



# The Impact of Meteorological Factors and Air Pollutants on Acute Coronary Syndrome

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## Abstract

**Purpose of Review** Several studies have found that air pollution and climate change can have an impact on acute coronary syndromes (ACS), the leading cause of death worldwide. We synthesized the latest information about the impact of air pollution and climate change on ACS, the latest data about the pathophysiological mechanisms of meteorological factors and atmospheric pollutants on atherosclerotic disease, and an overall image of air pollution and coronary heart disease in the context of the COVID-19 pandemic.

**Recent Findings** The variation of meteorological factors in different seasons increased the risk of ACS. Both the increase and the decrease in apparent temperature were found to be risk factors for ACS admissions. It was also demonstrated that exposure to high concentrations of air pollutants, especially particulate matter, increased cardiovascular morbidity and mortality.

**Summary** Climate change as well as increased emissions of air pollutants have a major impact on ACS. The industrialization era and the growing population cause a constant increase in air pollution worldwide. Thus, the number of ACS favored by air pollution and the variations in meteorological factors is expected to increase dramatically in the next few years.

**Keywords** Acute coronary syndrome · Coronary heart disease · Meteorological factors · Air pollutants · Risk factors

## Introduction

Cardiovascular diseases represent the main cause of morbidity and mortality globally, being responsible for important medical costs, despite the improvement of prevention and management measures [1, 2]. In 2016, almost a third of all deaths on the planet were caused by cardiovascular

diseases, with the prediction for 2030 being that this number will increase to 23 million [3, 4].

Acute coronary syndrome (ACS) is the clinical manifestation of coronary artery disease and includes acute myocardial infarction with/without ST-segment elevation (STEMI/NSTEMI) and unstable angina (UA). According to the Global Registry of Acute Coronary Events (GRACE Registry), STEMI represents 36% of all acute coronary events [5]. A similar percentage of STEMI cases has been reported by the Jakarta Acute Coronary Syndrome Registry (JAC Registry) [6]. Fortunately, the number of STEMI has significantly decreased since 1999 (133/100,000 people/years) up to 2008 (50/100,000 people/years), as was shown in a large US database [7]. At the same time, the proportion of patients with NSTEMI has increased from a third to more than half between 1995 and 2015 [8].

Besides the well-known risk factors for atherosclerosis (family history of ischemic heart disease, male gender, old age, smoking, dyslipidemia, high blood pressure, diabetes, etc.), more and more evidence shows that air pollutants and climate variations can influence the onset of ACS [9]. In the context of global warming, an important increase in cardiovascular mortality due to heat has been observed [10]. In 2017, the average global temperature increased by

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0.46 (+/−0.1 °C) above the 1981–2010 average and by 1.1 (+/−0.1 °C) above preindustrial levels [11]. Air temperature, which is the most studied climatic factor over the past years, seems to have a major impact on human health. During the last decades, climatic and epidemiological data have shown a disquieting increase in possibly harmful environmental effects on cardiovascular health. For the first time, an increase in the number of acute myocardial infarctions (AMI) during the winter months was reported at the beginning of the 1930s [12].

The relation between the degree of air pollution and the rate of early cardiovascular mortality was postulated as early as the beginning of the twentieth century, when the first extreme episodes of air pollution caused by industrial smog were reported [13, 14].

The extreme variation of meteorological factors and the concentration of air pollutants above the accepted limit may represent an important risk factor for decompensating coronary artery disease. This review offers the latest information about the impact of air pollution and climate change on ACS, the latest data about the pathophysiological mechanisms of meteorological factors and atmospheric pollutants on atherosclerotic disease, as well as an overall image of air pollution and coronary heart disease (CHD) in the context of the COVID-19 pandemic.

## The Impact of Meteorological Factors on Acute Coronary Syndrome

Acute myocardial infarctions cause more than 4 million deaths in Europe and North Asia and more than 2.4 million deaths in the USA [15]. Several epidemiological studies showed that the incidence of ACS was significantly higher in winter than in other seasons, as well as on days with heavy snowfall [16]. A study conducted in the USA reported a 53% increase in AMI cases in the winter months [17]. Likewise, an increase in cardiovascular and cerebrovascular mortality was observed among elderly patients in Canada during the cold season [18]. Data from studies performed in France, New Zealand, Japan, England, and Wales also reported an increase in the morbidity and mortality of CHD in the winter months [19–22]. In other countries with a Mediterranean climate, an increase in the number of acute coronary events was also observed in the cold season [23, 24]. Similar to the data reported in Europe and North America, a seasonal variation in cardiovascular mortality was observed in Brazil [25]. Yamaji et al. showed that low ambient temperatures can be a major risk factor for AMI, while air pollution and flu epidemics had a statistically insignificant impact [26]. The increased incidence of ACS in the winter months could be explained by intense physical activity due to “shoveling” on days with heavy snow [16]. Another possible cause was described by Kloner as the so-called “Merry Christmas

coronary” phenomenon, which is a mixture of circumstances such as late hospitalization, excessive alcohol and food consumption, and the increased emotional stress associated with the holidays [27].

In the context of global warming, heat has proven to be another risk factor for ACS. A small number of epidemiological data revealed that the incidence of ACS increased during the summer, on days with high temperatures, high relative humidity, and low atmospheric pressure [28–30]. Madrigano et al. reported that heat exposure increased the incidence and mortality of acute coronary events as a consequence of low socio-economic status, low level of education, and pre-existing chronic diseases (diabetes, dyslipidemia, etc.) [29, 31].

Aside from seasonal variations, epidemiological studies have looked at the relationship between ACS and various meteorological parameters like air temperature, atmospheric pressure, air humidity, wind speed, precipitation, and light. A “V,” “U,” “J” or linear-shaped correlation was observed between ischemic cardiac events and ambient temperature [24, 32–35]. The risk of acute coronary events increased by 22% when the temperature threshold of 26–29 °C was exceeded and increased by 2.8% for each decrease of 1 °C below this threshold [32].

The impact of atmospheric pressure on ACS is confusing. Several studies reported a “V”- or “J”-shaped relationship between atmospheric pressure and the incidence of AMI, while other studies did not identify significant effects of this parameter. The number of ACS was significantly higher with increasing or decreasing atmospheric pressure above or below 1016 mbar in France [19]. On the other hand, a significant increase in AMI admissions was observed on days with low atmospheric pressure in Japan and Canada [36, 37]. A recent study in Hiroshima, Japan, reported a higher incidence of ACS on days with an air pressure below 1005 hPa, while another study conducted also in Japan, in Kumamoto, reported an increase in ACS on days with high atmospheric pressures [36, 38]. Bijelović et al. observed a reduction in AMI cases on days with an atmospheric pressure below 1009 hPa, adjusted for air temperature and humidity [39].

Unlike air temperature and atmospheric pressure, which have been intensively studied so far, the impact of air humidity, wind speed, and precipitation on AMI hospitalizations has not been extensively investigated. The relationship between air humidity and CHD is unclear. A study conducted in 12 US cities found no correlation between atmospheric humidity and CHD hospitalizations, while a positive correlation between the incidence of ACS and relative humidity was reported in Athens, Greece [35, 40]. High wind speeds were associated with an increased incidence of AMI in Switzerland [41, 42]. In Italy, a significant impact of the variation of meteorological factors in different seasons on

the STEMI incidence was reported. STEMI risk was higher in certain meteorological conditions during the winter (on days with low temperatures, low atmospheric pressures, and low rainfall), spring (on days with high humidity and large variations in air pressure), and summer (on days with high temperatures) [43]. The SWEDEHEART registry reported an increased risk of ACS on days with low temperatures, low atmospheric pressure, decreased sunshine duration, and increased wind speed [44]. Other studies that analyzed the impact of air temperature on ACS types reported statistically significant results in terms of the incidence of STEMI, with no influence on the number of NSTEMI cases. A report from Israel showed an increase in STEMI cases in the winter season, while research from Japan showed that both the high peak temperature and the low average temperature the day before the acute coronary event caused a high incidence of STEMI [26, 45].

It was observed that air temperature alone does not accurately describe human thermal discomfort. Apparent temperature, a biometeorological index proposed by Steadman, seems to characterize more objectively the human perception of atmospheric temperature. This index is characterized by a combination of meteorological factors such as ambient temperature, humidity, and, optionally, solar radiation and wind speed [46, 47]. A few studies have analyzed the association between apparent temperature and the incidence of ACS, and the results have varied. In Iran, Moghadamnia et al. showed an increase in the number of ACS on days with a high apparent temperature, while Wichmann et al. identified that an increase in  $T_{app,max}$  (the daily 3-h maximum apparent temperature) was associated with a decrease in the incidence of AMI in the cold months [48, 49]. In Beijing, China, the number of STEMI cases increased on days with a high apparent temperature, while the incidence of NSTEMI was higher on days with a low apparent temperature [50••]. These data demonstrate the need for new studies to assess the impact of apparent temperature on the incidence of ACS subtypes in order to improve prevention measures and reduce cardiovascular mortality. The main studies that analyze the impact of seasonal variations and meteorological factors on ACS are summarized in Table 1.

## Pathophysiological Mechanisms of Meteorological Factors

Studies that analyzed the relationship between the season and the type of atherosclerotic plaque have reported that both cold and heat are risk factors for atheroma destabilization. In winter, the acute coronary event occurred due to rupture of the atheroma plaque, while in summer, the main cause was plaque erosion [51, 52]. Regarding the size of myocardial infarction, the summer months appear to be

associated with less extensive myocardial infarction, probably due to vasodilation, low preload and postload, low stimulation of the sympathetic nervous system, and low plasma catecholamine levels [53]. It was observed that a decrease in atmospheric temperature causes an increase in the activity of the sympathetic nervous system, resulting in an increase in blood pressure and heart rate [54]. The same physiological response is generated by the increase in serum catecholamines (vasoconstrictor effect) due to the stimulation of cold receptors in the skin [55]. Exposure to extremely low temperatures has prothrombotic and proinflammatory effects that promote atherothrombosis and the destabilization of already formed atheroma plaques [56, 57]. The cumulative action of these factors generates an imbalance between the need for and the supply of oxygen to the myocardium in the conditions of a pre-existing atherosclerotic disease, substantially increasing the risk of an acute coronary event in susceptible people. Heat, like low temperatures, increases blood viscosity, lipoprotein oxidation, and cholesterol deposits in blood vessel walls [58]. In people at risk of developing ACS, extreme heat can induce a systemic inflammatory response along with dehydration and vasodilation [54].

The mechanism by which changes in atmospheric pressure cause ACS is also controversial. Decreased air pressure causes an exaggerated response of the sympathetic nervous system and decreased oxygen saturation in the arterial blood [19, 59]. An *in vitro* study published in 2016 showed that epidermal keratinocytes play a major role in the body's response to sudden changes in atmospheric pressure. Reduced variations in air pressure by 5–20 hPa resulted in an increase in calcium influx into human keratinocytes. According to this research, the sudden change in atmospheric pressure stimulates the keratinocytes in the epidermis that synthesize nitric oxide (with a vasodilating role) and other hormones and neurotransmitters with an important role in the cardiovascular, nervous, immune, and endocrine systems [60]. High humidity causes dehydration and increased mental stress, while reduced sun exposure has been associated with vitamin D deficiency, depressive episodes, and a sedentary lifestyle [59]. The pathophysiological mechanisms by which meteorological factors can destabilise ACS are summarized in Fig. 1a.

## The Impact of Air Pollution on Acute Coronary Syndrome

Air pollution can be a key risk factor for ACS. Air pollution is currently the most important risk factor for global environmental health, with an estimated 3.7 million deaths per year due to outdoor air pollution and 4.3 million deaths per year due to exposure to indoor air pollution [61]. Up to 58%

**Table 1** Main studies that analyze the role of seasonal variations and meteorological factors on acute coronary syndrome

Seasonal variations and cardiovascular morbidity and mortality					
Author	Location/type of climate	Study period	Study population	Season with effect on ACS/Death	Result
Auger et al. [16]	Quebec (Canada)/continental climate	1981–2014	Patients with MI	Winter	Quantity and duration of snowfall ↑ risk of AMI admissions or death due to MI
Spencer et al. [17]	US cities/temperate climate	1994–1996	Patients with AMI	Winter	↑ risk of AMI
Sheth et al. [18]	Canada cities/continental climate	1980–1982 1990–1992	Patients with AMI and Stroke	Winter	↑ AMI and stroke mortality
Danet et al. [19]	Northern France/temperate climate	1985–1994	Patients with MI	Winter	↑ risk of MI and coronary deaths
Swampillai et al. [20]	Waikato (New Zealand)/temperate climate	1998–2007	Patients with STEMI	Winter	↑ risk of STEMI
Rumana et al. [21]	Takashima County, Shiga (Japan)/temperate climate	1998–2003	Patients with AMI	Winter, Spring	↑ risk of AMI
Ogbebor et al. [22]	England and Wales/temperate climate	1997–2005	Patients with AMI	Winter	↑ risk of AMI admissions and death due to MI
Vasconcelos et al. [23]	Lisbon and Oporto, (Portugal)/Mediterranean climate	2003–2007	Patients with AMI	Winter	↑ risk of AMI
Dilaveris et al. [24]	Athens (Greece)/Mediterranean climate	2001	Patients with AMI	Winter	↑ AMI mortality
Sharovsky et al. [25]	Sao Paulo (Brazil)/subtropical climate	1996–1997	Patients with MI	Winter	↑ AMI mortality
Yamaji et al. [26]	Japan/temperate climate	2011–2012	Patients with STEMI	Winter	↑ risk of STEMI
Akioka et al. [28]	Oita (Japan)/humid subtropical climate	2012–2013	Patients with AMI	Summer	↑ risk of AMI
Chen et al. [29]	Augsburg (Germany)/oceanic climate	1987–2014	Patients with MI	Summer	↑ risk of MI
Nastos et al. [30]	Crete Island (Greece)/Mediterranean climate	2004–2007	Patients with ACS	Summer	↑ risk of ACS
Madrigano et al. [31]	Worcester (USA)/humid continental climate	1995, 1997, 1999 2001, 2003	Patients with AMI	Cold months Warm months	↑ risk of AMI ↑ the risk of dying after an AMI
Versaci et al. [43]	Different regions of Italy with different types of climate	2012–2017	Patients with STEMI	Winter (↓ air temperature, ↓ ATM, ↓ rainfall) Spring (greater variations in ATM, ↑ humidity) Summer (↑ air temperature)	↑ risk of STEMI
Leibowitz et al. [45]	Jerusalem (Israel)/Mediterranean climate	2001–2005	Patients with AMI	Winter	↑ risk of STEMI

Table 1 (continued)

## Meteorological factors variations and cardiovascular morbidity and mortality

Author	Location/type of climate	Study period	Study population	Meteorological factors with effect on ACS/Death	Result
Danet et al. [19]	Northern France/temperate climate	1985–1994	Patients with MI	↓Atmospheric temperature <sup>a</sup> ↑/↓Atmospheric pressure <sup>b</sup>	↑ risk of MI and coronary deaths
Yamaji et al. [26]	Different regions of Japan with different types of climate	2011–2012	Patients with STEMI	↓Air temperature (Winter) ↓Minimum air temperature ↑ Maximum air temperature	↑ risk of STEMI
Akioka et al. [28]	Oita (Japan)/humid subtropical climate	2012–2013	Patients with AMI	↓Air temperature (Summer) ↑ Air humidity (Summer)	↑ risk of AMI
Pan et al. [32]	Taiwan (China)/subtropical climate	1981–1991	Patients with CHD	↑/↓ Ambient temperature <sup>c</sup>	↑ CHD mortality
Liang et al. [33]	Taiwan (China)/subtropical climate	2000–2003	Patients with ACS	↑/↓ Ambient temperature <sup>d</sup>	↑ risk of ACS
Guo et al. [34]	Yancheng (China)/humid subtropical climate	2013–2018	Patients with ACS	↑/↓ Ambient temperature <sup>e</sup>	↑ risk of ACS
Panagiotakos et al. [35]	Athens (Greece)/Mediterranean climate	2001–2002	Patients with ACS	↓ Air temperature <sup>a</sup> ↑ Relative humidity	↑ risk of ACS
Wang et al. [36]	Yamaguchi, Matsue, Tottori, Okayama, Hiroshima (Japan)/humid subtropical climate	2000–2005 1993–2002	Patients with AMI	↓Air temperature ↓Atmospheric pressure	↑ risk of AMI
Hong et al. [37]	Alberta (Canada)/humid continental climate	2002–2016	Patients with STEMI	↓Air pressure	↑ risk of STEMI
Honda et al. [38]	Kumamoto (Japan)/humid subtropical climate	2009–2013	Patients with AMI	↑ Air pressure ↓Air temperature ↓Air humidity ↑ Sunshine duration	↑ risk of AMI
Bijelović et al. [39]	Novi Sad (Serbia)/humid subtropical climate	2010–2011	Patients with CVD	↓Air temperature ↓Relative humidity ↓Air pressure	↑ risk of AMI ↓ risk of AMI
Goerre et al. [42]	Different regions of Switzerland with different types of climate	1990–1994	Patients with AMI	↑Ambient pressure ↑Wind activity	↑ risk of AMI
Mohammad et al. [44]	Sweden/temperate climate	1998–2013	Patients with MI	↓Air temperature ↓Atmospheric air pressure ↑Wind velocity ↓Sunshine duration	↑ risk of MI
Moghadamnia et al. [48]	Rasht (Iran)/humid subtropical climate	2005–2014	Patients with ACS	↑Apparent temperature	↑ risk of ACS

**Table 1** (continued)

Meteorological factors variations and cardiovascular morbidity and mortality					
Wichmann et al. [49]	Copenhagen (Denmark)/oceanic climate	1999–2006	Patients with AMI	↑ $T_{app_{max}}$ (in the cold period)	↓ risk of AMI
Li et al. [50••]	Beijing (China)/monsoon-influenced humid continental climate	2017–2019	Patients with ACS	↑ Apparent temperature ↓ Apparent temperature	↑ risk of STEMI ↑ risk of NSTEMI

ACS acute coronary syndrome, MI myocardial infarction, AMI acute myocardial infarction, STEMI ST-elevation myocardial infarction, ATM atmospheric pressure, CHD coronary heart disease, CVD cardiovascular disease,  $T_{app_{max}}$  daily 3-h maximum apparent temperature

<sup>a</sup>A linear association between air temperature and ACS admissions

<sup>b</sup>A V-shaped relation between atmospheric pressure and MI: ↑/↓ atmospheric pressure over/below 1016 mbar ↑ risk of MI

<sup>c</sup>A U-shaped relation between ambient temperature and CHD mortality: ↑/↓ air temperature over/below 26–29 °C ↑ CHD mortality

<sup>d</sup>A U-shaped relation between ambient temperature and ACS admissions: ↑/↓ air temperature over/below 27–29 °C ↑ ACS admissions

<sup>e</sup>An inverse J-shaped relation between ambient temperature and ACS admissions: ↑/↓ air temperature over/below temperature threshold (25 °C) ↑ ACS admissions

of premature deaths related to outdoor air pollution occurred in people with a history of CHD and stroke [62].

Indoor air pollution is mainly generated by the household combustion of fuels [63]. A recent study reported that the low socio-economic level and the lack of basic household utilities for cooking and daily heating have contributed to the increase in the total number of diseases due to air pollution to about 3 billion [64]. Most outdoor air pollutants come from industry, transportation, agriculture, power, and heating generation devices [63].

Atmospheric air pollution is caused by gaseous pollutants (sulfur dioxide, SO<sub>2</sub>; nitrogen dioxide, NO<sub>2</sub>; ozone, O<sub>3</sub>; carbon monoxide, CO) and fine or ultrafine particulate matter (particulate matter with a diameter ≤ 10 μm, PM<sub>10</sub>; particulate matter with a diameter ≤ 2.5 μm, PM<sub>2.5</sub>; particulate matter with a diameter ≤ 0.1 μm). The sources of air pollution are varied: NO<sub>2</sub> is a pollutant emitted primarily by exhaust fumes; SO<sub>2</sub> is generated by vehicles as well as by fossil fuel combustion; ground level ozone (O<sub>3</sub>) is a pollutant emitted by transport systems and industrial systems, with high concentrations on sunny days; CO is produced by incomplete combustion of fuels; PM results from natural processes, transportation systems, as well as fossil fuel combustion [62, 63].

A marked increase in cardiovascular morbidity and mortality due to short-term or long-term exposure to air pollutants was reported. On the other hand, there are few epidemiological studies that have assessed the impact of air pollution on ACS subtypes.

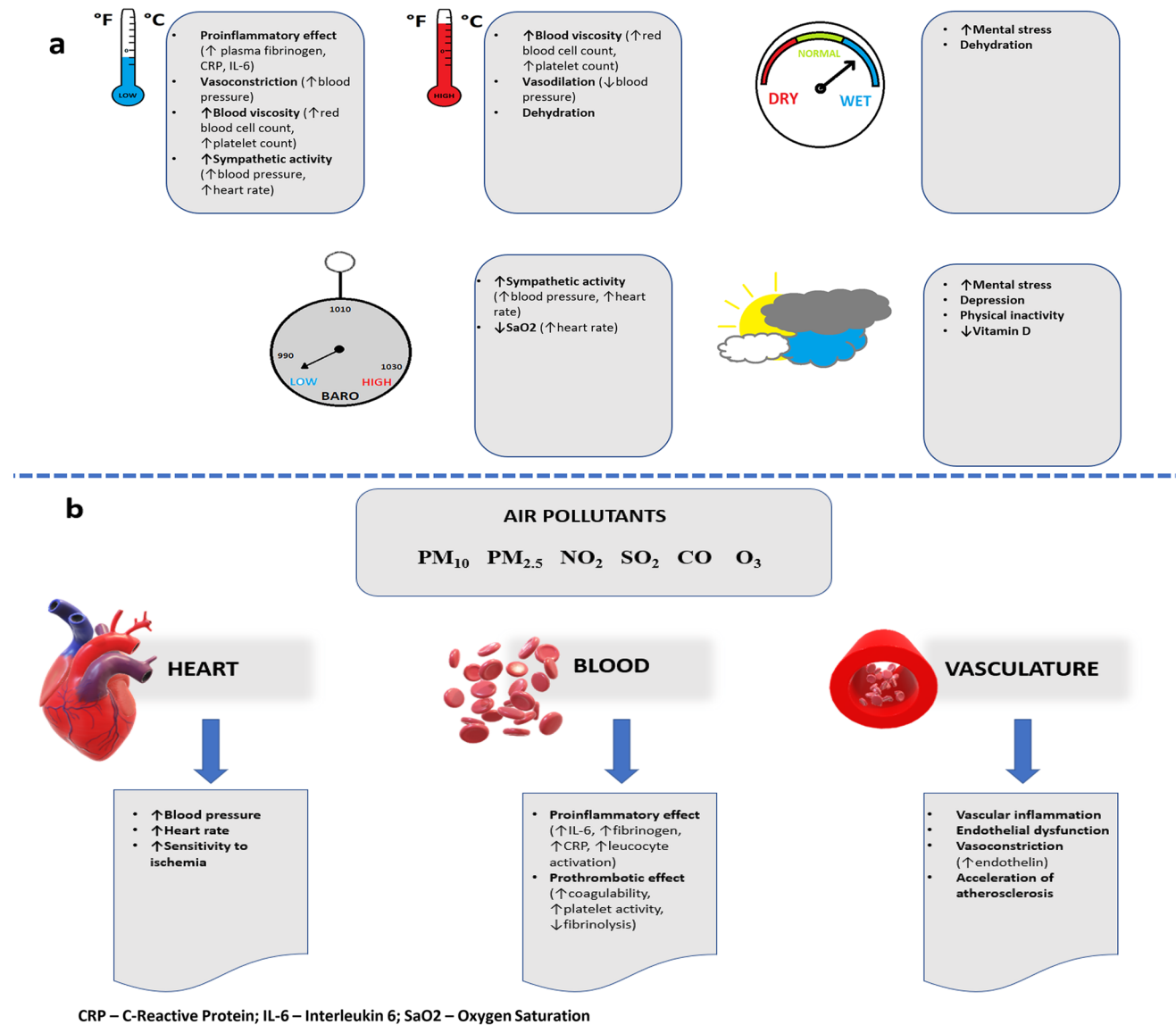
A harmful effect of fine particulate matter was observed when analyzing the relationship between long-term exposure to air pollution and cardiopulmonary mortality. In 2002, a large study conducted in the USA showed an increased risk

of all-cause (4%), lung cancer (8%), and cardiopulmonary (6%) mortality for each 10 μg/m<sup>3</sup> elevation of PM<sub>2.5</sub> particle concentrations [65]. Similar results have been observed in England and Wales, where the mortality of patients with a history of CHD increased as a result of chronic exposure to PM<sub>2.5</sub> [66]. In a multicenter European analysis, the incidence of acute coronary events increased by 13% in the case of chronic exposure to PM<sub>2.5</sub> and by 12% in the case of chronic exposure to PM<sub>10</sub> [67]. A recent meta-analysis of 27 cohort studies found a much more harmful effect of PM<sub>2.5</sub> compared to PM<sub>10</sub> on the risk of AMI [68•].

The results of epidemiological studies that analyzed the relationship between short-term exposure to air pollutants and the incidence of ACS were varied. The analysis of MINAP (Myocardial Ischaemia National Audit Project) data has noted a strong correlation between NO<sub>2</sub> levels and ACS risk [69, 70]. Each 10 μg/m<sup>3</sup> increase in NO<sub>2</sub> concentration caused a double rise in the risk of acute coronary events [69]. Likewise, each 10 μg/m<sup>3</sup> increase in NO<sub>2</sub> was associated with an important impact on NSTEMI cases, but without a significant correlation between STEMI and NO<sub>2</sub> levels [70]. Several authors showed that in Alberta, Canada, exposure to high concentrations of NO<sub>2</sub> caused an increase in NSTEMI hospitalizations, especially in elderly patients with high blood pressure [71]. There has also been an increase in AMI cases in France on days when the NO<sub>2</sub> concentration exceeded 30 μg/m<sup>3</sup>, while in Sweden, each 12.9 μg/m<sup>3</sup> increase in NO<sub>2</sub> levels was associated with a 4.2% increase in STEMI cases [72, 73].

Epidemiological data has suggested that fine particulate matter has much more obvious toxic cardiovascular effects than gaseous pollutants. High levels of PM<sub>2.5</sub> and





**Fig. 1** Pathophysiological mechanisms of meteorological factors and air pollutants on acute coronary syndrome. **a** Pathophysiological mechanisms of meteorological factors. **b** Pathophysiological mechanisms of air pollutants

PM<sub>10</sub> were associated with an increased risk of ACS in Italy, China, New York, and Poland [74–78]. In Italy, a 10 µg/m<sup>3</sup> increase in PM<sub>2.5</sub> levels caused a 2.3% rise in the risk of ACS, while in China, high concentrations of PM<sub>2.5</sub> determined an increase in cardiovascular morbidity and mortality [74, 75]. In New York, each 7.1 µg/m<sup>3</sup> increase in PM<sub>2.5</sub> concentration was associated with an 18% increase in STEMI risk [76]. A 10 µg/m<sup>3</sup> increase in PM<sub>10</sub> concentration was associated with high UA hospitalizations [77]. In industrial areas of Poland, exposure to high levels of gaseous pollutants (NO<sub>2</sub>, SO<sub>2</sub>, CO) and fine particulate matter (PM<sub>10</sub>, PM<sub>2.5</sub>) increased the incidence of STEMI, while NSTEMI hospitalizations were related to high NO<sub>2</sub> concentrations in

both industrial and non-industrial areas [78]. Data on the importance of O<sub>3</sub> on ACS is inconclusive [79, 80]. Table 2 summarizes the main epidemiological studies that analyze the impact of air pollutants on cardiovascular diseases, especially on ACS.

### Pathophysiological Mechanisms of Air Pollutants

Several pathophysiological mechanisms by which air pollution can influence the occurrence of acute coronary events have been described. Exposure to high concentrations of air

**Table 2** Main studies that analyze the role of air pollutants on cardiovascular disease, especially on acute coronary syndrome

Author	Location	Study period	Study population	Air pollutants analyzed	Air pollutants with effect on ACS/death	Result
<b>Long-term exposure to air pollution</b>						
Pope et al. [65]	USA	1982, follow-up 16 years	Random samples of adults	PM, sulfate, NO <sub>2</sub> , SO <sub>2</sub> , O <sub>3</sub> , CO	PM, sulfate	↑ risk of all-cause, cardiopulmonary, and lung cancer mortality
Tonne et al. [66]	England and Wales	2004–2007, average follow-up 3.7 years	Patients with ACS	PM <sub>10</sub> , PM <sub>2.5</sub> , NO <sub>2</sub> , NO <sub>x</sub>	PM <sub>2.5</sub>	↑ risk of all-cause mortality
Cesaroni et al. [67]	Germany, Finland, Denmark, Sweden, and Italy	1997–2007, average follow-up 11.5 years	Patients with ACS	PM <sub>10</sub> , PM <sub>2.5</sub> , NO <sub>2</sub> , NO <sub>x</sub>	PM <sub>10</sub> , PM <sub>2.5</sub>	↑ risk of coronary events
<b>Short-term exposure to air pollution</b>						
Bhaskaran et al. [69]	England and Wales	2003–2006	Patients with MI	PM <sub>10</sub> , NO <sub>2</sub> , SO <sub>2</sub> , O <sub>3</sub> , CO	PM <sub>10</sub> , NO <sub>2</sub>	↑ risk of MI
Butland et al. [70]	England and Wales	2003–2010	Patients with STEMI, NSTEMI	PM <sub>10</sub> , PM <sub>2.5</sub> , NO <sub>2</sub> , O <sub>3</sub>	NO <sub>2</sub>	↑ risk of NSTEMI
Wang et al. [71]	Alberta (Canada)	1999–2010	Patients with STEMI, NSTEMI	PM <sub>2.5</sub> , NO <sub>2</sub> , O <sub>3</sub> , NO, CO	NO <sub>2</sub>	↑ risk of NSTEMI
Vaudrey et al. [72]	Strasbourg (France)	2012–2014	Patients with coronary events	PM <sub>10</sub> , PM <sub>2.5</sub> , NO <sub>2</sub>	NO <sub>2</sub>	↑ risk of coronary events
Sahlén et al. [73]	Stockholm (Sweden)	2000–2014	Patients with MI	PM <sub>10</sub> , PM <sub>2.5</sub> , NO <sub>2</sub> , SO <sub>2</sub> , O <sub>3</sub>	NO <sub>2</sub>	↑ risk of STEMI
Belleudi et al. [74]	Rome (Italy)	2001–2005	Patients with CVD	PM <sub>10</sub> , PM <sub>2.5</sub> , UFP	PM <sub>10</sub> , PM <sub>2.5</sub>	↑ risk of ACS
Amsalu et al. [75]	Beijing (China)	2013–2017	Patients with CVD	PM <sub>2.5</sub> , NO <sub>2</sub> , SO <sub>2</sub> , O <sub>3</sub> , CO	PM <sub>2.5</sub>	↑ risk of CVD
Gardner et al. [76]	Rochester (New York)	2007–2010	Patients with STEMI, NSTEMI	PM <sub>2.5</sub> , UFP	PM <sub>2.5</sub>	↑ risk of STEMI
Kuźma et al. [77]	Białystok (Poland)	2008–2017	Patients with ACS	PM <sub>10</sub> , PM <sub>2.5</sub> , NO <sub>2</sub> , SO <sub>2</sub>	PM <sub>10</sub>	↑ risk of ACS
Kuźma et al. [78]	Poland	2008–2017	Patients with ACS	PM <sub>10</sub> , PM <sub>2.5</sub> , NO <sub>2</sub> , SO <sub>2</sub> , CO	PM <sub>10</sub> , PM <sub>2.5</sub> , NO <sub>2</sub> , SO <sub>2</sub> , CO	↑ risk of STEMI, NSTEMI
Argacha et al. [79]	Belgia	2009–2013	Patients with STEMI	PM <sub>10</sub> , PM <sub>2.5</sub> , NO <sub>2</sub> , O <sub>3</sub>	PM <sub>10</sub> , PM <sub>2.5</sub> , NO <sub>2</sub>	↑ risk of STEMI
Ruidavets et al. [80]	Toulouse (France)	1997–1999	Patients with AMI	NO <sub>2</sub> , SO <sub>2</sub> , O <sub>3</sub>	O <sub>3</sub>	↑ risk of AMI

ACS acute coronary syndrome, PM particulate matter, NO<sub>2</sub> nitrogen dioxide, SO<sub>2</sub> sulfur dioxide, O<sub>3</sub> ozone, CO carbon monoxide, PM<sub>10</sub> particulate matter with an aerodynamic diameter ≤ 10 μm, PM<sub>2.5</sub> particulate matter with an aerodynamic diameter ≤ 2.5 μm, NO<sub>x</sub> nitrogen oxides, MI myocardial infarction, STEMI ST-elevation myocardial infarction, NSTEMI non-ST-elevation myocardial infarction, NO nitrogen monoxide, CVD cardiovascular disease, UFP ultrafine particles

pollutants has been shown to cause a systemic inflammatory response, vascular dysfunction and vasoconstriction, increased heart rate and blood pressure, changes in clotting processes, and dysfunction of the sympathetic-parasympathetic systems [81, 82]. Elevated PM<sub>10</sub> and PM<sub>2.5</sub> levels have also been associated with elevated endothelin levels [83]. Increased blood pressure has been observed in patients undergoing cardiac rehabilitation

after exposure to high atmospheric concentrations of PM<sub>2.5</sub> [84]. The effects of air pollutants on the risk of AMI were also studied in the field of mechanics. Short-term exposure (1 h) to exhaust gases has been shown to induce a prothrombotic and proischemic effect in patients with CHD [85].

The process by which these pathophysiological mechanisms may differently affect the occurrence of ACS subtypes



remains debatable. STEMI and NSTEMI mechanics are not the same. STEMI appears after total occlusion of the vessel as a result of ruptured atheroma plaque with added thrombosis, whereas NSTEMI is distinguished by partial occlusion of the coronary arteries or the appearance of an imbalance between demand and oxygen supply in the myocardium. UA and NSTEMI have similar pathogenic mechanisms, with the difference that myocardial necrosis is not present in UA [86]. Some epidemiological data showed an increase in the number of STEMI cases after exposure to high concentrations of PM<sub>2.5</sub>, while other research reported a correlation between NO<sub>2</sub> exposure and an increased incidence of NSTEMI [70, 71, 76]. It is supposed that PM<sub>2.5</sub> air pollutants would stimulate the thrombotic process after atherosclerotic plaque rupture or that they would affect the thrombolysis process, resulting in complete occlusion of the vessel [76]. NO<sub>2</sub> appears to be involved in endothelial dysfunction, prothrombotic and proinflammatory effects, causing ACS [85–87]. Figure 1b summarizes the pathophysiological mechanisms of air pollutants on ACS subtypes. Further clinical and experimental studies are needed to analyze in detail the role of each air pollutant in the occurrence of ACS subtypes.

## Acute Coronary Syndrome and Air Pollution During the COVID-19 Pandemic

The new coronavirus, also called SARS-CoV-2, was first reported in December 2019 in Wuhan, China. The COVID-19 infection spread quickly, and the WHO declared it a global pandemic on March 11, 2020. This viral infection has caused more than 5.9 million deaths as of March 6, 2022 [88]. The lockdown imposed at the beginning of 2020 in most countries, as a measure of protection against infection with the new coronavirus, determined a decrease in the concentration of air pollutants, economic and social imbalances, increasing cases of depression and anxiety among the population, and uncertainty in the medical and scientific world [89, 90]. Recent reports have shown a definite correlation between COVID-19 infections and high levels of air pollution. Thus, air pollutants can facilitate the transport and spread of the SARS-CoV-2 virus [91•]. Both air pollution and COVID-19 infection may provoke a systemic inflammatory response, a procoagulant effect, endothelial dysfunction, increased oxidative stress, and an imbalance between the demand and oxygen supply in the cells, all of which favor the progression of atherosclerosis and unstable plaque rupture [81–87, 92, 93].

A decrease in the number of ACS hospitalizations was observed during the COVID-19 pandemic and lockdown period. In Austria and the USA, the number of STEMI/AMI cases decreased by 40% in the first half of 2020 [94, 95]. In Italy, NSTEMI cases were reduced by 65.1%, while

STEMI admissions decreased by 26.5% [96]. There was also an increase in out-of-hospital cardiovascular mortality, as well as numerous complications of AMI, due to late presentation to an emergency department (5 h after the onset of symptoms, compared to 1 h and a half in 2018–2019) [97].

Several theories have been proposed to justify the sudden reduction in ACS cases during the COVID-19 pandemic. One possible cause is the patient's fear of SARS-CoV-2 virus infection during a hospital visit. Another explanation could be the ignoring of patients with mild angina symptoms or stable CHD by medical staff overwhelmed by COVID-19 cases. The reduced number of ACS could be a result of less stress at work and congested traffic, a healthy lifestyle, reduced alcohol consumption, less smoking, increased adherence to medication, and improved air quality during the lockdown period [89].

The COVID-19 pandemic and the lockdown imposed in most countries of the world caused an increase in depression and anxiety cases, as well as socio-economic imbalances. Both SARS-CoV-2 virus infection and high concentrations of air pollutants may be risk factors for acute coronary events. It is possible that in the future, climate change and increased emissions of air pollutants could cause significant economic damage and far more deaths than the SARS-CoV-2 virus infection.

## Conclusions

ACS remains the main cause of death worldwide. Air temperature fluctuations in the global warming era as well as increased emissions of air pollutants have a major impact on acute coronary events. Cardiac patients are much more vulnerable to exacerbations of pre-existing heart disease, especially on days with extreme temperatures and sudden changes in air pressure or during periods of high air pollution. It is necessary to identify patients at risk and warn them in advance about weather variations in order to reduce the number of hospitalizations and the costs borne by public health programs. At present, the industrialization era and the growing population cause a constant increase in air pollution worldwide. Thus, the number of ACS caused by air pollution is expected to increase dramatically in the next few years.

## Compliance with Ethical Standards

**Conflict of Interest** The authors declare that they have no conflict of interest.

**Human and Animal Rights and Informed Consent** This article does not contain any studies with human or animal subjects performed by any of the authors.

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- Of importance
- Of major importance

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