

Depressed Mood and Survival in Seriously Ill Hospitalized Adults

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Objectives: To assess the relationship among depressed mood, physical functioning, and severity of illness and to determine the relationship between depressed mood and survival time, controlling for severity of illness, baseline functioning, and characteristics of patients.

Methods: Prospective cohort study of data for 3529 seriously ill hospitalized adults who received care at 5 tertiary care teaching hospitals and who completed a depressed mood assessment 7 to 11 days after admission to the study. The Profile of Mood States depression subscale was used to assess depressed mood. A stratified Cox proportional hazards model was used to assess the independent effect of depressed mood on survival time, adjusting for demographic characteristics of patients and health status.

Results: Greater magnitudes of depressed mood were associated with worse levels of physical functioning ($r=0.151$; $P<.001$) and more severity of illness. Depressed mood was associated with reduced survival time after adjusting for patient demographics and health status (hazards ratio, 1.134; 95% confidence interval, 1.071-1.200; $P\leq.001$).

Conclusion: Seriously ill patients should be assessed for the presence of depressed mood even if they have not been given a diagnosis of depression. Further study is needed to determine whether interventions aimed at relieving depressed mood may improve prognosis.

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SEVERAL INVESTIGATORS have found an association between depression and mortality.¹⁻⁶ However, depression also has been shown to be strongly associated with poorer functional status^{1,7-13} and severity of illness.¹⁴⁻¹⁷ Whether a causal relationship exists between depression and mortality or whether depressive symptoms are mainly markers for unmeasured severity of illness is unclear.⁵

Past researchers have not studied the associations among physical functioning, severity of illness, depressed mood, and mortality in a population with high mortality. To address this issue, we analyzed data from patients enrolled in the Study to Understand Prognoses and Preferences for Outcomes and Risks of Treatments (SUPPORT) project. In the SUPPORT project, patients were assessed for mood state during hospitalization; detailed measures of physical functioning and severity of illness were included.¹⁸ Patients were observed for 6 months after admission to the study. During this time, 47% of the patients died. Because detailed measures of physical func-

tioning and severity of illness were available for these patients, we were able to adjust for the relationships among depressed mood, severity of illness, and functional status to determine whether depressed mood was independently associated with mortality. This enabled us to study the independent effect of depressed mood on mortality while controlling for factors that may have confounded the relationship between depressed mood and mortality in past studies.

Specifically, we determined the association of depressed mood with physical functioning and severity of illness in a severely ill hospitalized population^{1,6-11} and the independent association of depressed mood with survival after adjusting for confounding by functional status and severity of illness.^{2,9-13}

RESULTS

CHARACTERISTICS OF THE SAMPLE

Of the 9105 patients enrolled in SUPPORT, 4092 were ineligible to complete the mood assessment interview. Reasons for ineli-

PATIENTS AND METHODS

PATIENTS

Patients were enrolled in the SUPPORT.¹⁸ This study was conducted from June 1989 to January 1994 at 5 teaching hospitals in the United States. Enrolled patients represented a range of adult patient populations: urban and rural, lower and higher income, and black, white, and Hispanic.

Patients were included in SUPPORT if they met predetermined selection criteria for a diagnosis of acute respiratory failure, exacerbation of chronic obstructive pulmonary disease, exacerbation of congestive heart failure, end-stage liver disease, nontraumatic coma, stage III or IV non-small cell lung cancer, colon cancer metastatic to the liver, or multisystem organ failure with sepsis or a malignant neoplasm. In aggregate, this population had a projected 6-month mortality of 50%. Patients were excluded if they did not speak English; had acquired immunodeficiency syndrome, head trauma, or burns; were pregnant; were younger than 18 years; were admitted to a hospital with an expected length of stay of less than 72 hours; died within 48 hours of hospital admission; or were transferred from another hospital to a hospital participating in the study.¹⁸

Data were collected by abstraction from the medical chart and by structured interviews. Data from the medical chart included diagnoses, comorbid illnesses, and physiological data including the acute physiology score from the Acute Physiology and Chronic Health Evaluation (APACHE) III.¹⁹ The SUPPORT prognostic model generated 2-month and 6-month survival estimates for each patient based on the burden of illness at the time of admission to the study.²⁰ The SUPPORT model has been shown to adjust well for severity of illness and has an area under the receiver operating characteristic curve of 0.78 for predicting survival.²⁰

Patients were interviewed between 2 and 5 days after admission to the study (the day-3 interview) and again

between 7 and 11 days after admission to the study, if the patient remained hospitalized, or within 5 days of discharge from the hospital. During the day-3 interview, patients were asked about demographic characteristics (including age, race, sex, marital status, and educational level) and functional status 2 weeks before hospitalization as measured by a modified Katz Index of Activities of Daily Living (ADL) scale.²¹ Mood assessment was performed during the second interview, approximately 1 to 2 weeks after admission to the study, if the patient remained hospitalized, or within 5 days of discharge from the hospital. Of the patients eligible for an interview, 74% completed the second interview. For 5% of these patients, data were missing for 3 or more depressed mood items. We included only patients who provided information about mood in this analysis (N=3529).

VARIABLES

Clinical

We used a modified Katz ADL scale as a guide to ask patients a series of questions about their self-care ability for bathing, washing, eating, walking, toileting, dressing, transferring (ie, independent moves in and out of bed and chair), and continence.²¹ The surrogate (the person identified by the patient or physician as the person who would make decisions for the patient if the patient were unable) was asked to assess the patient's ability using the same questions. If responses about ADLs were unavailable from the patient, the surrogate's responses for the ADL scale were used to calculate the ADL score. If data from the patient and surrogate were missing, an imputed score was used.²² The ADL scores ranged from 0 to 7, with 0 indicating independence in all activities and 7 indicating the worst physical functioning.

Three measures of the severity of illness were used in this analysis: the acute physiology score (APS) of the APACHE III score on day 3 after admission to the study; the number of comorbid illnesses present at the time of admission to the hospital and the estimate from the

gibility included the following: died before the interview, 1853; intubated or in a coma, 957; did not pass the cognitive screening test, 382; or unable to communicate, 900. Of the remaining eligible patients (n=5013), 3529 completed the mood assessment. Reasons for not completing the interview or scale were as follows: the patient refused, 572; the physician refused for the patient, 159; the surrogate refused for the patient, 300; the patient did not answer 3 or more of the mood assessment questions, 181; or the patient could not be located after discharge from the hospital, 272.

The median age for patients in the study was 63 years, and the median educational level was 12 years. Of the patients, 58% were men, 78% were white, and 52% were married. The most common disease groups were acute respiratory failure, congestive heart failure, chronic obstructive pulmonary disease, and lung cancer (**Table 1**). The median APS score at day 3 of the study was 29.0. The median number of comorbid illnesses was 2.0, and the median number of disabilities was about 0.5. Of the study patients, 42% died within 4½ years of admission to the study. Characteristics of the patients used in the

analyses are listed in Table 1. The median POMS depressed mood score was 0.37 on a 0 to 4 scale. **Figure 1** shows the depressed mood scores for the sample.

Patients who completed a depressed mood assessment interview and those who did not differed on several key demographic, severity of illness, and outcome variables. Those who completed the questionnaires were younger (mean age, 61 years vs 64 years; $P \leq .001$) and tended to be men (58% vs 42%; $P \leq .01$), had a lower day-3 APS (41 vs 31; $P \leq .001$), had more comorbid illnesses (mean, 2 vs 1.8; $P = .001$), but were more functional (mean, 1.2 vs 1.8 ADL dependencies; $P = .001$).

FACTORS ASSOCIATED WITH DEPRESSED MOOD SCORE

The associations of factors with depressed mood scores are given in **Table 2**. Older persons were less depressed than younger persons ($r = -0.121$; $P \leq .001$). More dependencies in ADLs were associated with worse depressed mood scores ($r = 0.151$; $P = .001$), as was greater severity of illness ($r = 0.083$; $P = .001$). Consistent with these

SUPPORT project model for 6-month survival,²⁰ which considers several clinical indicators of severity of illness.

Mortality

Survival time was calculated by subtracting the patient's date of death from the date of admission to the study. The result was the number of days the patient survived from admission to the study until death.

For analysis, the final vital status was defined by whether the patient was known to be alive 4½ years after admission to the study. We continued contacting patients up to 180 days from admission to the study for interviews, or next of kin to document deaths. After 6 months, the names and social security numbers of patients were traced through the National Death Index (US Dept of Health and Human Services, National Center for Health Statistics, Baltimore, Md) for a 4-year period to determine vital status.

Depressed Mood

Depressed mood was measured using the depression subscale from the shortened version of the Profile of Mood States depression scale (POMS).²³ The subscale consists of 8 items (ie, unhappy, sad, blue, hopeless, discouraged, miserable, helpless, and worthless). For each descriptor, patients were asked whether they had felt this way during the past week. The possible responses were as follows: 0, not at all; 1, a little; 2, moderately; 3, quite a bit; and 4, extremely. A depressed mood score was obtained by summing the points and dividing by the number of items in the scale. The range of depressed mood scores was thus 0 to 4, with a higher score indicating a more depressed mood. If 1 or 2 items were missing, the score was calculated by using mean substitution. If 3 or more items were unanswered, the depressed mood score was considered missing (n=181). The Cronbach α for this version of the POMS was .89, indicating good internal consistency or reliability.

STATISTICAL ANALYSIS

Age, years of education completed, marital status, and sex were used to describe the patient population. Because many of the variables had skewed distributions, nonparametric statistical procedures were used to compare groups within the sample and to study bivariate relationships. To determine whether significant differences existed between the 2 groups, independent sample Wilcoxon rank sum tests were used to compare the sample that completed the depressed mood assessment with the sample that did not complete the assessment. The Spearman rank correlation was used to evaluate the bivariate relationships between depressed mood and patient characteristics, illness characteristics, and mortality.

The mortality rates for the 9 disease categories in the SUPPORT project varied during the 6 months of observation. For example, patients with a primary diagnosis of acute respiratory failure or multisystem organ failure had higher 30-day mortality rates than patients with colon or lung cancer, but they all had similar 180-day mortality rates.²⁰ These differential mortality rates violate the assumption of the Cox proportional hazards model that baseline risk is the same across disease groups. Therefore, a Cox proportional hazards model stratified by disease group was used to test whether depressed mood had an independent effect on survival time. The disease groups included acute respiratory failure, chronic obstructive pulmonary disease, chronic heart failure, liver disease, cirrhosis, colon cancer, lung cancer, and multisystem organ failure with a malignant neoplasm or sepsis. The independent variables in the model included age, ADL score, APS, the number of comorbid illnesses, sex, the 6-month survival estimate from the SUPPORT model, and the POMS depressed mood score. The interaction of ADL with depressed mood also was tested. However, results proved to be insignificant and, therefore, are not included in the final analysis. All the analyses were performed using statistical software (SPSS for Windows, release 6.0, SPSS Inc, Chicago, Ill).

findings, a higher estimate of the probability of 6-month survival was negatively associated with depressed mood ($r=-0.057$; $P=.001$). Although these relationships were statistically significant, the relationships were weak.

To test whether depressed mood had an independent effect on survival time, age, ADL score, the APS on day 3 of the study, the number of comorbid illnesses, and sex, the 6-month survival estimate and depressed mood score were simultaneously entered into a stratified Cox proportional hazards model predicting survival. **Table 3** gives the coefficients, standard errors of the coefficients, the exponential value of the coefficients, and the 95% confidence intervals for each covariate in the model.

In this model, the ADL score ($P\leq.001$), the number of comorbid illnesses ($P\leq.001$), the 6-month estimate of survival from the SUPPORT model ($P\leq.001$), age ($P\leq.01$), and depressed mood ($P\leq.001$) independently predicted survival time. The χ^2 of the model was 308 when the *df* was 7. For example, an increase of 1 ADL dependency increased the odds of a shorter survival time by

9.5%. An increase of 1 comorbid illness increased the odds of a shorter survival time by 13%. The odds associated with survival time decreased by 13.4% with every unit increase in depressed mood score. Thus, compared with the odds of shorter survival time, depressed mood is in the same range as ADL dependencies and comorbid illnesses.

Figure 2 shows the estimated probability of survival time for increments of the POMS depressed mood score, the number of comorbid illnesses, and age. The estimated survival for each increment of the variable was calculated separately, holding all other variables in the model constant at their median. The difference between a score of 0 (ie, no depressed mood) and a score of 2 (ie, moderate level of depressed mood) was associated with an 11% decrease in the estimated survival time, whereas the difference between having no comorbid illnesses and 4 comorbid illnesses was a 17% decrease in the estimated survival time. On the other hand, differences in age were related less strongly to the estimated survival time: a 40-year increase in age led to a difference of a 9% reduction in the estimated survival time.

Table 1. Patient Characteristics (N=3529)*

Variable	Percentage	Mean	Percentile		
			25th	50th	75th
Age, y	...	60.9	51.1	62.9	71.6
Education, y	...	11.7	10.0	12.0	13.0
Sex, male	58.0
White	81.0
Married	52.0
Disease					
Acute respiratory failure	28.7
Congestive heart failure	24.1
Chronic obstructive pulmonary disease	14.3
Lung cancer	11.9
Colon cancer	7.8
Cirrhosis	7.5
Multisystem organ failure	5.2
Nontraumatic coma	0.4
Acute physiology score† at day 3	...	30.5	20	29	38
Activities of daily living	...	1.2	0.0	0.5	1.9
POMS* depressed mood score	...	0.7	0.0	0.4	1.1
No. of co-illnesses	...	2.1	1	2	3
SUPPORT model estimate for 6-month survival	...	0.64	0.53	0.68	0.78
Death by 4½ years	42

*Ellipses indicate not applicable; POMS, Profile of Mood States; and SUPPORT, Study to Understand Prognoses and Preferences for Outcomes and Risks of Treatments.

†Of the Acute Physiology and Chronic Health Evaluation III.

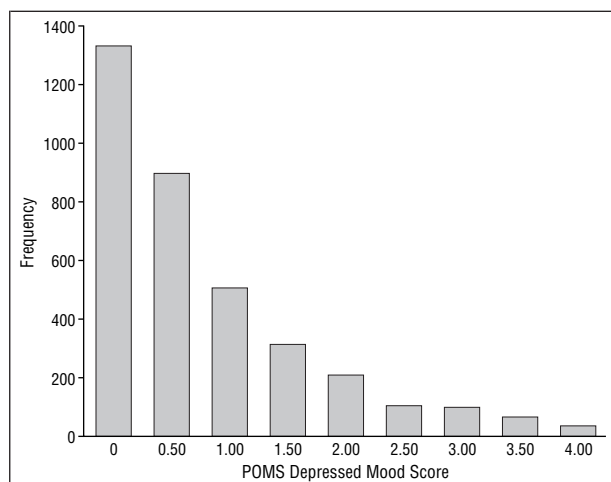


Figure 1. Depressed mood scale. Scores range from 0 to 4, with a higher score indicating a more depressed mood. N=3529; mean, 0.73; SD, 0.89. POMS indicates Profile of Mood States depression scale.

COMMENT

We studied the association of depressed mood and mortality in a group of severely ill hospitalized adults by using a stratified Cox proportional hazards model. What made the present study unique was our ability to assess a demographically and medically diverse group of hospitalized adults, whereas past research on depression or depressed mood had used mainly homogeneous groups of subjects, thus, limiting generalizability.

Depressive symptoms, or affect, have been found to be associated with increased mortality rates in patients in nursing homes.^{1,2} Many studies have found a predictive effect of depressive symptoms on mortality in pa-

Table 2. The Bivariate Relationship of Patient Characteristics and POMS Depressed Mood Score (N=3529)*

Patient Characteristics	POMS Depressed Mood Score
Age	-0.121†
Sex‡	-0.071†
Activities of daily living	0.151†
Acute physiology score at day 3§	0.083†
SUPPORT model 6-mo survival estimate	-0.057†
No. of comorbid illnesses	0.021

*Spearman rank correlation coefficients. POMS indicates Profile of Mood States; SUPPORT, Study to Understand Prognoses and Preferences for Outcomes and Risks of Treatment.

†P ≤ .001.

‡0=female; 1=male.

§Of the Acute Physiology and Chronic Health Evaluation III.

tients with various long-term diseases.^{1,5,8-11,24-29} By using a Cox proportional hazards model stratified for disease group, we found that depressed mood and severity of illness independently predicted survival time. Depressed mood had a significant association with survival while accounting for severity of illness, physical functioning, and patient demographics.

In contrast, some investigators have not found a relationship between depressive symptoms and mortality.^{5,30-32} Most studies with negative results have studied mortality in elderly populations in nursing homes rather than community-based samples. For an older population in poor health, factors other than depression may be stronger determinants of mortality; depression may be minimal and, thus, may not be significantly associated with mortality. Or, older persons may be more likely to die regardless of mood.

Table 3. Association of Survival Time With Patient Characteristics, Physical Functioning, Severity of Illness, and POMS Depressed Mood Score (N=3259)*

Variable	B Coefficient	Standard Error	ExpB†	95% CI of ExpB
Age‡	.065§	.022	1.067	1.023-1.113
Activities of daily living	.091	.016	1.095	1.061-1.130
Acute physiology score at day 3‡	.030	.029	1.034	0.981-1.089
Number of comorbid illnesses	.119	.022	1.127	1.078-1.177
Sex¶	.148§	.054	1.160	1.043-1.289
SUPPORT model 6-month survival estimate#	-.453	.055	0.636	0.571-0.708
POMS depressed mood score	.126	.029	1.134	1.071-1.200

*For the model $\chi^2=308$; $df=7$. POMS indicates Profile of Mood States; SUPPORT, Study to Understand Prognoses and Preferences for Outcomes and Risks of Treatments.

†The exponential value of the coefficient (ExpB) is the factor by which the odds of dying are increased or decreased by a unit change in the covariate.

‡Transformed by dividing the variable by 10 to represent a 10-year change in age and, for the acute physiology score; a 10-point change. The acute physiology score is a subscore of the Acute Physiology and Chronic Health Evaluation III.

§ $P \leq .001$.

|| $P \leq .01$.

¶0=female; 1=male.

#Because the SUPPORT Model survival estimate was skewed, a log transformation was performed ($\log_e - \log_e P$) to better fit the Cox proportional hazards model assumptions.

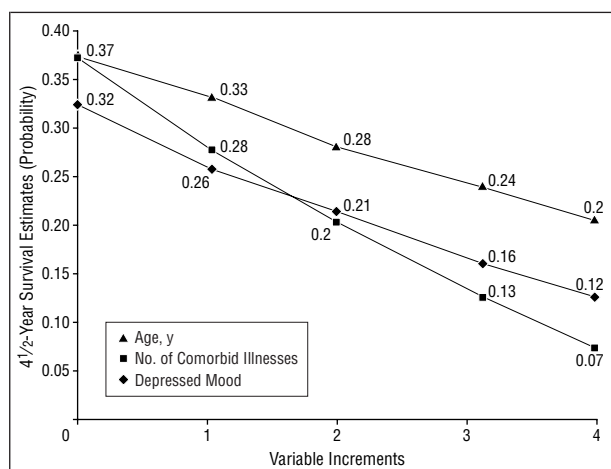


Figure 2. Predicted probability of survival for increments of depressed mood score, number of comorbid illnesses, and age; $N=3529$. The increments of depressed mood score for values of 0, 1, 2, 3, and 4, respectively, follows. Depressed mood score: 0, 1, 2, 3, and 4; number of comorbid illnesses: 0, 2, 4, 6, and 8; and age: 18, 38, 58, 78, and 98 years. The survival estimates are based on the Cox proportional hazards model, which also included the following variables: activities of daily living, the acute physiology score of the Acute Physiology and Chronic Health Evaluation III at day 3, and sex.

The literature on physical functioning and depression suggests a tendency for depression to worsen as physical health declines.^{8,11} In a review of 17 articles on physical functioning as measured by ADL scales, Schubert et al⁹ found a relationship between poor physical functioning and level of depression in 11 articles and no relationship in the other 6 articles. Our results suggest that patients who reported low levels of physical functioning, as measured by the ADL scale, also were more likely to report a greater magnitude of depressed mood than patients with higher levels of physical functioning.

Some have argued that for patients with chronic and severe illness, it is the illness that produces a decline in physical functioning and not depression. However, Wells et al¹⁶ found that although chronic illness alone did not affect physical functioning, the addition of depressive symptoms was associated with a significant reduction in

functioning. Koenig et al¹⁴ studied consecutive admissions to the neurologic service of a Veterans Administration medical center and found that physician-rated global severity of illness, as measured by a general summed rating of illnesses and the number of prescribed medications, explained 17.3% of the variance in depression. Parkerson et al¹⁵ also found that subjects with the highest combined severity of illness and disability scores also scored worse on depression scales than subjects with low severity of illness and disability scores.

When severity of illness is measured by patients' perceptions of their illness, the association with depression is significant, but when severity is assessed by using clinical data, the relationship diminishes.⁵ While clinical data may be important to the study of clinical outcomes, they may have little effect on specific patients' perceptions or understandings of their illness. Depression also may affect how patients interpret clinical information.

In the present study, the associations between depressed mood and severity were weak, but in the predicted direction. It is possible that because of the ongoing nature of their illnesses, patients in our study may have better clinical understanding of their medical conditions compared with patients in previous studies. This understanding, in turn, may have been reflected in their mood.

Our study had several limitations. First, our analysis was based on interviews of patients who agreed to participate in the study and were able to be interviewed. The sickest patients in the study could not be interviewed. We do not have data to suggest that the responses of the sicker patients would be different from or similar to those of the patients who were interviewed. Even so, our study included patients with greater severity of illness than in previous studies.

Second, our interview did not include a structured psychiatric evaluation. Therefore, we could not diagnose major depression or depressive disorders or assess the relationship between clinical depression and mortality. However, our analysis does show that a simple easy-to-administer depressed mood inventory is independently associated with mortality, emphasizing the

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importance of depressed mood regardless of the presence or absence of major depression.

Third, we cannot make causal linkages between the development of depressed mood and survival because we did not measure the development of depressed mood from before hospitalization until death. Still, we were able to control for some factors believed to confound the relationship between depressed mood and survival, so that we can conclude from our data that depressed mood has an independent relationship with survival time.

CONCLUSION

We found that depressed mood was independently related to the survival of seriously ill hospitalized patients. The relationship between depression and mortality is complex. Our study extends previous research because we controlled for the confounding effects of physical functioning and severity of illness on depression. However, our study does not explain the mechanisms underlying the relationship between depressed mood and mortality. Depressed mood may contribute to mortality through biological mechanisms, perhaps mediated by a link between mood and immunologic function.³³ Depressed mood may affect mortality because depressed mood can reduce social and psychological functioning and, thus, reduce a person's ability to cope with severe illness, which, in turn, may affect survival.³⁴⁻³⁸

Why does depressed mood affect survival? Is it because patients who have a depressed mood are more likely to be pessimistic about their future and make decisions that have a negative effect on outcome? Are patients with depressed moods more willing to forgo aggressive treatments than patients without depressed mood? Research to better answer these questions is urgently needed. We hope to address these questions in future research.

Our study indicates that clinicians need to be aware of the patient's mood, even if the patient has not been given a diagnosis of major depression. Because treating depression is easier than increasing the physical functioning of an ill patient, the treatment of depressed mood may be the most effective of available interventions.

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