Seasonal Periodicity of Ischemic Heart Disease and Heart Failure

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KEYWORDS

• Seasonal periodicity • Ischemic heart disease • Heart failure • Myocardial infarction

KEY POINTS

- Seasonal variation for ischemic heart disease and heart failure is known.
- The interplay of environmental, biological, and physiologic changes is fascinating.
- This article highlights the seasonal periodicity of ischemic heart disease and heart failure and examines some of the potential reasons for these unique observations.

INTRODUCTION

"Look to the Seasons when Choosing Your Cures" (Hippocrates)

An increase in deaths during winter was reported as early as 1847 when William Farr described the diagnostic composition of the excess deaths occurring in that year. There has been a considerable interest in the role of climate change and its potential as a trigger for new-onset or worsening ischemic heart disease (IHD) and heart failure. The complex role of environmental factors, external biological milieu, and temporary physiologic changes is fascinating. This article highlights the seasonal periodicity of IHD and heart failure and examines some of the potential reasons for these unique observations.

ISCHEMIC HEART DISEASE

Epidemiology

An increase in mortality from acute myocardial infarction (AMI) in the winter months compared with the summer months was first reported in the 1930s.[1] Previous studies have reported seasonal fluctuations in the onset of IHD and heart failure with a disproportionate number of admissions in the winter months compared with summer.[2–13] Far fewer studies have reported a higher incidence of AMI in the summer or no season variation.[14–20]

Furthermore, subsequent studies not only found an increase in mortality from AMI during the winter months but also from all forms of ischemic coronary disease during the winter.[21] Observational studies to determine whether cases of AMI reported to the second National Registry of Myocardial Infarction (NRMI-2) varied by season have been conducted previously as well.[22] Analysis of 259,891 cases revealed a significant peak in the winter months and a nadir in summer months. Moreover, this pattern was seen in all geographic areas, suggesting the chronobiology of season variation in AMI is independent of climate.

Analysis of 1252 patients in the Multicenter Investigation of Limitation of Infarct Size (MILIS) and Thrombolysis in Myocardial Infarction–4 (TIMI-4) trials found that mean infarct size, as measured by mean creatine-kinase in blood (CK-MB) infarct

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size index and TIMI flow grade, at 18 to 36 hours was decreased in the summer months.[23] A proposed mechanism includes an increase in vascular resistance in cold temperatures.[24–27] The subsequent increase in coronary vascular resistance would then be expected to result in reduced coronary flow. In the summer months, an increase in temperature has been hypothesized to contribute to overall reduced venous and arterial resistance, thus reducing preload as well as afterload.

Influence of Influenza

Other studies assessing potential factors contributing to seasonal fluctuations in IHD and heart failure have shown that respiratory infections are more frequent during the cold months. Given prior evidence of an association between respiratory infection and AMI,[28–30] respiratory infections may contribute to the higher rate of AMI in the winter. Vaccination against influenza has been associated with a 67% reduction in the risk of myocardial infarction during the subsequent influenza season.[31] Influenza has been shown to affect the vascular system in numerous ways. Inoculation of atherosclerotic apolipoprotein-E–deficient mice with influenza A resulted in heavy infiltration of atherosclerotic plaques by inflammatory cells as well as fibrin deposition, platelet aggregation, smooth muscle cell proliferation, and thrombosis.[32] These prothombotic and inflammatory changes mimic those seen in coronary plaques after myocardial infarction.[33] In addition, death rates from cardiovascular disease have been noted to increase during epidemics of influenza, and it has been suggested that acute respiratory tract infections before an AMI may be a cardiovascular risk factor.[34]

Biochemical Factors

Various other factors with seasonal variation have also been identified. Studies have shown seasonal variations in coagulation factors, such as fibrinogen and activated factor VII, with a significant increase during the winter months.[35–37] Analysis of 82 subjects, 47 of whom were free of clinical signs of coronary artery disease and 35 survivors of AMI, who had measurements of various metabolic and hemostatic coronary risk factors twice in the cold months (December and March) and twice in the warn months (June and September), revealed a significantly higher body mass index, glucose, total cholesterol, low-density lipoprotein, triglycerides, lipoprotein(a) (Lp[a]), fibrinogen, and platelet counts in the colder months compared with the warm months. Other studies have shown that fibrinogen levels were significantly higher in the winter with a more pronounced difference in fibrinogen levels in older patients (75 years of age and older) compared with subjects 55 to 75 years of age.[38]

Studies focusing on seasonal variation in cholesterol levels have also revealed total cholesterol and low-density lipoprotein cholesterol levels to be highest in wintertime.[39] A longitudinal study of seasonal variation in lipid levels in 517 healthy volunteers from a health maintenance organization serving central Massachusetts revealed a breadth of seasonal variation of 3.9 mg/dL in men, with a peak in December, and 5.4 mg/dL in women, with a peak in January.[40] Seasonal amplitude was greater in hypercholesterolemic participants compared with participants with normal cholesterol levels. Furthermore, 22% more participants had total cholesterol levels of 240 mg/dL or greater in the winter than in the summer.

Role of Air Pollution

There has been a growing amount of epidemiologic evidence underscoring a possible association between ambient air pollution and poor cardiovascular outcomes. This finding is important given the strong association between pollution levels, increased mortality, and winter months.[41–43] Specific air pollutants are implicated with an increased risk of cardiovascular disease, including carbon dioxide, oxides of nitrogen, sulfur dioxide, lead, ozone, and particulate matter less than 10 μm in diameter. These pollutants have been associated with increased hospitalizations[44,45] and mortality caused by cardiovascular disease,[46–48] with a disproportionate number of heart failures or baseline arrhythmias.[49] Exposure to fine particulate air pollutants may be associated with increased blood pressure caused by sympathetic activation.[50–52] Exposure to fine particulates has also been shown to possibly cause increase in baseline heart rate, fibrinogen levels, blood coagulation factor levels, arterial vasoconstriction, and endothelial dysfunction.[28] As a result, higher pollution levels in winter may be associated with myocardial ischemia,[29] angina pectoris, malignant ventricular arrhythmias,[30] and increased plaque vulnerability.[53]

Seasonal changes in temperature with subsequent endothelial dysfunction and changes in blood pressure may also contribute to seasonal variation in IHD. Research has shown a significant difference in seasonal variation of peak blood pressure values, with peak values in the spring and the lowest values in September.[54] Furthermore, a study of more than 17,000 European men and women found that systolic and diastolic pressures were highest in December and lowest in July, with more variation found in the elderly.[55]