In-Hospital Risk Prediction for Post-stroke Depression
Development and Validation of the Post-stroke Depression Prediction Scale

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Background and Purpose—The timely detection of post-stroke depression is complicated by a decreasing length of hospital stay. Therefore, the Post-stroke Depression Prediction Scale was developed and validated. The Post-stroke Depression Prediction Scale is a clinical prediction model for the early identification of stroke patients at increased risk for post-stroke depression.

Methods—The study included 410 consecutive stroke patients who were able to communicate adequately. Predictors were collected within the first week after stroke. Between 6 to 8 weeks after stroke, major depressive disorder was diagnosed using the Composite International Diagnostic Interview. Multivariable logistic regression models were fitted. A bootstrap-backward selection process resulted in a reduced model. Performance of the model was expressed by discrimination, calibration, and accuracy.

Results—The model included a medical history of depression or other psychiatric disorders, hypertension, angina pectoris, and the Barthel Index item dressing. The model had acceptable discrimination, based on an area under the receiver operating characteristic curve of 0.78 (0.72–0.85), and calibration (P value of the U-statistic, 0.96). Transforming the model to an easy-to-use risk-assessment table, the lowest risk category (sum score, <−10) showed a 2% risk of depression, which increased to 82% in the highest category (sum score, >21).

Conclusions—The clinical prediction model enables clinicians to estimate the degree of the depression risk for an individual patient within the first week after stroke. (Stroke. 2013;44:2441-2445.)

Key Words: depression ■ prediction ■ screening tool ■ stroke

Post-stroke depression (PSD) is a serious and common complication of stroke. A pooled estimate indicates that depressive symptoms are present in one third of all stroke survivors at any time during the follow-up. PSD negatively impacts patient participation in rehabilitation and associated patient outcomes. This is of major importance during patient recovery, when rehabilitation efforts are most critical to the outcome. There is increasing evidence that treatment with antidepressants decreases the severity of depression and improves functional status. Therefore, the early detection of PSD is essential to optimize the recovery of stroke patients.

Generally, PSD is defined using the criteria of the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV-TR). According to these criteria, depression is characterized as the consistent presence of ≥5 out of 9 depression symptoms during a 2-week period. Several instruments with acceptable diagnostic accuracy are available for screening depression in stroke patients. However, there is a trend toward a decreasing length of hospital stay with a mean of <14 days, and this short hospital stay complicates proper PSD screening, notably because of the DSM requirement that depression symptoms be present for ≥2 weeks. To enable the early detection of PSD while acknowledging a limited window of in-hospital opportunity, we developed a clinical prediction model to identify hospitalized stroke patients at risk for PSD after discharge. The focus was on the predictors available to clinicians in the first week after a stroke.

Materials and Methods

Study Design and Participant Selection
A prospective multicenter cohort study was conducted in 3 hospitals in The Netherlands. Ethical approval was obtained from the Medical Ethical Committee of the University Medical Centre Utrecht and the other participating hospitals. Between December 2009 and January 2011, 1033 consecutively admitted stroke patients (admitted with a clinical diagnosis of intracerebral hemorrhage or ischemic infarction), were approached for participation in the first week after stroke onset but before discharge. Patients (n=410; 39.7%) were included if they did not present with serious cognitive disorders, as indicated by a Mini Mental State Examination score ≥18 or with communicative disorders as indicated by a Frenchay Aphasia Screening Test.
score of ≥17 for patients <60 years of age; a score of ≥16 in patients aged ≥60 years and ≤70 years; and a score of ≥15 in patients ≥71 years of age. Written consent was obtained. Patients (n=623; 60.3%) who did not meet the inclusion criteria, who refused participation or who met any of the following criteria were excluded: presence of depressive disorders at stroke onset; presence of a major psychiatric comorbidity other than affective disorder; antidepressant medication use at stroke onset; or too ill to participate, based on the judgment of the clinicians or the researcher. Most of the excluded patients (69.0%) were too ill to participate because of stroke severity, severe aphasia, or severe cognitive impairments.

Primary Outcome
A diagnosis of major depressive disorder was made in the sixth to eighth week after stroke onset according to the DSM-IV-TR criteria, using the Composite International Diagnostic Interview (CIDI). For most patients (99.5%), this diagnosis occurred after hospital discharge. The CIDI, a structured diagnostic interview for DSM-IV and ICD-10 psychiatric disorders, shows good diagnostic concordance with the DSM-III-R (κ=0.84) and the ICD-10 diagnosis (κ=0.78) for major depression. The reliability is good as well; the inter-rater reliability measured with Cohen κ is 0.84, and the Cohen κ for the test–retest reliability is 0.90. The CIDI can be administered by trained lay interviewers. In this study, the CIDI-auto 2.1 version was used by a researcher (J.M.d.M.-v.G.) after formal training in the administration of CIDI. She visited the patient at home or at the residential healthcare facility to administer the CIDI.

PSD Risk Factors
From all participating patients, data were collected regarding potential risk factors for PSD. This included sociodemographic and stroke-related factors; medical history concerning vascular risk factors, vascular diseases, and other diseases such as depression or other psychiatric disorders; functional status post-stroke (measured using the Barthel Index and the modified Rankin Scale), and the patients’ perceived lack of or excess of social support before stroke (measured with the Social Support List-6). Details are described in Table 1. For a variable to be considered a candidate predictor for PSD, it had to be easily collected in a clinical setting with a view to future applicability. Consequently, the data collected were a proportion of the data normally collected in hospital care.

Data Analysis
The total percentage of missing values was 1.8. Missing values were substituted through multiple imputation to reduce the bias and to increase the statistical power. The imputation technique involves creating multiple copies of the data and replacing missing values with imputed values on the basis of a suitable random sample from their predicted distribution. We used the mice package (version MICE V2.10) of the statistical package R (version 2.14.0 [2011-10-31]) to obtain 5 completed data sets. We used a 2-step procedure to develop the prediction model for PSD. First, we selected the most strongly associated predictors from each subgroup of variables, using multivariable logistic regression with backward stepwise selection based on a likelihood-ratio test with a P value of 0.1. Second, the final model was selected from this set of variables and validated with backward stepwise selection in multivariable logistic regression. One thousand bootstrap samples were drawn from the original sample, estimating the overfitting-corrected regression coefficients from the final model and the overfitting-corrected measures of the model performance. These statistics may be considered as an estimate of the performance that is expected in future patients. We used the rms package (version 3.3-2) from the statistical package R (version 2.14.0 [2011-10-31]). In this backward step, selection was based on the Wald χ² test of the individual predictors with a P value of ≤0.1. To quantify the performance of the models, we determined the discrimination and calibration by comparing the actual presence of PSD with the calculated predictions for the presence of PSD.
In-Hospital Risk Prediction for PSD With the DePreS

discrimination indicates the extent to which the model distinguishes between patients with or without PSD. The ability to discriminate was expressed with the concordance-statistic, that is, the area under the receiver operating characteristic curve, by calculating the area under the receiver operating characteristic curve with a 95% confidence interval (CI) where the higher values indicate better discrimination.\textsuperscript{18,19} The calibration of a model describes the extent to which the predicted probabilities of PSD reflect the true probabilities of PSD.\textsuperscript{19} The calibration was judged with the $U$-statistic, which compares the actual slope and intercept of the calibration plot to the ideal values of 1 and 0, respectively, and was tested against a $\chi^2$ distribution with 2 degrees of freedom.\textsuperscript{18} We also calculated the following measurements for model accuracy: the Yates slope, a discrimination slope that measures the difference between the mean predicted probabilities for the patients with and without PSD; the Brier score, an expression of the squared differences between the actual presence of PSD and the calculated predictions for presence of PSD; and the Brier scaled, scaling the Brier score by its maximum slope to overcome the influence of PSD incidence on the Brier score. For the Yates slope and the Brier scaled, higher values indicate better accuracy, whereas a lower value of the Brier score represents better accuracy.\textsuperscript{18} All analyses were conducted in the 5 completed data sets. The 5 sets of regression coefficients, the performance estimates, and their variances were pooled according to Rubin’s\textsuperscript{22} rules to produce estimates and CIs that incorporate missing-data uncertainty. To construct an easily used clinical score card, the regression coefficients of the predictors from the final model were standardized, dividing all regression coefficients by the smallest coefficient and transforming them into points by multiplying by 3 and rounding off the results. The total scores were linked to the risk of PSD.

To enhance the clinical utility, we converted the regression model into a score table, the Post-stroke Depression Prediction Scale (DePreS), which can be used as a clinical prediction model (Table 2). We calculated the score risk for each of the participants and sorted them in ranges of total scores.

**Results**

The mean age of the 410 participating patients was 70 years (SD, 14.3; range, 20–97 years), and 221 (53.9%) were men.

### Table 2. Score Table DePreS

<table>
<thead>
<tr>
<th>Does the patient have a medical history of depression or other psychiatric disorders?</th>
<th>No</th>
<th>Yes</th>
</tr>
</thead>
<tbody>
<tr>
<td>n=54 (14.1%)</td>
<td>n=328 (85.9%)</td>
<td></td>
</tr>
<tr>
<td>Interactions</td>
<td>15.68 (3.2; 9–23)</td>
<td>14.99 (3.0; 6–24)</td>
</tr>
<tr>
<td>Perceived lack of support</td>
<td>7.13 (2.1; 6–14)</td>
<td>6.5 (1.3; 6–14)</td>
</tr>
<tr>
<td>Perceived excess of support</td>
<td>0.30 (0.7; 0–2)</td>
<td>0.08 (0.3; 0–3)</td>
</tr>
</tbody>
</table>

Table 3. Multivariable Logistic Regression Model

<table>
<thead>
<tr>
<th>Predictors</th>
<th>Odds Ratio (95% CI)</th>
<th>Coefficient</th>
<th>SE</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Depression or other psychiatric disorders</td>
<td>7.22 (3.63–14.35)</td>
<td>1.98</td>
<td>0.28</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Hypertension</td>
<td>0.49 (0.26–0.92)</td>
<td>0.71</td>
<td>0.35</td>
<td>0.08</td>
</tr>
<tr>
<td>Angina pectoris</td>
<td>2.82 (1.33–6.21)</td>
<td>1.04</td>
<td>0.39</td>
<td>0.01</td>
</tr>
<tr>
<td>Barthel item dressing</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Completely independent</td>
<td>*</td>
<td>*</td>
<td>*</td>
<td>*</td>
</tr>
<tr>
<td>Needs help but can do about half unaided</td>
<td>0.26 (0.08–0.82)</td>
<td>−1.34</td>
<td>0.58</td>
<td>0.03</td>
</tr>
<tr>
<td>Dependent</td>
<td>1.57 (0.80–3.09)</td>
<td>0.45</td>
<td>0.35</td>
<td>0.31</td>
</tr>
</tbody>
</table>

Coefficient: logistic regression coefficient, shrunken for future patients and pooled from the 5 completed data sets according to the Rubin’s rules. P values represent the highest value found in the 5 completed data sets.

The characteristics of the patients with and without incident PSD are summarized in Table 1, presenting the patients (n=382; 93.2%) in whom the outcome incident PSD was measured. Of these patients, 54 (14.1%; 95% CI, 10.9%–18.1%) were diagnosed with major depressive disorder in the aftermath of the stroke event. The patients who developed PSD showed a significant difference in the baseline medical history of impaired renal function, angina pectoris, depression or other psychiatric disorders, perceived lack of social support, and perceived excess of social support.

The selection of the candidate predictors for each subgroup of variables results in the candidate predictors: medical history of hypertension, alcohol consumption, angina pectoris and depression or other psychiatric disorder, Barthel Index item dressing, social support interactions, and perceived lack of support interaction.

A multivariable regression analysis showed that a medical history of depression or other psychiatric disorder was the most important predictor (odds ratio, 7.22; 95% CI, 3.63–14.35). Other variables remaining in the model were medical history of hypertension, angina pectoris, and Barthel Index item dressing, as shown in Table 3. The model showed a good discriminatory performance; the area under the receiver operating characteristic curve of the model was 0.78 (95% CI, 0.72–0.85). Additionally, the calibration was adequate with nonsignificant $U$-statistic ($P=0.96$). The other measures of the predictive performance are shown in Table 4.

Table 4. Predictive Performance of the Logistic Regression Model

<table>
<thead>
<tr>
<th>Yates</th>
<th>Brier</th>
<th>Brier AUC*</th>
<th>U-Statistic P</th>
<th>Mean Predicted Risk PSD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Model*</td>
<td>Score*</td>
<td>Scaled*</td>
<td>(95% CI)</td>
<td>Value (c)*</td>
</tr>
<tr>
<td>Final</td>
<td>0.19</td>
<td>0.11</td>
<td>0.07</td>
<td>0.78 (0.72–0.85)</td>
</tr>
</tbody>
</table>

*AUC indicates area under the receiver operating characteristic curve; and PSD, post-stroke depression.

*All statistics are scaled from 0 to 1. Higher Yates slope, lower Brier Score, higher Brier Scaled, higher discrimination AUC, and nonsignificant $P$ value of the calibration $U$-statistic represent better performance.
with low risk, we dichotomized the score at several thresholds and calculated the screening characteristics of the Prediction Scale. Table 6 summarizes the Prediction Scale screening characteristics at different cutoff values. At a cutoff score of ≥2, the best accuracy is achieved with a sensitivity of 0.73 (95% CI, 0.60–0.83) and specificity of 0.75 (95% CI, 0.70–0.80).

### Discussion

This study presents the development and performance of a clinical prediction model with its accompanying risk-assessment table to identify admitted stroke patients able to communicate adequately, who are at increased risk for PSD. The DePreS showed acceptable discrimination and calibration.

The structural use of a screening instrument in the daily care of stroke patients will promote the early recognition of depression.5,23 The trend toward decreasing hospital stays complicates proper screening for PSD during hospital stay and emphasizes the need for an easy-to-use prediction model to identify the risk for PSD. Our aim was to develop a prediction model that clinicians can apply in the daily care during the first week after stroke. Although a systematic review showed that several studies have been conducted on the prediction of PSD, the overall conclusion was that most of the available models lack precision, were not thoroughly developed or validated and were not clinically useful.11 In this study, we rigorously developed and internally validated the prediction model. Additionally, a few study characteristics must be noted to appreciate the findings. We included consecutively admitted stroke patients. This resulted in a sample reflecting the entire target population, as shown by the range of discharge destinations and by large variation in functional status. We imputed missing data to prevent biased estimates of the regression coefficients and their SEs. Multiple imputation is the best method available to deal with both random and nonrandom missing values.15,18 For the selection of the candidate predictors, we used predictors available to clinicians in the first week after stroke. These predictors will enhance the clinical utility of the prediction model in daily hospital care. The selection of candidate predictors was performed based on multiple logistic regression using the backward elimination, which is preferable compared with forward selection.24 Finally, to correct for optimism and prevent overfitting,25 we internally validated our model using bootstrap samples derived from the study sample. This resulted in a well-developed prediction model.

Most of the predictors in our PSD prediction model were previously reported as a predictor, boosting the potential applicability of the prediction model. However, there are also studies in which our predictors did not remain in a multivariable logistic regression.14 The strongest predictor for PSD was a medical history of depression or other psychiatric disorders. Another hospital-based study confirmed previous depressive episodes to be a predictor for PSD in a multivariable analysis, although less strongly.26 Functional status as a predictor of PSD has been studied more often than the medical history of depression and has been shown to contribute almost always in a multivariate regression model.11 None of the studies, however, investigated the association of the individual functional status items with PSD.11,27,28 In our prediction model the item dressing notably seems to be a stronger predictor than the total Barthel Index score. Moreover, the partial need for help in dressing protects from PSD, whereas the complete dependence in dressing was found to be a risk factor for PSD. This might be explained by the fact that the partial need for help in dressing gives patients the perspective of recovery. The correlation between PSD and vascular risk factors is less clear because in most studies these variables were not considered as predictors.11 In our study, a medical history of hypertension seems to protect from PSD, whereas angina pectoris is an independent predictor. In the few studies considering vascular risk factors as predictor, angina pectoris has not been reported to be an independent predictor for PSD, whereas hypertension was an independent predictor in most of the studies.11,29 Medication use may be a possible explanation for the protective effect of hypertension in our study. We did not register medication use; therefore, we were not able to verify the effect on the predictors. Note that a predictive relationship does not equal a causal relationship.30 The aim of prediction research is to predict, as accurately as possible, the risk of future outcomes based on a minimal set of predictors, using all of the variables that are potentially associated with the outcome.

### Table 5. DePreS Risk Scores With Corresponding Predicted and Observed Risks for PSD

<table>
<thead>
<tr>
<th>Total Score</th>
<th>Predicted Risk, %</th>
<th>Observed Risk, % (n/N)*</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;−10</td>
<td>2</td>
<td>0 (0/32)</td>
</tr>
<tr>
<td>−9 to −5</td>
<td>5</td>
<td>9 (11/127)</td>
</tr>
<tr>
<td>−4 to 0</td>
<td>11</td>
<td>6 (8/125)</td>
</tr>
<tr>
<td>1 to 5</td>
<td>19</td>
<td>19 (13/67)</td>
</tr>
<tr>
<td>6 to 10</td>
<td>31</td>
<td>33 (8/24)</td>
</tr>
<tr>
<td>11 to 15</td>
<td>49</td>
<td>47 (14/30)</td>
</tr>
<tr>
<td>16 to 20</td>
<td>67</td>
<td>77 (7/9)</td>
</tr>
<tr>
<td>&gt;21</td>
<td>82</td>
<td>100 (2/2)</td>
</tr>
</tbody>
</table>

DePreS indicates Post-stroke Depression Prediction Scale; and PSD, post-stroke depression.

*Number of patients diagnosed as depressed out of the total number of patients within a total score range.

### Table 6. Performance of the DePreS

<table>
<thead>
<tr>
<th>Cutoff Score</th>
<th>Sensitivity (95% CI)</th>
<th>Specificity (95% CI)</th>
<th>Positive Predicted Value (95% CI)</th>
<th>Negative Predicted Value (95% CI)</th>
<th>Number (%) False-Positive Risk Prediction</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥2</td>
<td>0.73 (0.60–0.83)</td>
<td>0.70 (0.70–0.80)</td>
<td>0.94 (0.91–0.97)</td>
<td>0.33 (0.25–0.42)</td>
<td>87 (25)</td>
</tr>
<tr>
<td>≥3</td>
<td>0.69 (0.57–0.80)</td>
<td>0.75 (0.75–0.84)</td>
<td>0.94 (0.90–0.96)</td>
<td>0.37 (0.28–0.47)</td>
<td>70 (20)</td>
</tr>
<tr>
<td>≥6</td>
<td>0.53 (0.39–0.66)</td>
<td>0.87 (0.87–0.94)</td>
<td>0.92 (0.88–0.94)</td>
<td>0.49 (0.37–0.62)</td>
<td>32 (9)</td>
</tr>
<tr>
<td>≥11</td>
<td>0.36 (0.24–0.49)</td>
<td>0.92 (0.92–0.97)</td>
<td>0.90 (0.86–0.93)</td>
<td>0.55 (0.38–0.71)</td>
<td>17 (5)</td>
</tr>
</tbody>
</table>

DePreS indicates Post-stroke Depression Prediction Scale; and PSD, post-stroke depression.
These variables, however, are not necessarily causally related to the outcome.\(^\text{30}\)

Our study has certain limitations. First, our target population comprised patients able to communicate adequately because the assessment of depression with the CIDI highly depends on verbal and cognitive competence. Although PSD is associated with communicative and cognitive impairment after stroke,\(^\text{1}\) it remains difficult to measure depression reliably in patients with cognitive and communicative disorders.\(^\text{31}\)

This restricts the application of our model to those patients. Second, the data collection in the first week after stroke resulted in a relatively high proportion of patients (69%) who were too ill to participate. This could also explain the relatively low cumulative incidence of PSD in our study of 14.1% (95% CI, 10.9%–18.1%) in the first 8 weeks after the event. A systematic review focusing on the frequency of PSD showed (for hospital-based studies) a pooled prevalence of 33% (95% CI, 23%–41%).\(^\text{1}\) However, for most of the studies included in the review, PSD was detected using a screening instrument and not a diagnostic interview. This could explain the difference because the use of screening instruments is associated with some misclassification.\(^\text{5}\)

Internal validation does not directly address the generalizability of the model.\(^\text{18}\) Therefore, to use this instrument with confidence, new data are needed for confirmation\(^\text{29}\) (collected from an appropriate patient population in a different center).

In conclusion, we have identified the most important clinical predictors for PSD in stroke patients who are able to communicate adequately. We have also developed a prediction model that enables clinicians to estimate the risk of PSD in the first week after stroke. The predictive performance of the prediction model is good. The use of the DePreS in daily practice may materially improve the clinical evaluation of stroke patients, provided it is followed by adequate treatment and follow-up.

Disclosures

None.

References

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