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Climatic influences on cardiovascular diseases

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Abstract

Classical risk factors only partially account for variations in cardiovascular disease incidence; therefore, also other so far unknown features, among which meteorological factors, may influence heart diseases (mainly coronary heart diseases, but also heart failure, arrhythmias, aortic dissection and stroke) rates. The most studied phenomenon is ambient temperature. The relation between mortality, as well as cardiovascular diseases incidence, and temperature appears graphically as a ''U'' shape. Exposure to cold, heat and heat waves is associated with an increased risk of acute coronary syndromes. Other climatic variables, such as humidity, atmospheric pressure, sunlight hours, wind strength and direction and rain/snow precipitations have been hypothesized as related to fatal and non-fatal cardiovascular diseases incidence. Main limitation of these studies is the unavailability of data on individual exposure to weather parameters. Effects of weather may vary depending on other factors, such as population disease profile and age structure. Climatic stress may increase direct and indirect risks to human health *via* different, complex pathophysiological pathways and exogenous and endogenous mechanisms. These data have attracted growing interest because of the recent earth's climate change, with consequent increasing ambient temperatures and climatic fluctuations. This review evaluates the evidence base for cardiac health consequences of climate conditions, and it also explores potential further implications.

Key Words: Weather; Climate; Meteorology; Cardiovascular diseases; Myocardial infarction; Angina pectoris

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Core Tip: Climatic stress may determine some risks to human health *via* complex pathophysiological pathways. Meteorological factors may influence coronary heart diseases, but also heart failure, arrhythmias, aortic dissection and stroke rates. The most studied phenomenon is temperature. The relation between mortality, as well as cardiovascular diseases incidence, and temperature appears graphically as a ‘‘U’’ shape. Other variables, such as humidity, atmospheric pressure, sunlight hours, wind strength and direction and rain/snow precipitations have been studied. These data have attracted growing interest because of the recent earth’s climate change. This review evaluates the evidence for cardiac health consequences of climate conditions.

INTRODUCTION

Despite considerable advances in identifying the conditions that may predispose to atherosclerosis, less information is known about the incident events leading to plaque rupture. Classical risk factors only partially account for variations in cardiovascular disease incidence and mortality. Therefore, also other so far unknown features, among which meteorological factors, may influence cardiovascular diseases rates.

AMBIENT TEMPERATURE AND MORTALITY

Seasonal peaks in respiratory, cardiovascular, and cerebrovascular mortality, with a winter increase in deaths, have been reported in different countries, referred to as ''excess winter mortality''[1-3]. This phenomenon has been strongly linked to changes in temperature[4-8].

The relation between environmental temperature and health has been known for a very long time. Several disorders, such as heat stroke and hypothermia, are directly linked to temperature extremes. Low seasonal temperatures increase the odds of mortality[9,10]. An association between extreme high temperatures and mortality has also been demonstrated[11,12], as confirmed by recent data[13-16]. Actually, a number of ecological time-series studies suggest that the relation between mortality and ambient temperature appears graphically as a ''U'' shape, with mortality rates lower on days in which the average temperatures range between 15° to 25°C, rising progressively as the ambient temperature becomes hotter or colder[17-20]. Most of mortality linked to heat occurs during first days after temperature increase, while the effect of cold has been prolonged for several weeks[21-23]. Spatial and temporal differences have been described in this phenomenon[24-27]. Many heat-related deaths occur in people before they come to medical attention[28]. Investigations carried out in a large number of cities have shown that temperature level corresponding to the minimum mortality varies from place to place and country to country according to the usual climate (heat thresholds were generally higher in communities closer to the equator), probably reflecting adaptations of the population to the usual range of temperature[29]. High respiratory, cardiovascular

and influenza mortality in winter leads to lower temperature effects in the following summer[30]. There was a progressive reduction in temperature related deaths over the 20th century, despite an aging population[31-33]. This trend is likely to reflect improvements in social, environmental, behavioural, and health-care factors[34,35]. In the recent COVID-19 pandemic, there was a negative correlation between the cumulative relative risk of death and temperature[36]. Table 1 shows main studies on the relations between weather and general mortality.

In particular, various epidemiological studies have reported greater coronary heart disease (CHD) and acute myocardial infarction (AMI) mortality both in winter[37-40] and in extremely hot summers[25,41,42]. Many authors have postulated that weather-related variables may also explain these seasonal trends, as well as substantial geographic variations in CHD mortality. Cold climate is independently associated to coronary mortality[43-45], but a U-shaped relationship between ambient temperature and cardiovascular mortality has been also described even in milder regions, where either low temperatures or heat waves are exceptional[46-48], with few exceptions[49]. Consensus is lacking, however, on whether this phenomenon reflects variations in incidence or in case fatality rate. Cold effect seems delayed, whereas heat effect is acute, both of which last for several days[34,46,50]. The delay between peak of cold is lower for all-cause mortality and CHD causes than for respiratory ones[51]. Mean temperature had better predictive ability than minimum and maximum one[35,46]. Table 2 shows main studies on the relations between weather and cardiovascular mortality.

AMBIENT TEMPERATURE AND CARDIOVASCULAR AND NON-CARDIOVASCULAR DISEASES

Weather exposure beyond certain thresholds affects human health negatively[52]. Both cold and heat temperature significantly increased risk of hospitalization for several diseases[53]. However, heat waves have documented a higher impact on mortality than on morbidity (hospital admissions)[41,54,55]. This phenomenon could be explained by the hypothesis that deaths from circulatory disease occur rapidly patients reach a

hospital[56]. There are relationships between temperature (in particular its short-term variability) and hospital admissions due to various forms of heart disease[57-61]. Hot and cold temperature are a risk factor for a wide range of cardiovascular, respiratory, and psychiatric illness; yet, in few studies, the increase in temperature reduced the risk of hospital admissions for pulmonary embolism and angina pectoris[62]. Table 3 shows main studies on the relations between weather and hospital admissions.

AMBIENT TEMPERATURE AND ACUTE CORONARY SYNDROMES

Seasonal variations in emergency admission rates and trial recruitment of patients suffering from acute coronary syndromes (ACS) are well described[37], and a number of epidemiological studies have reported a greater winter ACS incidence, with similar seasonal trends in all studied cohorts, including men and women, middle-aged and elderly patients, and patients from northern and southern hemispheres[4].

Over the past few decades, a growing body of epidemiological studies found the effects of ambient temperature on cardiovascular disease, including risk for ACS[63-66]. Inverse relationship between temperature and ACS is well known[67-71], even regardless of season[37,72,73]. In a previous study, we correlated the daily number of AMI cases admitted to a western Sicily hospital and weather conditions on a day-to-day basis over twelve years, showing a significant association between daily number of ACS hospital admission and minimal daily temperature[74]. Effects of low temperature on total ACS cases were more pronounced in years with higher average temperatures and also during summer, suggesting not a pure "cold effect" but an influence of unusual temperature decreases[64,75].

This relation, moreover, could be actually U-shaped, with higher short-term risk of ACS also in extremely hot summer[67,76-79]. Very few studies failed to demonstrate an association between temperature and ACS incidence[80]. A recent meta-analysis, however, confirmed that cold exposure, heat exposure, and exposure to heat waves were associated with an increased risk of ACS[81].

It has been hypothesized that angina's worsening occurs in cold weather, but few studies have investigated variations in hospitalizations due to angina pectoris in relation to climatic variables[3,59]. We showed a significant association between daily number of angina hospital admission and temperature[82]. Table 4 shows main studies on the relations between weather and hospital admissions for ACS.

Main limitation of these studies is the unavailability of data on individual exposure to temperature variability[57]. These seasonal changes, besides, do not seem universal[43,76], as they are absent near the equator or in subpolar regions, with less temperature fluctuations than in temperate regions. For this reason, it seems inadequate to extrapolate results to different environments.

ACS AND OTHER METEOROLOGICAL PHENOMENA BEYOND TEMPERATURE

Ambient humidity

We observed a negative significant relationship between the number of ACS admissions and maximal humidity[74]. This was confirmed as regards angina admissions only in males, in whom we showed also a positive significant relationship between angina and minimal humidity[82]. Previous data for ACS were confounding: although some studies showed an association with low humidity[83,84], and other no association[69], more researches showed high humidity being related to CHD in northern countries[68,76] and in other Mediterranean[48,78], Asian[75], and Oceanian[54] settings. Fernández-Raga *et al*[18] suggested as the optimal relative humidity 24% for patients with respiratory diseases, and 45% for cardiovascular ones.

Atmospheric pressure.

Consequences of atmospheric pressure on cardiovascular diseases have been studied less frequently. Associations between an increase in CHD occurrence and low atmospheric temperatures have been reported from mortality data and hospital admission registries. A morbidity registry (Lille-WHO MONICA Project) detected a linear V-shaped relationship with a minimum at 1016 mbar: a 10-mbar decrease and a

10-mbar increase were associated with significant 12% and 11% increase in event rates, respectively[73]. Ambient pressure had a statistical impact on the incidence of angina or ACS also in Sweden[72], Serbia[83], Slovenia[68], Lithuania[85], and Switzerland[86], but in Mediterranean population we did not observe any significant relation[82].

Sunlight

The amount of sunlight hours seems inversely related to winter mortality and ACS risk[72]. Our study in a Mediterranean area did not confirm any relation between sunlight hours and ACS daily admissions[74].

Wind, rain, and snow

ACS incidence during southern wind periods seems significantly greater than during the northern ones[75]. Also, the amount of rain and wind speed seems inversely related to winter mortality and ACS incidence[72,75,85,86]. We, however, failed to observe any significant relationship between wind force and direction, rain, and the number of hospital ACS admissions[74], suggesting these variables are not strong triggers, according to other authors[43]. It is likely that rain intermixed with snow may trigger increased mortality from cardiovascular disease. Snow is somewhat more significant in triggering deaths from heart disease than is air temperature, influencing mortality, mainly in males[87,88]. Snow fall exceeding 2 cm/d was identified as a significant predictor for ACS admission rates[89]. Snow- and rainfall had inconsistent effects in another study[87].

Combination of weather factors

The assessment of air temperature does not allow evaluation of actual discomfort perception caused by the combination of different meteorological parameters. Alternative biometeorological approaches consider Apparent Temperature Index in summer and New United States/Canada Wind Chill Temperature Index in winter, which combine air temperature, relative humidity and wind velocity[90], the presence of

anticyclonic and cyclonic air mass[91], as well as specific local climatic conditions, such as the Arctic Oscillation[92].

WEATHER AND OTHER CARDIOVASCULAR DISEASE BEYOND CHD

Heart failure

Environmental exposure is an important, but underappreciated, risk factor contributing to development and severity of heart failure. In European warm period (from June to October), there are significant less admissions than that in the cold period (from December to March). Air temperature is the most significant environmental factor related to heart failure hospital admissions, showing an inversed correlation[93,94]. Heart failure admissions peaked when temperature was between 0 and −10°C[68]. Every 1°C decrease in mean temperature and every 1hPa decrease in air pressure were associated, respectively, with an increase in the daily number of emergency admissions for heart failure by 7.83% (95%CI: 2.06-13.25) and 3.56% (95%CI: 1.09-5.96)[71]. Some other features, such as precipitation, are also relevant[94].

Arrhythmias

Current paradigm in sudden cardiac death (SCD) requires an abnormal myocardial substrate and an internal or external transient factor (such as a cold spell, an unusually cold weather event) that triggers cardiac arrest. An increased risk of ischaemic SCD was significantly associated with a preceding cold spell[95], and cardiac arrest admissions peaked when temperatures were between 0° and −10°C[60]. These associations were stronger for unexpected SCD than for SCD with prior CHD[45]. However, also higher average daily temperature and larger variation in humidity were associated with increase in appropriate ICD interventions in patients with arrhythmogenic right ventricular dysplasia/cardiomyopathy[96].

Aortic dissection

Days with spontaneous type A aortic dissections were significantly colder than those without dissections[97]. There appears to be a significant correlation between mean low monthly pressures and rupture incidence[98].

Stroke

Significant associations between temperature and hospital admission rates for stroke were apparent and generally stronger than in other cardiovascular disease[99-101]. Both increases and decreases in temperature had a marked relationship with stroke deaths, while hospital admissions were only associated with low temperature[102,103]. Overall, a 5°C drop in temperature was significantly associated with a 7% increase in admissions for stroke[69]. Every 1°C increase in mean temperature during the preceding 24 h was associated with a significant 2.1% increase in ischaemic stroke admissions. A fall in atmospheric pressure over the preceding 48 h was associated with increased rate of haemorrhagic stroke admissions. Higher maximum daily temperature gave a significant increase in lacunar stroke admissions than in other ischaemic strokes[100]. In another study, every 1°C decrease in mean temperature was associated with an increase in the daily number of emergency admissions by 35.57% for intracerebral haemorrhage and by 11.71% for cerebral infarction. An increase of emergency admissions due to intracerebral haemorrhage was observed at every 1 hPa decrease in air pressure[71]. A recent metanalysis, finally, confirmed that lower mean ambient temperature is significantly associated with the risk of intracerebral haemorrhage, but not with ischemic stroke and subarachnoid haemorrhage[104].

AGE, SEX, OTHER FACTORS AND CLIMATIC VARIABLES

Effects of weather vary depending on other factors, such as the population disease profile and age structure[19,74]. People with pre-existing medical conditions such as cardiovascular disease or carrying out physically demanding work, and the elderly, particularly those in nursing and care homes, are particularly vulnerable[68,105-108].

Mortality's increase with cold or heat was greater for older age groups[21,63,109]. Diurnal temperature range are related to hospital admissions for all cardiovascular and cerebrovascular disease among elderly, namely in males[59,83,110]. In the elderly, cardiovascular disease curve was U-shaped, showing higher values for cold stress than for heat one[107,109,111,112]. In general, longer duration of heat waves increases the risks of cardiovascular mortality for the elderly[113]. Main predictors of death are: the use of home public-integrated assistance, a higher comorbidity, a higher degree of disability[114], lack of thermal insulation and sleeping right under the roof[113], being confined to bed or unable to care for oneself and pre-existing cardiovascular diseases[115]. Home air-conditioning, visiting cool environments, dressing lightly, and increasing social contact were instead strongly associated with better outcomes[113,115]. Weak correlation between atmospheric air wind speed and ACS morbidity in older populations was determined[111].

Diurnal temperature range was significantly associated with hospital admissions for all cardiovascular disease, ischemic heart disease and cerebrovascular disease among elderly females[110]. We showed that, in females, a reduction in maximal temperature is associated with more hospital angina admissions[82], whereas the number of angina admissions is positively correlated with an increase in minimal temperature, as observed also by Ebi[59]. Increased outside temperature and sunshine hours were identified as strong positive predictors for ACS occurrence in women[89], as they tend to present with AMI at a later age than men, they will tend to exhibit a more marked seasonal variation[107-109]. A weak correlation between atmospheric air wind speed and MI morbidity in women was determined[111]. Snow fall was identified as a positive predictor for ACS admission rates with a significant effect in men, but not in women[89]. Other studies failed to detect significant difference according to sex[65].

Risk of heat-related death was significantly higher among Black people[112,116] and Australian indigens[105].

Heat-related mortality varied with sociodemographic characteristics such as in people living in low socioeconomic districts[12,106,107,117].

People living in areas with high PM2.5 concentration showed higher vulnerabilities to cold-ACS effects than other groups did[67].

MECHANISMS

Up to date, there are not clear pathophysiological links between weather and cardiovascular diseases. Climatic stress may increase direct and indirect risks to human health *via* different, complex pathophysiological pathways and exogenous and endogenous mechanisms. The pattern of well-known conventional risk factors (such as blood pressure, serum lipids, haematological and coagulation factors, body weight, glucose tolerance), a number of hormones including steroids, environmental factors (such as air pollution) as well as acute infections shows a marked seasonal variation, with a winter clustering of peak values[118,119]. In addition, humans display different seasonal behaviour in diet, activity, housing and smoking habits, psychosocial factors and mood disorders in winter[120]. Other factors, such as overindulgence, or stress on Christmas holidays, might also contribute[121].

Cold

Mechanisms leading to possible influence of cold on ACS or angina onset are most likely multifactorial. Different heart and circulation adjustments occur when humans are acutely exposed to low outdoor temperatures. Increase in circulating levels of catecholamines, secondary to cutaneous thermoreceptor activation[122]. lead to peripheral vasoconstriction and then to increase in blood pressure[123], heart rate, and left ventricular end-diastolic pressure and volume[3,124,125] with, in turn, increased cardiac work and peripheral resistance, greater heart oxygen requirement and reduction of ischemic threshold[3]; they may be clinically relevant when coronary circulation is already compromised[126]. People with normal cardiovascular function, in fact, are unaffected by cold stress, whereas those with IHD may be crippled, although rarely, by exposure to cold, especially if they perform physical work[122]. At the same time, reduced myocardial perfusion may lead to earlier ischemia, angina, and impaired

performance. Also having a heart failure deteriorates submaximal and maximal performance in cold conditions[127]. In cold conditions also a greater sodium intake lead to an increase in blood pressure. Cold-induced vasoconstriction results in an early return of reflected pressure waves from the periphery and an increase in central aortic systolic pressure, with increase of central aortic augmentation index[128]. Endothelial dysfunction may be another mechanism. Brachial flow-mediated dilation would vary by temperature (in the Framingham Offspring cohort it was highest in the warmest and lowest in the coldest outdoor temperature quartiles)[129]. Moreover, coronary artery spasm could occur if vasoconstriction extends to the heart vessels. Cold-intolerant patients had a steeper heart rate response in cold conditions and developed ischemia and angina earlier. In cold-tolerant patients, this increase may be offset by a reduction in heart rate if baroreceptor function is normal. Baroreceptor function was impaired in cold-intolerant patients. If baroreceptor function is abnormal, heart rate may not decrease in response to a cold-induced increase in blood pressure. This mechanism may account for some of the variability in tolerance to cold exposure that affects patients with exertional angina[124].

More dramatic events, such as sudden death, may be due to increased frequency of cardiac arrhythmias, or, perhaps through rises in blood pressure, to abrupt rupture of atherosclerotic plaques[3].

Cold, besides, exerts other biological negative effects on inflammatory markers, haemostasis, rheological factors, and lipids (probably related to haemoconcentration), alcohol consumption, and body weight gain[40,124,125,130,131]. A 10°C decrease in temperature led to an increase in platelet counts and fibrinogen and a decrease in C-reactive protein in CHD patients[131]. In cold weather, a greater tendency to clot in circulatory system has been demonstrated[119,132,133]. This could be related to plasma volume contraction (haemoconcentration) [119,126,134], induced by peripheral vasoconstriction, which can in part also explain the increase in serum lipids. These acute responses to cold conditions could trigger ACS.

Cold conditions may increase also the risk of respiratory infections through suppression of immune responses and direct effects on respiratory tree, and although no association can be claimed between respiratory infections and coronary deaths during cold season[124], a theory links pulmonary inflammation to stroke[99].

Finally, other causes hypothesized to explain the impact of cold are socioeconomic, mainly housing conditions[12,34].

Heat

During summer, ACS patients working outdoors show abnormal hemorheology (high haematocrit and blood viscosity)[135], as dehydration is more likely to occur[29]. Outdoor heat is associated with decreasing blood pressure, and cardiovascular vulnerability may vary primarily by central air conditioning[136]. Higher ambient temperature is associated with decreases in heart rate variability during warm season but not during cold one[137]. Hot weather is associated with an increase in systolic pressure at night in treated elderly hypertensive subjects, likely because of a nocturnal blood pressure escape from effects of a lighter summertime drug regimen[133].

Humidity

When air contains a high percentage of humidity, perspiration and the processes of temperature homeostasis may be hindered, making more difficult the automatic processes of internal temperature control, thus increasing respiratory fatigue and heart rate. However, this mechanism may be important only in more severe ischemic forms.

Rain and wind

A reduction of outdoor excursions when it is raining and windy prevents outdoor cold stress.

Sunshine

Several studies have demonstrated significantly lower levels of vitamin D, synthesized by skin following exposure to ultraviolet radiation, in subjects with CHD, particularly in winter[138]. It has been suggested that vitamin D may be a confounding factor in the association between cholesterol, structurally like it, and CHD risk. This is corroborated by findings of a strong, positive association between latitude and mean blood cholesterol, and a strong negative association between hours of sunshine and CHD mortality[120]. Association between vitamin D levels and CHD, however, has been shown to be independent of total serum cholesterol[138].

Age

With increasing age, winter peak increased. This is likely to reflect a combination of factors: poorer temperature autonomic control, lower physical activity levels, less use of protective clothing, greater time spent at home, more sensitivity to seasonal influenza and blood pressure changes, and poorer household heating and insulation. The predominance of effects of meteorological factors in the elderly could be also explained by the lower impact of genetic AMI determinants.

Sex

Different effects of weather on women may be related to different coronary anatomy in the female sex, as woman have less extensive coronary atherosclerosis, lower coronary size, and lower collateral circulation than males.

Pollution

Interaction between air pollution and weather is often missed in literature[139]. Studies show that ambient temperature and air pollution may interact to affect cardiovascular events *via* autonomic nervous system dysfunction[137]. Much higher PM10 effects on mortality were observed during warmer days[26,140-142], and the hypothesis that such an effect is attributable to enhanced exposure to particles in summer could not be rejected[143].

CONCLUSION

Implications and conclusions

Weather influences on heart diseases remind us that climatic stress can be considered as a new potential risk factor for cardiovascular events and even mortality[3,125]. Such an understanding has several potential implications for developing civil protection policy towards allocation of public healthcare resources and planning appropriate measures to prevent cardiovascular events[59,116]. Weather-related health effects have sharply attracted growing interest because of the recent observed and predicted earth's climate change, with consequent increasing ambient temperatures and climatic fluctuations, extremes of precipitation (floods and droughts), air pollution, and infectious diseases. Contrary to current predictions, this may mean a paradoxical increase in seasonal cycle of events with greater winter peaks, even as overall global temperatures rise[93]. Thus, increases in heat-related mortality due to global warming are unlikely to be compensated by decreases in cold-related mortality[112]. In a global environment of rapid and extreme climatic events, more populations will be exposed to conditions they are not readily adapted to from a bio-behavioural perspective[60,144]. Adaptation to such changes, that are expected to further increase, would seem to be imperative for medical professionals, health institutions, and general public[41,70].

Public health educational, behavioural and social measures[28,43] have been proposed to reduce adverse cardiovascular consequences of climate variability. We wish here to summarize the most important ones.

High risk identification: Prevention programs must be based around rapid identification of high-risk conditions and people, such as frails with cardiovascular disease, or the elderly[53,107]. Protective measures, in fact, should be directed towards susceptible groups, rather than the population as a whole, with the creation of an up-to-date database and care of vulnerable high-risk individuals[21,24,110,114].

Specific interventions: In the community, at home, and in institutions that care for elderly or vulnerable people, such as hospitals, a comfortable temperature should be granted[63,65]. Educational measures should be suggested to high-risk people. During the passing atmospheric front, as well as in extreme ambient temperature periods, *i.e.*, coronary patients should stay at home, and avoid both physical and psychological stress[78].

Provision of targeted advice: Many weather-related diseases may be preventable by and appropriate response to emergencies. Operative health weather watch/warning systems link public health actions to meteorological forecasts of dangerous weather. We need development of a short-term forecast system of daily demand using weather variables.

Remodulation of health services offer: During severe climatic conditions, it should be granted a greater deployment of ambulance services and an adequate reinforcement of health personnel in order to meet the unexpected increase in demands, and to avoid potential mismatch between the occurrence of acute cardiovascular events and medical service capacities[108].

Future perspectives: In the long term, improvements in infrastructures, residential architecture, working environment and urban planning must be adapted[113].

In conclusion, the problem of climate change is serious, urgent and getting worse[144]. Fairly obvious connections between climate change and cardiovascular health have been outlined in this article. Medical professionals, and societies of medical professionals, easily capable of understanding the physical and statistical methods used by climatologists, are in a good position to give politicians and leaders in industry and agriculture their necessary support[144].

Further large, exhaustive, population-based cohort research with consistent methodology over long periods in geographical areas with homogeneous

meteorological variables should be carried out to further clarify climatic influences on CHD occurrence, to identify underlying pathophysiological mechanisms, to show vulnerable populations and individuals and to develop cost-effective strategies to promote resilience against provocations of climate change[86,113].

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