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TRIGGERING OF ACUTE MYOCARDIAL INFARCTION BY HEAVY PHYSICAL EXERTION

Protection against Triggering by Regular Exertion

MURRAY A. MITTLEMAN, M.D.C.M., M.P.H., MALCOLM MACLURE, SC.D., GEOFFREY H. TOFLER, M.B., JANE B. SHERWOOD, R.N., ROBERT J. GOLDBERG, PH.D., AND JAMES E. MULLER, M.D., FOR THE DETERMINANTS OF MYOCARDIAL INFARCTION ONSET STUDY INVESTIGATORS*

Abstract *Background.* Despite anecdotal evidence suggesting that heavy physical exertion can trigger the onset of acute myocardial infarction, there have been no controlled studies of the risk of myocardial infarction during and after heavy exertion, the length of time between heavy exertion and the onset of symptoms (induction time), and whether the risk can be modified by regular physical exertion. To address these questions, we collected data from patients with confirmed myocardial infarction on their activities one hour before the onset of myocardial infarction and during control periods.

Methods. Interviews with 1228 patients conducted an average of four days after myocardial infarction provided data on their usual annual frequency of physical activity and the time, type, and intensity of physical exertion in the 26 hours before the onset of myocardial infarction. We compared the observed frequency of heavy exertion (6 or more metabolic equivalents) with the expected values using two types of self-matched analyses based on a new case-crossover study design. The low frequency of heavy exertion during the control periods was validated by data from a population-based control group of 218 subjects.

Results. Of the patients, 4.4 percent reported heavy exertion within one hour before the onset of myocardial infarction. The estimated relative risk of myocardial infarction in the hour after heavy physical exertion, as compared with less strenuous physical exertion or none, was 5.9 (95 percent confidence interval, 4.6 to 7.7). Among people who usually exercised less than one, one to two, three to four, or five or more times per week, the respective relative risks were 107 (95 percent confidence interval, 67 to 171), 19.4 (9.9 to 38.1), 8.6 (3.6 to 20.5), and 2.4 (1.5 to 3.7). Thus, increasing levels of habitual physical activity were associated with progressively lower relative risks. The induction time from heavy exertion to the onset of myocardial infarction was less than one hour, and symptoms usually began during the activity.

Conclusions. Heavy physical exertion can trigger the onset of acute myocardial infarction, particularly in people who are habitually sedentary. Improved understanding of the mechanisms by which heavy physical exertion triggers the onset of myocardial infarction and the manner in which regular exertion protects against it would facilitate the design of new preventive approaches. (N Engl J Med 1993; 329:1677-83.)

IT is well recognized that heavy physical exertion sometimes immediately precedes, and indeed appears to trigger, the onset of acute myocardial infarction.[1-3] Descriptive studies have established that in approximately 5 percent of patients with myocardial infarction, such exertion immediately precedes the onset of symptoms.[1,3] Since these studies lack control data, however, it has not been possible to quantify the association between heavy physical exertion and the onset of acute myocardial infarction or to examine factors that might alter the risk of triggering such an event.

Clarification of the role of physical exertion in triggering myocardial infarction is important for several reasons. First, it is estimated that more than 1.5 million myocardial infarctions occur annually in the United States,[4] and at least 75,000 of these infarcts — which lead to 25,000 deaths — may occur soon after exertion.[1,3] Second, since approximately two thirds of these deaths are sudden, knowledge leading to the prevention of the triggering of myocardial infarction is required to eliminate them. Third, a sedentary lifestyle has consistently been shown to increase the risk of coronary artery disease. The American Heart Association has recently recommended increased physical activity as an important method to reduce the risk of heart attack.[5] Heavy physical exertion therefore appears to be a two-edged sword, both triggering and preventing myocardial infarction. Finally, a better understanding of the triggering effect of physical exertion could lead to approaches to sever the link between potentially triggering activities and

From the Institute for Prevention of Cardiovascular Disease, Cardiovascular Division, Deaconess Hospital, and Harvard Medical School, Boston (M.A.M., M.M., G.H.T., J.B.S., J.E.M.); the Department of Epidemiology, Harvard School of Public Health, Boston (M.A.M., M.M.); and the Department of Medicine, University of Massachusetts Medical School, Worcester (R.J.G.). Address reprint requests to Dr. Mittleman at the Institute for Prevention of Cardiovascular Disease, Cardiovascular Division, Deaconess Hospital, 1 Autumn St., 5th Fl., Boston, MA 02215.

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*The participants in the study are listed in the Appendix.

the transient physiologic risk states that induce myocardial infarction.

The Determinants of Myocardial Infarction Onset Study was a multicenter, interview-based study of patients with acute myocardial infarction. In this study, we used a new case-crossover design to quantify the relative risk of myocardial infarction after heavy physical exertion as compared with periods of lighter exertion or no exertion, its timing, and its potential modification by habitual physical activity in 1228 patients with confirmed acute myocardial infarction.

Methods

Study Population

The study was conducted in 22 community hospitals and 23 tertiary care centers. A total of 1271 patients were interviewed a median of 4 days (range, 0 to 30) after myocardial infarction. Of these, 43 were unable to complete the interview and were excluded from this analysis. The remaining 1228 (836 men and 392 women; age range, 22 to 92 years) were interviewed between August 1989 and October 1992.

Interviewers identified eligible patients by reviewing the admission logs of coronary care units and patients' charts. For inclusion, patients were required to meet the following criteria: an elevated creatine kinase level, with MB isoenzymes; an identifiable onset of pain or other symptoms typical of infarction; and the ability to complete a structured interview. The protocol was approved by the institutional review board of each center, and informed consent was obtained from each patient.

Interview

The interviewers were trained by means of personal instruction, a training manual, and an instructional videocassette, and they received ongoing feedback from the study coordinator. Approximately one third of the interviews were audiotaped for randomly selected quality-control checks by the study coordinator to ensure the accuracy of coding. To minimize bias in ascertainment, the interviewers were not informed of the duration of the hypothesized hazard period before myocardial infarction.

In the interview, data were obtained on the time and place of the myocardial infarction, the type of pain experienced, other symptoms, the estimated usual frequency of physical exertion during the previous year, and the intensity and timing of heavy physical exertion and other potentially triggering factors during the 26 hours before the onset of myocardial infarction. Our findings regarding triggering factors other than physical exertion will be reported later.

The degree of physical exertion was quantified on a scale from 1 to 8 metabolic equivalents (MET) according to generally accepted values (Table 1)[6-10]; 1 MET is defined as the energy expended per minute by a subject sitting quietly and is equivalent to 3.5 ml of oxygen uptake per kilogram of body weight per minute by a 70-kg adult. Patients were asked to estimate how often they engaged in exertion at each level during the previous year (usual annual frequency) and to state the timing, type, and level of exertion during each of the 26 hours before the onset of myocardial infarction. Patients were considered to have been engaged in heavy exertion (exposed) if they reported a peak exertion level estimated to be 6 MET or more during the period of interest.

Study Design

A new epidemiologic technique, the case-crossover design, was developed for this study.[11] This approach was developed to assess the change in the risk of an acute event during a brief "hazard period" after exposure to a transient risk factor. With this method, each patient's previous exertion levels serve as his or her control information.[11]

A one-to-two-hour hazard period immediately before the onset of myocardial infarction was compared with two types of control data obtained from the patients: their usual frequency of heavy physical exertion over the past year, and their actual level of exertion in the comparable one-to-two-hour control period at the same time on the day before the onset of myocardial infarction. The use of this design explains why we collected detailed data about physical exertion during the 26 hours before the onset of infarction. To help maintain comparability of reporting of exertion levels for the hazard and control periods, the 26-hour period before the onset of myocardial infarction was treated as one long hazard period in the interview.

Matched neighborhood controls were also studied to obtain a third type of control data. Controls were matched to the case patients according to age (±2 years), sex, and area of residence. Each control was contacted for a preliminary telephone interview and then requested to carry a telephone-activated beeper. The beeper alarm was activated at the same time of day and day of the week as the matched patient's myocardial infarction began. Of 308 eligible controls, 218 (71 percent) participated.

Statistical Analysis

The analysis of case-crossover data is a new application of standard methods for stratified data analysis.[11-13] In this type of analysis, the stratifying variable is the individual patient, as in a crossover experiment.

The ratio of the observed frequency of physical exertion during the hazard period to the expected frequency (from the information on the control period or the neighborhood controls) was used to calculate estimates of the relative risk.[11] Expected frequencies were estimated in three ways: (1) according to the patient's usual annual frequency of heavy exertion, (2) according to the frequency of heavy exertion in the control period on the day before the onset of symptoms, and (3) according to the frequency of heavy exertion in neighborhood controls. Estimation on the basis of the usual annual frequency of exertion was the primary analytic method used. The amount of person-time spent in heavy exertion (exposure) was estimated by multiplying the reported usual annual frequency of physical exertion by its reported usual duration. Unexposed person-time (i.e., person-time not spent in heavy exertion) was then calculated by subtracting the exposed person-time in hours from the number of hours in a year. Hazard periods of varying lengths were analyzed with use of methods for cohort studies with sparse data in each stratum.[11,14] The calculated relative risk refers to the risk of having a myocardial infarction during a period of heavy exertion, as compared with the risk during periods of lighter exertion or no exertion.

Using the second method, based on the frequency of heavy exertion during the control period on the day before the onset of symptoms, we computed relative risks by standard methods for matched-pair case–control studies. Instead of concordant and discordant pairs of subjects, however, the pairs were made up of two intervals for each patient, a hazard period and a control period, which were either concordant or discordant for exposure to heavy exertion.[11,12] Ninety-five percent confidence intervals and two-sided P values were computed by exact methods based on the binomial distribution.[12]

A third approach to estimating the expected frequency of exertion before myocardial infarction was to use neighborhood controls. For this method, we interviewed controls in the community who had not had myocardial infarctions. Although the limited number of controls and the low frequency of heavy exertion precluded a detailed case–control analysis, the neighborhood controls provided additional data on the frequency of heavy physical exertion that could be used to validate the control data from the case sample.

Modification of the relative risk by various factors was assessed by comparing relative risks in subgroups, defined by different levels of the potential effect modifier. Subgroups were compared with the chi-square test for homogeneity.[12] To estimate induction time (the length of time from heavy exertion to the onset of myocardial infarction), relative risks were calculated for each one-hour period before the onset of myocardial infarction, with control for subsequent exposure.[15]

Results

The characteristics of the study sample are shown in Table 2. Of the 1228 patients, 54 (4.4 percent) had engaged in heavy physical exertion in the hour before the onset of myocardial infarction. The types of activities reported during this hazard period included predominately isometric exercise, such as lifting and

Table 1. Physical-Activity Rating Scale Used to Estimate the Level of Physical Exertion by Patients in the Determinants of Myocardial Infarction Onset Study.

Estimated No. of MET	Description	Type of Activity
1	Sleeping, reclining	Sunbathing, lying on a couch watching television
2	Sitting	Eating, reading, desk work, sitting watching television, driving on the highway
3	Very light exertion	Office work, driving in the city, personal care, standing in line, strolling in a park
4	Light exertion, with normal breathing	Mopping, slow walking (e.g., shopping), bowling, sweeping, golfing with a cart, gardening with power tools
5	Moderate exertion, with deep breathing	Normal walking, golfing on foot, slow biking, downhill skiing, calisthenics, raking leaves, cleaning windows, hanging wallpaper, interior painting, hunting, fishing, slow dancing, light restaurant work (e.g., waiting tables, serving drinks)
6	Vigorous exertion, with panting; overheating	Slow jogging, speed-walking, tennis, swimming, cross-country skiing, shoveling snow, fast biking, mowing with a push mower, pruning trees or shrubs, heavy gardening, factory assembly work, heavy household repairs, climbing up and down a ladder, overhead work, ice hockey, drills, softball, picking up garbage, laying bricks, hurried heavy restaurant work
7	Heavy exertion, with gasping; much sweating	Running, fast jogging, nonstop racquetball, pushing a car stuck in snow, moving boulders, changing tires, shoveling heavy or deep snow, mixing cement, competitive basketball, touch football, hanging drywall, putting down wall-to-wall carpet, ladder or stair climbing with a 23-kg load, using a jackhammer
8	Extreme or peak exertion	Sprinting, fast running, jogging uphill, aggressive sports with frequent sprinting and no rest, pushing or pulling with all one's might, unusually extreme work

pushing (18 percent); predominately isotonic or dynamic exercise, such as jogging and racquet sports (30 percent); and mixed activities such as gardening and splitting wood (52 percent). Symptoms began during the activity in 82 percent of the patients who had engaged in heavy exertion.

Usual Annual Frequency of Heavy Exertion as the Reference Value

In the analysis in which the usual annual frequency of heavy exertion served as the control value, the relative risk of myocardial infarction in the hour immediately after heavy exertion was 5.9 (95 percent confidence interval, 4.6 to 7.7). After we controlled for heavy physical exertion in the one-hour period before the onset of myocardial infarction, the relative risks for one-hour periods two to five hours before myocardial infarction were not significantly different from 1 (Fig. 1), indicating that the induction time was less than one hour. Therefore, all subsequent analyses were based on a one-hour hazard period.

Frequency of Heavy Exertion during the Control Period on the Day before Onset as the Reference Value

In the standard matched-pair analysis, there were 50 patients who reported heavy exertion only during the one-hour hazard period, as compared with 9 who reported heavy exertion only during the control period (the same one-hour period on the previous day). Four subjects reported heavy exertion at both times. This analysis yielded a relative risk of myocardial infarction of 5.6 (95 percent confidence interval, 2.7 to 12.8) for those who engaged in heavy exertion during the hazard period.

Frequency of Heavy Exertion in Neighborhood Controls as the Reference Value

Whereas among the matched cases there were 10 patients who reported heavy exertion, none of the 218 controls reported heavy physical exertion in the hour before the activation of the beeper alarm. Although the point estimate of the relative risk was infinite, the lower bound of the 95 percent confidence interval was 2.2. This finding confirms the validity of the low frequency of expected exposure to heavy exertion reported by the patients with myocardial infarction for both types of self-matched control data.

Modification of the Relative Risk by the Usual Frequency of Heavy Exertion

Patients who rarely exerted themselves (less than once a week) had a relative risk of myocardial infarction in the hour after heavy exertion of 107 (95 percent confidence interval, 67 to 171), as compared with a relative risk of 2.4 (95 percent confidence interval, 1.5 to 3.7) among those who reported physical exertion at a level of 6 MET or more at least five times per week (Fig. 2).

We also examined other potential modifiers of the relative risk of myocardial infarction (Table 3). Pa-

Table 2. Characteristics of the Study Population.

Characteristic*	Value
Mean age (yr) ±SD	62.0±12.7
	no. (%)
Sex	
Male	836 (68)
Female	392 (32)
Medical history	
MI as initial presentation of CAD	744 (61)
Previous MI	352 (29)
Angina	308 (25)
Hypertension	542 (44)
Diabetes mellitus	232 (19)
Medication use before MI	
Aspirin	299 (24)
Calcium-channel blockers	288 (23)
Beta-blockers	248 (20)
ACE inhibitors	119 (10)
Type of hospital where interviewed	
Community hospital	671 (55)
Tertiary care center (admitted)	241 (20)
Tertiary care center (transferred)	316 (26)

*MI denotes myocardial infarction, CAD coronary artery disease, and ACE angiotensin-converting enzyme.

tients with diabetes had a significantly higher relative risk of myocardial infarction after heavy physical exertion than nondiabetic patients ($P = 0.01$); this difference was not fully accounted for by lack of regular exertion. There was a nonsignificant trend ($P = 0.11$) toward an increased relative risk of myocardial infarction among patients over 70 years of age, in part because they had a lower prevalence of regular exercise. The relative risk of myocardial infarction in the hour after heavy physical exertion did not vary according to sex or the presence of obesity (body-mass index [weight in kilograms divided by the square of the height in meters] above 29), a history of hypertension, angina, or a previous myocardial infarction.

Discussion

For the total population in our study, an episode of heavy physical exertion was associated with a transient risk of myocardial infarction in the subsequent hour that was 5.9 times higher than the risk during periods of lighter exertion or no exertion. The relative risk varied greatly depending on the usual frequency of heavy exertion by the patient; it was 2.4 among those reporting regular physical exertion, but 107 among those who were habitually sedentary. These findings are unlikely to be accounted for by recall bias or confounding, since the patients were unaware of the hypothesis that the hazard period was one hour long and because the case-crossover design employed in this study eliminated the effect of confounding by factors that differed among patients.

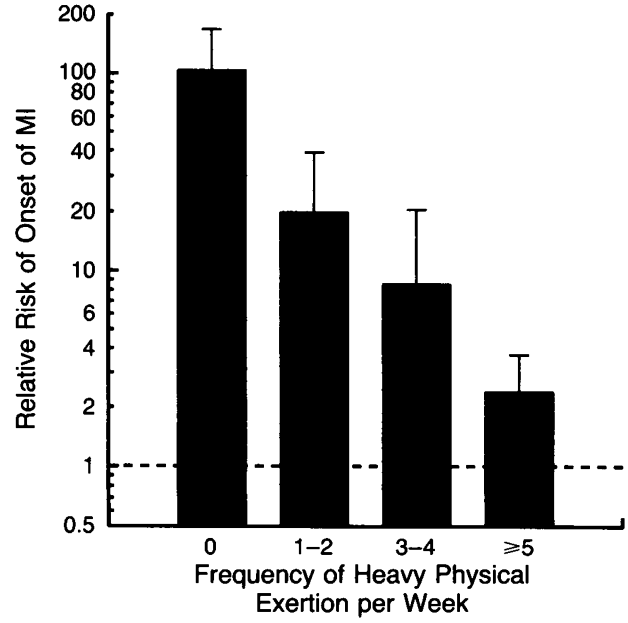

Figure 2. Relative Risk of Myocardial Infarction (MI) According to the Usual Frequency of Heavy Exertion.

Heavy exertion was defined as physical activity at a level of 6 MET or more. The relative risk is shown on a logarithmic scale. Habitually sedentary persons had an extreme relative risk (107), whereas those who reported heavy exertion five or more times per week had a risk only 2.4 times higher than the base-line risk ($P<0.001$). The T bars indicate the 95 percent confidence limits. The dotted line indicates the base-line risk.

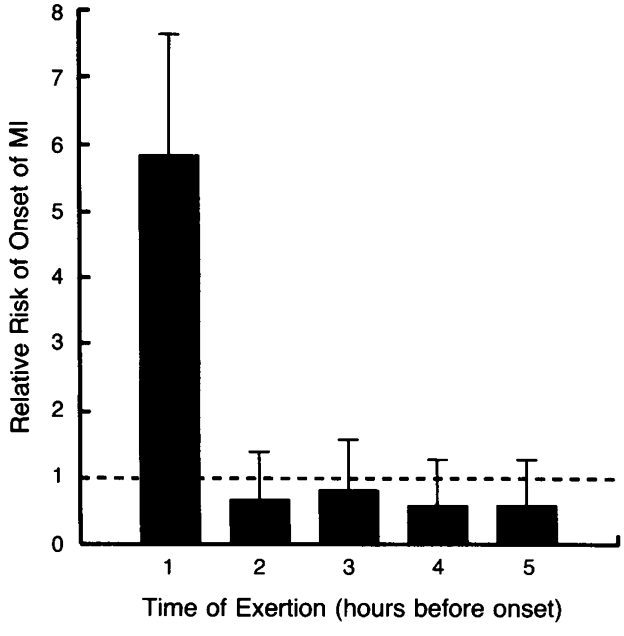

Figure 1. Time of Onset of Myocardial Infarction (MI) after an Episode of Heavy Physical Exertion (Induction Time).

Each of the five hours before the onset of myocardial infarction was assessed as an independent hazard period, and exertion during each hour was compared with that during the control period. Only exertion during the hour immediately before the onset of myocardial infarction was associated with an increase in the relative risk, suggesting that the induction time for myocardial infarction is less than one hour. The T bars indicate the 95 percent confidence limits. The dotted line indicates the base-line risk.

Approximately 4 percent of the patients we studied reported heavy physical exertion in the hour immediately before the onset of symptoms — a percentage similar to that reported in previous uncontrolled studies of the onset of myocardial infarction.[1-3] Our calculated relative risks are in agreement with those reported for a population-based case–control study in Germany, in which a relative risk of 2.1 was found for heavy physical exertion.[16] The relative risk observed in the German study was also lower for those who exercised regularly.

Although there has previously been only limited information on the association between heavy physical exertion and nonfatal myocardial infarction, several studies[17-20] have estimated the relative risk of sudden death from cardiac causes to be between 5 and 100 during periods of heavy physical exertion. Siscovick et al.[17] also found that the relative risk of sudden death from cardiac causes was lower among people who exercised regularly. The effects of the usual frequency of physical exertion on the relative risks of sudden death from cardiac causes and nonfatal acute myocardial infarction are remarkably similar, providing support for the possibility that many cases of sudden death due to cardiac causes that are triggered by exertion have a pathophysiology similar to that of nonfatal acute myocardial infarction.[21]

Since the case-crossover design uses self-matching,

Table 3. Relative Risk of Onset of Myocardial Infarction (MI) within One Hour after Heavy Physical Exertion, According to Patients' Characteristics.

Characteristic	No.	No. with Exertion in Hour before MI	Relative Risk (95% CI)*	P Value†
All patients	1228	54	5.9 (4.6–7.7)	—
Heavy physical exertion				
<1 time/wk	1027	19	107 (67–171)	<0.001
1–2 times/wk	68	10	19.4 (9.9–38.1)	
3–4 times/wk	40	6	8.6 (3.6–20.5)	
≥5 times/wk	93	19	2.4 (1.5–3.7)	
Age (yr)				
<50	227	21	5.7 (3.7–8.8)	0.11
50–69	629	26	5.4 (3.7–7.8)	
≥70	372	7	12.7 (6.0–27.2)	
Sex				
Male	836	50	5.9 (4.5–7.7)	0.77
Female	392	4	7.1 (2.1–23.5)	
Clinical history				
Diabetes				
Yes	232	7	18.9 (7.4–47.7)	0.01
No	996	47	5.4 (4.1–7.2)	
Angina				
Yes	308	5	3.7 (1.6–8.9)	0.25
No	920	49	6.3 (4.8–8.4)	
Hypertension				
Yes	542	17	5.2 (3.2–8.2)	0.47
No	686	37	6.4 (4.7–8.8)	
Obesity‡				
Yes	833	35	5.7 (4.1–7.9)	0.64
No	380	19	6.5 (4.2–10.0)	
Previous MI§				
Yes	352	7	3.5 (1.7–7.4)	0.12
No	857	47	6.6 (5.0–8.8)	
Medication use				
Beta-blockers				
Yes	248	5	4.2 (1.8–9.9)	0.40
No	980	49	6.2 (4.7–8.2)	
Aspirin				
Yes	299	5	4.3 (1.7–10.9)	0.46
No	929	49	6.2 (4.7–8.1)	

*CI denotes confidence interval.

†By the chi-square test for homogeneity.

‡Obesity is defined as a body-mass index above 29. Data were missing for some patients because they did not report their height or weight.

§Nineteen patients did not know whether they had had a myocardial infarction.

there is no variability in traditional risk factors for myocardial infarction within each stratum. Thus, there can be no confounding by these risk factors.[11,13] Confounding by factors limited to individual patients can occur if another transient risk factor often coincides with the exposure of interest. Although it is possible that there was some confounding by other transient exposures that coincided with exertion, it is unlikely to account for the strong association we observed.

A factor potentially limiting our study is recall bias. The case-crossover design helped to minimize this bias during the collection of data by treating the entire 26-hour period before the onset of myocardial infarction as one long hazard period. The observed modification of the relative risk by habitual physical exertion also argues against the effects of recall bias. Furthermore, heavy physical exertion is a relatively rare event and is easy to remember and assess. The consistency of the relative risks calculated with three types of control data also confirms the validity of the findings. Finally, even if some recall bias was present, it is unlikely to account for the strong associations we observed.

It is likely that there was some random error in measurement (nondifferential misclassification) of the degree of reported exertion and the actual energy expended during any given time period. The effect of this type of misclassification is to bias the relative risk toward a finding of no association.

There is also possible bias due to the differential survival of patients in whom myocardial infarction was triggered by different mechanisms. For example, if patients whose infarctions were triggered by physical exertion were more likely to survive than those whose infarctions were unrelated to exertion, then the apparent relative risk might be overestimated. This possibility seems unlikely in view of the association of heavy physical exertion and sudden death due to cardiac causes.

With regard to the frequency with which myocardial infarction is triggered by exertion, it is important to distinguish absolute risk from relative risk. On the basis of data from the Framingham Heart Study, the absolute risk that a 50-year-old nonsmoking, nondiabetic man will have a myocardial infarction during a given one-hour period is approximately 1 in 1 million.[22,23] If this man was habitually sedentary but engaged in heavy physical exertion during that hour, his risk would increase 100 times over the base-line value, but his absolute risk during that hour would still be only 1 in 10,000.

Although this study demonstrated that discrete episodes of physical exertion can increase the short-term risk of myocardial infarction, numerous studies[5,24-31] have found that regular exercise is associated with a reduction in the long-term risk of coronary events. People who exercise regularly not only have a lower base-line risk of myocardial infarction, but as demonstrated by this study, they also have a lower relative risk that an infarction will be triggered by heavy physical exertion.

From the public health perspective, our findings, which demonstrate protection against triggering of myocardial infarction with regular exertion, provide further evidence for encouraging regular physical activity, as recommended by the American Heart Association.[5] Such a physical-activity program is likely to lower the overall risk of myocardial infarction, since it may lower the base-line risk, and also decrease the relative risk that an episode of heavy physical exertion will trigger a myocardial infarction. Recommendations for patients with a history of myocardial infarction or angina are more complex. Patients in our study who had known coronary artery disease did not have a higher relative risk after heavy exertion than those without such a history. However, because of their elevated and variable base-line risk, the risks and benefits of heavy physical exertion for such patients must be assessed by their individual physicians and recommendations must be based on the guidelines for exercise.[5]

A proposed mechanism for the triggering of myo-

cardial infarction is the disruption of a vulnerable, but not necessarily stenotic, atherosclerotic plaque in response to hemodynamic stresses; thereafter, hemostatic and vasoconstrictive forces determine whether the resultant thrombus becomes occlusive.[32] The rarity with which a potential trigger becomes an actual trigger is probably a result of the infrequency of atherosclerotic plaques vulnerable to disruption and other conditions required for acute occlusive thrombosis.

It remains unclear whether beta-blockers or aspirin decreases the relative risk of myocardial infarction triggered by exertion. It is also unknown whether the risk that a myocardial infarction will be triggered by exertion varies at different times of the day. Murray et al.[33] found no significant increase in cardiac events in morning as compared with afternoon cardiac-rehabilitation classes, but the study had insufficient power to exclude a relative risk of 6 or less and many patients were taking beta-blockers, which might decrease a morning peak in onset.[34-36]

In our study population, given the relative risk of 5.9 and the exposure to heavy exertion of 4.4 percent of our population in the hour before the onset of myocardial infarction, heavy exertion may be considered to be the final component cause[12] in 3.8 percent of cases. Viewed from another perspective, approximately 80 percent of cases that occurred within one hour after an episode of exertion were triggered by it. The data available do not permit us to differentiate an earlier case from an excess case[37] — that is, we cannot distinguish an infarction that would have occurred several hours later even without heavy exertion from one that would never have occurred if the patient had avoided heavy exertion at that particular time, when an unfavorable combination of potentially reversible plaque vulnerability, vasoconstriction, and tendency to thrombosis was present. These conclusions and the limitation of the increased risk to the hour after exertion may be useful in considering workers' compensation and liability cases in which physical exertion preceded the onset of myocardial infarction.

Although heavy physical exertion could be identified as a trigger of myocardial infarction in only 3.8 percent of cases, it is possible that unidentified triggering by moderate exertion also occurs. Furthermore, other potential triggers, such as psychological stress or anger, which produce similar physiologic responses,[38-41] are more common than heavy exertion before myocardial infarction[1,3] and may be more frequent triggers. Further study of the triggering of acute vascular events may lead to new insights into the mechanisms involved, clarify some of the uncertainties regarding the beneficial effects of physical exertion,[42] and lead to new forms of preventive therapy.

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Appendix

The following hospitals or medical centers and investigators participated in the Determinants of Myocardial Infarction Onset Study: South Shore Hospital, South Weymouth, Mass. — C. Gaughan; Deaconess Hospital, Boston — S. Zarich; Carney Hospital, Boston — R. Rimmer; St. Vincent Hospital, Worcester, Mass. — R. Bishop; Carle Heart Center, Urbana, Ill. — B. Handler; Burbank Hospital, Fitchburg, Mass. — P. Block; Hahneman Hospital–Medical Center of Central Massachusetts, Worcester — J.A. Ferrullo and D. Miller; Beth Israel Hospital, Boston — R. Pasternak and A. Ware; Brigham and Women's Hospital, Boston — E. Antman; Newton–Wellesley Hospital, Newton, Mass. — J. Sidd; St. Luke's–Roosevelt Hospital Center, New York — J. Hochman; Memorial Hospital–Medical Center of Central Massachusetts, Worcester — J. Greenberg; Norwood Hospital, Norwood, Mass. — G. Bero and B. Heller; Faulkner Hospital, Jamaica Plain, Mass. — A. Ramirez; Washington Hospital Center, Washington, D.C. — L. Van Voorhees; New England Medical Center, Boston — S. Naimi; Massachusetts General Hospital, Boston — P. O'Gara; University of Massachusetts Medical Center, Worcester — J. Gore; Leominster Hospital, Leominster, Mass. — N. Mercadante; Overlook Hospital, Summit, N.J. — J. Gregory; Tampa General Hospital and James A. Haley Veterans Hospital, Tampa, Fla. — R. Zoble; Boston University Medical Center, University Hospital, Boston — M. Klein; Rush–Presbyterian–St. Luke's Medical Center, Chicago — P.R. Liebson; Stonybrook Health Sciences Center, Stonybrook, N.Y. — P. Cohn and R. Friedman; Memorial Hospital of Rhode Island, Pawtucket — A. Khan; Flushing Hospital Medical Center, Flushing, N.Y. — S. Zoneraich; West Virginia Veterans Affairs Medical Center, Huntington — R. Touchon; Milford Whitinsville Regional Hospital, Milford, Mass. — A. Sgalia; Quincy Hospital, Quincy, Mass. — A. Berrick; Montefiore Medical Center, Bronx, N.Y. — M. Goldberger; Veterans Affairs Medical Center, Long Beach, Calif. — A. Al-Zarka; Denver General Hospital, Denver — K. Nademanee; Concord Hospital, Concord, N.H. — C. Levick; St. Elizabeth's Hospital, Brighton, Mass. — B. Kosowsky; Danbury Hospital, Danbury, Conn. — D.L. Copen; Harlem Hospital Center, New York — J. Brown; Boston City Hospital, Boston — S. Bernard; Metro West Medical Center–Framingham Union Hospital, Framingham, Mass. — H.S. Smith; Goddard Memorial Hospital, Stoughton, Mass. — M. Mazur; Illinois Heart Institute, Peoria — P. Schmidt; New Britain General Hospital, New Britain, Conn. — M. Sands; New York Hospital–Cornell Medical Center, New York — R. Allan and S. Scheidt.

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