Timing of Depressive Symptom Onset and In-Hospital Complications Among Acute Coronary Syndrome Inpatients

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Abstract

Introduction—Recent research has reported an association between in-hospital depression and poorer long-term prognosis and a greater risk of in-hospital complications. The purpose of the current study was to examine the relationship between past and incident depressive symptoms and in-hospital complications in acute coronary syndrome (ACS) inpatients.

Methods—Nine hundred and six ACS inpatients from 12 coronary care units participated in the study. Incident depressive symptoms were assessed through the Beck Depression Inventory (BDI), and participants were asked if they had a past history of depressed mood for more than 2 weeks. In-hospital complications were noted as present or absent by nurses. Logistic regression analyses were conducted.

Results—Four hundred ninety-two patients (58.4%) experienced an in-hospital complication, the most common being ischemia (48.8%) and cardiac arrest (7.2%). After adjusting for prognostic indicators, incident (OR=2.19; 95% CI 1.38–3.45) and past combined with incident (OR=1.82; 95% CI 1.09–3.04) depressive symptoms were significantly associated with an increased risk of experiencing an in-hospital complication.

Conclusion—Depressive symptoms were significantly related to in-hospital complications. Corroborating other studies on the timing of depressive symptoms in relation to long-term mortality, incident symptoms in particular seem to be prognostic. This suggests that acute emotions may be triggering cardiac complications, and early identification of emotional symptoms is warranted.

Keywords

depression; complications; coronary artery disease

Introduction

The association between depression and coronary artery disease (CAD) has been well documented.^{1–3} Depression has been shown to be related to a greater risk of CAD onset, and poorer long-term prognosis among those with established CAD,^{1–3} although mixed results are found.⁴ More recently, research has shown that new onset depression at the time of a cardiac hospitalization is particularly prognostic. Our group⁵ and others^{6–8} have shown that new onset depression is related to mortality, and it is also shown to relate to recurrent events⁹ when compared to remitted or pre-cardiac hospitalization depression.

The relationship between new onset depression and cardiac outcome suggests acute pathophysiological mechanisms known to be associated with depression such as alterations in platelet activity, inflammation and the sympathetic nervous system rather than behavioural mechanisms might be responsible. However, to our knowledge only one study has examined levels of depression before or shortly after a cardiac event and its effect on in-hospital complications.¹⁰ This study which assessed major depression only at the time of hospitalization found that it was related to the occurrence of ventricular arrhythmias, heart failure, and reinfarction. More research is needed to determine whether depressive symptoms at the time of a cardiac event versus pre-event are related to acute cardiac health. The purpose of the current study was to examine the relationship of depressive symptom timing to in-hospital complications, including re-infarction, arrhythmias, ischemia and cerebrovascular accidents.

Methods

Procedure and Design

This was a cross-sectional substudy of a larger prospective longitudinal multi-site study, and the sample and methods are outlined in further detail elsewhere.¹¹ Participants were recruited in the CCU by a research nurse on the second to fifth day of hospitalization. Inclusion criteria were patients diagnosed with myocardial infarction (MI) or unstable angina (UA), and who were 18 years of age or older. Exclusion criteria consisted of patients who were too ill or confused to participate, in-hospital death, and lack of English language proficiency. Those who met study criteria and agreed to participate signed a consent form and were provided with a survey. The questionnaire included sociodemographic, disease-related, and psychosocial measures. Consent was also obtained to link participant's self-report questionnaire data with their clinical data from the Managing the Acute Coronary Syndromes – A Tracking Project (MACSTRAK) registry. The study was approved by the University Health Network and all participating institutions' Research Ethics Boards.

Participants

Consecutive patients who were diagnosed with an MI or UA in twelve coronary care units (CCUs) across south central Ontario, Canada were approached for the study. Some participating hospitals were urban teaching hospitals (22.6%), while others were community hospitals located in medium and small-sized cities. Of the almost 1800 patients approached, 906 (69% response rate) consented to participate in the study. Participants were significantly

younger than those who refused or were ineligible to participate ($p < .001$). Significantly more males agreed to participate than females ($p < .001$), and more married and fewer widowed individuals agreed to participate ($p < .001$). Participants' ages ranged from 31 to 93 years.

Measures

Sociodemographic data were collected via self-report and included marital status, level of education, level of income, and living situation. Participants also self-reported (yes/no) whether they smoked in the past 2 years, had a family history of cardiac disease, had diabetes or dyslipidemia. Date of birth and sex were recorded from patient charts. Other prognostic variables such as systolic blood pressure and Killip¹² class were recorded by the research nurse.

Outcome variable—In-hospital events or procedures following initial management (i.e., thrombolysis or primary angioplasty) were recorded prospectively in the CCU by the primary caregiver for the MACSTRACK registry. The complications assessed were as follows: requirement for intubation and ventilation, temporary transvenous pacemaker, receiving inotropes or thrombolysis, retrosternal chest pain, new or repeat MI, undergoing angioplasty, aortic balloon pump, ventricular fibrillation or tachycardia, sudden cardiac arrest, cerebrovascular accidents, and experiencing a major bleed. A variable was computed to denote presence or absence of any in-hospital complication.

Exposure variables—Depressive symptoms were assessed in hospital by two means: the Beck Depression Inventory (BDI) was administered to assess incident symptoms, and participants were also asked to self-report a history of depressed mood for more than 2 weeks (yes/no). The BDI¹³ is a reliable and well-validated 21-item scale using a forced-choice 4-alternative response format that has been widely used in the general population, and in chronic illness populations including cardiac patients.^{14–17} The internal consistency of the BDI was $\alpha = 0.87$ in the current sample. The BDI total score was dichotomized at a cutoff of 10, indicative of mild or greater symptomatology. A composite four-level variable was computed to reflect timing of depressive symptom onset: past history only, incident depressive symptoms only (i.e., BDI > 10), both past and incident depressive symptoms, and neither.

Statistical Analyses

A descriptive examination of the variables was performed. Differences in participant characteristics by in-hospital complications were tested using chi-square analyses and t-tests as appropriate. Finally, a logistic regression analysis controlling for prognostic variables was performed, to test the relationship between depressive symptom timing and presence of any in-hospital complications.

Results

Of the 906 participants in this study, 492 (58.4%) inpatients had an in-hospital complication. Specifically, 442 (48.8%) had ischemia, 65 (7.2%) had sudden cardiac arrest, 12 (1.3%) had

arrhythmia, 6 (0.7%) had thrombolysis, 5 (0.6%) had angioplasty, 4 (0.4%) had an MI, 4 (0.4%) had a major bleed, and 2 (0.2%) had a temporary transvenous pacemaker. Differences in sociodemographic and clinical characteristics of patients by in-hospital complications are presented in Table 1. Females were more likely to experience an in-hospital complication than males.

Descriptive statistics for the two depression variables, total BDI score and the composite timing of depressive symptoms variable, are presented in Table 2. Overall, 275 (31.2%) participants had elevated depressive symptoms ($BDI > 10$) during hospitalization. T-tests revealed that patients who had an in-hospital complication had significantly higher BDI scores, indicative of greater depressive symptomatology. They were not however more likely to have a history of depressed mood. Chi-square analysis revealed the composite depression timing variable was also significantly related to the presence of in-hospital complications.

The logistic regression analysis predicting in-hospital complications is presented in Table 3. The overall model was significant ($p < .001$). Patients of younger age, with higher systolic blood pressure were more likely to experience an in-hospital complication. Depressive symptom timing was significantly related to in-hospital complications, such that patients with elevated depressive symptoms in-hospital only were over two times more likely to have an in-hospital complication, and those with a history of depressed mood and elevated in-hospital depressive symptoms were almost two times as likely to have an in-hospital complication.

Discussion

This study examined the effect of timing of depressive symptom onset on a comprehensive range of in-hospital complications. Approximately one-quarter of cardiac patients reported a history of depressed mood for more than a continuous 2 week period, one-third had elevated depressive symptoms at the time of hospitalization, with 14% reporting both. Over half of the patients experienced an in-hospital complication, most notably ischemia. Results revealed that elevated in-hospital depressive symptoms in particular confer over 2 times greater risk of in-hospital complications. In addition, patients with both past and incident depressive symptoms had almost two times greater risk of in-hospital complications.

Much of the prior literature on depression and cardiac outcomes has focused on chronic affect.¹⁸ However, there have been several methodologically robust studies showing that depressive symptoms at the time of a coronary event or procedure rather than prior to or following hospitalization is most central to patient outcome.^{5, 9, 19} This study has been the first to compare timing of depressive symptom onset in relation to acute in-hospital complications. Our results generally corroborate those of Huffman et al.¹⁰ They examined the relationship between major depressive disorder at the time of hospitalization only to ischemia, ventricular arrhythmias, heart failure, and recurrent MI. They found that depression was related to each of these outcomes except ischemia. Given that the most frequent complication in the current study was ischemia, and the current study did find a relationship between depressive symptoms and ischemia, further investigation is warranted. However, the fact that Huffman et al. utilized psychiatric interviews to ascertain depression

provides further credence to the relationship between depression at the time of an event and in-hospital complications.

This has lead to questions regarding the mechanisms linking depressed mood and cardiac disease. These findings suggest that the mechanisms at play might not be behavioural in nature leading to a chronic atherosclerotic process but rather point to more acute mechanisms such as sympathetic nervous system activation leading to disruption of atherosclerotic plaque, instigation of arrhythmias, or increased platelet aggregation.¹⁸ Indeed there is a well-established literature demonstrating how acute emotional states are related to cardiac events. Studies have documented relationships between incident anger and MI,²⁰ and mental stress and silent myocardial ischemia for example.²¹ However, caution is warranted when interpreting the results herein given the limitations of the measure of a past history of depression. Further investigation into the effects of chronic depression on the atherosclerotic process is warranted.

Indeed the relationship of depressive symptoms both in the past and at the time of hospitalization to in-hospital complications deserves closer scrutiny. It was not found to be significant in our previous study examining mortality in cardiac patients.⁵ However, the common denominator here is in-hospital depressive symptoms, and what might be their acute effects on the heart. Future research, preferably prospective in design that can tease apart the effect of acute versus chronic negative affect on the heart, is needed. Such prospective research could also rule out the possibility of recall bias explaining the results.

There are important policy and clinical implications stemming from these findings. For instance, there are substantially higher hospital costs associated with complications in cardiac patients.²² Thus, there may be both financial and prognostic motives for detecting and treating depression in cardiac patients at risk for higher complications. While the identification of patients at an increased risk is important, there is as of yet no evidence that treating elevated symptoms of depression results in better outcomes in the long-term,^{23, 24} or during hospitalization. Physical activity has shown some promise for long-term benefit,²⁵ and interventions such as mindfulness-based stress reduction may serve to counteract acute negative mood states.²⁶

Limitations

There are several limitations to this study, related to design, measurement and generalizability. With regard to design, depression items were administered concurrently with outcome assessment. Thus, this analysis was cross-sectional in design and no causal conclusions can be drawn nor can we be certain of the direction of effect. With regard to measurement, depressive symptoms were assessed via self-report, which is subject to bias. In future studies, the use of clinical interviews to assess depression according to diagnostic criteria is warranted. Second, the study failed to assess two potentially confounding factors, namely cocaine abuse leading to in-hospital withdrawal and selective serotonin reuptake inhibitor (SSRI) use. Given the older mean age in the sample, the latter factor might have been more influential. Research suggest that SSRI use among cardiac patients might well be associated with fewer in-hospital complications, since chronic use appears to reduce recurrent MI and cardiac death.^{27–29} Unfortunately, the current study did not assess SSRI

use at the time of hospitalization. In a previous study however¹¹, we showed that only 5% of this sample reported antidepressant use 6 months post-hospitalization, suggesting again that this potential confound may be slight. Finally, with regard to generalizability, differences in patients consenting to participate in this study versus those who declined or were ineligible may have biased study results.

Conclusion

Both the presence of elevated incident depressive symptomatology and of past combined with incident depressive symptoms were associated with approximately two times greater risk of in-hospital complications among this sample of cardiac inpatients, after controlling for other prognostic factors. Such findings highlight the significance of the acute effects of negative mood on the heart, and the importance of identifying elevated depression symptoms among hospitalized cardiac patients. More research on the effective management of coronary intensive care patients with acute depressive symptoms is needed.

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Table 1

Participant Characteristics by In-Hospital Complications

	No complications (n=350, 41.6%)	Complications (n=492, 58.4%)	Total (N=906)	p value
Sociodemographic characteristics, n (%)				
Age (% <65 yrs)	186 (53.1%)	283 (57.5%)	498 (55.0%)	0.21
Sex (% female)	108 (30.9%)	187 (38.0%)	320 (35.3%)	0.03
Education (%HS or less)	226 (66.7%)	337 (70.5%)	602 (68.4%)	0.24
Family income (%< \$50,000CAD)	152 (51.9%)	241 (58.4%)	423 (55.5%)	0.09
Marital Status (% married/ common law)	256 (74.0%)	363 (74.5%)	664 (74.1%)	0.86
Clinical characteristics, n (%)				
Killip Class (% class I)	292 (85.4%)	392 (81.7%)	717 (83.8%)	0.16
Family history of CVD (%yes)	195 (60.9%)	310 (67.1%)	543 (64.3%)	0.08
Diabetes (%yes)	81 (25.6%)	115 (25.2%)	212 (25.5%)	0.90
Dyslipidemia (%yes)	130 (42.3%)	214 (49.0%)	372 (46.3%)	0.07
Hypertension (%yes)	151 (47.2%)	197 (43.6%)	371 (44.6%)	0.32

Percentages take into account missing data for some variables.

HS = high school

CVD = cardiovascular disease

Table 2

Depressive Symptoms by In-hospital Complications

	No complications (n=350)	Complications (n=492)	Total (N=906)	p Value
Past History of Depressed Mood (%yes)	77 (21.0%)	111 (25.5%)	188 (23.4%)	.133
BDI (mean $\pm$ SD)	7.84 $\pm$ 7.27	9.54 $\pm$ 7.80	8.68 $\pm$ 7.49	0.001
Depressive Symptom Timing				.003
Past History only	34 (9.4%)	41 (9.6%)	75 (9.5%)	
Past History and Incident BDI>10	42 (11.6%)	69 (16.1%)	111 (14.1%)	
Incident BDI>10 only	47 (13.0%)	87 (20.3%)	134 (17.0%)	
Neither	238 (65.9%)	231 (54.0%)	469 (59.4%)	

Percentages take into account missing data for some variables.

BDI = Beck Depression Inventory

Table 3
Logistic Regression Analysis Predicting Presence or Absence of In-Hospital Complications

Variables	Wald	p	OR	95% C.I.
Sex (Male)	0.92	0.34	0.84	0.59 1.20
Age	4.17	0.04	0.99	0.97 1.00
Systolic Blood Pressure (>130)	3.88	0.05	1.38	1.00 1.89
Smoking (yes)	0.42	0.52	0.89	0.61 1.28
Family history of cardiac disease (yes)	0.75	0.39	1.16	0.83 1.61
Diabetes (yes)	0.70	0.40	0.85	0.58 1.25
Dyslipidemia (yes)	0.01	0.93	1.02	0.74 1.40
Killip class (1)	1.63	0.20	0.75	0.48 1.17
Depressive Symptom timing	13.90	0.003		
Past history only	0.42	0.52	1.19	0.70 2.05
Past History and Incident BDI>10	5.24	0.02	1.82	1.09 3.04
Incident BDI> 10 only	11.22	0.001	2.19	1.38 3.45