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Seasonal Pattern of Acute Myocardial Infarction in the National Registry of Myocardial Infarction

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Objectives. **The purpose of this study was to determine whether the rate of hospital admission for acute myocardial infarction (AMI) varies seasonally in a large, prospective U.S. registry.**

Background. **Identification of specific patterns in the timing of the onset of AMI is of importance because it implies that there are triggers external to the atherosclerotic plaque. Using death certificate data, most investigators have noted a seasonal pattern to the death rate from AMI. However, it is unclear whether this observation is due to variation in the prevalence of AMI or to other factors that may alter the likelihood of a fatal outcome.**

Methods. **We examined the seasonal mean number of cases of AMI (adjusted for the length of days in each season) that were submitted to the National Registry of Myocardial Infarction (NRMI) by 138 high volume core hospitals over a 3-year period (December 21, 1990 through December 20, 1993) during which the number of hospitals participating in the Registry was stable. Data were analyzed using general linear modeling and analysis of variance.**

Results. **High volume core hospitals reported 83,541 cases of AMI to the Registry during the study period. Approximately 10% more such cases were entered into the Registry in winter or spring than in summer ($p < 0.05$). The same trends were seen in both northern and southern states, men and women, patients <70 versus ≥70 years of age and those with Q wave versus non-Q wave AMI.**

Conclusions. **We conclude that there is a seasonal pattern to the reporting rate of cases of AMI in the NRMI. This observation further supports the hypothesis that acute cardiovascular events may be triggered by events that are external to the atherosclerotic plaque.**

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The time of onset of both acute myocardial infarction (AMI) and cardiac death varies in a circadian pattern, with a peak from 6 AM to noon and a lower prevalence during the night (1–6). Variations in platelet aggregability and sympathetic activity have been proposed to explain the observation, but the actual mechanism is not completely understood (1–6). Although it is known that short-term climatic changes (e.g., a heat wave) can influence cardiovascular morbidity and mortality transiently, investigators throughout the world (7–23) have reported that there is a seasonal pattern of deaths due to AMI with more fatal events in winter than in summer. However, it is unclear whether this observation is due to variation in the prevalence of AMI or to other factors that may alter the likelihood of a fatal outcome. The purpose of this study was to further explore this distinction by determining whether the rate of hospital admission of patients with AMI varies seasonally in a large, prospective, United States registry of cases of AMI.

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Methods

Study inclusion characteristics. The National Registry of Myocardial Infarction (NRMI) Phase 1 (NRMI-1) was a nationwide, observational data base containing quantitative and qualitative information about characteristics, diagnosis, treatment, clinical course and outcome of patients with AMI. Patients with a Q wave or non-Q wave AMI and those treated with a thrombolytic agent or mechanical revascularization or neither were included in the Registry. A broad range of community and teaching hospitals from all across the United States participated voluntarily in this large, industry-sponsored, observational data base. At the time of this investigation, 1,073 hospitals participated in NRMI, representing 14.4% of all general medical/surgical hospitals in the United States. As a group, NRMI-1 hospitals were significantly larger, more likely to be certified by the Joint Commission on Accreditation of Health Care Organizations, more likely to be affiliated with a medical school and to have a residency teaching program and more likely to have an emergency department, coronary care unit, cardiac catheterization laboratory and cardiac surgery program than were non-Registry hospitals (24).

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Abbreviations and Acronyms

AMI	=	acute myocardial infarction
ANOVA	=	analysis of variance
MONICA	=	Monitoring Trends and Determinants in Cardiovascular Disease
NRMI	=	National Registry of Myocardial Infarction
NRMI-1	=	National Registry of Myocardial Infarction Phase 1
WHO	=	World Health Organization

Individual institutions participating in NRMI-1 designated a physician investigator to oversee the entire hospital project and an NRMI-1 coordinator who was a physician, nurse, pharmacist, resident or quality assurance representative. The NRMI-1 coordinator conducted periodic retrospective chart reviews of all patients with confirmed AMI, and completed a case report form for each patient. This form contained pertinent data about each patient with AMI, such as time from symptom onset, demographic data and interhospital transfer, infarct location, method of diagnosing AMI, pharmacotherapy, ancillary procedures performed, patient outcome and clinical complications. Completed case report forms were then sent to an independent data coordinating center (ClinTrials Research, Inc.) that compiled the data and generated the reports.

The NRMI-1 coordinator was instructed as to the importance and benefit of correctly completing the case report forms. NRMI-1 coordinators and physician investigators received detailed training manuals to increase their knowledge of how to collect data in a uniform, accurate manner. The data coordinating center generated quarterly reports including tables and charts of aggregate data from the completed case report forms. Each hospital received its own data and the national aggregate data for comparison. Biannual trend reports that compared these data sets in 6-month intervals were also distributed. Patient confidentiality was preserved assiduously.

For purposes of this analysis, we defined the northern hemisphere climatic seasons based on the official "calendar" definitions: winter (December 21 to March 19 [89 days]); spring (March 20 to June 20 [93 days]); summer (June 21 to September 22 [94 days]); fall (September 23 to December 20 [89 days]). We adjusted the length of each season to 91 days to take into account the difference in the length of each season.

A core group of 138 high volume hospitals that participated in NRMI-1 during the entire study period from July 1, 1990 to June 30, 1994 and consistently treated at least six patients for 1 month with AMI were chosen from the 1,073 participating NRMI-1 hospitals. These characteristics were not present in the remaining, excluded non-core hospitals. Non-core hospitals were enrolled continuously and were being added to the study at varying times during the 3-year data collection period. Submission of AMI data from sites other than the core hospitals was highly sporadic, resulting in the capture of only occasional AMI cases rather than a continuous series.

Only cases of AMI from high volume core hospitals were included in the analysis to increase the likelihood that the sample represented sites that were fully engaged in completing case reports on the majority of admitted patients with AMI. The date of AMI symptom onset was the variable analyzed in this study, not the date that the case report form was submitted to the Data Coordinating Center. The adjusted seasonal mean number of AMI cases was chosen as the outcome variable.

Study exclusion characteristics. We excluded from analysis all data collected during the 1st year of the study because hospitals were coming "on line" in the study and a steady state number of participating centers had not yet been reached. We excluded the last 6 months of data collection to avoid including only ½ year of data. Thus, the study period consisted of 3 full years, beginning December 21, 1990 and ending December 20, 1993. Geographic subgroup analysis was also performed to compare the primary outcome variable in northern (Maine, New Hampshire, Vermont, New York, Ohio, Michigan, Wisconsin, Minnesota, North Dakota, Montana, Washington) and southern (Florida, Georgia, Alabama, Mississippi, Louisiana, Texas, New Mexico, Arizona, California) states.

All data in this study were collected using the NRMI-1 data collection form. In the fall of 1994, a new data collection form was implemented and all subsequent cases are being entered into a new data base entitled NRMI-2.

Statistical analysis. Statistical analysis was conducted using general linear modeling and analysis of variance (ANOVA) to analyze the mean of the adjusted number of AMI cases. The factors in the model included season (treatment) effect (winter, spring, summer, fall) and year effect (1991, 1992, 1993). The F test from ANOVA (type III) determined the overall main effect of season. If it was significant (i.e., $p < 0.05$), then the least significant difference test was used for post-hoc comparison of multiple means to determine which seasons were different.

Results

High volume core hospitals reported 83,541 cases of AMI to NRMI-1 during the study period. The number of cases reported was significantly higher in winter or spring than in summer in the model analysis (Fig. 1). The seasonal variation was of substantial magnitude. Approximately 10% more patients with AMI were entered into NRMI-1 by the core hospitals in winter or spring than in summer (Table 1). There was no significant difference between the number of AMI cases in fall and that in any other season in the model analysis.

The same seasonal trends were seen in all subgroups studied (northern and southern states, men and women, patients <70 vs. ≥70 years of age and those with Q wave vs. non-Q wave AMI) (Table 1). In the model analysis, the results achieved statistical significance only for southern states, women and patients ≥70 years of age. We could not test for the effect of other potentially interesting variables such as aspirin or beta-blocker usage because such information was not captured in the NRMI-1 data base.

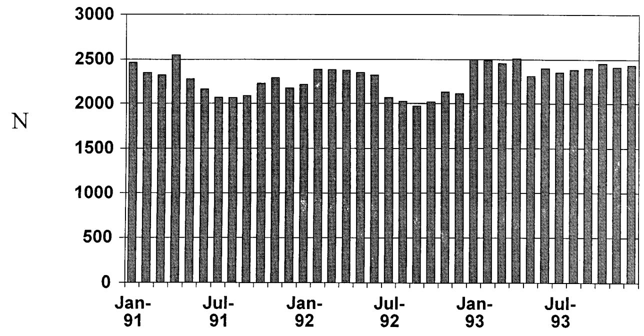

Figure 1. Number (N) of cases of acute myocardial infarction reported to the National Registry of Myocardial Infarction by all core hospitals per month. Monthly counts were adjusted on the basis of number of days in each month.

Discussion

Identification of specific patterns in the timing of the onset of AMI is of scientific importance because such patterns imply that there are triggers external to the atherosclerotic plaque. Using death certificate data, a large number of studies have confirmed that there is a seasonal pattern to deaths from AMI in the United States as a whole (23), Australia (23), New England (7), Philadelphia (8), Pittsburgh (9), New York (10), Boston (11), Cincinnati (12), Minneapolis-St. Paul (13), the Smolyan District of Bulgaria (16), London (14,17), England and Wales (18) and Romania (15). Only a handful of small, inadequately powered investigations (25–28) have not detected the seasonal pattern.

Muller et al. (6) recently discussed the appropriateness and limitations of using death certificate data to analyze the pattern of death from acute cardiovascular events such as AMI. Although death certificate diagnoses of specific causes of death are often inaccurate, general categories, such as death from ischemic heart disease, have been found to be reliable (6,29). The primary purpose of the previously cited studies was not to define the prevalence of death due to AMI but rather to determine whether there is a seasonal pattern to deaths attributed to AMI by the physician who signed the death certificate. Such studies cannot answer the most important question, which is whether there is a seasonal pattern to the actual prevalence of AMI.

The only way to definitively answer this question would be to look for a seasonal pattern in the prevalence of AMI in a large registry containing all cases of AMI in a geographic area (or in a representative sample of that area). All cases of AMI, including those presenting as sudden death or with atypical or no symptoms (i.e., "silent" infarction), would theoretically need to be confirmed in some way and counted. Unfortunately, there is no all inclusive, nationwide registry of cases of AMI in the United States and there is no practical way to detect and confirm the correct diagnosis in all AMI cases (e.g., "silent" infarctions).

The World Health Organization (WHO) MONICA (Monitoring Trends and Determinants in Cardiovascular Disease) Project uses a registry to track cardiovascular event and case fatality rates (30,31). Some sites, such as Augsberg, have captured virtually all hospitalized patients with AMI within a confined geographic area (32). Although most published reports from the MONICA Project have not reported looking for a seasonal patterns, a seasonal effect has been described in an Australian MONICA Project population (33). Coronary events, both fatal and nonfatal, were 20% to 40% more likely to occur in winter and spring than at other times of the year. It would be interesting to see whether such a trend exists in data from other MONICA Project centers and, if so, whether factors such as geographic latitude influence the pattern.

Limitations of the present study. The present study was undertaken to look for additional data that might support or refute the hypothesis that the onset of AMI has a seasonal prevalence. The NRMI-1 data base contains information on 354,435 patients with AMI and has been shown to be of great value in detecting trends in the treatment of AMI over time (24). However, it has certain limitations. NRMI-1 is not a random sample of all U.S. hospitals, but it does contain data from ~15% of all U.S. general medical/surgical hospitals. Participating hospitals tend to be larger and are more likely to have a coronary care unit, a cardiac catheterization laboratory or a cardiovascular surgery program than is the nationwide average hospital. None of these characteristics would be

Table 1. Cases of Acute Myocardial Infarction (AMI) Reported Each Season to the National Registry of Myocardial Infarction by All Core Hospitals During the Study

	Winter	Spring	Summer	Fall
All cases	7,218 (6,869–7,567)	7,222 (6,873–7,571)	6,574 (6,225–6,922)	6,765 (6,417–7,114)
Northern hospitals	2,153 (2,017–2,290)	2,188 (2,052–2,324)	2,000 (1,864–2,136)	2,091 (1,954–2,227)
Southern hospitals	1,632 (1,561–1,702)	1,557 (1,487–1,627)	1,397 (1,327–1,468)	1,460 (1,390–1,531)
Men	4,615 (4,356–4,875)	4,632 (4,372–4,892)	4,236 (3,976–4,496)	4,327 (4,063–4,587)
Women	2,545 (2,451–2,639)	2,531 (2,437–2,625)	2,292 (2,198–2,385)	2,381 (2,288–2,475)
Age <70 years	4,282 (4,042–4,522)	4,376 (4,136–4,615)	3,944 (3,704–4,184)	4,000 (3,760–4,240)
Age ≥70 years	2,873 (2,737–3,008)	2,775 (2,639–2,911)	2,563 (2,427–2,699)	2,716 (2,580–2,852)
Q wave AMI	5,095 (4,785–5,404)	5,071 (4,762–5,381)	4,594 (4,284–4,984)	4,675 (4,365–4,984)
Non-Q wave AMI	1,330 (1,278–1,382)	1,347 (1,295–1,399)	1,289 (1,237–1,340)	1,387 (1,335–1,438)

Data are presented as the mean (95% confidence interval) for all cases. Seasonal counts were adjusted on the basis of the number of days in each season.

expected to influence the seasonal pattern of AMI cases reported to NRMI-1.

Unlike other studies that have shown a higher prevalence of deaths attributed to AMI in the winter than in the summer, this investigation found more cases of AMI in both winter and spring than in summer (7–18,23). It is possible that the differences may be due to the fact that other studies have defined the seasons as arbitrary blocks of 3 months rather than by the official calendar definition.

Possible causes of the seasonal pattern. The cause of the seasonal pattern of AMI cases in NRMI-1 is unclear. Case report forms are sent into the data coordinating center from participating hospitals on a continuous basis. There are no administrative procedures (e.g., submission of reporting forms to meet a specific deadline at certain times of the year) that would generate an artificial, apparently seasonal pattern of cases. We do not believe it likely that an artifact, such as NRMI-1 coordinator summer vacations, had anything to do with the seasonal pattern because the analysis was based on the date of AMI onset rather than on the dates that the case report forms were submitted to NRMI-1. We believe that the most logical explanation is that the seasonal pattern of AMI NRMI-1 cases may, in fact, reflect an increased prevalence of AMI onset at certain times of the year.

Several theories have been proposed to explain an increased prevalence of AMI or its complications in winter (13,14,18,19,21,25,27,28) Cold weather or a sudden change in the climate can increase arterial blood pressure (22,34–39), arterial spasm (34–37,40), platelet and red blood cell counts (40), blood viscosity (40), plasma fibrinogen (41,42) and factor VII (42) and serum cholesterol levels (by ~2% to 3%) (43,44). Exposure to the cold also has important hemodynamic effects, including an increase in systemic vascular resistance, myocardial oxygen consumption and body metabolism. (34–37,40) It is unlikely that migration of persons from northern to southern states can explain the seasonal variation because similar trends were noted in both locations. Concurrent infections during the winter months, particularly those involving the respiratory tract, have also been postulated as a trigger for acute cardiovascular morbid events. Other mechanisms that have been proposed to explain the rise in cardiovascular events during cold weather include seasonal change in physical activity, diet, weight, stress during the holiday season and seasonal modulation in the secretion of physiologically active substances analogous to those that trigger seasonal depression (13,14,18, 19,21–23,25,27,28). The other possibility is that the seasonal pattern observed in this and other studies could be due to a summer *decrease* in events relative to other times of the year.

Magnitude of the seasonal variation. In the present study, the magnitude of the seasonal variation was relatively modest (~10%) compared to the 20% to 30% variation reported in the number of cardiovascular events in an Australian MONICA Project population (33). It was also less than the 20% to 38% seasonal variation reported in the incidence of cardiac death attributed to AMI based on death certificate data in the United States and Australia as a whole (23). The reason for these differences among studies is unclear.

Conclusions. We conclude that there is a winter and spring increase or summer decrease in the number of cases of AMI reported to a large, prospective United States registry of AMI cases. These observations, together with data indicating that there is a circadian pattern to the onset of AMI and a seasonal distribution of deaths reported to be due to AMI, further support the hypothesis that acute cardiovascular events may be triggered by events that are external to the atherosclerotic plaque.

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