CARDIOVASCULAR MEDICINE

Post-traumatic stress disorder in patients with cardiac disease: predicting vulnerability from emotional responses during admission for acute coronary syndromes

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Objectives: To assess frequency and predictors of post-traumatic stress disorder (PTSD), measured by the Post Traumatic Stress–self report version, at three months after admission for acute coronary syndromes (ACS).

Design: Two-phase prospective study.

Setting: Four coronary care units.

Patients: 135 patients admitted to hospital with ACS confirmed by ECG and cardiac enzyme changes.

Results: 20 patients (14.8%) showed a symptom pattern characteristic of PTSD at three months assessed by a conservative scoring criterion. Severity of chest pain and psychological factors during admission were predictive of PTSD severity. Acute stress symptoms, depression, negative affect, hostility, and pain scores were independent predictors of three-month PTSD symptoms ($R^2 = 0.495$, $p < 0.001$). In contrast, demographic factors (age, sex, education level and income) were unrelated to post-traumatic symptoms, as were markers of clinical disease severity.

Conclusions: Patient vulnerability to PTSD three months after ACS is predictable on the basis of psychological state and chest pain at the time of admission. This may be valuable to the clinician, as PTSD after myocardial infarction is associated with poorer quality of life, reduced adherence to drug treatment and increased likelihood of cardiovascular morbidity.

Post-traumatic stress disorder (PTSD) is a recognised psychiatric disorder, featuring a triad of symptoms: intrusions (flashback, nightmares); avoidance and emotional numbing (avoidance of reminders of the traumatic event, social withdrawal); and hyperarousal (sleeplessness, exaggerated startle response).¹ Diagnosis of PTSD requires that a person has been exposed to a traumatic event and that his or her response was characterised by intense fear, helplessness or horror, leading to persistence of the above three symptoms for one month or more and causing significant distress or impaired functioning. In recent years the definition of a “traumatic event” has been broadened to include having a diagnosed life threatening illness (*Diagnostic and statistical manual of mental disorders*, 4th ed (DSM IV), 1995).¹

Symptoms indicative of PTSD have been reported by people in the months after acute myocardial infarction (MI) and cardiac surgery. PTSD after MI is associated with poorer general functioning, reduced adherence to drug treatment and increased likelihood of cardiac readmission.^{2–3} It is therefore valuable to identify those people who are vulnerable to PTSD after MI. This study documented the prevalence and predictors of PTSD in a population of patients after admission for acute coronary syndromes (ACS).

The reported prevalence of PTSD after MI ranges from 6–22% according to the method of assessment and the point in time since the MI at which the patient is assessed.^{2–6} The reference standard for diagnosis of PTSD is the structured clinical interview for DSM IV, which tends to yield lower prevalences than self-report scales. Predictors of PTSD after MI are inconsistent within the existing literature and include younger age, greater depression during admission, lower social support and “distressed-type” personality.^{5–7}

Associations between PTSD and measures of objective clinical severity, such as cardiac enzymes or established indicators of prognosis after MI such as the GRACE (Global Registry of Acute Coronary Events) index,⁸ have rarely been assessed.^{2–9} In the present study we assessed prevalence and severity of PTSD in a group of patients with ACS three months after admission, and identified predictors of PTSD from psychological and clinical measures obtained during admission.

METHOD

Participants

We recruited 135 participants hospitalised for ACS from four London hospitals. Inclusion criteria were ACS with chest pain at onset confirmed by ECG changes (new ST elevation > 0.2 mV in two contiguous leads (V1, V2 or V3) and > 0.1 mV in two contiguous other leads, ST depression > 0.1 mV in two contiguous leads in the absence of QRS confounders, new left branch or brachial block, or dynamic T wave inversion in more than one lead) or cardiac enzymes (troponin T measurement > 0.01 µg/l or a creatine kinase measurement more than twice the upper range of normal for the measuring laboratory).¹⁰ Exclusions were the presence of severe psychiatric illness or cognitive decline impairing ability to complete an interview, and other conditions that might have stimulated raised cardiac enzymes. Patients were aged

Abbreviations: ACS, acute coronary syndromes; BDI, Beck Depression Inventory; DS16, Type D scale-16; DSM IV, *Diagnostic and statistical manual of mental disorders*, 4th ed; GRACE, Global Registry of Acute Coronary Events; MI, myocardial infarction; NSTEMI, non-ST elevation myocardial infarction; PSS-SR, PTSD Symptom Scale–self report version; PTSD, post-traumatic stress disorder; STEMI, ST elevation myocardial infarction

Table 1 Patient clinical and demographic characteristics

Characteristic	Non-PTSD (n = 115)	PTSD (n = 20)	p Value
Age	62.06 (11.33)	57.52 (10.79)	NS
Socioeconomic status index	0.82 (0.98)	1.14 (1.28)	NS
Admission pulse rate	80.45 (25.55)	73.52 (18.85)	NS
Troponin T (μg/l)	4.73 (5.47)	4.11 (9.40)	NS
No of vessels diseased on angiogram	1.68 (0.88)	1.83 (0.86)	NS
GRACE risk score	98.99 (27.94)	82.57 (20.40)	0.003
Subjective pain score	7.18 (2.15)	8.23 (2.33)	NS
Men	73.1%	76.2%	NS
Ethnicity (white European)	84.0%	66.7%	NS
Educational qualifications (v none)	53.8%	57.1%	NS
Type of ACS (STEMI v NSTEMI/UA)	69.7%	76.1%	NS
Management (PTCA/CABG v medical)	71.3%	85.7%	NS

Data are mean (SD) (t test comparisons, required significance level adjusted to $p < 0.007$ by the Bonferroni method) or percentage (χ^2 comparisons).

ACS, acute coronary syndromes; CABG, coronary artery bypass graft; GRACE, Global Registry of Acute Coronary Events; NSTEMI, non-ST elevation myocardial infarction; PTCA, percutaneous transluminal coronary angioplasty; PTSD, post-traumatic stress disorder; STEMI, ST elevation myocardial infarction; UA, unstable angina.

between 18 and 80, and were able to complete the interview in English.

Procedure

Interviews were conducted and data were collected at phase 1 within five days of admission. Patients completed questionnaire psychological measures 7–10 days after admission. Presence and severity of PTSD and depression were assessed at phase 2 (three months later) by questionnaire. Of 233 patients in the participating hospitals with clinical eligibility, 184 (79.0%) consented to take part in the initial phase of the study. Of these, 135 returned phase 2 questionnaires on PTSD, giving a response rate of 73.4% of those who took part in phase 1 of the study and a response rate of 57.9% of all clinically eligible patients. Phase 2 participants did not differ in baseline clinical or demographic characteristics from those who took part in phase 1 but not phase 2. The study was approved by research ethics committees at participating hospitals and the University College London/University College London Hospitals.

Measures

Clinical characteristics of ACS were assessed at phase 1 yielding the following variables: type of ACS (ST elevation MI (STEMI) versus non-ST elevation MI (NSTEMI)/unstable angina); history of MI; severity of ACS indexed by cardiac enzymes (troponin T and creatine kinase); and number of vessels diseased at angiography. We computed risk scores on the GRACE index, a composite measure of severity shown to be predictive of mortality over six months,⁸ and patient-assessed severity of chest pain based on a standard numerical rating scale (1–10). Information about level of education and household income was also collected during the interview.

Psychological factors

The psychological factors assessed fell into three groups. Firstly, self-reported history of depression and the frequency, duration and severity of self-reported depression in the six months before onset were recorded. Secondly, emotional state during admission was assessed by questionnaires measuring depression (Beck Depression Inventory (BDI)),¹¹ anxiety (Hospital Anxiety Scale)¹² and acute stress symptoms.

Acute stress symptoms were assessed with a composite scale derived from the Peritraumatic Dissociative Experiences Questionnaire¹³ and the Acute Stress Disorder Scale.¹⁴ The scale consisted of 14 items rated on a 1–5 scale (*not at all true to extremely true*), with higher scores indicating greater

dissociation, flashbacks, intrusions and fear during the event. Cronbach's α showed good reliability of the full scale ($\alpha = 0.87$).

Thirdly, psychosocial factors were assessed with measures of hostility,¹⁵ optimism (Life Orientation Test),¹⁶ type D personality—comprising the two components negative affectivity and social inhibition (Type D scale-16 (DS16))¹⁷—and a social network questionnaire assessing size of network and frequency of contact.

The presence of PTSD and the severity of post-traumatic symptoms were assessed at phase 2 (three months after ACS) with the PTSD Symptom Scale—self report version (PSS-SR).¹⁸ The scale consists of 17 items scored for frequency on a 0–3 scale (*not at all to five or more times a week*). Each item corresponds to one of the 17 DSM-IV criteria for diagnosis of PTSD for the dimensions intrusions, avoidance and arousal.¹ Sensitivity for the PSS-SR based on DSM criteria is 62% and specificity 100%.¹⁸ The current study used scoring criteria whereby a score of ≥ 2 (*two to four times a week*) on one intrusion, three avoidance and two arousal items indicated the presence of PTSD,¹⁹ which is more conservative than the original guidelines but has been found to be closer to the original DSM-IV criteria. The PSS-SR is listed as a suitable index for screening for PTSD in recent national guidelines.²⁰ Cronbach's α showed high internal reliability in our sample ($\alpha = 0.91$).

Statistical analyses

Participants assigned to the PTSD group were compared on demographic, psychological and clinical variables with the non-PTSD group by χ^2 and t tests for categorical and continuous measures, respectively. The significance level required was corrected for multiple t test comparisons by the Bonferroni method. Predictors of total score on the PSS-SR at three months were identified from variables collected at the time of admission by linear regression. Forced entry was used for the initial steps of the regression for those variables identified as predictors of PTSD by previous studies, namely age, history of depression and acute stress symptoms. For the final step, the most predictive in-hospital psychological variables were selected by a stepwise method (entry criterion $p \leq 0.050$, removal criterion $p \geq 0.100$). Results from previous studies are not consistent enough to draw strict hypotheses about the relative importance of the various psychological predictors and, as several of these variables overlap conceptually, a stepwise selection method is more appropriate than forced entry.

RESULTS

Patient characteristics

Mean age was 61.4 (SD 11.3) years and 99 of the 135 patients were men (73.3%). Patients were predominantly white and with limited education (28.9% educated above high school level). Seventeen participants (12.6%) had a history of MI, and 95 (70.4%) were admitted with STEMI and the remainder with NSTEMI or unstable angina. Just over half the patients (56.7%) were managed with percutaneous transluminal coronary angioplasty and the remainder either medically (26.9%) or with coronary artery bypass grafting (16.4%). Scores on the GRACE algorithm averaged 96.53 (SD 27.51) equating to a moderate 2.5% risk of mortality over six months.

The mean score for all participants on the PSS-SR at three months was 12.1 (SD 9.9). According to the scoring criteria of Brewin *et al*¹⁹ to determine prevalence of PTSD in the sample, 20 patients (14.8%) met the criteria for PTSD.

Predictors of PTSD and symptom severity at three months

Demographic variables, indices of severity of ACS, characteristics of the cardiac event and in-hospital psychological factors were examined to identify predictors of PTSD three months later.

The presence of PTSD or the PSS-SR scores were not significantly associated with the type of ACS (STEMI versus NSTEMI/unstable angina), number of diseased vessels, or troponin T or creatine kinase concentrations (table 1). Scores on the GRACE were higher in the PTSD group, although not when adjusted for age and sex. Subjective intensity of acute pain did not differ by group but was significantly correlated with PSS-SR scores at three months ($p = 0.033$).

Age, sex and the indicator of socioeconomic status (education and income) were not associated with PTSD or with PSS-SR scores (table 1).

Psychological factors

A history of clinical depression and experiencing two weeks of severe depression in the six months before ACS were both associated with higher PSS-SR scores ($p < 0.001$). Acute stress symptoms during admission were also strongly associated with both the presence of PTSD and the severity of post-traumatic stress symptoms (table 2). Patients who later developed PTSD had significantly greater acute stress symptoms while in hospital ($p < 0.001$). All three components of the acute stress questionnaire (dissociation and emotional distress during the event and experience of intrusions) were correlated with PSS-SR severity at three

Figure 1 Scores on the post-traumatic stress disorder (PTSD) Symptom Scale-self report version (PSS-SR) at three months in relation to Beck Depression Inventory (BDI) scores at admission (divided into quartiles).

months (all at $p < 0.012$). In addition, patients with PTSD at three months reported significantly greater levels of depression but not anxiety at the time of admission (table 2). Patients with PTSD also had greater levels of type D personality ($p = 0.013$), specifically negative affectivity ($p < 0.001$), as well as hostility ($p = 0.001$). PTSD was not associated with social inhibition, optimism or size of social network. Figure 1 illustrates the relationship between depression in hospital and later PSS-SR severity, where patients were divided into quartiles of BDI scores. A strong linear relationship was apparent. Of those patients fulfilling the criteria of the present study for PTSD, 83% also scored more than 10 on the BDI, indicating mild to moderate depression, compared with 26% of patients without PTSD at three months ($\chi^2 = 22.92$, $p < 0.001$).

Multiple regression analysis was conducted to identify significant predictors of three-month PSS-SR symptoms. Age was entered as the first step, six-month history of depression as the second, pain ratings as the third and acute stress symptoms as the fourth (table 3). These factors in combination accounted for 26.8% of the variance in three-month PSS-SR scores. Lifetime history of depression was also a significant predictor of PSS-SR scores but six-month history of depression, being a stronger predictor, was used in step 2. A final step entering all psychological measures at admission used a stepwise selection method and identified depression, DS16 negative affectivity and hostility as independent predictors. In other analyses, a categorical variable for the presence or absence of type D personality was used rather than separate variables for negative affectivity and social inhibition, but was not significant. None of the selected psychological variables showed multicollinearity according to variance inflation factor and tolerance values. Table 3 shows the final model, which achieved a regression coefficient of $r = 0.735$ ($p < 0.001$), accounting for 50.4% of the total variance.

Co-morbidity of depression and PTSD

In-hospital depression was shown to predict PTSD severity at three months and explained more variance than acute stress symptoms. Although depression was assessed prospectively, it is difficult to disentangle the directionality of such associations. Firstly, a history of depression was associated with higher scores on the PSS-SR (see above), so depression was a risk factor for PTSD after exposure to trauma. Secondly, in-hospital depression was associated with in-hospital acute stress symptoms ($r = 0.527$, $p < 0.001$), depression and PTSD were highly correlated at three months ($r = 0.811$, $p < 0.001$), and so the two were highly comorbid at both time points. Thirdly, in-hospital depression

Table 2 Comparisons of psychological variables between PTSD and non-PTSD groups

Variable	Non-PTSD (n = 115)	PTSD (n = 20)	p Value
PSS-SR score	8.95 (6.31)	29.60 (7.35)	<0.001
Acute stress symptoms	26.84 (8.92)	35.85 (10.36)	<0.001
Social Network Questionnaire	4.97 (1.87)	4.92 (2.05)	NS
DS16 negative affectivity	9.18 (6.44)	16.54 (6.75)	<0.001
DS16 social inhibition	11.07 (6.16)	13.16 (6.37)	NS
Hostility scale	14.67 (7.25)	21.73 (8.68)	0.001
Life Orientation Test	20.48 (3.27)	18.32 (3.64)	NS
Hospital Anxiety Scale	5.76 (3.89)	6.79 (5.11)	NS
Beck Depression Inventory	6.96 (5.97)	17.78 (9.49)	<0.001
Type D personality	30.9%	61.1%	0.013

Data are mean (SD) (t test comparisons, required significance level adjusted to $p < 0.007$ by the Bonferroni method) or percentage (χ^2 comparisons).

DS16, Type D scale-16; PSS-SR, PTSD Symptom Scale-self report version; PTSD, post-traumatic stress disorder.

Table 3 Linear regression model predicting post-traumatic stress symptom severity at three months

	β	Adjusted R ²	Accumulative R ²
First step			
Age	-0.016	0.017	0.017
Second step			
Depression in 6 months preceding ACS	0.082	0.086	0.103
Third step			
Pain score	0.089	0.038	0.141
Fourth step			
Acute stress score	0.116	0.127	0.268
Fifth step			
Beck Depression Inventory	0.361	0.186	0.454
DS16 negative affect	0.208	0.029	0.483
Hostility scale	0.178	0.021	0.504

ACS, acute coronary syndromes; DS16, Type D scale-16.

was shown to predict PTSD independently, but in-hospital acute stress symptoms also predicted depression at three months, even after history of depression and in-hospital depression were covaried ($p = 0.003$). These data suggest a complex relationship where both depression and traumatic stress syndromes were risk factors for each other.

DISCUSSION

This study investigated prevalence and predictors of PTSD three months after admission for ACS. We found that 14.8% of patients admitted for ACS could be classified as experiencing PTSD three months after admission. This falls within the range reported in previous studies.²⁻⁶ No demographic variables were predictive of PTSD or symptom severity at three months, whereas studies of PTSD in the general population have found education, female sex and younger age to be associated with PTSD.²¹ This does not appear to be the case in cardiac populations, however, suggesting that PTSD may have distinctive correlates in medically ill patients. Objective clinical severity of ACS was not predictive of PTSD, despite use of a broad range of indices, and this is in agreement with previous studies in cardiac populations² and literature on PTSD after a wider range of medical events.⁹ Subjective severity or intensity of the ACS as indexed by degree of chest pain, however, was a predictor of PTSD severity.

In-hospital psychological factors were the strongest predictors of PTSD at three months. Negative affect, whether measured in terms of depressive symptoms or a personality dimension, is the most robust predictor of PTSD in cardiac populations.⁵⁻⁷ Although in a previous study type D personality predicted PTSD,⁷ in our data only the dimension negative affect, rather than type D as a whole, predicted PTSD independently of other covariates. One other study found an association with hostility⁵ and, as with the present study, anxiety has not been found to be predictive.⁶ In addition, history of depression was associated with PTSD, and previous mental illness is a risk factor for PTSD in the general population.²¹

One limitation of the current study is that PTSD was assessed by questionnaire rather than by clinical interview. A full diagnostic interview was not possible within the confines of the study, given sample size and the two-phase design. Standard clinical interviews tend to give lower prevalences than self-report scales, causing some authorities to suggest that clinical PTSD is rare in cardiac patients. Two recent studies contradict this argument; O'Reilly *et al*⁴ found a 7% prevalence among patients with MI by using structured clinical interview diagnosis, and Ladwig *et al*²² recorded an exaggerated startle response, an established physiological marker of PTSD,²³ in survivors of life threatening cardiac

events with PTSD. The present study therefore provides only an estimate of PTSD frequency. Conservative scoring criteria were applied,¹⁹ however, and therefore only patients with frequent symptoms were assigned to the PTSD group. This method also avoids confounding by high scores on somatic items, which is problematic when assessing mood state in populations with chronic illness. From a clinician's perspective, in which the goal is to identify patients at risk of distress and poor outcomes, post-traumatic stress severity may be a more useful concept than PTSD. PTSD symptoms occur on a continuum of severity, as do those of depression; therefore, subclinical PTSD may exert a detrimental effect on cardiac patients as does depression,²⁴ where increasing severity predicts increasing risk of mortality. Another limitation is lack of psychological data on those patients who were clinically eligible but did not consent to take part, as those with severe traumatisation may have avoided participation, thus underestimating PTSD in this sample. Strengths of the study are the consideration of the full range of ACS rather than just MI, its sample size and the prospective design.

It is not surprising that depression (in-hospital or before onset) is predictive of PTSD, given the high levels of comorbidity between the two and the finding that depression and PTSD are risk factors for one another.²⁵ This raises a number of issues, the first being the specificity of the measures used in this study and the influence of "reporting bias" (the tendency to endorse any negative items). Although PTSD and depression may co-occur, symptoms are distinct and the measures used in this study are specific to PTSD. Furthermore, the scales were adapted to refer to ACS as the index "traumatic event" and therefore reflect distress arising from ACS rather than pre-existing distress. Statistical control for reporting bias on the PTSD scale was provided by entering acute stress symptoms into the regression model before other psychological predictors.

A second issue is whether psychological predictors identified by this study constitute a non-specific dimension of vulnerability to PTSD. The predictors (depression, negative affect and hostility), however, were independent of one another. Rather than being a single factor of "distress", these psychological factors may operate through different pathways to precipitate PTSD and may importantly require different kinds of intervention.

A third issue addresses the implications of PTSD in cardiac populations and concerns the value of screening for PTSD as well as for depression. PTSD in patients with cardiac disease is associated with a reduced quality of life, reduced adherence to drug treatment, and cardiac readmission after MI.²⁻³ Depression in patients with coronary heart disease has also been associated with poor outcomes,²⁴ and plausible biological pathways leading to progression of coronary heart disease

have been delineated. Neuroendocrine, immunological and autonomic pathways are found to be disrupted in PTSD; the proinflammatory cytokines tumour necrosis factor and interleukin 6 are raised²⁶ and heart rate variability is reduced.²⁷ Both of these patterns are established risk factors for coronary heart disease.^{28–29} Although cortisol concentrations are raised in patients with depression, however, studies of patients with PTSD but without cardiac disease find lower concentrations of cortisol and downregulation of the hypothalamic–pituitary–adrenal axis.²⁵

Screening patients only for depression may overlook those with severe PTSD and the risks that this incurs. Furthermore, different types of treatment are required for depression and PTSD. Recently published national guidelines on the management of PTSD recommend “trauma-focused therapy” as the first line of treatment, which differs from standard cognitive–behavioural techniques used to treat depression.²⁰ One group investigated efficacy of administering corticosteroids to patients recovering from cardiac surgery, finding that the incidence of traumatic stress symptoms was lower in the treatment group.³⁰

In conclusion, the association of PTSD with harmful behavioural and biological factors and with raised levels of depression means that, whatever the direction of causality, coexisting PTSD and coronary heart disease are a potentially malignant problem with a clear threat to well-being and future risk of death.

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