PHYSICAL EXERTION AS A TRIGGER OF ACUTE MYOCARDIAL INFARCTION

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Abstract *Background.* It is controversial whether the onset of myocardial infarction occurs randomly or is precipitated by identifiable stimuli. Previous studies have suggested a higher risk of cardiac events in association with exertion.

Methods. Consecutive patients with acute myocardial infarction were identified by recording all admissions to our hospital in Berlin and by monitoring a general population of 330,000 residents in Augsburg, Germany. Information on the circumstances of each infarction was obtained by means of standardized interviews. The data analysis included a comparison of patients with matched controls and a case-crossover comparison (one in which each patient serves as his or her own control) of the patient's usual frequency of exertion with the last episode of exertion before the onset of myocardial infarction.

Results. From January 1989 through December 1991, 1194 patients (74 percent of whom were men; mean age [±SD], 61±9 years) completed the interview 13±6 days after infarction. We found that 7.1 percent of the case patients had engaged in physical exertion (≥6 metabolic equivalents) at the onset of infarction, as compared with 3.9 percent of the controls at the onset of the control event. For the patients as compared with the matched controls, the adjusted relative risk of having engaged in strenuous physical activity at the onset of infarction or the control event was 2.1 (95 percent confidence interval, 1.1 to 3.6). The case-crossover comparison yielded a similar relative risk of 2.1 (95 percent confidence interval, 1.6 to 3.1) for having engaged in strenuous physical activity within one hour before myocardial infarction. Patients whose frequency of regular exercise was less than four and four or more times per week had relative risks of 6.9 and 1.3, respectively ($P<0.01$).

Conclusions. A period of strenuous physical activity is associated with a temporary increase in the risk of having a myocardial infarction, particularly among patients who exercise infrequently. These findings should aid in the identification of the triggering mechanisms for myocardial infarction and improve prevention of this common and serious disorder. (N Engl J Med 1993;329: 1684-90.)

THROUGHOUT this century, the possible association of external stimuli with the onset of acute myocardial infarction has been debated.[1-10] Among the factors that have been suggested as precipitating myocardial infarction are strenuous physical activity and emotionally upsetting life events. Some studies have suggested that cardiac events occur with increased frequency during or within a few hours after physical exertion.[1-3,8-10] Others have concluded that acute myocardial infarction is a random event among patients with coronary artery disease.[4,7] Many of these studies, however, were based on anecdotal reports, studied selected patient populations, or were limited by the lack of adequate control data.

The documentation of circadian variation in the incidence of acute myocardial infarction indicated that the onset of infarction is not a random event; such studies thus provided a basis for the study of the triggering mechanisms.[11-13] The Triggers and Mechanisms of Myocardial Infarction Study was designed to determine the frequency and importance of physical activity and other external stimuli associated with the transition from chronic coronary artery disease to acute nonfatal myocardial infarction.

METHODS

Study Population

In Berlin, Germany, data were recorded for all patients admitted to the coronary care unit at Klinikum Steglitz with a primary diagnosis of acute myocardial infarction. In Augsburg (a midsize city in southern Germany), a predefined general population of 330,000 residents (48 percent men and 52 percent women, 25 through 74 years of age) was monitored with use of the registration procedures developed for the Monitoring Trends and Determinants in Cardiovascular Disease project of the World Health Organization.[14] The study personnel in Augsburg identified patients with myocardial infarctions by routine monitoring of hospitalizations in the Central Hospital (on a daily basis), in the other 12 hospitals within the study area (once a week), and in 13 hospitals adjacent to the study area (once a week).[15]

The diagnostic criteria for acute myocardial infarction included chest pain lasting 20 minutes or more that was not relieved by nitrates, electrocardiographic changes suggestive of evolving myocardial infarction according to the Minnesota coding system,[16] and a subsequent increase in the level of at least one of three cardiac enzymes (creatine kinase, aspartate aminotransferase, and lactate dehydrogenase) to more than twice the upper limit of normal. Electrocardiographic data (available for 98 percent of the patients) were coded independently by two specially trained coders, and a final decision about the diagnosis was subsequently made by a supervisor. Exclusion criteria for the study were poor health (such as a critical illness or moribund condition), inability to communicate with the investigators, and death before the scheduled interview. Informed consent for participation was requested and received from all patients.

Control subjects were recruited from the general population of Augsburg and matched to the Augsburg patients in terms of age, sex, and precinct. Case patients were frequency-matched to controls in a projected ratio of 2:1. All residents in Germany are legally required to register with the local administration. After approval of the study by the Department of Health, state officials in Augsburg and the surrounding communities provided a stratified random sample of residents matched to the case patients. Within seven days after mailing them a request for cooperation in a "study on heart disease," we contacted the members of the sample by telephone and asked them to participate in the study. Seventy percent of the initial random sample of controls were successfully contacted and consented to a telephone interview. The stratification scheme was preserved by the use of backup stratified samples of matched residents.

Collection of Data

All the study patients underwent a standardized interview after their transfer from the coronary care unit to a general ward. The

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interview covered demographic variables, medical history, cardiac risk factors, the timing and characteristics of symptoms, physical activity, unusual life events, location and circumstances of the myocardial infarction, sleeping and waking habits, the times of awakening and arising, medications used, typical meals and activities, and any factors suspected by the patients of triggering myocardial infarction.

During an initial pilot phase,[17] the questionnaire was tested and revised to improve its clarity, minimize redundancy, and facilitate statistical analysis. The interviews with the patients were conducted by three study nurses with extensive clinical experience with cardiovascular disease. Adherence to standardized interview and coding procedures was ensured by the initial training of the interviewers, subsequent routine supervision, and a policy of immediately contacting the study investigators in the case of unforeseen problems. If necessary, supporting information was retrieved from the patients' medical records or obtained from their physicians (for example, to obtain complete information on medications). If data conflicted, medical reports were considered more reliable than information furnished by the patients.

The telephone interview with the controls was conducted by study personnel who used a standardized questionnaire that was almost identical to the patient-interview form but that excluded questions about acute symptoms and suspected triggers of myocardial infarction. The controls were instructed by the interviewer to assume that they had experienced acute chest pain (the "control events") at specific times within the previous 24 hours, distributed in a circadian pattern identical to the pattern of onset of myocardial infarction among the patients.

Physical activity was measured in terms of metabolic equivalents (MET), defined as the energy expended per minute by a resting subject. Activity was categorized as follows: sleep (1 MET), sedentary activity (2 MET), mild-to-moderate activity (3 to 5 MET), or strenuous activity (≥6 MET) on the basis of the subjects' assessment; this method was similar to that used by Paffenbarger et al.[18] The time of occurrence of the myocardial infarction was defined as time of onset of the most severe symptoms.

Statistical Analysis

After the questionnaires were checked for completeness and accuracy, the data were coded and double-entered into a D-BASE IV data base on a PS/2-70 computer, and the plausibility of the responses was checked. The data were evaluated with SAS and Epi Info 5 statistical-software packages.

The primary statistical approach (Fig. 1) was a case–control analysis of the frequency of exposure (in this case, the frequency of strenuous physical activity) in the patients as compared with the matched controls. We also used a self-matched case-crossover method that was recently developed to identify transient effects on the risk of acute events.[19] Briefly, the patients' usual frequency of physical exertion over the past year (for purposes of the analysis, the daily frequency of strenuous activity assuming 16 potential one-hour episodes of activity per day and eight hours of sleep) was compared with the length of time between the last episode of physical activity and the onset of myocardial infarction. The risk period was prospectively defined as the hour before the onset of myocardial infarction. For each patient, we calculated the observed odds of occurrence of physical exertion (1:0 or 0:1) within the hour before the onset of myocardial infarction and the expected odds (x:y) that exertion would have occurred within one hour before the onset of symptoms, given the usual frequency of physical exertion. Algebraically, the sum of y in patients who reported exertion within one hour before onset represents the numerator and the sum of x in patients who reported no exertion represents the denominator of the risk ratio.

In our analysis of the length of time from exertion to the onset of myocardial infarction, adjusted for the time of awakening, the probability of onset in patients in whom symptoms were present when they awakened was evenly distributed during the six hours before the time of awakening, as described previously.[17]

Conventional statistical techniques were used to determine the differences between the study groups in terms of categorical or continuous variables. The relative risk of myocardial infarction (odds ratio) associated with a suspected trigger and a corresponding estimate of the variance of its logarithm were calculated with use of the Mantel–Haenszel procedure.[19-22] Multivariate logistic-regression analysis was performed to adjust for factors known to influence the risk of myocardial infarction or to differ between cases and controls. All P values were two-tailed; values below 0.05 were considered to indicate statistical significance.

Results

Study Population

From January 1989 through December 1991, a total of 1194 patients (74 percent men and 26 percent women; mean age [±SD], 61±9 years) were enrolled in the study and completed the interview 13±6 days after myocardial infarction. Of all patients hospitalized during this period with documented nonfatal myocardial infarctions, 75 percent were eligible and consented to participate in the study. The differences between the 224 patients from Berlin and the 970 patients from Augsburg (Table 1) were probably related mainly to the study design. A total of 532 controls were matched to the Augsburg patients (Table 1). The controls did not differ from the patients in age, sex, marital status, proportion of blue-collar workers, educational level, or usual frequency of physical exertion, but a higher proportion of the control group was employed. As would be expected, there were substantial differences between the patients and the controls in medical history and use of cardiac medications (Table 1).

Physical-Activity Status

As compared with the matched controls, the Augsburg patients had a crude relative risk of 1.9 (95 per-

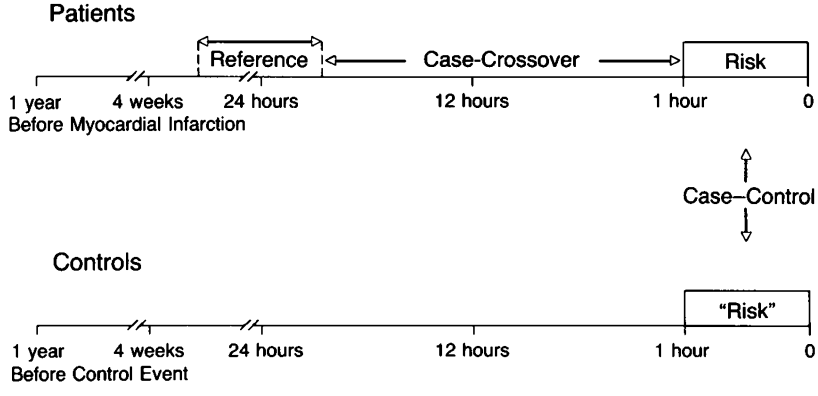

Figure 1. Design of the Study.

The time point 0 indicates the onset of acute myocardial infarction in the patients and coincides with the control event for the matched controls (a specified time during the 24 hours before the interview). The case–control analysis compared the patients' exposure to a suspected trigger (strenuous physical activity) before the onset of myocardial infarction (risk period) with the controls' exposure to the same trigger before the control event ("risk" period). An additional case-crossover analysis compared the patients' exposure to a suspected trigger (strenuous physical activity) during the risk period with their usual frequency of exposure.

cent confidence interval, 1.1 to 3.5) of having engaged in strenuous physical activity (≥6 MET) at the onset of myocardial infarction (69 patients [7.1 percent] vs. 21 controls [3.9 percent]). The activities reported by the patients included housework (9 patients), physical activity at work (6), yardwork (4), shopping and carrying bags (8), lifting heavy objects (6), walking up flights of stairs (8), jogging (5), bicycling (2), aerobics (1), and other activities (19); in the case of 1 additional patient, myocardial infarction began during an exercise treadmill test. Patients were less likely to have been sleeping at the onset of myocardial infarction than were the controls at the times of the control events (194 patients [20 percent] vs. 157 controls [30 percent]). A total of 509 patients (52 percent) and 233 controls (44 percent) had been sedentary, and 198 patients (20 percent) and 121 controls (23 percent) had been engaged in mild-to-moderate activity; these percentages did not differ significantly between patients and controls.

Multivariate logistic-regression analysis with adjustment for factors known to influence the risk of myocardial infarction or to differ between case patients and controls confirmed an independent relative risk of 2.1 (95 percent confidence interval, 1.1 to 3.6) that the patients had engaged in physical exertion at the onset of myocardial infarction (Table 2).

Patients with a previous diagnosis of coronary heart disease (myocardial infarction or angina pectoris) appeared not to have an increased risk in association with physical exertion (Table 3), but this finding may be an artifact caused by the small number of controls who reported physical activity. Subgroups of patients defined according to sex and age had similar relative risks of myocardial infarction in association with physical exertion: men, 2.0 (95 percent confidence interval, 0.9 to 3.7), and women, 2.0 (95 percent confidence interval, 0.5 to 9.0); patients 60 years of age or older, 2.4 (95 percent confidence interval, 1.0 to 5.9), and patients less than 60 years of age, 1.6 (95 percent confidence interval, 0.8 to 3.5). Among patients who reported exertion before the event, the onset of myocardial infarction was fairly evenly distributed throughout the day.

Table 1. Demographic Characteristics and Medical History of the Study Population.*

VARIABLE	PATIENTS		CONTROLS (N = 532)
	BERLIN (N = 224)	AUGSBURG (N = 970)	
Age (yr)	63±13†	60±8	59±9
Male (%)	64†	77	77
Married (%)	63†	81	81
Employed (%)	38	38‡	48
Blue-collar worker (%)	18†	36	39
College education (%)	11§	6	5
Regular exercise (%)	21†	38	35
Previous myocardial infarction (%)	24§	17‡	6
Angina pectoris (%)	35	33‡	8
Hypertension (%)	47	50‡	30
Hyperlipidemia (%)	54§	63‡	33
Diabetes (%)	14§	20‡	9
Smoking (%)	48§	41‡	23
Nitrates (%)	18	20‡	4
Calcium-channel blockers (%)	23	21‡	7
Beta-blockers (%)	14	15‡	6
Aspirin (%)	13	12‡	3
ACE inhibitors (%)	6	5¶	3

*Plus–minus values are means ±SD. Regular exercise was defined as usual strenuous physical activity four or more times per week. ACE denotes angiotensin-converting enzyme.

†P<0.01 for the comparison with the Augsburg patients.

‡P<0.01 for the comparison between the Augsburg patients and the controls.

§P<0.05 for the comparison with the Augsburg patients.

¶P<0.05 for the comparison between the Augsburg patients and the controls.

Table 2. Adjusted Odds Ratios of Physical-Activity States among Augsburg Patients at the Onset of Myocardial Infarction as Compared with Controls.*

VARIABLE	NO. OF PATIENTS (N = 882)	NO. OF CONTROLS (N = 531)	ODDS RATIO (95% CI)
Strenuous activity	56	21	2.1 (1.1–3.6)
Mild-to-moderate activity	178	121	0.9 (0.8–1.0)
Sedentary activity	454	232	1.1 (0.9–1.4)
Sleep	194	157	0.8 (0.7–0.9)
Time from awakening to onset ≤3 hr	399	138	1.9 (1.4–2.4)

*From a multivariate logistic-regression analysis, adjusted for standard risk factors (hypertension, hyperlipidemia, diabetes, and smoking), previous myocardial infarction, angina pectoris, use of any cardiac drug, current employment, age, sex, and time of awakening. Only subjects for whom complete information was available for all variables were included in this analysis. CI denotes confidence interval.

The case-crossover comparison of the combined patient population, in which each patient served as his or her own control (Table 4), yielded a relative risk of 2.1 (95 percent confidence interval, 1.6 to 3.1) of having engaged in strenuous physical activity within the hour before the onset of myocardial infarction; for patients in Berlin, the relative risk of having engaged in physical exertion was 3.2 (95 percent confidence interval, 1.5 to 6.9), whereas for patients in Augsburg the relative risk was 1.9 (95 percent confidence interval, 1.3 to 2.9). The subgroups of patients who usually engaged in exertional physical activity less than four times a week (n = 125) had a relative risk of having engaged in physical exertion in the hour before the onset of myocardial infarction of 6.9 (95 percent confidence interval, 4.1 to 12.2), as compared with 1.3 (95 percent confidence interval, 0.8 to 2.2) for patients who reported a usual frequency of physical activity of four or more times a week (P<0.01). Patients had a similar relative risk whether or not they had a previous diagnosis of coronary disease (Table 4).

Time of Myocardial Infarction Adjusted for Time of Awakening

There was significant circadian variation (P<0.01) in the onset of myocardial infarction, with a peak during the morning from 8 to 11 a.m. (Fig. 2). The relative risk of myocardial infarction during this three-hour period was 1.8 (95 percent confidence interval, 1.5 to 2.1). After adjustment for the individual awak-

Table 3. Effect of Physical Exertion in Augsburg Patients at the Onset of Myocardial Infarction as Compared with Controls, According to Presence or Absence of Previous Coronary Heart Disease.*

Group	No. with Physical Exertion		Odds Ratio (95% CI)†
	Patients (N = 882)	Controls (N = 531)	
Previous coronary heart disease	17	3	1.0 (0.3–4.0)
No previous coronary heart disease	39	18	2.2 (1.1–4.1)

*Previous coronary heart disease included a diagnosis of either myocardial infarction or angina pectoris. Only subjects for whom complete information was available for all variables were included in this analysis.

†This multivariate logistic-regression model controlled for standard risk factors (hypertension, hyperlipidemia, diabetes, and smoking), use of any cardiac drug, current employment, age, and sex. CI denotes confidence interval.

ening times of patients, the morning peak of myocardial infarction was markedly sharper. The relative risk of myocardial infarction during the initial three-hour period after awakening was 2.7 (95 percent confidence interval, 2.3 to 3.1). The length of time between awakening and arising was less than 15 minutes for 94 percent of the patients.

Unusual Life Events

The cumulative frequency of unusual life events in the 24 hours or the 24 hours to four weeks before either a myocardial infarction or a control event was similar in the patient and control populations (Table 5). However, as compared with the control subjects, patients more often reported unusual emotionally upsetting events ($P<0.05$) in the 24 hours before the onset of myocardial infarction or from 24 hours to four weeks before it, and there was a nonsignificant trend toward more frequent reporting of stress at work from 24 hours to four weeks before the event (Table 5). Within the same time period, the death of a friend and disease in the respondent were reported more frequently by the controls than by the patients ($P<0.05$). The other types of life events that we evaluated occurred with similar frequency among patients and controls.

Discussion

We have documented an increased risk of acute myocardial infarction during strenuous physical activity or within the one-hour period after it. In a subgroup analysis a particularly high risk was associated with physical exertion by patients who usually exercised only infrequently. Moreover, an analysis of the time of onset of myocardial infarction adjusted for the time of awakening demonstrated an approximately threefold increase in risk during the three-hour period after awakening, as compared with other times of day.

On the basis of anecdotal reports and clinical experience, precipitating factors of acute myocardial infarction have previously been suspected.[1-13] Since the potential triggers of myocardial infarction are likely to be nonspecific, however, adequate control data are needed to determine their importance. To overcome the limitations of previous studies, we used a case–control design in which patients from a large, predefined, and carefully monitored population were compared with matched controls. To minimize possible recall bias, the controls were asked about their activities at a specific time during the 24 hours before the interview. Although the rate of participation among the initial group of eligible controls was high (70 percent), the possibility of selection bias cannot be entirely excluded. Similarly, the difference in technique between the interviews conducted with the case patients and those conducted with the controls permits the possibility of some bias with regard to the information obtained.

In order to eliminate these sources of potential bias, we undertook an additional case-crossover comparison, in which each patient served as his or her own control.[19] This analysis confirmed the results of the conventional case–control analysis. Although only patients who exerted themselves reasonably often and for whom complete information on physical activity could be obtained were included in this analysis (23 percent of total), the statistical power was sufficient to demonstrate a significant association. The slightly higher relative risk associated with physical exertion in this analysis may be due to the longer exposure period — activity one hour before the onset of myocardial infarction, as compared with activity at the onset of the event in the case–control analysis. The case-crossover method appears to be a power-

Table 4. Case-Crossover Comparison of the Patients' Usual Frequency of Physical Exertion with the Last Episode of Physical Exertion before Myocardial Infarction.*

Variable	All Patients (N = 270)	Frequency of Exertion		Previous CHD	
		<4 times/wk (N = 125)	≥4 times/wk (N = 145)	Yes (N = 95)	No (N = 175)
No. with physical exertion <1 hr before onset	44	20	24	14	30
Usual weekly frequency of exertion					
Mean ±SD	6±2	2±3	7±3	5±4	6±3
Median	4	1	7	4	4
Expected daily frequency in patients with exertion (numerator)†	484	221	263	156	328
Expected daily frequency in patients without exertion (denominator)‡	235	32	202	83	152
Odds ratio (95% CI)§	2.1 (1.6–3.1)	6.9 (4.1–12.2)	1.3 (0.8–2.2)	1.9 (1.1–2.7)	2.7 (1.4–3.3)

*Only patients who reported usual exertional physical activities and for whom complete information on these activities was available are included. CHD denotes coronary heart disease.

†The total daily frequency (assuming 16 hours per day) of potential exposure to physical exertion for all patients who reported exertion within one hour before the onset of myocardial infarction.

‡The total daily frequency of potential exposure to physical exertion for all patients who did not report exertion within one hour before the onset of myocardial infarction.

§The Mantel–Haenszel estimate of the relative risk of having engaged in physical exertion within one hour before the onset of myocardial infarction. CI denotes confidence interval.

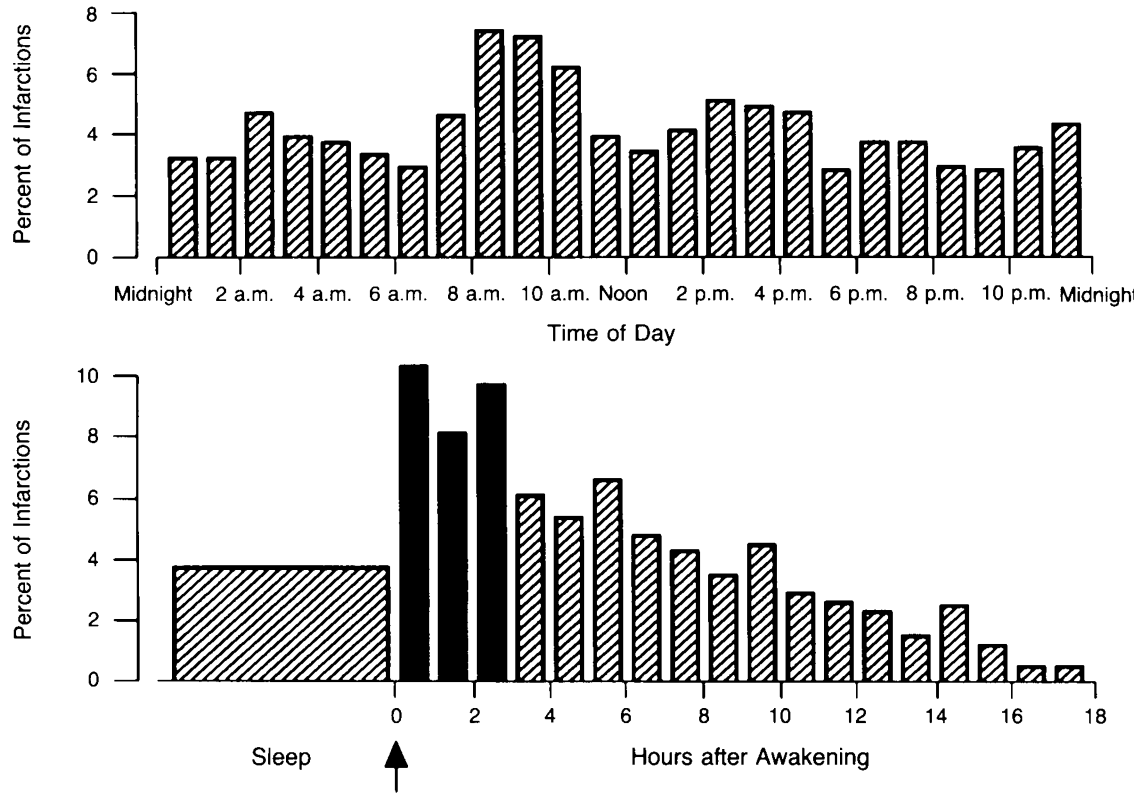

Figure 2. Distribution of Times of Onset of Myocardial Infarction.

The time of onset of myocardial infarction showed a significant circadian variation ($P<0.01$), with a peak incidence from 8 to 11 a.m. (upper panel). The relative risk of myocardial infarction during this three-hour period, as compared with other times of day, was 1.8 (95 percent confidence interval, 1.5 to 2.1). After adjustment for the individual patients' times of awakening (lower panel), the morning peak was more pronounced. The relative risk of myocardial infarction during the initial three-hour period after awakening was 2.7 (95 percent confidence interval, 2.3 to 3.1).

ful tool, although it may not eliminate the influence of transient confounding factors or preclude information bias due to differential recall of the time of events (for example, patients may overestimate possible triggers in the recent past and underestimate the frequency of their usual exposure to those factors).

The results of this study are compatible with the findings of another study in which the case-crossover analysis was the primary method used.[23] Several additional studies have found that the onset of myocardial infarction occurred during physical exertion in 5 to 13 percent of cases, which is in the same range as our findings.[2,3,6,7]

During the morning and the hours just after awakening, the risk of acute coronary events is markedly increased as compared with the risk at other times of the day — a pattern confirmed by our results.[11-13,24-28] In multivariate analyses we found independent significant associations between the onset of myocardial infarction and both physical exertion and the time of awakening (Table 2). This suggests that both physical exertion at any time during the day and routine activities after awakening and arising may be triggers of myocardial infarction in patients with coronary artery disease. Suspected underlying physiologic changes responsible for circadian variation in the incidence of

Table 5. Unusual Life Events within 24 Hours and between 24 Hours and Four Weeks before the Onset of Myocardial Infarction or before the Control Event in Augsburg Patients and Controls.*

Event	<24 Hours			24 Hours–Four Weeks		
	Patients (N = 970)	Controls (N = 532)	Odds ratio (95% CI)	Patients (N = 970)	Controls (N = 532)	Odds ratio (95% CI)
	percent			*percent*		
Death in family	0.3	0.4	0.3 (0.1–2.5)	4.6	2.8	1.3 (0.6–2.9)
Death of friend	0.1	0.2	2.1 (0.1–34.0)	1.5	3.2	0.2 (0.1–0.6)
Disease in subject	1.7	3.2	0.3 (0.1–0.8)	7.5	11.1	0.5 (0.3–0.8)
Emotional stress at work	5.3	5.3	0.9 (0.5–1.6)	19.2	14.8	1.4 (1.0–2.1)
Emotional upset	4.4	2.6	2.7 (1.1–6.6)	19.9	9.8	2.5 (1.7–3.8)
Unusual dreams or nightmares	2.0	1.1	2.1 (0.6–8.1)	5.5	5.5	1.0 (0.5–1.4)
Sleep disturbances	6.2	6.2	0.8 (0.4–1.4)	13.9	13.7	0.8 (0.5–1.5)
Change of job	0.2	0.0	—	1.0	0.4	1.5 (0.3–7.6)
Change of relationship	0.1	0.0	—	1.2	0.0	—
Any of the above	13.3	15.2	0.8 (0.6–1.1)	42.4	40.0	1.1 (0.8–1.4)

*Odds ratios have been adjusted for standard risk factors (hypertension, hyperlipidemia, diabetes, and smoking), age, and sex. CI denotes confidence interval.

myocardial infarction include the sharp morning increases in blood pressure, heart rate, coronary tone, and platelet aggregability and the simultaneous decrease in fibrinolytic activity.[29-35] Platelet activation has been reported to occur during exercise-induced myocardial ischemia in patients with coronary artery disease, directly after physical exercise in normal subjects, and during other types of stress.[36-39] Furthermore, in persons who do not exercise regularly, endogenous fibrinolytic activity is lower both at base line and after bicycle exercise testing than in trained controls; this reduction further enhances the tendency to thrombosis.[40] Consistent with these pathophysiologic observations is our finding of a particularly high relative risk of myocardial infarction among "unfit" patients during or shortly after exertion.

The benefit of regular physical activity in providing long-term protection against the manifestations of coronary heart disease has been documented.[18,41,42] The risk of an acute cardiac event, however, may actually be increased during vigorous exercise,[9,10,43] at least in the case of patients with coronary disease who do not exercise regularly — a concept that is supported by the present results. In the light of the large number of people who have myocardial infarctions in Western industrialized societies,[44] even a small excess risk associated with physical exertion may translate into a hazard for many patients with coronary disease. Our results also suggest that it is not only patients with known, previously diagnosed coronary heart disease who may be at increased risk during exertion, but also those without a previous event — that is, those with "silent" coronary disease. The important clinical implications of this increase in risk emphasize the need to investigate further the relations among the type and duration of physical activity, training status, physiologic changes, and the risk of acute coronary disease, including sudden death.[45]

The increased incidence of acute myocardial infarction during the first hours after awakening and arising suggests that, in addition to strenuous exertion, routine morning activities are associated with an increased risk in some patients. Therefore, scheduling cardiac medication some time after arising may not be the most protective method of administration. Controlled studies are needed to investigate the preventive potential of either long-acting medication taken at night or medication taken before arising. Although physical activity is an essential aspect of life and may reduce the incidence of coronary disease,[18,41,42] pharmacologic or behavioral intervention may be required to attenuate the risk of cardiac events associated with physical exertion in patients with coronary artery disease, especially if they are usually sedentary.

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