DEPRESSION, HEALING, AND RECOVERY FROM CORONARY ARTERY BYPASS SURGERY

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• Background  Effects of postoperative depression on recovery from coronary artery bypass grafting have not been widely studied.

• Objectives  To evaluate emotional and physical recovery after bypass surgery and investigate associations between depressive symptoms and infections and impaired wound healing in patients with high and low levels of depressive symptoms.

• Methods  A nonrandomized, comparative, longitudinal design was used to study 72 bypass surgery patients without serious noncardiac comorbidities who were available for follow-up after discharge. Patients completed questionnaires to assess depressive symptoms, emotional recovery, and physical recovery within 48 hours after extubation, at discharge from the hospital, and 6 weeks later and performed 6-minute walk tests at the last 2 times. Infections and impaired wound healing (as indicated by positive cultures, antibiotic treatment, or extra treatments, such as debridements or incisions and drainage) were identified by chart audit.

• Results  At discharge, patients with higher depressive symptom scores (indicating more symptoms) reported poorer emotional recovery (P < .001) and poorer physical recovery (P = .007) and achieved shorter walking distances (P < .001) than did patients with lower scores (indicating fewer symptoms). Six weeks after discharge, emotional and physical recovery remained lower in patients with more depressive symptoms (P < .001). Infections and impaired wound healing were more common among patients with higher depressive symptom scores (46%) than among patients with lower scores (19%, P = .03).

• Conclusions  After bypass surgery, depressive symptoms are associated with infections, impaired wound healing, and poor emotional and physical recovery. (American Journal of Critical Care. 2005;14:316-324)

Coronary artery bypass grafting (CABG) is one of the most common operations in the United States; approximately 519,000 procedures are performed each year.1 CABG accounts for more healthcare resources than any other single procedure and for more than $10 billion in healthcare costs annually.2,3 The relationship between (1) emotional states and clinical affective disorders and (2) outcomes in cardiac patients has been the subject of increasing scrutiny by researchers and clinicians. In particular, depression has been associated with adverse outcomes, including increased mortality and morbidity after acute myocardial infarction.4,5

Depressive symptoms are common before CABG6 and are associated with increased healthcare costs. Depressive symptoms have been reported in up to 60% of patients undergoing bypass grafting,7 a prevalence that exceeds that of other patients with cardiac problems. In initial studies8 in CABG patients, higher levels of depressive symptoms preoperatively were correlated with increases in readmissions postoperatively. Also, preoperative distress, including both anx-
The effect of postoperative major depression on cardiac events after CABG has been evaluated in only a single study. Although depression is thought to be associated with immune dysregulation, no studies to date have linked depressive symptoms after CABG to higher rates of postoperative infectious complications. The purpose of this study was 3-fold:

1. to describe depressive symptoms associated with CABG at 3 time points: in the hospital, at the time of discharge from the hospital, and 6 weeks after discharge;
2. to evaluate emotional and physical recovery after CABG; and
3. to determine the association between depressive symptoms and infections and impaired wound healing at the time of discharge and 6 weeks later in patients who had had CABG.

Depressive symptoms occur in as many as 60% of patients before coronary artery bypass graft surgery and are associated with higher rates of cardiac events and hospital readmission after surgery.

Methods
Sample and Setting
The sample consisted of 72 patients undergoing CABG at a single urban, university-affiliated medical center. After approval by the institutional review board, patients were included in the study if they gave signed consent to participate in it, spoke English and were available for follow-up after hospital discharge, were free of cognitive impairment that could interfere with their ability to participate, and had no noncardiac serious or life-threatening comorbid conditions, such as stroke, sepsis, or acute renal failure.

Procedure
A nonrandomized, comparative, longitudinal design was used. Data were collected 3 times after surgery: in the hospital, either in the intensive care unit or in the step-down unit within 48 hours after extubation; at the time of discharge from the hospital; and 6 weeks after discharge. The initial in-hospital time was chosen to provide data on the early postoperative critical care experience, which most likely is associated with the highest level of emotional distress. The time of discharge from the hospital was selected to mark the transition to home care. The time after discharge was selected because at that time limitations on activities such as driving and lifting are removed and patients are usually encouraged to resume their previous level of physical activity.

Within 48 hours after extubation, either in the intensive care unit or in the step-down unit, patients were approached by a research assistant. After giving informed consent, they completed a questionnaire booklet. On the evening before discharge from the hospital or on the morning of discharge, patients completed a 6-minute walk test and answered the questions in the booklet again. For each patient, 6 weeks after discharge, a research assistant visited the patient’s home, administered a 6-minute walk test, and asked the patient to complete a final questionnaire booklet. Chart audits to determine infectious complications and wound-healing problems were conducted at the time of discharge from the hospital and 6 weeks later.

Instruments
The Parsonnet score, a measure of preoperative 30-day mortality risk, was used to characterize the sample. Depressive symptoms were measured by using the Multiple Affect Adjective Check List (MAACL). Physical recovery was measured by using the 6-minute walk test, the Wolfer-Davis Recovery Index, the Physical Health Composite score of the Short-Form 12 (SF-12), and chart review to determine documented infections and episodes of prolonged wound healing requiring treatment. Emotional recovery was measured by using the Cardiac Attitudes Index (CAI) and the Mental Health Composite score of the SF-12.

Parsonnet Score. The Parsonnet score has been well established as a valid and reliable measure of preoperative risk and is useful because it aids in comparisons of samples across studies. Demographic and clinical characteristics are weighted and summed, so that advanced age (>70 years), being female, low ejection fraction (<0.50), diabetes, obesity, renal failure, previous cardiac surgery, urgent surgery, and presence of catastrophic or rare circumstances (such as cardiogenic shock) confer added risk. Scores, which range from 0 to 55, are then grouped to yield risk categories of good (0-4), fair (5-9), poor (10-14), high (15-19), and very high (≥20).

Multiple Affect Adjective Check List. The MAACL, a self-report measure consisting of 132 alphabetically arranged adjectives, was used to assess emotional states of anxiety, depression, and hostility. Higher scores mean that the subject has higher symptomatic levels of the given dysphoria. Subjects receive a separate score for anxiety, depression, and hostility. The MAACL has been used extensively in research and clinical practice and has established reliability and validity.
The CAI consists of 19 belief statements used to measure perceived control in the context of cardiac disease. This instrument was developed specifically to measure the degree to which patients feel they have control related to their cardiac disease. Subjects rate agreement with statements on a Likert scale, and responses for each item are summed to arrive at a total score. A higher score indicates a higher level of perceived control. Rather than measuring locus of control, a conceptually related measure, the CAI is used to measure control relevant to patients’ current health problems. Compared with more general locus-of-control instruments, the CAI is better for predicting outcomes. The reliability of the Instrument as assessed by internal consistency is high, with a Cronbach α of .89. Validity of the instrument has also been established.

Six-Minute Walk Test. The 6-minute walk test provides an objective measure of functional status and exercise tolerance, is often used to assess these parameters in cardiac patients, and is a useful indicator of changes in functional status after intervention. Patients are instructed to walk at a brisk pace as far as they can within 6 minutes, resting as needed. The distance walked is measured in feet. Each assessment of the 6-minute walk was done by the same research assistant, who used a wheeled metering device to measure the distance each patient walked on a flat surface and who used a standardized script to instruct patients, as recommended by previous investigators. Concurrent validity of the 6-minute walk was established by Lipkin et al, who used maximal oxygen consumption in subjects on a treadmill. Reproducibility of the 6-minute walk test is impressive and is higher than that of the pulmonary function test. The within-person coefficient of variation over 6-minute walking tests is 8.2%, attesting to high reliability.

Short-Form 12. The SF-12 is a shorter version of the 36-item Short-Form 36 Health Survey developed as part of the Medical Outcomes Study to assess mental and physical health. The 12 items of the SF-12 are summarized as 2 scores: a physical component and a mental component; the instrument does not yield a total score. The physical component includes physical function, role limitations due to physical health problems, bodily pain, and general health. The mental component reflects vitality, social functioning, role limitations due to emotional problems, and mental health (psychological distress and psychological well-being). Each of the 12 items contributes to the physical and mental component scores according to a prespecified weight used in the calculation. The weights are based on results from the general population in the United States and yield standardized scores. Higher scores indicate better health status. In the US general population, the SF-12 items explained more than 90% of the variance in the Short Form-36 physical and mental health summary measures.

Wolfer-Davis Recovery Index. The Wolfer-Davis Recovery Index is an 8-item self-report instrument used to measure perceived surgical recovery. Patients are asked to rate their recovery from surgery on a 5-point Likert scale from 1 (the poorest possible recovery) to 6 (the best possible recovery). Recovery items include ones related to general health, such as appetite, strength and energy, interest in what is going on around oneself, and ones related to activities of daily living, such as ability to move around and ability to do things for oneself. The range of scores extends from 8 to 48; a higher score indicates a more favorable state of recovery. The scale has been used in a variety of surgical patients, with reliability coefficients of .85. Construct validity in comparison with a pain scale and an ambulation scale during a period of 4 postoperative days has been supported.

Data Analysis
Baseline characteristics of the sample were examined by using measures of central tendency. In order to reduce the possibility that any indicated association between higher scores for depressive symptoms and physical recovery measures could be explained by clinical or sociodemographic variables, differences in baseline characteristics between patients with higher and lower scores for depressive symptoms were examined at each time point. For these comparisons, χ² statistics were used for categorical variables, and 1-way analysis of variance was used for continuous variables.

Because scores for depressive symptoms were greater than the community norm of 11 in most patients, median scores at each time point were used to form the 2 groups of patients with higher and lower scores. At the time of discharge from the hospital and at 6 weeks after discharge, groups with higher and lower
scores were compared by using physical and emotional recovery instruments. At the time of discharge, the inhospital scores were used; at 6 weeks, the hospital discharge scores were used. Multivariate analysis of variance was used to compare subsequent outcomes between groups with high and low scores for depressive symptoms. For the second time point (groups based on scores for depressive symptoms at the time of discharge), age was used as a covariate and diabetes was used as a second fixed factor to control for differences between the groups. The incidence of infections and impaired wound healing was compared by using \( \chi^2 \) statistics. Because age and presence of diabetes differed by group and because obesity is a known risk factor for poor wound healing after CABG, \(^{29}\) logistic regression analysis was used to control for the effects of these variables. The Bonferroni adjustment was used to control for multiple comparisons.

## Results

Of the 72 patients who enrolled in the study, 67 participated at the time of discharge from the hospital, and 60 completed an evaluation 6 weeks after discharge. The most common reason for dropping the study was to return to presurgical activities (ie, work). Demographic and clinical characteristics of the sample are summarized in the Table. We found no differences in demographic and clinical characteristics between patients who completed the study and those who did not or between patients with higher and lower scores for depressive symptoms within 48 hours after extubation. At the time of discharge from the hospital, however, patients with higher scores for depressive symptoms were younger than patients with lower scores (mean 60.2 years, SD 8.9 years vs mean 68.1 years, SD 10.1 years, respectively; \( P = .02 \)) and were more likely to have diabetes (83.7% vs 16.7%, respectively; \( P = .04 \)).

### Table: Demographic and clinical characteristics of the sample

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Whole sample (N = 72)</th>
<th>Group with lower scores for depressive symptoms at discharge from the hospital (n = 36)</th>
<th>Group with higher scores for depressive symptoms at discharge from the hospital (n = 31)</th>
<th>( P )</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years</td>
<td>64.9 10.3</td>
<td>68.1 10.1</td>
<td>60.2 8.9</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Education, years</td>
<td>15.4 2.8</td>
<td>15.0 2.8</td>
<td>16.0 2.7</td>
<td>.17</td>
</tr>
<tr>
<td>Ejection fraction</td>
<td>0.53 0.14</td>
<td>0.54 0.11</td>
<td>0.51 0.18</td>
<td>.43</td>
</tr>
<tr>
<td>No. of bypass grafts</td>
<td>3.1 1.0</td>
<td>3.2 1.1</td>
<td>3.0 1.1</td>
<td>.47</td>
</tr>
<tr>
<td>Postoperative length of hospital stay, days</td>
<td>6.4 2.5</td>
<td>6.6 3.0</td>
<td>6.0 1.7</td>
<td>.43</td>
</tr>
<tr>
<td>Previous infarction or coronary artery bypass grafting</td>
<td>26 36.1</td>
<td>10 27.8</td>
<td>11 35.5</td>
<td>.50</td>
</tr>
<tr>
<td>Female</td>
<td>27 37.5</td>
<td>15 41.7</td>
<td>10 32.3</td>
<td>.43</td>
</tr>
<tr>
<td>Diabetes</td>
<td>19 26.4</td>
<td>6 16.7</td>
<td>12 38.7</td>
<td>.04</td>
</tr>
<tr>
<td>Married</td>
<td>44 61.1</td>
<td>20 55.6</td>
<td>21 67.7</td>
<td>.17</td>
</tr>
<tr>
<td>Preoperative risk (Parsonnet score):</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Good/fair</td>
<td>42 58.3</td>
<td>20 55.6</td>
<td>20 64.5</td>
<td>.46</td>
</tr>
<tr>
<td>Poor</td>
<td>19 26.4</td>
<td>11 30.6</td>
<td>6 19.4</td>
<td></td>
</tr>
<tr>
<td>High/very high</td>
<td>11 15.3</td>
<td>5 13.9</td>
<td>5 16.1</td>
<td></td>
</tr>
<tr>
<td>Urgency of operation</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Elective</td>
<td>45 62.5</td>
<td>24 66.7</td>
<td>19 61.3</td>
<td></td>
</tr>
<tr>
<td>Urgent</td>
<td>21 29.2</td>
<td>10 27.8</td>
<td>9 29.0</td>
<td></td>
</tr>
<tr>
<td>Emergency</td>
<td>6 8.3</td>
<td>2 5.6</td>
<td>3 9.7</td>
<td></td>
</tr>
<tr>
<td>Ethnicity</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>59 81.9</td>
<td>28 77.8</td>
<td>26 83.9</td>
<td>.38</td>
</tr>
<tr>
<td>African American</td>
<td>5 6.9</td>
<td>4 11.1</td>
<td>1 3.2</td>
<td></td>
</tr>
<tr>
<td>Hispanic</td>
<td>3 4.2</td>
<td>1 2.8</td>
<td>2 6.5</td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>5 6.9</td>
<td>3 8.3</td>
<td>2 6.5</td>
<td></td>
</tr>
</tbody>
</table>

Depressive symptoms are greatest at the time of transfer from the intensive care unit, about the second to third postoperative day.
For the whole sample at the 3 time points (in hospital, discharge from the hospital, and 6 weeks after discharge), mean scores for depressive symptoms on the MAACL were 19.8 (SD 6.3), 18.8 (SD 7.1), and 16.4 (SD 7.8), respectively. At the 3 respective time points, 92%, 88%, and 72% of patients in the sample scored higher than the population norm of 11.

At 6 weeks after discharge, 19 (26%) of the 72 patients met criteria for wound infections or wound-healing problems. Of those, 9 (12%) had positive blood cultures, 15 (21%) received antibiotics, and 11 (15%) required extra treatment. A total of 5 patients (7%) had wound problems of the sternum, 8 (11%) had complications at the donor graft site, and 2 (3%) had complications at both the sternal and donor graft sites. Among the 9 patients with positive cultures, 4 (44%) had cultures positive for multiple microorganisms. The most common organisms reported were coagulase-negative staphylococci and Staphylococcus aureus, both detected in 4 patients (44%) who had positive cultures.

Seventy-seven percent of patients recovering from bypass surgery had greater levels of depression than community norms 6 weeks after discharge.

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Figures 1 through 3 are comparisons of outcomes (1) at the time of discharge from the hospital in groups according to in-hospital scores for depressive symptoms and (2) at 6 weeks after discharge in groups according to scores for depressive symptoms at the time of discharge. Patients with higher scores within 48 hours after extubation had poorer mental and physical health.
scores on the SF-12, poorer self-rated recovery, and poorer perceived control at the time of discharge than did patients with lower scores (Figure 1A). They also had shorter walking distances on the 6-minute walk test than did patients with lower scores (Figure 2). Six weeks after discharge, patients who had had higher scores for depressive symptoms at the time of discharge continued to have poorer self-rated recovery and poorer perceived control than did patients who had had lower scores (Figure 1B). Patients with higher scores at discharge were 3.7 times more likely than patients with lower scores to experience wound infections and wound-healing problems 6 weeks after discharge (odds ratio 3.71; 95% CI 1.15-12.0; \( P = .03 \); Figure 3). These findings persisted even when the effects of age and diabetes, both of which differed between the groups, and the effects of obesity, which is a known risk factor for infections at surgical sites, were controlled for statistically. Patients with higher scores at the time of discharge did not differ significantly from patients with lower scores in the distance traveled in the 6-minute walk test at 6 weeks after discharge.

**Discussion**

Our findings support a growing body of evidence that documents the high prevalence of depressive symp-

toms after CABG and links the symptoms to adverse outcomes after surgery. In particular, the high levels of depressive symptoms prevalent immediately after surgery, at the time of discharge from the hospital, and 6 weeks after discharge, support the findings of McCrone et al\(^ {31} \) that depression is greater than population norms during the early postoperative period. Our finding that depressive symptoms were highest within 48 hours after extubation is consistent with this earlier report\(^ {11} \) that dysphoria peaks during the second to third postoperative day. Factors related to the surgical experience, such as pain, sleep deprivation, isolation, and loss of control, may intensify feelings of depression in the first few days after CABG, a situation that could explain this phenomenon. Together, these studies establish a consistent pattern in which dysphoria peaks after surgery and diminishes over time.

The proportion of patients (72%) who had scores for depressive symptoms greater than community norms 6 weeks after discharge was higher in our study than in studies by other investigators,\(^ {6,31} \) who found evidence of clinical depression in 23% and 26% of patients at 6 weeks and 12 weeks, respectively. Our finding that a large majority of patients experienced depressive emotions greater than the community norm indicates the pervasive presence of a wide spectrum of depressive states after CABG.

Although cardiac events have been associated with major depression after CABG, findings about the relationship between lesser depressive states and emotional and physical recovery have been equivocal. Some investigators\(^ {6} \) found that even marked depressive symptoms just short of meeting criteria for major depression were not correlated with postsurgical car-
Cardiac events. Our findings that walking distances, self-reported physical and emotional recovery, and perceived control over one’s health after CABG were diminished in patients with higher scores for depressive symptoms supports the theory that depression need not be at the level of a clinical syndrome in order to influence recovery outcomes. Although symptoms consistent with major depression have been associated with major cardiac events, lesser symptoms appear to be associated with poorer quality of life and with increased incidence of incomplete symptom relief after CABG. However, differences in study methods and instruments make it difficult to compare results across studies. Further investigation is warranted to evaluate the severity of symptoms in relation to surgical outcomes after CABG.

The most intriguing finding from our study is the positive association between depressive symptoms and infections and impaired wound healing. This finding supports a biobehavioral model in which psychological, behavioral, and biological pathways influence wound healing. In the model, surgery is a form of stress. Patients’ responses to the stress of surgery are influenced by psychological states, such as depression and anxiety. Together with the stress of surgery, dysphoria may act indirectly via the hypothalamic-pituitary-adrenal axis to modulate immune function or may affect immune cells directly so that secretion of proinflammatory cytokines becomes dysregulated. Consistent with this model, studies in animals and preliminary studies in humans indicate that increased short-term stress results in a large reduction in wound healing. In addition, adverse behavioral changes, such as poorer hygiene, nutrition, and self-care and reduced adherence to medical recommendations, are often associated with depression. These factors may act directly to increase the likelihood that patients who are depressed after surgery will have postoperative complications.

**Patients’ responses to the stress of surgery is influenced by depression, which may enhance the production of proinflammatory cytokines.**

Most likely cytokines provide an important link between delayed postoperative infectious complications and impaired wound healing and depressive symptoms. Evidence exists that depression and anxiety enhance the production of proinflammatory cytokines, particularly interleukin-6. In animal models, stress elevates plasma levels of interleukin-6, probably through stimulation of α-adrenergic receptors. Elevated circulating levels of proinflammatory cytokines may, in turn, activate multiple feedback loops involving prostaglandins, soluble receptors for interleukin-2, and hyperactivity of the hypothalamic-pituitary-adrenal axis, which result in a blunted cellular immune response to pathogens. Further study is warranted to investigate possible immune-mediated and behaviorally mediated pathways that may explain the association of depressive symptoms with infections and impaired wound healing after CABG.

The independence of the association we found is consistent with the results of earlier experimental studies in which investigators showed that stress has a large effect on wound healing. This finding is important because wound healing and postoperative infections are a major source of postoperative morbidity and dramatically increase the cost of CABG. The overall incidence of infections at the surgical site and of impaired healing of the incisions used to obtain the saphenous vein can be as high as 9.9% and 43.8%, respectively. In addition, infections at surgical sites are associated with longer hospital stays and increased costs.

To date, evidence on the effect of negative emotions on wound healing has been based largely on experimental studies in community samples of healthy persons. Few investigators have examined this relationship in patients. Our findings are among the first to establish a relationship between depressive symptoms and infections and impaired wound healing after CABG.

For 2 reasons of note, the association between depressive symptoms and infections and impaired wound healing remained significant even when the effects of age, diabetes, and obesity were taken into account. First, controlling statistically for these factors limits the likelihood that our findings are spurious, because both increased age and diabetes could mediate an association between depressive symptoms and postoperative infections and wound healing in patients after CABG. Immunocompetence declines with age, and the vascular, neuropathic, and biochemical abnormalities of diabetes inhibit wound healing. Second, and more important, the number of patients more than 70 years old who have CABG and the number of patients with diabetes who have this surgery continue to increase steadily. As a result, increasing numbers of patients who have CABG will be predisposed to infections and impaired wound healing. The added burden of depressive symptoms in this increasingly vulnerable population most likely will have a marked effect on postoperative morbidity, use of healthcare resources, and costs of surgical recovery.
Our findings are limited by the use of a single recruitment site, by the use of a single instrument to measure depressive symptoms, and by a relatively small sample size. We recruited patients from an urban tertiary care center, where patients were well educated and primarily white, so our findings may not be generalizable to other populations. In addition, we used a single instrument to measure depressive symptoms. Depressive symptoms might have been better characterized if additional instruments designed to identify clinical depression and symptom severity had been added. Finally, with a modest sample size, we were unable to consider psychosocial variables, such as social support, and behavioral factors, such as compliance with activity and self-care recommendations, that are thought to influence surgical recovery. Other factors germane to surgical recovery, such as the involvement of home healthcare and cardiac rehabilitation and the level of primary care follow-up after surgery, also warrant inclusion in future, larger studies.

In summary, our findings add to the accumulating body of evidence for high levels of psychological morbidity after CABG and support the association between depressive symptoms and poor postoperative outcomes after surgery. Our findings that functional status as reflected by walking distances, self-reported physical and emotional recovery, and perceived control over one’s health after CABG were diminished in patients with depressive symptoms provides meaningful information that clinicians can use to provide patients with specific support and intervention to improve recovery outcomes. The finding that depressive symptoms are associated with increased postoperative infectious complications and impaired wound healing further underscores the need for early recognition and treatment of patients at risk for depression after CABG. Confirmation of these findings in a larger, more diverse sample is needed, along with studies designed to test specific immune pathways that most likely influence the development of infectious complications and impaired wound healing after CABG.

ACKNOWLEDGMENTS
This study was funded by a Critical Care Research Award from the American Association of Critical-Care Nurses and by grant K01 017001 from the National Institutes of Mental Health.

Commentary by Mary Jo Grap (see shaded boxes).

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AMERICAN JOURNAL OF CRITICAL CARE, July 2005, Volume 14, No. 4
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Am J Crit Care 2005;14 316-324
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