

# Sex differences in potential daily triggers of the onset of acute myocardial infarction: a case-crossover analysis among an Iranian population

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**Objective** Despite an increasing knowledge of the importance of triggering in cardiac events and their mortality and morbidity, awareness concerning the types of physical and psychological triggers is unsatisfactory. This study aimed to address the main daily triggers of typical chest pain as a marker of acute coronary syndrome onset and assessed the sex-related differences regarding these triggers among Iranians.

**Basic methods** A case-crossover study was conducted on 198 consecutive patients with a first event of acute myocardial infarction admitted to the coronary care unit of Shafa hospital in Kerman. Patients were interviewed about the baseline characteristics as well as potential triggers of chest pain experienced over the day before the diagnosed onset of disease. The start of diagnostic chest pain was used as a marker of disease onset. The hazard period was defined as 12-h period of onset of chest pain.

**Main results** Among probable triggers, only unsuspected sudden bad news and sexual activity had significant relationships with chest pain appearance during the hazard period. Among patients with the experience of bad news, the risk of chest pain occurrence during the hazard period was 6.9 [95% confidence interval (CI) 1.5–31.8]. Also, among those who were exposed to sexual activity, this risk

was 3.4 (95% CI 1.1–10.4). Risk of chest pain following bad news was specific to men with a risk of 9.9 (95% CI 1.1–87.6) and risk of event following sexual activity was specific to women with a risk of 13.3 (95% CI 1.4–120.9).

**Conclusion** Unsuspected sudden bad news can be an important trigger for acute cardiac events in men, whereas sexual activity can act as a strong trigger for these events among women. Counseling in high-risk groups should be focused on men with considerable sudden emotional stressors in their lives and also on women during the ages of active sexual function. *J Cardiovasc Med* 11:723–726 © 2010 Italian Federation of Cardiology.

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**Keywords:** myocardial infarction, risk factors, sex, sexual activity, stress

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## Introduction

The impact of sociodemographic and psychological factors on cardiovascular events is well known in terms of chronic cardiovascular and ischemic states. Various probable external triggers have been hypothesized as risk factors for the onset of acute coronary syndrome (ACS), such as heavy physical activities, emotional stress, sexual activity, meteorological stress and large meals. Some of these triggers, such as heavy physical exertion, can precede approximately half of the onsets of ACS in men, whereas some others, such as emotional stress, may play a more important role in triggering ACS in women [1]. However, it seems that the mental or physical stress alone is not a common trigger of either silent or symptomatic ischemia, whereas combined physical/mental stress has a major role for ischemic cardiac events [2]. These effects of physical and mental triggers may be effectively induced by several processes. It has been suggested that cardiac vagal modulation and increased procoagulant

activities have a major role in the onset of acute cardiac events following physical or psychological stresses [3]. A number of hypotheses have also been raised to explain that the appearance of the stresses may lead to plaque rupture and therefore occlusive coronary thrombosis. In addition, induction of coagulability or vasoconstriction triggered by stressors may contribute to complete occlusion of the coronary artery lumen [4,5]. Although the knowledge of clinicians regarding triggering in cardiac events and their mortality and morbidity has an increasing trend [6], awareness concerning the types of physical and psychological triggers is unsatisfactory. This fact creates the need to identify the acute triggers of ACS and sudden cardiac death, especially in our population with notable prevalence of ACS and its potential risk factors. This paper describes our study to determine the main daily triggers of typical chest pain as a marker of ACS onset and to assess the sex-related differences regarding these triggers among Iranians.

## Methods

### Study population

This was a case-crossover study nested in the Shafa hospital in Kerman. The details of case-crossover studies have been described previously [7]. Briefly, in this study, three types of data are needed: the time of disease onset; knowledge of whether the trigger was present during a defined period immediately before onset and the usual frequency of trigger exposure. It also defined a hazard period variable that is the period before disease onset during which the trigger has an effect. The main goal of this study was to calculate the relative risk of disease after an episode of its probable trigger.

The study population consisted of 198 consecutive patients with a first event of acute myocardial infarction (AMI) who were admitted to the coronary care unit of Shafa hospital between January and July 2009. Among 200 patients who were eligible in this study, 198 patients were interviewed. In the current study, patients who were too sick to be contacted for the onset study and also those with missing, unreliable or inaccurate information regarding time of disease onset were excluded. AMI was diagnosed according to the criteria developed by the European Society of Cardiology and the American College of Cardiology jointly published guidelines [8]. The start of diagnostic chest pain was used as a marker of disease onset. Typical chest pain was defined as pressure-like retrosternal pain being exacerbated by exercise and relieved at rest or with administration of nitroglycerin. Additionally, if the pain radiated to the neck or left shoulder or arm, it was classified as typical [9]. The hazard period was defined as a 12-h period of onset of chest pain. The Ethical Committee of Kerman University of Medical Sciences approved the study to be carried out and all patients gave consent for participation in the scientific study.

### Study data

Study information was obtained by interviews conducted by a trained physician during the first day of admission. The data were collected using a self-administered questionnaire which included sociodemographic characteristics and medical history as well as information on the episode of chest pain such as time, type and duration of pain. Patients were also interviewed about eight potential triggers of chest pain experienced over the day before the diagnosed onset of disease. Probable triggers included severe anger, bad news, emotional stress, heavy physical activity, being cold, cigarette smoking, opium use/addiction and sexual activity. Exposure to each trigger was identified in the interview by this question: 'When was the last time before your chest pain that you were exposed to the trigger?'. Opium addiction was defined on the basis of the DSM-IV Criteria for Substance Dependence as regular consumption of inhalatory opium more than three times per week and/or oral opium daily.

However, opium users included all cases with regular or irregular use of opium [10].

### Statistical analysis

Data were presented as mean  $\pm$  SD for continuous variables and percentages for categorical variables. Comparisons of categorical variables across the groups were performed using an overall chi-square test or Fisher's exact test if required, whereas comparisons of continuous variables were performed using an independent *t*-test. For determining the main predictors of chest pain onset, we first evaluated univariately associations between the probable triggers for this event (including anger, bad news, cold situation, heavy physical activity, smoking, opium use and sexual activity) and appearance of chest pain as a marker of disease onset by chi-square test. Then, in the subsequent analysis, factors obtained in univariate analysis were considered in multivariable binary logistic regression analyses for determining relationships between these triggers and onset of pain as dependant variable in the presence of cofounders such as age, marital status, education level and history of coronary artery disease (CAD) risk factors. The effect of triggers was measured as a relative risk, estimated by the ratio between the observed exposure odds at the time of disease onset and the expected exposure odds and presented as odds ratio (OR) and 95% confidence intervals (95% CIs) for OR. Model calibration was estimated using the Hosmer–Lemeshow goodness-of-fit statistics that higher  $\chi^2$  values implied that the model fits the observed data better. *P* values of 0.05 or less were considered statistically significant. All the statistical analyses were performed using SPSS version 16.0 (SPSS Inc., Chicago, Illinois, USA).

## Results

As shown in Table 1, the mean age of study patients was  $59.8 \pm 12.0$  (range 30–88 years) and 62.1% of them were men. There were significant differences in the overall incidence rates of social characteristics and risk factors for CAD between the two sexes, in that a history of hypertension and diabetes mellitus was found more in women than men, whereas education level was significantly

**Table 1 Baseline characteristics and clinical data of study patients**

Characteristics	Total ( <i>n</i> = 198)	Men ( <i>n</i> = 123)	Women ( <i>n</i> = 75)	<i>P</i> value
Age (years)	59.8 $\pm$ 12.0	57.8 $\pm$ 11.9	63.1 $\pm$ 11.6	0.002
Marriage	133 (67.2)	92 (74.8)	41 (54.7)	0.003
Education level				
Primary	116 (58.6)	55 (44.7)	61 (81.3)	<0.001
Secondary	64 (32.3)	50 (40.7)	14 (18.7)	
Higher	18 (9.1)	18 (14.6)	0 (0)	
Diabetes mellitus	67 (33.8)	32 (26.0)	35 (46.7)	0.039
Hypertension	79 (39.9)	38 (30.9)	41 (54.7)	0.033
Current smoking	61 (30.8)	57 (46.3)	4 (5.3)	<0.001
Opium addiction	75 (38.4)	54 (43.9)	21 (28.0)	0.127

Data are presented as mean  $\pm$  SD or *n* (%).

**Table 2 Oral medication in study patients before admission**

Characteristics	Total (n = 198)	Men (n = 123)	Women (n = 75)	P value
Aspirin	188 (94.9)	115 (93.5)	73 (97.3)	0.232
Beta-blocker	167 (84.3)	109 (88.6)	58 (77.3)	0.034
Calcium-blocker	29 (14.6)	23 (18.7)	6 (8.0)	0.039
ACE inhibitor	59 (29.8)	29 (23.6)	30 (40.0)	0.014
Diuretic	33 (16.7)	13 (10.6)	20 (26.7)	0.003
Nitrate	140 (70.7)	89 (72.4)	51 (68.0)	0.513

Data are presented as *n* (%). ACE, angiotensin-converting enzyme.

lower in women. With regard to oral medications before admission, although administration of aspirin and nitrates were similar between the two sexes, beta-blockers and calcium-blockers were administered more in men, whereas ACE inhibitors and diuretics were used more in women (Table 2). Regarding exposure to triggers (Table 3), except for cigarette smoking and opium use, which were more frequent in men, no significant differences were observed in the exposure to other triggers between the two sexes.

Among eight probable triggers in univariate analysis, only bad news and sexual activity had significant relationships with chest pain appearance during the hazard period. Among patients with the experience of bad news, the risk of chest pain occurrence during the hazard period was 6.9 (95% CI 1.5–31.8). Also, among those who were exposed to sexual activity, this risk was 3.4 (95% CI 1.1–10.4). With regard to the risk of chest pain following trigger exposure in the two sexes, risk of chest pain following bad news was specific to men with a risk of 9.9 (95% CI 1.1–87.6) and risk of an event following sexual activity was specific to women with a risk of 13.3 (95% CI 1.4–120.9) (Table 4).

## Discussion

The current study tried to assess the triggering effects of some usual physical and emotional stimulators on the onset of typical cardiac chest pain as a marker of AMI onset. Our assessment mainly focused on the effects of these factors in men and women separately. In our study, although bad news and sexual activity have been identified as the two main risk triggers of cardiac events, the influence of the first trigger was higher in men and the

**Table 3 Frequency of probable triggers of the onset of cardiac chest pain during the 12 h before the diagnosis of disease**

Characteristics	Total (n = 198)	Men (n = 123)	Women (n = 75)	P value
Anger	48 (24.2)	29 (23.6)	19 (25.3)	0.780
Bad news	11 (5.6)	5 (4.1)	6 (8.0)	0.339
Emotional stress	30 (15.3)	21 (17.2)	9 (12.2)	0.341
Heavy physical activity	18 (9.1)	13 (10.6)	5 (6.7)	0.354
Cold situation	5 (2.5)	2 (1.6)	3 (4.0)	0.302
Cigarette smoking	42 (21.6)	39 (32.0)	3 (4.2)	<0.001
Opium use	81 (41.1)	62 (50.8)	29 (38.7)	<0.001
Sexual activity	17 (8.6)	9 (7.3)	8 (10.7)	0.414

Data are presented as *n* (%).

**Table 4 Multivariable analysis of the effects of bad news and sexual activity as the triggers of cardiac chest pain during the 12 h directly after these triggers**

Triggers	Number of exposed cases	Odds ratio	95% CI	P value	HLS ( $\chi^2$ )
Bad news					
Total	11/198	6.944	1.512–31.894	0.013	7.259
Men	5/123	9.908	1.120–87.614	0.039	7.337
Women	6/75	4.849	0.536–43.839	0.160	2.622
Sexual activity					
Total	17/198	3.424	1.125–10.420	0.030	3.897
Men	9/123	1.303	0.312–5.441	0.717	5.320
Women	8/75	13.378	1.480–120.946	0.021	4.045

HLS, Hosmer–Lemeshow goodness of fit.

other trigger in women. First, we showed that bad news within the 12 h before chest pain appearance could increase the risk of event by 9.9 times in men. It seems that the role of bad news as a trigger of the onset of typical chest pain is more likely due to the effect of sudden emotional stress. In fact, bad news can be defined as a sudden emotional stress. Between 20 and 40% of sudden cardiac deaths are precipitated by acute emotional stressors [6,11]. Studies in both animal models and humans confirmed a causal relationship between emotional stress and coronary atherosclerosis [12,13].

Mental stresses are able to increase the risk for myocardial infarction about two-fold. It has been suggested that the stress is characterized by an increase in plasma catecholamines and cortisol associated with a rise in heart rate and blood pressure. Plasma epinephrine can increase by a factor of eight through emotional or physical stress [14]. Some studies have indicated that the effect of acute emotional stress on the onset of cardiac event was more common in younger patients and those with lower socioeconomic levels [15]. However, specification of this relationship in men should be studied further, because contrary to our study, some researchers have shown that heavy physical activity and eating were more likely to precede the infarction onset in men, whereas women were more likely to report emotional stress [1]. Apart from this, although in some previous studies it has been mentioned that physical activity and emotional stress are common triggers of ACS in men and women [1], respectively, we showed that emotional stress was a major trigger of ACS particularly in men. It seems that men in our society are more subjected to emotional triggers of typical chest pain compared to women, and this may be explained by the prominence of occupational stressors in the profiles of men that was also previously observed [16].

Another finding in the present study focused on the strong trigger effect of sexual activity on the onset of cardiac chest pain in women, but not in men. It was revealed that the relative risk of AMI was 2.1 during 1 h after sexual activity, and the risk among patients with a sedentary life style was 4.4 [7]. However, it seems that sexual activity, especially in men, represents a small risk

of triggering an AMI compared with vigorous physical activity and intense emotional responses. Furthermore, sexual activity has a moderate stress on the heart in terms of the responses that impact on myocardial oxygen requirement [17–20]. Additionally, sexual activity only once a week can increase the annual risk of myocardial infarction slightly [7].

The prevalence of opium addiction in our study group was estimated as 38.4%, which was considerably high for our society. In a study by Ziaaddini and Ziaaddini [21] it was suggested that the prevalence of substance abuse in a rural area in Kerman was 22.5%. Regarding the prevalence of opium addiction among patients with coronary artery disease, some other studies on the Iranian population confirmed a significantly high prevalence of opium dependence in those with early-onset CAD in comparison with normal individuals [22]. It seems that cultural factors and socioeconomic status are the most important plausible reasons for high opium dependence among the Kerman population. These effective factors have been identified on the basis of population-based studies so that positive attitudes towards drug consumption and faulty knowledge of the therapeutic use of opium were recognized as factors affecting addiction tendency in the Kerman population [23].

In conclusion, acute emotional stress such as bad news can be an important trigger for acute cardiac events in men, whereas sexual activity can be a strong trigger for these events among women. On the basis of our findings, counseling in high-risk groups should be focused on men with considerable emotional stressors in their life and also on women during the ages of active sexual function.

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## References

- 1 Culić V. Acute risk factors for the onset of acute coronary syndromes. *Acta Med Croatica* 2006; **60**:439–445.

- 2 Freedman SB, Wong CK. Triggers of daily life ischaemia. *Heart* 1998; **80**:489–492.
- 3 González Pliego JA. Triggering of acute coronary syndromes. Pathophysiologic relationships. *Arch Cardiol Mex* 2006; **76**:208–221.
- 4 Johnstone MT, Mittleman M, Tofler G, Muller JE. The pathophysiology of the onset of morning cardiovascular events. *Am J Hypertens* 1996; **9**:22–28.
- 5 Stone PH. Triggers of transient myocardial ischemia: circadian variation and relation to plaque rupture and coronary thrombosis in stable coronary artery disease. *Am J Cardiol* 1990; **66**:32–36.
- 6 Vlastelica M. Emotional stress as a trigger in sudden cardiac death. *Psychiatr Danub* 2008; **20**:411–414.
- 7 Möller J, Ahlbom A, Hulting J, Diderichsen F, de Faire U, Reuterwall C, Hallqvist J. Sexual activity as a trigger of myocardial infarction. A case-crossover analysis in the Stockholm Heart Epidemiology Programme (SHEEP). *Heart* 2001; **86**:387–390.
- 8 Macfarlane PW. *Update on ACC/ESC criteria for acute ST elevation myocardial infarction. Current news in cardiology*. Milan: Springer; 2007.
- 9 Goldman L, Weinberg M, Weisberg M, Olshen R, Cook EF, Sargent RK, et al. A computer-derived protocol to aid in the diagnosis of emergency room patients with chest pain. *N Engl J Med* 1982; **307**:588–596.
- 10 APSY. *Diagnostic and statistical manual of mental disorders text revision*. 4th ed. Washington DC: American Psychiatric Pub.; 2000.
- 11 Willich SN. Circadian variation and triggering of cardiovascular events. *Vasc Med* 1999; **4**:41–49.
- 12 Chernigovskaya SV, Cherkovich GM, Uzunyan LA. Effect of emotional stress on blood-clotting system indices in monkeys. *Bull Experiment Biol Med* 2006; **75**:250–252.
- 13 Kones RJ. Emotional stress, plasma catecholamines, cardiac risk factors, and atherosclerosis. *Angiology* 1979; **30**:327–336.
- 14 Klein HH. Stress and myocardial infarction. *Herz* 2001; **26**:360–364.
- 15 Strike PC, Perkins-Porras L, Whitehead DL, McEwan J, Steptoe A. Triggering of acute coronary syndromes by physical exertion and anger: clinical and sociodemographic characteristics. *Heart* 2006; **92**:1035–1040.
- 16 Knox SS. Work stress and chest pain in men and women under age 65. *J Women's Health* 1993; **2**:125–132.
- 17 Fries R, König J, Schäfers HJ, Böhm M. Triggering effect of physical and mental stress on spontaneous ventricular tachyarrhythmias in patients with implantable cardioverter-defibrillators. *Clin Cardiol* 2002; **25**:474–478.
- 18 Stein RA. Cardiovascular response to sexual activity. *Am J Cardiol* 2000; **86**:27–29.
- 19 Muller JE. Triggering of cardiac events by sexual activity: findings from a case-crossover analysis. *Am J Cardiol* 2000; **86**:14–18.
- 20 Muller JE, Mittleman MA, Maclure M, Sherwood JB, Tofler GH. Triggering myocardial infarction by sexual activity. Low absolute risk and prevention by regular physical exertion. Determinants of Myocardial Infarction Onset Study Investigators. *JAMA* 1996; **275**:1405–1409.
- 21 Ziaaddini H, Ziaaddini MR. The household survey of drug abuse in Kerman. *Iran J Appl Sci* 2005; **5**:380–382.
- 22 Najafi M, Sheikhvatan M, Montazeri A, Sheikhfathollahi M. Quality of life in opium-addicted patients with coronary artery disease as measured with WHOQOL-BREF. *Int J Soc Psychiatr* 2009; **55**:247–256.
- 23 Shamsi Meymandi M, Ziaaddini H, Sharifi Yazdi A. Opinion of high school students of Kerman towards affecting factors on narcotics tendency. *JQUMS* 2008; **12**:80–88.