted for average temperature and average relative humidity. Models are adjusted for seasonality and day of the week by design

* $p<0.05$

Stratified analyses for the association of AF onset and IQR elevation of CO average concentration showed that groups at higher risk for AF were Bedouin-Arab patients (OR=1.29, p=0.021), DM patients (OR=1.15, p=0.036), and COPD patients (OR=2.06, p=0.016). The effect of CO on AF onset was similar among patients younger and older than 65 years of age (OR=1.06, p=0.340 and OR=1.03, p=0.473, respectively). NO_2 effect, on the other hand, was positively associated with AF onset only among patients younger than 65 years of age (OR=1.08, p=0.025). Although no significant associations were found with O_3 and SO_2, AF hospitalizations were positively associated with O_3 only among patients with diabetes (RR 1.6, p=0.189) and COPD (RR 1.14, p=0.327). A protective effect of PM_{10} on AF onset was observed among patients with ischemic heart disease (OR=0.92, p=0.036) (Table 4).

When comparing the characteristics of the eligible study population to the 548 patients excluded from the study, no significant differences in the average age at admission were observed. Groups were also similar in terms of gender, DM, and COPD proportions. The proportions of IHD patients and Bedouin-Arab patients were higher among patients eligible for the study compared to those excluded from the analysis (29 vs. 24.4 % and 11 vs. 7 %, respectively).

Discussion

In this large population-based study of patients admitted to the hospital with AF for the first time in their life during the years 2006–2010, we have demonstrated an association between mainly traffic-originating air pollutants (CO, NO_2, and SO_2) and onset of AF. Identifying possible triggers and risk factors for AF onset may help in developing prevention strategy. The clinical guidelines for susceptible patients may include the recommendations for the exposure reduction or preparing for arrhythmia by implementing the "pill in the pocket" approach (Alboni et al. 2010) during highly polluted days.

Israel is a small densely populated country, with several potential industrial and transportation sources for air pollution (Goldreich 2003). In addition, this region is frequently subjected to high concentrations of atmospheric particles originating from non-anthropogenic sources such as dust storms (Asaf et al. 2008; Krasnov et al. 2014), negatively impacting human health (Vodonos et al. 2014; Yitshak Sade et al. 2014).

There are a number of published epidemiologic studies showing significant associations between CO, NO_2, SO_2, and AF. The results of these studies are somewhat contradictory, and some did not show the association between the pollutants and AF. The main characteristics and principal findings of these studies are summarized in Table 5.

The main results of our study are consistent with previously reported 5.1 and 2.5 % increases in arrhythmia hospital admissions associated with an IQR increase of 24-h average NO_2 and 8-h average CO, respectively (Barnett et al. 2006). Berger and colleagues also observed a significantly increased risk for supraventricular runs, recorded by 24-h electrocardiogram (ECG), associated with NO_2 (Berger et al. 2006). Positive and significant associations of supraventricular arrhythmias and 2-day mean concentrations of SO_2 were observed in a study performed among 195 cardiac patients with ICDs (Dockery et al. 2005). On the other hand, several studies did not observe significant associations with either of these pollutants (Rich et al. 2004, 2006; Metzger et al. 2007).

Table 4 Odd ratios for AF onset associated an interquartile range (IQR) increase of the average pollutants concentrations

Stratified by	Odd ratios and 95 % confidence intervals				
	PM_{10} IQR 23.9 μg/m^3	SO_2 IQR 2.6 ppb	NO_2 IQR 11.1 ppb	O_3 IQR 25.2 ppb	CO IQR 139.46 μg/m3
Diabetes mellitus					
Yes	1.00 (0.95 to 1.05)	1.02 (0.87 to 1.21)	0.99 (0.85 to 1.15)	1.14 (0.87 to 1.50)	*1.15 (1.00 to 1.33)**
No	0.99 (0.95 to 1.05)	1.04 (0.94 to 1.15)	1.03 (0.98 to 1.09)	0.88 (0.75 to 1.04)	0.99 (0.90 to 1.09)
Ischemic heart disease					
Yes	*0.92 (0.86 to 0.99)**	1.08 (0.92 to 1.27)	1.06 (0.97 to 1.15)	0.99 (0.76 to 1.31)	1.07 (0.93 to 1.23)
No	1.01 (0.98 to 1.04)	1.02 (0.92 to 1.13)	1.00 (0.94 to 1.05)	0.93 (0.79 to 1.10)	1.03 (0.94 to 1.13)
Chronic obstructive pulmonary disease					
Yes	1.06 (0.96 to 1.17)	1.09 (0.75 to 1.56)	0.81 (0.52 to 1.26)	1.60 (0.79 to 3.23)	*2.06 (1.14 to 3.73)**
No	0.99 (0.96 to 1.02)	1.03 (0.95 to 1.13)	1.04 (0.96 to 1.13)	0.93 (0.80 to 1.07)	1.03 (0.95 to 1.11)
Ethnicity					
Bedouin Arabs	0.99 (0.91 to 1.07)	1.29 (0.98 to 1.69)	1.09 (0.96 to 1.69)	0.79 (0.51 to 1.25)	*1.28 (1.03 to 1.60)**
Jewish	0.99 (0.96 to 1.02)	1.02 (0.93 to 1.12)	1.02 (0.96 to 1.06)	0.97 (0.83 to 1.12)	1.01 (0.92 to 1.10)
Age, years					
<65	0.98 (0.95 to 1.02)	1.01 (0.87 to 1.18)	*1.08 (1.01 to 1.16)**	0.86 (0.68 to 1.09)	1.06 (0.93 to 1.20)
65+	1.02 (0.97 to 1.08)	1.04 (0.94 to 1.16)	0.98 (0.92 to 1.04)	1.00 (0.84 to 1.19)	1.03 (0.93 to 1.14)

Odd ratios (OR) and 95 % confidence intervals (CI) are presented for stratified analyses by ethnicity and the presence of the following chronic conditions: diabetes mellitus (DM), ischemic heart disease (IHD), and chronic obstructive pulmonary disease (COPD). ORs and 95 % CI are presented for the association of atrial fibrillation (AF) onset, defined by hospitalizations, with an interquartile range (IQR) elevation of the 24 h average concentration of PM_{10}, SO_2, NO_2, and O_3. Each pollutant effect was modeled separately and was adjusted for average temperature and average relative humidity. Models are adjusted for seasonality and day of the week by design

*$p<0.0$

In our study, increase of CO and SO_2 levels was positively associated with all AF-related hospitalizations. However, stratified analysis by season revealed significant association only during the cold seasons. The increased cardiovascular risk during the cold seasons can be associated to the stimulation of the sympathetic nervous system leading to higher susceptibility to the arrhythmia (Schneider et al. 2008).

In accordance with our findings, Vedal and colleagues reported consistent positive and significant associations between the frequency of ICD discharge and SO_2, only during the winter season (Vedal et al. 2004). Similarly, a study that investigated the air pollution effect on heart rate variability (HRV), a known marker for AF and other arrhythmias, found negative associations of SO_2 and HRV indicators during the winter (Santos et al. 2005), supporting previous reports of a possible effect of SO_2 on the activation of autonomic nervous system, leading to changes in the cardiac rhythm (Tunnicliffe et al. 1999; Ghelfi et al. 2008).

The significant CO effect found only in the winter season can be explained by the higher concentrations observed in the winter season. Since CO originates mainly from transportation, cooking, and heating sources (Moeller 2005), the exposure to CO is more frequent in the winter season. Accordingly, the higher magnitude of an effect found among the Bedouin-Arab population in the study may be due to the indoor use of open fire for heating and cooking, which are frequent among this ethnic group (Kordysh et al. 2005).

The effect found in our study was more pronounced among patients with diabetes and chronic obstructive pulmonary disease. Patients diagnosed with chronic cardiac and pulmonary conditions have reported to be more susceptible to the air pollution effect (Bateson and Schwartz 2004). Zanobetti and colleagues found that patients with a secondary diagnosis of concurrent respiratory infections were at a greater risk for air pollution-associated hospital admissions due to cardiac diseases (Zanobetti et al. 2000). Diabetes comorbidity has also been previously reported as a modifier of the effect of airborne particle exposure on hospital admissions for heart and lung diseases. The authors found a higher risk for air pollution-associated hospital admissions, both for heart and lung diseases, among diabetic patients (Zanobetti and Schwartz 2001).

The age-stratified analysis showed a higher risk associated with NO_2 among patients younger than 65 years. This is in line with a study performed by Barnett and colleagues, in which positive association was detected only in the younger age group (Barnett et al. 2006). This effect might be explained by higher overall incidence of AF in the older population, which would reduce the pollutant-associated relative risk.

In Southern Israel, the main reasons for higher PM concentrations during the winter and spring seasons are dust

Table 5 Epidemiological association between air pollutants and atrial fibrillation

Location	Cohort	Main findings
Massachusetts, USA (Peters et al. 2000)	Defibrillator discharge interventions among 100 patients	26-ppb increase in NO_2 was associated with 1.8 (95 % CI 1.1; 2.9) increase in defibrillator interventions 2 days later
Columbia and Puerto Rico (Pope et al. 2004)	Part of the Cancer Prevention Study II (CPS-II), a prospective study of 1.2 million adults	10-μg/m^3 increase in $PM_{2.5}$ increased the risk of cardiovascular outcomes (dysrhythmias, heart failure, and cardiac arrest) by 1.13 (95 % CI 1.05; 1.21)
Vancouver, Canada (Rich et al. 2004)	34 Patients with ICDs	No statistically significant results were found with $PM_{2.5}$, PM_{10}, O_3, SO_2, NO_2, and CO. There were trends that might indicate positive associations between $PM_{2.5}$ and ICD discharges.
Boston, USA (Dockery et al. 2005)	195 Cardiac patients with ICDs	4-ppb increase of 2-day mean SO_2 increased the risk of supraventricular arrhythmias by 1.33 (95% CI 1.04, 1.70)
Australia and New Zealand (Barnett et al. 2006)	Cardiovascular emergency hospital admission data for 12,118,024 patients hospitalized in 7 large cities	Increase in IQR of 24-h NO_2 and 8-h CO was associated with 5.1 % (95 % CI 2.2 %; 8.1 %) and 2.5 % (0.1 %; 4.9 %) increase in arrhythmia admissions, respectively
Boston, USA (Rich et al. 2006)	203 Patients with a third-generation implantable cardioverter defibrillators (ICDs)	Positive not significant associations with NO_2, $PM_{2.5}$, and black carbon
Erfurt, Germany (Berger et al. 2006)	57 Men with coronary heart disease were subjected to six 24-h electrocardiogram recordings	5-day average IQR of NO_2, CO and $PM_{2.5}$ increased the risk for supraventricular runs by 1.31 (95 % CI 1.11; 1.53), 1.18 (95 % CI 1.04; 1.35), and 1.24 (95 % CI 1.05; 1.46), respectively
Atlanta, USA (Metzger et al. 2007)	518 Patients with 6287 tachyarrhythmia event-days over a 10-year period	No associations were found with PM_{10}, $PM_{2.5}$ O_3, NO_2, CO, or SO_2
Pennsylvania, USA (Liao et al. 2011)	Community dwelling sample of 106 nonsmokers	An adverse effect of AF predictors (P-wave complexity and PR duration) was associated with $PM_{2.5}$ exposure within 1.5–2 h
Boston, USA (Link et al. 2013)	176 Patients with dual chamber ICDs	14 % increases in AF onset for each 5.0 μg/m^3 increase in 24-h $PM_{2.5}$

OR odds ratio, *O_3* ozone, *NO_2* nitrogen dioxide, *CO* carbon monoxide, *$PM_{2.5}$* PM with diameter less than 2.5 μm, *PM_{10}* PM with diameter less than 10 μm, *IQR* interquartile range, *SO_2* sulfur dioxide

storms. The chemical properties of PM may differ and partially depend on whether the dust originated from Saudi-Arabian or North-African storms (Ganor et al. 2009). Increased levels of PM_{10} exposure were not associated with AF incidence in our study. The existing evidence regarding the association of cardiac arrhythmia and PM is in fact contradictory. In accordance with our findings, several studies did not find significant associations of AF and other supraventricular arrhythmias and PM exposure (Rich et al. 2004, 2006; Metzger et al. 2007). However, a few studies that used ICD or continuous ECG recordings to identify AF episodes, did find an association with PM (Berger et al. 2006; Liao et al. 2011). People's tendency to stay at home during days with high PM levels during dust storms may explain the lack of association found in our study and potentially different biological effect of non-anthropogenic and anthropogenic source PM.

One of the notable strengths in this study is the ability to identify, without exclusion, all the AF hospitalizations during 2006–2010 and to verify that the event was the first in life. The unique setup of the local medical system ensured the completeness of the medical data in the study. In addition, the large sample size and relatively long study period enabled the investigation of the confirmed AF onset diagnosis as the main outcome of interest.

The study had a few limitations. First, the study population was limited to the hospitalized patients and did not include asymptomatic episodes of AF. In addition, the exposure was measured based on the ambient pollutant measurements retrieved from a monitoring site. In both cases, the obtained assessments might have resulted in a non-differential bias in exposure, which might have reduced the magnitude of the association at study toward the null hypothesis. Secondly, given the multiple comparisons used in this study, there is a possibility of increased family-wise alpha level. However, the findings observed in our study are biologically plausible and are supported by previous studies. Yet, the results of our study should be interpreted with caution due to the potential type 1 error. Lastly, since the only available monitor is located in the city, the rural and suburban populations are underrepresented.

Summary and conclusions

In conclusion, short-term exposure to pollutants such as CO, NO_2, and SO_2 was associated with first-time AF events leading to hospitalization, suggesting that these pollutants might trigger the onset of the disease. The clinical guidelines for patients who were diagnosed with AF may include the

importance of minimizing exposure when possible or preparing for the arrhythmia by implementing the "pill in the pocket" approach (Alboni et al. 2010) during highly polluted days.

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