Impact of particulate matter on the incidence of atrial fibrillation and the risk of adverse clinical outcomes

A review

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Review

Impact of particulate matter on the incidence of atrial fibrillation and the risk of adverse clinical outcomes: A review

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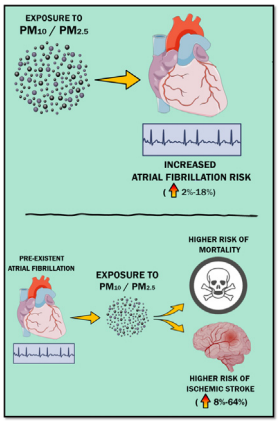
HIGHLIGHTS

- Previous evidence showed that air pollution increases atrial fibrillation (AF) risk.
- Short and long-term exposure to $PM_{2.5}$ or PM_{10} leads to a higher risk of new-onset AF.
- In patients with previous AF, exposure to high $PM_{2.5}$ or PM_{10} concentrations raises mortality and stroke risks.
- Air pollution should be considered as a risk factor for both AF and adverse events.

GRAPHICAL ABSTRACT

Upper panel = Association between particulate matter exposure and new-onset atrial fibrillation.



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ABSTRACT

Background: Atrial fibrillation (AF) is common and increases the risk of stroke and mortality. Previous studies have suggested that air pollution is an important risk factor for new-onset AF. Herein, we review the evidence regarding: 1) the association between exposure to particulate matter (PM) and new-onset AF, and 2) the risk of worse clinical outcomes in patients with pre-existent AF and their relation to PM exposure.
Methods: A selection of studies between 2000 and 2023 linking PM exposure and AF was performed through searches in PubMed, Scopus, Web of Science, and Google Scholar.
Results: 17 studies from different geographical areas demonstrated that exposure to PM was associated with an increased risk of new-onset AF, although the results were heterogeneous regarding the temporal pattern (short- or long-term) ultimately related to AF. Most of the studies concluded that the risk of new-onset AF increased between 2 %–18 % per 10 μg/m^3 increment in $PM_{2.5}$ or PM_{10} concentrations, whereas the incidence (percentage of change of incidence) increased between 0.29 %–2.95 % per 10 μg/m^3 increment in $PM_{2.5}$ or PM_{10}. Evidence about the association between PM and adverse events in patients with pre-existent AF was scarce but 4 studies showed a higher risk

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of mortality and stroke (between 8 %–64 % in terms of hazard ratio) in patients with pre-existent AF when PM exposure was higher.

Conclusions: Exposure to PM (both $PM_{2.5}$ and PM_{10}) is a risk factor for AF, and a risk factor for mortality and stroke in patients who already suffer from AF. Since the relationship between PM and AF is independent of the region of the world, PM should be considered as a global risk factor for both AF and worse clinical outcomes in AF patients. Specific measures to prevent air pollution exposure need to be adopted.

Contents

1. Introduction

One of the main challenges facing humanity in modern times is air pollution, because its presence in the atmosphere can cause an irreversible impact on human health. Both long-term and short-term effects of air pollutants are of great importance as there is a high risk of harm even at low concentrations (Kim et al., 2015).

The term “air pollution” includes environmental pollution and indoor pollution. The main difference between both is the source of the pollution itself. In the case of environmental pollution, it is caused by the release into the atmosphere of products resulting from the combustion of fossil fuels, while indoor pollution is mainly produced by the combustion of natural gas and aerosols from different sprays (Al-Kindi et al., 2020).

The most studied pollutant that gives rise to the harmful effects of environmental pollution on health is the particulate matter (PM), which consists of a heterogeneous mixture of solid organic and inorganic particles such as dust, pollen, dirt, soot, smoke, as well as liquid droplets suspended in the air (Fig. 1). Sulphate and nitrate are also major components of PM. These particles are classified into coarse particles (with a size diameter < 10 μm [PM_{10}]), fine particles (<2.5 μm [$PM_{2.5}$]) and ultrafine particles (<0.1 μm [$PM_{0.1}$]) (Rajagopalan and Landrigan, 2021).

Cardiovascular diseases are the leading cause of death and morbidity worldwide. In 2019, it was estimated that this set of diseases caused

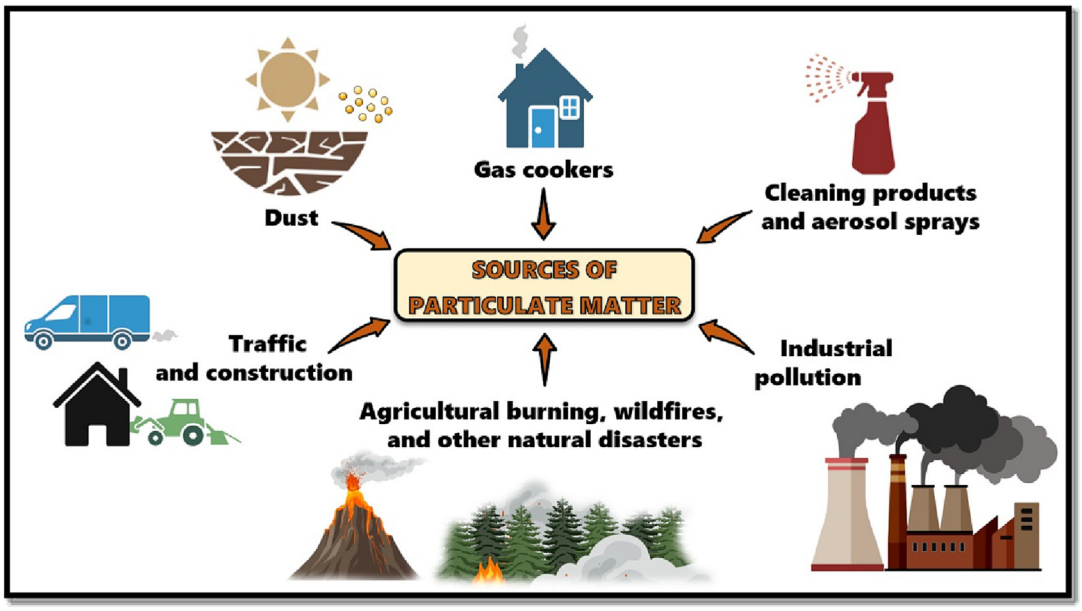

Fig. 1. Main sources contributing to particulate matter release into the atmosphere.

about 18.6 million deaths globally (Murray et al., 2020). For this reason, an attempt has been made to identify those risk factors that favour the onset of cardiovascular diseases (Gibbons et al., 2021). Pollution is now one of these risk factors (Sartini et al., 2016), and evidence has linked exposure to PM with cardiovascular morbidity and mortality, as well as with myocardial infarction, heart failure and a wide range of cardiovascular diseases (Brook et al., 2010a; de Bont et al., 2022; Chen et al., 2022).

Among the most frequent cardiovascular diseases in the general population, atrial fibrillation (AF) is a heart rhythm disturbance caused by dysfunction of the electrical conductivity of the heart, and it is the most common arrhythmia with an estimated prevalence of 37.574 million cases (Lippi et al., 2021). AF is an important risk factor for stroke so that the morbidity and mortality of this disease are substantial, being responsible for increasing healthcare costs and hospitalizations (Burdett and Lip, 2022). Thus, AF is a major public health problem.

Several risk factors yield to a substrate for AF, including advanced age, hypertension, diabetes mellitus, myocardial infarction, heart failure, and overweight/obesity (Kornej et al., 2020). Simultaneously, lifestyle factors such as smoking, alcohol consumption, physical inactivity, and non-adherence to the Mediterranean diet, are risk factors for AF development and perpetuation (Kornej et al., 2020; Biccirè et al., 2022). In addition, the increasing prevalence of this arrhythmia along with the increasing levels of ambient pollution worldwide, particularly PM, might also have important inter-relationships. Therefore, PM can lead to a higher incidence of AF.

Various mechanisms may be involved in this process, including systemic oxidative stress, endothelial dysfunction, systemic inflammation, and the promotion of autonomic nervous system dysfunction. In turn, these changes rise the likelihood of developing atherosclerosis and thrombosis, thus increasing the risks of worse clinical outcomes in patients who already have AF. However, several issues require further clarification, and systematic reviews and meta-analyses published to date have only included some studies from this field.

In this review, we aim to explore the potential association of PM and AF by providing an overview of the clinical evidence linking short-term and/or long-term exposure to $PM_{2.5}$/PM_{10} and new-onset AF, and second, to summarize studies in relation to clinical events in AF patients and PM exposure.

2. Methods

The data published in this review were identified after a search and selection in PubMed, Scopus, Web of Science and Google Scholar. The search for information related to the association between PM and AF was conducted using the keywords: “air pollution” OR “particulate matter” AND “atrial fibrillation”. On the other hand, the search for manuscripts related to the association between PM and adverse outcomes in AF patients were conducted using the keywords “air pollution” OR “particulate matter” OR “$PM_{2.5}$” OR “PM_{10}” AND “atrial fibrillation” AND “mortality” OR “stroke” OR “bleeding” OR “adverse events”. Additionally, the reference lists of some of the articles used in the present study were reviewed to include other relevant articles. Articles published in English and Spanish between 2000 and 2023 were reviewed and included, if appropriate.

3. Initiating mechanisms of cardiovascular events after PM exposure

The biological mechanisms involved in the occurrence of cardiovascular events triggered by exposure to PM are complex and may vary depending on the source of the pollutant, time of exposure and pollutant characteristics. There is evidence supporting short term effects of pollutants such as autonomic dysfunction, and on the other hand, evidence of chronic effects derived from exposure to PM also exist like hypertension, cardiac fibrosis, and type 2 diabetes mellitus (T2DM), among others (Rajagopalan et al., 2018).

To better understand the mechanisms of which pollutants may result in cardiovascular dysfunction, controlled animals as well as human exposure studies have been conducted to reveal the pathways underlying by which cardiovascular damage occurs (Campen et al., 2002; Gong et al., 2003). Regarding PM, three different biological pathways have been described as potentially responsible for instigating cardiovascular events (Fig. 2). These pathways link PM exposure with cardiovascular diseases through the effect of PM in the pulmonary alveoli (Miller and Newby, 2020).

The first biological pathway linking PM to cardiovascular diseases is the release of pro-inflammatory mediators (IL-1β, IL-6, TNF-α) from lung cells, leading to a systemic oxidative stress and inflammation (Long et al., 2020a). Oxidative stress as a response to air pollution is suggested to be

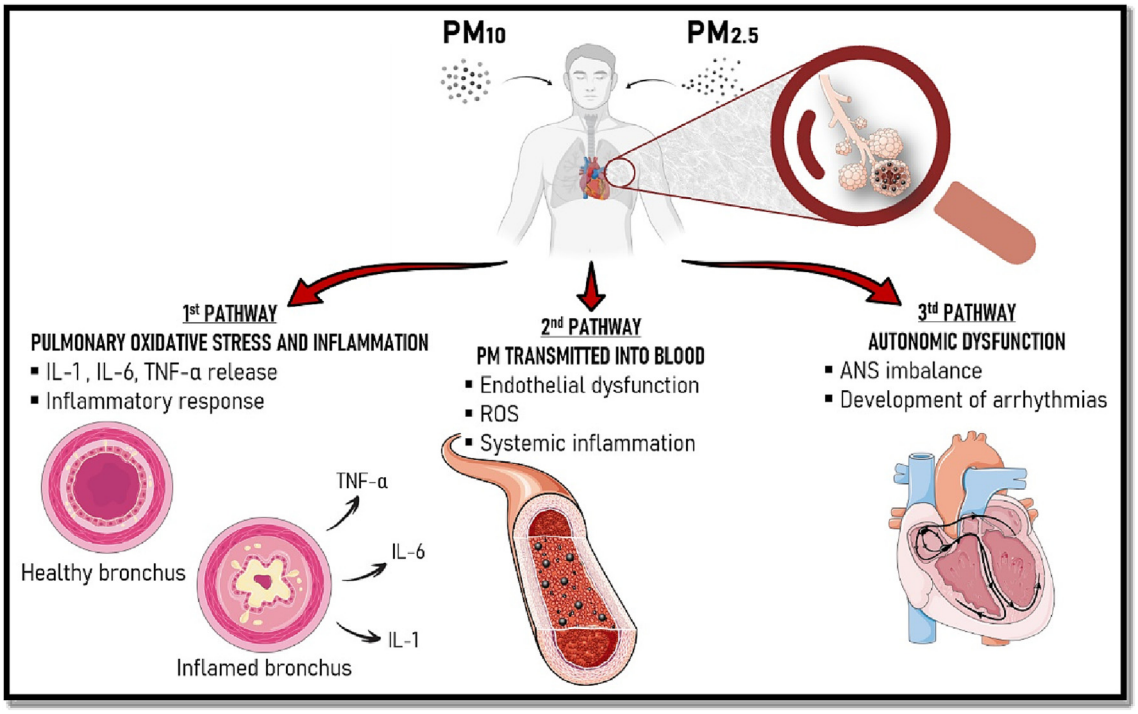

Fig. 2. Potential biological pathways by which particulate matter may trigger cardiovascular diseases.

an early step in humans, and the haemostasis pathway responds gradually over a 2–3 day period. That initial pulmonary response may contribute to the systemic changes the ultimately involve the cardiovascular system (Roy et al., 2014). Indeed, the activation of Toll-like receptor 4 (TLR4) and Nicotinamide adenine dinucleotide phosphate (NADPH) oxidase pathways by oxidized phospholipids in lungs may mediate a systemic cellular inflammatory response triggered by $PM_{2.5}$ (Kampfrath et al., 2011) and also, exposure markers of systemic inflammation and oxidative stress have been found in the blood of human patients and animal models after exposure to PM (Forbes et al., 2009).

The second pathway involves translocation of the PM directly into the systemic circulation resulting in direct effects in remote deposition sites, triggering endothelial dysfunction, PM-mediated reactive oxygen species (ROS), and systemic inflammation, all leading to the development of different risk factors (thrombosis, hypercoagulable state, hypertension, dyslipidaemia, T2DM, etc.) and progressive atrial remodelling that can lead to different cardiovascular outcomes (Long et al., 2020b; Brook et al., 2010b). This potential pathway was tested in a recent study using inhalation of gold particles in healthy volunteers, where these particles were detected in the blood within 15 min after initial exposure, and within 24 h all the volunteers had levels of particles in both blood and urine. At 3 months of follow-up, these particles were still present in the urine and blood of the participants (Miller and Newby, 2020).

The third biological pathway is the activation of lung autonomic nervous system reflex arcs driving to an autonomic dysfunction, triggering an increase of the heart rate, arrhythmias, blood pressure through a reduced parasympathetic activity and an increased sympathetic activity (Brook et al., 2010a). Nasal, bronchial, and pulmonary C-nerve fiber subtypes play a role in the response to air pollution through the activation of several receptors such as transient receptor potential ankyrin 1 (TRPA1) and transient receptor potential vanilloid 1 (TRPV1). These receptors act like sensors that initiate sensory nerve excitation, suggesting a sympathetic predominance (Taylor-Clark, 2020). Some studies also evidence that TRPA1 mediates pollution-evoked autonomic dysfunction in animals with cardiovascular diseases (Hazari et al., 2011). Moreover, air pollution exposure might promote electrical disturbances in the atria, and there is previous evidence that $PM_{2.5}$ levels are associated with relevant ECG predictors of AF (P-wave complexity and PR-duration) (Liao et al., 2011).

4. New-onset atrial fibrillation and exposure to PM

Through the mechanisms highlighted above, it is possible to hypothesize that PM may be implicated in the development of AF. Indeed, a large number of clinical studies have reported to date a relationship between AF and exposure to air pollutants, particularly $PM_{2.5}$.

Of note, studies showing the relationship between PM and AF are not limited to a particular region of the world, but evidence has been derived from all over the globe. These are summarized below and in Table 1.

4.1. North America

In this region, various studies observed a positive association between PM exposure and the development of AF. In the first study, patients were recruited between 2006 and 2010 in Boston, and the study evidenced that short exposure windows (2 h) to fine PM were associated with an increase in the risk of developing AF episodes, whereby the odds of AF increased by 26 % (95 % CI 8 %–47 %) for each 6.0 $\mu g/m^3$ increment in $PM_{2.5}$ in the 2 h before the event (Link et al., 2013). One Canadian study also investigated the relationship between ambient air pollution and the risk of AF in a population-based cohort between 2001 and 2015 (Shin et al., 2019). The study identified 313,157 incident cases of AF, showing a positive association between long-term exposure to $PM_{2.5}$ and the risk of AF (HR 1.07, 95 % CI 1.04–1.10; per 10 $\mu g/m^3$ of increase in $PM_{2.5}$) (Shin et al., 2019). A study including Medicare users from 2000 to 2016 determined that for each 1.0 $\mu g/m^3$ rise in annual exposure to $PM_{2.5}$, the risk of AF increased (HR 1.0059, 95 % CI 1.0054–1.0064), which was confirmed using a 3-year average $PM_{2.5}$ concentration (HR 1.0044, 95 % CI 1.0033–1.0054) (Jin et al., 2022).

On the other hand, one study conducted in Utah in 2011 examined 10,457 hospitalizations due to AF from 1993 to 2008 exploring air pollutants in concurrent days and up to 21 days, showing that a 10 $\mu g/m^3$ increase in lagged cumulative exposures to $PM_{2.5}$ was not significantly associated with a higher estimated relative risks of AF hospitalization (Bunch et al., 2011). However, a limitation of this study was that subclinical arrhythmia or short duration episodes were not recorded, and cannot exclude the association of subclinical AF and PM exposure (Bunch et al., 2011).

4.2. East and Central Asia

In Asia, several studies have also confirmed the association between exposure to the ambient air pollutants $PM_{2.5}$ or PM_{10} and the development of new-onset AF. Most concluded that an increase of 10 $\mu g/m^3$ for the concentration of PM results in a significant raise in the risk of incident AF.

In a study conducted in Beijing (China) with patients enrolled between 2012 and 2013, Liu et al. reported a significant association between $PM_{2.5}$ and PM_{10} and the risk of new-onset AF (OR 3.8, 95 % CI 1.4–6.2 and 2.7, 95 % CI 0.6–4.8; respectively) for each 10 $\mu g/m^3$ increase in patients with a cardiac implantable electronic device (Liu et al., 2018). Of note, they also described that multi-day exposure had stronger effects than single-day exposure and that such effects were higher in males (Liu et al., 2018). Likewise, a nationwide cross-sectional study among 1,374,423 Chinese individuals, an increase of 10 $\mu g/m^3$ in $PM_{2.5}$ (OR 1.031, 95 % CI 1.010–1.053) and PM_{10} (OR 1.021, 95 % CI 1.009–1.033) was positively associated with AF prevalence, and these associations were stronger in females, age < 65 years, and those with hypertension and diabetes (Sun et al., 2023).

Another study from Beijing reported 24,455 hospital admissions for AF between 2013 and 2017 (Amsalu et al., 2019). The authors found that a 10 $\mu g/m^3$ increase of $PM_{2.5}$ from the previous day to the current day (lag 0–1) associated with increases in hospital admissions for AF (0.29 %, 95 % CI 0.03–0.55 %) (Amsalu et al., 2019).

Kwon et al. examined both the short-term and long-term effects of air pollution on AF using a cohort of 1,011,638 participants randomly selected from South Korea (Kwon et al., 2019). The investigators reported that a 10 $\mu g/m^3$ increase in $PM_{2.5}$ was associated with a 4.5 % increase of the emergency visits for AF in three days; however, long-term exposure to air pollution did not affect the development of new-onset AF, but an analysis suggested that long-term effects of $PM_{2.5}$ in patients with heart disease were present (Kwon et al., 2019). On the contrary, another study from South Korea investigated the relationships between long-term exposures of air pollution and incident AF using a nationwide cohort (N = 432,587), and found that long-term exposures to air pollution were associated with the incidence of new-onset AF by 17.9 % (for $PM_{2.5}$) and 3.4 % (for PM_{10}) (Kim et al., 2019). This relationship was more prominent in older and obese subjects with hypertension or myocardial infarction, suggesting that subjects with AF risk factors were more sensitive to air pollution than those without risk factors for AF (Kim et al., 2019).

Similar results were described by Lee et al. in Taiwan, who analysed 670 patients with first-time AF hospitalization and the air quality related data in 77 monitoring stations from 2006 to 2011, and found a 8.6 % higher risk per 10 $\mu g/m^3$ increase in $PM_{2.5}$ (Lee et al., 2019). Additionally, a study from Shanghai assessed the association of PM and the incidence of different arrhythmias in patients with a remote ECG followed-up between 2014 and 2016. For AF, they demonstrated a lag effect of $PM_{2.5}$ at lag 2 (percentage of change: 0.59 %, 95 % CI 0.22–0.96 %), with the greatest effect on AF at lag 0–2 (percentage of change: 0.71 %, 95 % CI 0.18–1.25 %) (Yang et al., 2020). Finally, in a cohort of 15,171 inpatients from two Chinese hospitals from 2015 to 2020, a 10 $\mu g/m^3$ increase in $PM_{2.5}$ and PM_{10} on lag 0–4 days was associated with 2.81 % (95 % CI 1.44–4.20) and 1.67 % (95 % CI 0.77–2.59) increased hospitalizations for AF, respectively (Fang et al., 2021).

Table 1
Summary of studies regarding new onset AF in relation to PM.

Study	Design	Location	Sample size	Participants	Main results
Link et al. (2013)	Prospective observational study	USA	176	Patients with dual (atrial and ventricular) chamber ICD	AF incidence increased with the exposure to $PM_{2.5}$ (percent change): • 26 % (95 % CI 8–47) for each 6.0 μg/m^3 increase in mean $PM_{2.5}$ in the 2 h prior to the event. • 14 % (95 % CI 3–47) for each 5.0 μg/m^3 increase in mean $PM_{2.5}$ in the 24-h prior to the event.
Shin et al. (2019)	Retrospective observational cohort study	Canada	5,071,956	General population (age 35–85) free of AF or stroke	AF risk increased with the long-term exposure to $PM_{2.5}$ (hazard ratio): • 1.03 (95 % CI 1.01–1.04) for each interquartile range increase in mean $PM_{2.5}$
Jin et al. (2022)	Retrospective observational cohort study	USA	4,939,663	Medicare patients (aged ≥65) diagnosed with AF	AF risk increased with the exposure to $PM_{2.5}$ (hazard ratio): • 1.0059 (95 % CI 1.0054–1.0064) for each 1.0 μg/m^3 increase in mean annual $PM_{2.5}$ • 1.0044 (95 % CI 1.0033–1.0054) for 3-year average $PM_{2.5}$ concentration.
Bunch et al. (2011)	Case-crossover study	USA	10,457	Patients hospitalized for AF	Hospitalization for AF was not found to be significantly associated with PM exposure.
Liu et al. (2018)	Case-crossover study	China	100	Patients with CIEDs due to sick sinus syndrome, high-grade atrioventricular block, or sinus bradycardia	AF risk increased with the exposure to $PM_{2.5}$ or PM_{10} (odds ratio): • 3.8 (95 % CI 1.4–6.2) for each 10 μg/m^3 increase in mean $PM_{2.5}$ • 2.7 (95 % CI 0.6–4.8) for each 10 μg/m^3 increase in mean PM_{10}
Sun et al. (2023)	Cross-sectional study	China	1,374,423	General population (aged ≥35)	AF risk increased with the exposure to $PM_{2.5}$ or PM_{10} (odds ratio): • 1.031 (95 % CI 1.010–1.053) for each 10 μg/m^3 increase in mean $PM_{2.5}$ • 1.021 (95 % CI 1.009–1.033) for each 10 μg/m^3 increase in mean PM_{10}
Amsalu et al. (2019)	Ecological time-series	China	24,455	Patients hospitalized for AF	AF incidence increased with the exposure to $PM_{2.5}$ (percent change): • 0.29 % (95 % CI 0.03–0.55) for each 10 μg/m^3 increase in mean $PM_{2.5}$ at lag 0–1 prior to the event.
Kwon et al. (2019)	Retrospective observational cohort study	South Korea	1,011,638	General population	AF risk increased with the exposure to $PM_{2.5}$ (relative risk): • 1.045 (95 % CI 1.002–1.089) for each 10 μg/m^3 increase in mean $PM_{2.5}$ at lag 3 prior to the event.
Kim et al. (2019)	Retrospective observational cohort study	South Korea	432,587	General population	AF risk increased with the exposure to $PM_{2.5}$ or PM_{10} (hazard ratio): • 1.179 (95 % CI 1.176–1.183) for each 10 μg/m^3 increase in mean $PM_{2.5}$ • 1.034 (95 % CI 1.033–1.036) for each 10 μg/m^3 increase in mean PM_{10}
Lee et al. (2019)	Case-crossover study	Taiwan	670	General population	AF risk increased with the exposure to $PM_{2.5}$ (odds ratio): • 1.22 (95 % CI 1.03–1.44) for each interquartile range increase (26.2 μg/m^3) in mean $PM_{2.5}$ at lag 0 prior to the event.
Yang et al. (2020)	Retrospective observational cohort study	China	1,016,579	General population with remote electrocardiogram	AF incidence increased with the exposure to $PM_{2.5}$ (percent change): • 0.59 % (95 % CI 0.22–0.96) for each 10 μg/m^3 increase in mean $PM_{2.5}$ at lag 2 prior to the event. • 0.71 % (95 % CI 0.18–1.25) for each 10 μg/m^3 increase in mean $PM_{2.5}$ at lag 0–2 prior to the event.
Fang et al. (2021)	Ecological time-series	China	15,171	Patients hospitalized for AF	AF incidence increased with the exposure to $PM_{2.5}$ or PM_{10} (percent change): • 2.81 % (95 % CI 1.44–4.20) for each 10 μg/m^3 increase in mean $PM_{2.5}$ at lag 0–4 prior to the event. • 1.67 % (95 % CI 0.77–2.59) for each 10 μg/m^3 increase in mean PM_{10} at lag 0–4 prior to the event.
Vaduganathan et al. (2016)	Cross-sectional study	Italy	830	Patients hospitalized for AF	AF risk increased with the exposure to PM_{10} (relative risk): • 1.008 (95 % CI 1.003–1.012) for each standard deviation μg/m^3 increase in mean PM_{10} at lag 0 prior to the event.
Solimini and Renzi (2017)	Ecological time-series	Italy	79,892	General population	AF incidence increased with the exposure to $PM_{2.5}$ or PM_{10} (percent change): • 2.95 % (95 % CI 1.35–4.67) for each 10 μg/m^3 increase in mean $PM_{2.5}$ at lag 0–1 prior to the event.

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Table 1 (*continued*)

Study	Design	Location	Sample size	Participants	Main results
Gallo et al. (2020)	Retrospective observational cohort study	Italy	145	Patients with ICDs, CRT, or pacemakers	• 1.44 % (95 % CI 0.65–2.26) for each 10 μg/m^3 increase in mean PM_{10} at lag 0–1 prior to the event. AF risk increased with the exposure to $PM_{2.5}$ or PM_{10} (odds ratio): • 1.80 (95 % CI 1.34–2.40) for an increase of 50 μg/m^3 above the WHO threshold in mean $PM_{2.5}$ • 2.48 (95 % CI 1.44–4.28) for an increase of 50 μg/m^3 above the WHO threshold in mean PM_{10}
Dahlquist et al. (2020)	Randomized, controlled, non-blinded cohort study	Sweden	242	Elderly (age 75 and 76 years) individuals with a history of intermittent AF	AF risk increased with the exposure to PM_{10} (odds ratio): • 1.10 (95 % CI 1.01–1.19) for each interquartile range increase (7.8 μg/m^3) in mean $PM_{2.5}$ at lag 12–24 h prior to the event.
Andersen et al. (2021)	Retrospective observational cohort study	Denmark	23,528	Nurses free of prior AF	AF risk increased with the exposure to $PM_{2.5}$ (hazard ratio): • 1.09 (95 % CI 1.00–1.20) for each 3.9 μg/m^3 increase in 3-years mean $PM_{2.5}$.
Dahlquist et al. (2022)	Time-stratified case-crossover study	Sweden	91	Patients with CIED	AF risk increased with the exposure to $PM_{2.5}$ (odds ratio): • 1.05 (95 % CI 1.01–1.09) for each interquartile range increase in mean $PM_{2.5}$ at lag 48–72 h prior to the event. • 1.05 (95 % CI 1.00–1.10) for each interquartile range increase in mean $PM_{2.5}$ at lag 72–96 h prior to the event.

AF = atrial fibrillation; CIED = cardiac implantable electronic device; CRT = cardiac resynchronization therapy; ICD = implantable cardioverter-defibrillators; PM_{10} = particulate matter with an aerodynamic diameter of <10 μg/m^3; $PM_{2.5}$ = particulate matter with an aerodynamic diameter of <2.5 μg/m^3.

In summary, some of these studies describe that long-term exposure had stronger effects than single-day exposure (Liu et al., 2018; Sun et al., 2023; Kim et al., 2019; Lee et al., 2019; Yang et al., 2020; Fang et al., 2021), but other conclude that the exposure of PM in a short-time period had more effects than long-term exposure (Amsalu et al., 2019; Kwon et al., 2019).

4.3. Western Europe

In Western Europe, six studies identified an association between the exposure to PM and new-onset AF.

In 2016, Vaduganathan et al. studied the risk of cardiovascular hospitalizations in Italy derived from exposure to PM_{10} from 2004 to 2007, and observed that each standard deviation increase of μg/m^3 PM_{10} at lag 0-day was independently associated with higher rates of acute hospitalizations for AF (RR 1.008, 95 % CI 1.003–1.012) (Vaduganathan et al., 2016). Another study from Rome evaluated the association between air pollution and 79,892 patients admitted to emergency rooms because of AF during the period from 2001 to 2014 (Solimini and Renzi, 2017). They found that AF incidence increased 2.95 % (95 % CI 1.35–4.67) with the exposure to $PM_{2.5}$ and 1.44 % (95 % CI 0.65–2.26) with the exposure to PM_{10}, for each 10 μg/m^3 increase at lag 0–1 prior to the event with the associations being greater for older patients (≥75 years old) and in those patients with previous cardiovascular conditions (Solimini and Renzi, 2017).

A study conducted in the Northeast region of Italy including a cohort of patients followed in nine cardiology centers from 2011 to 2012 found that the odds of AF increased by 1.80-fold (95 % CI 1.34–2.40) for an increase of 50 μg/m^3 above the WHO threshold in mean $PM_{2.5}$ and by 2.48-fold (95 % CI 1.44–4.28,) for an increase of 50 μg/m^3 above the WHO threshold in mean PM_{10} (Gallo et al., 2020). Similarly, in a study conducted in Sweden, the relationship between short-term exposure to ambient air pollution and AF was examined in elderly patients with a history of intermittent AF episodes (Dahlquist et al., 2020). An increased risk of new-onset AF for each interquartile range increase in mean $PM_{2.5}$ at lag 12–24 h prior to the event was found (OR 1.10, 95 % CI 1.01–1.19), and this association was higher in overweighed subjects, and among participants with diabetes (Dahlquist et al., 2020). In Denmark, a study using the Danish Nurse Cohort assessed the relationship between long-term exposure to air pollution and incident AF (Andersen et al., 2021). During the follow-up, 1522 nurses developed AF and each 3.9 μg/m^3 increase in 3-years mean $PM_{2.5}$ was associated with higher risk of incident AF (HR 1.09, 95 % CI 1.00–1.20) (Andersen et al., 2021). Finally, one Sweden study aimed to estimate the association between short-term air pollution levels and risk of AF episodes among patients with intracardiac devices, and showed a higher risk of AF for each interquartile range increase in mean $PM_{2.5}$ at lag 48–72 or 72–96 h prior to the event (OR 1.05, 95 % CI 1.01–1.09 and OR 1.05, 95 % CI 1.00–1.10; respectively) (Dahlquist et al., 2022).

5. Adverse events in atrial fibrillation patients and relation to PM exposure

In contrast to the effect of PM on the incidence of AF, scarce data are available regarding the association of adverse events caused by PM exposure in patients with pre-existent AF. Four studies were identified reporting such an information, all of them demonstrating a positive association between ambient PM exposure and adverse events in AF patients.

Milojevic et al. reported a case-crossover study including all nationwide mortality data from 2003 to 2006, aimed to identify the short-term effects of air pollution on some cardiovascular events in England and Wales (Milojevic et al., 2014). During the follow-up, the study revealed a higher mortality in AF patients exposed to a 10th–90th centile change of $PM_{2.5}$ at lags 0–4 days (percentage of change: 21 %, 95 % CI 3.9–41 %) (Milojevic et al., 2014).

One study analysed the association between fine PM and the risk of stroke in a cohort of 31,414 AF patients from 2007 to 2015 and during a median follow-up time of 3.5 years, 1546 patients suffered an ischemic stroke, with an increased risk of stroke in AF patients residing in places with the highest quartile of 1-year mean $PM_{2.5}$ compared to the lowest quartile (HR 1.21, 95 % CI 1.01–1.45) (Rhinehart et al., 2020).

Similarly, another study of 1361 anticoagulated patients with AF reported a higher risk of ischemic stroke (aHR, 1.64; 95 % CI 1.28–2.09), major bleeding (aHR, 1.44; 95 % CI, 1.22–1.70) and mortality (aHR, 1.50; 95 % CI 1.34–1.69) for each 10 μg/m^3 increase in mean PM_{10} (Rivera-Caravaca et al., 2020).

Finally, a recent study from China recruited 155,616 patients diagnosed with acute ischemic stroke between August 2015 and December 2017, whereby 15,430 (≈10 %) patients had previous documented history of AF (Wang et al., 2022). The investigators found that a 10 μg/m^3 increase in $PM_{2.5}$ was associated with greater risk of stroke in individuals with AF, with the highest impact at lag 0–4 days prior to the event (OR 1.008, 95 % CI 1.002–1.014; per 10 μg/m^3 increase in $PM_{2.5}$) (Wang et al.,

2022). In elderly patients (age ≥ 65 years), the association was higher at lag 0–5 days prior to the event (OR 1.009, 95 % CI 1.002–1.015), while no significant results were shown in younger patients (aged <65) (Wang et al., 2022). In female patients, the highest risk of stroke was found at lag 0–5 days prior to the event (OR 1.010, 95 % CI 1.002–1.018), but no significant difference was observed in male patients (Wang et al., 2022) (Table 2).

In summary, these studies demonstrate that PM can also promote different adverse events in those patients suffering from AF, increasing the risk of stroke and even mortality.

6. Considerations and future perspectives

Beyond the well-known negative impact of pollution on the environment -reducing biodiversity and contributing to climate change- it has also become a major concern for public health. Air pollution (especially PM) increases the risk of respiratory infections, lung cancer, and cardiovascular diseases, including AF (Błaszczyk et al., 2023). Indeed, there is strong evidence demonstrating that exposure to PM (both $PM_{2.5}$ and PM_{10}) is a risk factor for AF. One systematic review in 2016 demonstrated a statistically significant association between AF development and $PM_{2.5}$, with a population-attributable risk of 0.89 (95 % CI 0.20–1.57) (Shao et al., 2016). In patients with an implantable cardioverter-defibrillator, a meta-analysis also found that a 10 μg/m^3 increase in $PM_{2.5}$ was associated with a 24 % (9 % CI 0.00–53.00) excess risk of AF (Yue et al., 2020).

Another systematic review and meta-analysis assessed the short- and long-term effects of ambient air pollution on AF. Using a random-effects model to estimate the excess risk (ER) percentage, the authors showed that for the short term, ER per 10 μg/m^3 increase was 1.8 % (95 % CI 0 %–3.7 %) for $PM_{2.5}$ and 1.1 % (95 % CI -0.2 %-2.4 %) for PM_{10} (Chen et al., 2021). Another systematic review and meta-analysis showed the underlying short-term exposure effects for each increase of 10 μg/m^3 in $PM_{2.5}$ and PM_{10} concentrations, which derived in an OR for AF of 1.01 (95 % CI 1.00–1.02), and 1.03 (95 % CI 1.01–1.05) (Yue et al., 2021), respectively. Regarding the long-term exposure effect for each increment of 10 μg/m^3 in the $PM_{2.5}$ concentration, the combined OR for AF was 1.07 (95 % CI 1.04–1.10); for PM_{10} it was 1.03 (95 % CI 1.03–1.04) (Yue et al., 2021). More recently, an umbrella review of systematic reviews and meta-analyses showed that few high-quality reviews evaluated the relationship of exposure to $PM_{2.5}$ or PM_{10} with AF, but they generally reported positive statistical associations (de Bont et al., 2022).

In the present review, we have encompassed all the previous evidence from 2000 to 2023 so that exposure to ambient PM independently of the period of exposure and the level, seems to increase the risk of new-onset AF by between 1.10 % (Dahlquist et al., 2020) and 3.80 % (Liu et al., 2018), per every 10 μg/m^3 rise in PM. Importantly, we show that there is evidence of this association among different geographical areas thus confirming that the link between PM and AF is independent of the region of the world. However, conflicting results were observed regarding the appropriate lag. For this reason, it is unclear what is the period of exposure to air pollution which may increase AF development. In addition, the level of PM that might lead to AF is uncertain, and it is not well described if the WHO threshold would apply or whether lower levels should be considered.

On the other hand, several studies included in this review suggest that the effect of PM is greater in subjects with traditional risk factors for AF (ie elderly, diabetes, hypertension, obese, coronary artery disease, etc.), so pollution could be a trigger in these patients. Therefore, patients and healthcare professionals should be aware of the effects of PM to prevent AF. For that reason, it is important to reduce PM emissions and to avoid exposure as much as possible, along with other risk factor management which will lead to a reduction of AF incidence.

Regarding the association of the exposure to PM and subsequent adverse events in patients with pre-existent AF, the evidence available is limited. Notwithstanding, PM is also a risk factor for mortality and stroke in AF patients. Despite the few studies investigating this issue, this is an important public health concern given how common AF is, and after exposure to air pollutants, these AF patients may have even an increased risk of suffering AF-related outcomes.

In light of the evidence shown in the present study, acting on pollution and the management of patients living in areas with increased levels of pollution requires special attention. Indeed, current guidelines on cardiovascular disease prevention provide for the first time some recommendations regarding air pollutants (Visseren et al., 2021). Patients at very high risk for cardiovascular diseases may be encouraged to avoid long-term exposure to regions with high air pollution; and opportunistic cardiovascular risk screening programs may be considered for people living in regions with long-term exposure to high levels of air pollution (both Class IIb, Level of

Table 2
Summary of studies regarding the risk of adverse events in patients with previous AF in relation to PM.

Study	Design	Location	Sample size	Participants	Results
Milojevic et al. (2014)	Case-crossover study	England (UK)	600,000	CVDs related deaths	Mortality rates in AF increased with the exposure to $PM_{2.5}$ (percent change): • 21 % (95 % CI 3.90–41.0) for a 10th–90th centile increase in mean $PM_{2.5}$ at lags 0–4 days.
Rhinehart et al. (2020)	Prospective observational cohort study	Pennsylvania (U·S)	31,414	Patients with previous AF	Ischemic stroke risk in AF increased with the exposure to $PM_{2.5}$ (hazard ratio): • 1.08 (95 % CI 1.03–1.14) for each standard deviation μg/m^3 increase in 1-year mean $PM_{2.5}$ • 1.21 (95 % CI 1.01–1.45) for the highest quartile of 1-year mean $PM_{2.5}$ compared to the first quartile. Ischemic stroke risk in AF increased with the exposure to PM_{10} (hazard ratio): • 1.64 (95 % CI 1.28–2.09) for each 10 μg/m^3 increase in mean PM_{10}
Rivera-Caravaca et al. (2020)	Retrospective observational cohort study	Murcia (Spain)	1361	Patients with previous AF	Major bleeding risk in AF increased with the exposure to PM_{10} (hazard ratio): • 1.44 (95 % CI 1.22–1.70) for each 10 μg/m^3 increase in mean PM_{10} All-cause mortality risk in AF increased with the exposure to PM_{10} (hazard ratio): • 1.50 (95 % CI 1.34–1.69) for each 10 μg/m^3 increase in mean PM_{10}
Wang et al. (2022)	Case-crossover study	China	15,430	Patients with previous AF	Ischemic stroke risk in AF increased with the exposure to $PM_{2.5}$ (odds ratio): • 1.008 (95 % CI 1.002–1.014) for each 10 μg/m^3 increase in mean $PM_{2.5}$ at lag 0–4 days prior to the event.

AF = atrial fibrillation; CVD = cardiovascular disease; PM_{10} = particulate matter with an aerodynamic diameter of <10 μg/m^3; $PM_{2.5}$ = particulate matter with an aerodynamic diameter of <2.5 μg/m^3.

recommendation C). In addition, policy interventions at the population level are suggested such as putting in place measures to reduce air pollution, including reducing PM emissions (Class I). Some of these measures may include encouraging the use of public transport use, reducing taxes on electric and hybrid cars and building houses and schools far away from the highways and polluting industries (Visseren et al., 2021).

7. Conclusions

Exposure to PM (either $PM_{2.5}$ or PM_{10}) is a risk factor for AF, as well as a risk factor for mortality and stroke in AF patients. Since the relationship between PM and AF is independent of the region of the world, more specific measures to prevent PM exposure should be adopted, and future clinical practice guidelines need to consider air pollution as a risk factor for both AF and adverse clinical outcomes.

Abbreviations

AF	Atrial Fibrillation
aHR	adjusted hazard ratio
CIED	Cardiac Implantable Electronic Devices
CI	Confidence Interval
CVD	Cardiovascular disease
ESC	European Society of Cardiology
HR	Hazard Ratio
ICD	Implantable Cardioverter Defibrillator
IL	Interleukin
IQR	Inter Quartile Range
IRR	Interaction Rate Ratio
NADPH	Nicotinamide adenine dinucleotide phosphate
NO_2	NitrogenDioxide
OR	Odds Ratio
PM	Particulate Matter
ROS	Reactive Oxygen Species
TLR4	Toll-like receptor 4
TNF	Tumor Necrosis Factor
TRPA1	Transient receptor potential ankyrin 1
TRPV1	Transient receptor potential vanilloid 1
WHO	World Health Organization

CRediT authorship contribution statement

Darío Mandaglio-Collados, Raquel López-Gálvez and José Miguel Rivera-Caravaca performed the search and selection of potential papers in appropriate databases, and drafted the manuscript. Raquel López-Gálvez and Antonio Ruiz-Alcaraz supervised and corrected the basic side of the review. Cecilia López-García and Vanessa Roldán critically revised the manuscript. Gregory Y.H. Lip and Francisco Marín conceived and supervised the study, and critically revised the manuscript. All authors read and approved the final version of the manuscript.

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Data availability

No data was used for the research described in the article.

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