ORIGINAL ARTICLE

Depression and Other Psychological Risks Following Myocardial Infarction

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Background: There is consistent evidence that depression symptoms predict long-term mortality following a myocardial infarction, and recent results show a dose-related gradient. The importance of other psychological variables remains unclear.

Methods: This study examines the relative importance of depression, anxiety, anger, and social support in predicting 5-year cardiac-related mortality following a myocardial infarction and assesses the role of any common underlying dimensions. The design of this cohort analytic study involves self-reports (Beck Depression Inventory, state scale of the State-Trait Anxiety Inventory, 20-item version of the General Health Questionnaire, Modified Somatic Perception Questionnaire, Anger Expression Scale, Perceived Social Support Scale, number of close friends and relatives, and visual analog scales of anger and stress). The study was conducted in 10 Montreal-area hospitals. The patients included 896 persons who experienced a myocardial infarction, aged 24 to 88 years (232 were women), followed up for 5 years using Medicare records; baseline data were complete for 95.0% of the patients. The intervention was usual care, and the main outcome measure was 5-year cardiac-related mortality.

Results: The Beck Depression Inventory ($P<.001$), the State-Trait Anxiety Inventory ($P=.04$), and the 20-item version of the General Health Questionnaire ($P=.048$) were related to outcome), but only depression remained significant after adjustment for cardiac disease severity (hazards ratio per SD, 1.46; 95% confidence interval, 1.18-1.79) ($P<.001$). Exploratory factor analysis revealed 3 underlying factors: negative affectivity, overt anger, and social support. There was also a covariate-adjusted trend between negative affectivity scores and outcome ($P=.08$). Furthermore, residual depression scores ($P=.001$) and negative affectivity scores ($P=.05$) were linked to cardiac-related mortality after adjustment for each other and cardiac covariates.

Conclusions: Negative affectivity and some unique aspect of depression predict long-term cardiac-related mortality following a myocardial infarction independently of each other and cardiac disease severity. Additional research is needed to characterize the mechanisms involved.

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SEVERAL RECENT literature reviews[1-3] have concluded that although there is evidence that various psychological and social variables are related to prognosis in patients with established coronary disease, the cumulative evidence is greatest for depression. However, most of the studies summarized by these reviews examined only one psychological or social variable, usually using only one measure for that variable, making it impossible to compare the prognostic importance of the different concepts in the same individuals, to assess the relative importance of cardiac disease severity, or to examine the degree to which the variables represent one or more common dimensions. Furthermore, some[4,5] have suggested that when measures of anger or social support have prognostic importance, the relationships are probably mediated by depression or anxiety. As Watson and Clark[6] noted, another problem with the single concept approach, and even with the multiple concept approach using only one indicator of each psychological concept, is that individual scales are never pure measures of the concepts they are intended to measure. All scales contain a certain amount of error, and self-reports of negative emotions are also likely to be correlated with an underlying dimension reflecting a general tendency to experience or report negative emotions (negative affectivity or neuroticism).[7,8] Without using multiple measures, it is difficult to know whether any apparent prognostic relationships are due to specific psychological concepts or to one or more

hidden underlying dimensions, including negative affectivity.

We administered a battery of self-report indexes of depression symptoms, anxiety, anger, and social support to a large group of patients hospitalized for an acute myocardial infarction (MI). Patients were followed up for cardiac-related mortality for 5 years to examine the relative importance of the different psychological variables in long-term prognosis, to assess the role of cardiac disease severity in accounting for any observed relationships, to examine the extent to which prognostic relationships could be explained by common dimensions, and to determine whether there was evidence of specific importance for any of the 4 concepts.

METHODS

The sample involves 896 patients post-MI who completed a self-report measure of depression symptoms as part of a psychosocial interview during hospitalization. Participants were recruited from 10 Montreal-area hospitals between January 17, 1991, and September 20, 1994. They participated in 2 previously described studies: the Emotions and Prognosis Post-Infarct project (n=218), an epidemiological study of the prognostic importance of psychosocial factors in patients post-MI,[9,10] and the usual care group of the Montreal Heart Attack Readjustment Trial (n=678), a randomized trial of psychosocial intervention following MI.[11] Details of the methods of each study, and of the combined sample, appear in previous publications.[12-14]

Both studies received ethical approval from all participating hospitals. Following discharge from the hospital, patients were followed up for 5 years based on physician contacts recorded in Quebec Medicare data. Patients with any physician contact after 1825 days were classified as alive at the 5-year point. For nonsurviving patients, these data were supplemented with information from hospital medical records and death certificates. A cardiologist and a trained research assistant independently and blindly classified all deaths as cardiac and noncardiac related. The 5-year survival status was obtained for all but 26 (2.9%) of the 896 patients.

Depression symptoms were measured with the 21-item Beck Depression Inventory (BDI).[15] We subdivided the BDI into separate cognitive (first 13 items) and somatic subscales,[16] to examine the relative importance of the 2 types of depression symptoms. We included 2 measures related to the concept of anxiety: the 20-item state portion of the Spielberger State-Trait Anxiety Inventory (S-STAI)[17] and the 13-item Modified Somatic Perception Questionnaire,[18] which measures somatic symptoms often associated with anxiety. We also included the 20-item version of the General Health Questionnaire (GHQ-20),[19] which evaluates psychological distress as a combination of symptoms of depression, anxiety, and dysfunction. Anger was assessed with the 8-item anger-in and anger-out subscales of the Spielberger Anger Expression Scale (AX).[20] This was supplemented with 3 visual analog scales (VAS) to assess the frequency, intensity, and duration of anger (n=896) during the past month and 2 separate VAS for feelings of stress during the week before the MI and during the past week (n=895). The 12-item Perceived Social Support Scale[21] was used to measure perceived availability and satisfaction with social support from family and friends. There were also 2 questions related to the size of patients' social networks: the number of close friends and the number of close relatives. Of the patients, 851 (95.0%) completed all baseline self-report measures. Patients were also questioned about their marital status, education, medical history, and cardiac risk factors; they were also asked whether they lived alone. Additional medical data were abstracted from hospital medical records. The following medical and background variables were included in the data set: years of education, daily smoking, history of treatment for hypertension, previous MI, thrombolytic treatment at the index admission, Q-wave MI, Killip class greater than 1, revascularization at the index admission, a left ventricular ejection fraction of 35% or less (n=879), prescription of hypoglycemic agents (for those with diabetes mellitus), and prescription of β-blockers and angiotensin-converting enzyme inhibitors at discharge from the hospital.

Data were analyzed with SPSS for Windows, version 10.07.[22] All tests were 2-tailed, with $P \leq .05$ considered statistically significant and $P > .05$ but $\leq .10$ indicative of trends. Because of skewed distributions for the BDI (skewness=2.0), the reported number of close friends (skewness=6.6), and the number of close relatives (skewness=5.1), these data were analyzed using logarithmic transformations, reducing the skewness of all variables to below 0.80. To facilitate comparisons between measures, standardized scores were calculated. Cox proportional hazards regression analysis was used to assess the relationships between the standardized score for each baseline measure and the time to cardiac-related death during the follow-up of 5 years. Patients whose survival status at 5 years was unknown were censored on the last date known to be living. To construct survival curves, we divided standard scores at the upper quartile (or the lower quartile for social support) to illustrate the prognostic values of the various measures in an equitable fashion.

We performed an exploratory principal component factor analysis with varimax rotation to assess the number of factors underlying the baseline psychosocial measures. However, because of the theoretical possibility that the underlying factors show some degree of correlation with each other, we performed a second analysis with oblique rotation using the direct oblimin procedure (oblimin with a δ of 0). The appropriateness of factor analysis was assessed using the Kaiser-Meyer-Olkin measure of sampling adequacy[23] and the Bartlett test of sphericity.[24] Because we wanted to calculate factor scores, final analyses were performed with variables considered missing on a listwise basis. However, sensitivity analyses were also performed using pairwise exclusion and substitution of means for missing values. Because results were similar, only the listwise exclusion analyses are presented herein.

Eigenvalues above 1.0 and inspection of the scree plot were used to determine the number of factors. Factor scores were calculated using regression analysis based on results from the factor analysis, and the prognostic values of the resulting factor scores were assessed using Cox proportional hazards regression analysis. To assess the degree to which any of the baseline measures made unique contributions to prognosis beyond their common factor components, multiple linear regression analysis was used to compute residual scores for each measure. Cox proportional hazards regression analysis was used to assess the degree to which each residual score improved prognostic models based on the factor scores alone.

To select cardiac disease severity–related covariates for statistical adjustment, we used the approach for small data sets suggested by Steyerberg et al.[25] All baseline characteristics and treatment variables were entered together into a Cox proportional hazards regression analysis to predict 5-year cardiac-related mortality. Those independently associated with prognosis ($P \leq .50$) were retained for covariate adjustment.

RESULTS

SAMPLE

The 896 patients ranged in age from 24 to 88 years (mean, 59.4 years; SD, 11.2 years), and about one third (n=232)

Table 1. Correlation Matrix Among Baseline Psychological and Social Measures*

Variable	GHQ-20	S-STAI	MSPQ	VAS for Stress		AX Subscales		VAS for Anger in the Past Month			PSSS	No. of Close Friends	No. of Close Relatives
				Week Before the MI	Past Week	Anger In	Anger Out	Frequency	Duration	Intensity			
BDI†													
Total	0.53	0.56	0.37	0.36	0.35	0.32	0.10	0.21	0.23	0.19	−0.20	−0.12	−0.05‡
Somatic subscale§	0.50	0.45	0.38	0.29	0.30	0.27	0.04‡	0.14	0.18	0.12	−0.14	-0.11	−0.02‡
Cognitive subscale§	0.48	0.56	0.30	0.37	0.33	0.34	0.16	0.25	0.24	0.24	−0.21	−0.11	−0.07‖
GHQ-20		0.50	0.47	0.44	0.37	0.29	0.13	0.29	0.25	0.22	−0.13	−0.09	−0.10
S-STAI			0.29	0.34	0.46	0.29	0.09	0.24	0.24	0.16	−0.23	−0.06‡	−0.05‡
MSPQ				0.33	0.28	0.23	0.10	0.25	0.22	0.19	−0.06‖	−0.05‡	−0.05‡
VAS for stress													
Week before the MI					0.32	0.28	0.11	0.32	0.26	0.30	−0.10	−0.11	−0.14
Past week						0.17	0.05‡	0.17	0.17	0.13	−0.13	−0.07‖	−0.07‖
AX subscales													
Anger in							0.11	0.17	0.22	0.19	−0.21	−0.14	−0.12
Anger out								0.40	0.26	0.41	0.02‡	0.04‡	−0.01‡
VAS for anger in the past month													
Frequency									0.49	0.59	−0.10	−0.04‡	−0.07‖
Duration										0.50	−0.13	−0.07‖	−0.04‡
Intensity											−0.09	−0.11	−0.06‡
PSSS												0.30	0.24
No. of close friends†													0.23
No. of close relatives†													

Abbreviations: AX, Anger Expression Scale; BDI, Beck Depression Inventory; GHQ-20, 20-item version of the General Health Questionnaire; MI, myocardial infarction; MSPQ, Modified Somatic Perception Questionnaire; PSSS, Perceived Social Support Scale; S-STAI, state portion of the State-Trait Anxiety Inventory; VAS, visual analog scale.

*All values are significant ($P \leq .01$) unless otherwise indicated.

†Analysis based on logarithmically transformed data.

‡$P > .05$.

§The correlation between the somatic and cognitive subscale scores is 0.57.

‖$P \leq .05$ and $P > .01$.

were women. Most (n=685) were recovering from their first MI; 47.1% were daily smokers, and 63.1% were prescribed β-blockers at hospital discharge. Additional baseline characteristics have been reported previously.[14]

BASELINE PSYCHOLOGICAL AND SOCIAL MEASURES AND LONG-TERM SURVIVAL

The correlation matrix for the continuous baseline self-report measures is shown in **Table 1**. With such a large sample size, it is not surprising that almost all of the correlations are significant. Factor analysis of the data (measure of sampling adequacy for the total matrix, 0.84; $P < .001$ for the Bartlett test of sphericity) revealed 3 underlying factors that accounted for a total of 51.3% of the variance. As **Table 2** shows, the factor structure was similar when the somatic and cognitive subscales of the BDI were included instead of the total score. Results using oblique rotation did not alter the factor pattern, and correlations between the oblique factors indicated less than 10% shared variance between them.[26] Therefore, we restricted our analyses to results for the orthogonal rotation. We applied linear regression analysis to estimate factor scores labeled negative affectivity, overt anger, and social support, based on the measures that loaded most heavily on each factor.

Within the group of 870 patients whose 5-year status was known, there were 155 deaths, including 121 cardiac- and 34 non–cardiac-related deaths. There were no significant interactions involving age ($P > .20$ for all) or sex (smallest $P = .08$; all others, $P > .15$) and any of the self-report measures or factor scores. The age- and sex-adjusted results of the Cox proportional hazards regression analyses for 5-year cardiac-related mortality for each of the continuous self-report measures, the factor scores, and the dichotomous measures of social support appear in **Table 3**. To illustrate the relationships for cardiac survival, **Figure 1** shows the 5-year age- and sex-adjusted survival curves for cardiac-related mortality, with scores dichotomized at the upper quartile for the overall BDI score (>11), the BDI cognitive subscale (>5), the BDI somatic subscale (>6), the S-STAI (>43), the GHQ-20 (>10), the Modified Somatic Perception Questionnaire (>16), the AX anger-in subscale (>18), and the AX anger-out subscale (>17). The lower quartiles were used to categorize the social support measures (<65 for the Perceived Social Support Scale, <2 for close relatives, and <1 for close friend). **Figure 2** shows similar survival curves for the dichotomized factor scores of negative affectivity (upper quartile), overt anger (upper quartile), and social support (lower quartile).

We observed significant relationships between the BDI ($P < .001$), its somatic ($P < .001$) and cognitive ($P < .001$) subscales, the GHQ-20 ($P = .048$), and the S-STAI ($P = .04$) and long-term cardiac-related mortality, with no long-term links for any of the measures of anger, VAS for stress, or any measures of social support. The negative affectivity score derived from factor analysis was also significantly ($P = .002$) associated with 5-year

Table 2. Component Matrix From Principal Components Factor Analysis With Varimax Rotation*

Variable	Measure of Sampling Adequacy	Scale α Value	Negative Affectivity		Overt Anger		Social Support	
			Analysis With Total BDI	Analysis With BDI Subscales	Analysis With Total BDI	Analysis With BDI Subscales	Analysis With Total BDI	Analysis With BDI Subscales
BDI†								
Total	0.86	.87	0.76	NA	0.07	NA	–0.10	NA
Somatic subscale	0.85	.72	NA	0.75	NA	–0.03	NA	–0.04
Cognitive subscale	0.86	.85	NA	0.74	NA	0.14	NA	–0.12
GHQ-20	0.87	.88	0.77	0.75	0.16	0.17	–0.05	–0.05
S-STAI	0.83	.93	0.76	0.75	0.06	0.07	–0.08	–0.08
MSPQ	0.88	.81	0.61	0.59	0.17	0.18	0.05	0.05
VAS for stress								
Week before the MI	0.91	NA	0.57	0.54	0.28	0.30	–0.13	–0.13
Past week	0.88	NA	0.65	0.61	0.006	0.03	–0.04	–0.05
AX subscales								
Anger in	0.91	.71	0.41	0.41	0.17	0.17	–0.30	–0.30
Anger out	0.81	.78	0.009	0.02	0.68	0.67	0.11	0.11
VAS for anger in the past month								
Frequency	0.82	NA	0.22	0.20	0.79	0.80	–0.05	–0.05
Duration	0.87	NA	0.23	0.22	0.68	0.68	–0.10	–0.10
Intensity	0.79	NA	0.13	0.12	0.82	0.82	–0.11	–0.11
PSSS	0.73	.90	–0.16	–0.16	–0.01	–0.01	0.71	0.71
No. of close friends*	0.68	NA	–0.03	–0.04	–0.01	–0.003	0.72	0.72
No. of close relatives*	0.70	NA	–0.01	–0.003	–0.04	–0.04	0.65	0.66
Eigenvalue (rotated)	NA	NA	4.01 (3.18)	4.34 (3.55)	1.74 (2.39)	1.81 (2.43)	1.43 (1.61)	1.45 (1.62)
% of variance (rotated)	NA	NA	28.6 (22.7)	28.9 (23.7)	12.4 (17.1)	12.1 (16.2)	10.2 (11.5)	9.6 (10.8)

Abbreviations: AX, Anger Expression Scale; BDI, Beck Depression Inventory; GHQ-20, 20-item version of the General Health Questionnaire; MI, myocardial infarction; MSPQ, Modified Somatic Perception Questionnaire; NA, data not applicable; PSSS, Perceived Social Support Scale; S-STAI, state portion of the State-Trait Anxiety Inventory; VAS, visual analog scale.

*Analysis based on logarithmically transformed data.

cardiac-related mortality, but the other factor scores were not. The survival curves based on the upper quartiles of each scale illustrate that the BDI showed the strongest relationship to long-term cardiac-related mortality, with survival curves continuing to separate over time. The patterns for the BDI subscales were similar, as were the somewhat less strong links with the S-STAI, the GHQ-20, and the factor score for negative affectivity. There was also some evidence of a relationship between the AX anger-in subscale score and survival during the first postdischarge year (1-year hazards ratio per SD, 1.10; 95% confidence interval, 1.03-1.18; $P=.004$), with the curves coming together after that point.

ADJUSTMENT FOR CARDIAC DISEASE SEVERITY AND TREATMENTS

When all baseline characteristics and treatment variables were entered together into a Cox proportional hazards regression analysis to predict 5-year cardiac-related mortality, only previous hypertension treatment and prescription of angiotensin-converting enzyme inhibitors at hospital discharge had multivariate values of $P>.50$. All of the other variables were retained as covariates. Table 3 shows the fully adjusted hazards ratios for 5-year cardiac-related mortality for each of the baseline self-reports and the factor scores.

While the relationships between the BDI score and both of its subscale scores and cardiac-related mortality remained independent of baseline covariates, the associations with the GHQ-20 and the S-STAI were entirely explained by covariate adjustment. Finally, although the relationship with the factor score for negative affectivity remained close to significant, adjustment for covariates increased the value to $P>.05$.

UNIQUE PREDICTIVE VALUE OF INDIVIDUAL MEASURES

We sought to determine the degree to which the associations between each of the individual self-report measures and long-term cardiac-related mortality were due to their relationships with the dimensions of negative affectivity, overt anger, and social support or whether any of the different measures had some unique predictive value beyond their shared variance. Multiple linear regression analysis was used to calculate standardized residual scores for each measure after taking into account the variance explained by the factor scores. Cox proportional hazards regression analyses assessed the degree to which each residual score improved the factor scores' prediction of cardiac-related mortality.

Only the BDI score had unique predictive value for cardiac-related mortality beyond the factor scores (**Table 4** and Figure 2). Furthermore, the residual BDI score remained significant ($P=.001$) when included in the same model with all 3 factor scores and full control for covariates. The trend for negative affectivity also remained apparent in this model. In a parallel analysis based on the BDI subscales, the values for the negative affec-

Table 3. The HRs for Baseline Psychological and Social Measures and 5-Year Cardiac-Related Mortality–Free Survival*

Variable	Age- and Sex-Adjusted HR (95% CI)	*P* Value	Fully Adjusted HR (95% CI)†	*P* Value
Continuous Baseline Measures of Psychological and Social Factors				
BDI (n = 896)‡				
Total	1.74 (1.41-2.14)	<.001	1.46 (1.18-1.79)	<.001
Somatic subscale	1.84 (1.47-2.30)	<.001	1.51 (1.21-1.88)	.001
Cognitive subscale	1.51 (1.26-1.81)	<.001	1.34 (1.12-1.61)	.002
GHQ-20 (n = 893)	1.21 (1.00-1.45)	.05	1.03 (0.85-1.25)	.79
S-STAI (n = 893)	1.21 (1.01-1.46)	.04	1.14 (0.93-1.38)	.21
MSPQ (n = 895)	1.12 (0.93-1.35)	.22	1.03 (0.85-1.26)	.76
VAS for stress (n = 895)				
Week before the MI	1.07 (0.89-1.30)	.48	0.98 (0.81-1.20)	.87
Past week	1.10 (0.92-1.31)	.29	1.02 (0.85-1.23)	.81
AX subscales				
Anger in (n = 894)	1.15 (0.97-1.37)	.12	1.07 (0.90-1.27)	.46
Anger out (n = 869)	1.09 (0.91-1.31)	.36	1.05 (0.87-1.26)	.64
VAS for anger in the past month				
Frequency (n = 895)	1.05 (0.87-1.27)	.62	1.06 (0.87-1.28)	.58
Intensity (n = 896)	1.09 (0.91-1.31)	.36	1.02 (0.85-1.22)	.83
Duration (n = 896)	1.10 (0.92-1.32)	.29	1.13 (0.95-1.35)	.18
PSSS (n = 889)	1.01 (0.85-1.21)	.90	1.07 (0.89-1.29)	.49
No. of close friends (n = 896)‡	1.02 (0.86-1.22)	.81	1.07 (0.90-1.28)	.45
No. of close relatives (n = 893)‡	1.07 (0.90-1.26)	.44	1.10 (0.93-1.34)	.24
Factor Score				
Negative affectivity	1.38 (1.12-1.69)	.002	1.20 (0.98-1.47)	.08
Overt anger	1.04 (0.85-1.26)	.73	1.02 (0.84-1.24)	.81
Social support	1.08 (0.90-1.31)	.39	1.12 (0.93-1.36)	.23
Additional Dichotomous Measures of Social Support				
Married	0.87 (0.57-1.33)	.53	0.82 (0.54-1.25)	.35
Living with other(s)	1.05 (0.66-1.67)	.83	1.02 (0.63-1.63)	.95

Abbreviations: AX, Anger Expression Scale; BDI, Beck Depression Inventory; CI, confidence interval; GHQ-20, 20-item version of the General Health Questionnaire; HR, hazards ratio; MI, myocardial infarction; MSPQ, Modified Somatic Perception Questionnaire; PSSS, Perceived Social Support Scale; S-STAI, state portion of the State-Trait Anxiety Inventory; VAS, visual analog scale.

*For continuous measures, the HRs are per SD increase.

†Adjusted for age, sex, educational level, daily smoking, previous MI, thrombolytic treatment at index admission, Q-wave MI, Killip class greater than 1, revascularization at index admission, left ventricular ejection fraction, and prescription of hypoglycemic agents (for those with diabetes mellitus) and β-blockers at hospital discharge.

‡Analysis based on logarithmically transformed data.

tivity score ($P=.02$) and the residual BDI somatic ($P=.02$) and cognitive ($P=.03$) subscale scores all remained $P<.05$ in the total model (**Table 5**).

COMMENT

Our data suggest that the previously reported strong link between self-report BDI scores and long-term cardiac-related mortality is related to the BDI's ability to measure 2 separate prognostic components: negative affectivity and some unique aspect of depression itself. Not only do these results imply that there may be more than one psychological target for improving post-MI prognosis, and that the mechanisms underlying the prognostic importance of psychological factors are likely to be complex, but they also help to explain some of the inconsistencies between previous studies of anxiety, distress, and depression symptoms in patients with established cardiac disease.

When our psychological indexes were analyzed separately, we found that although the relationship with long-term cardiac prognosis was most marked for depression symptoms (as assessed with the BDI), the S-STAI, a measure of state anxiety, and the GHQ-20, a measure of psychological distress, were also related to 5-year cardiac-related mortality. While there were no apparent long-term links for any measures of social support or anger, one component of anger, the AX anger-in subscale, also had a significant relationship, but only during the first post-MI year. After adjustment for multiple indexes of cardiac disease severity and treatment, only the long-term link with the BDI remained significant.

The issue of covariate control is complex.[27-29] If a factor is part of the causal pathway between a given psychological variable and prognosis (eg, low perceived social support in the case of depression), control for that factor will eliminate part of the relationship between the psychological factor and the outcome. This is not true confounding, and statistical adjustment leads to an underestimation of the prognostic importance of the psychological factor being explored. To ensure that this was not the case with covariate adjustment in our study, as suggested by Algra,[29] we reassessed the associations between the S-STAI and the GHQ-20 and prognosis, controlling for each individual baseline covariate alone. For the S-STAI, no individual adjustments increased the *P* value to above .20; separate control for previous MI, Killip class, and left ventricular ejection fraction each increased the *P* value for the GHQ-20 score to above .20.

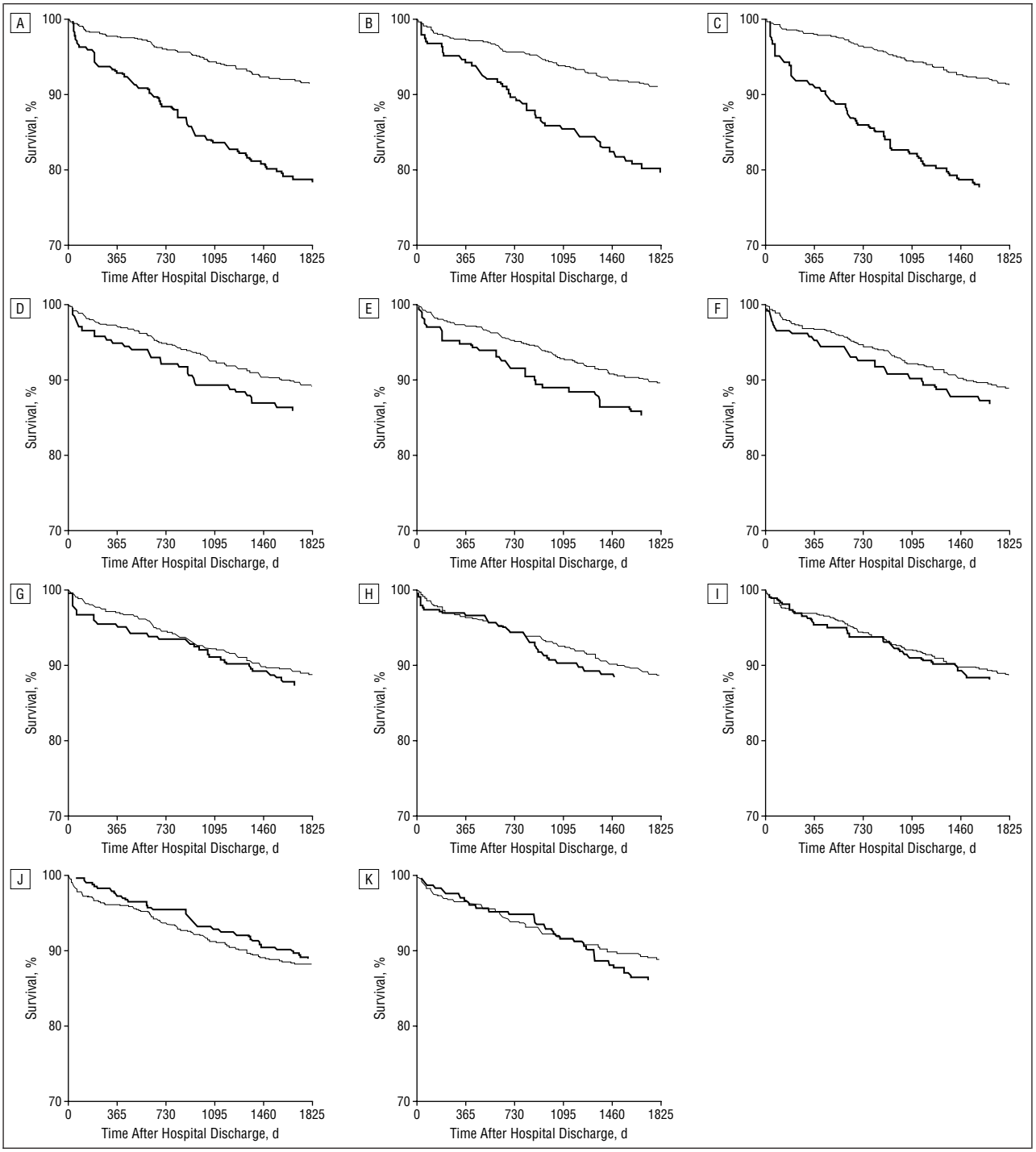

Figure 1. Five-year sex- and age-adjusted cardiac-related-death–free survival after a myocardial infarction in relation to psychological and social variables during admission (dichotomization based on the upper vs the lower 3 quartiles, except for social support measures, which are dichotomized at the lower vs the upper 3 quartiles). A, Beck Depression Inventory (BDI). B, The cognitive subscale of the BDI. C, The somatic subscale of the BDI. D, The state portion of the State-Trait Anxiety Inventory. E, The 20-item version of the General Health Questionnaire. F, Modified Somatic Perception Questionnaire. G, The anger-in subscale of the Anger Expression Scale (AX). H, The anger-out subscale of the AX. I, Perceived Social Support Scale. J, Number of close relatives. K, Number of close friends.

It is hard to argue that current distress caused a previous MI or poor cardiac functioning, and it is more likely that the apparent link between the GHQ-20 score and prognosis is truly confounded by cardiac disease severity.

All of the measures with significant prognostic associations were fairly strongly intercorrelated, and factor analysis revealed that all, including the AX anger-in subscale score, shared a common underlying dimension of negative affectivity. Friedman et al[30] administered the BDI, the S-STAI, the AX, several measures of hostility, and the NEO Five-Factor Inventory,[31] including a neuroticism subscale, to a sample of undergraduates. They found that the S-STAI, the BDI, and the AX anger-in subscale all loaded most heavily on the same factor as the NEO Five-Factor Inventory neuroticism subscale, with the other measures of anger, including the AX

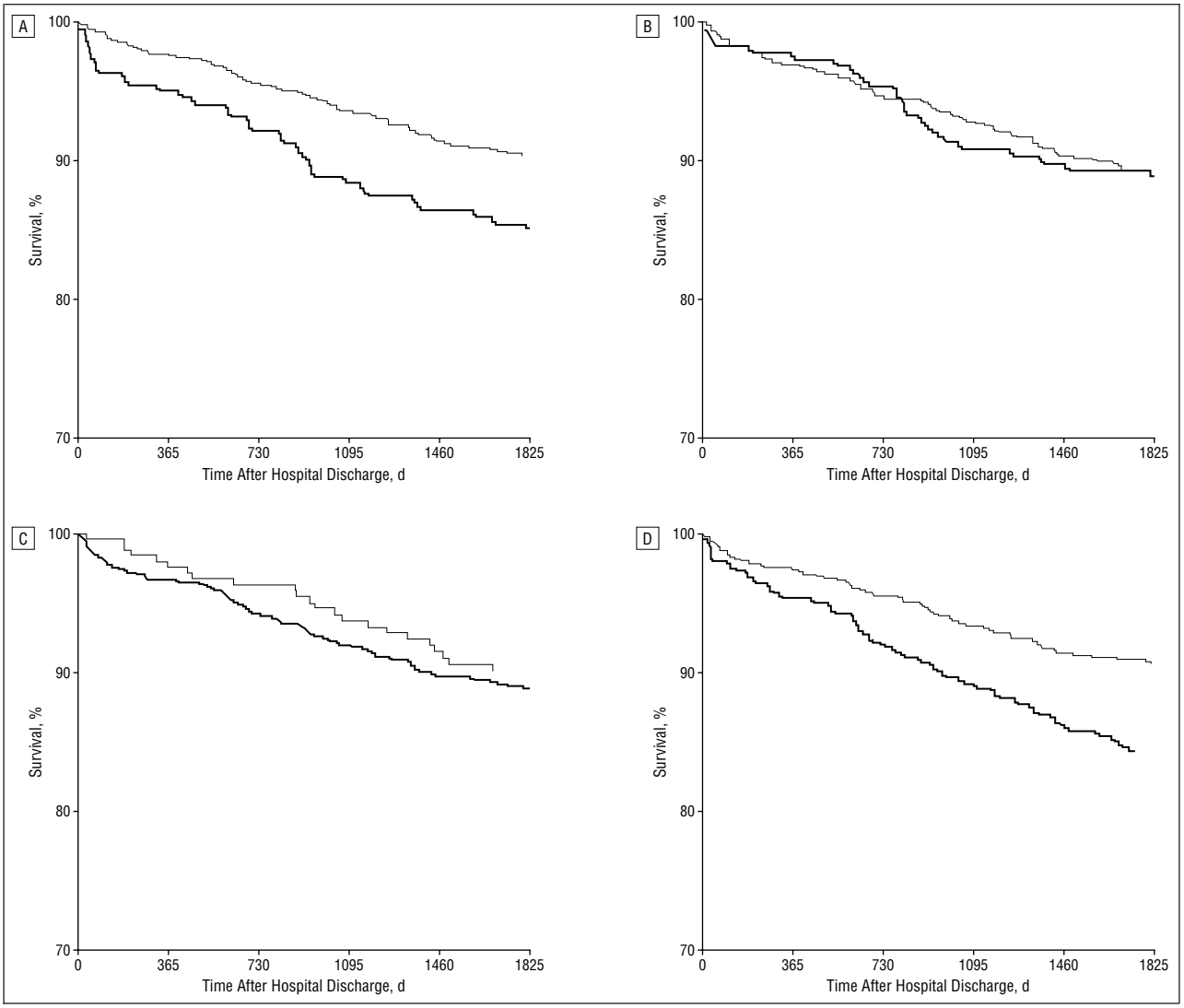

Figure 2. Five-year sex- and age-adjusted cardiac-related-death–free survival after a myocardial infarction in relation to factor scores (A, negative affectivity; B, overt anger; and C, social support) and the residual Beck Depression Inventory score (D) during admission (dichotomization based on the upper vs the lower 3 quartiles, except for the social support factor, which is dichotomized at the lower vs the upper 3 quartiles).

anger-out subscale, loading on factors linked to cynicism, overt hostility, and, to a lesser extent, the personality dimension of low agreeableness. Similar results were found by Martin and colleagues.[32,33] However, once the negative affectivity dimension was removed from our data, neither the resulting overt anger nor the social support factor had any relationship with cardiac survival, paralleling the results for the individual scales.

While there are data suggesting that some aspects of anger may be related to the development of coronary artery disease in initially healthy subjects, and there have been many laboratory stress studies showing the short-term pathophysiological consequences of anger, there is little evidence that anger or the related concepts of hostility, cynicism, or type A behavior are associated with objective health outcomes in patients with established coronary artery disease.[2,4,34] Thus, the present results showing no association with long-term prognosis for the overt anger dimension, the AX anger-out subscale, or any of the individual VAS for anger frequency, intensity, and duration are not surprising.

The literature[28] on social support in patients with cardiac disease is more complicated, not only in terms of results, but also in terms of the various measurement approaches used. While some investigators have studied perceptions of positive social support or the presence of a close confidant, others have looked at the frequency of various social contacts, and still others have investigated the size and complexities of social networks; most studies have simply used various proxy measures of social support, primarily marital status or living alone. Although a review of this extensive literature is beyond the scope of this article, the results of studies using proxy measures are the most heterogeneous. Most recent publications,[35-37] evaluating social support using more extensive measures, have shown that less social support or fewer social ties are associated with higher risks of major cardiac events in patients with coronary artery disease. However, none of the individual measures in our data set, including a measure of perceived support, indexes of network size, and the proxy measures of marital status and living alone, was associated with long-

Table 4. Multivariate Model for 5-Year Cardiac-Related Mortality Based on the Total BDI Score

Variable	Fully Adjusted HR (95% CI)	*P* Value
Residual BDI score	1.44 (1.17-1.78)	.001
Factor score		
Negative affectivity	1.23 (1.00-1.53)	.05
Overt anger	1.04 (0.86-1.26)	.71
Social support	1.12 (0.93-1.35)	.23
Age (per year increase)	1.04 (1.02-1.07)	<.001
Female sex	0.74 (0.48-1.16)	.19
<8 Years of education	0.89 (0.59-1.33)	.56
Daily smoker	1.20 (0.77-1.87)	.43
Previous MI	2.09 (1.37-3.18)	.001
Thrombolysis at index admission	0.63 (0.39-1.00)	.05
Q-wave MI	1.24 (0.83-1.86)	.29
Killip class >1	1.37 (0.87-2.17)	.18
Left ventricular ejection fraction ≤35%	2.00 (1.27-3.14)	.003
Revascularized at index admission	0.52 (0.29-0.91)	.02
Prescribed at hospital discharge		
Antidiabetic medication	2.11 (1.36-3.27)	.001
β-Blockers	0.71 (0.47-1.07)	.10

Abbreviations: BDI, Beck Depression Inventory; CI, confidence interval; HR, hazards ratio; MI, myocardial infarction.

Table 5. Multivariate Model for 5-Year Cardiac-Related Mortality Based on the BDI Cognitive and Somatic Subscales

Variable	Fully Adjusted HR (95% CI)	*P* Value
Residual BDI subscale		
Cognitive	1.23 (1.02-1.48)	.03
Somatic	1.33 (1.06-1.67)	.02
Factor score		
Negative affectivity	1.28 (1.03-1.58)	.02
Overt anger	1.01 (0.83-1.23)	.90
Social support	1.14 (0.95-1.37)	.16
Age (per year increase)	1.04 (1.02-1.07)	<.001
Female sex	0.74 (0.48-1.16)	.19
<8 Years of education	0.87 (0.58-1.31)	.51
Daily smoker	1.22 (0.78-1.91)	.39
Previous MI	2.09 (1.37-3.19)	.001
Thrombolysis at index admission	0.63 (0.39-1.01)	.05
Q-wave MI	1.26 (0.84-1.88)	.26
Killip class >1	1.37 (0.86-2.17)	.19
Left ventricular ejection fraction ≤35%	1.99 (1.26-3.13)	.003
Revascularized at index admission	0.52 (0.30-0.92)	.02
Prescribed at hospital discharge		
Antidiabetic medication	2.10 (1.35-3.27)	.001
β-Blockers	0.73 (0.48-1.12)	.15

Abbreviations: BDI, Beck Depression Inventory; CI, confidence interval; HR, hazards ratio; MI, myocardial infarction.

term prognosis. Furthermore, there was a good deal of overlap between our measures of social support and all 3 factored together independently from negative affectivity and overt anger. The factor score for social support was also unrelated to long-term prognosis. It is unclear why our sample showed no evidence of impact of any measure of social support; it is possible that the literature on social support has a publication bias against negative results. However, a previous publication on our data concerning the importance of social support in 1-year prognosis revealed a significant interaction between the dichotomized BDI score and perceived social support. Patients with high levels of social support did not experience an increase in risk associated with depression, probably because they were the most likely to experience an improvement in depressive symptoms during the year.[13] Additional analysis[14] showed that baseline social support was only linked to changes in depressive symptoms in those with mild depression, but not in those with more severe depression, suggesting a complicated relationship between changes in self-reported depression, social support, and prognosis over time. Initial analyses for the present article examining interactions between the individual measures of support, and the factor score for social support, and each of the other measures of negative emotions and the other factor scores showed no significant interactions in predicting long-term prognosis (data not shown).

While the dimension of negative affectivity was tapped in our data by the cognitive and somatic symptoms of depression (BDI), state anxiety (S-STAI), somatic anxiety symptoms (Modified Somatic Perception Questionnaire), psychological distress (GHQ-20), anger-in subscale (AX), and higher scores on the VAS of stress, in previous studies in patients with cardiac disease, it has probably been reflected by various other individual self-report measures related to anxiety and distress. Some of these studies[37-40] have found significant associations with prognosis, and others[41,42] have not. Although many differences exist between these studies, the lack of consistent results is at least in part due to the increased error in measurement inherent in the use of single measures. Although some studies of psychological risks in patients with cardiac disease have measured more than one concept, most typically anxiety and depression, the theoretical importance of including multiple measures of multiple concepts[6,30] has been largely ignored. This is probably because of concerns over type II error rates with multiple measures in small samples, coupled with the need for clinically feasible approaches to screening.

Our results are limited by the characteristics and medical treatment of the current sample of Canadian patients treated at major medical centers in the early 1990s. They are also limited by the original choice of measures. While we included multiple measures of anxiety, anger, and social support, there was only one measure of depression, the BDI. As described in previous publications,[12-14] because of budget and time constraints in conducting interviews with hospitalized patients, there was no diagnostic assessment of either current or past depression. However, such dichotomous measures could not have been included in factor analyses. Furthermore, previous analyses of the present data showed that increases in the risk of long-term cardiac-related mortality are apparent even with BDI scores below the traditional cut point of 10 (considered indicative of at least mild to moderate depression symptoms), and that after adjustment for cardiac disease severity, patients with moderate BDI scores (11-18) experience as great an increase in risk as those with the highest scores (≥19 [probably representing major depression]).[14] Thus, it seems un-

likely that the increased risk is dependent on the diagnostic entity of major depression during hospitalization. Many[43,44] have argued that even minor elevations of depression symptoms represent time fluctuations in the same chronic affective illness, and that distinctions between major and subthreshold depression may not be important. However, psychiatric practice guidelines remain based on expert clinician diagnosis, and the evidence of treatment efficacy in patients with milder conditions remains to be demonstrated in patients with cardiac disease and in those with depression in general.

Although not all studies have reported a significant relationship between measures of depression symptoms and cardiac prognosis,[45] or one that remained significant after covariate adjustment,[46-48] most recent studies[36,37,40,49-52] supported a link in patients with established cardiac disease. The combined quality and quantity of the published data continues to support the strong relationship summarized in several major literature reviews.[1-3,53,54] Our results extend this literature to suggest that there is some mortality-related aspect of self-reported depression that goes beyond simple negative affectivity, neuroticism, or the tendency to respond with negative emotions. It probably also goes beyond the somatic symptoms of depression, including fatigue, as suggested by the evidence of an independent impact of the residual cognitive and somatic BDI subscale scores and control for our ability to measure patients' cardiac conditions. Furthermore, beyond the residual BDI score, overt anger, and social support, the negative affectivity score probably reflects the interplay between personality traits, coping, perception of cardiac disease severity, health behavior, and active efferent pathways between emotions and the cardiovascular system. We can speculate that negative affectivity represents a persistent personality factor, whereas the aspect of self-reports of depression symptoms that is independent of negative affectivity represents cyclical symptom changes associated with depression. Perhaps it is negative affectivity that is most associated with damaging health behaviors, and it is the residual aspect of depression that has the strongest pathophysiological correlates. In combination with the recent disappointing results of randomized trials of cognitive behavioral therapy[55] and sertraline hydrochloride[56] as separate treatments for post-MI depression, our data also suggest that cognitive behavioral therapy or other structured psychotherapy and antidepressants may be needed to optimally target the behavioral and physiological mechanisms of psychological risk in patients following an MI. Additional research is needed to learn more about the active ingredients of the relationships observed and their implications for treatment.

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