

# Transthyretin Concentrations in Acute Stroke Patients Predict Convalescent Rehabilitation

Naofumi Isono,\* Yuki Imamura,† Keiko Ohmura,† Norihide Ueda,†‡  
Shinji Kawabata,§ Motomasa Furuse,§ and Toshihiko Kuroiwa§

*Objective:* For stroke patients, intensive nutritional management is an important and effective component of inpatient rehabilitation. Accordingly, acute care hospitals must detect and prevent malnutrition at an early stage. Blood transthyretin levels are widely used as a nutritional monitoring index in critically ill patients. Here, we had analyzed the relationship between the transthyretin levels during the acute phase and Functional Independence Measure in stroke patients undergoing convalescent rehabilitation. *Methods:* We investigated 117 patients who were admitted to our hospital with acute ischemic or hemorrhagic stroke from February 2013 to October 2015 and subsequently transferred to convalescent hospitals after receiving acute treatment. Transthyretin concentrations were evaluated at 3 time points as follows: at admission, and 5 and 10 days after admission. After categorizing patients into 3 groups according to the minimum transthyretin level, we analyzed the association between transthyretin and Functional Independence Measure. *Results:* In our patients, transthyretin levels decreased during the first 5 days after admission and recovered slightly during the subsequent 5 days. Notably, Functional Independence Measure efficiency was significantly associated with the decrease in transthyretin levels during the 5 days after admission. Patients with lower transthyretin levels had poorer Functional Independence Measure outcomes and tended not to be discharged to their own homes. *Discussion:* A minimal transthyretin concentration (<10 mg/dL) is predictive of a poor outcome in stroke patients undergoing convalescent rehabilitation. In particular, an early decrease in transthyretin levels suggests restricted rehabilitation efficiency. Accordingly, transthyretin levels should be monitored in acute stroke patients to indicate mid-term rehabilitation prospects. **Key Words:** Transthyretin—stroke—convalescent rehabilitation—Functional Independence Measure—monitoring—outcome—efficiency—National Institutes of Health Stroke Scale.

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From the \*Department of Neurosurgery, Higashi-Sumiyoshi Morimoto Hospital, Osaka, Japan; †Clinical Nutrition and Food Service, Higashi-Sumiyoshi Morimoto Hospital, Osaka, Japan; ‡Clinical Nutrition and Food Service, Kokuho Central Hospital, Shiki, Japan; and §Department of Neurosurgery, Osaka Medical College, Takatsuki, Japan.

Received November 8, 2016; revision received February 6, 2017; accepted February 15, 2017.

Address correspondence to Naofumi Isono, MD, Department of Neurosurgery, Higashi-Sumiyoshi Morimoto Hospital, 3-2-66 Takaai Higashisumiyoshi-ku, Osaka, 546-0014, Japan. E-mail: [neuisono@tachibana-med.or.jp](mailto:neuisono@tachibana-med.or.jp).

1052-3057/\$ - see front matter

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<http://dx.doi.org/10.1016/j.jstrokecerebrovasdis.2017.02.020>

## Introduction

Malnutrition is a common complication observed in stroke patients.<sup>1,2</sup> According to previous reports, the proportion of malnourished patients continues to increase within several weeks after the onset of stroke<sup>3-5</sup> and approximately half of all patients in convalescent rehabilitation are undernourished.<sup>6,7</sup> Intensive nutritional supplementation has recently been found to improve the functional recovery of undernourished patients receiving intensive inpatient rehabilitation after stroke,<sup>2,8</sup> a finding that raised questions regarding whether undernutrition during the acute recovery phase would affect outcomes and efficiency of convalescent rehabilitation.

Although early and ongoing detection of malnutrition is recommended immediately after stroke onset,<sup>9</sup> a clear definition of malnutrition has yet to be established; as a result, evaluation methods differ among facilities. Currently, blood transthyretin levels are widely used as a biochemical index for nutrition management during acute illness.<sup>10,11</sup> Notably, the strong ability of transthyretin to reveal changes in protein status has been attributed to its relatively short biological half-life (approximately 2 days). In this study, we evaluated the nutritional status of acute stroke patients using transthyretin measurements obtained at 3 time points and analyzed the relationship between the transthyretin levels and Functional Independence Measure (FIM) outcomes in the convalescent rehabilitation setting.

## Methods

### *Subjects*

This retrospective single-center study investigated patients who were admitted consecutively to Higashi-Sumiyoshi Morimoto Hospital after a recent stroke and subsequently transferred to convalescent hospitals after acute treatment between February 2013 and October 2015. For each patient, we registered the following variables: age, sex, neurologic impairments, stroke type (hemorrhagic or ischemic), and length of hospital stay. Neurologic impairment was evaluated using the National Institutes of Health Stroke Scale (NIHSS), a well-validated instrument used to assess impairment levels in 15 neurological functions frequently affected by stroke.<sup>12</sup> Patients with subarachnoid hemorrhage were excluded because the severity of this condition could not be estimated using the NIHSS, and patients with severe liver cirrhosis were excluded because transthyretin is synthesized in the liver.<sup>11</sup> Patients with cancer or acute myocardial infarction were also excluded. In all cases, the diagnosis was confirmed using computed tomography or magnetic resonance imaging, and standard treatments were implemented according to the 2009 Japanese Guidelines for the Management of Stroke.

### *Transthyretin Analysis*

Blood transthyretin levels were evaluated at 3 time points: at admission, and at 5 and 10 days after hospitalization. Some leeway in the postadmission blood sampling (e.g.,  $\pm 1$  day) was allowed according to the patient's condition. C-reactive protein (CRP) at admission was also used as a marker of inflammation.

On the basis of an earlier report that transthyretin levels of lower than 20 mg/dL are associated with a 4-month weight loss,<sup>13</sup> we categorized all patients into 3 groups according to the minimal transthyretin level measured during the analysis. Accordingly, patients with high transthyretin levels ( $\geq 20$  mg/dL) at all 3 time points would be expected to have more favorable outcomes during con-

valescent rehabilitation because they were able to maintain the lean body mass. Such patients were defined as group A. Another previous study defined undernutrition as having transthyretin level of lower than 10 mg/dL and found that this level correlated with a poor outcome at 3 months.<sup>5</sup> Accordingly, we defined patients with a minimum transthyretin level of lower than 10 mg/dL as group C. The remaining patients were defined as group B. We designated a change in the transthyretin levels from admission to the second and third time points as  $\Delta 1-2\text{TTR}$  and  $\Delta 1-3\text{TTR}$ , respectively.

### *Factors Affecting Nutrition*

To determine the factors that affected a patient's nutritional status, we investigated several clinical parameters. Surgery under general anesthesia within 10 days after admission was included as was chest infection during the acute care period. The latter was defined as an infection requiring antibiotic treatments and manifesting with the following symptoms: febrile body temperature, respiratory crackles, new purulent sputum, radiographic evidence, abnormal laboratory findings (leukocytosis or increased erythrocyte sedimentation rate), decrease in oxygen saturation, and/or positive culture. We also considered a requirement for swallowing rehabilitation during acute hospital care.

### *Functional Outcome and Efficiency of Convalescent Rehabilitation*

We adopted FIM parameters used by physicians at convalescent hospitals. FIM is a standard, clinically relevant scale for measuring a patient's functional status.<sup>14</sup> Items are scored according to the level of assistance required for the patient to perform activities of daily life. The scale includes 18 items, and each is scored from 1 (total dependence) to 7 (complete independence). The total summed scores thus range from 18 to 126, with higher scores indicating greater independence. The rate of functional gain (FIM efficiency) was calculated as the total change in FIM (discharge FIM score minus transfer FIM score) divided by the length of stay in a convalescent rehabilitation facility. The final discharge disposition (home or not home) was also recorded.

### *Nutrition Management*

Each patient consumed a standard oral diet after a nurse, speech and language therapist, or physician confirmed that the patient could manage oral intake. The required amount of energy was calculated using the Harris-Benedict equation.<sup>15</sup> Extraordinary nutritional diets were not routinely given and very-low-calorie diets were not prescribed for diabetic patients. Oral dietary or peripheral parenteral nutrition supplementation was added if the patient's oral intake was insufficient. For dysphagic

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