Usefulness of Persistent Symptoms of Depression to Predict Physical Health Status 12 Months After an Acute Coronary Syndrome

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Brief Title: Symptoms of Depression and Physical Health Status Post-ACS

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Abstract

Past research has focused on the relation between post-ACS depression and subsequent cardiac morbidity and mortality. However, the relationship between depression and quality of life during recovery remains unclear. We investigated whether symptoms of depression during hospitalization for acute coronary syndrome (ACS) or the course of depressive symptoms post-ACS predict physical health status 12 months post-ACS, controlling for physical health status at the time of the ACS. This was a prospective study of 425 ACS patients assessed with the Beck Depression Inventory (BDI) and SF-12 Health Survey during hospitalization and 12 months later. Linear regression was used to assess the relationship between in-hospital BDI scores and BDI symptom trajectory post-ACS with physical health status 12 months later, controlling for baseline physical health status, age, gender, Killip class, history of acute myocardial infarction, and cardiac diagnosis. Baseline BDI scores predicted 12-month physical health ($p < .001$). Compared to nondepressed patients, only patients with persistent symptoms of depression were at risk for poorer physical health. Patients with newly-developed depressive symptoms post-ACS were at slightly increased risk for worsened physical health ($p = .060$), whereas patients with transient depressive symptoms were not at increased risk. In conclusion, these results underscore the importance of assessing depression both at the time of ACS and on an ongoing basis.

It is not clear from existing studies whether symptoms of depression measured during hospitalization for acute coronary syndrome (ACS) predict changes in physical health status or the degree to which the course of depressive symptoms over time might be related to physical health outcomes. The main objectives of this study were to investigate whether symptoms of depression measured during hospitalization for ACS predict physical health status 12 months later controlling for baseline levels and to determine whether the course of physical health status over 12 months post-ACS is related to the course of depressive symptoms over the same time period.

Methods

Adult patients who were diagnosed with an ACS (i.e., acute myocardial infarction [AMI] or unstable angina [UA]) were recruited by a research nurse on the 2nd to 5th day of acute hospitalization. Patients were recruited from 12 coronary care units in both large urban teaching hospitals and community hospitals in small- and medium-sized cities across Southcentral Ontario, Canada. The methods of the study have been described previously.[1] Patients were excluded if they were medically unstable or unable to read or speak English. Eligible patients who agreed to participate gave informed, written consent and were provided with a self-report questionnaire. All patients received standard aftercare for their ACS. In addition to the self-report questionnaire that was completed during the index hospitalization, patients were followed-up at home by mail 6 and 12 months after the ACS and completed an additional self-report questionnaire that included an assessment of depressive symptoms and physical health status. The original study protocol was approved by the Research Ethics Boards of the University of Toronto and University Health Network.

Symptoms of depression were assessed using the BDI,[2] which is a 21-item measure of depressive symptoms. Each item has four possible answers, scored 0-3, indicating increasing symptom severity. Total scores range from 0-63. Respondents are instructed to describe the way they have been feeling during the past week. The authors of the BDI recommend a cutoff score of ≥ 10 for at least mild symptoms of depression.[3] The Physical Component Summary (PCS) of the SF-12 was used to measure physical health status. The SF-12[4] is a 12-item version of the SF-36.[5] It provides empirically-derived physical and mental health composite summary measures, which reproduce the composite scores of the SF-36 with considerable accuracy (multiple R squares of 0.91 and 0.92, respectively).[4] Raw scores on the SF-12 PCS are standardized to range from 0 to 100 with 0 representing the poorest health status. The mean standardized score for the U.S. population is 50.[4] During the hospitalization for the ACS, patients rated their health status during the 4 weeks prior to admission. Killip class, measured on a 4-point scale, was used to indicate the presence of heart failure at the time of the AMI. Killip class and history of previous AMI were determined from the medical record. Other health status variables, such as comorbidities and smoking status were determined from the patient health questionnaire. Sociodemographic data, including age, sex, marital status, education, and income, were assessed in-hospital. Depressive symptoms and physical health status were assessed during the hospitalization and at each follow-up.

Patient demographic and medical data were compared between patients with at least mild symptoms of depression in the hospital (BDI ≥ 10) and patients who scored < 10 on the BDI in-hospital. Differences between the groups on categorical variables were assessed using the χ^2 statistic and on continuous variables with independent samples 2-tailed *t* tests. Patients were included in analyses if they were missing 3 or fewer items on the BDI and the SF-12 both in-

hospital and 12 months post-ACS and if they were not missing any of the demographic or cardiac disease severity variables that were included in the initial specifications of the multiple regression equations. For patients missing fewer than 3 items on the BDI or SF-12, missing values were imputed using the SPSS Missing Values Analysis module expectation maximization algorithm (SPSS version 14.0, Chicago, IL).

To assess the association between depressive symptoms in-hospital and change in physical health status from pre-ACS to 12 months post-ACS, multiple linear regression analysis was conducted. SF-12 PCS score 12 months post-ACS was the dependent variable. Predictor variables were pre-ACS PCS, age, sex, diagnosis (AMI versus UA), history of AMI, Killip class > 1, and in-hospital BDI scores. Thus, the regression weights for BDI scores can be interpreted as an estimate of the degree of change in physical health status from pre-ACS to 12 months post-ACS associated with symptoms of depression after controlling for confounders.

To assess whether different patterns of depressive symptoms over time related differently to change in health status outcomes, we classified depressive symptoms as *not present*, *persistent*, *transient*, or *new*.[6] Depressive symptoms were classified as *not present* if patients scored < 10 on the BDI both in-hospital and 12 months post-ACS. Symptoms were classified as *persistent* if patients scored ≥ 10 on the BDI at both time points. Symptoms were classified as *transient* if patients scored ≥ 10 on the BDI in the hospital, but scored < 10 a year later and symptoms improved by a statistically reliable amount. Depressive symptoms were labeled *new* if patients scored below 10 on the BDI in-hospital, scored 10 or higher 12 months later, and experienced a statistically reliable increase in symptoms. Statistically reliable change was defined to have occurred if the magnitude of change in BDI score was large enough to be statistically reliable compared to normal test-retest fluctuations.[7] Jacobson and Truax's reliable

change index (RCI)[8] was used to determine if statistically reliable change occurred for each patient, assuming a test-retest reliability of the BDI of .90.[9] Statistically reliable change was included in the study definitions in order to avoid classifying patients whose BDI scores changed non-meaningfully (e.g., from 10 to 9) as having experienced *transient* or *new* symptoms of depression.

To evaluate whether particular patterns of depressive symptoms (*not present, persistent, transient, new*) were differentially associated with change in physical health status from pre-ACS to 12 months post-ACS, multiple linear regression analysis was conducted, similar to the multiple regression that was conducted with baseline BDI symptoms. The only difference was that instead of baseline BDI scores, dummy-coded symptom classification variables (*persistent, transient, new*) were entered into the prediction equations with *not present* as the reference category. All analyses were conducted using SPSS version 14.0 (Chicago, IL), and all statistical tests were 2-sided with a $p < .05$ significance level.

Results

A total of 913 patients consented to participate, and 812 patients had complete BDI, SF-12, sociodemographic, cardiac disease, and risk factor data in-hospital. Of the 812 patients who had complete baseline data, 331 did not provide complete data at 12 months, 45 died within 12 months of the index ACS, and the vital status of 11 patients was unknown. Thus, a total of 425 patients with complete baseline and follow-up data were included in the analyses. Patients with complete data were significantly older (mean age 62.4 years vs. 59.5 years, p = .001), and more likely to be male (71.5% vs. 59.8%, p < .001), to earn over CAD$50,000 per year (49.2% vs. 41.3%, p = .046), to be married (79.9% vs. 69.9%, p = .002), to have education beyond high school (35.2% vs. 26.9%, p = .015), and to have an admission diagnosis of AMI (58.4% vs.

47.4%, p = .003) than those without complete data. They were less likely to have smoked in the last 2 years (29.7% vs. 39.7%, p = .004). Patients with complete data also had fewer depressive symptoms (i.e., mean BDI scores 7.7 vs. 9.6, p < .001) and better physical function (i.e., mean SF-12 PCS scores 41.9 vs. 39.7, p < .001) than those without complete data.

As shown in Table 1, patients with a BDI score ≥ 10 in-hospital were significantly less likely to be male, to report family income over CAD$50,000, to be married or living with a partner, or to have more than high school education. They were also significantly more likely to have hypertension and diabetes mellitus and to have smoked in the last 2 years, but less likely to have an admission diagnosis of AMI.

The percentage of patients classified as having at least mild symptoms of depression (BDI ≥ 10) was 28.9% (n = 123) in-hospital and 24.0% (n = 102) 12 months post-ACS. Based on the overall in-hospital mean and standard deviation of the BDI (7.7 ± 7.1) the RCI required an increase or decrease of at least 6.2 points on the BDI for statistically reliable change. Of 425 patients, 66.1% (n = 281) were classified as symptoms *not present*, 20.0% (n = 85) as having *persistent* symptoms, 8.9% (n = 38) as having *transient* symptoms, and 4.9% (n = 21) as having *new* symptoms emerge between the index ACS and 12 months post-ACS. The mean BDI score during the index hospitalization was highest for patients with *transient* symptoms (19.3 ± 9.2), followed by patients with *persistent* symptoms (14.8 ± 5.8), patients classified as *not present* (4.2 ± 2.7), and patients with *new* symptoms (3.9 ± 2.8). Based on t tests and adjusting for multiple comparisons, all mean BDI differences between groups were significant (p < .05) with the exception of the comparison between patients in the *not present* and *new* groups. Mean BDI scores at 12 months were highest for patients with *new* symptoms (17.0 ± 8.0), followed by patients with *persistent* symptoms (14.0 ± 7.3), patients with *transient* symptoms (6.3 ± 4.4), and

patients in the *not present* group (3.8 ± 3.0). All differences between groups were significant ($p < .05$) except the difference between patients with *persistent* and *new* symptoms.

Patients with a BDI score ≥ 10 in-hospital had significantly poorer physical health status 12 months after the ACS compared to patients with a BDI score < 10 (Table 1). After controlling for pre-ACS physical health status, age, sex, diagnosis, history of AMI, and Killip class, higher BDI scores during the index hospitalization continued to be significantly associated with both poorer physical health status 12 months post-ACS ($p< .001$). Younger age ($p < .001$) and male sex ($p = .018$) were associated with better physical function at 12 months, controlling for baseline physical function (Table 2).

When BDI symptom classifications (*persistent, new, transient* with *not present* as reference) were entered into the regression equation instead of baseline BDI scores (Table 3), *persistent* symptoms significantly predicted worse physical health at 12 months compared to pre-ACS physical health ($\beta = -.220$, $p < .001$). *New* symptoms tended to predict worse physical health, but non-significantly ($\beta = -.073$, $p = .060$). Using change definitions based on 6-month BDI scores rather than 12-month BDI scores did not affect predictions meaningfully (*persistent*, $\beta = -.178$, $p < .001$; *new*, $\beta = -.061$, $p = .152$; *transient*, $\beta = .037$, $p = .379$). The significance or non-significance of other predictors did not change when symptom classifications rather than in-hospital BDI scores were used to predict physical health status.

Variables that were not initially specified for entry into the regression equations (Table 1) were added, but none of these variables significantly predicted 12-month physical health status. In addition, since BDI and SF-12 score distributions were somewhat skewed, all regression equations were redone using transformed BDI and SF-12 variables. Because results

remained unchanged, only non-transformed variables are presented in Tables 2 and 3 to facilitate interpretation.

Discussion

The major finding of this study is that symptoms of depression as measured by the BDI during hospitalization for ACS predict physical health status 12 months later, even after controlling for pre-ACS physical health status, demographic, and health-related predictor variables. Only patients with *persistent* symptoms of depression, however, were at significant risk for poorer physical health outcomes at 12 months compared to pre-ACS levels. Patients who did not have elevated symptoms of depression during the hospitalization (i.e., patients who had an initial BDI score below 10), but who did have elevated symptoms 12 months later (*new* symptoms) tended to have worse physical health outcomes, although this was not significant. Patients with *transient* symptoms of depression were not at risk for worse physical health outcomes 12 months after ACS. This is particularly interesting because patients who were classified as having *transient* symptoms of depression had significantly higher mean BDI scores during the ACS hospitalization than any other patient group, and in-hospital depressive symptoms have typically been used to assess the relationship between depression and health outcomes, including morbidity and mortality, following ACS. The finding that patients with *persistent* or *new* symptoms of depression were at greater risk for poor outcomes compared to patients with initially high, but *transient,* symptoms, is consistent with findings recently reported by de Jonge and colleagues. Patients with incident depression after AMI in their study were at increased risk for cardiovascular events compared to non-depressed patients.[10] In another study, patients with significant depressive symptoms that increased after the AMI were also at increased risk for cardiovascular events.[11] These findings underscore the importance of

considering the trajectory of depressive symptoms in relation to health outcomes and the importance of re-assessing depression periodically during follow-up from an AMI. Despite very high initial levels of depressive symptoms, patients who experienced *transient* symptoms of depression were not at risk for poorer physical health 12 months after ACS compared to pre-ACS levels. It may also explain why some studies have not found a prospective relationship between symptoms of depression during the ACS hospitalization and physical health status 4 to 12 months later,[12-15] since this relationship appears to depend not only on initial symptom levels, but also on the trajectory of depressive symptoms subsequent to discharge.

This is the first study that has examined the relation between the course of depressive symptoms and physical health outcomes that has incorporated the construct of statistically reliable change of depressive symptoms. Parashar et al.[6] also examined the effect of *persistent*, *transient*, and *new* symptoms of depression (determined by change from baseline to 1 month post-ACS) on physical limitations 6 month post-ACS, but did not include statistically reliable change of depressive symptoms in their analyses. They found that patients in each of these categories were at significantly greater risk for increased physical limitation with the highest risk for patients with *persistent* symptoms, followed by *new* symptoms and *transient* symptoms. Compared to our results showing only marginally significant effects of *new* symptoms of depression on risk for poorer physical health status, Parashar et al. found a large and significant effect for patients with *new* symptoms. However, this difference may have resulted from the lack of specification of a minimum magnitude of change for statistical reliability in their analyses. Similarly, the presence of *transient* symptoms in the present study was not a risk factor for worse physical function outcomes, but was a significant risk factor in the Parashar et al. study. Thus,

our findings underscore the importance of specifying statistically reliable change scores when analyzing changes in depression as a predictor for physical health outcomes.

There are several limitations to our study. Approximately half of the patients who were recruited for this study did not have complete baseline and follow-up data. Patients without complete data differed from those with complete data on several variables. For example, patients without complete data had more depressive symptoms and worse physical health at baseline. Thus, patients who were included in our follow-up analyses may have had a better psychosocial/health status at baseline, which could have introduced a bias to our results.

The most recent guidelines of the American College of Cardiology and American Heart Association for the management of patients with ST-elevation myocardial infarction give a Class I recommendation to assessing psychosocial status. The guidelines note "the psychosocial status of the patient should be evaluated, including inquiries regarding symptoms of depression, anxiety, or sleep disorders and the social support environment."[16] The findings of this study emphasize the importance of assessing symptoms of depression, not only at the time of the acute ACS hospitalization, but also subsequently during follow-up visits.

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