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Air pollution and cardiovascular diseases

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Abstract: It is well known that air pollution is a major risk factor for non-infectious diseases and that it contributes more to global morbidity and mortality than all other known environmental risk factors collectively. Still, guidelines for the prevention of cardiovascular illnesses have almost exclusively concentrated on individual behavioral and metabolic risk factors, and pollution reduction has been overlooked in programs for the control of cardiovascular disease. This is a significant oversight since including pollution reduction into the prevention of cardiovascular disease could result in millions of lives being saved. The focus of this review is to try to summarize the evidence supporting a strong link between the risk of cardiovascular diseases and cardiovascular risk factors with air pollution through a spectrum of exposure levels, possible mechanisms that increase cardiovascular risk are described, and evidence supporting the effects of air pollution on cardiovascular health is investigated, and some knowledge gaps that could help improve the rising cardiovascular morbidity and mortality linked to air pollution are discussed.

Keywords: air pollution, non-infectious diseases, cardiovascular disease.

Introduction

The main cause of disability and death worldwide is cardiovascular disease. An estimated 18.6 million deaths worldwide and 957,000 deaths in the United States were caused by these diseases in 2019. (GBD 2019; Roth *et al*., 2019). In high-income countries, significant progress has been made in lowering the prevalence of cardiovascular disease and related mortality. It has proven crucial to identify risk factors in sizable, prospective, multiyear epidemiologic investigations, such as cigarette use, hypertension, dyslipidemia, physical inactivity, and diabetes (Roth *et al*., 2019). Understanding these risk factors has improved early identification, raised awareness of cardiovascular disorders, and directed therapy and prevention. Since 1950, the death rate in the United States from cardiovascular disease has decreased by more than 50% as a result of these developments (Ratcliff *et al*., 2021).

The evidence on the effects of ambient air pollution on cardiovascular diseases (CVDs) has grown significantly. It is commonly established that air pollution has a greater impact on global morbidity and mortality than all other known environmental risk factors combined, and that it is a significant risk factor for chronic non-communicable diseases (Al-Kindi *et al*., 2020).

Pollution

Pollution is the undesired materials that human activity releases into the environment. It is a significant but frequently disregarded risk factor for cardiovascular disease (Bevan *et al*., 2021). According to the Global Burden of Disease (GBD) study, pollution is thought to have caused 9 million deaths globally in 2019, with cardiovascular disease accounting for 61.9% of those deaths, including ischemic heart disease (31.7%) and stroke (27.7%). Because they are based on only a portion of environmental risk factors, these statistics, whatever great they may be, very probably understate the actual contribution of pollution to the worldwide burden of cardiovascular disease (Bevan *et al*., 2021).

Prior until recently, recommendations for the prevention of cardiovascular illnesses have mostly focused on a person's unique behavioural and metabolic risk factors, and efforts for the treatment of cardiovascular disease have paid little attention to pollution reduction (Varieur *et al*., 2022). Since including pollution reduction into the prevention of cardiovascular disease could result in the saving of millions of lives, this is a serious omission (Varieur *et al*., 2022).

Air Pollution

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Weather has a significant impact on air pollution since it is a complex combination that varies in quantity and composition depending on place and time (Varieur *et al*., 2022; Brook *et al*., 2010). It comprises both primary and secondary pollutants, such as ozone, which are produced in the atmosphere. Primary pollutants include nitrogen oxides (NOx), sulphur dioxide, and carbon monoxide, which are directly discharged into the air. Volatile and semivolatile organic aerosols, such as benzene, toluene, xylene, 1,3-butadiene, and polycyclic aromatic hydrocarbons, are additional components (Bevan *et al*., 2021).

Ambient (outdoor) and household (indoor) pollution are both types of air pollution. The burning of fossil fuels is the main cause of ambient air pollution. The main causes of ambient air pollution are pollutants that are emitted into the atmosphere by stationary sources like coal-fired power plants and steel mills as well as mobile sources like cars, trucks, and ships (Bevan *et al*., 2021).

Burning biomass fuels such wood, coal, straw, dung, and charcoal in home cook stoves primarily contributes to household air pollution in low-income countries, primarily affects women and children (Urrutia-Pereira *et al*., 2022). Natural gas combustion, wood-burning stoves, fireplaces, incense, candles, aerosol sprays, and volatile cleaning products are all causes of indoor air pollution in high-income countries. Inefficiently ventilated houses with poor design amplify household air pollution (Varieur *et al*., 2022).

The most well researched aspect of air pollution is particulate matter (PM), that has a number of significant health consequences (Regan *et al*., 2021). PM can be classified into coarse particles (aerodynamic-mass median diameter, <10 μm [PM10]), fine particles (<2.5 μm [PM2.5]), and ultrafine particles (<0.1 μm [PM0.1]). Numerous studies have also linked increased morbidity and mortality to gaseous pollutants, most notably ozone (Di, Q *et al*., 2017; Beckerman *et al*., 2012; Kim *et al*., 2020).

Air Pollution and Cardiovascular Disease

Air pollution has variable degrees of a consequence on cardiovascular disease around the world. Air pollution no longer kills as many people from cardiovascular disease as it used to in high-income countries because of the major reduction in pollution carried about by laws, regulations, and technological advances. Air pollution levels in the US have dropped by 70% since the Clean Air Act was adopted in 1970 (Hopkinson *et al*., 2019).

On the other hand, pollution is frequently hazardous and is getting worse in some regions in low- and middle-income countries. In many developing countries, the proportion of cardiovascular deaths linked to pollution is much greater than the proportion linked to smoking and other behavioral and metabolic risk factors (Krishna *et al*., 2017).

Short-term (from hours to days) alterations in PM2.5 levels are associated with increased risks of myocardial infarction, stroke, and cardiovascular death (Varieur *et al*., 2022; Peters *et al*., 2021). The probability of these events increases by 0.1% to 1.0% for each transient elevation in PM2.5 levels of 10 g/cm^3 (Varieur *et al*., 2022). There have also been dose-related increases in risk with nitrogen oxides (NOx) and sulphur oxides (SOx), although not usually with ozone, according to certain studies (Tonne *et al*., 2017; Zhao *et al*., 2022; Kazemiparkouhi *et al*., 2020).

Prospective cohort studies show a strong causal relationship between higher ischemic heart disease mortality and longer-term PM2.5 exposures (1 to 5 years). For every 10 g/cm3 increase in annual mean PM2.5 exposures, there are increases of 16 to 31% documented at a variety of concentrations (Crouse *et al*., 2012; Alexeeff *et al*., 2021; Shah et al., 2015). Increased risk of both atrial fibrillation and ventricular arrhythmias have been also linked to air pollution (Varieur *et al*., 2022; Zhang *et al*., 2021).

Cardiovascular Risk Factors and Air Pollution

Ambient PM2.5 pollution has a causal relationship with a number of cardiovascular disease risk factors, most notably diabetes and hypertension (Varieur *et al*., 2022; Bevan *et al*., 2021; Balti *et al*., 2017). Variations in vascular tone and elevated blood pressure have been linked to short-term increases in ambient PM2.5 levels and short-term experimental human

exposure to pollution (Bevan *et al*., 2021). On average, a rise in PM2.5 exposure of 10 µg per cubic millimetre the day before increases systolic and diastolic blood pressure by 0.5 to 1.0 mm Hg, with a broad range of effects and, in some persons, elevations as high as 5 to 10 mm Hg. The fact that long-term exposures are linked to an increased incidence of newly developed hypertension suggests that air pollution is an underestimated risk factor for the world's leading cause of death (Cai *et al*., 2016; Fuks *et al*., 2017; Tibuakuu *et al*., 2018; Jaganathan *et al*., 2022).

Chronic kidney disease development, left ventricular hypertrophy, increased carotid intima media thickness, coronary artery calcification, abdominal aortic calcification, susceptibility to atherosclerotic plaque formation, are all linked to long-term PM2.5 exposure (Liang *et al*., 2021; Kaufman *et al*., 2016; Bevan *et al*., 2021; Singh *et al*., 2020; Hicken *et al*., 2016; Bowe *et al*., 2019). Additionally, there is proof that links PM2.5 exposure to insulin resistance and type 2 diabetes from clinical, epidemiologic, and experimental trials (Varieur *et al*., 2022; Bevan *et al*., 2021; Le Glass *et al*., 2021). These links go all the way down to pollution concentrations beneath 5 g per cubic millimetre. Worldwide, it is estimated that airborne PM2.5 pollution causes 3.2 million new diagnoses of diabetes each year and 196,792 diabetes-related deaths (Bowe *et al*., 2018).

Household Air Pollution and CVD

One of the major sources of the health effects of global air pollution is household air pollution. According to the GBD study, household air pollution caused 2.6 million avoidable deaths worldwide in only 2016 alone. The term "household air pollution" refers to a variety of particles from various sources (GBD 2016). Depending on geographic, social, and cultural factors, the constitution of household air pollution can vary greatly. When people are indoors, they can breathe in up to 65% of the particles from outdoor air (Fisk et al., 2017).

In low- and middle-income countries, cooking and heating using biomass fuels may contribute to household air pollution levels (Rajagopalan *et al*., 2012). In developed countries, using gas stoves for cooking, lighting candles and incense, using aerosol sprays, and using cleaning supplies all cause indoor particle emission. During the winter, areas in the western United States where wood burning is prevalent may be exposed to high amounts of ultrafine particles. Evidence linking indoor air pollution to cardiovascular events is still developing, despite the fact that the link between lung cancer and respiratory outcomes is well known (Fisk *et al*., 2017; Yu, K *et al*., 2018).

Pathophysiology of Air Pollution on CVD

Mechanistic evidence from animal and experimental research supporting the link between air pollution exposure and CVD. Over the past ten years, the number of studies examining the processes underlying how air pollution affects CVD has significantly increased. The three most frequent starting mechanisms are direct particle translocation, autonomic nerve imbalance, and oxidative stress and inflammation. These pathways could trigger further pathways, including epigenomic alterations, endothelial dysfunction, thrombotic pathways, and stimulation of the hypothalamic-pituitary-adrenal axis (HPA). Although the mechanisms are different and may occur at various points of time and areas throughout the body, they are highly interrelated and their effects may eventually converge to raise the risk of CVD events (Al-Kindi *et al*., 2020).

Additionally, other pathways have similar intermediate endpoints for CVD that might result in atherosclerosis, arrhythmogenesis, elevated blood pressure, or increased arterial stiffness in variable degrees. The risk of experiencing specific CVD clinical events, such as cardiac arrest, IHD, heart failure, stroke, and ultimately CVD mortality, may be elevated as a result of all these. Depending on how long or in what order you are exposed to air pollution, numerous pathways may be activated (Brook *et al*., 2010). Short-term exposures may stimulate some pathways (such as autonomic imbalance), whereas long-term exposures may boost others (e.g., atherosclerosis). Overall, the impact on the pathways will be affected by the nature of the pollutant, the amount and length of exposure, the exact cardiovascular endpoints, and the condition of the individual's health (Brook *et al*., 2010).

Ischemic Heart Disease and Myocardial Infarction

Increased levels of air pollution may make the heart more susceptible to ischemic stress via a variety of mechanisms, according to controlled human exposure studies and toxicological research (De Bont *et al*., 2022; Regan *et al*., 2021; Mutlu *et al*., 2019). Experimental research conducted over the past few decades have demonstrated that breathing in PM2.5 for both short and long periods of time causes oxidative stress and systemic inflammation (De Bont *et al*., 2022; Regan *et al*., 2021). Oxidative stress is a condition in which the body's organs, including the lungs, vascular bed, and even local cellular and tissue levels, accumulate high levels of free radicals, reactive oxygen species (ROS), and reactive nitrogen species. The disruption of crucial redox-sensitive signalling pathways, the depletion of vasodilators and antioxidants, the perturbation of cellular mechanisms, and the oxidation of proteins and lipids are all believed to increase adverse biological effects (e.g., lipid/protein/deoxyribonucleic acid [DNA] oxidation and initiation of proinflammatory cascades) and may alter cardiac and vascular function. For instance, it has been demonstrated that PM2.5 lowers cardiomyocyte contractility and antioxidant capacity in mice (Wold *et al*., 2012). Vascular function and hemostasis are further affected by a cascade of molecular mechanisms that are triggered by both inflammation and oxidative stress (Mills *et al*., 2011). These experimental research have shown that a rise in PM was correlated with a rise in cellular and molecular markers of pulmonary and systemic inflammation, such as interleukin-6 and C-reactive protein, among others. The cytokine release can affect hemostasis and raise thrombosis risk (Mills *et al*., 2011). In both animal models and humans, nitrogen oxides have shown a similar reaction to that of PM, starting with pulmonary inflammation and inflammatory marker migration leading to systemic inflammation and oxidative stress, which can activate cells lining the blood vessels. However, it is still believed that there is little and conflicting evidence to support the NOx's biological plausibility. Overall, endothelial dysfunction, vasoconstriction, and coagulation are only a few of the pathological reactions that oxidative stress and systemic inflammation may cause. These reactions could raise the risk of IHD, MI, and other CVD events (July *et al*., 2020; Scheers *et al*., 2015). Moreover, short-term exposure to air pollution has been shown to increase blood viscosity, activate thrombotic reactions, and hypercoagulability in controlled human exposure and toxicological studies (Zou *et al*., 2021; Franchini *et al*., 2009). In both animal and human experimental trials, PM also results in impaired flow-mediated dilation, vasoconstriction, acute coronary obstruction, and ischemia, all of which have been proposed as potential mechanisms underlying cardiovascular morbidity, including IHD and MI. Experimental human and animal model research reveal that atherosclerotic plaque progression and alterations, as well as atherothrombotic events including MI and ischemic stroke, are related to exposure to air pollution (Mannucci *et al*., 2015).

Atherosclerosis and Arterial Stiffness.

The interactions between inflammation, plasma lipoproteins, endothelial activation, neutrophil attraction to the endothelium, extravasation, and lipid uptake can be used to explain the relationships between long-term exposure to air pollution and, specifically, atherosclerosis. Additionally, studies on both animals and humans have shown that both short- and long-term exposure to air pollution can result in persistent changes in vascular function, including an increase in arterial stiffness, a reduction in the conduit artery flow-mediated dilatation, inflammation, arteriolar dysfunction, and changes to the retinal arteries (Rajagopalan *et al*., 2021). Controlled short-term exposures to PM2.5 in human studies were linked to reduced brachial artery flow, elevated blood levels of the vasoconstrictor endothelin-1, and elevated levels of vascular endothelial growth factor, a marker for vascular injury (Liu *et al*., 2015; Andersen *et al*., 2017; Tong *et al*., 2015; Zhong *et al*., 2015). The effects of vascular remodelling may be explained by the long-term reduction of endothelial progenitor cells caused by air pollution (Ying et al., 2015; Wold *et al*., 2012). High PM concentrations have also been linked in both animal and human studies to increased plaque development and decreased plaque stability, which is consistent with these vascular effects. Generally, short-term changes in endothelial function may cause alterations in vascular tone and stiffness, but long-term changes may result in elevated cardiac afterload, diastolic

dysfunction, changes to coronary flow reserve, and left ventricular hypertrophy and fibrosis (Regan *et al*., 2021).

Other Suggested Pathways

Air pollution can affect HPA activation and might be a significant mechanism for CVD risk, according to recent research. Insulin resistance, white adipose inflammation, and brown adipose dysfunction may all increase with hypothalamic activation, but glucocorticoids may rise with adrenal axis activation (Rao *et al*., 2018; Liu *et al*., 2014). Epigenomic alterations might be connected to other pathways. According to various research, exposed over time to long-term ambient air pollution may exhibit unique connections with site-specific DNA methylation in purified monocytes. It is necessary to further study the conflicting data on long-term NO_2 exposure and genome-wide DNA methylation. Human observational studies have proposed that exposure to PM may affect blood DNA methylation loss, which may indicate the activation of proinflammatory processes in blood leukocytes (Chi *et al*., 2016; Lange *et al*., 2012; Lichtenfels *et al*., 2018). Several documented pathways for the onset and progression of CVD are supported by evidence from animal, experimental, and epidemiological studies investigating the effect of PM and NOx exposure on the risk of developing and death from CVD. The progressive reduction of biological and physiological processes associated with ageing may render the older population more vulnerable as a result, decreasing their resistance to exposure to air pollution. Populations predisposed to a higher risk for underlying disease processes exacerbations include those with pre-existing cardiovascular problems. According to their altered state of blood coagulability and metabolism, those with a greater body mass index may be at an increased risk of cardiovascular events after exposure to ambient air pollution (Murray *et al*., 2020).

Epidemiology of Air Pollution- Related CVD

Cardiovascular Deaths

Both low and high exposure levels to PM2.5 have been associated with cardiovascular death. The relationship between PM2.5 and cardiovascular mortality has been examined in a time series analysis that evaluated the hourly, daily, and monthly fluctuations in PM2.5 levels as causes of cardiovascular death (Brook *et al*., 2010; Pope *et al*., 2006). For instance, overall short-term rises in areas with modest daily exposure to PM2.5 (35 g/m3) correlate to a 0.3-1.0% rise in the relative risk of cardiovascular death per 10 g/m3 increase in PM2.5 (Lu *et al*. 2015).

Chronic exposure studies use cohort designs, often use annual PM2.5 values as the exposure, and monitor subjects over time to assess their long-term risk of cardiovascular mortality. One of the largest cohort studies on chronic pollution conducted in the USA to date, the American Cancer Society Study (involving 1.2 million people from 172 urban areas), found that each 10 g/m3 increase in PM2.5 was associated with a 15% relative increase in IHD deaths (Krewski *et al*., 2009). After an acute MI, continued exposure, even at low levels, appears to increase the risk of cardiovascular death. Long-term exposure to PM2.5 was linked to a lower quality of life and an increased 5-year mortality in a study of patients who had experienced a MI event (Chen *et al*., 2020). In comparison to PM2.5, the link between chronic ozone gas exposure and cardiovascular mortality is weak and milder than for other causes of death, such as COPD (Lim *et al*., 2019).

Atherosclerosis

Numerous longitudinal and cross-sectional epidemiologic studies have found a link between expected long-term exposure to PM2.5 and the prevalence of atherosclerosis in humans, as determined by the thickness of the carotid intima media, as well as the calcium levels in the coronary and abdominal aorta (Rajagopalan *et al*., 2018). A 5 g/m3 increase in long-term exposure to PM2.5 was related with a progression of coronary artery calcification (4.1 Agatston units each year), according to the Multi-Ethnic Study of Atherosclerosis and Air Pollution (Pal *et al*., 2020).

Hypertension

Men, Asians, and residents of high-pollution locations appeared to be more likely to experience a relationship between PM2.5 and blood pressure (BP) than other groups (Yang *et al*., 2018). Observational trials have clearly proven that exposure to PM (fine, coarse, and diesel exhaust) causes short-term elevations in

systolic blood pressure (SBP; 1–5 mmHg) and diastolic blood pressure (DBP; 1-3 mmHg) (Münzel *et al*. 2017, 2018). At least four meta-analyses have demonstrated a significant correlation between ambient PM2.5 concentrations and a rise in SBP of 1-3 mmHg. Long term exposure to PM2.5 has also been linked to incident hypertension and relatively greater elevations in blood pressure (Cai *et al*., 2016, Pedersen *et al*., 2014). Importantly, relationships between PM2.5 and hypertension have been seen in research from both nations with exceptionally high exposure to PM2.5 (China) and low levels of pollution (Canada and the USA), with no evidence that the response flattens with higher doses (Zhao *et al*., 2014). Air filtration has consistently been linked to lower blood pressure with less exposure to air pollution, according to small randomized control trials (Langrish *et al*., 2012; Shi *et al*., 2017; Morishita *et al*., 2018).

Rapid changes in autonomic tone that are made worse by endothelial dysfunction may be one of the pathways behind short-term BP rises (Langrish *et al*., 2013). DBP levels increased linearly in at least one human research after exposure to concentrated PM2.5 but not ozone gas, and this change was connected with alterations in indicators of autonomic function, including heart rate variability. The same study found no connection between inflammatory marker levels and BP variations, and endothelin activity and oxidative stress were both inhibited by vitamin C and the endothelin receptor antagonist bosentan, respectively, but this did not change the BP responsiveness to exposure to concentrated PM2.5. It is yet unclear if strict BP regulation can reduce the cardiovascular consequences of air pollution (Brook *et al*., 2009).

Acute Coronary Syndrome

A significant amount of research (case-crossover studies and time series) has linked PM2.5 exposure to an increased risk of a non-fatal MI. A higher risk is observed in patients who have angiographic evidence of coronary artery disease, according to the data, which is stronger for ST segment elevation MI (STEMI) than for non-STEMI. These relationships remain true regardless of sociodemographic characteristics (Pope *et al*., 2006; Weaver *et al*. 2019).

Insulin Resistance and Diabetes

There is a lot of research that links PM2.5 inhalation to the development of insulin resistance and diabetes, including both animal and human studies (Tang *et al*., 2020; Rajagopalan *et al*. 2012). Each 10 g/m3 rise in PM2.5 was shown to be associated with a 10% relative increase in incident diabetes in a meta-analysis of 13 published studies, with some data suggesting a higher link in women. Another meta-analysis of eleven studies found that the chance of developing diabetes increased by 39% with every 10 g/ m3 increase in long-term exposure to PM2.5. This connection maintained even at very low levels of exposure. Additionally, a 49% rise in the risk of diabetes-related mortality was linked to every 10 g/m3 increase in PM2.5 exposure. Ambient PM2.5 has been linked to 206,105 diabetes-related deaths worldwide, and roughly 3.2 million incident cases of diabetes (Eze *et al*., 2015; Wang *et al*., 2014; Brook *et al*., 2013; Bowe *et al*., 2018).

Inflammation in brown and white adipose tissue, insulin resistance in skeletal muscle, inflammation in hepatic tissue, and inflammation in the hypothalamus of the central nervous system may all play a role in the mechanisms underlying the development to insulin resistance and diabetes. A role for pulmonary oxidative stress in facilitating pollution- induced insulin resistance has also been suggested, considering that treatment with the antioxidant tempol or lung- specific overexpression of the endogenous antioxidant extracellular superoxide dismutase stopped vascular insulin resistance and inflammation caused by exposure to concentrated PM2.5 (Tang *et al*., 2020; Rajagopalan *et al*., 2012; Haberzettl *et al*., 2016).

Arrhythmias

In people with an automated implantable cardioverter-defibrillator (ICD), several studies have established a link between air pollution and ventricular arrhythmias (Rich *et al*., 2006; Folino *et al*., 2017; Shao *et al*., 2016).Exposure to PM2.5 was linked to an increased risk of ventricular tachycardia or ventricular fibrillation in a 2017 study involving patients with left ventricular dysfunction (mean left ventricular ejection fraction of 35%) and an automated ICD or ICD plus cardiac resynchronization therapy device, with patients with a prior MI appearing to

be most at risk. Furthermore, each 10 g/m3 increase in PM2.5 was linked to a rise in the relative risk of atrial fibrillation of 0.89% in a meta-analysis of four studies including more than 450,000 people (Folino *et al*., 2017; Shao *et al*. 2016).

Heart failure

A meta-analysis of 35 studies found that the risk of heart failure hospitalizations or mortality increased by 2.1% for every 10 g/m3 increase in short-term exposure to PM2.5, with the highest effects found on the exposure day (Shah *et al*, 2013). Based on these findings, the researchers hypothesized that a reduction in PM2.5 of 3.9 g/m3 would prevent 7,978 heart failure hospitalizations annually in the USA, saving around US$300 million annually (Shah *et al*. 2013). Furthermore, each 1 g/m3 increase in PM2.5 was linked to an increased risk of acute heart failure in a research comprising 136,094 Seoul, South Korea residents without CVD who were followed up for a median of 7 years (with mean personal exposure PM2.5 levels of 25.6 g/m3). The sensitivity of patients with ischemic or non-ischaemic heart failure to air pollution levels has not yet been studied (Kim *et al*. 2017).

Peripheral Arterial Disease

Several studies have found that endothelial function is impaired by acute exposure to PM2.5. Brachial artery flow-mediated dilatation was frequently used in human research as a marker for endothelial dysfunction. There are few population-based studies investigating the link between chronic exposure to PM2.5 and the prevalence of peripheral artery disease. According to one study, hospital admissions for peripheral artery disease increased by 0.26% and 4.40% , respectively, for every 10 g/m3 increase in acute and chronic exposure to PM2.5 (Kloog 2016) . An increased prevalence of both low and high ankle-brachial indexes was linked to a 5th to 95th percentile increase in exposure to PM2.5 in a population-based study conducted in Germany with 4,544 participants (Zhang *et al*. 2018).

Venous Thromboembolism

There are few and conflicting studies examining the link between venous thromboembolism and exposure to PM2.5. PM2.5 levels (per 10 ug/m3) were linked to an increased risk of both DVT (0.63% for short-term exposure and 6.98% for long-term exposure) and pulmonary embolism (0.38% for short-term exposure and 2.67% for long-term exposure) in a study involving 453,413 hospital admissions for deep-vein thrombosis (DVT) and 151,829 hospital admissions for pulmonary embolism. This association needs to be confirmed by additional research (Kloog et al., 2013).

Cerebrovascular Disease

The risks of stroke (short-term or long-term) and death from stroke (short-term) were found to increase with exposure to PM2.5 (per 10 g/m3 increments) in a 2019 meta-analysis of 80 studies from 26 countries. The links with ischemic and hemorrhagic stroke were strongest. The risk of dementia, Alzheimer disease , and Parkinson disease were all elevated by long-term exposure to PM2.5. These risks were comparable to those observed in a previous meta-analysis of 103 studies, which discovered a relative risk increase of 1.1% for stroke or death from stroke for every 10 g/m3 rise in PM2.5, with the greatest risk on the exposure day. The Women's Health Initiative study indicated that long-term exposure to PM2.5 in the USA was associated with some of the highest estimated risks of stroke and mortality from cerebrovascular diseases, with relative increases of 35% and 83%, respectively, per 10 g/m3 increase. The mechanisms underlying the link between PM2.5 and cerebrovascular diseases are probably similar to those underlying the link between MI and coronary artery disease (Fu *et al*., 2019; Nhung *et al*., 2017; Miller *et al*. 2007).

Conclusion

The acknowledgment of pollution as a serious cardiovascular risk factor which is frequently neglected clinically creates numerous chances for prevention and treatment. Evidence-based national strategies for the prevention of pollution related cardiovascular diseases should be adopted. As a part of a complex network of factors, air pollutants frequently coexist with other pollutants and exposures . We still don't completely understand the separate and maybe combined (or synergistic) cardiovascular effects that these various exposures cause, which needs more researches. Personal and governmental protective strategies should be established to prevent pollution related cardiovascular diseases.

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