Do depression and anxiety predict recurrent coronary events 12 months after myocardial infarction?

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Summary

We examined the association between depression and anxiety and recurrent coronary heart disease events during the first 12 months subsequent to myocardial infarction. The Beck Depression Inventory and the State-Trait Anxiety Inventory were completed during hospitalization by 288 myocardial infarction patients. Peel Index score and Killip class were used as indices of disease severity. The 12-month incidence of recurrent coronary heart disease events (fetal and non-fatal) was determined. Eighty-two patients experienced recurrent coronary heart disease events, including 27 cardiac fatalities, during follow-up. Whereas the Peel Index differentiated patients who experienced recurrent events from those who did not (OR 3.00, 95% CI 1.46–6.20), symptoms of depression (OR 0.97, 95% CI 0.55–1.70) and anxiety (OR 1.00, 95% CI 0.98–1.02) were unrelated to outcome. Depression and anxiety did not predict subsequent coronary heart disease events and were not associated with either Peel Index scores or Killip class.

Introduction

Symptoms of depression and anxiety are common following myocardial infarction (MI),1–3 and have been observed to persist in the months subsequent to MI.4–5 In addition, several recent studies have reported that depression predicted subsequent mortality in MI patients,5–15 although counterexamples exist.16–18 The study of anxiety in this context has produced even more inconsistent results. Of the three studies to date, only one reported an unequivocal association between anxiety and mortality.14 While one found no association,9 the other reported a relationship for men but not women.10 Power is frequently low in such studies of mortality following MI, with the inevitable consequences for type I as well as type II errors.19 Power is not only dependent on sample size, but is also a function of the outcome incidence rate.19 Thus, one way of increasing power in this context is to examine non-fatal as well as fatal coronary heart disease (CHD) events. Both depression9,13,14 and anxiety9,14,20 have also been linked with an increased risk of recurrent CHD events following MI.

However, depression and anxiety would appear to predict mortality and recurrent CHD events where researchers have either not controlled statistically for disease severity14 or where disease severity was significantly correlated with depression and anxiety.5,7–11,13,15,20 In studies in which depression was confounded with disease severity, statistical control abolished the relationship between depression and mortality in two studies,11,15 although the association survived such correction in another.5,7–9 With regard to the two analyses of depression and recurrent CHD events, correction for disease severity abolished the significant association between depression and combined fatal and non-fatal events in the study by Frasure-Smith et al.,9 but not the association between depression and angina pectoris in the other.13 Of the two recent published studies which
have examined the relationship between anxiety and recurrent CHD events following MI, controlling for disease severity, both reported associations that withstood correction for disease severity.\textsuperscript{9,20}

Given such inconsistencies, the present prospective study was undertaken to examine further the relationship between depression and anxiety measured during hospitalization for MI and fatal and non-fatal CHD events during the subsequent 12 months. In addition, at entry to the study, indices of disease severity were derived and a variety of demographic and behavioural measures taken.

**Methods**

Consecutive admissions, who met established criteria for MI, were recruited from the coronary care units in two general hospitals in the West Midlands, between January 1997 and August 1998. The study was approved by the Ethics Committee review board at both hospitals. Patients had to meet at least two of the following criteria for MI: typical ischaemic chest pain lasting at least 20 minutes; presence of new pathological Q-waves on the electrocardiogram (ECG); a peak creatine phosphokinase (CK) level greater than 1.5 times the normal limit, or a CK-MB (the myocardial isoenzyme of CK) value $\geq 25$ IU/l or $> 5\%$ of a simultaneous CK value exceeding the normal limit. Patients were excluded if their MI resulted from coronary artery bypass graft (CABG) surgery, angioplasty (PTCA), or angiography; if they had a co-morbidity likely to cause death within the next 12 months; if they were unable to speak English; if they were cognitively impaired; or if they were too unstable medically to complete the baseline assessment within 15 days of their infarction. There were no age or gender restrictions. All patients in the study received routine hospital and post-discharge care.

Participants were interviewed as soon as they were medically stable, on average 6 days after their MI (SD 2.1, range 2–15 days). Routine demographic data including age, gender, education, living arrangements, current partner status, ethnicity, and employment status were collected. Socio-economic position was indexed by the deprivation score attached to individuals’ postal codes.\textsuperscript{21} Deprivation scores are composites of the extent of household overcrowding, unemployment, and lack of car and home ownership in small postal code areas across England and Wales. Scores range from $-7.3$ to $10.2$, with higher positive scores indicating greater deprivation.

Patients also completed a battery of questionnaires. The 21-item self-report Beck Depression Inventory (BDI)\textsuperscript{22} was used to assess current depressive symptoms. A meta-analysis of the BDI’s internal consistency revealed a mean Cronbach’s alpha of 0.86 for psychiatric patients and 0.81 for non-psychiatric patients, and test-retest reliability coefficients as high as 0.86 and 0.83 in these populations, respectively.\textsuperscript{23} Scores of 10 or more were used to indicate the presence of depression.\textsuperscript{5,7–10}

The State-Trait Anxiety Inventory (STAI),\textsuperscript{24} comprising two self-report scales was used to assess both state and trait anxiety. Both scales have acceptable internal consistency, with Cronbach’s alpha of 0.92 and 0.90, for state and trait scales, respectively. The Health Behaviours Profile, adapted from the Whitehall II study, was used to assess current smoking status, and the frequency, intensity, and duration of exercise behaviour.\textsuperscript{25} Patients were asked to rate the frequency of exercise undertaken as, ‘three times a week or more’, ‘once or twice a week’, ‘once to three times a month’, or ‘hardly ever’. This was scored using a four-point ordinal scale with higher scores indicating more frequent exercise. These scores were then weighted according to intensity; for moderate exercise, scores were multiplied by two and for vigorous exercise by three. Overall scores ranged from 0 to 18. The patients were also asked to indicate the duration of exercise at each intensity, reporting the number of hours per week spent exercising. Duration was weighted for intensity of exercise in the same way as frequency.

Baseline clinical variables, including administration of thrombolytic therapy, history of previous MI, history of hypertension, diabetes mellitus, hypercholesterolaemia, or angina pectoris were obtained from patients’ hospital records. The Peel Index,\textsuperscript{26} which was used to gauge the severity of infarction, is a composite of a number of potential prognostic indicators, namely: age, sex, previous medical history, degree and severity of shock, presence and severity of heart failure, cardiac rhythm, and the nature and extent of ECG signs. The total score ranges from 1 to 28, with higher scores denoting a poorer prognosis. In addition, Killip class, a standardized four-point clinical assessment of the degree of left ventricular dysfunction, was determined from chest X-ray, heart and lung sounds, and signs of shock,\textsuperscript{27} by a consultant physician blind to clinical outcome. The higher the Killip class, the greater the degree of heart failure. Length of hospital stay was also used as a proxy for CHD severity.

Recurrent cardiac events (fatal and non-fatal) requiring hospitalization within the first 12 months following the index MI were recorded from medical records and the Patient Information System held at each hospital. Non-fatal recurrent events included unstable angina pectoris, recurrent MI, heart failure, CABG surgery, angioplasty, and arrhythmic events.
For fatal events, cause of death was established from hospital and general practitioner records and death certificates. Deaths were confirmed as cardiac or non-cardiac by a consultant cardiologist (GL), who was blind to baseline data. Fatal cardiac events were further classified as secondary to arrhythmia, MI, heart failure, or underlying ischaemic heart disease.

Data analysis

Data were analysed using SPSS for Windows (version 8.0).26 All statistical tests were two-tailed; p-values ≤0.05 were considered statistically significant. As indicated above, the main outcome was one or more recurrent cardiac events requiring hospitalization within 12 months of the index MI. Analysis was by logistic regression. In these analyses, BDI scores were treated both as a continuous variable and a dichotomous variable, <10 and ≥10.8 Peel Index scores were dichotomized using a <17 and ≥17 split; scores of ≥17 are considered to signify a mortality risk of at least 50% within the first 28 days following MI.26 Given the negatively skewed distribution of patients among the four Killip classes, Killip class was also reconstituted as a dichotomous variable: class I (no heart failure) and classes II, III, and IV (heart failure). In addition, the length of initial hospital stay was dichotomized around the median, <8 and ≥8 days. χ² and t-tests were used to compare baseline indices of disease severity (Peel Index, Killip class, and length of hospital stay) between those who were depressed (BDI ≥10) and those who were not, and between those with high (≥40) and low state or trait anxiety. For these analyses, Peel Index scores and length stay were treated as continuous variables.

Results

Comparison of participants and non-participants

Overall, 288 (65.9%) of the 437 patients who were eligible for participation provided informed consent and completed the baseline interview. There were few differences between participants and those who refused, although the latter were more likely to be Afro-Caribbean (p<0.001), non-smokers (p=0.007), and have diabetes mellitus (p=0.002). Those who refused to participate did not have more severe cardiac disease than those who participated, as evidenced by Peel Index scores, Killip class, and mean length of hospital stay (data not shown).

Twelve-month incidence of recurrent CHD events

By 12 months, 82 (30.1%) patients had experienced at least one recurrent CHD event requiring hospitalization, including 27 (9.9%) cardiac deaths. The non-fatal events included 24 (8.8%) cases of unstable angina pectoris, 14 (5.1%) instances of recurrent MI, 13 (4.8%) admissions for CABG surgery, 13 (4.8%) for PTCA, eight (2.9%) with heart failure, and eight (2.9%) with arrhythmias. Of the 27 cardiac deaths, 16 were due to recurrent MI, eight to heart failure, and three to arrhythmias. Four patients died from non-cardiac causes during the 12-month follow-up period and the hospital records were unavailable for 12 other patients. Accordingly, the effective sample size was 272, 190 (69.9%) of whom were event-free at 12 months.

Predictors of CHD events

There were no statistically significant demographic predictors of recurrent CHD events (see Table 1). None of the behavioural and psychological variables differentiated patients with recurrent events from event free survivors (see Table 1). Neither depression nor anxiety were associated with recurrent cardiac events: the mean BDI scores of the event-free survivors (7.4) was virtually identical to that of the patients who had suffered a recurrent cardiac event (7.5); the same was true for both state and trait anxiety.2

The only variables predicting prognosis at 12 months were Peel Index score (p=0.003) and initial length of hospital stay (p=0.05) (see Table 2). While for the purposes of analysis the Peel Index was dichotomized, the mean (SD) Peel Index scores of those who experienced a recurrent event and those who were event-free were 11.5 (5.3) and 9.9 (4.6), respectively. Logistic regression analysis confirmed that Peel Index scores, treated as a continuous variable, also predicted outcome (OR 1.07, 95% CI 1.01–1.13, p=0.02). In a final multiple logistic regression model in which both the dichotomized Peel and initial length of hospital stay were entered, only Peel Index score emerged as a significant predictor of 12-month recurrent CHD events (OR 2.73, 95% CI 1.28–5.83, p=0.009).

Depression, anxiety and indices of disease severity

Those characterized as depressed (BDI ≥10, n=81) had longer hospital stays (mean 11.4 days, SD 11.0) than patients who were not depressed (mean 9.4 days, SD 4.3) (t=2.21, p=0.03). However, neither Peel Index scores (t=1.51, p=0.13) nor
Table 1  Baseline demographic, psychological, and behavioural data of participants and CHD incidence within the first 12 months after MI

| Age (years)* | 61.9 (11.3) | 64.2 (12.4) | 1.02 (0.99–1.04) | 0.14
| Males | 142 | 58 | 1.22 (0.69–2.18) | 0.49
| Partnered | 138 | 53 | 1.45 (0.83–2.53) | 0.19
| Living alone | 40 | 21 | 1.29 (0.70–2.37) | 0.41
| Ethnicity | | | | |
| Caucasian | 173 | 80 | 0.43 (0.17–1.10) | 0.08
| Afro-Caribbean | 6 | 1 | | |
| Asian | 1 | 1 | | |
| Employed | 129 | 54 | 0.91 (0.53–1.58) | 0.74
| Education (years)* | 10.2 (2.0) | 9.8 (1.1) | 0.85 (0.70–1.03) | 0.09
| Deprivation score* | 3.4 (3.1), n = 186 | 3.2 (2.8), n = 81 | 0.98 (0.90–1.07) | 0.67
| BDI score* | 7.4 (5.8) | 7.5 (5.9) | 1.00 (0.96–1.05) | 0.92
| BDI score ≥ 10 | 57 | 24 | 0.97 (0.55–1.70) | 0.90
| State anxiety score* | 33.3 (11.8) | 33.6 (12.1) | 1.00 (0.98–1.02) | 0.86
| Trait anxiety score* | 32.1 (10.4) | 30.3 (9.4) | 0.98 (0.95–1.01) | 0.16
| Frequency of exercise* | 6.1 (3.8) | 5.7 (4.4) | 0.97 (0.91–1.04) | 0.43
| Duration of exercise* | 18.0 (31.0), n = 184 | 14.4 (20.0) | 0.99 (0.98–1.01) | 0.34
| Smoking status | | | | |
| Current smoker | 85 | 34 | 1.08 (0.77–1.52) | 0.66
| Ex-smoker | 70 | 32 | | |
| Non-smoker | 35 | 16 | | |

Patients who were depressed (BDI score ≥ 10) at baseline were more likely to be female (p < 0.001). Higher state anxiety was evident in women (p = 0.006) and younger patients (p = 0.03), whereas higher trait anxiety was associated only with age (p < 0.001). As indicated, age and sex were not significantly related to recurrent CHD events in the present sample, although those who had suffered an event tended to be older. However, BDI scores were not related to age and it was younger patients who registered higher levels of state and trait anxiety. *Mean (SD).

Table 2  Baseline clinical data of participants and CHD incidence within the first 12 months after MI

| Peel Index score ≥ 17 | 17 | 18, n = 79 | 3.00 (1.46–6.20) | 0.003
| Previous MI* (≥ 1) | 34 | 22, n = 81 | 1.71 (0.93–3.16) | 0.09
| Hypertensive* | 77 | 30, n = 81 | 0.86 (0.51–1.48) | 0.59
| Angina pectoris* | 59 | 25, n = 81 | 0.99 (0.56–1.74) | 0.98
| Killip class* (II–IV) | 95 | 44, n = 79 | 1.26 (0.74–2.13) | 0.39
| Thrombolysed | 116 | 46, n = 81 | 1.19 (0.70–2.02) | 0.51
| Hypercholesterolaemia** | 141, n = 180 | 55, n = 74 | 0.80 (0.43–1.50) | 0.49
| Diabetes mellitus (type I or II) | 25 | 10, n = 81 | 0.93 (0.42–2.04) | 0.86
| Mean (SD) hospital stay (days) | 9.4 (4.6) | 11.5 (10.7) | 1.04 (1.00–1.08) | 0.05

*This variable is assessed as part of the Peel Index. **Cholesterol ≥ 5.2 mmol/l.

Killip class (χ² = 0.99, p = 0.32) varied significantly with depression status. Using the criterion of ≥ 40, those identified as high in either state or trait anxiety did not have higher Peel Index scores, poorer Killip class, or longer hospital stays. For the state anxiety comparisons, the relevant statistics for length of hospital stay, Peel Index, and Killip class, were t = 0.26, p = 0.80; t = 0.83, p = 0.41; and χ² = 0.11, p = 0.75, respectively. For trait anxiety, the analogous statistics were t = 0.85, p = 0.40; t = 1.15, p = 0.25; and χ² = 0.00, p = 0.97, respectively.

Discussion

In the present study, depression and anxiety, measured in hospital 2–15 days after acute MI, did not predict fatal and non-fatal CHD events in the subsequent 12 months. This finding would appear to be at odds with the results of other recent prospective studies of the relationship between depression and anxiety following MI and recurrent CHD events.9,13,14,20 Since studies have varied in location, patient population, and the
manner in which depression and anxiety was measured, some variation in results is hardly surprising. However, it is difficult to explain the present null result in terms of the extent of depressive and anxious symptomatology in the current sample, since it is similar to that reported by others using the same measures.\textsuperscript{5,7,9} Further, given that positive relationships have emerged from studies with uniformly smaller sample sizes and lower event rates than the present one,\textsuperscript{9,14,20} it is difficult to attribute our failure to find associations to low power. Given the distribution of BDI scores \( \geq 10 \) among those with and without recurrent CHD events observed in a previous study,\textsuperscript{9} power analysis indicated that with the present sample size and number of CHD events, and the power to detect effects for depression with an odds ratio of at least 3.32 was 96%.

As indicated earlier, depression and anxiety would appear to predict fatal and non-fatal events in studies that have either failed to control for disease severity\textsuperscript{14} or in which markers of disease severity were strongly correlated with depression and anxiety.\textsuperscript{5,7,13,15} Indeed, a recent editorial by Mendes de Leon\textsuperscript{29} cautioned, ‘One of the main issues regarding the role of depression is the potential confounding with disease severity’ (p. 738). In the present study, indices of disease severity, although associated with CHD incidence, were not, with the exception of length of hospital stay, associated with depression and anxiety. However, the relationship between anxiety and recurrent CHD events observed in other studies has tended to survive statistical correction for measures of disease severity,\textsuperscript{9,20} and the association for depression withstood such correction in one previous study\textsuperscript{13} but not in the other.\textsuperscript{9}

It would be premature to conclude, on this basis, that depression and anxiety constitute independent risk factors for CHD events following MI. The ability of multivariate statistical models to determine independence depends on the accuracy of measurement of potential confounding variables, and any inaccuracy will inevitably result in under-estimation of the true impact of the confounder. As Davey Smith and Phillips\textsuperscript{30} asserted, ‘it can appear that a risk factor is related to risk of disease because of under-adjustment for these confounding factors’ (p. 257). Accordingly, in previous positive studies it is possible that depression and anxiety were primarily consequences of baseline disease severity, and that it is disease severity which is the underlying cause of recurrent CHD events.

It is unclear why depression and anxiety are related to disease severity in some studies\textsuperscript{9,20} but not in the present study, although cultural differences in perceptions of personal control and fatalism in relation to health may be implicated. A fatalistic orientation towards disease, claimed to characterize the British,\textsuperscript{31,33} may serve to uncouple disease severity from affect, whereas an ideology of personal control, more characteristic of North American populations in particular,\textsuperscript{34} would optimize the association between disease severity and negative affect. Symptoms of serious illness are more likely to elicit depression and anxiety when illness is perceived as a personal failing than when it is regarded as a matter of fate.

Although depression and anxiety were not predictive of prognosis in the present study, they remain a cause for concern in MI patients. Nevertheless, the present finding, echoing earlier results,\textsuperscript{1–5} that a substantial proportion of MI patients exhibited mild to severe symptoms of depression and/or high levels of anxiety, emphasizes the need to both assess mood and develop appropriate intervention strategies for survivors of MI.\textsuperscript{15}

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References


