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Anxiety and anger immediately prior to myocardial infarction and long-term mortality: Characteristics of high-risk patients

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ABSTRACT

Objective: Acute high levels of anger and anxiety are associated with an elevated risk of myocardial infarction (MI) in the following two hours. MIs preceded by these acute negative emotions may also have a poor long-term prognosis, but information about high-risk patients is lacking. We examined whether young age and female sex are associated with MIs that are preceded by negative emotions and whether age and sex moderate the subsequent increased mortality risk following MI preceded by negative emotions.
Methods: We conducted a secondary analysis of the Determinants of Myocardial Infarction Onset Study (N = 2176, mean age = 60.1 ± 12.3 years, 29.2% women). Anxiety and anger immediately prior to (0−2 h) MI and the day before (24–26 h) MI were assessed using a structured interview. Subsequent 10-year all-cause mortality was determined using the US National Death Index.
Results: Anxiety during the 0–2 h pre-MI period was associated with younger age (OR = 0.98,95% CI = 0.96–0.99 per year) and female sex (OR = 1.50,95% CI = 1.11–2.02). Anger in the 0–2 h pre-MI period was also associated with younger age (OR = 0.95,95% CI = 0.94–0.96) but not with sex (OR = 0.93,95% CI = 0.67–1.28). During follow-up, 580 (26.7%) patients died. Mortality rate was higher if MI occurred immediately after high anxiety, particularly in patients ≥65 years (HR = 1.80,95% CI = 1.28–2.54) vs. younger patients (HR = 0.87,95% CI = 0.55–1.40; p-interaction = 0.015). Other interactions with sex or anger were not significant.
Conclusions: Patients with high anxiety or anger levels in the critical 2-hour period prior to MI are younger than those without such emotional precipitants. In addition, pre-MI anxiety is associated with an elevated 10-year mortality risk in patients aged ≥65 years.

1. Introduction

Transient exposure to physical, chemical and psychological stressors are potential triggers of cardiovascular events [1,2]. An elevated risk of myocardial infarction (MI) has been documented minutes to hours following episodes of heavy physical exertion [3], sexual activity [4,5], chemical exposures including air pollution [6], use of marijuana [7] and cocaine, [8] as well as psychological states such as high levels of anger and anxiety [9,10] and depressed mood [11]. In addition to the consistent evidence of an immediately higher cardiovascular risk associated with short-term experiences of negative emotions, the long-term prognosis may be poor among people surviving an MI following these potential acute triggers [12]. However, other studies have not found an association between acute emotional precipitants of MI and long-term mortality [13]. Clinical characteristics of patients whose MI is preceded by negative emotions may partly account for these observed differences in long-term prognosis.

Biological hyper-reactivity to physical or emotional perturbations is a plausible biobehavioral mechanism accounting for MIs that are preceded by exogenous stressors. Acute mental stress can induce myocardial ischemia in controlled laboratory settings and during daily life activities [14–17]. The cardiac demand at which psychological factors induce myocardial ischemia is lower than with physical exertion [17], suggesting that coronary supply-related processes and/or more severe underlying myocardial disease may characterize patients with emotionally triggered ischemia [18]. Mental stress-induced ischemia is also

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associated with an increased long-term mortality risk in patients with coronary artery disease [19,20]. These mechanistic laboratory studies are important because it is difficult to unequivocally determine whether the preceding emotions and behaviors prior to MI are actually exposures that "trigger" acute cardiac events, or whether these emotional precipitants reflect a third common factor and/or reporting bias independent of the pathophysiology of MI Knowledge about the immediate emotional precipitants of MI and the characteristics of these patients may therefore be of clinical utility because these factors may add to the long-term risk stratification of post-MI patients.

Evidence suggests that age is inversely related to emotional wellbeing such that younger adults report more negative emotions than older individuals [21,22]. This age-related pattern has also been found in patients with coronary heart disease [23] and heart failure [24]. In addition, women tend to report higher levels of anxiety and other negative emotions compared to men [25–27] whereas men tend to report higher levels of hostility [28,29]. However, there has been no research examining whether the prevalence of emotional factors in the critical 2 h immediately prior to MI onset varies by age and sex. Vaccarino et al. [30] showed that women ≤50 years of age with a recent history of MI had substantially more mental stress-induced myocardial ischemia compared to age-matched men (52% vs. 25%). No sex-related differences were observed for ischemia induced with physical stress or in patients older than 50 years. Therefore, younger age and female sex are likely to be associated with a higher risk of myocardial infarction preceded by acute negative emotions such as anxiety and anger. In addition, MIs that develop in the context of these acute negative emotions might have a poor subsequent long-term prognosis.

This study builds on our recent observations that immediate (0–2 h pre-MI) [31] and distant (24–26 h pre-MI) [32] emotional states prior to MI (particularly anxiety) are predictive of adverse long-term mortality outcomes whereas MIs preceded by exercise were not associated with a subsequent elevated mortality risk [31]. The present article builds on these observation by investigating three new aspects of emotional precipitants of MI: on [1] the identification of high-risk sub-groups of patients who experience an MI following negative emotions based on age and sex; [2] determine whether age and sex influence the higher mortality rate following MIs that occur following negative emotions; and [3] the investigation of immediate vs. distant emotional precipitants of MI as predictors of subsequent (long-term) mortality. Anxiety and anger were examined by a structured interviews derived from the State-Trait Personality Inventory at a median of 4 days post-MI; patients reported about immediate (0–2 h pre-MI) and distant (24–26 h pre-MI) experiences of these emotions. Patients were then followed for up until 10 years after the MI. We tested the hypothesis that: [1] younger age and female sex are associated with a higher likelihood of MI onset preceded (i.e., potentially triggered) by anxiety or anger; [2] the risks of adverse long-term mortality outcomes following MIs that are preceded by high levels of anxiety and/or anger are higher in young patients and women; and [3] the 10-year mortality rate is elevated in patients with high anxiety and anger levels in the *immediate* (0–2 h pre-MI) premonitory phase compared to patients with high anxiety and anger levels occurring *distant* from the MI (24–26 h pre-MI). These data provide important novel information as current research and clinical assessments focus on an individual's psychosocial characteristics in general, rather than focusing on the specific emotional state at the time when the actual MI occurred.

2. Methods

2.1. Patients

Patients with a documented MI who participated in the Determinants of Myocardial Infarction Onset Study (MIOS) were followed up for 10 years. In total, 3886 MI patients were recruited from 64 centers between 1989 and 1996 to establish potential physical and emotional triggers of MI. Inclusion criteria were: creatine kinase levels above the upper limit of normal for the laboratory at each centre, positive MB isoenzymes, an identifiable onset of symptoms preceding MI (chest pain or other cardiac symptoms), and the ability to complete a structured interview. Eligible patients were identified by reviewing coronary care unit admission reports and patient charts.

After providing informed consent, patients were interviewed using structured forms. Interviews were administered within a median of 4 days after hospital admission (range 0–30 days). The interview for emotional state (anxiety and anger derived from the STPI, see below) was administered in a sub-cohort of the overall MIOS sample (N = 2176/3886 = 55.9%), comprising the study sample presented in this report. The cohort was prospectively followed for the occurrence of all-cause mortality, using the National Death Index, through December 31, 2007.

The Institutional Review Board of each center approved the protocol, and subsequent approval for the follow-up assessments based on publically available mortality records was obtained from the Beth Israel Deaconess Medical Center Committee on Clinical Investigations.

2.2. The present investigation as related to prior MIOS-based publications

Initial reports from this study were based on a subsample of the final full MIOS cohort [3,10]. These early reports were used to document the triggering potential of exposures such as exercise and anger. More recently we examined the long-term predictive value of these emotional experiences for prognosis after the incident MI [31,32]. The paper by Wrenn et al. focused on the emotional data 24–26 h prior to MI [32] and the research letter by Smeijers et al. [31] provides only a brief evaluation of the 10-year mortality outcomes in MI patients with exercise, anxiety or anger in the 2-hour pre-MI exposure period. The present study expands these findings in three new aspects: (a) the clinical characteristics of MIs immediately (0–2 h) prior to MI, (b) subgroup that are at disproportionately elevated risk of post-MI mortality during 10 years follow-up; and (c) the differential prognostic value of immediate (0–2 h pre-MI) vs. distant (24–26 h pre-MI) emotional states.

2.3. Assessment of anxiety and anger prior to MI

Trained research staff conducted a standardized interview to obtain information about the time, place and nature of symptom onset, health behaviors (e.g., smoking) and emotional state prior to MI. Patients were asked about several potential triggers, such as physical exertion, anxiety and anger. Patients were asked about immediate experiences during 0–2 h prior to MI onset and more distant experiences in the 24–26 h prior to MI (for details of the original study see [3,10,32]).

Levels of anxiety and anger prior to MI were assessed using the interviewer-administered subscales of the State-Trait Personality Inventory (STPI) [33] modified to assess short-term exposures prior to MI. Patients reported about the 0–2 h prior to MI (N = 2176) and this information was compared with "distant" anxiety and anger levels during the same time period the day before (24–26 h prior to MI; 1824/2176 patients (83.8%) had valid data for the distant pre-MI period). Participants were also asked additional questions about anger using an hour-by-hour preceding MI scale designed for this study [10], but these hourly ratings were not obtained for anxiety. This report therefore focuses on the 0–2 h and 24–26 h STPI-based interview data for anxiety and anger. Scores ranged from 10 to 40 and were analyzed as continuous variables and dichotomized at the 90th percentile for the primary analyses (consistent with prior reports based on this study [10,31,32].

2.4. Assessment of demographic and clinical characteristics

Patient interviews and medical records were used to collect information about demographics, health behaviors, medical history and medication use. Demographic variables included the primary subgroup