

Psychological Symptom Clusters, Psychiatric Comorbidity and Poor Self-Reported Health Status Following Myocardial Infarction

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ABSTRACT

Background: Depression is a risk factor for adverse outcomes following myocardial infarction (MI). However, the importance of various other psychological factors is less well established. **Purpose:** The purpose is (a) explore the degree to which self-reported psychological symptoms in post-MI patients represent one or more underlying dimensions and (b) examine whether psychological symptom profiles based on these dimensions are differentially associated with major depressive disorder (MDD) and anxiety disorder (AD), and impaired health status. **Methods:** Two months post-MI, the Beck Depression Inventory, State-Trait Anxiety Inventory, and Global Mood Scale were used to measure symptoms of depression, anxiety, and mood status in 324 patients. The Composite International Diagnostic Interview was administered to diagnose DSM-IV MDD and AD. Health status was assessed by the Seattle Angina Questionnaire. **Results:** Principal component analysis revealed 4 essential features of post-MI distress: depressed affect, anxious apprehension, positive affect, and emotional exhaustion. Cluster analysis using these components identified 3 subgroups with different symptom profiles: A no distress subgroup (high positive affect, low on the remaining components), a first increased distress subgroup (ID1; elevated anxious apprehension/emotional exhaustion scores and decreased positive affect, $p < .001$, but absence of depressed affect, $p = .56$), and a second increased distress subgroup (ID2; decreased positive affect and elevated scores on the other components, all $p < .001$). Both increased distress subgroups were more likely to have psychiatric disorder (ID1: odds ratio [OR] = 5.4, 95% confidence interval [CI] = 1.3–22.1, $p = .018$; ID2: OR = 27.1, 95% CI = 6.4–114.7, $p < .0001$) and worse health status (ID1: $-.38 < \beta < -.12$; all $p < .05$; ID2: $-.48 < \beta < -.20$; all $p < .05$). **Conclusions:** In addition to standard depressive symptoms, other affective components are important in understanding emotional adjustment in post-MI patients. These components are closely related to psychiatric comorbidity and poor health status post-MI.

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INTRODUCTION

About one in five patients is affected by major depressive disorder (MDD) following myocardial infarction (MI) (1). In turn, both MDD and depressive symptoms have been associated with (a) a twofold increased risk of mortality and (b) increased morbidity and rehospitalisation post-MI (2–6). Although several literature reviews have concluded that there is evidence that various other psychological factors are related to prognosis in established coronary artery disease (CAD) (7–9), the importance of these factors is less well established. In addition, it is not known which symptoms are specific to post-MI distress and whether there are reliably identifiable subgroups of post-MI patients with different psychological symptom profiles.

According to Frasura-Smith and Lespérance (10), most studies on psychosocial risk factors in CAD patients used only one psychological or social variable, making it impossible to examine the degree to which the variables represent one or more common dimensions. Without using multiple measures, it is difficult to know whether the essential features of distress in post-MI patients concern specific psychological concepts or one or more underlying dimensions, including negative affectivity. In addition, little is known about the psychological symptom profiles based on these dimensions and their relationship with adverse outcomes post-MI. Identification of CAD risk profiles across the spectrum of symptoms and syndromes characterizing psychological discomfort, including subsyndromal conditions, might increase the sensitivity of our epidemiologic prediction models and clarify the pathophysiological pathways linking negative psychological states to CAD (11).

The objectives of this study were (a) to explore the degree to which psychological variables of distress in post-MI patients represent one or more underlying dimensions and (b) to examine whether psychological symptom profiles based on these dimensions are differentially associated with the *Diagnostic and Statistical Manual of Mental Disorders* (4th ed. [DSM-IV]) (12) MDD and anxiety disorder (AD) and impaired self-reported health status.

METHODS

Patient Population and Design

Between May 2003 and August 2005, 402 patients hospitalized for acute MI were recruited from four teaching hospitals (Catharina Hospital, Eindhoven; St. Elisabeth

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Hospital, Tilburg; TweeSteden Hospital, Tilburg; and St. Anna Hospital, Geldrop) in the Netherlands. Two months post-MI, during an appointment specifically for this study, patients were evaluated by a trained psychologist using the Composite International Diagnostic Interview (CIDI) (13) and completed self-report measures of depression, anxiety, emotional distress, and disease-specific health status in the cardiology department of the participating hospitals. Inclusion criteria were age above 30 and hospitalization due to acute MI. Exclusion criteria were significant cognitive impairments (e.g., dementia), severe comorbidities (e.g., cancer) in addition to their cardiac condition, and psychiatric comorbidities other than MDD and AD (e.g., psychosis). Criteria for the diagnosis of MI included troponin I levels more than twice the upper limit, with typical ischemic symptoms (e.g., chest pain) lasting for more than 10 min or electrocardiogram (ECG) evidence of ST segment elevation or new pathological Q-waves. The study was approved by the medical ethics committees of the participating hospitals. The study was conducted in accordance with the Helsinki Declaration, and all patients provided written informed consent.

Analyses were based on patients who were alive 2 months after discharge from the index hospitalization for MI, who were assessed with the CIDI and had completed the self-report questionnaires 2 months post-MI. Of the original 402 patients, 10 patients refused to participate at 2 months follow-up, 5 patients died prior to the 2-months assessment, and 63 patients were excluded due to missing CIDI diagnosis or missing self-report measures. Hence, the final population for this study comprised 324 patients.

Measures

Symptoms of depression, anxiety, and mood status. The Beck Depression Inventory (BDI) is a 21-item self-report measure developed to assess the presence and severity of depressive symptoms during the past week (14). Each item is rated on a 0 to 3 scale. The BDI is a reliable and well-validated measure of depressive symptomatology (15,16) and is the most widely used self-report measure of depression. BDI scores 10 or higher are indicative of at least mild to moderate symptoms of depression and have been associated with poor prognosis in MI patients (4,6,17,18).

The State-Trait Anxiety Inventory (STAI) is a self-report measure consisting of two 20-item scales developed to measure the level of general state and trait anxiety (19). In this study we included the state scale of the STAI, which assesses the current level of general anxiety. Each item is rated on a 4-point Likert scale. Elevated scores on the STAI have been associated with poor prognosis in MI patients (20). The STAI has been demonstrated to have adequate validity and reliability (21).

The Global Mood Scale (GMS) is a self-report measure assessing both positive (energy and sociability) and negative (fatigue and malaise) mood states in patients with

heart disease (22). It consists of 10 positive and 10 negative mood terms answered on a 5-point Likert scale. The respondent is asked to rate the extent to which he or she has experienced each mood state lately. The GMS has been shown to be a valid and reliable measure of affective mood states (22,23) and is very responsive to treatment-related changes in mood status (24).

Clinical diagnoses of depression and anxiety disorder. The CIDI was used to assess current diagnoses of MDD and AD (consisting of panic disorder, social phobia, and/or generalized anxiety disorder) based on the diagnostic criteria of the *DSM-IV* (12). The CIDI was administered 2 months post-MI (1.8 ± 0.6 months).

Health status. Health status was measured with the Seattle Angina Questionnaire (SAQ) (25). The SAQ is a 19-item disease-specific self-report measure for patients with CAD and has been used to assess patient outcomes in acute coronary syndromes (26). It has been demonstrated to be a valid and reproducible measure and to be sensitive to clinical change (25,27). In addition, it has been shown to be predictive of 1-year mortality (28). The SAQ is composed of five scales: physical limitations caused by CAD, angina frequency, angina stability over the preceding month, treatment satisfaction, and patients' perceptions of how their disease limits their quality of life. Scores range from 0 to 100. Higher scores indicate higher functional levels in the preceding 4 weeks, for example, less physical limitations and better quality of life.

Demographic and clinical characteristics. Demographic variables included gender, age, educational level, and marital status. Clinical variables were obtained from the patients' medical records and included comorbidity (arthritis, renal insufficiency, and chronic obstructive pulmonary disease), cardiac history (MI, angina, percutaneous coronary intervention or coronary artery bypass graft surgery prior to the MI), multivessel disease, diabetes mellitus, percutaneous coronary intervention versus conservative treatment, current smoking (self-report), and cardiac medication at discharge (β -blockers, ACE-inhibitors, Ca-antagonists, anti-coagulants, statins, diuretics, A2-antagonists, vasodilators, aspirin).

Statistical Analysis

Principal component analysis (PCA) with oblimin rotation was used to determine the underlying structure of the psychological distress measures (BDI, STAI, GMS). A Scree-plot was adopted to identify the number of components, and subsequent Kaiser-Meyer-Olkin (KMO) and Bartlett's test of sphericity were applied as fit indexes. The resulting components were used to construct homogeneous subscales of psychological distress. For each subscale, those six items with the highest compo-

nent loadings and cross loading differences less than .20 were selected. Subscale homogeneity was examined by Cronbach’s alpha. Identification of groups was obtained through cluster analysis. We used a two-stage clustering procedure as recommended by Hair and Black (29). First, hierarchical clustering analysis (wards method; squared Euclidean distance) with standardized subscale measures ($M = 50, SD = 10$) derived the number of clusters through inspection of the agglomeration schedule. Second, the cluster centers obtained from hierarchical cluster analysis were used as initial seed points in nonhierarchical cluster analysis (i.e., K-means clustering) to fine-tune the solution. The combination of hierarchical and non-hierarchical methods results in a more valid cluster solution. For comparison between groups we used the chi-square test for discrete variables and analysis of variance (ANOVA) for continuous variables. A multivariate ANOVA (MANOVA) was employed to examine differences on subscale measures between groups identified by cluster analysis. The Student-Neuman-Keuls test was used for post hoc analysis. Logistic regression (method = enter) was used to assess the relationship between group membership and current

psychiatric comorbidity (i.e., MDD and/or AD). Relevant assumptions were checked and met using the criteria recommended by Ottenbacher et al. (30). Multiple regression analysis (method = enter) was used to assess the relationship between group membership and health status while controlling for potential confounders. The following assumptions for multiple linear regression were checked and met (31): multicollinearity (VIF: range = 1.04–1.23), independent observations (Durbin-Watson: range = 1.85–2.10), homoscedasticity (plot of standardized predicted dependent variable vs. standardized residuals; random patterns were found), normally distributed error (histogram of residuals). Linearity was not checked, because all independent variables were dichotomous. Data were analyzed using SPSS 12.0.1 for Windows.

RESULTS

Components of Psychological Distress

A PCA revealed a four-component solution in the underlying structure of the psychological symptom measures (see Table 1). KMO (0.95) and Bartlett’s test of

TABLE 1
Four-Component Rotated Solution for Psychological Distress Measures

Items	Scale (#)	Comp-1	Comp-2	Comp-3	Comp-4
Depressed affect					
Guilty feelings	BDI (5)			-.87	
Self-dislike	BDI (7)			-.84	
Self-criticism	BDI (8)			-.79	
Sense of failure	BDI (3)			-.79	
Punishment feelings	BDI (6)			-.61	
Feelings of sadness	BDI (1)			-.45	
Anxious apprehension					
Being jittery	STAI (13)	.75			
Feeling restless	STAI (4)	.75			
Feeling calm	STAI (1)	-.73			
Feeling nervous	STAI (12)	.72			
Feeling at ease	STAI (5)	-.68			
Being tense	STAI (3)	.66			
Positive affect					
Hard working	GMS (7)		.79		
Lively	GMS (9)		.79		
Enterprising	GMS (13)		.78		
Dynamic	GMS (4)		.76		
Active	GMS (2)		.74		
Bright	GMS (5)		.73		
Emotional exhaustion					
Feeling tired	GMS (12)				.81
Feeling fatigued	GMS (18)				.80
Feeling tired	BDI (17)				.77
Feeling weakened	GMS (19)				.77
Feeling worn out	GMS (3)				.72
Feeling feeble	GMS (8)				.70

Note. No cross-loadings of .30 or more were found in the six-item subscales. Only the six items with the highest component loadings are shown. Comp = component. BDI = Beck Depression Inventory; STAI = State-Trait Anxiety Inventory; GMS = Global Mood Scale.

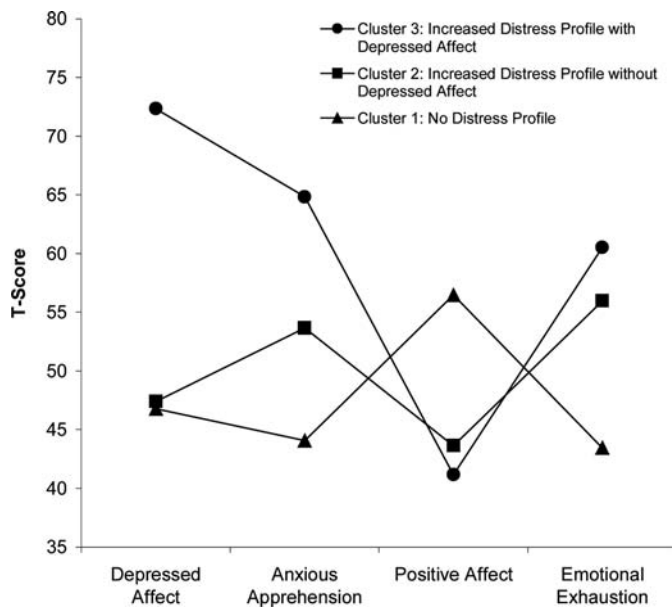


FIGURE 1 Psychological symptom clusters.

sphericity, $\chi^2(1830) = 15,217, p < .001, N = 324$ indicated that PCA was adequate for these data. The six-item subscales that were constructed from the PCA reflected, respectively, Depressed Affect (Component 3; Cronbach's $\alpha = .82$; BDI Items 1, 3, 5, 6, 7, 8), Anxious Apprehension (Component 1; $\alpha = .90$; STAI Items 1, 3, 4, 5, 12, 13), Positive Affect (Component 2; $\alpha = .91$; GMS Items 2, 4, 5, 7, 9,

13), and Emotional Exhaustion (Component 4; $\alpha = .92$; GMS Items 3, 8, 12, 18, 19; BDI Item 17). The labeling of the components was based on previous literature (22,23). For example, the items included in the Emotional Exhaustion subscale were drawn from the negative affect subscale of the GMS. The range of component loadings for items not reported in Table 1 was .30 to .63 for Component 1, .46 to .69 for Component 2, .30 to .41 for Component 3, and .38 to .69 for Component 4.

Psychological distress profiles. The agglomeration schedule obtained by hierarchical cluster analysis suggested a three-cluster solution. There was a sharp increase in within-cluster sum of squares between two and three clusters. Subsequently, K-means cluster analysis resulted in a final solution with 168 (52%) patients in the first cluster, 118 (36%) in the second cluster, and 38 (12%) in the third cluster. Figure 1 visualizes the three psychological distress profiles. Cluster 1 can be characterized by a relative absence of psychological distress and presence of positive affect and is therefore labeled the no distress group. Clusters 2 and 3 can both be labeled as increased distress groups. Cluster 2 is characterized by low positive affect and increased anxious apprehension/emotional exhaustion but also by the absence of depressed affect. Cluster 3 is characterized by the presence of psychological distress, including depressed affect and a relative absence of positive affect.

Cluster characteristics are shown in Table 2. Patients in Cluster 1 were more likely to be male and to have a high

TABLE 2 Demographic and Medical Characteristics Stratified by Cluster Membership

	No Distress ^a	Increased Distress Without Depressed Affect ^b	Increased Distress With Depressed Affect ^c	P
Age (M, SD)	60.1 (11.0)	60.0 (11.5)	56.7(11.5)	.22
Male sex	89 (149)	73 (86)	68 (26)	.001
Low educational level ^d	72 (120)	84 (99)	84 (32)	.03
Having no partner	13 (21)	14 (17)	34 (13)	.004
Being a smoker	37 (61)	35 (41)	66 (25)	.002
Cardiac history ^e	19 (31)	32 (36)	34 (13)	.03
Multi-vessel disease ^f	42 (67)	46 (51)	40 (15)	.75
Comorbidity ^g	13 (20)	29 (32)	29 (11)	.002
Diabetes	12 (19)	14 (16)	11 (4)	.77
PCI ^h	63 (100)	60 (67)	63 (24)	.89
β -blockers	87 (139)	85 (94)	84 (32)	.84
ACE-inhibitors	40 (64)	43 (47)	32 (12)	.48
Ca-antagonists	15 (24)	25 (27)	13 (5)	.09
Anti-coagulants	83 (133)	85 (94)	76 (29)	.49
Statins	94 (145)	94 (104)	87 (33)	.40
Diuretics	18 (28)	21 (23)	29 (11)	.28
A2-antagonists	8 (13)	10 (11)	8 (3)	.84
Vasodilators	24 (39)	33 (37)	26 (10)	.26
Aspirin	88 (141)	77 (85)	82 (31)	.06

Note. Unless noted, values are % (n). In 4% of the cases medical data were unknown. Bold indicates significant values. ^an = 168. ^bn = 118. ^cn = 38. ^dNo education completed, first level (primary school), or secondary level (first phase). ^eMyocardial infarction (MI), angina, percutaneous coronary intervention or coronary artery bypass graft prior to the MI. ^fReference group: one-vessel disease. ^gArthritis, renal insufficiency, chronic obstructive pulmonary disease. ^hReference group: noninvasive treatment.

TABLE 3
Mean Levels of Health Status, as Assessed by the Seattle Angina Questionnaire, Stratified by Cluster Membership

	<i>No Distress</i>		<i>Increased Distress Without Depressed Affect</i>		<i>Increased Distress With Depressed Affect</i>		<i>P</i>
	<i>M</i>	<i>SD</i>	<i>M</i>	<i>SD</i>	<i>M</i>	<i>SD</i>	
Physical limitation	39.7	7.4	33.1	9.8	29.9	9.9	<.0001
Angina stability	5.6	0.9	4.8	1.5	4.3	1.6	<.0001
Angina frequency	11.5	1.3	10.6	2.0	9.8	2.5	<.0001
Treatment satisfaction	17.5	2.3	16.4	3.3	15.5	3.5	<.0001
Quality of life	12.4	2.1	9.8	2.8	7.9	3.0	<.0001

Note. Results of pairwise comparisons were all significant ($p < .05$). Higher scores indicate better health status, e.g. less angina frequency and better quality of life.

educational level and less likely to have comorbidities and a cardiac history. Cluster 2 is characterized by more females, more patients with a low educational level, and more comorbidities than would be expected from the independence hypothesis. Finally, Cluster 3 contains relatively more females, more patients without a partner, and more current smokers.

A MANOVA revealed that there was an overall significant main effect for cluster membership on psychological distress (Wilks's lambda = 0.32), $F(8, 450) = 42.7$, $p < .0001$, adjusting for sex, marital status, educational level, smoking, cardiac history, and comorbidity. This indicates that differences between clusters on psychological distress variables cannot be explained by the included covariates. Therefore, the clusters provide unique information on the identification of subgroups in CAD patients.

Psychological distress profiles and psychiatric comorbidity. Because of the relative low prevalence of MDD and AD in our sample, we created a single dichotomous variable: psychiatric comorbidity. Value 1 was assigned to those patients with current MDD and/or AD. The prevalence of psychiatric comorbidity was 2% ($n = 3/168$; MDD, $n = 2$; AD, $n = 2$) in Cluster 1, 9% ($n = 11/118$; MDD, $n = 10$, AD, $n = 2$) in Cluster 2, and 37% ($n = 14/38$; MDD, $n = 12$, AD, $n = 8$) in Cluster 3. Cluster membership was recoded into two dummy variables with the no distress group as reference category. Subsequently, logistic regression analysis revealed that both the increased distress group with depressed affect (Cluster 3; odds ratio = 27.1; 95% confidence interval = 6.4–114.7, $p < .0001$) as well as the increased distress group without depressed affect (Cluster 2; odds ratio = 5.4; 95% confidence interval = 1.3–22.1, $p = .018$) were associated with psychiatric comorbidity (Nagelkerke $R^2 = 0.25$; Hosmer and Lemeshow test: $p = 1$). Hence, a subgroup of CAD patients was more likely to have psychiatric comorbidity despite their low levels of self-reported depressed affect. These patients were characterized, however, by increased levels of self-reported

anxious apprehension and emotional exhaustion and the relative absence of positive affect. The exact strength of the associations should be interpreted with some caution given the large confidence intervals and the small cell sizes, especially in Cluster 1 (the reference category).

Psychological distress profiles and health status. Mean levels of health status were lowest among patients in Cluster 3, whereas patients in Cluster 2 reported lower levels of health status compared to Cluster 1 patients (Table 3).

In multivariate analyses, all health status subscales were associated with cluster membership. Patients in the increased distress group with depressed affect (Cluster 3; $-.48 < \beta < -.20$; all $p < .05$) and the increased distress group without depressed affect (Cluster 2; $-.38 < \beta < -.12$; all $p < .05$) experienced decreased health status compared with the no distress subgroup. In addition, age, current smoking, aspirin usage, multivessel disease, cardiac history, and comorbidity were also associated with decreased self-reported health status.

DISCUSSION

The aim of the study presented here was to examine dimensions of psychological distress in post-MI patients and the associations of psychological symptom profiles with psychiatric comorbidity and health status. The underlying structure of self-reported psychological symptoms post-MI consisted of four components: depressed affect, anxious apprehension, positive affect, and emotional exhaustion. Cluster analysis based on these components revealed three psychological symptom clusters: a no distress subgroup, characterized by a relative absence of psychological distress and presence of positive affect, and two increased distress subgroups characterized by absence of positive affect and presence of anxious apprehension and emotional exhaustion. Remarkably, one increased distress subgroup was characterized by a relative absence of depressed affect as well. Patients in the two increased

distress subgroups were more likely to have MDD/AD and decreased health status as compared with the no distress subgroup. This suggests that some post-MI patients may be more likely to have MDD/AD and impaired health status despite their low levels of self-reported depressed affect. Moreover, these results imply that the spectrum of psychological factors associated with CAD is larger than previously considered.

An increasing body of literature has demonstrated a relationship between depressive symptoms and the likelihood of subsequent adverse cardiac events (32), although negative findings have been reported (33–35). It is interesting to note that in our study one increased distress subgroup without elevated scores on depressed affect, but characterized by the absence of positive affect and presence of anxious apprehension and emotional exhaustion, was associated with psychiatric comorbidity and decreased health status. This “subclinical” group can be an interesting study target because it seems that these patients are more likely to have psychiatric comorbidity and decreased health status without having increased depressed affect. It is possible that the absence of positive affect is important in this subgroup.

In contrast to the data linking negative emotional states to CAD, the potential protective effect of positive psychological factors has been less extensively investigated (36), and data linking positive affect and health is not definitive (37). In the largest study to date, participants were assessed for optimistic versus pessimistic explanatory style and followed for 10 years. Results revealed a gradient relationship between levels of optimism and cardiac outcomes, with optimism halving the risk for cardiac events (38). In addition, several studies have shown that positive psychological factors can dampen the physiologic reactivity to negative emotional stimuli (39) and can enhance immune function (40). These findings point to the importance of further exploring positive emotional states and their potential protective effects against disease.

In addition, our findings show that anxious apprehension could be a potentially harmful negative emotion. Several large studies have noted a relationship between phobic anxiety and sudden cardiac death (41,42). In addition, Grace et al. (18) reported nonphobic anxiety to have a negative effect on self-reported recurrent cardiac events following an ischemic coronary event. However, data linking the various forms of anxiety to CAD are relatively rare and more work is needed.

According to Suls and Bunde (43), there needs to be more appreciation that the clustering and overlap of negative affective dispositions may make specificity of emotion less critical for CAD risk, that is, anxiety and depression may not have distinctive, independent effects. They may all increase risk because they share a general disposition to experience chronic and intense negative emotions. Kubzansky and colleagues (11) also argued for the need to study various potential psychosocial risk factors and

their relationship with CAD and CAD recurrence. Identifying various forms of distress, even in their less severe states, may provide an important avenue for early intervention. Effective treatment targeting psychosocial risk factors in CAD patients requires an accurate characterization of who is at risk for adverse outcomes. A more detailed examination of the CAD distress profiles may better inform the development of more effectively timed and more specifically tailored behavioral interventions. However, more research is needed to replicate these results and to study potential treatment implications.

Results of this study show that the increased distress profiles were associated with MDD/AD and impaired health status. According to the European Society of Cardiology (44), primary goals of therapy include symptom control and maximizing health status. In addition, health status has been shown to be predictive of 1-year mortality (28). Understanding the association of negative and positive mood states with health status may help to guide development of interventions to enhance health status and outcome following MI.

The results of our study should be interpreted with some caution. Because the study was cross-sectional, we were not able to assess the predictive value of the psychological symptom clusters. It would be interesting to evaluate the effect of the symptom clusters on cardiac morbidity and mortality. Ultimately, these profiles will need to be examined prospectively against hard medical outcomes. Furthermore, we had no information on left ventricular ejection fraction, which could influence psychological symptoms post-MI. However, we did adjust for other measures of disease severity (e.g., cardiac history). We did not take into account the potential influence of history of psychiatric disorder. Our study also has a number of strengths, including the use of valid and reliable measures of multiple concepts, making it possible to identify various underlying dimensions of psychological symptoms post-MI. We also used a structured diagnostic interview to assess psychiatric comorbidity. In addition, health status was assessed with a disease-specific measure that may be more sensitive to capture symptoms in this patient group than a generic measure.

In conclusion, the underlying structure of self-reported psychological symptoms post-MI can be characterized by depressed affect, anxious apprehension, positive affect, and emotional exhaustion. Symptom profiles based on these features revealed a no distress subgroup and two increased distress subgroups. Both increased distress subgroups were associated with psychiatric comorbidity and decreased health status, despite the relative absence of depressed affect in one of these subgroups. This study needs to be replicated in a similar sample using confirmatory factor analysis, measures of objective health status, and longitudinal data. The distress profiles based on the underlying structure reported here provide a basis for profile analysis of psychological symptom change in outcome studies with post-MI patients and are potentially valuable for both research and clinical practice.

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