Serum Albumin Level as a Predictor of Ischemic Stroke Outcome

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**Background and Purpose**—Animal studies showed that human albumin therapy is strongly neuroprotective in focal ischemia. The aim of our study was to determine if relatively high serum albumin level is associated with decreased risk of poor outcome in ischemic stroke patients.

**Methods**—Seven hundred fifty-nine consecutive patients with acute ischemic stroke were included. Functional outcome was measured 3 months after stroke using modified Rankin Scale (mRS). Poor outcome was defined as mRS >3 or death. Serum albumin level was measured within 36 hours after stroke onset.

**Results**—Patients with poor outcome had significantly lower serum albumin level than patients with nonpoor outcome (34.1±7.4 versus 36.8±6.7 g/L). On logistic regression analysis, serum albumin level remained independent predictor of poor outcome (odds ratio [OR]: 0.43; 95% confidence interval [CI]: 0.26 to 0.70).

**Conclusions**—Relatively high serum albumin level in acute stroke patients decreases the risk of poor outcome. (**Stroke.** 2004;35:e156-e158.)

**Key Words:** stroke ▪ cerebral ischemia ▪ outcome ▪ albumins

Human serum albumin is a unique multifunctional protein with neuroprotective properties. Experimental studies showed that human albumin therapy substantially improves neurological function, markedly reduces the volume of cerebral infarction, and eliminates brain swelling in animals with acute stroke.1-3

We hypothesize that relatively high serum albumin level in acute stroke patients is associated with decreased risk of poor outcome.

**Materials and Methods**

Patients in this study were recruited from 818 consecutive patients with first-ever ischemic stroke admitted to our stroke unit between January 2000 and December 2002. Patients admitted to the hospital >24 hours after stroke onset (56 patients) and patients with cancerous disease or other serious diseases (3 patients) were excluded.

Arterial hypertension was diagnosed when its presence was documented in medical records or when at least 2 readings of blood pressure were ≥140 mm Hg (systolic) or ≥90 mm Hg (diastolic) after the acute phase of stroke. Ischemic heart disease was diagnosed when there was a history of angina pectoris or myocardial infarction. Diabetes mellitus was diagnosed if its presence was documented in medical records or patient was using insulin or an oral hypoglycemic agent. A patient was defined as a smoker if there was a history of cigarette smoking during the past 5 years.

All patients underwent head computed tomography (CT) scan within 24 hours after stroke onset. The second CT scan was performed 4 to 6 days after stroke onset in 90.5% of patients. Large infarcts were so designated when the sum of the largest transverse and sagittal diameter divided by 2 was >1.5 cm.

Stroke severity on admission was assessed using Scandinavian Stroke Scale (SSS).4 The patients were divided into 2 groups on the basis of the stroke severity on admission. SSS <25 was selected as a cutoff point because patients with lower scores were all nonambulatory.5 Functional outcome was measured 3 months after stroke using modified Rankin Scale (mRS).6 Poor outcome was defined as mRS >3 or death.7 Nonpoor outcome was defined as mRS ≤4.

Serum albumin level was measured between 12 and 36 hours after stroke onset using Roche/Hitachi analyzer. Fasting total cholesterol (TC) and fibrinogen levels were measured at the same time.

The study protocol was approved by the local Bioethics Committee and informed consent was obtained from all patients.

The chi-square test was used to compare proportions and Student t test was used to compare continuous variables between groups. Logistic regression analysis was used to assess the independent contribution of variables statistically significant on univariate analysis in the prediction of outcome. Poor outcome was coded as 1, and good outcome was coded as 0. Backward logistic regression including only variables with a P<0.1 was followed by a forward logistic regression including the same variables. Values of P<0.05 were considered statistically significant.

**Results**

We included 759 patients with acute ischemic stroke. Mean age was 68.3±12, and 372 were men. During the 3-month follow-up period, 98 patients (12.9%) died.

The characteristics of patients with poor outcome and those with nonpoor outcome are shown in the Table. Two hundred sixty-six patients had poor outcome. These patients were significantly older, more often female, and more frequently had ischemic heart disease and atrial fibrillation. The patients with poor outcome had significantly more severe neurological deficit on admission measured on SSS scale and more...
frequently had large infarct on CT (76.9% versus 53.7%, \( P \leq 0.01 \)). Serum albumin and TC levels were significantly lower in patients with poor outcome than in those with nonpoor outcome. The Figure shows albumin levels versus mRS.

The following variables were put into logistic regression model: age (\( \geq 65 \) versus \(< 65 \) years), sex, atrial fibrillation, ischemic heart disease, smoking, SSS score on admission (\( \geq 25 \) versus \(< 25 \)), infarct size (large versus small), TC (\( \geq 6.2 \) versus \(< 6.2 \) mmol/L), and serum albumin level (\( \geq 49 \) versus \(< 49 \) g/L). Subjects within the upper quartile of the albumin distribution (\( \geq 49 \) g/L) were considered to be at lower risk for poor outcome. On multiple logistic regression analysis, ischemic heart disease (odds ratio [OR]: 1.71; 95% confidence interval [CI]: 1.09 to 2.69), SSS score on admission (OR: 0.06; 95% CI: 0.04 to 0.10), infarct size (OR: 2.01; 95% CI: 1.30 to 3.12), and serum albumin level (OR: 0.43; 95% CI: 0.26 to 0.70) remained independent predictors of poor outcome. In next analysis, we put into the model the same variables, but age, SSS score, TC, and albumin levels were given as continuous variables. We found the following independent predictors: age (OR: 1.03; 95% CI: 1.01 to 1.05), ischemic heart disease (OR: 1.73; 95% CI: 1.07 to 2.78), SSS

<table>
<thead>
<tr>
<th>Characteristics of Stroke Patients With Poor Outcome and Those With Nonpoor Outcome</th>
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<tbody>
<tr>
<td>Patients With Poor Outcome (N=266)</td>
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<tr>
<td>Age, mean (SD)</td>
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<tr>
<td>Men, n (%)</td>
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<tr>
<td>Hypertension, n (%)</td>
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<tr>
<td>Diabetes mellitus, n (%)</td>
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<tr>
<td>Ischemic heart disease, n (%)</td>
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<tr>
<td>Atrial fibrillation, n (%)</td>
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<tr>
<td>TIA, n (%)</td>
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<td>Smoking, n (%)</td>
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<td>SSS score on admission, mean (SD)</td>
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<tr>
<td>Systolic blood pressure on admission (mm Hg), mean (SD)</td>
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<td>Diastolic blood pressure on admission (mm Hg), mean (SD)</td>
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<td>Fibrinogen g/L, mean (SD)</td>
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<td>TC mmol/L, mean (SD)</td>
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<td>Albumin g/L, mean (SD)</td>
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TIA indicates transient ischemic attack; SD, standard deviation; SSS, Scandinavian Stroke Scale; TC, total cholesterol.
score on admission (OR: 0.87; 95% CI: 0.86 to 0.89), and albumin level (OR: 0.96; 95% CI: 0.93 to 0.99).

When poor outcome was defined as mRS ≥2, logistic regression analysis identified the following independent predictors: ischemic heart disease (OR: 1.96; 95% CI: 1.27 to 3.01), SSS ≥25 (OR: 0.06; 95% CI: 0.04 to 0.09), infarct size (OR: 2.28; 95% CI: 1.51 to 3.43), and albumin level ≥49 g/L (OR: 0.63; 95% CI: 0.40 to 0.98). When poor outcome was defined as mRS >1, we found the following independent predictors: ischemic heart disease (OR: 1.81; 95% CI: 1.20 to 2.72), SSS ≥25 (OR: 0.05; 95% CI: 0.03 to 0.09), infarct size (OR: 2.10; 95% CI: 1.43 to 3.08), and albumin level ≥49 g/L (OR: 0.58; 95% CI: 0.38 to 0.89).

Discussion

Experimental studies of focal cerebral ischemia showed that high-dose (2.0 to 2.5 g/kg) or moderate-dose (0.63 to 1.25 g/kg) human albumin therapy, if administered promptly (2 to 4 hours) after stroke onset, is highly effective in improving neurological status and in reducing infarction volume and extent of brain swelling.1–3

Albumin has multifaceted intravascular effects. It not only reduces hematocrit level but also influences erythrocyte aggregation by increasing low shear viscosity and decreasing erythrocyte sedimentation under no-flow conditions.8 Albu-

there is no consensus on the most appropriate method and timing of the stroke outcome assessment. We defined poor outcome as mRS >3 or death, because it was suggested that using this cutoff point makes it easier to define poor outcome as opposed to favorable outcome.7 However, in the next analysis, we used other cutoff points, also. Regardless of chosen cutoff point, serum albumin level remained an independent predictor of stroke outcome.

So far, albumin therapy for stroke was assessed in only 1 small, prospective, clinical study in which albumin was administered in an individually customized fashion.12 The results of that study suggest a treatment-associated reduction in mortality rate of ≥10%. Further studies are needed to verify whether albumin therapy could be beneficial for acute stroke patients.

References


