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ORIGINAL ARTICLE

Depressive symptom dimensions and cardiac prognosis following myocardial infarction: results from the ENRICHD clinical trial

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Background. Depression following myocardial infarction (MI) independently increases risk for early cardiac morbidity and mortality. Studies suggest that somatic, but not cognitive, depressive symptoms are responsible for the increased risk. However, the effects of somatic depressive symptoms at follow-up, after sufficient time has elapsed to allow for physical recovery from the initial infarction, are not known. Our aim was to examine the relationship between cognitive and somatic depressive symptom dimensions at baseline and 12 months post-MI and subsequent mortality and cardiovascular morbidity.

Method. Patients were 2442 depressed and/or socially isolated men and women with acute MI included in the Enhancing Recovery in Coronary Heart Disease (ENRICHD) clinical trial. We used principal components analysis (PCA) of the Beck Depression Inventory (BDI) items to derive subscales measuring cognitive and somatic depressive symptom dimensions, and Cox regression with Bonferroni correction for multiple testing to examine the contribution of these dimensions to all-cause mortality, cardiovascular mortality, and first recurrent non-fatal MI.

Results. After adjusting for medical co-morbidity and Bonferroni correction, the somatic depressive symptom dimension assessed proximately following MI did not significantly predict any endpoints. At 12 months post-MI, however, this dimension independently predicted subsequent all-cause [hazard ratio (HR) 1.43, 95% confidence interval (CI) 1.13–1.81] and cardiovascular mortality (HR 1.60, 95% CI 1.17–2.18). No significant associations were found between the cognitive depressive symptom dimension and any endpoints after Bonferroni correction.

Conclusions. Somatic symptoms of depression at 12 months post-MI in patients at increased psychosocial risk predicted subsequent mortality. Psychosocial interventions aimed at improving cardiac prognosis may be enhanced by targeting somatic depressive symptoms, with particular attention to somatic symptom severity at 12 months post-MI.

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Key words: Coronary heart disease, depression, mortality, myocardial infarction, prognosis.

Introduction

Depression following myocardial infarction (MI) is common (Schleifer *et al*. 1989; Forrester *et al*. 1992; Frasure-Smith *et al*. 1993) and has been associated with a 2- to 2.5-fold increased risk of recurrent non-fatal cardiac events and mortality (Barth *et al*. 2004; van Melle *et al*. 2004). Although several mechanisms linking depression to adverse cardiac outcomes have been proposed, the exact mechanisms are not known (de Jonge *et al*. 2010). Furthermore, randomized controlled trials (van Melle *et al*. 2007), including the Enhancing Recovery in Coronary Heart Disease (ENRICHD) trial (Berkman *et al*. 2003), have not found that treating depression reduces risk for subsequent cardiac events. Given the substantial overlap between symptoms of depression and cardiac disease, it is not clear to what extent the association between post-MI depression and worse cardiac prognosis is confounded by cardiac disease severity (de Jonge *et al*. 2006*a*; Martens *et al*. 2010). For instance, in their meta-analysis, Nicholson *et al*. (2006) found that almost half of the increased risk of death in depressed coronary heart disease (CHD) patients was accounted for by CHD severity, especially left ventricular ejection

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fraction (LVEF). Some reports have suggested the utility of distinguishing between depressive symptom clusters in modeling cardiovascular prognosis. Three such studies among general CHD populations (de Jonge *et al*. 2006*a*; Linke *et al*. 2009; Martens *et al*. 2010) used factor analysis to examine the dimensional structure of the Beck Depression Inventory (BDI), resulting in two or three depressive symptom dimensions: cognitive/affective, somatic/affective and appetitive.

de Jonge *et al*. (2006*a*) found that, after controlling for LVEF, Killip class and previous MI, only somatic/affective symptoms predicted cardiovascular mortality in MI patients. Martens *et al*. (2010) and Linke *et al*. (2009) replicated this finding in samples of MI patients and in women with suspected myocardial ischemia respectively, and furthermore found appetitive depressive symptoms to be associated with a more adverse cardiac prognosis (Linke *et al*. 2009). Cognitive/affective depressive symptoms were, however, not related to cardiac prognosis in these studies. Similarly, in a study of chronic heart failure patients, only somatic/affective depressive symptoms were associated with all-cause mortality (Schiffer *et al*. 2009). In light of the ongoing debate as to whether somatic depressive symptoms are another manifestation of CHD severity, it should be noted that the association between somatic depressive symptoms and cardiac prognosis remained after controlling for cardiac disease severity.

Using data from the ENRICHD clinical trial, our aim was to examine the effects on subsequent prognosis of BDI depressive symptom dimensions at the time of an index MI and at 12-month follow-up in a sample of patients who were depressed and/or socially isolated at baseline. We examined the effects of these symptom dimensions 12 months after the index event to expand our understanding of the link between depression and post-MI prognosis, because transient depressive symptoms at baseline, when patients may be faced with acute adjustment of a major life-threatening event, may influence prognosis differently than depressive symptoms occurring several months after the life-threatening cardiac event. The effects on prognosis of somatic depressive symptoms at follow-up, after sufficient time has elapsed to allow for physical recovery from the initial MI, are not known.

Method

Study design and participants

ENRICHD was a National Heart, Lung, and Blood Institute (NHLBI)-funded randomized clinical trial conducted from October 1996 to April 2001 that recruited 2481 patients with acute myocardial infarction (AMI) meeting the study criteria for depression and/or low perceived social support (LPSS). Patients were recruited from 73 hospitals affiliated with eight clinical centers and randomized to a cognitive behavior therapy (CBT) intervention or treatment as usual. The main study objective was to evaluate the effect of intervention, relative to usual care, on the primary endpoint of combined all-cause mortality and recurrent MI. Follow-up assessments were conducted at 6, 12, 18, 30 and 42 months. Prior to initiation of recruitment, the study protocol was approved by the eight local institutional review boards. The study organization, design, methods and results have been described in detail elsewhere (ENRICHD Investigators, 2000, 2001*a*; Berkman *et al*. 2003).

The criteria for AMI were a characteristic increase in at least one biomarker of myocardial injury to twice the upper limit as established within the recruiting institution. Additionally, symptoms compatible with AMI or characteristic evolutionary electrocardiographic ST-T changes or new Q waves had to be present. Moreover, patients undergoing interventions for ST elevation were suitable for inclusion, regardless of the biomarker criteria (ENRICHD Investigators, 2000; Berkman *et al*. 2003).

Patients were excluded from ENRICHD if they had a non-cardiac illness likely to be fatal within 1 year; were too ill to participate; had major psychiatric co-morbidity (including imminent risk for suicide, schizophrenia, bipolar disorder, severe dementia or current substance abuse); were already receiving psychotherapy for depression; could not be enrolled within 28 days of their cardiac event; were not accessible for follow-up; could not provide informed consent; or were participating in another trial (Berkman *et al*. 2003).

Psychosocial measures

Depressive symptoms

Patients were eligible for the study if they met modified DSM-IV (APA, 1994) diagnostic criteria for dysthymia, minor depressive disorder or major depressive disorder on the Depression Interview and Structured Hamilton (DISH), developed for the ENRICHD trial (Freedland *et al*. 2002; Berkman *et al*. 2003). The BDI was also administered to patients as part of the baseline assessment and at follow-up assessments. The BDI is a 21-item questionnaire with each item representing an aspect of the depression clinical presentation and rated on a 0–3-point scale of symptom severity (Beck *et al*. 1988). BDI scores of 10–15 indicate mild depression, 16–23 moderate depression, and 24–63 severe depression.

Perceived social support (PSS)

PSS was assessed with the ENRICHD Social Support Instrument (ESSI), which has been described in detail elsewhere (ENRICHD Investigators, 2000, 2001*b*). In brief, the ESSI is a five-item questionnaire designed for the ENRICHD trial to assess perceived functional and emotional support. A total score $\leqslant 18$ with a score $\leqslant 3$ on at least two items or a score $\leqslant 2$ on two items regardless of the total score was used to classify patients with LPSS (ENRICHD Investigators, 2000; Berkman *et al*. 2003).

Sociodemographic and clinical variables

The baseline variables included in the ENRICHD trial have been described in detail elsewhere (ENRICHD Investigators, 2001*b*; Watkins *et al*. 2003; Jaffe *et al*. 2006). For this secondary analysis, sociodemographic and clinical covariates were selected on the basis of a medical risk model developed from the ENRICHD dataset, and reported previously (Jaffe *et al*. 2006). Baseline sociodemographic variables included age, gender, ethnicity, marital status, education, and annual household income. We further included information on ejection fraction (EF), previous MI, congestive heart failure (CHF), diabetes, chronic pulmonary disease, malignancy, and renal disease.

Main outcome measures

The primary endpoint in the ENRICHD trial was a composite of recurrent non-fatal MI and all-cause mortality. Secondary endpoints included, among others, cardiovascular mortality and cardiovascular hospitalizations (ENRICHD Investigators, 2000). In the present study, endpoints included all-cause mortality, cardiovascular mortality, and first recurrent non-fatal MI. Hospital readmissions and deaths were identified at follow-up visits and through telephone contact with patients and their family (Jaffe *et al*. 2006). If an event had occurred, supporting documentation from the medical record was obtained and, if necessary, a death certificate (Jaffe *et al*. 2006). In addition, at the annual follow-up visits, a resting electrocardiogram (ECG) was performed and unrecognized MI was determined by the ECG Core Laboratory. Endpoints were classified according to standardized criteria (Jaffe *et al*. 2006).

Statistical analyses

Of the 2481 patients included in the ENRICHD trial, 98.4% ($n=2442$) provided BDI information at baseline and were thus included in this secondary analysis. Of these, 72.8% ($n=1777$) completed the BDI at 12 months. Of those ($n=665$) who did not complete the BDI at 12 months, mortality prior to 12 months was confirmed for 233. Differences in sociodemographic, clinical and psychosocial baseline characteristics between responders ($n=1777$) and non-responders ($n=432$) at 12 months were examined with an independent-samples t test and χ^2 tests for independence, for continuous and categorical variables respectively.

We first established the underlying structure of the BDI for the ENRICHD sample at baseline, using principal components analysis (PCA) with direct oblimin rotation (Field, 2009). An oblique method was chosen over an orthogonal, as the factors were expected to correlate. The contribution of depressive symptom dimensions at baseline and 12 months to subsequent prognosis was determined by Cox regression analysis. We standardized the depression subscale scores for ease of interpretation. The initial model entered baseline cognitive and somatic symptom dimensions simultaneously, with adjustment for treatment assignment (intervention *versus* usual care). The covariates added to the second model included age, gender, ethnicity, marital status, education, annual household income, and LPSS. Three indicators of cardiac disease severity (LVEF, history of CHF, previous MI), were entered in a third model, and pulmonary disease, diabetes, malignancy, and renal disease were added in a fourth model. All of these baseline covariates were included in models testing the effects of 12-month depressive symptom dimensions, controlling for baseline somatic and cognitive symptom dimensions, and for interim cardiac and non-cardiac hospitalizations. To adjust for multiple testing, a Bonferroni correction was applied ($0.05/12=0.0042$). All statistical analyses were performed with SPSS version 18 (SPSS Inc., USA).

Results

Patient characteristics

The baseline characteristics of the ENRICHD sample ($n=2481$) have been described previously (ENRICHD Investigators, 2001*b*). Selected sociodemographic, clinical and psychosocial baseline characteristics of the present subsample ($n=2442$) are shown in Table 1 along with differences in baseline characteristics between responders and non-responders at 12 months. Differences were found with respect to gender and minority status.

Factor structure of the BDI

Bartlett's test of sphericity ($p < 0.001$) and the Kaiser–Meyer–Olkin measure of sampling adequacy (0.90)

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Table 1. *Baseline characteristics of the ENRICHD subsample and differences at baseline between responders and non-responders at 12 months*

Characteristics	Baseline ($n=2442$)	Responders at 12 months ($n=1777$)	Non-responders at 12 months ($n=432$)	p value for responder *versus* non-responder differences
Sociodemographic variables				
Male gender	1372 (56.2)	989 (55.7)	265 (61.3)	0.04
Age (years), mean (S.D.)	60.8 (12.6)	60.2 (12.2)	59.9 (12.5)	0.68
Non-minority	1620 (66.3)	1192 (67.1)	266 (61.6)	0.04
Married/partnered	1265 (51.8)	933 (52.5)	220 (50.9)	0.59
⩽High school	1331 (54.5)	942 (53.0)	230 (53.2)	0.97
Annual household income				0.26
<US$20 000	851 (34.8)	610 (34.3)	149 (34.5)	
⩾US$20 000 and <US$40 000	514 (21.0)	394 (22.2)	78 (18.1)	
⩾US$40 000	454 (18.6)	337 (19.0)	89 (20.6)	
Unknown	623 (25.5)	436 (24.5)	116 (26.9)	
Clinical variables				
Ejection fraction (% LVEF)				0.55
EF <35%	321 (13.1)	219 (12.3)	50 (11.6)	
35% ⩽EF <40%	183 (7.5)	122 (6.9)	27 (6.3)	
40% ⩽EF <45%	243 (10.0)	171 (9.6)	47 (10.9)	
45% ⩽EF <50%	242 (9.9)	182 (10.2)	42 (9.7)	
50% ⩽EF <55%	335 (13.7)	265 (14.9)	53 (12.3)	
EF ⩾55%	641 (26.2)	486 (27.3)	117 (27.1)	
Unknown	477 (19.5)	332 (18.7)	96 (22.2)	
Previous MI	651 (26.7)	429 (24.1)	116 (26.9)	0.27
History of CHF	329 (13.5)	187 (10.5)	53 (12.3)	0.34
Diabetes	800 (32.8)	567 (31.9)	134 (31.0)	0.77
Chronic pulmonary disease	450 (18.4)	308 (17.3)	77 (17.8)	0.86
Malignancy	218 (8.9)	160 (9.0)	31 (7.2)	0.26
Renal disease	238 (9.7)	149 (8.4)	34 (7.9)	0.80
Psychosocial variables				
Intervention	1225 (50.2)	895 (50.4)	210 (48.6)	0.55
Psychosocial risk group				0.08
Depressed	964 (39.5)	708 (39.8)	148 (34.3)	
LPSS	632 (25.9)	463 (26.1)	117 (27.1)	
Depressed/LPSS	846 (34.6)	606 (34.1)	167 (38.7)	

ENRICHD, Enhancing Recovery in Coronary Heart Disease trial; LVEF, left ventricular ejection fraction; MI, myocardial infarction; CHF, congestive heart failure; LPSS, low perceived social support; S.D., standard deviation.

Values given as n (%) of total unless stated otherwise.

indicated that the data were suitable for PCA. In the initial analysis, four components with eigenvalues above 1 emerged; however, the screeplot revealed a break after the second component, and only two items (loss of appetite and loss of weight) loaded above 0.3 on the third component. This was also the case in a forced three-factor solution, suggesting that a two-factor solution would be appropriate because at least three items per component is advised (Costello & Osborne, 2005). In the forced two-factor solution, the weight loss item loaded weakly on both components (–0.08 and 0.28). Given the problematic contingent scoring of this item, coupled with poor factor loadings, we excluded it from the measurement model. The refined two-factor model provided an acceptable solution, although the irritability item loaded weakly on both components, and the dissatisfaction item loaded above 0.3 on both components. Table 2 shows the pattern and structure matrix of the final two-factor model. The total variance explained by the two-factor

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Table 2. *Factor loadings of BDI depressive symptom dimensions*[a]

	Pattern coefficients		Structure coefficients	
	Cognitive	Somatic	Cognitive	Somatic
Sadness	**0.46**	0.24	**0.55**	0.42
Pessimism	**0.58**	0.11	**0.62**	0.33
Sense of failure	**0.72**	−0.10	**0.68**	0.17
Dissatisfaction	**0.36**	0.33	**0.49**	0.47
Guilt	**0.67**	−0.12	**0.62**	0.14
Punishment	**0.64**	−0.16	**0.58**	0.08
Self-dislike	**0.72**	−0.04	**0.70**	0.23
Self-accusations	**0.65**	−0.03	**0.64**	0.22
Suicidal thoughts	**0.47**	−0.05	**0.46**	0.13
Crying	**0.36**	0.23	**0.45**	0.37
Irritability	**0.26**	0.24	**0.35**	0.33
Social withdrawal	**0.40**	0.20	**0.48**	0.36
Indecisiveness	**0.37**	0.28	**0.47**	0.42
Body image change	**0.45**	0.11	**0.49**	0.28
Work difficulties	−0.10	**0.74**	0.18	**0.70**
Insomnia	0.06	**0.52**	0.26	**0.54**
Fatigability	−0.07	**0.77**	0.22	**0.74**
Loss of appetite	−0.11	**0.61**	0.13	**0.57**
Somatic preoccupation	0.23	**0.34**	0.35	**0.42**
Decreased libido	0.11	**0.38**	0.25	**0.42**

BDI, Beck Depression Inventory.
The highest loadings are in bold.
[a] Principal components analysis (PCA) with direct oblimin rotation.

model was 33.6%, and the correlation between components was 0.38, supporting the use of an oblique rotation.

Cognitive and somatic dimensions

The internal consistency of the BDI cognitive dimension was satisfactory for the baseline ($\alpha = 0.82$) and 12-month follow-up assessments ($\alpha = 0.88$). Cronbach's α on the somatic dimension at baseline was marginally satisfactory ($\alpha = 0.62$), and satisfactory at the 12-month follow-up ($\alpha = 0.76$). The correlation between subscale scores measuring the two dimensions of depression was moderate at baseline ($r = 0.47$, $p < 0.001$) and strong at the 12-month follow-up ($r = 0.68$, $p < 0.001$). The mean BDI total scale score and symptom dimensions scores at baseline and at the 12-month follow-up are shown in Table 3. At baseline, the mean total scale score corresponded to moderate depressive symptoms, which decreased to mild depressive symptoms at the 12-month follow-up. No differences in baseline cognitive and somatic symptoms of depression were found between those who provided BDI data at 12 months and those who did not.

Table 3. *BDI total scale and symptom dimension scores at baseline and 12 months post-MI*

	Total (21 items)	Cognitive (14 items)	Somatic (6 items)
Baseline	15.8 (8.4)	8.5 (6.1)	6.6 (3.4)
12-month follow-up	9.3 (8.9)	5.0 (5.9)	4.0 (3.5)

BDI, Beck Depression Inventory; MI, myocardial infarction.
Values given as mean (standard deviation).

Depressive symptom dimensions and cardiovascular prognosis

The mean follow-up time was 2.3 years for all-cause and cardiovascular mortality, and 2.1 years for non-fatal MI. A total of 335 patients died during the follow-up period and 62.4% (209) were classified as cardiovascular deaths. In addition, 336 patients experienced recurrent non-fatal MI. The number of events before and after 12 months is shown in Table 4. A total of 639 cardiovascular hospitalizations and 624 non-cardiovascular hospitalizations occurred within

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Table 4. *Number of events before and after 12 months*

	Number of events (% of total)		
Time period	All-cause mortality Total = 335	CV mortality Total = 209	Non-fatal MI Total = 336
Baseline to 12 months	233 (69.6)	145 (69.4)	243 (72.3)
After 12 months	102 (30.4)	64 (30.6)	93 (27.7)

CV, Cardiovascular; MI, myocardial infarction.

the first 12 months. The results from Cox regression analyses on depressive symptom dimensions and subsequent outcomes are shown in Table 5.

Somatic and cognitive symptoms of depression at baseline

The associations between the somatic depressive symptom dimension at baseline and all-cause mortality, cardiovascular mortality and recurrent non-fatal MI were statistically significant when adjusting for treatment group. The effect on cardiovascular mortality became non-significant when additionally adding sociodemographic variables and co-morbid LPSS to the model, as did all-cause mortality with the further addition of cardiac disease severity. The effect of somatic depressive symptoms on subsequent non-fatal MI became non-significant in the fully adjusted model. The baseline cognitive depressive symptom dimension was associated with all-cause mortality when adjusting for treatment group; however, this effect was not statistically significant in the subsequent adjusted model.

Somatic and cognitive symptoms of depression at the 12-month follow-up

The somatic depressive symptom dimension at 12 months predicted all-cause and cardiovascular mortality after adjusting for baseline depressive symptom dimensions and all other covariates, including interim cardiovascular and non-cardiovascular hospitalizations. An increase in score of one standard deviation on the somatic subscale predicted a 43% increase in risk of all-cause mortality and a 60% increase in risk of cardiovascular mortality whereas no significant associations were found for non-fatal MI. Subsequent outcomes were not significantly predicted by the cognitive depressive symptom dimension at 12 months.

Discussion

Contrary to our expectations, when adjusting for sociodemographic factors, cardiac disease severity and co-morbidity, somatic depressive symptoms measured at the time of the index cardiac event were not associated with cardiac morbidity or mortality. However, somatic depressive symptoms 12 months post-MI were associated with all-cause and cardiovascular mortality. Cognitive depressive symptoms were found to be unrelated to prognosis in all fully adjusted models after Bonferroni correction; however, a non-significant trend was found for cognitive depressive symptoms at 12 months predicting lower cardiovascular mortality.

Our finding that baseline post-MI somatic depressive symptoms did not predict prognosis differs from the results of several prior studies (de Jonge *et al*. 2006*a*; Linke *et al*. 2009; Schiffer *et al*. 2009; Smolderen *et al*. 2009; Hoen *et al*. 2010; Martens *et al*. 2010; Roest *et al*. 2011) demonstrating a significant effect of baseline somatic depressive symptoms on cardiac prognosis. Differences between the present study and previous studies with respect to sample composition, included covariates, and factor analytic solutions may in part explain these inconsistencies. Furthermore, the timing of the baseline depression assessment may have influenced our results. In their meta-analysis, Nicholson *et al*. (2006) found that depression assessed more than 2 weeks after an MI showed a stronger association with cardiac prognosis than depression assessed closer to the event. In the ENRICHD trial, patients were enrolled an average of 11 days post-MI (Jaffe *et al*. 2006), making it plausible that some initial depressive symptoms were transient.

Most prior studies (Linke *et al*. 2009; Smolderen *et al*. 2009; Hoen *et al*. 2010; Martens *et al*. 2010; Roest *et al*. 2011) have not found a significant association between cognitive depressive symptoms and cardiac prognosis; however, one recent study demonstrated that a cognitive depressive symptom dimension marked by pessimism, past failure, self-criticalness and worthlessness predicted cardiac morbidity and mortality (Tully *et al*. 2011). Although cognitive symptoms were not significant predictors of post-MI prognosis in the current study, after Bonferroni correction, one prior study found a protective effect of cognitive depressive symptoms on cardiovascular mortality (de Jonge *et al*. 2006*a*). The authors of that study concluded that the effect estimate for cognitive symptoms was being overcorrected by statistical control for somatic depressive symptoms. It is possible that their finding was not spurious and that our conservative use of Bonferroni criteria resulted in failure to demonstrate an association between cognitive symptoms of depression and improved prognosis. However, we can offer only speculative hypotheses regarding mechanisms to explain this association and instead focus our discussion on the findings that were significant in the current study.

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Table 5. *Results from Cox regression analyses: depressive symptom dimensions at baseline and 12-month follow-up and subsequent outcomes*

	Main outcome measures					
	All-cause mortality		CV mortality		Non-fatal MI	
	HR (95% CI)	*p* value[a]	HR (95% CI)	*p* value[a]	HR (95% CI)	*p* value[a]
Baseline						
Model 1[b]						
Cognitive	0.79 (0.70–0.90)	<0.001	0.84 (0.72–0.98)	0.03	1.00 (0.90–1.13)	0.94
Somatic	1.41 (1.26–1.58)	<0.001	1.36 (1.18–1.58)	<0.001	1.30 (1.16–1.46)	<0.001
Model 2[c]						
Cognitive	0.94 (0.83–1.07)	0.38	0.99 (0.84–1.16)	0.85	1.05 (0.93–1.18)	0.44
Somatic	1.24 (1.10–1.40)	0.001	1.21 (1.03–1.41)	0.02	1.25 (1.10–1.41)	<0.001
Model 3[d]						
Cognitive	0.95 (0.84–1.09)	0.46	1.00 (0.85–1.18)	0.99	1.05 (0.93–1.18)	0.46
Somatic	1.14 (1.01–1.29)	0.04	1.09 (0.93–1.28)	0.27	1.21 (1.07–1.37)	0.003
Model 4[e]						
Cognitive	0.93 (0.82–1.06)	0.30	0.98 (0.83–1.16)	0.83	1.05 (0.93–1.18)	0.46
Somatic	1.09 (0.96–1.24)	0.18	1.05 (0.89–1.23)	0.56	1.16 (1.03–1.32)	0.02
12 months						
Model 5[f]						
Cognitive	0.85 (0.66–1.11)	0.23	0.66 (0.45–0.95)	0.03	1.17 (0.89–1.52)	0.26
Somatic	1.49 (1.18–1.88)	0.001	1.64 (1.21–2.23)	0.002	1.05 (0.79–1.40)	0.74
Model 6[g]						
Cognitive	0.87 (0.67–1.13)	0.30	0.66 (0.45–0.98)	0.04	1.16 (0.89–1.52)	0.27
Somatic	1.43 (1.13–1.81)	0.003	1.60 (1.17–2.18)	0.003	1.05 (0.79–1.41)	0.73

CV, Cardiovascular; MI, myocardial infarction; HR, hazard ratio; CI, confidence interval.

[a] Bonferroni correction for multiple testing ($\alpha < 0.0042$).

[b] Adjusted for treatment group.

[c] Adjusted additionally for age, gender, ethnicity, marital status, education, household income, and low perceived social support (LPSS).

[d] Adjusted additionally for history of congestive heart failure (CHF), ejection fraction (EF), and previous MI.

[e] Adjusted additionally for pulmonary disease, diabetes, malignancy, and renal disease.

[f] Depressive symptoms at 12 months adjusted for somatic and cognitive depressive symptoms at baseline, treatment group, age, gender, ethnicity, marital status, education, household income, LPSS, history of CHF, EF, previous MI, pulmonary disease, diabetes, malignancy, and renal disease.

[g] Depressive symptoms at 12 months adjusted for all baseline variables in the previous model, and for CV and non-CV hospitalizations occurring between baseline and the 12-month follow-up.

Our findings suggest that somatic depressive symptoms 12 months following MI may be more predictive of post-MI prognosis than somatic depressive symptoms measured close to the acute event. Although the present analyses do not distinguish between pre-existing and new-onset depression, other studies have suggested that new-onset rather than pre-MI depression predicts subsequent adverse cardiac events (Grace *et al*. 2005; de Jonge *et al*. 2006*b*; Dickens *et al*. 2008).

Possible mechanisms

Several mechanisms by which depression might increase cardiovascular disease (CVD) risk have been proposed (Lett *et al*. 2004; de Jonge *et al*. 2010) and it is possible that somatic depressive symptoms may highlight specific mechanisms. Consistent with this hypothesis, de Jonge *et al*. (2007) found that somatic symptoms of depression (such as fatigue and psychomotor changes) were associated with reduced heart rate variability, a risk factor for CVD, whereas cognitive symptoms (such as negative self-image) were not. Patients with a more severe depression, which is often accompanied by somatic symptoms, have evidence of hypercortisolemia, which also increases CVD risk (Gillespie & Nemeroff 2005). Some types of depression may be secondary to underlying cerebrovascular disease, which may be greater in patients with heart disease (Sheline *et al*. 2010). In previous reports, de Jonge

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et al. (2010) and others (Gold & Chrousos, 2002; Schiffer *et al*. 2009) have argued that different subtypes of depression may have different risks. Recently, Davidson *et al*. (2010) reported that anhedonia (loss of interest or pleasure in all or most activities), but not depressed mood, was an independent predictor of adverse cardiac events and mortality. Anhedonia has been associated with perturbations in sleep, appetite, weight and libido in psychiatric patients (Davidson *et al*. 2010), and our results are consistent with those findings. In addition, somatic depressive symptoms may reflect an entirely different disease process, such as sleep apnea (Takama & Kurabayashi, 2009). Thus, a range of factors may underlie the current finding.

Implications for clinical practice

The ENRICHD intervention improved depression but failed to improve event-free survival (Berkman *et al*. 2003). The present results suggest that psychosocial interventions directed at improving cardiac prognosis may be enhanced by targeting post-recovery somatic depressive symptoms. The ENRICHD intervention lasted for up to 6 months and interventions of longer duration might be considered in patients with persistent somatic symptoms. Although psychosocial interventions aimed at cognitive symptoms of depression are not likely to improve post-MI prognosis, quality of life, independent of cardiovascular prognosis, may be enhanced by such interventions through improved mood and psychosocial functioning.

Limitations

The present study relied on secondary analyses of the ENRICHD data. Consequently, the data analyses were bounded by the design of the ENRICHD trial. Given the comprehensive collection of data in the ENRICHD trial, sufficient information was available to test the present hypotheses. However, it should be noted that the ENRICHD sample was limited to post-MI patients at increased psychosocial risk at baseline, and our results may not therefore be generalizable to post-MI patients who are neither depressed nor socially isolated. Of the medically eligible patients in the ENRICHD trial ($n = 9279$), a total of 35% were depressed and/or socially isolated (ENRICHD Investigators, 2001*b*). Based on these findings, it is estimated that the present findings would apply to approximately one-third of AMI patients. In addition, approximately half of the ENRICHD participants received CBT. Although the intervention did not improve event-free survival, depressive symptoms were improved in the intervention group (Berkman *et al*. 2003). We took this into account by controlling for the treatment group status.

In the 12-month models we used interim cardiovascular and non-cardiovascular hospitalizations as a proxy for worsening cardiac disease severity and co-morbidity. Although this seems a reasonable proxy, and we did adjust for baseline CVD severity and medical co-morbidity, some patients may have experienced a worsening of their CVD and other co-morbid diseases without being hospitalized. Thus, the findings in the 12-month models could have been confounded to some extent by disease severity. Moreover, we were not able to distinguish between pre-MI and post-MI depressive symptoms based on our present analyses. Future studies could benefit from taking this distinction into account.

Conclusions

The present secondary analyses of ENRICHD data are the first to examine the association between depressive symptom dimensions at 12 months post-MI and subsequent medical prognosis. Somatic depression symptom severity at baseline among post-MI patients who were depressed and/or socially isolated at baseline was not a significant predictor of cardiac morbidity and mortality. By contrast, somatic depressive symptoms at 12 months post-MI were associated with increased all-cause and cardiovascular mortality. These findings suggest that psychosocial interventions aimed at improving cardiac prognosis may be enhanced by targeting somatic depressive symptoms, with particular attention to somatic symptom severity several months post-MI.

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Declaration of Interest

None.

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