Background and Purpose—To investigate whether neuroimaging information has added predictive value compared with clinical information for independency in activities of daily living (ADL) 1 year after stroke.

Methods—Seventy-five first-ever middle cerebral artery stroke survivors were evaluated in logistic regression analyses. Model 1 was derived on the basis of clinical variables; for model 2, neuroimaging variables were added to model 1. Independent variables were stroke severity (National Institutes of Health Stroke Scale), consciousness (Glasgow Coma Scale), urinary continence, demographic variables (age, gender, relationship, educational level), hospital of admission, and clinical instruments: sitting balance (trunk control test), motor functioning (Motricity Index), and ADL (Barthel Index). Neuroimaging variables, determined on conventional MRI scans, included: number of days to scanning, lesion volume, lesion localization (cortex/subcortex), hemisphere, and the presence of white matter lesions. ADL independency was defined as 19 and 20 points on Barthel Index. Differences in accuracy of prediction of ADL independence between models 1 and 2 were analyzed by comparing areas under the curve (AUC) in a receiver operating characteristic analysis.

Results—Model 1 contained as significant predictors: age and ADL (AUC 0.84), correctly predicting 77%. In model 2, number of days to scanning, hemisphere, and lesion volume were added to model 1, increasing the AUC from 0.84 to 0.87, accurately predicting 83% of the surviving patients.

Conclusions—Clinical variables in the second week after stroke are good predictors for independency in ADL 1 year after stroke. Neuroimaging variables on conventional MRI scans do not have added value in long-term prediction of ADL. (Stroke. 2006;37:1050-1054.)

Key Words: activities of daily living ■ magnetic resonance imaging ■ stroke
predicting ADL 1 year after stroke compared with information derived from clinical assessment only.

The aim of the present study was to examine the added value of neuroimaging information from MRI scans obtained in the second week after stroke by comparing infarct volume and lesion localization with clinical variables in predicting independency in ADL of stroke survivors with middle cerebral artery (MCA) infarctions at 1 year after stroke.

Methods

Patients admitted to stroke units of 6 hospitals in the Netherlands in 1999 to 2001 were asked to participate. After informed consent, an MRI scan was obtained at a mean of 11 days (SD 3.5) after stroke. Data about stroke severity (NIHSS13 and Glasgow Coma Scale [GCS]14) on hospital admission were retrospectively retrieved from medical records,15 and demographic variables (age, gender, relationship) were collected. Other measures of functional status (Barthel Index [BI]16; trunk control test),17 Morbidity Index, MI18) were part of a physical examination. An experienced researcher tested patients ~6 days after stroke (mean 5.6 days; SD 2.6; range 1 to 13 days), blinded for the neuroimaging findings. The research protocol was approved by the medical ethics committee of University Medical Center Utrecht.

Patients

Patients included had a nonlacunar first-ever ischemic MCA infarction, were between 18 and 85 years of age, had a premorbid BI ≥18, and a stable neurological condition 1 week after stroke. All patients had a visible lesion on the MRI scan. Patients with other lesions, infarctions other than MCA infarctions such as subcortical infarctions, and patients with border-zone infarctions, multiple infarctions, and lacunar infarctions were excluded. Lacunar infarctions were defined as infarctions with a diameter ranging from 3 to 4 mm to 15 to 20 mm and located at the site of the basal ganglia, internal capsule, or corona radiate.19,20 Patients with premorbid cognitive limitations or comorbidity influencing functional outcome were excluded. Patients who died or had another stroke during the follow-up period were excluded so that ADL of stroke survivors 1 year after stroke could be predicted.

Dependent Variable

Level of independency with the BI was assessed face to face by the same researcher 1 year after stroke (mean 377 days after stroke; SD 22). Persons with BI scores 19 and 20 were considered independent.9

Independent Variables

Clinical Variables

The NIHSS13 was normally distributed in our study group and used as a continuous variable. For the GCS,14 a cutoff point of 15 (male/female), relationship (Yes/No [Y/N]), and urinary incontinence in the second week after stroke were used as independent candidate variables for model development. Based on bivariate logistic regression analysis, significant determinants were selected for the development of a multivariate logistic model necessary for the prediction of ADL independency 1 year after stroke. Odds ratios and 95% CIs were calculated. Candidate determinants for model development were allowed if odds ratio reached a liberal level of significance (P ≤ 0.15). To prevent overfitting of the derived model in relation to the number of positive events per variable27 and improve stability of the regression model, determinants were removed if collinearity diagnostics showed correlation coefficients between candidate determinants of ≥0.7.28 Because of the large number of variables compared with number of patients involved, the maximum likelihood estimation of parameters in the multivariate clinical model (model 1) was based on a conditional “stepwise forward” approach. Probability for entry of a variable was set at 0.05, for removal at 0.10. Each hypothesis was 2-tailed tested with a significance level of 0.05.

To evaluate the added value of neuroimaging variables, neuroimaging variables significant after bivariate analysis were added at once (“enter” approach) to the clinical variables of model 1 in a second logistic regression analysis (model 2).

Subsequently, surplus value of model 2 compared with model 1 was investigated by comparing the area under the curve (AUC) in an ROC curve for both models. An area of 0.5 implies perfect sensitivity and specificity, whereas an area of 0.5 implies that the predictions of the model are no better than would be obtained by chance. The trapezoid rule was used to calculate the AUC for each model.29,30

The ROC curves of both models were graphically displayed and tested if the AUC of model 2 was significantly different from that of model 1. Models were significantly different if z ≥ 1.96. The paired z score between model 2 and model 1 was calculated by the equation: z = AUC2 − AUC1 ~/SE2 − SE1 √2 − 2SE2∗SE1, with r as the Pearson product moment correlation coefficient between model 1 and model 2.31 All analyses were performed using SPSS (version 12.0.1 for Windows).
Results

Of 115 patients scanned, 21 were excluded because of MRI findings: other lesions (4 patients); infratentorial lesions (10 patients); multiple infarctions (left and right hemisphere; 5 patients); border-zone infarction (1 patient); and in 1 patient, the MRI scan could not be evaluated because of movement artifacts. At 1 year after stroke, 19 of these 94 patients were excluded from further analysis: 9 patients died; 4 patients had recurrent stroke; 2 patients developed comorbidity seriously affecting functional outcome; and 4 patients refused further examination. The 13 patients who died or had another stroke incident were analyzed and compared with the remaining 75 patients with MCA strokes. Both groups did not differ significantly in terms of age (P=0.19); gender (P=0.63); stroke severity (NIHSS; P=0.71); lesion location (cortex/subcortex, P=0.89; hemisphere, P=0.83), and mean lesion volume (P=0.87).

Measurements were available for 75 stroke patients. Table 1 presents patient characteristics and neuroimaging variables. Eighty-four percent of the patients were admitted to the hospital at the day of stroke onset. Median GCS at admission was 15 (interquartile range [IQR], 25% to 75%; 15 to 15), indicating that most patients had moderate neurological deficits. Median BI at 6 days after stroke was 8 of 20 (IQR, 4 to 17). At 1 year after stroke, 33 patients (56%) were independent in ADL (BI, 19 or 20). Discharge status of patients after hospital stay was: 35% home; 37% rehabilitation center; 4% geriatric home; 23% nursing home; and 1% elsewhere.

**TABLE 1. Patient Characteristics and Neuroimaging Variables**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Total</th>
<th>Percentages</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>75</td>
<td></td>
</tr>
<tr>
<td>Gender, male/female</td>
<td>35/40</td>
<td>(47%; 53%)</td>
</tr>
<tr>
<td>Age, mean (SD)</td>
<td>63 (15)</td>
<td></td>
</tr>
<tr>
<td>Relationship, Y/N</td>
<td>53/22</td>
<td>(71%; 29%)</td>
</tr>
<tr>
<td>Educational level (low/high)</td>
<td>42/33</td>
<td>(56%; 44%)</td>
</tr>
<tr>
<td>NIHSS; median, (IQR)</td>
<td>15 (15–15)</td>
<td></td>
</tr>
<tr>
<td>BI (0–20), day 6; median, (IQR)</td>
<td>8 (4–17)</td>
<td></td>
</tr>
<tr>
<td>MMSE; median, (IQR)</td>
<td>26 (23–28)</td>
<td></td>
</tr>
<tr>
<td>Motricity Index, arm; median, (IQR)</td>
<td>50 (0–92)</td>
<td></td>
</tr>
<tr>
<td>Motricity Index, leg; median, (IQR)</td>
<td>75 (14–100)</td>
<td></td>
</tr>
<tr>
<td>Motricity Index, total; median, (IQR)</td>
<td>120 (14–191)</td>
<td></td>
</tr>
<tr>
<td>Modified Rankin; median, (IQR)</td>
<td>3 (2–4)</td>
<td></td>
</tr>
<tr>
<td>Urinary incontinence, N/Y</td>
<td>41/34</td>
<td>(55%; 45%)</td>
</tr>
<tr>
<td>Sitting balance, Y/N</td>
<td>54/21</td>
<td>(72%; 28%)</td>
</tr>
<tr>
<td>No. of days MRI poststroke, mean (SD)</td>
<td>11 (3.5)</td>
<td></td>
</tr>
<tr>
<td>White matter lesions, N/Y</td>
<td>51/24</td>
<td>(68%; 32%)</td>
</tr>
<tr>
<td>Hemisphere, left/right</td>
<td>38/37</td>
<td>(51%; 49%)</td>
</tr>
<tr>
<td>Pure subcortex/cortex</td>
<td>27/48</td>
<td>(36%; 64%)</td>
</tr>
<tr>
<td>Median volume (IQR)</td>
<td>31.9 (6.3–91.2)</td>
<td></td>
</tr>
<tr>
<td>Volume (0≤22 mL; 1&gt;22 mL)</td>
<td>32/43</td>
<td>(43%; 57%)</td>
</tr>
</tbody>
</table>

IQR indicates 1st, 3rd percentile; Y/N, yes/no; MMSE, mini mental status examination.

**TABLE 2. Bivariate Analysis of Acute Impairments and Disabilities Associated With ADL Assessed Using BI (0<19; 1≥19) 1 Year After Stroke**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Odds Ratio</th>
<th>95% CI</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinical variables</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td>0.99</td>
<td>0.99–1.00</td>
<td>0.10*</td>
</tr>
<tr>
<td>Gender, male/female</td>
<td>0.54</td>
<td>0.28–1.03</td>
<td>0.06*</td>
</tr>
<tr>
<td>Educational level (high/low)</td>
<td>0.56</td>
<td>0.30–1.04</td>
<td>0.07*</td>
</tr>
<tr>
<td>Relationship, Y/N</td>
<td>0.29</td>
<td>0.11–0.80</td>
<td>0.02*</td>
</tr>
<tr>
<td>NIHSS</td>
<td>0.97</td>
<td>0.93–1.00</td>
<td>0.06*</td>
</tr>
<tr>
<td>GCS (0–15; 1≤15)</td>
<td>0.67</td>
<td>0.18–2.36</td>
<td>0.53</td>
</tr>
<tr>
<td>BI (0&gt;9; 1≤9)</td>
<td>0.26</td>
<td>0.12–0.54</td>
<td>0.00*</td>
</tr>
<tr>
<td>Motricity Index, total (0&gt;100; 1≤100)</td>
<td>0.10</td>
<td>0.03–0.34</td>
<td>0.00*</td>
</tr>
<tr>
<td>Urinary incontinence, N/Y</td>
<td>0.21</td>
<td>0.09–0.52</td>
<td>0.00*</td>
</tr>
<tr>
<td>Sitting balance, Y/N</td>
<td>0.11</td>
<td>0.03–0.45</td>
<td>0.00*</td>
</tr>
<tr>
<td>Hospital of admission (1–6)</td>
<td>0.88</td>
<td>0.74–1.05</td>
<td>0.17</td>
</tr>
<tr>
<td>Neuroimaging variables</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No. of days to poststroke MRI scanning</td>
<td>0.97</td>
<td>0.93–1.01</td>
<td>0.13*</td>
</tr>
<tr>
<td>White matter lesions, N/Y</td>
<td>0.60</td>
<td>0.26–1.37</td>
<td>0.23</td>
</tr>
<tr>
<td>Hemisphere (0: left; 1: right)</td>
<td>0.54</td>
<td>0.28–1.06</td>
<td>0.08*</td>
</tr>
<tr>
<td>Subcortex/cortex (0: purely subcortical; 1: subcortex and cortex involved)</td>
<td>0.78</td>
<td>0.44–1.38</td>
<td>0.39</td>
</tr>
<tr>
<td>Volume (0≤22 mL; 1&gt;22 mL)</td>
<td>0.48</td>
<td>0.26–0.91</td>
<td>0.03*</td>
</tr>
</tbody>
</table>

*P<0.25.
IQR indicates 1st, 3rd percentile; Y/N, yes/no.

Bivariate and Multivariate Analyses

Table 2 shows odds ratios and 95% CIs from bivariate logistic regression analyses for independent variables. Of 16 variables, 12 were significantly related to the probability of independency at 1 year after stroke. MI and urinary continence were removed because both determinants showed collinearity with the BI. The remaining 10 variables were used as candidate determinants for developing multivariate logistic models (models 1 and 2).

Table 3 shows regression coefficients of included clinical determinants and the derived logistic regression model of probability for regaining ADL independency 1 year after stroke in model 1 (sensitivity 77%; specificity 83%; false-positives 21%; false-negatives 19%). Model 2 shows the logistic regression model with added neuroimaging variables (sensitivity 83%; specificity 82%; false-positives 24%; false-negatives 12%). The Figure shows the AUC in ROC analysis for models 1 and 2.

The AUC was 0.84 for model 1 (SE 0.05; P=0.00; 95% CI, 0.75 to 0.94) and 0.87 for model 2 (SE 0.04; P=0.00; 95% CI, 0.79 to 0.95). Comparison of the 2 derived ROC curves shows that the AUC was not significantly different between models 1 and 2 (R=0.95; z=1.85).

Discussion

The aim of the present study was to evaluate whether neuroimaging variables combined with clinical variables (model 2) have added value in predicting functional outcome compared with a model based on clinical determinants alone (model 1).
Model 1 contained only 2 clinical variables (age and BI) and was already highly predictive of ADL independency measured at 1 year after stroke. Adding neuroimaging variables (model 2) did not significantly increase the accuracy of predicting long-term outcome of ADL.

The clinical predicting variables in model 1 were recognized before as important factors that independently predict outcome of ADL. This finding further underpins the prognostic value of age and ADL in the acute phase of stroke (BI) as factors that are highly associated with outcome of ADL.

Our results agree with findings from the study of Johnston et al. They showed that the NIHSS at 1 week after stroke was highly predictive of excellent or devastating outcomes using the NIHSS, BI, and GCS at 3 months after ischemic stroke, and that a combination of clinical information and infarct volume assessed on computed tomography scans 1 week after stroke did not improve predictive value. Our findings also agree with those of Wardlaw et al. In their logistic regression analysis, lesion volume was not found to be an independent predictor for 6-month outcome above age and stroke severity, although lesion volume was found to be bivariately associated with functional outcome ($P=0.009$).

However, our results disagree with those from Baird et al. They concluded that imaging predictors assessed with diffusion-weighted magnetic resonance (time in hours of scanning and lesion volume) in combination with neurological predictors (NIHSS) were more accurate in predicting 3-month BI than either clinical or imaging factors alone.

Found differences between the above mentioned studies may be attributable to differences in: (1) moment of measuring functional outcome (3, 6, or 12 months after stroke); (2) clinical variables used as candidate determinants for regression modeling; (3) outcome assessment instruments, and (4) criteria applied for selecting patients. For example, the present study included patients with MCA stroke, whereas Wardlaw et al included patients with stroke in anterior and posterior cerebral circulation using Rankin scores 6 months after stroke, whereas Baird et al restricted to patients with anterior circulation infarctions using the BI at 3 months after stroke.

Our study adds to the literature by providing a long-term follow-up of a homogenous group of stroke survivors with MCA infarcts in which functional outcome was predicted. However, our study had some limitations. First, patients were included within the first week after admission in a stroke unit leading to a selection of patients for our study population. Second, the number of determinants included in both derived regression models was restricted by the limited number of events per variable. Third, the T2-weighted MRI slices used for lesion segmentation were relatively thick (6 mm), which could have resulted in an underestimation of lesion volume, particularly when lesions were small. However, a study in patients with multiple sclerosis showed that estimations of computed lesion volumes did not increase substantially if lesion slice thickness of 6 mm was further minimized. It appears unlikely that minimization of lesion slice thickness would have led to different results in our study.

Our study implicates that patient characteristics and clinical instruments obtained in the early phase after stroke are
sufficient to predict long-term independency in ADL of the stroke survivor after MCA stroke. Neuroimaging information does not have added predictive value compared with clinical information.

Acknowledgments

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