Depressive Symptoms as a Predictor of 6-Month Outcomes and Services Utilization in Elderly Medical Inpatients

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Background: Depressive symptoms have been associated with higher mortality in hospitalized elderly persons, but few data are available associating depressive symptoms with other outcomes.

Objective: To determine the association between depressive symptoms and the risk of hospital readmission, nursing home admission, and death as well as inpatient services utilization during a 6-month follow-up period in a cohort of elderly medical inpatients.

Methods: We enrolled 401 patients, 75 years and older, admitted to the internal medicine service of an academic hospital in Lausanne, Switzerland. Data on demographic, medical, physical, social, and mental status were collected on admission. Depressive symptoms were defined as a score of 6 or higher on the Geriatric Depression Scale short form. Follow-up data were gathered from the centralized billing system (hospital and nursing home admissions) and from proxies (in cases of death).

Results: In bivariate analysis, depressive symptoms were associated with an increased risk of hospital readmission, nursing home placement, and death. After adjustment for demographic, socioeconomic, and functional status and comorbidity, depressive symptoms remained associated with an increased risk of hospital readmission (adjusted hazard ratio, 1.50; 95% confidence interval, 1.03-2.17; \( P = .03 \)). In addition, depressive symptoms were associated with increased average costs of both acute and rehabilitation services, resulting in higher overall costs of inpatient services. ($175.70 vs $126.00; \( P < .001 \)). This association remained after adjusting for differences in functional status, comorbidity, and living situation, although it was just short of statistical significance (\( P = .07 \)).

Conclusions: Elderly medical inpatients with depressive symptoms were more likely than those without to be readmitted and had higher inpatient services utilization during the follow-up period, independent of functional and health status. These results emphasize the need for interventions directed at improving management of depressive symptoms, given the low recognition and treatment rates of this problem in elderly populations.

Arch Intern Med. 2001;161:2609-2615

Depression is frequently encountered in hospitalized elderly persons. In these persons, several studies have found an independent association between depressive symptoms and mortality, as well as functional decline. For example, in a study of elderly medical inpatients, subjects who scored 6 or higher on the Geriatric Depression Scale (GDS) had a 34% higher mortality (95% confidence interval [CI], 3%-73%) during a 3-year follow-up. While the association between depressive symptoms at hospital admission and mortality has been well studied in this setting, few studies looked specifically at other potential effects of depressive symptoms, such as subsequent hospital readmission or nursing home admission. Similarly, whereas the association between depressive symptoms and increased health services utilization is well described for community-dwelling elderly, similar data are sparse for inpatients. In a study of inappropriate hospital utilization among elderly medical inpatients, depressive symptoms were associated with an increased likelihood of spending inappropriate days in the hospital.

The objective of the present study was to investigate the relationship between depressive symptoms and 6-month outcomes as well as services utilization in a cohort of elderly medical inpatients. Specifically, we wanted to test the hypothesis that depressive symptoms are associ-
PATIENTS AND METHODS

STUDY POPULATION AND SETTING

Participants were patients enrolled in a larger study on functional assessment in the acute care setting. The sample selection process has been described previously. Briefly, eligible patients were alternate patients 75 years or older admitted to the internal medicine service of an academic medical center in French-speaking Switzerland over a 6-month period. From the original 649 patients, 135 (20.8%) were not included because they (1) stayed less than 24 hours in the hospital (n = 10), (2) were transferred from a regional or out-of-state hospital for an elective procedure (n = 32), (3) were already living in a nursing home (n = 43), or (4) had private insurance (n = 50). These latter patients were not included because of the inability to access administrative and follow-up data needed for the larger study.

In addition, 106 patients (16.3%) were excluded because of inability to answer questions because of severe cognitive impairment (defined as the inability to provide their name and date of birth, n = 29), aphasia or stroke (n = 9), unstable medical condition (n = 20), terminal illness or coma (n = 23), or other reasons (eg, language barrier) (n = 25). In addition, 7 patients (1.1%) refused to participate in the study. Thus, a total of 401 patients were eventually recruited. Excluded patients had a similar age and sex distribution, but, as expected, were more likely to die during their hospital stay (25.0% vs 5.0%; P < .005). The study was approved by the institutional review board of the Faculty of Medicine, University of Lausanne, Lausanne, Switzerland. Written informed consent for participation was systematically contacted. For those who died during the study, the exact date of death was ascertained through contact with the sample met or exceeded the GDS cutoff score (≥6) for depressive symptoms.

RESULTS

At baseline, participants ranged in age from 75 to 99 years (mean age, 82.4 years); 60.9% were women; 57.6% lived alone; and 54.1% had at least a high school education. The most frequent admitting diagnoses were cardiovascular disorders (39.4%), pulmonary disease (13.0%), and falls (11.0%). At the time of admission, 64.6% had at least one comorbidity as measured by the Charlson Comorbidity Index, and 13.2% had 3 or more. Dependency in one or more basic and/or instrumental ADLs was reported by 38.9% and 86.3% of patients, respectively. Abnormal MMSE scores (<24) were present in 32.2% of the patients. Overall, 90 (22.4%) of the 401 patients of the sample met or exceeded the GDS cutoff score (≥6) for depressive symptoms. Median length of stay was 8.0 days (mean, 10.3; range, 1-100). Overall, 20 patients (5.0%) died during the index stay. During the 6-month follow-up, 82 patients (21.5%) died, 137 (36.0%) were readmitted at least once to an acute care hospital, and 36 (9.4%) were permanently admitted to a nursing home. At 6-month follow-up, cross-sectional analysis showed that, compared with subjects without depressive symptoms, those with depressive symptoms were more frequently readmitted at least once (45.5% vs 34.2%; P = .02), were more frequently living in a nursing home (18.5% vs 6.3%; P = .002), and died more frequently (27.8% vs 18.3%; P = .05).

Kaplan-Meier estimations of survival without hospital readmission, survival without permanent nursing home admission, and survival among patients with and without depressive symptoms are given in Figure 1. In bivariate analysis using Cox proportional hazard analysis (Tables 1, 2, and 3), patients with depressive symptoms were about 1.6 times more likely to be readmitted, more than twice as likely to be permanently admitted to

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a proxy whose name was registered at the baseline interview. If a proxy was not available, the primary care physician was contacted, and, if necessary and applicable, representatives of the in-home services or nursing home were questioned. We were able to determine the place of living and vital status (ie, alive vs dead) in all subjects. Data on hospital and nursing home date of admission and discharge were gathered through the centralized, statewide, billing office. This office bills for all hospital, rehabilitation, and nursing home stays throughout the Canton of Vaud (Switzerland) for patients with basic insurance coverage (72.4% of women and 51.2% of men 65 years or older in the canton in 1993).

To assess the validity of this database, we used data collected on discharge destination immediately following the index hospitalization and compared them with the data extracted from this database. There was a 96.9% agreement (κ = 0.94; P = .02). Data on nursing home admission during the 6-month follow-up period were systematically correlated with proxy information. No unexpected nursing admission was found. We excluded 29 patients (7.2%) from the analysis of hospital readmission because data on their index hospitalization were missing in the billing database; however, none had a nursing home admission.

Total costs related to inpatient services utilization were calculated for each patient. The number of days spent at each level of care was multiplied by the average daily cost billed to the insurance system ($630 for acute care, $261 for rehabilitation care, $124 for nursing home care). All inpatient costs were totaled and divided by the number of days the patient remained in the study.

STATISTICAL ANALYSIS

Subjects were placed into 2 categories according to their GDS result: with or without depressive symptoms. Kaplan-Meier survival curves were plotted and tested for differences using the log-rank test. Risks of hospital readmission, nursing home admission, and death were estimated from bivariate and multivariate Cox proportional hazards regression using a stepwise procedure. In the analysis of hospital readmission, 2 variables were added to demographic and socioeconomic status and functional covariates: the length of the index hospitalization and a dummy variable indicating whether the subject had been admitted in the previous year. Statistical significance level for variables to enter and remain in the model were set at P < .10 and P < .20, respectively.

Multivariate analyses were performed with and without the depressive symptoms variable forced into the model (no differences). Death was a censoring event in all these analyses. For all models developed in the study, no statistically significant departure from the proportional hazard assumption occurred, based on the tests of Grambsch and Therneau.

To eliminate the possible confounding effect on GDS results of an undetected terminal disease at the time of the index hospitalization, we repeated the analysis of permanent nursing home admission after exclusion of subjects who died within the 6-month follow-up period. As a sensitivity analysis, we repeated all the analyses using higher GDS scores (one at ≥8 and one at ≥10) to define the presence of depressive symptoms.

Cost data were analyzed in bivariate and multivariate linear regression analyses after logarithmic transformation to normalize data distribution. We used a stepwise procedure with demographic, socioeconomic, and functional status and medical data (admitting diagnosis and comorbidity) included in the model. The final multivariate model was tested for the potential disproportionate influence of outliers, (ie, patients with an extremely low or high daily cost). We studied the residuals and used robust regression techniques to detect any departure from linearity assumptions. None was found. Statistical analyses were performed using Stata 6.0 (Stata Corp, College Station, Tex).

a nursing home, and 1.6 times more likely to die. Using multivariate stepwise analysis to adjust for demographic, socioeconomic, and functional status and comorbidity (third and fourth columns of Tables 1-3), we found that depressive symptoms remained independently associated with an increased risk of hospital readmission (adjusted hazard ratio [adj HR], 1.50; 95% CI, 1.03-2.17; P = .03). Sensitivity analyses using higher GDS cutoff scores gave a similar result for a cutoff of 8 or higher (adj HR, 1.60; 95% CI, 1.03-2.47; P = .04), but not for a cutoff of 10 or higher (adj HR, 1.31; 95% CI, 0.68-2.50; P = .42). This latter result is likely explained by the very small proportion of patients (5.5%) with depressive symptoms in the sample when using this higher cutoff.

In addition, because previous studies have shown that the GDS might not be appropriate for subjects with severe cognitive impairment,56 we repeated the analyses after excluding subjects with an MMSE score lower than 16 (n = 30). Results were not modified except for the analysis of permanent nursing home admission, in which the instrumental ADL variable disappeared from the model. However, results for the abnormal GDS variable were unchanged. Finally, the secondary analysis of permanent nursing home admission after exclusion of the subjects who died during the 6-month follow-up provided the same independent predictors with the addition of the abnormal GDS variable, although the relationship did not reach statistical significance (adj HR, 1.73; 95% CI, 0.82-3.64; P = .15).

Overall, mean (SD) inpatient services costs per day of follow-up were significantly higher for subjects with depressive symptoms than for those without ($175.70 [182.40] vs $126.00 [167.10], respectively; P < .001; Kruskall-Wallis rank sum test). Although the cost of all types of inpatient services was increased (Figure 2), the difference was mostly due to average (SD) costs of acute services ($140.90 [180.60] for patients with depressive symptoms vs $106.90 [163.90] for those without; P = .03) and rehabilitation services ($20.60 [37.50] for those with symptoms vs $10.70 [30.00] for those without; P = .007). The association between overall costs and depressive symptoms remained after adjusting for comorbidity, functional status, and living situation, although it fell just short of statistical significance (β = .25; SE = 0.139; P = .07).
Our results point to 2 main findings that support and extend other research that has demonstrated a strong relationship between depressive symptoms and poor health outcomes. First, we found an increased likelihood for subjects with depressive symptoms to be readmitted to the hospital within 6 months of an index acute hospital admission. Second, we found a clear trend for these subjects to have a higher utilization of inpatient services during the follow-up period, resulting in higher costs. Unfortunately, we were unable to confirm the increased risk of mortality associated with depressive symptoms, but this is most likely owing to our limited follow-up period.

Three major mechanisms can be proposed to explain the link between depressive symptoms and hospital readmission. First, a direct effect of depressive symptoms on health is possible. For example, a meta-analytic review found a significant association between depression and alteration in cellular immunity, potentially resulting in a reduced capability to resist stressors. In other studies focusing on the relationship of depression to cardiovascular diseases, depression has been associated with alteration in neuroendocrine function, autonomic nervous system activity, and platelet reactivity.

Alternatively, an indirect effect of depressive symptoms may be postulated. Hospital readmission might be secondary to poor adherence to medical treatment and recommendations, as found in previous studies. In addition, subjects with depressive symptoms might be more vulnerable when facing an acute situation because of a poorer social support system. These subjects will more likely end up in the hospital, while a nondepressed person might be able to more efficiently mobilize social resources to avoid hospital readmission. However, if that were the case, one would expect to find a significant relationship between the presence of formal help provided prior to the index hospital admission and hospital readmission outcome. This was not the case in our study. Of interest, a previous study of the possible modifying effect of social support on the relation between depression and mortality in older adults also failed to demonstrate a substantial effect.

A third hypothesis is that depressive symptoms as measured at baseline were an indicator of some underlying but unrecognized clinical disease that modified the readmission risk. Although complete risk adjustment is impossible, we controlled for comorbidity and functional status in the multivariate model, and the relationship was not affected.

Clearly, further studies are needed to clarify the exact mechanisms linking depressive symptoms to adverse outcomes such as hospital readmission. Nevertheless, our results add to the evidence supporting the need to further test the effects of better detection and treatment of depressive symptoms in elderly persons on a wide range of outcomes. Unfortunately, available evidence suggests no simple interventional strategy to achieve better outcomes in elderly persons with depres-
Finally, we did not confirm the previously well-described association between depressive symptoms and mortality. However, Kaplan-Meier survival curves (eg, Figure 1C) strongly suggest that the limited follow-up period was the main factor explaining this negative result. Interestingly, the curves for subjects with and without depressive symptoms begin to clearly separate at around 100 days, as previously found in similar studies of elderly medical inpatients.8,10

Several limitations to this study should be mentioned. First, as already discussed, we had a short follow-up period that likely affected our results, especially the analysis on mortality. Second, the use of the GDS to define depressive symptoms might be criticized because it is primarily a screening tool. However, the GDS has been widely used and has been shown to perform adequately in studies of similar elderly patients who have

Table 2. Results From Bivariate and Multivariate Cox Proportional Hazard Regression Analysis Predicting 6-Month Risk of Permanent Nursing Home Admission

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Unadjusted HR (95% CI)</th>
<th>P Value</th>
<th>Adjusted HR (95% CI)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abnormal GDS score (≥6)†</td>
<td>2.10 (1.06-4.14)</td>
<td>.03</td>
<td>1.18† (0.58-2.43)†</td>
<td>.65†</td>
</tr>
<tr>
<td>Age</td>
<td>1.09 (1.02-1.16)</td>
<td>.01</td>
<td>...</td>
<td>...</td>
</tr>
<tr>
<td>Male sex</td>
<td>0.45 (0.21-0.99)</td>
<td>.05</td>
<td>...</td>
<td>...</td>
</tr>
<tr>
<td>Living alone</td>
<td>2.21 (1.04-4.89)</td>
<td>.04</td>
<td>2.26 (0.98-5.24)</td>
<td>.06</td>
</tr>
<tr>
<td>Less than high school education</td>
<td>1.90 (0.97-3.71)</td>
<td>.06</td>
<td>2.21 (1.11-4.40)</td>
<td>.02</td>
</tr>
<tr>
<td>Comfortable self-rated income‡</td>
<td>2.58 (1.13-5.89)</td>
<td>.02</td>
<td>2.85 (1.22-6.63)</td>
<td>.02</td>
</tr>
<tr>
<td>In-home formal help prior to hospital admission (per independent function)§</td>
<td>2.84 (1.42-5.69)</td>
<td>.003</td>
<td>...</td>
<td>...</td>
</tr>
<tr>
<td>Fall as major admitting diagnosis</td>
<td>5.05 (2.52-10.11)</td>
<td>&lt;.001</td>
<td>3.25 (1.54-6.86)</td>
<td>.002</td>
</tr>
<tr>
<td>Independence in instrumental ADL prior to hospital admission (per independent function)‖</td>
<td>0.79 (0.68-0.92)</td>
<td>.002</td>
<td>0.77 (0.65-0.93)</td>
<td>.005</td>
</tr>
<tr>
<td>Abnormal MMSE score (&lt;24)</td>
<td>4.46 (2.26-8.81)</td>
<td>&lt;.001</td>
<td>2.35 (1.10-5.00)</td>
<td>.03</td>
</tr>
</tbody>
</table>

*HR indicates hazard ratio; CI, confidence interval; GDS, Geriatric Depression Scale; ellipses, not included in multivariate model; ADL, activities of daily living; MMSE, Mini-Mental State Examination.
†Adjusted HR, 95% CI, and P value for GDS result from stepwise multivariate Cox regression with GDS forced in the model.
‡Measured using a 5-point Likert scale (no financial difficulties at all to many difficulties).
§Measured using the Lawton scale.20
‖Measured using a 5-point Likert scale (no difficulties at all to many difficulties).

Table 3. Results From Bivariate and Multivariate Cox Proportional Hazard Regression Analysis Predicting 6-Month Risk of Death

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Unadjusted HR (95% CI)</th>
<th>P Value</th>
<th>Adjusted HR (95% CI)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abnormal GDS score (≥6)†</td>
<td>1.57 (0.98-2.52)</td>
<td>.06</td>
<td>1.04† (0.65-1.73)†</td>
<td>.81†</td>
</tr>
<tr>
<td>Male sex</td>
<td>1.70 (1.11-2.63)</td>
<td>.02</td>
<td>...</td>
<td>...</td>
</tr>
<tr>
<td>Living alone</td>
<td>0.67 (0.44-1.04)</td>
<td>.08</td>
<td>...</td>
<td>...</td>
</tr>
<tr>
<td>In-home formal help prior to hospital admission</td>
<td>1.78 (1.15-2.75)</td>
<td>.01</td>
<td>...</td>
<td>...</td>
</tr>
<tr>
<td>Comorbid illness (per point)‡</td>
<td>1.45 (1.31-1.60)</td>
<td>&lt;.001</td>
<td>1.36 (1.22-1.52)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Independence in instrumental ADL prior to hospital admission (per independent function)‖</td>
<td>0.77 (0.70-0.85)</td>
<td>&lt;.001</td>
<td>0.86 (0.77-0.97)</td>
<td>.01</td>
</tr>
<tr>
<td>Abnormal MMSE score (&lt;24)</td>
<td>1.87 (1.21-2.99)</td>
<td>&lt;.001</td>
<td>0.86 (0.74-1.00)</td>
<td>0.06</td>
</tr>
</tbody>
</table>

*HR indicates hazard ratio; CI, confidence interval; GDS, Geriatric Depression Scale; ellipses, not included in multivariate model; ADL, activities of daily living; MMSE, Mini-Mental State Examination.
†Adjusted HR, 95% CI, and P value for GDS result from stepwise multivariate Cox regression with GDS variable forced in the model.
‡Measured using the Charlson Comorbidity Index score.22
§Measured using the Lawton scale.20
‖Measured using the Katz scale.19

sive symptoms.41-42 For example, a recent randomized trial of simple case finding for depression in elderly outpatients did not result in any reduction in health care utilization during a 2-year follow-up period.41 Achieving better results will likely require more complex and intensive strategies, combining provider education with psychosocial and/or antidepressant drug interventions targeted at patients meeting appropriate criteria.

We were unable to confirm the hypothesized association between depressive symptoms and permanent nursing home admission. Most likely this is because of the limited number of subjects admitted to nursing homes in this population during the study period. Nevertheless, results of the subgroup analysis restricted to subjects who survived during the 6-month follow-up suggest a potential independent effect that should be investigated with a larger sample.
Conclusions

The relationship between depressive symptoms and undesirable health outcomes such as hospital readmission is probably complex, but the low detection and treatment rates for depression found in previous studies suggest that improved detection and treatment of this condition might result in improved outcomes. Such an approach needs to be tested in an interventional trial.

Accepted for publication March 29, 2001.

This project was supported by Fonds de Performance grant 20-1994 from the Public Health Service, Canton of Vaud, Lausanne, Switzerland (Dr Bula).

We are grateful to Nadine Corbaz for secretarial assistance and John C. Beck, MD, for comments on the manuscript.

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