Increased Winter Mortality From Acute Myocardial Infarction and Stroke: The Effect of Age

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OBJECTIVES
We examined seasonal variations in mortality from acute myocardial infarction (AMI) and stroke by age using 300,000 deaths in the Canadian Mortality Database for the years 1980 to 1982 and 1990 to 1992.

BACKGROUND
The effect of age on environmental determinants of AMI and stroke is not well understood.

METHODS
Seasonal variations were analyzed by month and for the four seasons (winter beginning in December). A chi-square test was used to test for homogeneity at \( p < 0.01 \), and relative risk ratios (RRs) for high and low periods were determined in relation to the overall mean. For each of four age subgroups, the magnitude of the seasonal variation was reported as the difference in mortality between the highest and lowest frequency seasons.

RESULTS
By month, AMI deaths were highest in January (RR = 1.090) and lowest in September (RR = 0.904), a relative risk difference of 18.6%. The seasonal mortality variation in AMI deaths (winter vs. summer) increased with increasing age: 5.8% for <65, 8.3% for 65 to 74, 13.4% for 75 to 84 and 15.8% for >85 years (\( p < 0.005 \) for trend). Stroke mortality peaked in January (RR = 1.113) and had a trough in September (RR = 0.914), a relative risk difference of 19.9%. The seasonal variation in stroke mortality also increased with age.

CONCLUSIONS
The elderly demonstrate a greater winter increase in AMI and stroke mortality than younger individuals. An understanding of these seasonal patterns may provide novel avenues for research in cardiovascular disease prevention. (J Am Coll Cardiol 1999;33:1916–9) © 1999 by the American College of Cardiology

The influence of environmental factors on the onset and course of cardiovascular events is not well understood. Studies from European (1,2) and Asian (3–5) countries have observed an increase in death rates from acute myocardial infarction (AMI) and stroke in the winter. Reports from North America, although restricted to small sample sizes or to specific cities, have suggested a similar trend (6–8). It is hypothesized that exposure to winter weather conditions may induce physiologic stresses including sympathetic activation, hypercoagulability and infection that increase the incidence or case fatality of AMI and stroke (1). The elderly, with their reduced physiologic reserve, may be more vulnerable to these influences than younger people. Data on the effect of age on seasonal variations in AMI and stroke are limited. We therefore investigated seasonal variations on mortality from AMI and stroke among different age groups in a large sample of deaths from Canada, a country with substantial differences in temperatures between seasons.

METHODS
This study utilized data from the Canadian Mortality Database for the years 1980 to 1982 and 1990 to 1992. The International Classification of Diseases (9th edition) was used to select deaths from AMI (code 410) and stroke (code 430–438). Data were analyzed by month of the year and by season as follows: winter (December to February), spring (March to May), summer (June to August) and autumn (September to November). Deaths by month were corrected for the number of days in each month. Subgroup analyses of seasonal patterns were performed by age groups: <65, 65 to 74, 75 to 84 and >85 years, and by gender.

The temporal distribution of deaths was tested for homogeneity with a chi-square goodness of fit (9). If differences were significant, the periods with the highest and lowest frequency were tested to evaluate differences from the average of all periods combined. The overall mean was set at a relative risk (RR) of one. The seasonal variation in mortality was expressed as the difference in RR between the
periods with the highest and lowest mortality. The trend in seasonal variation by age group was tested by linear regression, with age group as the independent variable. To account for multiple comparisons, a p value of less than 0.01 was considered significant.

RESULTS

A total of 159,884 deaths from AMI and 136,157 deaths from stroke were analyzed. The seasonal and monthly variations are shown for all deaths by season in Figure 1 and by month in Figure 2.

Acute myocardial infarction. Acute myocardial infarction deaths showed significant seasonal changes overall (p < 0.001). Deaths were highest in the winter (RR = 1.052, p < 0.001) and lowest in the summer (RR = 0.954, p < 0.001) with a seasonal variation in mortality of 9.8%. The month with the highest AMI mortality was January (RR = 1.090, p < 0.001), and the month with the lowest mortality was September (RR = 0.904, p < 0.001), with a 18.6% difference between January and September. Seasonal variation became dramatically more pronounced with increasing age. It was 5.8% in those <65 years, compared with 8.3% for ages 86 to 74, 13.4% for ages 75 to 84 and 15.8% for ages >85 years (Fig. 3). The slope of this trend was an increase of 3.51% in seasonal variation for every 10-year increase in age (p < 0.005). Acute myocardial infarction deaths among men were highest in the winter (RR = 1.049, p < 0.001) and lowest in the summer (RR = 0.955, p < 0.001), with a RR difference of 9.4%. A similar pattern was seen in women with a winter peak (RR = 1.056, p < 0.001) and a summer trough (RR = 0.953, p < 0.001) and a RR difference of 10.3%.

Figure 1. Mortality from acute myocardial infarction (AMI) and stroke by season. Relative risks for high and low months are compared with the average of all seasons combined. There are significant winter peaks (AMI p < 0.001, stroke p < 0.001) and summer troughs (AMI p < 0.001, stroke p < 0.001) in cardiovascular disease mortality, with a large difference in AMI (9.8%) and stroke (14.3%) mortality between these two seasons.

Figure 2. Mortality from acute myocardial infarction (AMI) and stroke by month. Relative risks for high and low months are compared with the average of all months combined. For both AMI and stroke, deaths peak in January (AMI p < 0.001, stroke p < 0.001) and then progressively decrease to a low in September (AMI p < 0.001, stroke p < 0.001). The difference in mortality from January to September is 18.6% for AMI and 19.9% for stroke.

Figure 3. Seasonal mortality variation by age at death. At younger ages, seasonal changes have little effect on mortality from cardiovascular diseases. However, seasonal variations are more pronounced with increasing age. Among those over 85 years old, there were 15.8% more AMI and 19.3% more stroke deaths in the winter than in the summer. The slope for this trend was significant at p < 0.005 for AMI and p < 0.005 for stroke.
Stroke. Stroke deaths also showed significant seasonal changes overall (p < 0.001). Deaths were highest in the winter (RR = 1.072, p < 0.001) and lowest in the summer (RR = 0.929, p < 0.001) with a seasonal mortality variation of 14.3%. By month, deaths were most frequent in January (RR = 1.113, p < 0.001) and fewest in September (RR = 0.914, p < 0.001), for a RR difference of 19.9%. Seasonal variation in mortality from stroke increased markedly with increasing age. In those aged <65 years, there was a RR difference of 4.8%, which increased to 11.6% in those aged 65 to 74, 15.2% for ages 75 to 84 and 19.3% for age >85 years (Fig. 3). The slope of this trend was a 4.71% increase in seasonal variation for every 10-year increase in age (p < 0.005). In men, a winter peak (RR = 1.068, p < 0.001), a summer trough (RR = 0.941, p < 0.001) and a RR difference of 12.7% were observed. Women showed similar variations, having higher death rates in the winter (RR = 1.075, p < 0.001) than in the summer (RR = 0.920, p < 0.001), with a RR difference of 15.5%.

DISCUSSION

We have studied seasonal variations in cardiovascular mortality using 300,000 deaths from the Canadian Mortality Database, in the largest study of seasonal mortality thus far in North America. A pronounced age effect in seasonal variations of death rates was observed. Winter increases in mortality from AMI and stroke were greater in the elderly compared with younger individuals.

Acute myocardial infarction. In Canada, a country with marked seasonal changes in climate, we have shown a seasonal variation in AMI mortality of 9.8%, suggesting that a large number of events are due to seasonal effects. Previous studies from Europe (1,10) and Asia (3,4) have also demonstrated a winter peak in cardiovascular deaths that is consistent with our results. However, our data suggest that age is a major determinant of the extent of environmental influence. A graded increase in mortality from AMI with increasing age was observed.

The mechanisms by which cardiovascular mortality increases in the winter and by which age differences occur are unclear. The winter peaks in AMI mortality have been correlated with daily (11) and monthly (10) temperature and shown to be greater among those with less personal protection from the cold (12). This would suggest the importance of climatic factors, particularly temperature, in causing seasonal variation. Climatic effects may potentially be mediated through increases in disease incidence or case fatality rates.

Epidemiologic data on seasonal changes in the incidence of AMI are limited. Two previous reports suggest that the incidence of AMI does, in fact, peak in the winter for older patients, whereas younger patients, particularly male patients, actually have a spring peak (1,10) in incidence. However, these data were based on hospital admissions records that may be subject to substantial referral biases and, therefore, may not account for all events in a community. Data on incidence rates from prospective cohorts are required.

On a physiologic level, knowledge of the determinants of acute cardiovascular disease incidence is evolving. The onset of AMI has been related to the presence of a vulnerable plaque, plaque disruption and fissuring and superimposed thrombosis (13). Several physiologic changes have been identified which may increase the probability of these events (14). Elevated lipid levels (15) and the presence of active inflammation (16) may make plaques more vulnerable to rupture. Disruption of plaques may be precipitated by hemodynamic forces, especially increases in blood pressure (17); subsequent thrombosis may be accelerated by higher levels of fibrinogen and other procoagulants (18). It has been shown that serum cholesterol (19), C-reactive protein (20), blood pressure (21), fibrinogen (20,22) and factor VII activity (20) are all higher in the winter. Elevation of these parameters may contribute to an increased tendency toward arterial thrombosis and a higher winter incidence of acute coronary syndromes (14).

There are several possible mechanisms by which the elderly may be subject to greater winter increases in AMI incidence than younger people. The elderly may have greater cold exposure. Exposure to cold is greater among poorer individuals and the elderly have lower income levels than other age groups. Alternatively, the elderly may demonstrate exaggerated responses to winter weather conditions, with greater increases in blood pressure and coagulation parameters, or a greater likelihood of infection (23). Further research is required to document age differences in these seasonal physiologic changes.

The winter increase in AMI mortality may be accounted for, at least in part, by winter increases in case fatality rates. It may be that the rates of complications and death are higher among patients who suffer myocardial infarction during colder temperatures. Furthermore, the elderly, with their decreased physiologic reserve, may be more susceptible. This hypothesis, however, remains to be tested because data on seasonal changes in case fatality rates for AMI have not been reported.

Stroke. Our data demonstrate a substantial seasonal variation in stroke mortality of 14.3%. A prior report from the U.K. also suggests a winter increase in deaths from stroke (2). Data on stroke incidence by season have been studied in hospital admission records and population cohorts. A number of studies of hospital admission data suggest that there is a winter peak in cerebral infarction that is not observed for hemorrhagic strokes (24–26). Because these studies utilized hospital admission data, they may be subject to referral bias. Though data from population-based cohorts provide a more accurate estimate of incidence rates, published studies thus far are conflicting. The Framingham cohort and an Italian stroke community registry show a winter peak in cerebral infarction (27,28), whereas no seasonal variation in stroke...
incidence by any subtype was seen in a U.K. community-based study (29).

If seasonal variations in incidence do not occur, then our results suggest that patients who suffer a stroke in the winter have a substantially worse prognosis than patients who have a stroke at other times of the year, particularly if they are older. Respiratory infections complicate stroke frequently. They are more common in the winter and may contribute to higher winter case fatality rates (2).

Limitations. This investigation utilized data from national and provincial statistics. Although these data are complete and encompass records of deaths in the country, vital statistics databases have less diagnostic accuracy than data derived from hospital admissions or clinical trials. On the other hand, such diagnostic misclassifications would tend to reduce differences between seasons and therefore, the real differences may be more marked than our data suggest. The use of broad diagnostic categories such as AMI and stroke reduces the potential for misclassification.

Conclusions. We have demonstrated a greater winter increase in mortality from AMI and stroke among the elderly than younger individuals in a large North American sample. These data suggest that environmental factors may play a major role in the triggering of acute cardiovascular events or in determining their outcome. An understanding of the potential role of seasonal stresses and other physiologic mechanisms responsible for these effects may provide novel avenues for research in the prevention of cardiovascular disease.

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