



## Association between ambient air pollution and hospitalization caused by atrial fibrillation

Amir Saifipour<sup>(1)</sup> , Amirhossein Azhari<sup>(2)</sup> , Ali Pourmoghaddas<sup>(3)</sup>, Sayed Mohsen Hosseini<sup>(4)</sup>, Tohid Jafari-Koshki<sup>(5)</sup>, Mojtaba Rahimi<sup>(6)</sup>, Ali Nasri<sup>(7)</sup>, Mansour Shishehforoush<sup>(8)</sup>, Ahmadreza Lahijanzadeh<sup>(9)</sup>, Babak Sadeghian<sup>(10)</sup>, Elham Moazam<sup>(11)</sup>, Mohammad Bagher Mohebi<sup>(12)</sup>, Victoria Ezatian<sup>(13)</sup>, Katayoun Rabiei<sup>(14)</sup>, Nizal Sarrafzadegan<sup>(15)</sup>

### Original Article

#### Abstract

**BACKGROUND:** Many studies have shown the worst effects of air pollution on cardiovascular diseases (CVDs). Present study focused on the relationship between atrial fibrillation (AF), as one of the common arrhythmias, and air pollutants in Isfahan, Iran, an industrial city in the Middle East.

**METHODS:** A case-crossover design was used to explore the associations between air pollution and AF hospitalized patients with ventricular response (VR) > 90 beats per minute (bpm) (fast response) and those with VR ≤ 90 bpm. All patients' records were extracted from their hospital files. Air pollutants data including particulate matter less than 10 μ (PM<sub>10</sub>), PM<sub>2.5</sub>, carbon monoxide (CO), nitrogen dioxide (NO<sub>2</sub>), sulfur dioxide (SO<sub>2</sub>), and ozone (O<sub>3</sub>) were obtained from the Correlation of Air Pollution with Hospitalization and Mortality of Cardiovascular and Respiratory Diseases (CAPACITY) study. Conditional logistic regression test was used to measure the relationship between pollutants and hospitalization due to AF.

**RESULTS:** Records of 369 patients, including 173 men (46.9%) who were hospitalized for AF during the study period and had complete data were extracted. Although a positive but not statistically significant relationship was shown between 10-unit increases in all pollutants (except PM<sub>10</sub>) and the hospitalization due to AF in patients with rapid VR (RVR), the only significant relationship was observed in case of NO<sub>2</sub> [odds ratio (OR) = 1.26, 95% confidence interval (CI) = 1.0-2.1, P = 0.031].

**CONCLUSION:** This study showed positive significant relationships between NO<sub>2</sub> and the hospitalization due to AF in patients with RVR. NO<sub>2</sub> is a greenhouse gas whose levels are expected to increase due to global environmental changes. Therefore, relevant strategies should be adopted to decrease its levels, especially in industrial cities like Isfahan.

**Keywords:** Air Pollution, Atrial Fibrillation, Nitrogen Dioxide

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#### Introduction

Recent studies by the World Health Organization (WHO) have shown that more than 90% of the world's population is exposed to air pollution. Ambient air pollution was responsible for about

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- 1- Cardiology Resident, Cardiac Rehabilitation Research Center, Cardiovascular Research Institute, Isfahan University of Medical Sciences, Isfahan, Iran
  - 2- Assistant Professor, Heart Failure Research Center, Cardiovascular Research Institute, Isfahan University of Medical Sciences, Isfahan, Iran
  - 3- Professor, Hypertension Research Center, Cardiovascular Research Institute, Isfahan University of Medical Sciences, Isfahan, Iran
  - 4- Professor, Department of Biostatistics and Epidemiology, School of Public Health, Isfahan University of Medical Sciences, Isfahan, Iran
  - 5- Assistant Professor, Road Traffic Injury Research Center AND Department of Statistics and Epidemiology, School of Health, Tabriz University of Medical Sciences, Tabriz, Iran
  - 6- Associate Professor, Department of Anesthesiology, School of Medicine, Isfahan University of Medical Sciences, Isfahan, Iran
  - 7- Assistant Professor, Interventional Cardiology Research Center, Cardiovascular Research Institute, Isfahan University of Medical Sciences, Isfahan, Iran
  - 8- Isfahan Disaster Management Office, Isfahan Governor's Office, Isfahan, Iran
  - 9- Khuzestan Department of Environment, Ahvaz, Iran
  - 10- Central Laboratory and Air Pollution Monitoring, Isfahan Province Environmental Monitoring Center, Isfahan Department of Environment, Isfahan, Iran
  - 11- Cancer Prevention Research Center, Isfahan University of Medical Sciences, Isfahan, Iran
  - 12- Information Technology Office, Isfahan University of Medical Sciences, Isfahan, Iran
  - 13- Isfahan Meteorological Office, Isfahan, Iran
  - 14- PhD Candidate, Isfahan Cardiovascular Research Center, Cardiovascular Research Institute, Isfahan University of Medical Sciences, Isfahan, Iran
  - 15- Professor, Isfahan Cardiovascular Research Center, Cardiovascular Research Institute, Isfahan University of Medical Sciences, Isfahan, Iran
- Correspondence to: Amirhossein Azhari, Email: [amirazhari2@gmail.com](mailto:amirazhari2@gmail.com)

four million deaths, mainly due to cardiovascular diseases (CVDs) in 2017. In addition to an increase in death rate due to CVD, air pollution is associated with increased complications and duration of hospitalization in patients suffering from heart problems. Hypertension (HTN),<sup>1-3</sup> cardiac arrhythmias,<sup>4,5</sup> heart failure (HF) deterioration, and acute ischemic and atherosclerotic cardiovascular complications are among the short-term consequences of air pollution.<sup>6</sup> Exposure to airborne contaminants causes a variety of cardiac arrhythmias, including atrial fibrillation (AF).<sup>7</sup> Independent relationships have been reported between death due to AF and concentrations of contaminants on the day before death.<sup>8</sup> Cardiac autonomic dysfunction caused by air pollution leads to various complications including AF.<sup>9</sup> In addition, air pollution can cause inflammation, oxidative stress, changes in atrial pressure, and ultimately AF.<sup>10</sup>

AF is the most widespread treatable cardiac arrhythmia.<sup>11</sup> It is associated with increased risk of stroke,<sup>12</sup> myocardial infarction (MI),<sup>13</sup> HF,<sup>14</sup> dementia,<sup>15</sup> and chronic kidney disease (CKD).<sup>15</sup> This prevalent arrhythmia doubles the risk of mortality following acute coronary disease and stroke.<sup>16,17</sup> There is an association between the incidence of AF and age, i.e., the prevalence of this arrhythmia varies from 1% in people younger than 60 years to 9% in those over 80 years of age. In Iran, the prevalence of AF in individuals over 70 years of age has been reported as high as 6%.<sup>18</sup> The prevalence of this disorder may even reach 14% in patients with stroke.<sup>19</sup>

The prevalence of AF in Iranians over 50 years of age has been estimated as 3%.<sup>20,21</sup> Considering the prevalence of AF and its potential irreversible complications, identification of its risk factors, determination of risk factor exposure, and planning of risk factor control policies can be a priority in the management of irrelevant diseases. This study investigated the relationship between AF and different air pollutants as part of a study on "The Correlation of Air Pollution with Hospitalization and Mortality of Cardiovascular and Respiratory Diseases (CAPACITY)" conducted in Isfahan, Iran, from March 20, 2010 to March 20, 2012.<sup>22</sup>

Increased ambient air pollution was associated with increased risk of episodes of rapid ventricular response (RVR) and AF, and we analyzed this association using a case–crossover design.

## Materials and Methods

This case-crossover study was part of the

CAPACITY research which evaluated the relationship between hospitalization and death from cardiovascular and respiratory diseases and airborne contaminants during March 20, 2010 to March 20, 2012. Data about all cases of hospitalization and/or death due to cardiovascular and respiratory diseases in Isfahan City during the mentioned period were collected from the hospitals and cemetery of Isfahan. Data on the concentrations of gaseous and non-gaseous pollutants including particulate matter < 10  $\mu$  and < 2.5  $\mu$  (PM<sub>10</sub> and PM<sub>2.5</sub>, respectively), nitrogen dioxide (NO<sub>2</sub>), sulfur dioxide (SO<sub>2</sub>), carbon monoxide (CO), and ozone (O<sub>3</sub>) were collected from fixed air monitoring stations in the city of Isfahan. The CAPACITY study used two time-series and case-crossover models to assess the relationships between cardiovascular and respiratory diseases and air pollutants.<sup>22</sup>

The present study extracted the names and characteristics of all patients who were diagnosed with AF [I48 in the International Classification of Diseases, 10<sup>th</sup> revision (ICD-10)] and admitted to Isfahan hospitals during March 20, 2010 to March 20, 2012 from the CAPACITY study. The causes of hospitalization were determined by the hospital physician but were re-examined in this study. The patients' additional information, including symptoms at the time of admission, history of diabetes, and history of HTN, along with ejection fraction (EF) in the echocardiography performed during hospitalization, were extracted from the relevant hospitals. Patients with incomplete data were excluded from the study.

Air pollutant data including PM<sub>10</sub>, PM<sub>2.5</sub>, CO, SO<sub>2</sub>, NO<sub>2</sub>, and O<sub>3</sub>, as well as weather information, including temperature, humidity, and wind speed were collected from the CAPACITY study (obtained from the Department of Environment, Isfahan Province). This information was collected from six fixed air monitoring stations installed in different areas of Isfahan recording the hourly concentrations of each pollutant. The CAPACITY study collected data on temperature, humidity, and wind speed from Isfahan Weather Forecast Organization and the National Oceanic and Atmospheric Administration (NOAA) National Environmental Satellite, Data, and Information Service (<http://www.nesdis.noaa.gov>). All data were evaluated in the CAPACITY study and the outliers and missing points were determined. The average daily values of weather pollutants were merged into a single file.

A case-crossover design allowed for investigation of the acute effects of exposure to air

pollution. The subject exposure before the time of the event (case period) was compared with the distribution of exposure estimated from separate control periods and the matched sets were analyzed using conditional logistic regression. Thus, each patient served as his or her own control.

Case periods were defined by the time prior to onset of each confirmed arrhythmic event. Daily pollution concentrations and weather conditions were then matched to the case and control time periods for analysis.

The effect of 10-unit increase of air pollutants on hospitalization with heart rate more than 90 beats per minute (bpm) was determined using conditional logistic regression and crude and adjusted odds ratios (ORs) by temperature ( $^{\circ}$ f), dew point ( $^{\circ}$ f), and wind speed (mile/h).

The patients were divided in two groups: VR rate  $> 90$  bpm and  $\leq 90$  bpm. Qualitative variables were expressed as number and percentage and for comparison between them, chi-square test or Fisher's exact test were used. Quantitative variables were expressed as mean  $\pm$  standard deviation (SD) and compared with independent t-test or Mann-Whitney U test (if normality assumption was not hold).

Kolmogorov-Smirnov test (K-S test) was used to determine whether normality assumption existed.

Statistical analysis was conducted using Stata software (version 9, Stata Corporation, College Station, TX, USA). P-value less than 0.050 was considered statistically significant.

## Results

A total of 451 patients with AF were hospitalized in seven educational hospitals affiliated to Isfahan University of Medical Sciences, Isfahan City, during the study period. However, only 369 patients, including 173 men (46.9%), had complete data and were entered into the study. The patients' mean age was  $66.3 \pm 15.9$  years. The patients visited the hospital mainly due to chest pain ( $n = 61$ , 16.0%), dyspnea ( $n = 41$ , 10.7%), dyspnea on exertion (DOE) ( $n = 81$ , 21.2%), dizziness ( $n = 19$ , 5.0%), and tachycardia ( $n = 17$ , 4.5%). The frequency of these complaints did not differ significantly between the two groups. Table 1 shows the history of diseases, symptoms, and results of echocardiography in all patients and the two groups.

**Table 1.** Demographic characteristics of hospital admissions for atrial fibrillation (AF) in Isfahan, Iran, 2010-2012

Variable	All subjects (n = 369)	Subjects with PR $\leq 90$ bpm (n = 108, 29.3%)	Subjects with PR $> 90$ bpm (n = 261, 70.7%)	P
	Total	PR $\leq 90$	PR $> 90$	
Age (year)	66.31 $\pm$ 15.88	65.55 $\pm$ 15.06	66.56 $\pm$ 16.24	0.657**
SBP (mmHg)	130.30 $\pm$ 27.78	129.17 $\pm$ 29.69	130.58 $\pm$ 27.25	0.693**
DBP (mmHg)	78.90 $\pm$ 13.42	77.41 $\pm$ 13.75	79.43 $\pm$ 13.32	0.227 <sup>†</sup>
Number of pulses (bpm)*	117.80 $\pm$ 33.05	75.78 $\pm$ 51.50	130.91 $\pm$ 26.19	$< 0.001$ **
EF value	50.70 $\pm$ 15.10	48.69 $\pm$ 15.27	51.27 $\pm$ 15.06	0.278**
Hb concentration	13.41 $\pm$ 2.60	13.16 $\pm$ 2.92	13.48 $\pm$ 2.53	0.443**
Creatinine (mg/dl)	1.22 $\pm$ 0.49	1.20 $\pm$ 0.40	1.23 $\pm$ 0.51	0.560 <sup>†</sup>
Arterial oxygen saturation	90.71 $\pm$ 8.76	88.75 $\pm$ 5.12	90.90 $\pm$ 9.16	0.221 <sup>†</sup>
History of VHD	87 (23.6)	23 (21.3)	64 (24.5)	0.539*
Medicines received in the hospital				
- Beta blocker	105 (28.5)	27 (25.0)	78 (29.9)	0.596*
- Statin	53 (14.4)	17 (15.7)	36 (13.8)	0.118*
- Warfarin	67 (18.2)	22 (20.4)	45 (17.2)	0.056*
Male gender	173 (46.9)	39 (36.1)	134 (51.3)	0.581*
History of diabetes	86 (23.3)	23 (21.3)	63 (24.1)	0.472*
History of HTN	148 (40.1)	33 (30.5)	115 (44.1)	0.567*
Status (death)	13 (3.5)	2 (1.8)	11 (4.2)	0.529*

Values are presented as mean  $\pm$  standard deviation (SD) or median [interquartile range (IQR)] for quantitative variables and number and percentage for qualitative variables.

\* Chi-square or Fisher's exact test were used where appropriate.

\*\* Two independent samples t-test was used.

<sup>†</sup> Mann-Whitney U test was used.

PR: Pulse rate; SBP: Systolic blood pressure; DBP: Diastolic blood pressure; EF: Ejection fraction; Hb: Hemoglobin; Bpm: Beats per minute; VHD: Valvular heart disease; HTN: Hypertension

**Table 2.** The mean daily concentrations of pollutants in Isfahan, Iran, during the study period (March 20, 2010 to March 20, 2012)

Variable	Mean $\pm$ SD	Minimum	Maximum
O <sub>3</sub> (ppb)	29.09 $\pm$ 15.18	3.00	101.0
CO (ppm)	3.93 $\pm$ 2.46	0.00	16.0
SO <sub>2</sub> (ppb)	41.33 $\pm$ 35.04	0.00	147.5
NO <sub>2</sub> (ppb)	40.53 $\pm$ 23.11	0.01	128.0
PM <sub>10</sub> ( $\mu\text{g}/\text{m}^3$ )	129.86 $\pm$ 58.85	36.40	528.3
PM <sub>2.5</sub> ( $\mu\text{g}/\text{m}^3$ )	54.14 $\pm$ 29.61	8.00	296.1
Temperature ( $^{\circ}\text{f}$ )	55.77 $\pm$ 18.58	27.80	92.2
Dew point ( $^{\circ}\text{f}$ )	27.42 $\pm$ 9.23	7.30	46.6
Wind speed (mile/h)	4.82 $\pm$ 2.52	0.80	15.5

Ppb: Particle per billion; Ppm: Part per million; O<sub>3</sub>: Ozone; CO: Monoxide carbon; SO<sub>2</sub>: Sulfur dioxide; NO<sub>2</sub>: Nitrogen dioxide; PM: Particulate matter; SD: Standard deviation

As seen in table 1, the two groups (VR  $\leq$  90 and VR  $>$  90 bpm) had no significant differences except in the number of pulses. This difference was expected due to the classification of patients based on pulse rate (PR). Table 2 presents the mean concentrations of pollutants and weather factors during the study period.

Table 3 presents the details of the effect of air pollution on hospitalization due to AF using a crude and adjusted model for temperature ( $^{\circ}\text{f}$ ), dew point (%), and wind speed (mile/h).

As seen, the only significant relationship was observed between a 10-unit increase in NO<sub>2</sub> and the hospitalization due to AF. However, 10-unit increases in other pollutants, except PM<sub>10</sub>, had positive but not statistically significant associations with the hospitalization due to AF and RVR (VR  $>$  90 bpm).

## Discussion

The direct association between NO<sub>2</sub> concentration and rate of hospitalization due to AF was the only significant relationship in this study. Although increments in other pollutants increased the

frequency of hospitalization due to AF, these relationships were not significant. Various studies have investigated the effects of pollutants on the incidence of cardiac arrhythmias, including AF, around the world. A cohort study followed patients with implantable cardioverter-defibrillator (ICD) for three years and found 798 cases of ventricular fibrillation (VF). The incidence of these cases was related with PM<sub>2.5</sub> and O<sub>3</sub>.<sup>5</sup> Another cohort study reported a significant relationship between ventricular arrhythmias and SO<sub>2</sub> concentration. It evaluated 56 patients and a total of 139 VF events and found increased NO<sub>2</sub> 24 hours before the incidence of arrhythmia. However, this increase had no significant associations with arrhythmias.<sup>23</sup>

A cohort study extracted electrocardiographic (ECG) changes from the records of patients with ICD and identified significant relationships between the incidence of AF and exposure to PM, CO, and NO<sub>2</sub>, especially two hours before AF. Overall, 124 AF events occurred in individuals who had no previous AF records and the incidence of the arrhythmia was strongly associated with the mentioned contaminants, especially NO<sub>2</sub>.<sup>24</sup>

**Table 3.** The effects of a 10-unit increase in pollutants at 24 hours before the onset of atrial fibrillation (AF) in patients with rapid ventricular response (RVR)

Pollutants	Crude			Adjusted*		
	OR	95% CI	P	OR	95% CI	P
PM <sub>2.5</sub>	1.017	0.950-1.089	0.612	1.019	0.951-1.092	0.579
PM <sub>10</sub>	0.992	0.930-1.059	0.830	0.994	0.931-1.062	0.879
SO <sub>2</sub>	1.017	0.849-1.218	0.854	1.014	0.846-1.215	0.878
CO**	1.064	0.864-1.310	0.557	1.062	0.862-1.309	0.570
NO <sub>2</sub>	1.260	1.024-1.551	0.029	1.259	1.020-1.553	0.031
O <sub>3</sub>	1.082	0.763-1.533	0.657	1.083	0.760-1.544	0.655

\* Adjusted for temperature ( $^{\circ}\text{f}$ ), dew point(%), and wind speed (mile/h)

\*\* For CO effect, 1-unit increase was conducted

OR: Odds ratio; CI: Confidence interval; PM: Particulate matter; SO<sub>2</sub>: Sulfur dioxide; CO: Monoxide carbon; NO<sub>2</sub>: Nitrogen dioxide; O<sub>3</sub>: Ozone

A two-year time-series study on emergency room (ER) visits in Brazil revealed associations between arrhythmias and air contaminants. The study designed a model based on generalized linear Poisson regression with seasonal adjustment to investigate the relationship between contaminants and the incidence of arrhythmias. The results showed that atrial arrhythmias, including flutter and fibrillation, and other arrhythmias were associated with increases in CO, NO<sub>2</sub>, and PM<sub>10</sub> concentrations within the quartiles.<sup>25</sup>

A 14-year time-series study in Rome, Italy, investigated the relationship between the frequency of patients with AF referring to ER and air pollutants (PM<sub>10</sub>, PM<sub>2.5</sub>, NO<sub>2</sub>) at different time intervals. Models based on two pollutants and adjusted for temperature, humidity, individual characteristics, and consumed drugs were also developed. During the study, nearly 80000 people were admitted to ERs due to AF. The study showed an association between hospitalization due to AF and exposure to PM 24 hours before the incidence of arrhythmia. Hospitalization due to AF had the strongest relationships with PM in men over 75 years of age and with NO<sub>2</sub> in women over 75 years of age. It was also associated with exposure to NO<sub>2</sub>, and more strongly with PM<sub>2.5</sub> 24 hours before the incidence in all ages.<sup>26</sup>

In a large case-crossover study in the United Kingdom (UK), patient registration programs, e.g., the Myocardial Ischaemia National Audit Project (MINAP), were used to extract the data of around 2 million patients admitted to ERs due to CVD during 2003-2008. Data about the mean daily concentrations of CO, PM<sub>10</sub>, PM<sub>2.5</sub>, SO<sub>2</sub>, and NO<sub>2</sub>, as well as the maximum 8-hour concentrations of O<sub>3</sub> per day, were extracted from air monitoring stations with minimum distance from each individual patient. The designed model was examined based on different time intervals and up to four days before the event. The strongest relationship was observed between NO<sub>2</sub> levels and hospitalization due to different cardiovascular causes, including AF. In addition, the hospitalization of patients after non-ST-segment elevation MI (NSTEMI) had significant relationships with SO<sub>2</sub> and NO<sub>2</sub> during the four-day period before the incidence. The effects of NO<sub>2</sub> were more profound in subjects over 70 years old and also in women.<sup>27</sup>

NO<sub>2</sub> is produced from diesel fuel and secondary reactions of NO with O<sub>3</sub>. It is usually related with other pollutants and can exacerbate their effects.

NO<sub>2</sub> per se can cause autonomic system dysfunction and increase the risk of AF.<sup>26,28</sup>

It should be borne in mind that although AF is a major risk factor for stroke and MI, it is often asymptomatic and undetectable. Consequently, the treatment may not be initiated until a complication occurs. Therefore, based on the results of this study, it is preferable to control the risk factors of AF, e.g., airborne contaminants, especially NO<sub>2</sub>. Furthermore, in addition to pollutant reduction policies, screening methods to diagnose and treat AF should be adopted in the country. A combination of these measures and control strategies, especially on polluted days, will reduce the hospitalization due to both AF and its complications.

Another important point is the rapid change in the AF process and the development of symptoms, due to which studies on the effects of pollutants on the hospitalization due to AF should consider the few hours before hospitalization as the exposure time.<sup>24</sup> Based on the results of other studies, obtaining reliable results regarding the effects of environmental factors, such as pollutants, on the incidence of AF requires larger research, cohort studies, using large databases such as health information system (HIS) and Iranian electronic health record (SEPAS) in Iran, updating the available databases, and recording patients' full information (e.g., history of hospitalization, diseases, and medication use) and changes in their home and work addresses.

Another finding of this study was that the mean annual concentrations of NO<sub>2</sub>, PM<sub>10</sub>, PM<sub>2.5</sub>, and SO<sub>2</sub> within the study period were almost twice the Iranian and global standards. High levels of pollutants can be attributed to the presence of various industries using fossil fuels, as well as the increased number of vehicles, in particular diesel cars, followed by elevated use of fossil fuels in the city of Isfahan. Moreover, due to sanctions in 2011, Iran could not import gasoline and had to use the gasoline produced in the country which did not have Euro 4 standard according to some sources. It is, hence, critical to pay attention to high levels of pollutants and develop relevant measures to control them.

Another notable result of this study was the high frequency of women hospitalized for AF in Isfahan. Similar to our findings, Habibzadeh et al. studied patients referred to a first-level health center and showed a higher frequency of women among the 463 50-80-year-old patients with AF.<sup>20</sup> In contrast, Schnabel et al. reviewed a 50-year record of patients admitted for AF and reported a higher incidence of this arrhythmia in men.<sup>29</sup> In the Gulf Survey of

Atrial Fibrillation Events (Gulf SAFE) on 2043 patients with AF visiting ERs, men had a higher overall frequency, but the frequency of women was higher in patients with comorbidities and resistant AF.<sup>30</sup> Accordingly, it seems necessary to assess gender distribution of Iranian patients with AF, especially those at a high risk of complications.

### Conclusion

The greater frequency of women among patients with AF, higher concentrations of pollutants compared to global standards, and a relatively strong significant relationship between NO<sub>2</sub>, as an important pollutant, and the hospitalization due to AF or development of its symptoms were the most important findings of this study. Therefore, relevant strategies should be adopted to identify patients and examine the reasons for the higher rate of hospitalization due to AF in women. It is also essential to develop effective measures to decrease the levels of pollutants (especially NO<sub>2</sub>) and precursor pollutants (e.g., O<sub>3</sub>). Timely AF control methods should also be used before the development of complications on highly-polluted days. In addition, due to the possibility of quick effects of pollutants on the hospitalization due to AF, further studies are required to design models assessing very short exposure times before the hospitalization due to AF symptoms. Models should also consider combinations of pollutants in order to study the impacts of precursor pollutants on other contaminants.

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### Conflict of Interests

Authors have no conflict of interests.

### References

- Zanobetti A, Canner MJ, Stone PH, Schwartz J, Sher D, Eagan-Bengston E, et al. Ambient pollution and blood pressure in cardiac rehabilitation patients. *Circulation* 2004; 110(15): 2184-9.
- Dvonch JT, Kannan S, Schulz AJ, Keeler GJ, Mentz G, House J, et al. Acute effects of ambient particulate matter on blood pressure: Differential effects across urban communities. *Hypertension* 2009; 53(5): 853-9.
- Urch B, Silverman F, Corey P, Brook JR, Lukic KZ, Rajagopalan S, et al. Acute blood pressure responses in healthy adults during controlled air pollution exposures. *Environ Health Perspect* 2005; 113(8): 1052-5.
- Peters A, Liu E, Verrier RL, Schwartz J, Gold DR, Mittleman M, et al. Air pollution and incidence of cardiac arrhythmia. *Epidemiology* 2000; 11(1): 11-7.
- Rich DQ, Schwartz J, Mittleman MA, Link M, Luttmann-Gibson H, Catalano PJ, et al. Association of short-term ambient air pollution concentrations and ventricular arrhythmias. *Am J Epidemiol* 2005; 161(12): 1123-32.
- Franchini M, Mannucci PM. Air pollution and cardiovascular disease. *Thromb Res* 2012; 129(3): 230-4.
- Hoek G, Brunekreef B, Fischer P, van Wijnen J. The association between air pollution and heart failure, arrhythmia, embolism, thrombosis, and other cardiovascular causes of death in a time series study. *Epidemiology* 2001; 12(3): 355-7.
- Dominici F, McDermott A, Daniels M, Zeger SL, Samet JM. Mortality among residents of 90 cities. In: Dominici F, McDermott A, Daniels M, Zeger SL, Samet JM, Editors. Revised analyses of time-series studies of air pollution and health. Boston, MA: Health Effects Institute; 2003. p. 9-24.
- Link MS, Dockery DW. Air pollution and the triggering of cardiac arrhythmias. *Curr Opin Cardiol* 2010; 25(1): 16-22.
- Aviles RJ, Martin DO, Apperson-Hansen C, Houghtaling PL, Rautaharju P, Kronmal RA, et al. Inflammation as a risk factor for atrial fibrillation. *Circulation* 2003; 108(24): 3006-10.
- Piccini JP, Hammill BG, Sinner MF, Jensen PN, Hernandez AF, Heckbert SR, et al. Incidence and prevalence of atrial fibrillation and associated mortality among Medicare beneficiaries, 1993-2007. *Circ Cardiovasc Qual Outcomes* 2012; 5(1): 85-93.
- Lip GY, Nieuwlaat R, Pisters R, Lane DA, Crijns HJ. Refining clinical risk stratification for predicting stroke and thromboembolism in atrial fibrillation using a novel risk factor-based approach: the euro heart survey on atrial fibrillation. *Chest* 2010; 137(2): 263-72.
- Soliman EZ, Safford MM, Muntner P, Khodneva Y, Dawood FZ, Zakai NA, et al. Atrial fibrillation and the risk of myocardial infarction. *JAMA Intern Med* 2014; 174(1): 107-14.
- Miyasaka Y, Barnes ME, Gersh BJ, Cha SS, Bailey KR, Abhayaratna W, et al. Incidence and mortality risk of congestive heart failure in atrial fibrillation patients: A community-based study over two decades. *Eur Heart J* 2006; 27(8): 936-41.
- Kwok CS, Loke YK, Hale R, Potter JF, Myint PK.

- Atrial fibrillation and incidence of dementia: A systematic review and meta-analysis. *Neurology* 2011; 76(10): 914-22.
16. Stewart S, Hart CL, Hole DJ, McMurray JJ. A population-based study of the long-term risks associated with atrial fibrillation: 20-year follow-up of the Renfrew/Paisley study. *Am J Med* 2002; 113(5): 359-64.
  17. Miyasaka Y, Barnes ME, Bailey KR, Cha SS, Gersh BJ, Seward JB, et al. Mortality trends in patients diagnosed with first atrial fibrillation: A 21-year community-based study. *J Am Coll Cardiol* 2007; 49(9): 986-92.
  18. Krijthe BP, Kunst A, Benjamin EJ, Lip GY, Franco OH, Hofman A, et al. Projections on the number of individuals with atrial fibrillation in the European Union, from 2000 to 2060. *Eur Heart J* 2013; 34(35): 2746-51.
  19. Behrouz R, Powers CJ. Epidemiology of classical risk factors in stroke patients in the Middle East. *Eur J Neurol* 2016; 23(2): 262-9.
  20. Habibzadeh F, Yadollahie M, Roshanipoor M, Haghghi AB. Prevalence of atrial fibrillation in a primary health care centre in Fars Province, Islamic Republic of Iran. *East Mediterr Health J* 2004; 10(1-2): 147-51.
  21. Ahmadi A, Etemad K, Khaledifar A. Risk factors for heart failure in a cohort of patients with newly diagnosed myocardial infarction: A matched, case-control study in Iran. *Epidemiol Health* 2016; 38: e2016019.
  22. Rabiei K, Hosseini SM, Sadeghi E, Jafari-Koshki T, Rahimi M, Shishehforoush M, et al. Air pollution and cardiovascular and respiratory disease: Rationale and methodology of CAPACITY study. *ARYA Atheroscler* 2017; 13(6): 264-73.
  23. Rich DQ, Kim MH, Turner JR, Mittleman MA, Schwartz J, Catalano PJ, et al. Association of ventricular arrhythmias detected by implantable cardioverter defibrillator and ambient air pollutants in the St Louis, Missouri metropolitan area. *Occup Environ Med* 2006; 63(9): 591-6.
  24. Link MS, Luttmann-Gibson H, Schwartz J, Mittleman MA, Wessler B, Gold DR, et al. Acute exposure to air pollution triggers atrial fibrillation. *J Am Coll Cardiol* 2013; 62(9): 816-25.
  25. Santos UP, Terra-Filho M, Lin CA, Pereira LA, Vieira TC, Saldiva PH, et al. Cardiac arrhythmia emergency room visits and environmental air pollution in Sao Paulo, Brazil. *J Epidemiol Community Health* 2008; 62(3): 267-72.
  26. Solimini AG, Renzi M. Association between air pollution and emergency room visits for atrial fibrillation. *Int J Environ Res Public Health* 2017; 14(6).
  27. Milojevic A, Wilkinson P, Armstrong B, Bhaskaran K, Smeeth L, Hajat S. Short-term effects of air pollution on a range of cardiovascular events in England and Wales: Case-crossover analysis of the MINAP database, hospital admissions and mortality. *Heart* 2014; 100(14): 1093-8.
  28. Brook RD, Rajagopalan S, Pope CA 3<sup>rd</sup>, Brook JR, Bhatnagar A, Diez-Roux AV, et al. Particulate matter air pollution and cardiovascular disease: An update to the scientific statement from the American Heart Association. *Circulation* 2010; 121(21): 2331-78.
  29. Schnabel RB, Yin X, Gona P, Larson MG, Beiser AS, McManus DD, et al. 50 year trends in atrial fibrillation prevalence, incidence, risk factors, and mortality in the Framingham Heart Study: A cohort study. *Lancet*. 2015; 386(9989): 154-62.
  30. Shehab A, Zubaid M, Bhagavathula AS, Rashed WA, Alsheikh-Ali AA, AlMahmeed W, et al. Sex differences in management and outcomes of patients with atrial fibrillation in the Middle East: Gulf survey of atrial fibrillation events (Gulf SAFE). *PLoS One* 2017; 12(5): e0175405.