Effects of Depression and Anxiety Improvement on Adherence to Medication and Health Behaviors in Recently Hospitalized Cardiac Patients

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Impaired adherence to medications and health behaviors may mediate the connection between psychiatric symptoms and mortality in cardiac patients. This study assessed the association between improvements in depression/anxiety and self-reported adherence to health behaviors in depressed cardiac patients in the 6 months after cardiac hospitalization. Data were analyzed from depressed patients on inpatient cardiac units who were hospitalized for acute coronary syndrome, heart failure, or arrhythmia and enrolled in a randomized trial of collaborative care depression management (n = 134 in primary analysis). Measurements of depression (Patient Health Questionnaire-9), anxiety (Hospital Anxiety and Depression Scale, Anxiety subscale), and adherence to secondary prevention behaviors (Medical Outcomes Study-Specific Adherence Scale items) were obtained at baseline, 6 weeks 12 weeks, and 6 months. The association between improvement in depression/anxiety and adherence was assessed by linear regression after accounting for the effects of multiple relevant covariates. At all time points improvement in the Patient Health Questionnaire-9 was significantly and independently associated with self-reported adherence to medications and secondary prevention behaviors. In contrast, improvement in the Hospital Anxiety and Depression Scale, Anxiety subscale was associated with improved adherence only at 6 weeks. In conclusion, in a cohort of depressed cardiac patients, improvement in depression was consistently and independently associated with superior self-reported adherence to medications and secondary prevention behaviors across a 6-month span, whereas improvement in anxiety was not. **(Am J Cardiol 2012;109:1266–1271)**

Depression is common in patients with cardiac illness and has been independently associated with poor functional status, recurrent cardiac events, and increased mortality in patients with acute coronary syndrome (ACS), heart failure, and arrhythmias.[1–3] Although depression may affect cardiac outcomes through direct physiologic mechanisms (e.g., increased inflammation or abnormal platelet function),[4] poor adherence to medication and recommended health behaviors clearly plays a role in this association and may further explain the increased rates of adverse medical events in depressed cardiac patients.[5,6] Nevertheless, little is known about whether an improvement of mood symptoms is associated with adherence in depressed cardiac patients and even less is known about the connection between anxiety and adherence in these patients. Anxiety has been increasingly identified as a risk factor—possibly independent of depression—for adverse outcomes in cardiac patients.[7] However, few studies have examined the effects of anxiety or anxiety improvement on treatment adherence in patients with acute heart disease[8] or simultaneously assessed the independent effects of anxiety and depression. In this secondary analysis of data from a depression care management trial, we assessed whether improvements in depression and anxiety were independently associated with greater adherence to health behaviors over a 6-month period in a cohort of hospitalized cardiac patients who met criteria for depression during hospitalization.

Methods

This was a secondary analysis from a prospective randomized trial (http://clinicaltrials.gov, identifier NCT00847132) of a 12-week collaborative care depression treatment program versus usual care for depressed patients admitted to inpatient cardiac units.[9] All study procedures were approved by the hospital's institutional review board.

Eligible patients for the collaborative care study were admitted for ACS, decompensated heart failure, or arrhythmia to inpatient cardiac units at an urban academic medical center from September 2007 through September 2009. These 3 diagnoses were selected because they provide a representative sample of patients in cardiac inpatient units (accounting for approximately 80% of admission diagnoses) and because depression has been associated with poor medical outcomes in patients with each of these conditions.[3,10,11] To meet study criteria for clinical depression,

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patients were required to have a Patient Health Questionnaire-9 (PHQ-9)[12] score ≥10 with ≥5 symptoms—including depressed mood or anhedonia—present >1/2 the days for the preceding ≥2 weeks. Patients meeting depression criteria were evaluated further for psychiatric exclusion criteria including bipolar disorder, psychosis, active substance use disorder, cognitive impairment, and active suicidal ideation.

Subjects who met all eligibility criteria and were enrolled were randomized to a 12-week collaborative care intervention (a multipronged intervention using a care manager to provide serial depression assessments and coordinate psychiatrists' recommendations regarding depression care) or to usual care. Results of the main study have been published elsewhere; briefly, patients receiving the collaborative care intervention had significantly greater decreases in anxiety and depressive symptoms at 6 and 12 weeks (during the intervention) compared to those in usual care. In addition, at 6 months (postintervention) the intervention was associated with greater decreases in the number and intensity of cardiac symptoms and greater self-reported adherence to medication and health behaviors, although its effect on depression waned at this time point.

On enrollment, study staff obtained information about a patient's sociodemographic characteristics, medical conditions, depression history, and baseline study outcome measurements. Outcome measurements included measures of depression (PHQ-9), anxiety (Hospital Anxiety and Depression Scale, Anxiety subscale [HADS-A]),[13] and health-related quality of life (Medical Outcomes Study Short Form-12 [SF-12] Mental and Physical Component scores).[14] The PHQ-9 was chosen because it is a widely used instrument with high validity and reliability[12] and because it has been used in similar studies of cardiac patients.[15] We used the HADS-A to measure anxiety because it has been used in previous studies of patients with cardiac illness[16] and because it does not contain somatic symptom items that could represent physical symptoms of cardiac illness, unlike such other scales as the Beck Anxiety Inventory or Generalized Anxiety Disorder-7. The SF-12 was used because it is a brief well-validated measurement of health-related quality of life previously used in cardiac patients.[17]

Follow-up assessments by a staff member blinded to group assignment were conducted 6 weeks 12 weeks, and 6 months after enrollment. At all follow-up time points, study measurements (PHQ-9, HADS-A, and SF-12) were repeated. Adherence was also measured during these follow-up assessments using 4 items from the Medical Outcomes Study Specific Adherence Scale (MOS-SAS). These items assessed adherence to a healthy diet, exercise, stress reduction, and medication. For each item, subjects were asked the frequency (from "none of the time" to "all of the time," scored from 1 to 6) with which they had followed each of these health behaviors in the previous month. We did not measure adherence at baseline because some patients may not have had pre-existing cardiac disease or may not have been prescribed medication before their admission.

We chose to measure self-reported adherence for several reasons. First, other more objective methods of assessing adherence were not appropriate for the present study because measuring adherence using electronic pill caps, dietary logs, multiaxial accelerometers, and other invasive methods is expensive, burdensome, and difficult for this population of patients with complex medical problems. Second, such methods have their own limitations in the accurate measurement of health behavior (e.g., electronic pill caps measure only the number of cap openings and not necessarily the actual pill intake).[18] Third, self-reported adherence has been validated as a reliable predictor of health outcomes.[15,19] We specifically selected items from the MOS-SAS because of its ease of administration to cardiac patients and because it has been used in multiple previous studies in patients with heart disease[5,20,21] including patients who, as in the present study, had been recently hospitalized for an acute cardiac event.[5]

At each time point, all subjects who completed that follow-up assessment were included in the analysis. We initially performed preliminary unadjusted analyses comparing adherence scores between depressed and nondepressed patients (using an established PHQ-9 cutoff score ≥10[22]) at our primary time point (6 months) and exploratory time points (6 and 12 weeks) and compared groups using independent-samples *t* tests.

To determine differences in baseline characteristics between subjects completing follow-up and subjects with

Table 1
Baseline sociodemographic and medical characteristics for patients with all follow-up data at primary time point (6 months, n = 134)

Age (years), mean ± SD	61.49 ± 11.8
Men	64 (48%)
Married	55 (41%)
Employed	36 (27%)
Diabetes mellitus	43 (32%)
Hypercholesterolemia*	76 (57%)
Hypertension*	78 (58%)
Current smoking	26 (19%)
Previous myocardial infarction	39 (29%)
Admission diagnosis	
Heart failure	44 (33%)
Unstable angina	38 (28%)
Myocardial infarction	23 (17%)
Arrhythmia	29 (22%)
Previous depression	96 (72%)
Duration of current depression >1 month	106 (79%)
Prescribed antidepressant at admission	59 (44%)
Medications prescribed at discharge	
Aspirin	100 (75%)
β-Adrenergic blocker	106 (79%)
Angiotensin-converting enzyme inhibitor	68 (51%)
Statin	97 (72%)
Diuretic	70 (52%)
Antidepressant	98 (73%)
Baseline outcome variables, mean ± SD	
Depression (Patient Health Questionnaire-9 score)	17.8 ± 3.6
Anxiety (Hospital Anxiety and Depression Scale, Anxiety subscale)	10.5 ± 4.1
Physical health-related quality of life (Medical Outcomes Study Short Form-12 Physical Component score)	32.0 ± 9.8
Length of hospital stay (days), mean ± SD	7.2 ± 7.8

Variables are reported as mean ± SD or number (percentage).
* Hypertension and hypercholesterolemia diagnoses were determined by medical record review.

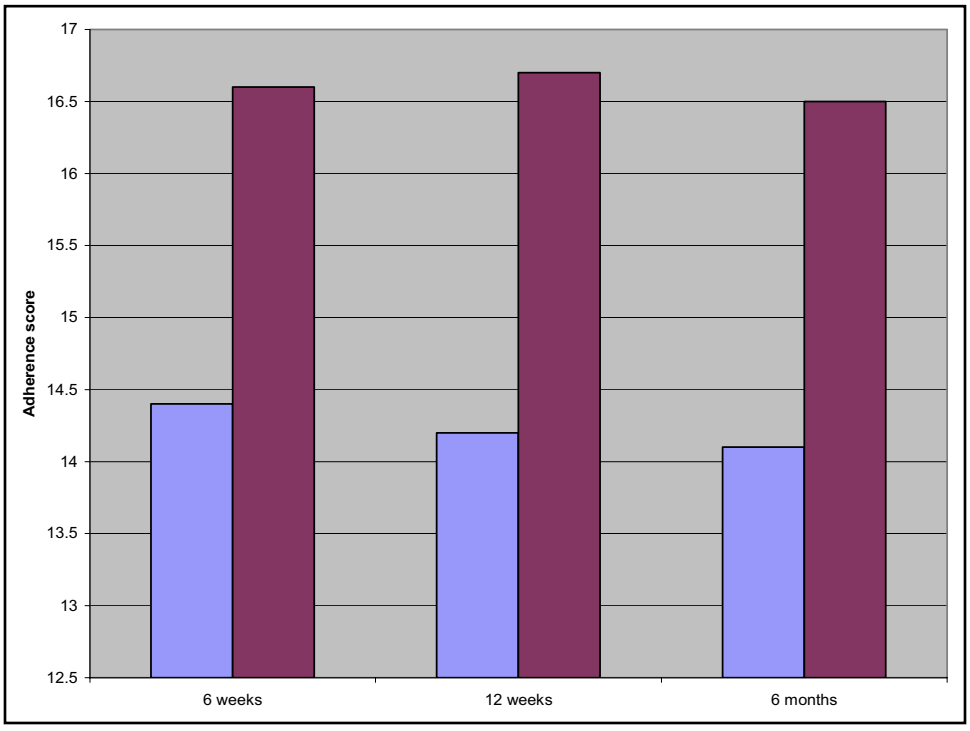

Figure 1. Adherence in depressed (Patient Health Questionnaire-9 ≥10) *(light bars)* versus nondepressed *(dark bars)* subjects (between-group differences p <0.001 at all time points).

Table 2
Linear regression assessing variables associated with improvement in self-reported adherence at six months (primary time point, n = 134)

Variable	Coefficient	SE	95% CI	p Value
Change in depression (Patient Health Questionnaire-9) from baseline	0.27	0.05	0.15–0.37	<0.001
Change in anxiety (Hospital Anxiety and Depression Scale, Anxiety subscale) from baseline	−0.02	0.07	−0.15 to 0.11	0.75
Age	−0.39	0.02	−0.09 to 0.01	0.14
Gender	0.42	0.57	−0.72 to 1.56	0.47
Employment status	1.04	0.69	−0.34 to 2.42	0.14
Diabetes mellitus	0.08	0.61	−1.13 to 1.29	0.89
Admission diagnosis	0.24	0.36	−0.47 to 0.96	0.51
Physical health-related quality of life (initial Medical Outcomes Study Short Form-12 Physical Component Scale score)	−0.007	0.03	−0.06 to 0.05	0.82
Current smoker	−0.99	0.75	−2.48 to 0.49	0.19
Living alone	−0.56	0.66	−1.85 to 0.74	0.39

CI = confidence interval.

missing data at the primary time point (6 months), we compared baseline sociodemographic variables, medical characteristics, and psychiatric symptom measurements using chi-square analysis for dichotomous variables and *t* tests for continuous variables. We selected 6 months as the primary time point to assess longer-term change, which may be more difficult to sustain and more important in longitudinal prognosis than transient changes in health behaviors.

For the primary analyses, we performed multivariate linear regression using continuous adherence (MOS-SAS) scores at 6 months as the dependent variable. To ensure the most robust analyses, we chose to measure adherence as a continuous variable rather than using a predefined "cutoff" for adherence. To avoid overfitting and to use a rational model creation, we also selected independent variables a priori based on previous literature rather than preselecting variables with favorable bivariate comparisons and limited the number of variables in the model.

Independent variables selected for the model included age, gender, admission diagnosis, living alone (social support and living status have been linked to adherence in patients with heart disease[23,24]), baseline functional status as measured by the SF-12 Physical Component Scale (this scale/domain has been linked to treatment adherence), smoking status at admission (smoking has been linked to health behavior adherence and itself is a target behavior[23]), employment (a predictor of poor treatment adherence in cardiac patients), diabetes mellitus (linked to poor adherence), change in depression score from baseline (PHQ-9), and change from baseline anxiety score (HADS-A).

Table 3
Linear regression assessing variables associated with improvement in self-reported adherence at six weeks (secondary time point, n = 124)

Variable	Coefficient	SE	95% CI	p Value
Change in depression (Patient Health Questionnaire-9) from baseline	0.10	0.05	0.008–0.20	0.048
Change in anxiety (Hospital Anxiety and Depression Scale, Anxiety subscale) from baseline	0.16	0.07	0.04–0.30	0.012
Age	0.01	0.02	−0.03 to 0.06	0.56
Gender	0.61	0.53	−0.43 to 1.67	0.25
Employment status	0.81	0.70	−0.57 to 2.19	0.25
Diabetes mellitus	−0.52	0.68	−1.88 to 0.82	0.44
Admission diagnosis	1.12	0.57	−0.004 to 2.25	0.051
Physical health-related quality of life (initial Medical Outcomes Study Short Form-12 Physical Component Scale score)	−0.011	0.03	−0.71 to 0.48	0.91
Current smoker	0.40	0.65	−0.87 to 1.68	0.53
Living alone	−0.10	0.61	−1.30 to 1.11	0.88

Abbreviation as in Table 2.

Table 4
Linear regression assessing variables associated with improvement in self-reported adherence at 12 weeks (secondary time point, n = 134)

Variable	Coefficient	SE	95% CI	p Value
Change in depression (Patient Health Questionnaire-9) from baseline	0.2	0.06	0.09–0.31	<0.001
Change in anxiety (Hospital Anxiety and Depression Scale, Anxiety subscale) from baseline	−0.04	0.07	−0.19 to 0.11	0.58
Age	−0.01	0.05	−0.07 to 0.04	0.61
Gender	0.42	0.63	−0.83 to 1.67	0.51
Employment status	−0.04	0.79	−1.59 to 1.51	0.96
Diabetes mellitus	−0.52	0.68	−1.88 to 0.82	0.44
Admission diagnosis	0.57	0.40	−0.23 to 1.38	0.16
Physical health-related quality of life (initial Medical Outcomes Study Short Form-12 Physical Component Scale score)	0.003	0.03	−0.06 to 0.07	0.91
Current smoker	0.80	0.82	−0.82 to 2.44	0.33
Living alone	−0.06	0.74	−1.52 to 1.41	0.94

Abbreviation as in Table 2.

We also performed exploratory supplemental analyses to identify factors associated with combined and medication adherence at 6 and 12 weeks after hospitalization. These analyses used multivariate linear regression in the same manner as the 6-month assessments. All analyses were performed using STATA 11.0 (STATA Corp., College Station, Texas). Because the predetermined primary analysis was for 6 months (a single time point) p values were 2-tailed with significance set at ≤0.05. If we had used a Bonferroni correction to account for the 3 time-point analyses, a p value of 0.0167 would have been needed to achieve significance.

Results

One hundred seventy-five participants enrolled in the trial; 14 subjects (8.0%) died during the 6-month study period. Of the 161 surviving patients, 134 (83.2%) completed all portions of the 6-month follow-up evaluation and were included in the primary analysis. Of these 134 subjects, 70 (52.2%) were randomized to the collaborative care intervention and 64 (47.8%) to usual care. Baseline characteristics of these 134 subjects are listed in Table 1. There were no significant differences on any baseline sociodemographic, medical, medication-related, or psychiatric measurement between those who did and those who did not compete the 6-month follow-up, with 1 exception: patients who completed follow-up were more likely to be younger than patients who did not complete follow-up (61.5 vs 65.1 years, $t = 1.64$, $p = 0.05$). Regarding supplementary time points, 124 patients completed 6-week follow-up assessments and 134 completed the 12-week follow-up. Initial mean PHQ-9 score at enrollment was 17.8 (SE 0.33). Rates of depression response (50% decrease in PHQ-9 score from baseline) at each time point were 52.8% at 6 weeks, 58.5% at 12 weeks, and 54.7% at 6 months.

At 6 months, patients with PHQ-9 scores signaling depression (PHQ-9 ≥10, n = 63) had significantly lower MOS-SAS adherence scores than nondepressed patients (PHQ-9 <10, n = 71, adherence score 14.1 vs 16.5 in depressed vs nondepressed patients, $t = 3.98$, $p < 0.001$). Results were similar at 6 weeks (14.4 in depressed vs 16.6 in nondepressed patients, $t = 4.19$, $p < 0.001$) and 12 weeks (14.2 vs 16.7, $t = 4.08$, $p < 0.001$; Figure 1).

Multivariate linear regression at the primary time point (6 months) revealed a strong and significant relation between change in PHQ-9 score and adherence at 6 months (beta 0.263, $p < 0.001$) independent of all covariates (Table 2). A change in HADS-A score and other covariates were not associated with 6-month adherence measured by the MOS-SAS.

Analysis at supplementary time points revealed that improvement in depression and improvement in anxiety were

independently associated with improved adherence scores (depression, beta 0.101, p = 0.048; anxiety, beta 0.167, p = 0.012) at 6 weeks after hospitalization (Table 3). Twelve weeks after hospitalization, a strong and significant relation was present between a change in depression score and adherence (beta 0.249, p <0.001), with no significant relation between anxiety and adherence (Table 4).

Discussion

Our results are consistent with previous findings that depression is associated with impaired subsequent adherence behavior (e.g., medication adherence, heart-healthy diet) in cardiac patients.[5,15] However, to our knowledge, only 2 previous studies have assessed whether improvement of depression is associated with improved adherence to cardiac treatment.

First, a pair of reports by Rieckmann et al[25,26] from 1 study found that improvement of depression (assessed during hospitalization and 3 months later) was associated with improved medication (aspirin) adherence at 3 months in patients admitted with an ACS. However, that study did not assess adherence to other health behaviors, the impact of other psychological factors, other cardiac illnesses, or a longer period. A second study, by Kronish et al,[27] examined the effect of depression on adherence to secondary prevention behaviors and medications at 3 months and found associations between persistent depression and lower adherence to medications, exercise, cardiac rehabilitation, and quitting smoking. This second study did not involve treatment of depression, did not measure anxiety, assessed a single time point, and followed patients for a shorter period than the present study.

The present study is the first to assess the impact of changes in depression symptoms on adherence in patients with a wide range of cardiac diagnoses, representing approximately 80% of admitted patients to cardiac units. It is the first to assess the impact of anxiety improvement on adherence and uniquely addresses the independent effects of anxiety and depression improvement on adherence outcomes. This project examined multiple time points and a longer follow-up period (6 months) than previous studies assessing the effects of changes in depressive symptoms on adherence.

Our findings suggest that improvement of depression symptoms (whether spontaneously or by treatment) appears to lead to improved adherence in patients with a broad range of cardiac diagnoses, and this may have important clinical implications. Adequate adherence to healthy-lifestyle interventions and medication has been shown to improve some cardiac risk factors (increased lipids, high blood pressure, increased glucose, and obesity)[28] and has been linked to fewer cardiac events and increased survival in patients after ACS.[15,29] Therefore, decreasing depression might prevent future cardiac events by increasing adherence to treatment recommendations; of note, in nearly 1/2 of patients there was a nonresponse of depression symptoms over the 6 months after admission (despite an active depression intervention or notification of treaters) consistent with a previous study on this topic.[30] This suggests that aggressive management of depression may be needed to decrease depression and affect adherence. Indeed, our findings may further encourage clinicians to aggressively address depression in cardiac patients, especially those recently hospitalized, and suggest a potential mediating factor (adherence) by which such treatment may improve function and survival.

In contrast, change in anxiety was not independently associated with adherence beyond 6 weeks in this study. One explanation for this difference may be that the core symptoms of depression—such as poor motivation, impaired concentration, and low energy—may directly affect participation in health behaviors, whereas symptoms of anxiety including activation and restlessness may have a lesser impact on the adherence outcomes measured. Furthermore, patients with anxiety may be highly anxious about (and focused on) health concerns, leading to greater vigilance regarding recommendations about their health.

This study has several important limitations. As noted, adherence was determined by self-report rather than by electronic pill caps, food diaries, accelerometers, and other methods; although these other methods are more burdensome and have their own limitations, they may serve as more objective adherence assessment methods. Also, self-reported assessment of stress reduction as part of the adherence measurement may not be independent of anxiety and depression scales, which could introduce a methodologic bias. Furthermore, not all patients whose depression improved received depression treatment and thus we can say only that depression improvement (rather than depression treatment) is linked to adherence. Directionality/causality of the link between depression and improvement in adherence could not be assessed; indeed, improved adherence to exercise, diet, and other behaviors may have led to improved mood. In addition, other factors that may affect adherence, mood, or anxiety such as participation in cardiac rehabilitation were not measured. This study was performed in a single urban academic medical center with a largely Caucasian population. Despite these limitations, this study reinforces the strong and independent connection between depression and critical health behaviors in patients with a wide range of cardiac diagnoses.

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