Undernutrition as a Predictor of Poor Clinical Outcomes in Acute Ischemic Stroke Patients

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Objective: To determine whether changes in nutritional status in the first week after acute ischemic stroke and undernutrition predicts poor clinical outcomes.

Design: Prospective observational study.

Setting: Tertiary university hospital.

Patients: We included 131 acute ischemic stroke patients who underwent nutritional assessments within 24 hours and at 1 week after symptom onset.

Main Outcome Measures: Undernutrition was diagnosed when 1 or more of the following 5 parameters were present: (1) weight loss 10% or more during the past 3 months or 6% or more during the week after admission, (2) a weight index less than 80%, (3) a serum albumin level less than 3.0 g/dL, (4) a transferrin level less than 150 mg/dL, or (5) a prealbumin level less than 10 mg/dL. We assessed poststroke complications and 3-month outcome using modified Rankin Scale responder analysis.

Results: Of 131 patients included in this study, undernutrition was observed in 16 (12.2%) patients at admission and in 26 (19.8%) at 1 week. Multiple logistic regression analysis showed that baseline undernutrition independently predicted 1-week undernutrition (odds ratio [OR], 14.85; 95% confidence interval [CI], 3.52-62.76; P < .001) and poststroke complications (OR, 6.72; 95% CI, 1.09-41.56; P = .04), and that 1-week undernutrition (OR, 4.49; 95% CI, 1.07-18.94; P = .04) and 1-week National Institutes of Health Stroke Scale score (OR, 1.76; 95% CI, 1.31-2.37; P < .001) independently predicted poor 3-month outcomes.

Conclusions: These findings suggest that acute ischemic stroke patients with baseline undernutrition are being undernourished during hospitalization. Strategic nutritional support, particularly in patients with baseline undernutrition, may improve clinical outcomes.


Although undernutrition is common in medical,1 geriatric,2 and stroke3-12 patients, its treatment has received little attention. Because undernutrition may influence clinical outcomes, it is important to assess nutritional status and treat undernutrition particularly during acute stage of stroke.

For editorial comment see page 15

In investigating the association between undernutrition and clinical outcomes in stroke patients, several studies have shown that undernutrition contributes to clinical outcomes,5-7,9 whereas others have not.8,10 These inconsistent results may be because of the following reasons: Nutritional parameters and the definitions of undernutrition differ among studies. Many studies have evaluated undernutrition using a combination of hematologic and anthropometric parameters,5,6,8,9,11 while others have used subjective assessments, such as clinician’s decision5 or patient-generated global assessment.6,10 The time point of nutritional assessment has also varied among studies, including within 24 hours,4-6,8,9 or 7 days7 after stroke onset. Serial nutritional assessments have been performed rarely. Moreover, many of these studies have evaluated ischemic and hemorrhagic stroke patients together,3,5-8,10-12 despite undernutrition being more prevalent in hemorrhagic than in ischemic stroke.5 There are also differences in clinical outcome measures, which have included the Barthel index,5 the modified Rankin Scale (mRS),6 hospital stay,3,10 poststroke complications,7 and mortality.8,9 and in the confounding variables considered in the data analysis. With these considerations in mind, we sought to determine whether undernutrition independently predicts poststroke complications and long-term poor clinical outcomes in acute ischemic stroke patients by serial measurements of
more objective nutritional parameters and by adjusting for all potential confounding factors.

METHODS

PATIENTS

This was a prospective study performed between December 8, 2004, and December 12, 2005, at the Asan Medical Center, Seoul, Korea. Patients were included if they had an acute ischemic stroke confirmed by diffusion-weighted imaging performed within 24 hours of symptom onset and if they had serial nutritional assessments within 24 hours and 1 week after onset. We excluded patients who were treated with intravenous or intra-arterial thrombolysis or who might need angioplasty, stenting, or an operation such as craniectomy within 1 week after stroke onset, because these invasive treatments may strongly influence subsequent nutritional status and clinical outcomes. This study was approved by the institutional review boards of the Asan Medical Center, and written informed consent was obtained from each patient, family, or legal guardian.

DATA COLLECTION

Demographics, risk factors for vascular disease, comorbid disease (such as cancer, recent surgery, or recent infection), pre-morbid mRS score, stroke severity, stroke subtype according to the Trial of ORG 10172 in Acute Stroke Treatment classification, nutritional status, diet methods (regular, dysphagic, or enteral feed) and amount (sufficient vs insufficient), and clinical outcomes were assessed. Stroke severity was assessed using the National Institutes of Health Stroke Scale (NIHSS) within 24 hours and at 1 week after onset or at the time of discharge. Swallowing function at admission was evaluated at bed side by a physician and, if necessary, by video fluoroscopic swallow study. Patients were given a regular oral diet, dysphagic diet, or enteral feed via Levin tube according to the results of a swallowing function test and were supplied with daily calories as total energy expenditure based on the Harris-Benedict equation and activity factor. Patients were considered to have been given enteral feed if they were fed via Levin tube for more than half of the first week. Patients were encouraged to intake total calories and were considered as having consumed a sufficient diet when they were fed more than 80% of total desired calories.

NUTRITIONAL ASSESSMENT

Nutritional status was evaluated at admission and at 1 week or discharge using the following 5 nutritional parameters: (1) weight loss, measured as actual body weight in relation to reference weight, (3) serum albumin level, measured as actual body weight in relation to reference weight, (3) serum albumin level, (4) serum transferrin level, and (5) serum prealbumin level. These parameters were selected because they reflected global assessment (weight loss), somatic protein compartment (weight index), and visceral protein compartment (albumin, transferrin, and prealbumin levels). Previous weight loss was assessed by a face-to-face interview with the patients or their significant others at admission. Body weight was measured using a portable in-bed scale for immobile patients and a fatness measuring system for ambulatory patients at admission. Undernutrition was diagnosed when 1 or more of 5 parameters showed moderate or severe undernutrition: (1) weight loss of 10% or more of body weight for the past 3 months or 6% or more during the first week after admission, (2) weight index less than 80%, (3) serum albumin level of less than 30 g/dL (to convert to grams per liter, multiply by 10), (4) serum transferrin level of less than 150 mg/dL, or (5) serum prealbumin level of less than 10 mg/dL (to convert to milligrams per liter, multiply by 10). Nutritional changes from baseline to 1 week were categorized as no change (from healthy to healthy, or from undernutrition to undernutrition), improved (from undernutrition to healthy), or worsened (from healthy to undernutrition).

CLINICAL OUTCOMES

The presence of poststroke complications was assessed immediately after admission and up to discharge or transfer to a rehabilitation unit and included pneumonia, urinary tract infection, extracranial hemorrhage, deep vein thrombosis, and pressure sore. Pneumonia was diagnosed as probable by the presence of (1) high fever (> 38.0°C), (2) 1 or more clinical symptoms or signs (purulent sputum or rale), and (3) abnormal laboratory findings (leukocytosis or increased erythrocyte sedimentation rate or C-reactive protein level) and as definite when these 3 criteria were accompanied by lung infiltrates on chest radiography. Myocardial infarction was diagnosed when 2 of the following 3 criteria were met: chest pain continuing for more than 30 minutes, increased cardiac enzyme (creatinine kinase MB, troponin I, or troponin I) levels, and diagnostic electrocardiographic changes. Urinary tract infection was diagnosed when clinical symptoms, such as high fever and pyuria, were present or when bacteria (> 10^5 colony-forming units/mL) were grown from urine culture. Extracranial hemorrhage, such as gastrointestinal bleeding or gross hematuria, was defined as clinically significant hemorrhage that needed close observation, transfusion, or operation. Deep vein thrombosis was diagnosed by swelling or pain in the calf, with or without abnormal image (ultrasound scan or venography) findings. A pressure sore was defined as an abrasion or necrosis of the skin and tissue due to sustained pressure, friction, or moisture.

Long-term clinical outcome was assessed by mRS score at 3 months, with outcome categorized as good or poor according to responder analysis, which judges outcome based on baseline NIHSS score. Good outcome was defined as an mRS score of 0 if baseline NIHSS score was less than 8, an mRS score of 0 to 1 if baseline NIHSS score was 8 to 14, and an mRS score of 0 to 2 if baseline NIHSS score was 15 or higher. Serial NIHSS scores, poststroke complications, and long-term clinical outcome were assessed by one investigator blinded to baseline characteristics and nutritional status.

DATA ANALYSIS

The McNemar test was used to compare baseline and 1-week undernutrition. To identify the factors associated with baseline and 1-week undernutrition, poststroke complication, and 3-month outcome, the Fisher exact test, t test, and the Mann-Whitney test were used where appropriate. Multiple logistic regression analysis was used to determine independent predictors of 1-week undernutrition, poststroke complication, and poor 3-month outcome. Variables were selected for entry into the model based on the results of univariate analyses (P < .05). Because we tried to identify predictors of clinical outcomes, the precedent variables to poststroke complications and 3-month outcome were entered into the models. The odds ratios (ORs) and 95% confidence intervals (CIs) were calculated. The Hosmer-Lemeshow goodness-of-fit test was used to assess how well the model accounted for outcomes. SPSS, version 12.0 (SPSS Inc, Chicago, Illinois), for Windows was used for statistical analyses. Two-tailed P < .05 was considered to indicate a significant difference.

RESULTS

A total of 264 patients were screened for this study, but 133 were excluded: 40 for thrombolysis, 9 for angio-
plasty or other operation, 75 for unavailable nutritional assessment, and 9 for refusal of consent or withdrawal. There were no differences in demographic characteristics, risk factors, or stroke subtypes between included and excluded participants, except that baseline NIHSS scores were higher in included (median, 7; range, 0-30) than in included (median, 4; range, 0-23; P < .001) patients.

Of the 131 patients included in this study, 84 (64.1%) were men. Patients had a mean (SD) age of 64.8 (10.3) years and a median (range) baseline NIHSS score of 4 (0-23). Stroke intensity was mild (baseline NIHSS score, 0-7) in 109 patients (83.2%), moderate (baseline NIHSS score, 8-14) in 15 (11.5%), and severe (baseline NIHSS score, ≥ 15) in 7 (5.3%). Premorbid mRS score was 0 in all patients.

Undernutrition was observed in 16 (12.2%) patients at admission and in 26 (19.8%) at 1 week, showing a significant increase during the first week (P < .03 by McNemar test) (Table 1). Nutritional status according to each parameter also deteriorated during hospitalization, with the most profound being serum albumin concentration (P < .001 by McNemar test). During the first week, there were no nutritional changes in 113 (86.3%) patients, improved nutrition in 4 (3.1%), and worsened nutrition in 14 (10.7%).

FACTORS ASSOCIATED WITH UNDERNUTRITION AT BASELINE AND 1 WEEK

Age (P = .001), cardioembolic stroke (P = .001), and higher baseline NIHSS score (P = .04) were associated with the presence of baseline undernutrition. The baseline characteristics associated with 1-week undernutrition included age (P = .01), absence of hypercholesterolemia (P = .04), baseline undernutrition (P < .001), and enteral feed (P = .049). Multiple logistic regression analysis showed that only baseline undernutrition (OR, 14.85; 95% CI, 3.52-62.76; P < .001) independently predicted subsequent undernutrition.

PREDICTORS OF POSTSTROKE COMPLICATIONS

Poststroke complications were observed in 11 of 131 (8.3%) patients, with aspiration pneumonia in 5, extracranial hemorrhage in 3, myocardial infarction in 2, and bed sores in 1. Univariate analysis showed that old age (P = .001), cardioembolic stroke (P = .003), higher baseline NIHSS score (P < .001), baseline undernutrition (P < .001), and enteral feed (P < .001) were associated with more frequent poststroke complications (Table 2). Multiple logistic regression analysis showed that baseline NIHSS score (OR, 1.21; 95% CI, 1.01-1.45; P = .04) and baseline undernutrition (OR, 6.72; 95% CI, 1.09-41.56; P = .04) were independent predictors of poststroke complications during hospitalization (Table 3).

PREDICTORS OF POOR OUTCOME AT 3 MONTHS

During the 3-month follow-up period, recurrent stroke occurred in 2 (1.5%) patients and death occurred in 4 (3.1%) patients, 2 due to respiratory failure, 1 due to cancer, and 1 unknown cause. Baseline and 1-week undernutrition were not associated with recurrent stroke or death.

Poor outcome, as defined by 3-month mRS responder analysis, was observed in 87 (66.4%) patients and was significantly associated with female sex (P = .01), 1-week undernutrition (P = .01), insufficient diet for the first week (P = .02), and higher baseline (P < .001) and 1-week (P < .001) NIHSS scores by univariate analysis (Table 2). Multiple logistic regression analysis revealed that 1-week undernutrition (OR, 4.49; 95% CI, 1.07-18.94; P = .04) and 1-week NIHSS score (OR, 1.76; 95% CI, 1.31-2.37; P < .001) predicted poor 3-month outcome (Table 3).

When we defined poor outcome as an mRS score of 2 to 6 (n = 47 [35.9%]) or of 3 to 6 (n = 24 [18.3%]), 1-week undernutrition was associated with poor outcomes (mRS score, 2-6; P = .01; mRS score, 3-6; P = .006). However, multivariate analyses showed that both 1-week NIHSS score (OR, 2.19; 95% CI, 1.27-3.60) and age (OR, 1.16; 95% CI, 1.05-1.27) and 1-week NIHSS score (OR, 2.48; 95% CI, 1.59-3.87) remained independent predictors of poor outcome (mRS score, 2-6) and that age (OR, 1.16; 95% CI, 1.05-1.27) and 1-week NIHSS score (OR, 2.48; 95% CI, 1.59-3.87) remained independent predictors of poor outcome (mRS score, 3-6).

This study shows that undernutrition was an independent predictor of poststroke complications and poor clinical outcome in acute ischemic stroke patients. This study has several methodological advantages over previous ones. Serial nutritional assessments using more objective nutritional parameters were performed in the acute stage of stroke. Only acute ischemic stroke patients were included. All potential confounding variables, such as vascular risk factors, comorbid diseases, stroke severity, stroke subtypes, and diet methods and amount, were considered in the analysis to demonstrate the independent contribution of undernutrition to poor clinical outcomes.

Baseline undernutrition was an independent predictor of subsequent undernutrition in our sample. We also observed significant associations between baseline undernutrition and poststroke complications during hospitalization and between 1-week undernutrition and poor 3-month clinical outcomes. These results suggest that patients undernourished at admission do not recover well with general hospital diets and are more likely to have
poststroke complications and that undernourished patients during hospitalization are more likely to develop poor functional outcomes. However, baseline undernutrition was not directly associated with long-term outcome, a finding similar to previous work. For an explanation of this lack of correlation, we speculate that long-term outcome may be more affected by progress during hospitalization than by baseline characteristics. We also consider that these results emphasize the significance of nutritional support during hospitalization.

The frequency of undernutrition in our study was 12.2% at admission (24 hours after onset) and 19.8% at 1 week, which was relatively lower than in previous studies. The difference in the frequency may be related to different definitions of undernutrition. We defined only moderate to severe undernutrition of each patient.

### Table 2. Factors Associated With Clinical Outcome in Acute Ischemic Stroke Patients

<table>
<thead>
<tr>
<th>Variables</th>
<th>Poststroke Complications</th>
<th>Poor 3-mo Outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Patients With (n=11)</td>
<td>Patients Without (n=120)</td>
</tr>
<tr>
<td>Demographics</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean age (SD), y</td>
<td>74.3 (7.3)</td>
<td>63.9 (10.1)</td>
</tr>
<tr>
<td>Male sex</td>
<td>8 (72.7)</td>
<td>77 (64.2)</td>
</tr>
<tr>
<td>Risk factors</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypertension</td>
<td>10 (90.9)</td>
<td>100 (83.3)</td>
</tr>
<tr>
<td>Diabetes</td>
<td>4 (36.4)</td>
<td>35 (29.2)</td>
</tr>
<tr>
<td>Hypercholesterolemia</td>
<td>3 (27.3)</td>
<td>52 (43.3)</td>
</tr>
<tr>
<td>Current smoker</td>
<td>1 (9.1)</td>
<td>37 (30.8)</td>
</tr>
<tr>
<td>Heavy drinker</td>
<td>0</td>
<td>12 (10)</td>
</tr>
<tr>
<td>Previous stroke</td>
<td>2 (18.2)</td>
<td>28 (23.3)</td>
</tr>
<tr>
<td>Cancer</td>
<td>1 (9.1)</td>
<td>2 (1.7)</td>
</tr>
<tr>
<td>Recent operation or trauma, &lt;1 mo</td>
<td>1 (9.1)</td>
<td>1 (0.8)</td>
</tr>
<tr>
<td>Recent infection, &lt;2 wk</td>
<td>2 (18.2)</td>
<td>11 (11.7)</td>
</tr>
</tbody>
</table>

### Table 3. Independent Predictors of Clinical Outcomes in Acute Ischemic Stroke Patients

<table>
<thead>
<tr>
<th>Outcome Predictor</th>
<th>Poststroke Complications</th>
<th>Poor 3-mo Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>OR (95% CI)</td>
<td>P Value</td>
</tr>
<tr>
<td>Age</td>
<td>1.09 (0.99-1.20)</td>
<td>.07</td>
</tr>
<tr>
<td>Male sex</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cardioembolism</td>
<td>2.08 (0.28-15.76)</td>
<td>.49</td>
</tr>
<tr>
<td>Baseline NIHSS score</td>
<td>1.21 (1.01-1.45)</td>
<td>.03</td>
</tr>
<tr>
<td>Baseline undernutrition</td>
<td>6.67 (1.08-41.35)</td>
<td>.04</td>
</tr>
<tr>
<td>Enteral feed</td>
<td>4.89 (0.43-55.27)</td>
<td>.20</td>
</tr>
<tr>
<td>Insufficient diet</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1-wk NIHSS score</td>
<td>2.13 (0.64-7.04)</td>
<td>.22</td>
</tr>
<tr>
<td>Undernutrition at 1 wk</td>
<td>4.49 (1.07-18.94)</td>
<td>.04</td>
</tr>
</tbody>
</table>

Abbreviations: LAA, large-artery atherosclerosis; SVO, small-vessel occlusion; NIHSS, National Institutes of Health Stroke Scale.

Values are number (percentage) unless otherwise specified.
parameter as undernutrition, whereas other studies have included mild undernutrition in the definition. In addition, we included patients who had relatively mild strokes while excluding patients receiving thrombolysis or emergency interventional treatments. Because stroke severity was significantly associated with undernutrition, excluding severe stroke patients may have resulted in a lower prevalence of undernutrition. We also excluded hemorrhagic stroke patients in whom undernutrition has been shown to be more prevalent than in ischemic stroke patients.

The parameters for nutritional assessment also differ among studies. As a visceral protein compartment, serum albumin level has been used for nutritional assessment and is known to be a good predictor of clinical outcome. However, serum albumin level is of limited utility in detecting acute nutritional changes owing to its long half-life (18 days). We therefore also measured transferrin and prealbumin levels, which have shorter half-lives, 8 and 2 days, respectively. In this study, undernutrition was more likely detected in the transferrin parameter than in the albumin parameter at admission, but temporal changes during 1 week were more pronounced in the albumin parameter. The mechanism of these findings is unclear, and the advantages of transferrin and prealbumin over albumin levels in detecting undernutrition were not demonstrated in this study. Moreover, whereas other studies have used anthropometric parameters, such as caliper skin fold measures at multiple body sites, for nutritional assessment, we did not use these parameters, as they have been shown to be unsuitable for stroke patients with tetraparesis or spasticity as a sequela of stroke, especially in assessing acute nutritional change.

We used mRS responder analysis, which is influenced by initial stroke severity, to assess long-term clinical outcome. Because most of our patients had had mild or moderate strokes, we thought that responder analysis might be more appropriate than conventional mRS categorical analysis.

Our study has several limitations. First, it was conducted in a single tertiary hospital in an Asian country, thus limiting generalization of our results to other communities or countries where dietary patterns are likely different. Second, not all acute ischemic stroke patients were included, which resulted in including patients with relatively milder stroke in this study. The low incidence of poststroke complications may have resulted in wide CI of ORs. The incidence of recurrent stroke or death was too low to find an association with undernutrition. Third, undernutrition was not an independent predictor of poor outcome when we defined poor outcome as an mRS score of 2 to 6. Thus, further studies with a larger sample size should be conducted to confirm our findings.

In conclusion, this study shows that acute ischemic stroke patients with baseline undernutrition are being undernourished during hospitalization and that undernutrition independently predicts poor clinical outcomes in these patients. Strategic nutritional support, particularly in patients with baseline undernutrition, may improve clinical outcomes after acute ischemic stroke.

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