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The Impact of Pain and Depression on Post-CABG Recovery

Natalia E. Morone, MD, MS, Debra K. Weiner, MD, Bea Herbeck Belnap, Dr Biol Hum, Jordan F. Karp, MD, Sati Mazumdar, PhD, Patricia R. Houck, MS, Fanyin He, BS, and Bruce L. Rollman, MD, MPH

Department of Medicine, Division of General Internal Medicine (N.E.M., B.H.B., B.L.R.), Clinical and Translational Sciences Institute (N.E.M., J.F.K.), Department of Medicine, Division of Geriatric Medicine (D.K.W.), Department of Psychiatry (D.K.W., J.F.K., S.M., P.R.H.), Department of Anesthesiology (D.K.W., J.F.K.), Department of Biostatistics, Graduate School of Public Health (S.M., F.H.), University of Pittsburgh, Geriatric Research Education and Clinical Center, VA Pittsburgh Healthcare System (D.K.W.), Pittsburgh, PA, USA

Abstract

Objective—To describe the relationship between pain and depression on recovery after coronary artery bypass grafting (CABG).

Methods—A secondary data analysis on 453 depressed and nondepressed post-CABG patients enrolled in a randomized, controlled, effectiveness trial of telephone-delivered collaborative care for depression. Outcome measures were collected from March 2004 to September 2007 and included pain, physical function, and mood symptoms.

Results—Depressed patients (baseline Patient Health Questionnaire-9 score ≥ 10) versus those without depression reported significantly worse pain scores on the SF-36 Bodily Pain Scale at baseline and up to 12-months post-CABG, $p < 0.05$. Among patients with depression, those who received collaborative care reported significantly better pain scores at each time point between 2 and 12-months post-CABG vs. depressed patients randomized to the usual care control group, $p < 0.05$. Regardless of intervention status, depressed participants with at least moderate pain at baseline reported significantly lower functional status (measured by the Duke Activity Status Index) at 8 and 12-months vs. depressed patients with none or mild pain, $p < 0.05$. Depressed patients with at least moderate pain at baseline were also significantly less likely to show improvement of depressive symptoms throughout the course of follow-up vs. depressed patients with little or no pain, $p < 0.05$. These findings controlled for age, gender, education, race, comorbid conditions and baseline pain diagnosis.

Conclusions—Depression and pain appear to influence functional recovery post-CABG. The relationship between these two conditions and 12-month outcomes should be considered by clinicians when planning treatment.

Keywords

Depression; Pain; CABG; Collaborative Care

INTRODUCTION

There is compelling evidence that patients with depression have worse outcomes after cardiac surgery as compared to nondepressed patients. Studies have shown lower functional status and

lower health related quality of life (HRQoL), as well as an increased incidence of hospitalizations after discharge and increased mortality. The latter is true even after controlling for cardiac status, comorbidity, the extent of bypass surgery and despite a satisfactory surgical result (1–4). The research demonstrating worse outcomes in depressed patients undergoing cardiac surgery has not examined the additional impact of pain on clinical outcomes. Yet there is robust evidence for the negative clinical consequences of both pain and depression on non-surgical patients. For example, depressed patients with pain are less likely to respond to treatment for depression, and describe poorer physical function and quality of life as compared to depressed patients without pain (5–8).

The impact of co-occurring pain and depression has not been studied in patients undergoing coronary artery bypass grafting (CABG). To address this gap we studied depressed and nondepressed patients who had undergone bypass surgery and had participated in a clinical trial of collaborative care for depression. We had the following four questions; 1) What are the demographic and clinical characteristics of depressed and nondepressed patients with and without at least a moderate level of pain? 2) What is the course of pain among post-CABG patients with and without depression? 3) Among depressed post-CABG patients, what is the relationship between higher levels of pain and recovery of physical function? and 4) Are higher levels of post-CABG pain associated with reduced rate of recovery from depression?

METHODS

We performed a secondary data analysis on the National Institutes of Health (NIH) funded Trial “Bypassing the Blues”. This was a randomized, controlled effectiveness trial comparing a telephone-delivered collaborative care intervention for depression to “usual” care depressed patients post-CABG. The trial also included a post-CABG nondepressed group to facilitate study comparison. The intervention did not assess pain or make recommendations about pain control. Outcome measures were obtained from March 2004 to September 2007. Trial details (9) and main outcome findings (10) are presented elsewhere and briefly described below. The study was approved by the University of Pittsburgh Institutional Review Board, and all participants provided written informed consent.

Participants

A total of 453 post-CABG patients were recruited into the study from seven Pittsburgh-area hospitals. They included 150 depressed patients randomized to the intervention group, 152 randomized to the usual care group, and 151 nondepressed assigned to the comparison group. Before the commencement of trial enrollment, NHLBI, our sponsor, set a 15% target enrollment of non-whites in our overall study (target N=450). To achieve this goal, we programmed a software algorithm into the Tablet PCs used by our nurse-recruiters to guide them through our recruitment procedures at patients’ bedsides that deliberately limited the number of white subjects enrolled in our trial’s nondepressed comparison arm (target N=150). This resulted in our effectively oversampling non-whites into our nondepressed comparison group (19%), and as just 9% of the depressed subjects we enrolled and randomized were non-white (target N=300), we achieved 13% overall enrollment of non-whites (57/453) into our study.

These patients were screened for mood symptoms prior to discharge using the 2-item Patient Health Questionnaire (PHQ-2). If either item was positive, the patient was enrolled in the study and the PHQ-9 (11) was administered via telephone two-weeks following hospitalization. Inclusion criteria were: 1) depression, defined by a PHQ-9 score ≥ 10 ; 2) a Folstein Mini-Mental Status Exam (12) score ≥ 24 ; 3) medical stability and life expectancy > 1 year; 4) no active suicidality; 5) no history of psychosis or bipolar disorder; 6) no current alcohol or substance abuse; 7) not currently in treatment with a mental health specialist; 8) English

speaking; 9) no communication barrier; and 10) own a household telephone. The nondepressed comparison group could not have a current or previous history of depression treatment, had to score zero on the PHQ-2 inpatient screen, and at 2-weeks post-CABG had to score < 5 on the PHQ-9.

Procedures

Collaborative Care Intervention—The intervention lasted for eight months and consisted of several components:

1. A nurse care manager who telephoned depressed patients at baseline (2-weeks following hospitalization) to obtain details of the psychiatric history, provide a workbook about depression (13), initiate or recommend an antidepressant (prescribed by their PCP) and/or refer to a local mental health specialist, or “watchful-waiting” for mildly elevated mood symptoms. The care manager then telephoned patients bi-weekly for two to four months. After the initial active treatment phase the contacts decreased to every 1 to 2 months until the end of the 8-month intervention if the patient was in remission. Pain control was not addressed in the intervention.
2. Weekly Case-Review: the nurse care manager presented her clinical information to the study psychiatrist and general internist. Following a case discussion, the clinical management team typically formulated one to three treatment recommendations. The nurse conveyed these recommendations to the patient via telephone, and to his/her PCP for consideration via fax, telephone, or mail depending upon the urgency of response.

Usual Care—For ethical reasons, both depressed patients randomized to the “usual care” control group and their PCP were informed of the participant’s depression status. However, no treatment advice was provided unless suicidality was detected during a follow-up assessment.

Measures

Medical diagnoses (including pain diagnoses) were obtained by abstracting patients’ medical records after enrollment. In addition to sociodemographic information, medical diagnoses and medications, the following measures were obtained at baseline (2-weeks following hospitalization), then at two, four, six, eight, and twelve months by a trained assessor blinded as to baseline treatment assignment and depression status:

1) Medical Outcomes Study (MOS) 36-Item Short Form Health Survey (SF-36)—

Pain was assessed using the Bodily Pain Scale of the widely used, comprehensive, and generic SF-36 rating scale (14). The instrument can differentiate between levels of health among post-CABG individuals at a single time point, in the same individuals over time, and it has been well validated, including when administered to cardiac patients over the telephone (15). Higher scores indicate better HRQoL (and less bodily pain). We used this scale to dichotomize the sample into two pain groups, which is described below. For the baseline assessment, the time period of the SF-36 was the previous week (which was post-CABG). For all follow-up assessments it was over the past month.

2) Depression Interview and Structured Hamilton (DISH)—Generates a reliable Hamilton Rating Scale for Depression (HRS-D) score in cardiac patients in an efficient, integrated interview format permitting easy telephone follow-up (16).

4) Duke Activity Status Index (DASI)—This brief 12-item measure provides a standardized assessment of functional status that correlates well with peak oxygen uptake

during exercise (Spearman correlation 0.81). The DASI addresses various common activities of daily living including personal care, ambulation, household tasks, sexual function, and recreational activities (17).

Statistical Analyses

We divided participants into the two pain intensity groups by their answer to the following question on the SF-36 Bodily Pain Scale at baseline: “How much bodily pain have you had during the past week?” If participants answered none, very mild, or mild they were considered to be in the “none or mild pain” group and if they answered moderate, severe, or very severe they were considered to be in the “at least moderate pain” group.

Descriptive statistics were used to summarize demographic characteristics of study participants. A two way logistic regression model was used for categorical variables to detect differences in demographic characteristics between the depressed group (depressed with at least moderate pain and depressed with little or no pain) and the pain group (depressed and nondepressed with none or mild pain vs. depressed and nondepressed with at least moderate pain), as well as the interaction, and a two-way ANOVA was used for the continuous variables with the depression and pain groups as the two factors. To test the report of pain over time in depressed vs. nondepressed participants, a repeated measures mixed effect model was run on the SF-36 Bodily Pain Scale score. In our model, participant intercept was a random effect and time was a fixed categorical variable. Group by time interaction was included in the model. To test the effects of baseline pain on outcomes of depression (HRS-D) and function (DASI) in depressed participants a second mixed model was run between depressed patients assigned to intervention or usual care with pain level (little or no pain vs. at least moderate pain) as the grouping factor. Mixed effect models are able to accommodate missing data so that all available data are utilized. All repeated measures controlled for age, gender, education, race, comorbid conditions and baseline pain diagnosis.

RESULTS

Question 1: What are the demographic and clinical characteristics of depressed and nondepressed patients with and without at least a moderate level of pain?

Baseline sociodemographic and clinical characteristics of the sample by pain and depression status are presented in Table 1. Overall, 45% (202/453) of participants were depressed and reported at least a moderate level of pain, 22% (100/453) were depressed and reported none or mild pain, 9% (39/453) were nondepressed with at least moderate pain, and 25% (112/453) were nondepressed with none or mild pain. Depressed post-CABG patients vs. nondepressed patients were also more likely to report at least moderate pain 67% (202/302) vs. 26% (39/151). Depressed patients were more likely to have a diagnosis of a painful condition vs. nondepressed patients; 68% (204/302) vs. 48% (73/151; $p = 0.002$) and to use opioids; 34% (104/302) vs. 19% (28/151; $p = 0.056$). The sample was predominantly white and well-educated. Those with depression as compared to nondepressed patients were more likely to report worse scores on the DASI ($p < 0.0001$). Those with at least moderate pain as compared to those with none or mild pain were more likely to report higher symptoms on the depression scales (PHQ-9, $p = 0.070$, HRS-D, $p < 0.0001$) and worse functional status on the DASI ($p = 0.005$).

Question 2: What is the course of pain among post-CABG patients with and without depression?

Regardless of intervention status, patients with depression vs. those without depression self-reported significantly worse scores on the SF-36 Bodily Pain Scale at baseline and all subsequent time points up to 12 months, $p < 0.05$ (Figure 1). This finding was controlled for age, gender, education, race, comorbid conditions and baseline pain diagnosis. Moreover,

depressed post-CABG patients randomized to the study intervention reported significantly less pain as measured by the SF-36 Bodily Pain Scale over the twelve month course of follow-up vs. the depressed usual care group, $p < 0.05$ (Figure 1). The nondepressed group had only 39 patients, making the sample size too small to accurately follow outcomes of physical function and depression over time.

Question 3: Among depressed post-CABG patients, what is the relationship between higher levels of pain and recovery of physical function?

The depressed patients with at least moderate pain in the usual care group improved the least in physical function as measured by the DASI and the depressed patients with none or little pain who received the intervention improved the most (Figure 2). The patients with moderate pain who received the intervention improved at the same rate as patients with none or mild pain in the usual care group. Thus, the intervention had a significant effect on improvement in physical function at 12-months ($p = 0.04$). While the presence of at least moderate pain had a significant negative effect on physical function at 8 and 12 months ($p < 0.05$). These findings controlled for age, gender, education, race, comorbid conditions, and baseline pain diagnosis. While there was a main effect of pain level and intervention status on physical function, there was no interaction between the two, indicating that the collaborative care intervention did not work differentially between patients with none or mild pain or at least moderate pain.

Question 4: Are higher levels of post-CABG pain associated with reduced recovery from depression?

The intervention had a significant effect on improvement of depression as compared to patients in the usual care group, $p = 0.02$ (Figure 3). This effect was regardless of pain status. While participants with depression and at least moderate pain (both intervention and usual care groups) were significantly less likely to show improvement of depressive symptoms at the 12-month follow-up period as compared to depressed participants with little or no pain, $p < 0.05$ (Figure 3). Thus, there was a main effect of pain level and intervention status on recovery from depression. There was no interaction between pain and depression, indicating that the collaborative care intervention did not work differentially based on pain level. These findings controlled for age, gender, education, race, comorbid conditions and baseline pain diagnosis.

We also determined how many participants had a clinical response to the depression intervention as defined by a $\geq 50\%$ reduction from baseline HRS-D score. Within the intervention group, those with moderate pain tended to be less likely to achieve a clinical response (45% vs. 60%) than participants with little or no pain, $p = 0.08$. Participants in the usual care group had a clinical response of 41% and 40% respectively (at least moderate pain vs. little or no pain), and this difference was not statistically significant.

DISCUSSION

This is the first study to describe the effects of co-occurring pain and depression in post-CABG patients. Depressed post-CABG patients self-reported significantly more bodily pain as compared to nondepressed patients consistently over the 12-month period following surgery. Among depressed patients, there was a main effect of pain level on improvement of physical function and improvement in depressive symptoms, with those who reported at least a moderate pain level being significantly less likely to improve in physical function and less likely to improve in depressive symptoms. There was no interaction between pain and depression, indicating that the collaborative care intervention did not work differentially based on pain level. These findings controlled for a broad variety of baseline variables.

Functional recovery after CABG surgery is a clinical outcome of critical importance. We found that depressed patients who reported at least moderate pain post-CABG were less likely to have improvement in physical function throughout the 12-month follow-up period compared to those with depression and none or little pain. Other researchers have also found a significant relationship between depression and functional recovery among post-surgical populations. Brander et al. found that baseline depression predicted more pain and decreased function one year after total knee replacement surgery (18). Their study focused on knee-specific pain and function and not cardiac status or global pain and function as ours did. Our finding underscores the importance of not only addressing depression symptoms on clinical follow-up post-CABG, but also asking about and treating pain to potentially enhance functional recovery.

Depressed patients with at least moderate pain at baseline were less likely to respond to the collaborative care intervention than depressed patients with none or mild pain. Thielke reported similar results among depressed older adults who participated in a collaborative care intervention for depression. He found that those with higher pain interference at baseline were less likely to achieve a depression response (19). Another study of 573 depressed patients treated with one of three selective serotonin reuptake inhibitors found the odds of poor treatment response was 2.0 for participants with at least moderate pain (20). However, both studies were in primary care and not surgical populations.

Patients with depression were more likely to report increased pain throughout the 12-month follow-up than nondepressed patients. While we cannot distinguish the source of the pain from our data, our finding is consistent with other research findings that describe a relationship between pain and post-CABG depression. Taillefer found that depression predicted chronic nonanginal postoperative pain after cardiac surgery and Karlsson found depression predicted chest pain up to 12-months post-CABG (21,22).

A large proportion of our sample with depression (67%) had at least moderate pain at baseline assessment two weeks after hospitalization. This is consistent with a literature review of depression and pain comorbidity which reported the prevalence of pain in patients with depression was about 65% (8). In comparison, the lifetime prevalence of painful symptoms in the general population is 24%–37% (23). Our depressed sample not only had higher symptoms of pain at baseline, but they also reported higher pain scores on the SF-36 Bodily Pain scale throughout the 12-month follow-up period.

Our study is limited by the lack of assessment of pre-surgical pain condition and pain medication and depression data since these were all collected post-CABG. The pain question was not specific to post-surgical pain, but on the other hand this allowed us to examine the effect of any type of pain on outcomes. Pain was assessed with the SF-36 Bodily Pain Scale and not any other instrument. The sample was predominantly white and well-educated and confined to one geographic region of the United States. The information on co-morbid medical conditions was collected by chart review.

In conclusion, our study is the first to describe the complex interrelationship between pain and depression after CABG surgery: patients with depression are more likely to express symptoms of pain, pain is associated with a decreased clinical response to depression treatment, and those with both pain and depression are less likely to report improvement in physical function. Since treatment for both pain and depression is readily available it is important for clinicians to inquire about these post-operatively. Treating one but not the other could result in a suboptimal post-surgical outcome. The lack of interaction between treatment and pain in the presence of significant main effects further supports the need for novel interventions that address both of these linked conditions simultaneously. Future research should study the effects of treating pain and depression in cardiac populations and not depression alone. Important research

questions should address whether more aggressive pain and depression treatment prior to surgery affects surgical outcomes or whether more aggressive post-op pain management leads to improved outcomes.

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Acronyms

HTN	Hypertension
CVA	Cerebral vascular accident
COPD	Chronic obstructive pulmonary disease
CHF	Chronic heart failure
PHQ	Patient Health Questionnaire
HRS-D	Hamilton Rating Scale-Depression
DASI	Duke Activity Status Index
NSAIDs	Non-steroidal anti-inflammatory drug

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Figure 1.

Course of pain symptoms post-CABG among depressed and nondepressed patients.

Higher score less pain.

*Nondepressed vs. depressed (includes both intervention and usual care groups), $P < 0.05$

**Depressed/intervention vs. depressed/usual care, $P < 0.05$.

INT: Depressed/intervention; UC: Depressed/usual care; ND: Nondepressed; CABG:

Coronary artery bypass graft.

N at each assesment:

UC, with pain:	102	90	89	84	79
UC, without pain:	50	44	45	42	36
Int, with pain:	100	81	81	84	76
Int, without pain:	50	39	42	42	39

Figure 2.

Course of functional status post-CABG among depressed patients assigned to collaborative care intervention group or usual care group by pain level.

Higher score is better.

$P < 0.05$ at 8 and 12 months for: INT/moderate pain + UC/moderate pain vs. INT/none or mild pain + UC/none or mild pain.

$P = 0.04$ at 12 months for: INT/moderate pain + INT/none or mild pain vs. UC/moderate pain + UC/none or mild pain.

INT: Depressed/intervention; UC: Depressed/usual care; CABG: Coronary artery bypass graft. The sample size (N) at each timepoint reflects the mean of those who completed the assessment for that timepoint.

N at each assesment:

UC, with pain:	102	90	89	84	79
UC, without pain:	50	46	46	42	36
Int, with pain:	100	82	81	83	76
Int, without pain:	50	39	42	42	39

Figure 3.

Course of depression symptoms post-CABG among depressed patients assigned to the collaborative care intervention group or usual care group by pain level.

Lower score is better.

$P < 0.05$ at every time point for: INT/moderate pain + UC/moderate pain vs. INT/none or mild pain + UC/none or mild pain.

$P = 0.02$ at 12 months for: INT/moderate pain + INT/none or mild pain vs. UC/moderate pain + UC/none or mild pain.

INT: Depressed/intervention; UC: Depressed/usual care; CABG: Coronary artery bypass graft. The value of the Hamilton Rating Scale-Depression score at each timepoint reflects the mean of those who completed the assessment for that timepoint.

TABLE 1

Baseline Demographic and clinical characteristics of sample

Characteristic	Depressed with at least moderate pain <i>n</i> = 202	Depressed with little or no pain <i>n</i> = 100	Nondepressed with at least moderate pain <i>n</i> = 39	Nondepressed with little or no pain <i>n</i> = 112	<i>P</i> -value [†]	<i>P</i> -value [‡]
Age, mean ± SD	62.7 ± 11.2	66.5 ± 10.2	66.8 ± 7.2	66.0 ± 10.4	0.12	0.19
Gender (%)					0.58	0.53
Female	87 (43.1)	38 (38.0)	15 (38.5)	41 (36.6)		
Male	115 (56.9)	62 (62.0)	24 (61.5)	71 (63.4)		
Ethnicity (%)					0.002	0.17
White	180 (89.1)	94 (94.0)	30 (76.9)	92 (82.1)		
African American	21 (10.4)	6 (6.0)	8 (20.5)	17 (15.2)		
Greater than a high school education (%)	118 (58.4)	50 (50.0)	22 (56.4)	56 (50.0)	0.85	0.18
Measures, mean ± SD						
PHQ-9	13.7 (3.4)	13.2 (3.2)	2.3 (1.3)	1.7 (1.4)	< .0001	0.07
HRS-D	17.6 (7.0)	13.5 (6.1)	4.6 (3.3)	3.1 (2.6)	< .0001	< .0001
DASI	6.9 (6.9)	8.5 (6.4)	11.3 (5.5)	13.9 (6.5)	< .0001	0.005
SF-36 Bodily Pain	33.8 (5.7)	49.3 (7.1)	38.3 (5.9)	53.1 (6.8)	< .0001	< .0001
Comorbid conditions, (%)						
Pain Diagnosis*	146(72.3)	58(58.0)	19(48.7)	54(48.2)	0.002	0.15
Diabetes	88 (43.6)	40 (40.0)	16 (41.0)	43 (38.4)	0.71	0.57
HTN	164 (81.2)	89 (89.0)	32 (82.1)	90 (80.4)	0.30	0.39
CVA	18 (8.9)	6 (6.0)	2 (5.1)	6 (5.4)	0.46	0.69
COPD	52 (25.7)	15 (15.0)	6 (15.4)	8 (7.1)	0.03	0.02
Chronic Renal Insufficiency	24 (11.9)	5 (5.0)	4 (10.3)	12 (10.7)		
CHF	34 (16.8)	25 (25.0)	6 (15.4)	18 (16.1)	0.26	0.35
Pain Medications, (%)						
NSAIDs	5 (2.5)	0 (0.0)	1 (2.6)	3 (2.7)	0.97	0.97
Opioids	84 (41.6)	20 (20.0)	9 (23.1)	19 (17.0)	0.056	0.007

Characteristic	Depressed with at least moderate pain <i>n</i> = 202	Depressed with little or no pain <i>n</i> = 100	Nondepressed with at least moderate pain <i>n</i> = 39	Nondepressed with little or no pain <i>n</i> = 112	<i>P</i> -value [†]	<i>P</i> -value [‡]
Acetaminophen	17(8.4)	7 (7.0)	1 (2.6)	6 (5.4)	0.21	0.65
Antidepressant Medications, (%)						
Serotonin reuptake inhibitor	44 (21.8)	13 (13.0)	0	0		
Tricyclic antidepressant	4 (2.0)	1 (1.0)	0	1 (0.9)		
Sedative/hypnotic	11 (5.5)	8 (8.0)	0	0		
Serotonin-Norepinephrine reuptake inhibitor	12 (5.9)	2 (2.0)	0	0		

[†] Depressed with at least moderate pain + depressed with little or no pain vs. nondepressed with at least moderate pain + nondepressed with little or no pain.

[‡] Depressed/nondepressed with little or no pain vs. with depressed/nondepressed with at least moderate pain.

* Any painful condition in the following areas: musculoskeletal, gastrointestinal, genitourinary, neurological/sensory, back pain, migraine/chronic headaches, chronic pain syndrome.

HTN: Hypertension; CVA: Cerebral vascular accident; COPD: Chronic obstructive pulmonary disease, CHF: Chronic heart failure; PHQ: Patient Health Questionnaire, higher is worse; HRS-D: Hamilton Rating Scale-Depression, higher is worse; DASI: Duke Activity Status Index, higher is better; SF-36 Bodily Pain Scale, higher is better; NSAIDs: Non-steroidal anti-inflammatory drug.