Weekly Variation of Acute Myocardial Infarction
Increased Monday Risk in the Working Population

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**Background**  Seasonal and circadian variations in the occurrence of myocardial infarction and sudden cardiac death have been documented, suggesting that triggering factors may play a role in the causation of cardiac events. However, there are only sparse and conflicting data on the weekly distribution of the disorders.

**Methods and Results**  To determine the weekly variation of acute myocardial infarction and sudden cardiac death, 5596 consecutive patients (71% men; age, 63±1 years) were analyzed in a regionally defined population (n=330 000; age, 25 to 74 years) monitored from 1985 to 1990. The exact time of onset of symptoms was used to determine the day of the event. Patients with myocardial infarction (n=2636) demonstrated a significant weekly variation (P<.01) with a peak on Monday, whereas patients with sudden cardiac death (n=2960) were evenly distributed throughout the week. A similar weekly pattern was observed in subgroups of patients with myocardial infarction defined with respect to age, sex, cardiac risk factors, prior cardiac medication, and infarct characteristics. The working population demonstrated a weekly variation of myocardial infarction as opposed to the nonworking population, with a 33% increase in relative risk of disease onset on Monday (P <.05) and a trough on Sunday compared with the expected number of cases, if homogeneity was assumed.

**Conclusions**  The onset of acute myocardial infarction demonstrates a peak on Monday primarily in the working population. If this finding is confirmed in other communities, it may aid in identifying acute triggering events of myocardial infarction and perhaps in improving prevention of the disease.  

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**Key Words**  • myocardial infarction • sudden cardiac death • circadian variation

The triggering mechanisms of acute myocardial infarction and sudden cardiac death are poorly understood, and means of efficient prevention are therefore limited. A new basis for investigation of the acute causation of the disorders has been provided by the observation of circadian and seasonal variations in the onset of myocardial infarction and sudden cardiac death. Both disorders occur more frequently during the initial hours after awakening compared with other times of day1-4 and during the winter months compared with other seasons.5-8 These findings support the hypothesis that identifiable triggering factors may play a role in the causation of cardiac events.9,10

There are only sparse and conflicting data on the weekly distribution of acute myocardial infarction and sudden cardiac death. Furthermore, some previous studies on the weekly distribution of cardiac events were based on select patients or limited sample size or did not provide sufficient subgroup analyses.5,6,11-16 Preliminary analyses of the Triggers and Mechanisms of Myocardial Infarction (TRIMM) Study suggested a weekly variation of myocardial infarction.17 Therefore, we determined the weekly variation of acute myocardial infarction and sudden cardiac death based on the exact time of onset of symptoms in a large, unselected population of the Monitoring Trends and Determinants in Cardiovascular Disease (MONICA) register18,19 and in patient subgroups categorized with regard to cardiac risk factors, cardiac medication, and sociodemographic variables including working status.

**Methods**

**Study Population**  The primary objective of the World Health Organization MONICA project is to measure the trends and determinants in cardiovascular mortality and morbidity and to assess the extent to which these trends are related to changes in risk factors and medical care.18 The present study was conducted in the Augsburg MONICA center, which shares the organizational structure of all participating MONICA sites and furthermore uses additional extensive standardized patient interviews.18,19 The Augsburg center includes a study population of 330 000 residents (48% men, 52% women; 25 to 74 years of age).

**Entry Criteria and Data Collection**  The diagnostic criteria for acute myocardial infarction included chest pain for ≥20 minutes not relieved by nitrates, ECG changes suggestive of evolving myocardial infarction according to Minnesota coding,20 and subsequent elevation above twice the upper normal limit of at least one of three enzymes: creatine phosphokinase, aspartate aminotransferase, and lactate dehydrogenase. The Minnesota code is a standardized classification system for ECG readings. A maximum of four 12-lead ECGs (first, second, and third day after admission and discharge recordings) were available for 98% of patients, coded independently by two specially trained coders and subsequently compared and decided on by a supervisor coder. All the diagnostic parameters were available as primary items from each patient. The diagnostic criteria for sudden cardiac death included chest pain for ≥20 minutes not relieved by nitrates, ECG changes suggestive of evolving myocardial infarction according to Minnesota coding,20 and sudden death.
death included death within 24 hours after onset of cardiac symptoms in individuals with a history of coronary artery disease or no evidence for another cause of death. For the purpose of the present study, all diagnostic evidence including necropy findings, if available, was used to classify the registered event as sudden cardiac death or acute myocardial infarction.

The study personnel learns of a myocardial infarction or sudden cardiac death by routine monitoring of hospitalizations in the Central Hospital and all further 12 hospitals within and 13 hospitals adjacent to the study area and by routine review of death certificates.\textsuperscript{19} Data on hospital-treated myocardial infarctions were collected primarily at the time when the patients were still hospitalized (average time in hospital for patients with myocardial infarction, 25 days). Using a list of specific admission diagnoses, the admission books of the within-region hospitals were regularly (Central Hospital daily, other hospitals weekly) screened for suspected acute myocardial infarction or ischemic events; the adjacent hospitals were called on a weekly or monthly basis. Subsequently, ward physicians were questioned by telephone to determine whether there was clinical evidence of acute myocardial infarction in patients meeting the screening diagnoses. If so, patients were interviewed with a standardized questionnaire within 2 weeks after hospital admission by three specially trained nurses employed exclusively for registration purposes. Information on medical history, cardiac medication, working status, and exact time of onset of symptoms was obtained in these interviews and by questionnaires sent to the physicians of deceased patients. Additional information was retrieved from hospital charts if needed (eg, in case of incomplete medical or medication history). The diagnosis was confirmed and treatment data were collected in a final chart review approximately 6 weeks after discharge. The time of onset of symptoms as recollected by the patient was used to determine the day and time of the cardiac event.

**Statistical Analysis**

Implementation and data handling procedures and quality control measures of the MONICA study have been described previously.\textsuperscript{18,19} The data were evaluated with SAS and EPINFO 5. The patients were classified as having had the cardiac event on the day of onset of symptoms, not on the day of presentation to a hospital. The weekly distribution of cardiac events was first tested for homogeneity by $\chi^2$ goodness-of-fit tests including Bonferroni correction for multiple hypothesis testing.\textsuperscript{21,22} An excess relative risk of cardiac events on individual days of the week was calculated by age-adjusted Mantel-Haenszel statistics. Stratified analyses and multivariate logistic regression models were used to assess the contribution of sociodemographic and medical factors to the weekly distribution of cardiac events. The circadian variation of cardiac events on different days of the week was first tested by $\chi^2$ tests to determine differences among four 6-hour intervals (midnight to 6 AM, 6 AM to noon, noon to 6 PM, and 6 PM to midnight) as described previously.\textsuperscript{1} Subsequently, the circadian variation on Sunday versus midweek days also was tested to determine differences among twelve 2-hour intervals. A value of $P<.05$ was considered significant.

**Results**

From January 1985 to December 1990, a total of 5596 events of myocardial infarction or sudden cardiac death were recorded in the Augsburg MONICA register. The patient population included 71% men and 29% women with a mean age of 63 years. Compared with the patients with sudden cardiac death, the patient group with myocardial infarction included more men, was younger and more frequently currently employed, and was generally "healthier" as indicated by a lower frequency of previous angina, myocardial infarction, diabetes, and use of cardiac medication (Table 1). The weekly distribution of disease onset in patients with myocardial infarction (n=2636) demonstrated a significant variation ($P<.01$), with a peak on Monday (Fig 1). The relative risk to experience myocardial infarction on Monday was increased by 20% ($P<.05$) compared with the expected number of cases, if homogeneity was assumed. Sudden cardiac death (n=2960) was rather evenly distributed without a day of significantly increased incidence (Fig 1).

A similar weekly pattern in onset of myocardial infarction was observed in stratified subgroups of patients categorized with respect to age, sex, known cardiac risk factors, and use of medication (Table 1). The daily distribution of disease onset in patients with myocardial infarction (n=2636) demonstrated a significant variation ($P<.01$), with a peak on Monday (Fig 1). The relative risk to experience myocardial infarction on Monday was increased by 20% ($P<.05$) compared with the expected number of cases, if homogeneity was assumed. Sudden cardiac death (n=2960) was rather evenly distributed without a day of significantly increased incidence (Fig 1).
TABLE 2. Weekly Variation of Onset of Myocardial Infarction in Patient Subgroups, Categorized With Respect to Sociodemographic Variables, Cardiac Risk Factors, Prior Cardiac Medication, and Infarct Characteristics by Age-Adjusted Mantel-Haenszel Odds Ratio Observed Versus Expected Number of Cases per Weekday

<table>
<thead>
<tr>
<th>Odds Ratios</th>
<th>Sunday</th>
<th>Monday</th>
<th>Tuesday</th>
<th>Wednesday</th>
<th>Thursday</th>
<th>Friday</th>
<th>Saturday</th>
<th>Total (n)</th>
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<td>1.20*</td>
<td>0.93</td>
<td>1.00</td>
<td>1.10</td>
<td>0.94</td>
<td>0.98</td>
<td>2636</td>
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<td>Age, y</td>
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<td></td>
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<td>25-54</td>
<td>0.86</td>
<td>1.23</td>
<td>1.01</td>
<td>1.07</td>
<td>1.00</td>
<td>0.87</td>
<td>1.01</td>
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<td>0.98</td>
<td>1.11</td>
<td>0.91</td>
<td>0.99</td>
<td>1.10</td>
<td>0.93</td>
<td>0.99</td>
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<td>1.21*</td>
<td>0.92</td>
<td>0.97</td>
<td>1.17</td>
<td>0.99</td>
<td>0.96</td>
<td>1097</td>
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<tr>
<td>Men</td>
<td>0.88</td>
<td>1.16</td>
<td>0.95</td>
<td>1.02</td>
<td>1.07</td>
<td>0.90</td>
<td>0.94</td>
<td>1987</td>
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<tr>
<td>Women</td>
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<td>1.29</td>
<td>0.82</td>
<td>0.90</td>
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<td>1.33*</td>
<td>0.94</td>
<td>0.90</td>
<td>1.14</td>
<td>0.84</td>
<td>1.00</td>
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<td>0.92</td>
<td>1.01</td>
<td>1.04</td>
<td>0.97</td>
<td>1.00</td>
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<td>Diabetes</td>
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<td>0.96</td>
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<td>1.15</td>
<td>0.92</td>
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<td>Hypertension</td>
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<td>1.22</td>
<td>0.92</td>
<td>0.96</td>
<td>1.04</td>
<td>1.00</td>
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<td>1.21</td>
<td>0.94</td>
<td>1.02</td>
<td>1.18</td>
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<td>1.19</td>
<td>0.96</td>
<td>0.96</td>
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<td>0.99</td>
<td>0.92</td>
<td>1.04</td>
<td>0.95</td>
<td>0.99</td>
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<td>0.88</td>
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<td>Yes</td>
<td>0.79</td>
<td>1.19</td>
<td>1.06</td>
<td>0.98</td>
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<tr>
<td>First myocardial infarction</td>
<td>0.86</td>
<td>1.18</td>
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<td>0.99</td>
<td>1.12</td>
<td>0.92</td>
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<td>Recurrent myocardial infarction</td>
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<td>1.29</td>
<td>0.97</td>
<td>0.94</td>
<td>1.14</td>
<td>1.00</td>
<td>0.93</td>
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<td>1.20*</td>
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<td>1.00</td>
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<td>0.93</td>
<td>0.95</td>
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<td>Nontransmural</td>
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<td>1.13</td>
<td>0.90</td>
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<td>1.13</td>
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<td>Anterior</td>
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<td>1.21</td>
<td>0.97</td>
<td>0.87</td>
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<td>0.95</td>
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<td>Inferior</td>
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<td>0.89</td>
<td>1.06</td>
<td>1.05</td>
<td>0.93</td>
<td>0.99</td>
<td>1206</td>
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</tbody>
</table>

*P<.05.

Risk factors, prior cardiac medication, and infarct characteristics (Table 2). However, there was a marked difference in groups of patients with myocardial infarction categorized with respect to working status (Fig 2). In the working population (n=884) there was the most prominent Monday peak of myocardial infarction, with a 33% increase in relative risk (P<.05) and a trough on Sunday compared with the expected number of cases, if homogeneity was assumed. In the nonworking population (n=1191), there was a more even weekly distribution. In the remaining 561 patients, information on the working status was not available. The majority of these patients (87%) were 60 years of age or older. The weekly pattern was similar in patients with blue collar or white collar professions, with a relative risk increase on Monday by 41% and 18%, respectively.

In a multivariate analysis, no variable alone could explain the Monday peak of onset of myocardial infarction. Sunday was the only day on which the observed number of myocardial infarction was consistently lower than the expected number under the assumption of homogeneity (odds ratios <1).

Hospital admission was delayed if myocardial infarction occurred on a Sunday compared with each midweek day (Fig 3). Of all patients with onset of symptoms on Sunday, 32% were admitted on a later day compared with only 19% of patients with onset of symptoms on Monday, the day of smallest delay (P<.01). There was a

![Graph showing the effect of the working status on myocardial infarction](http://circ.ahajournals.org/)

*Fig 2. Bar graph: Day of week of myocardial infarction in the working population (n=884) and in the nonworking population (n=1191). The occurrence of myocardial infarction demonstrates a weekly variation in the working population, with a peak on Monday (relative risk increased by 33%), as opposed to the nonworking population (P<.05) with a more even distribution.*
marked overall circadian variation \( (P<.001) \) of myocardial infarction and of sudden cardiac death that did not, however, reach statistical significance on each day of the week (Fig 4). In the working population, the peak of myocardial infarction appeared to occur somewhat earlier on midweek days compared with Sunday, but this was not statistically significant (Fig 5).

**Discussion**

The present study demonstrates a weekly variation of acute myocardial infarction of hospitalized patients, with an increased relative risk on Monday. This weekly pattern appears to reflect primarily the distribution of disease onset in the working population.

Previous studies on the weekly distribution of cardiac events presented conflicting views. Some authors suggested an increased risk on Mondays, whereas others indicated a peak on other days of week or no significant weekly variation at all. Some of these prior studies were not population based, did not distinguish clearly between sudden cardiac death and myocardial infarction, or did not present subgroup analyses related to important demographic variables. In the present study, selection bias appears to be an unlikely source of error because of the design of the MONICA registry. The population-based registry in the MONICA Augsburg study region was an ideal tool to provide complete documentation of fatal and nonfatal coronary events and to determine the day and time of disease based on the onset of symptoms. Time of onset of symptoms of myocardial infarction has been shown previously to correlate well with the timing of disease onset, based on enzymatic time activity analysis. The only group of patients impossible to include into the present analysis were those with “silent” myocardial infarction, but a similar weekly pattern may be assumed in these patients.

In the present study, the delay from onset of cardiac symptoms to hospital admission was greater on Sunday compared with midweek days. This observation may reflect an increased likelihood in patients whose infarct began on Sunday to stay home and delay hospital admission until Monday. Since in our analysis, determination of time of an event was based on the time of onset of symptoms rather than time of admission, this phenomenon was an unlikely source of bias of the present results. However, this observation may provide clues to a possible “referral bias” of previous reports, although other analyses suggested a longer delay to admission on Monday compared with weekend days (Weaver, personal communication).

The observation of a weekly variation of myocardial infarction is compatible with the hypothesis that external triggering factors may play a role in the acute causation of the disease. Therefore, the secondary finding of a difference in weekly variation according to working status of the patients was of particular interest. Although precise information on the working schedule of the patients was not obtained routinely, it is reasonable to assume an increase in physical and mental burden from leisurely weekend activities to stressful work on Monday in the majority of working patients. Furthermore, the suggestion of an earlier peak in the circadian variation of myocardial infarction on Monday and on other midweek days compared with Sunday (Fig 5) may reflect an earlier onset of these activities. The speculation of an association of work burden and disease onset is indirectly supported by recent results of a large cohort study indicating a higher hospitalization rate as a result of ischemic heart disease among men with frequent night or shift working schedules compared with those having day work only. Further investigation of the weekly pattern of myocardial infarction in relation to the kind of work done and in patients of a different cultural background with different work schedules may provide further insight into the relation between activities and cardiac risk. One also might speculate that medication compliance differs between midweek and weekend days, perhaps resulting in medication withdrawal on Mondays, although to our knowledge, no studies have addressed this issue yet.

External stimuli may act as triggers in subjects predisposed to coronary artery disease and may explain the excess relative risk of myocardial infarction on Mondays. Prominent external stress factors including physical exercise, natural disasters such as earthquakes or blizzards, and warfare have been observed to increase short-term cardiac mortality. In patients suddenly changing their activity pattern on the transition from weekend to workday, more subtle stimuli might increase the risk of myocardial infarction. The possible pathophysiologic links between external factors and acute coronary events include changes in thrombotic tendency, platelet aggregability, fibrinolytic activity, blood viscosity, and body temperature during physical or mental stress and increases in blood pressure and coronary tone secondary to changes in the sympathetic nervous system activity level. However, further investigation is needed to determine the precise association between external events and underlying pathophysiological mechanisms and to identify means of possible intervention.

In view of the fact that the presumed pathophysiology of myocardial infarction and sudden cardiac death is often similar, it is enigmatic that the Monday peak
phenomenon was only observed with myocardial infarction. Because a substantial proportion of sudden cardiac deaths are probably fatal myocardial infarctions as assessed by thrombotic coronary occlusion in autopsy studies, a similar onset pattern was expected for both disorders. The overall circadian variation of myocardial infarction and sudden cardiac death is similar in the present study (although not statistically significant on each day, presumably because of small sample sizes) and consistent with observations in prior studies. The only inconsistency is that the weekly variation of sudden cardiac death does not parallel that of acute myocardial infarction. There is no clear explanation for the discrepancy observed in the present study. The possibility of undersampling of sudden cardiac death as a potential source of bias appears unlikely because of the extensive screening of the MONICA registry. However, the accuracy of mortality records has certain limitations, perhaps causing some recording bias. Furthermore, the marked differences in baseline characteristics of patients with sudden cardiac death compared with those with myocardial infarction may have contributed to the observed differences between the two cardiac events (Table 1). It also appears to be possible that the absence of a weekly variation of sudden cardiac death as opposed to myocardial infarction reflects a difference in categories of possible external triggers of the disorders. Therefore, our observations and these hypothetical explanations need to be confirmed or refuted in the future.

Limitations and Conclusions

Although our main findings were statistically significant and compatible with prior epidemiological observations and pathophysiological hypotheses, the MONICA study was not primarily designed to address the aims of the present study. The retrospective subgroup analyses may yield significance by chance alone and therefore warrant
Further investigation. The primary value of the present results is their adding evidence to the emerging concept of triggering of onset of myocardial infarction and sudden cardiac death. If the present finding of an increased Monday risk of myocardial infarction in the working population is confirmed in other communities, it may help to identify triggering mechanisms of the disease. This approach may eventually lead to improved means of prevention.

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References


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