Emotional Events and Anger at the Workplace as Triggers for a First Event of the Acute Coronary Syndrome: A Case-Crossover Study

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Key words: triggers, emotion, acute coronary syndrome, myocardial infarction, work

Abstract

Background: Previous studies found that some factors such as physical exertion, anger and heavy meals were triggers for acute coronary syndrome.

Objectives: To estimate the relative risk of an ACS episode associated with positive and negative emotional experiences and anger as potential work-related triggers.

Methods: A total of 209 consecutive patients were interviewed a median of 2 days after a cardiac event that occurred at work or up to 2 hours later. The case-crossover design was used. Positive and negative emotional experiences and anger episodes in the hours immediately before the onset of ACS were compared with episodes in the comparable hours during the previous workday. For anger the episodes were compared with the usual frequency at work during the previous year. Positive and negative emotional experiences were assessed by the PANAS questionnaire (Positive and Negative Affect Scale), and anger by the Onset Anger Scale.

Results: The relative risks of an acute coronary event during the first hour after exposure to negative and positive emotional experiences were RR = 14.0 (95% confidence interval 1.8–106.5) and RR = 3.50 (95% CI 0.7–16.8) respectively and RR = 9.0 (95% CI 1.1–71) for an episode of anger. Using conditional logistic regression analysis, the highest relative risk was associated with negative emotional experiences.

Conclusions: Negative emotional experiences and anger at work can trigger the onset of an ACS episode. This could have implications for recognizing a cardiac event as a work accident. The implementation of stress-reduction programs in the workplace or use of preventive medications in workers at high risk for coronary heart disease should be investigated.

IMAJ 2007;9:310–315

In case-crossover studies, individual factors such as physical exertion [1,2], anger [3], sexual activity [4] and heavy meals [5] were found to be triggers for acute coronary syndrome. In as many as 50% of patients in previous studies, patients who suffered an ACS episode reported possible triggers before the event [6,7]. An analysis of periodicity showed a significant 30% increase in cardiac episodes on Mondays among working people [8]. Older and retired people had their heart attacks more evenly distributed across the days of the week [8,9].

A recent meta-analysis showed a significant 40% increase in risk of heart attack between 6 a.m. and 12 noon compared with what would have been expected if heart attacks occurred randomly and were evenly distributed throughout the 24 hours [10]. Increases in blood pressure and pulse rate [11], serum cortisol, plasma catecholamines and platelet aggregability levels [12] on awakening can explain only the first few hours of the increase in risk of ACS. These findings suggest that work-related factors may contribute to the triggering of a cardiac event.

In the present study, we used the case-crossover design to estimate the relative risk of a cardiac episode associated with positive and negative emotional experiences and anger as potential work-related triggers. To the best of our knowledge, this is the first report on the role of negative and positive emotional experiences and anger at the workplace as triggers for ACS.

Patients and Methods

The study was conducted in four intensive coronary care units in the center of Israel. Patients who worked and were free of previous cardiac events were selected from the admissions register. A total of 209 patients (194 men and 15 women, age range 26–77 years) who participated were interviewed a median of 2 days (range 1–5 days) after an ACS episode that occurred during working hours or up to 2 hours thereafter. The same interviewer conducted all the interviews. The institutional review board of each center approved the protocol and informed consent was received from all patients.

* Deceased

ACS = acute coronary syndrome
RR = relative risk
CI = confidence interval

Study design

We used a case-crossover method that was originally developed to assess the change in risk of an acute event during a brief "hazard period" after exposure to a transient risk factor [1-4,13,14]. The occurrence of negative and positive emotional experiences and experiences of anger during the hazard period immediately before the ACS onset at work were compared with the occurrence of experiences during the same period on the working day before the onset of the cardiac event. The hourly relative risk was obtained by asking the patient the length of time of the emotional situation, the length of time from the emotional experience to the onset of symptoms, and if it occurred at work time or at another time. For anger, a comparison was also made with the usual frequency of anger at work during the past year. Positive and negative emotional experiences could not be assessed by the "usual frequency during the past year."

Case definition

The diagnostic criteria for ACS were either a first event either of chest pain or other symptoms associated with myocardial infarction together with an elevated creatine kinase level or new onset of angina pectoris with electrocardiographic changes suggestive of evolving myocardial ischemia. The first time the patient reported experiencing the typical symptoms was taken as the reference time for the onset of the ACS (acute myocardial infarction).

Interview questionnaires

Positive and negative emotional experiences were assessed by the PANAS questionnaire (Positive and Negative Affect Scale) [15], comprising two mood scales of 10 items at three levels [Appendix 1]. This was translated into Hebrew. Patients were considered to have experienced positive or negative emotional experiences if they reported at least three positive or negative emotional experiences during the period of interest.

The Anger Onset Scale, a seven-level scale previously used in studies of coronary heart disease [3], was translated into Hebrew [Appendix 2]. Patients were considered exposed if they reported a peak level of anger ≥ level 4 during the interval of interest.

Patients were also asked about unusual emotional situations on the same day of the week prior to the onset of symptoms in order to determine whether the person is exposed to a fixed trigger on a particular day of the week.

Validation of the questionnaires

We assessed the validity and reliability of the Hebrew version of the PANAS scales by interviewing a group of 30 workers twice within a period of one week and obtained good results for test-retest reliability and internal consistency.

Statistical analysis

The data were analyzed using the SPSS package for Windows. When the control period was the day before onset, relative risks were computed using standard methods for matched-pair case-control studies, in which each patient contributed a pair of intervals – a "hazard period" and a "control period" [13,14,16]. For the usual annual frequency of episodes, the amount of person-time "exposed" was estimated by multiplying the reported usual annual frequency of exposure at work by its usual duration. Unexposed person-time was then calculated by subtracting the exposed person-time in hours from the number of hours in a year. The data on the case-day was taken for working hours, thus for annual frequency of exposure at work we assumed 8 hour workdays and 5.5 working days a week. Hazard periods of various duration were analyzed using methods for cohort studies with sparse data in each stratum [13,16,17].

We used 95% confidence intervals for the calculated relative risks using exact methods based on the binomial distribution. Conditional multiple logistic regression analysis was used to control for within-person confounding [13,16]. Interactions were assessed by comparing relative risks in subgroups defined by different levels of the potential effect modifier. To estimate induction time (the length of time from the episode to the onset of acute ischemic event), relative risks were calculated for each 1 hour period before the onset of ACS, with statistical control for subsequent exposure [18]. Correlation between negative emotional experiences and anger was assessed by the Phi correlation coefficient.

Results

Characteristics of the study sample are shown in Table 1. Twenty-three patients (11%) reported negative emotional experiences, 8 (3.8%) reported positive emotional experiences and 15 (7.2%) reported anger on the day of the ACS event.

Negative and positive emotional experiences

In the matched-pair analysis for negative emotional experiences, the relative risk for the 1 hour period prior to the ACS event was RR 14.0 (95% CI 1.8–106.5) [Table 2]. The relative risk declined to

Table 1. Study sample characteristics

	No. of patients	% patients	Mean ± SD
Age (yrs)	–*	–*	52.4 ± 8.7
High (cm)	–*	–*	173.0 ± 6.53
Weight (kg)	–*	–*	80.1 ± 12.75
BMI (kg/m^2)	–*	–*	27.0 ± 3.7
Male	194	92.8	–*
Salaried	130	62.2	–*
Physical work	68	32.5	–*
Smoker	125	59.8	–*
Past smoker	36	17.2	
Non-smoker	48	23.0	
CHD family history	93	44.5	–*
Hypertension	64	30.6	–*
Diabetes	32	15.3	–*

* Category not applicable

BMI = body mass index, CAD = coronary heart disease.

PANAS = Positive and Negative Affect Scale

7.5 (95% CI 1.0–63.9) during the 1 hour period 5 hours before the acute coronary event [Figure 1].

In the matched-pair analysis for positive emotional experiences, the relative risks for all the 1 hour periods before an ACS event were not statistically significant [Table 2]. There were significant findings in the comparison of emotional experiences on the day of the coronary event with the same day a week before.

Anger

The relative risk of an ACS event was RR = 9.0 (95% CI 1.1–71) for those exposed to anger during the hazard period [Table 2]. After controlling for episodes of anger in the 1 hour period before the onset of a coronary event, the relative risks for the 1 hour periods 2–5 hours before an ACS event were not statistically significant, indicating that the induction time was less than 1 hour. The usual annual frequency of episodes of anger as the control value yielded relative risks of an ACS event in the hour immediately after exposure of RR = 6.2 (95% CI 3.6–10.9) and of RR = 4.3 (95% CI 2.2–8.6) in the 2–3 hour periods before an acute coronary event, declining to lower and non-statistically significant relative risks thereafter [Table 2].

Table 2. Relative risk for an acute coronary syndrome after a 1–2 hour period after exposure to anger, positive emotional experience, or negative emotional experience

	Hours before ACS onset	Day before RR (95% CI)	*P*	Annual frequency RR (95% CI)	*P*
Negative emotion	First hour	14 (1.8–106.5)	0.001	–*	–*
	Second hour	7.5 (1.7–32.8)	0.002		
Positive emotion	First hour	3.5 (0.7–16.8)	0.18	–*	–*
	Second hour	5 (0.6–42.8)	0.22		
Anger	First hour	9 (1.1–71)	0.004	6.2 (3.6–10.9)	0.00001
	Second hour	7 (0.9–56.9)	0.07	4.3 (2.2–8.6)	0.00001

* Category not applicable

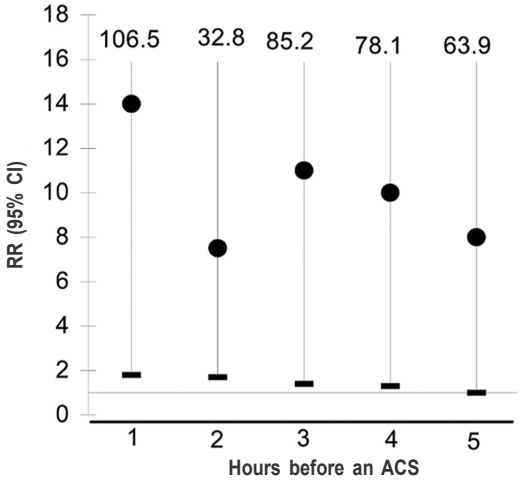

Figure 1. Relative risks for acute coronary syndrome after exposure to negative emotional experiences

Effect modification analysis

For the exposed to negative emotions, the effect modification analysis yielded a non-significantly lower relative risk among regular users of aspirin, angiotensin-converting enzyme inhibitors or statins (RR = 1.0, 95% CI 0.1–16) than among non-users (RR = 13.0, 95% CI 1.7–99.4), but the difference between the two was of borderline significance ($P = 0.062$). For non-diabetics the relative risk was higher than for diabetics ($P = 0.062$). We did not find any statistically significant modifiers for positive emotional experiences [Table 3]. No patients reported two kinds of triggers at the same time.

Table 3. Relative risks for an ACS event by stratification for potential effect modifiers in the first hour after exposure to a potential trigger compared with the day before

	No. of patients	Negative emotion RR (95% CI)	Positive emotion RR (95% CI)	Anger RR (95% CI)
All patients	209	14 (1.8–106.5)	3.5 (0.7–16.8)	9 (1.1–71.0)
Age (yrs)				
< 50	81	6 (0.7–49.8)	2.5 (0.5–12.9)	5 (0.6–42.8)
50–69	123	7 (0.9–56.9)	2 (0.2–22.1)	4 (0.4–35.8)
> 69	5	1 (0.1–16.0)	1 (0.1–16.0)	1 (0.1–16.0)
BMI				
≤ 25	66	3 (0.3–18.8)	1 (0.1–16.0)	4 (0.4–35.8)
> 25	142	11 (1.4–85.2)	6 (0.7–49.8)	5 (0.6–42.8)
Hypertension				
Yes	64	5 (0.6–42.8)	4 (0.4–35.8)	4 (0.4–35.8)
No	145	9 (1.1–71.0)	1.5 (0.2–9.0)	5 (0.6–42.8)
Diabetes				
Yes	32	1 (0.1–16.0)	1 (0.1–16.0)	3 (0.3–28.8)
No	177	13 (1.7–99.4)	3 (0.6–14.9)	6 (0.7–49.8)
Aspirin				
Yes	9	1 (0.1–16)	1 (0.1–16)	2 (0.2–22.1)
No	200	13 (1.7–99.4)	3.5 (0.7–16.8)	7 (0.9–56.9)
Beta-blockers				
Yes	12	1 (0.1–16)	1 (0.1–16)	1 (0.1–16)
No	197	14 (1.8–106.5) (NS)	3 (0.6–14.9)	8 (1–63.9)
Calcium blockers				
Yes	21	2 (0.2–22.1)	2 (0.2–22.1)	1 (0.1–16.0)
No	188	12 (1.6–92.3)	2.5 (0.5–12.9)	8 (1–63.9)
ACE inhibitors				
Yes	9	1 (0.1–16)	1 (0.1–16)	2 (0.2–22.1)
No	200	13 (1.7–99.4)	3.5 (0.7–16.8)	7 (0.9–56.9)
Statins				
Yes	11	1 (0.1–16.0)	1 (0.1–16.0)	1 (0.1–16.0)
No	198	13 (1.7–99.4)	3.5 (0.7–16.8)	8 (1–63.9)
Physical work				
Yes	68	1 (0.1–16.0)	3 (0.3–28.4)	4 (0.4–35.8)
No	141	13 (1.7–99.4)	2 (0.4–10.9)	5 (0.6–42.8)
Smoke				
Yes	125	7 (0.9–56.9)	4 (0.4–35.8)	6 (0.7–49.8)
No	84	7 (0.9–56.9)	3 (0.3–28.8)	3 (0.3–28.8)

The relative risk for patients exposed to anger tended to be lower among users of beta-blockers, calcium channel blockers, ACE inhibitors, statins, and among diabetics, and higher in smokers, patients with a family history of heart disease, and patients holding a job [Table 3]. However, sample sizes were small and these differences were not statistically significant. None of the women were exposed to anger or a negative emotional experience before the onset of symptoms. The modifier effect of cholesterol was checked and found to be non-significant.

Negative emotional experiences (PANAS scale) and the Onset Anger Scale

The comparison between the results of the PANAS Scale (negative emotional experiences) and the Onset Anger Scale yielded a Phi correlation of coefficient between 0.57 and 0.54 ($P < 0.0001$) for the three first 1 hour periods before the onset of symptoms.

Conditional logistic regression

In the conditional logistic regression analysis, after controlling for the potential confounding variables, the association with negative emotional experiences remained strong and statistically significant (odds ratio = 6.09, 95% CI 1.36–27.32). Anger was also strongly associated with ACS, but with borderline significance (OR = 7.94, 95% CI 0.94–66.89). The association with positive emotional experiences was weak and not statistically significant (OR = 1.51, 95% CI 0.33–6.82).

Discussion

In the present study, the relative risk of an ACS event associated with a negative emotional experience was statistically significantly increased at 2 hours. It remained increased, although less so, up to 5 hours after the trigger. The relative risk for an ACS event after a positive emotional experience was not statistically significant. As previously reported by others [3,19], there was an increased relative risk associated with an episode of anger for several hours prior to the coronary event but it was statistically significant for the first hour only.

To the best of our knowledge, this is the first study dealing with triggers at work independently of those occurring during leisure time. Negative emotional experiences were associated with a 6 to 14-fold risk of the onset of ACS in the subsequent 5 hours. In the present study most patients who reported negative emotional experiences reported a level "more than usual," and not the maximal level "much more than usual." Therefore, relatively low levels of negative emotions appear to be capable of triggering the symptoms of ACS. These findings contrast with previous findings negating the possible association between a negative emotion at work and a cardiac event [20].

Thirty percent of any type of trigger found in our study was related to negative emotional experiences. This is consistent with several case series where about 30% reported emotional upset prior to myocardial infarction [6,21]. The percentage of patients who reported a negative emotional experience in the first hour before the onset of ACS symptoms was 6.7%, which is higher than previously reported for anger [3]. This is logical because the spectrum of negative experiences in the PANAS Scale is wider than the Onset Anger Scale and includes such concepts as distressed, upset, guilty, scared, hostile, irritable, ashamed, nervous, jittery and afraid – which are not included in the anger scale.

The 5 hours induction time (which is the time between the emotional experience and the cadiac event) for a coronary event induced by a negative emotional experience at work was much longer than the induction time that others found for an acute myocardial infarction induced by physical exertion [1,2], anger [3] and a heavy meal [5]. To the best of our knowledge, this is the first report of negative emotional experiences having such a long induction time when the trigger causing the cardiac event was external. This suggests that a negative emotional experience related to work has a "longer range effect" on a worker compared to an experience such as an outburst of anger, a sudden physical exertion, or a heavy meal. Thus, the induction time for a work-related ACS episode appears to be longer than the induction time by spontaneous experiences not related to work. In the present study 4.3% of patients reported an experience of anger compared with 2.0–2.4% in previous studies [3,19]. An important difference is that in our study only a very small group of patients reported a level of 5 in the Onset Anger Scale, so we used a borderline level of 4 compared with a level of 5 in the previous investigations. Furthermore, our endpoint included both acute myocardial infarction and acute ischemia in contrast to acute myocardial infarction only, in the previous studies [3,19].

Positive emotional experiences at work were not related to ACS using the day before the event. As described before, we were not able to use the usual annual frequency of experiences as control data in combination with the PANAS questionnaire. Because traumatic experiences are usually remembered more vividly than positive or pleasant experiences that occurred during the year [22], we believe that even if we could perform this analysis, it would be inappropriate to compare memories related to negative and positive experiences. Results obtained using the day before the cardiac event as the control period should be less subject to recall bias.

Our results are consistent with a case-crossover study that examined positive and negative emotions associated with transient ischemia on 48 hour ECG monitoring, following new-onset coronary heart disease patients [23]. Only negative emotional experiences were significantly related to transient ischemia in everyday life. The strength of the relative risk was different to that in the present study (RR = 3 vs. 14). However, the endpoints in this study differed, the research population was different, and the emotion items were different (only three items of negative emotions compared with ten in the PANAS Scale). Nevertheless, the results for transient ischemia resembled our results for ACS. Another recent study affirmed that emotional stress can precipitate severe but reversible left ventricular dysfunction caused by an exaggerated sympathetic response [24]

ACE = angiotensin-converting enzyme
OR = odds ratio

The results of this investigation contribute to the debate on whether an ACS episode occurring at work could be considered an occupational accident. If a negative emotional experience at work can trigger a cardiac episode, it is possible that some may regard it as a work accident.

The relative risks tended to vary by subgroups. These results are only suggestive since the subgroups yielded small numbers for analysis. There was some evidence that regular use of aspirin, ACE inhibitors and statins may be protective, although the results were close to statistical significance ($P = 0.062$).

Potential biases and study limitations

All patients admitted to the intensive cardiac care units and who matched the inclusion criteria were recruited to the study, with a compliance of 97%. Thus, there was essentially no self-selection bias. Interviewer selection bias was excluded by collecting the patient criteria for inclusion before the exposure data. Only one interviewer was used in the present study, thereby avoiding "interviewer bias." In addition, in order to minimize the bias resulting from possible secondary gain, questions were asked in such a way that it was not clear to the patient which was the control and which was the hazard period. So, the misclassification, if it exists, is non-differential, and the true relative risk is likely to be higher than the calculated risk. Finally, the high test-retest reliability argues against recall bias. The lower relative risk obtained, when the control time was the usual annual frequency of anger, could be explained by the tendency of patients to over-report their annual frequency of experiences, yielding a lower relative risk [3].

Conclusions

Negative emotional experiences and sudden anger at work can trigger the onset of a cardiac episode. More studies are required to understand the physiological changes which may explain the association between external triggers and the pathological outcome. The implementation of stress-reduction programs in the workplace and the possible use of preventive medications in workers at high risk for coronary heart disease should be investigated.

Acknowledgments. This work was supported by a grant from the Committee for the Prevention and Research of Health at Work, Israel Ministry of Labor.

We are grateful to Dr. Yael Villa for helping with the statistical analysis, and Prof. Michael Eldar and Prof. Zahava Salomon for feedback on the design and report of the study.

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Appendix 1

The PANAS Scale

Negative affect level		Positive affect level	
Did you feel distressed	3 4 5	Did you feel interested	3 4 5
Did you feel upset	3 4 5	Did you feel excited	3 4 5
Did you feel guilty	3 4 5	Did you feel strong	3 4 5
Did you feel scared	3 4 5	Did you feel enthusiastic	3 4 5
Did you feel hostile	3 4 5	Did you feel proud	3 4 5
Did you feel irritable	3 4 5	Did you feel alert	3 4 5
Did you feel ashamed	3 4 5	Did you feel inspired	3 4 5
Did you feel nervous	3 4 5	Did you feel determined	3 4 5
Did you feel jittery	3 4 5	Did you feel attentive	3 4 5
Did you feel afraid	3 4 5	Did you feel active	3 4 5

3 = as usual, 4 = more than usual, 5 = much more than usual

Appendix 2

The Anger Onset Scale

Anger level description
1. Calm
2. Busy but not hassled
3. Mildly angry, irritated, and hassled, but it does not show
4. Moderately angry, so hassled it shows in your voice
5. Very angry, body tense, clenching fists or teeth
6. Furious, almost out of control, very angry, pound table, slam door
7. Enraged! Lost control, throwing objects, hurting yourself or others

If all men knew what others say of them, there would not be four friends in the world

Blaise Pascal (1623-1662), French theologian, mathematician and physicist

Capsule

HIV evolution: host or virus?

During infection, the human immunodeficiency virus (HIV) is under pressure to mutate in order to escape immune detection. A population-level study has suggested that polymorphisms in genes that encode the major histocompatibility complex (MHC) proteins responsible for presenting viral antigens to cytotoxic T cells have a strong influence on how the virus evolves. However, Bhattacharya et al. now present an analysis that takes into account other confounding effects of viral phylogeny and reveals that the majority of such associations result from effects of viral lineages, rather than immune escape. Although MHC polymorphism is still likely to have some influence on viral evolution, this effect could be significantly less than previously suggested.

Science 2007;315:1583

Eitan Israeli

Capsule

Streptomycin resistance

Streptomycin was the first antibiotic found to target the ribosome; specifically, it works by promoting the misreading of the genetic code during translation. Although resistance to high levels of streptomycin has been assigned to mutations in *rrs*, the gene encoding 16S ribosomal RNA (rRNA), this mechanism does not account for the observed high prevalence of resistance to low levels of the drug. Okamoto et al. have found that spontaneous mutations occur rapidly within the bacterially conserved gene *gid*B, which encodes a 7-methylguanosine methyltransferase specific for 16S rRNA. As a consequence of these mutations, there is a failure to methylate the invariant nucleotide G527, and hence low level streptomycin resistance is conferred. Even though resistance to most drugs that interact with the ribosome occurs via changes in rRNA sequence, this finding suggests that this mechanism of resistance could be more frequent among bacteria than previously expected. Moreover, it is worrisome that these mutations do not appear to exact any fitness cost and seem to constitute a first step toward the evolution of high level resistance.

Mol Microbiol 2007;63:1096

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