Posttraumatic stress disorder in first-time myocardial infarction patients

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OBJECTIVES: The objectives of this study were to investigate the prevalence of posttraumatic stress disorder in patients with a first myocardial infarction compared with a random sample of healthy controls and to determine variables associated with the disorder.

DESIGN: A questionnaire was distributed to 112 consecutive patients 4 to 6 weeks after infarction and to 115 healthy controls selected randomly from the general population. Objective clinical measures were obtained from the patients’ medical records.

RESULTS: Twenty-five (22%) patients qualified for a diagnosis of posttraumatic stress disorder (PTSD) compared with 8 (7%) controls with patients being more than a three-fold (OR: 3.84; 95% CI: 1.65 to 8.94) risk of having the disorder. When adjusting for other variables, the risk was reduced to above a two-fold risk (OR: 2.71; 95% CI: 0.99-7.41). In patients and controls, depression and neuroticism were associated with a diagnosis of PTSD adjusting for other variables. In patients, anxiety was associated with a diagnosis of PTSD adjusting for other variables. Left ventricular ejection fraction and symptoms of angina pectoris were not related to a diagnosis of PTSD in the patient group.

CONCLUSIONS: Given that previous research has shown that persons with PTSD are at increased risk of cardiovascular diseases, cardiac patients with the disorder may be at a higher risk of recurrent cardiac events. Although longitudinal studies are needed to confirm such a relationship, this disorder should not be overlooked because of its potential role in reinfarctions and mortality. (Heart Lung® 2003;32:300-7.)

INTRODUCTION

Evidence is accumulating that survivors of myocardial infarction (MI) may be at risk for posttraumatic stress disorder (PTSD).1-6 PTSD was first introduced as a separate diagnostic entity in the Diagnostic and Statistical Manual III (DSM-III)7, but the diagnostic criteria for PTSD have evolved since then. In the present DSM-IV, the emphasis is placed on the two-part stressor criterion, ie, (A1) the qualifying stressor (comprising a range of potential traumatic events), and (A2) the response to the event, which must involve “intense fear, helplessness, or horror.”8 Symptoms of PTSD include episodes of repeatedly reliving the event, avoidance of situations reminiscent of the trauma, and hyperarousal. These are known as the symptom clusters intrusion (criterion B), avoidance (criterion C), and arousal (criterion D). Symptoms have to be present for 1 month (criterion E), and must lead to impairment in functioning (criterion F).8

As indicated in a recent review, the majority of studies on PTSD in survivors of MI have included 50 patients or fewer with the largest study to date having included 100 patients.9 Few studies have controlled for confounders, such as psychiatric history, neuroticism, comorbid diagnoses, and disease severity, and information about the criteria used for diagnosing MI often has not been provided.9 No studies have estimated the prevalence of PTSD in MI patients compared with healthy controls.9 Although comparison groups have been included in some investigations, they were either veterans or victims of rape-related trauma.4,5,10 These compari-
son groups are themselves at increased risk of PTSD. Identification of patients at risk for PTSD may have implications for prognosis given evidence suggesting that MI patients with PTSD may be at increased risk of recurrent cardiac events. PTSD related to the heart transplantation experience has been associated with a fifteen-fold risk of mortality 1 to 3 years after transplantation. In addition, PTSD is often associated with substance abuse, such as smoking and the use of alcohol. Smoking is a traditional risk factor for coronary artery disease. Furthermore, studies have shown a direct association between PTSD and an increased risk of cardiovascular diseases. Boscarino and Chang found a relationship between PTSD and increased risk of MI (OR: 4.44, \(P \leq 0.05\)) independent of smoking, body mass index, and alcohol use. Levels of social support may also be affected in MI patients who develop PTSD. Lack of social support is a known risk factor for coronary artery disease and has also been related to adverse prognosis. Finally, in a recently published study, PTSD was associated with nonadherence to medication in survivors of MI, which in turn was related to poor medical outcome. Only limited information is available with regard to variables associated with a diagnosis of PTSD. In clinical practice, knowledge of these variables is important to determine which patients are at risk.

The objectives of the present study were: 1) to investigate the prevalence of PTSD in MI patients compared with a random sample of healthy controls drawn from the general population and 2) to determine variables that may be associated with a diagnosis of PTSD.

MATERIAL AND METHODS

Participants

Consecutive patients with a first MI were recruited from August 1999 to January 2001 from Aarhus University Hospital and Horsens Hospital, Denmark. Patients were asked to fill in a questionnaire 4 to 6 weeks after MI when visiting the outpatient clinic. A diagnosis of MI was based on increased levels of troponin T (>0.10 microgram/liter) and electrocardiogram changes according to the most recent guidelines. Troponin T was measured on admittance and after 6 and 12 hours. Patients were excluded if they had other life-threatening diseases (eg, cancer or HIV), had cognitive impairments, had a history of psychiatric disorders, or were unable to understand and read Danish. Of 164 patients screened for inclusion in the study, 3 were excluded because of other life-threatening diseases and previous psychiatric history. Twelve were not approached because of personnel error. Of the remaining 149 patients, 37 (25%) refused to participate. Thus, analyses are based on 112 (75%) patients and a random sample of 115 healthy controls drawn from a national register. Controls were excluded if they reported that they had coronary artery disease or other life-threatening diseases (eg, cancer or HIV), had cognitive impairments, had a history of psychiatric disorders, or were unable to understand and read Danish. For ethical and privacy reasons, and because controls were volunteers, they were not required to reveal whether nonparticipation was because of nonfulfillment of the inclusion criteria or unwillingness to participate. Hence, it is not possible to calculate an exact response rate for the controls, but 600 controls were initially approached. Ethical approval was obtained from the ethical committees in Aarhus and Vejle Municipalities, and the study was carried out in accordance with the Helsinki Declaration.

Procedure

Patients were approached and informed about the project by staff in the departments of cardiology. Patients who agreed to participate were given a questionnaire with written information about the project and a consent form. Patients returned the questionnaire by mail to the institute of psychology and sent the informed consent form to the departments of cardiology. A written reminder was sent to patients who had not returned their questionnaires within 2 weeks. Controls were approached in writing informing them about the project and that their addresses had been obtained through the national register. They were asked to sign an informed consent form and to return it with the questionnaire if they were interested in participating and fulfilled the inclusion criteria.

Measures

Demographic variables. Sociodemographic variables included gender, age, marital status, living arrangement, education, working status, and smoking status.

Clinical variables. Clinical variables (eg, left ventricular ejection fraction [LVEF], beta-blocker therapy, and presence of angina pectoris) were obtained for the patients from their medical records. LVEF was assessed by means of echocardiography and
categorized as: 1) severely reduced (0-40%), 2) moderately reduced to normal (>41%).

**Psychological variables.** The Posttraumatic Diagnostic Scale (PDS) was used to assess PTSD. The PDS assesses all of the diagnostic criteria (A-F) for PTSD according to DSM-IV. To qualify for a diagnosis of PTSD, the respondent has to have been exposed to a potentially life-threatening event (criterion A1), to respond to the event with “intense fear, helplessness, or horror” (criterion A2), to endorse at least 1 of 5 “intrusion” symptoms (criterion B), at least 3 of 7 “avoidance” symptoms (criterion C), and at least 2 of 5 “arousal” symptoms (criterion D). Symptoms also have to be present for 1 month (criterion E) and lead to impairment in functioning (criterion F). Criteria B, C, and D are assessed on a four-point Likert scale from 0 (not at all or only 1 time) to 3 (5 or more times a week or almost always) (score range 0-51). A score of 1 on a given symptom is sufficient for it to count towards a potential diagnosis. The PDS has been validated against the Structured Clinical Interview for DSM-IV, and has good sensitivity and specificity.

The Trauma Symptom Checklist was used to assess anxiety and depression. Depression is often found as a comorbid diagnosis in persons with PTSD. The psychometric properties are adequate with Cronbach α = 0.72 for the anxiety and depression subscales, respectively. Both subscales also have been shown to discriminate between abused and nonabused (P < .05). The 2 subscales contain 9 items, respectively, that are answered on a four-point Likert scale from 0 (never) to 3 (very often), yielding a score range of 0-27.

We assessed the 2 personality traits neuroticism and extroversion by means of the short version of the Eysenck Personality Questionnaire. Each of the subscales contains 12 items with the response categories 1 (yes) and 0 (no). The total score for each of the subscales ranges from 0 to 12 with a high score indicating more of the personality trait. The validity and reliability of the 2 subscales have proven satisfactory.

**Statistical analyses**

Differences in baseline characteristics between patients and controls were evaluated by Fisher’s exact test for categorical variables and the Student’s t-test for continuous variables. All tests were two-tailed. To quantify differences between patients and controls on psychological outcome measures, we calculated the effect size using Cohen’s thresholds for independent samples: (mean1 – mean2/SDpooled).

An effect size of <0.20 is considered trivial, >0.20 to 0.50, small, >0.50 to 0.80, moderate, and >0.80, large. Univariate and multivariate logistic regression analyses were used to examine whether MI, gender, age, depression, anxiety, neuroticism, and extroversion were associated with PTSD. Only variables significant at P = .10 in univariate analyses were entered as independent variables in the multivariate analyses with PTSD as the dependent variable. The significance level of P = .10 to retain variables in the model was selected to reduce the possibility of a Type II error. The first regression analysis was based on both patients and controls. The second regression analysis was based on patients only and was performed in the same way, although LVEF and angina pectoris were added to the independent variables used in the first analysis to examine whether LVEF and symptoms of angina are associated with a diagnosis of PTSD. To test the overall goodness of fit of the 2 models, the Hosmer-Lemeshow statistics was used. A good model produces a nonsignificant Chi-square. For all statistical analyses, we used SPSS 10.1 for Windows.

**RESULTS**

**Patient responders versus nonresponders.** We found no statistically significant differences between patient responders and nonresponders on demographic (gender and age) and clinical variables (LVEF, angina pectoris, and treatment with beta-blockers).

**Patients versus controls.** Comparisons between patients and controls revealed no statistically significant differences on gender, living arrangement, and years of continuing education (Table I). However, patients were slightly older, had fewer years of schooling, were less likely to be employed, and were less likely to smoke. To analyze the potential influences of these differences on PTSD, we entered all demographic variables that were significant in univariate analyses together with the psychological variables into a logistic regression model with PTSD as the endpoint. None of the demographic variables was related to a diagnosis of PTSD.

**Differences on psychological measures between patients and controls.** On psychological measures, patients scored significantly higher on intrusion, arousal, total PDS, depression, and neuroticism compared with controls (Table II). No statistically significant differences were found on avoidance, anxiety, and extroversion. As indicated by Cohen’s effect sizes, the most clinically significant differ-
ences between patients and controls were found on arousal, PDS total, and depression.

**Prevalence of PTSD.** Twenty-five (22%) of the patients versus 8 (7%) of the controls qualified for a diagnosis of PTSD according to DSM-IV.

**Variables associated with a diagnosis of PTSD.** As presented in Table III, anxiety, depression, neuroticism, and MI were associated with PTSD in patients and controls in univariate analyses. Patients were above a three-fold risk of having PTSD compared with controls (OR: 3.84; 95% CI: 1.65-8.94). In multivariate analyses, depression (OR: 1.28; 95% CI: 1.09-1.50) and neuroticism (OR: 1.28; 95% CI: 1.10-1.50) were associated with a diagnosis of PTSD adjusting for anxiety, whereas MI was no longer statistically significant (OR: 2.71; 95% CI: 0.99-7.41). The Hosmer-Lemeshow goodness of fit statistic was used and showed a good concordance between the estimated and expected probability of the independent variables on PTSD in the higher deciles of risk ($\chi^2 = 12.39, df = 8, P = .14$).

In a separate analysis of the MI patients, none of the clinical variables (LVEF and angina pectoris) was related to a diagnosis of PTSD (Table IV). How-

### Table I
Characteristics of MI patients and controls

<table>
<thead>
<tr>
<th></th>
<th>MI Patients (n = 112)</th>
<th>Controls (n = 115)</th>
</tr>
</thead>
<tbody>
<tr>
<td>n (%)*</td>
<td>Mean (SD)</td>
<td>Range</td>
</tr>
<tr>
<td>Females</td>
<td>33 (30)</td>
<td>43 (37)</td>
</tr>
<tr>
<td>Age (yrs)</td>
<td>60 (9.7) 40-79</td>
<td>57 (10.8) 41-79</td>
</tr>
<tr>
<td>Schooling (yrs)</td>
<td>8.5 (1.5)</td>
<td>9.3 (1.9)</td>
</tr>
<tr>
<td>Continuing education (yrs)</td>
<td>3.2 (3.7)</td>
<td>4.5 (6.4)</td>
</tr>
<tr>
<td>Marital status:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Married/partner</td>
<td>98 (87)</td>
<td>90 (78)</td>
</tr>
<tr>
<td>Single</td>
<td>14 (13)</td>
<td>23 (20)</td>
</tr>
<tr>
<td>Living arrangement:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>With others</td>
<td>98 (88)</td>
<td>94 (82)</td>
</tr>
<tr>
<td>Alone</td>
<td>13 (12)</td>
<td>19 (17)</td>
</tr>
<tr>
<td>Employment status:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Working</td>
<td>47 (42)</td>
<td>67 (58)</td>
</tr>
<tr>
<td>Not working</td>
<td>64 (57)</td>
<td>44 (38)</td>
</tr>
<tr>
<td>Smokers</td>
<td>13 (12)</td>
<td>36 (31)</td>
</tr>
</tbody>
</table>

*Not all percentages add up to 100 due to missing values

### Table II
Comparisons between MI patients and controls on psychological measures

<table>
<thead>
<tr>
<th></th>
<th>MI Patients (n = 112)</th>
<th>Controls (n = 115)</th>
<th>P</th>
<th>Effect Size</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean (SD)</td>
<td>Mean (SD)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intrusion</td>
<td>2.46 (2.50)</td>
<td>1.63 (2.31)</td>
<td>.023</td>
<td>0.34</td>
</tr>
<tr>
<td>Avoidance</td>
<td>2.09 (2.18)</td>
<td>1.37 (2.87)</td>
<td>.051</td>
<td>0.28</td>
</tr>
<tr>
<td>Arousal</td>
<td>2.33 (2.14)</td>
<td>1.21 (2.03)</td>
<td>.001</td>
<td>0.54</td>
</tr>
<tr>
<td>PDS total</td>
<td>6.88 (5.60)</td>
<td>4.21 (5.98)</td>
<td>.002</td>
<td>0.46</td>
</tr>
<tr>
<td>Depression</td>
<td>4.28 (3.15)</td>
<td>2.86 (2.35)</td>
<td>.001</td>
<td>0.51</td>
</tr>
<tr>
<td>Anxiety</td>
<td>2.61 (2.06)</td>
<td>2.32 (1.74)</td>
<td>.276</td>
<td>0.15</td>
</tr>
<tr>
<td>Neuroticism</td>
<td>4.08 (3.18)</td>
<td>3.10 (2.96)</td>
<td>.018</td>
<td>0.31</td>
</tr>
<tr>
<td>Extroversion</td>
<td>7.20 (2.36)</td>
<td>6.93 (2.31)</td>
<td>.391</td>
<td>0.12</td>
</tr>
</tbody>
</table>
ever, anxiety, depression, and neuroticism were also associated with PTSD in patients in univariate analyses. When adjusting for depression and neuroticism, anxiety (OR: 1.50; 95% CI: 1.08-2.09) was the only variable associated with a diagnosis of PTSD. The Hosmer-Lemeshow goodness of fit statistic was $\chi^2 = 7.83$, df = 8, $P = .45$.

**DISCUSSION**

Psychiatric disorders in the medically ill have been underdiagnosed and undertreated, perhaps because symptoms are seen as a normal reaction to a major life event. In particular, PTSD has been neglected as a sequel of MI. Our results showed that 22 percent of consecutive patients with a first MI qualified for a diagnosis of PTSD and that they were above a three-fold risk of having the disorder compared with healthy controls. When adjusting for anxiety, only depression and neuroticism contributed significantly to PTSD risk; the risk from MI was reduced to above a two-fold risk although it was no longer statistically significant. Anxiety was identified as being associated...
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with a diagnosis of PTSD in the patient group adjusting for depression and neuroticism.

Because of the sample size and the relatively small number of PTSD events, the statistical power may have been too low to retain several predictors in the regression model. Hence, this may explain why MI in a pooled sample of patients and controls was no longer statistically significantly associated with PTSD in multivariate analyses. However, patients were above a two-fold risk of having PTSD compared with controls, which indicates a clinically relevant risk.

The number of patients included in previous studies of PTSD in MI survivors has ranged from 20 to 100 with 50 patients or fewer in 5 out of 8 studies. The latter study to date included 100 patients. The latter study found a prevalence rate similar to that in the current study. Prevalence rates in other studies have generally been lower compared with that in the current study. However, the majority of these studies assessed PTSD according to DSM-III. A recent investigation showed that the change in the stressor criterion for PTSD has lead to an increase in PTSD cases. Alternatively, the assessment of PTSD already between 4 to 6 weeks after MI in the current study may account for the higher prevalence rate.

Anxiety was associated with a diagnosis of PTSD in survivors of MI in the current study. A previous study also found that negative affect was associated with a diagnosis of PTSD, but the study did not control for disease severity.

It is noteworthy that a diagnosis of PTSD among the MI patients was not related to symptoms of angina and disease severity in the current study. In other words, cardiac disease severity could not explain why some patients had PTSD whereas others did not. Two previous studies have found similar results. This is also consistent with a large number of studies that have shown that psychopathology is not a result of more severe cardiac disease and that psychosocial variables predict outcome after coronary artery disease independent of disease severity.

As pointed out in a recent review, MI-related PTSD may comprise an acute reaction to a life-threatening event, and therefore symptoms may abate with time. This may also be the case for patients in the current study, which will become clear when follow-up is complete. Hence, therapeutic intervention at this early stage also cannot be recommended. However, the early identification of patients at risk, even 1 month after MI, may be important, because PTSD has been associated with nonadherence to medication in survivors of MI and poor medical outcome. PTSD has also been associated with a fifteen-fold risk of mortality in heart transplantation patients 1 to 3 years after transplantation. Thus, there is preliminary evidence suggesting that survivors of MI who have PTSD may be at increased risk of recurrent cardiac events. Longitudinal studies are now needed to substantiate the long-term consequences of PTSD in survivors of MI.

The current study attempted to address some of the limitations of previous research concerning the risk to cardiac patients of having PTSD after MI. First, diagnosis of MI was based on objective clinical measures. Second, we excluded patients with other life-threatening diseases and previous psychiatric history, and adjusted for disease severity in statistical analyses. Third, a healthy control group was included as the comparison group, which allowed us to determine the risk to cardiac patients of having PTSD.

Despite these methodological improvements, the results of the current study should be interpreted with caution. First, no information was available about the psychological status of patient nonresponders, which comprised 25%. Although responders and nonresponders did not differ on demographic and clinical variables, they may have differed on psychological variables. Second, the study was underpowered, and when adjusting for other variables we were therefore not able to show that MI was related to a diagnosis of PTSD at the required significance level. Third, psychological outcome was assessed by self-report measures, which may not be as accurate as standardized diagnostic interviews. This might particularly have been a problem in the assessment of anxiety and depression, because the Trauma Symptom Checklist has not been validated against a diagnostic interview. Fourth, we cannot exclude that the controls constituted a selected sample. Although they were selected as a random sample from the general population, those who volunteer to participate in research projects may have a different psychological makeup than nonvolunteers. We could also not calculate the exact response rate for the controls. Moreover, patients differed from controls on age, schooling (years), employment status, and smoking status. However, differences between patients and controls on employment status and smoking status were to be expected given that patients were assessed 4 to 6 weeks after MI. At this point in time, the majority of patients is unlikely to have returned to work yet and they will also have received a smoking cessation advice from the cardiologist. Concerning differences between patients and controls on age, a study by Bennett et al (1999) showed an inverse relationship between age and symptoms of...
PTSD in MI patients.\textsuperscript{1} Because our patients were older than controls, age is not likely to have inflated the prevalence of PTSD in the patient group. Moreover, even though the difference is statistically significant, when calculating the effect size according to Cohen’s thresholds, the difference between groups on age is small ($d = 0.29$). Similarly, although differences between groups on schooling is statistically significant, the effect size is small ($d = 0.47$). Furthermore, in regression analysis none of these characteristics was related to a diagnosis of PTSD. Finally, causation cannot be inferred, because patients were not assessed before their MI.

In conclusion, these results indicate that patients after MI may be at increased risk of having PTSD compared with healthy controls, although the results should be replicated in a larger sample with a matched case-control design. The results also underscore the importance of identifying cardiac patients at risk for PTSD in clinical practice, particularly in light of preliminary evidence that PTSD has implications for prognosis. For this end, a simple screening procedure may be sufficient, as suggested in a recent review.\textsuperscript{28} Follow-up of the patients in the current study at 9 months after MI is currently ongoing. We hope that information obtained from the follow-up will increase knowledge about the clinical course of PTSD in this particular patient group. An important step for future research will be to conduct studies that investigate the consequences of PTSD on health-related behaviors, compliance, and long-term morbidity and mortality in MI patients.

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