

# Malnutrition Increases the Incidence of Death, Cardiovascular Events, and Infections in Patients with Stroke after Rehabilitation

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*Background:* Although the impact of malnutrition in patients with acute stroke has been reported, its significance after rehabilitation is not well understood. The geriatric nutritional risk index (GNRI) is a simple and well-established nutritional screening tool that predicts poor prognosis in elderly patients and in those with a high risk of cardiovascular events. We investigated the associations between GNRI and all-cause mortality, cardiovascular events, and infectious diseases in patients with stroke after rehabilitation. *Methods:* This study included 138 patients aged 80 years or below who were discharged between 2010 and 2013 in a single center, and followed up for more than 1 year. Malnutrition was defined as a GNRI of 96 or lower. *Results:* The mean age was  $63.9 \pm 11.0$  years, the mean GNRI at discharge was  $98.8 \pm 6.5$ , and the mean total functional independence measure (FIM) score at discharge was  $91.8 \pm 25.8$ . Among the patients, 37 (27%) had malnutrition. During the follow-up period, all-cause mortality, cardiovascular events, and infectious diseases were recorded in 11 (8%), 21 (15%), and 20 (15%) patients, respectively. Kaplan–Meier curves showed a significantly higher incidence of each outcome in patients with a GNRI of 96 or lower. In the Cox proportional analysis, GNRI was an independent determinant of all-cause mortality (hazard ratio [HR], .71; 95% confidence interval [CI], .61-.83), cardiovascular events (HR, .87; 95% CI, .80-.95), and infectious diseases (HR, .80; 95% CI, .74-.87) after adjusting for age, gender, and total FIM score. *Conclusions:* Malnutrition has a negative impact on prognosis in patients with stroke even after rehabilitation. **Key Words:** Nutritional status—geriatric nutritional risk index—functional independence measure—all-cause mortality—cardiovascular events—infections. © 2017 National Stroke Association. Published by Elsevier Inc. All rights reserved.

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## Introduction

Stroke is one of the leading causes of mortality and disability worldwide.<sup>1</sup> Although the mortality of stroke has declined steadily, it is still the fourth major cause of death in Japan. Therefore, further efforts are needed to sustain this decline and to improve mortality.

Recently, it has been noted that malnutrition in patients with acute stroke is associated with poor prognosis.<sup>2</sup> The geriatric nutritional risk index (GNRI) is a simple, well-established nutritional assessment tool for elderly individuals, dialysis patients, and other critically ill patients.<sup>3,4</sup> It is based on only 3 objective parameters: body weight, height, and serum albumin level. We recently reported that the cutoff value of GNRI for predicting all-cause and

cardiovascular mortality is 96 in hemodialysis patients and that a GNRI of 96 or lower predicts the long-term incidence of cardiovascular events irrespective of echocardiographic left ventricular hypertrophy and chronic kidney disease (CKD).<sup>5,6</sup> However, this assessment has not yet been applied to long-term prognosis and complications in patients with stroke after rehabilitation.

Although the prevalence of malnutrition is significantly higher in the rehabilitation stage than that in the acute stage,<sup>7</sup> it is still poorly understood how malnutrition affects the long-term incidence of all-cause mortality, cardiovascular events, and infectious diseases in patients with stroke who are discharged after poststroke rehabilitation. In the present study, we investigated the associations between GNRI and all-cause mortality, cardiovascular events, and infectious diseases in patients post stroke.

## Methods

### *Participants*

We enrolled 163 patients with stroke aged 80 years or below who were admitted to Asahikawa Rehabilitation Hospital (266 hospital beds) for poststroke rehabilitation, discharged from a convalescent rehabilitation ward between April 2010 and March 2013, and were followed up for more than 1 year. Forty-four physical therapists, 26 occupational therapists, and 10 speech therapists offer rehabilitation therapy in the facility. The hospital has a nutritional support team that includes doctors, nurses, and nutritionists, and they round on each patient before offering nutritional problems. Stroke was defined as cerebral infarction, cerebral hemorrhage, or subarachnoid hemorrhage. After excluding patients who were on dialysis and had comorbidities with malignancies, nephrotic syndrome, or liver cirrhosis, and those with missing data, the present analysis included 138 patients (male,  $n = 90$ ; female,  $n = 48$ ; mean age,  $63.9 \pm 11.0$  years). Age, gender, blood pressure, heart rate, lipid parameters, electrolytes, and conventional cardiovascular risk factors were also recorded. A current smoker was defined as one who regularly smoked at least 1 pack per day before the onset of stroke. The present study was performed in strict accordance with the ethical guidelines of the Declaration of Helsinki and was approved by the Ethical Scientific Committee of Asahikawa Rehabilitation Hospital. All study participants provided written informed consent.

### *Data Collection*

The following data were collected for each patient at discharge. Body mass index (BMI) was calculated by dividing weight by height squared ( $m^2$ ). We calculated the GNRI using serum albumin values, weight, and ideal body weight. GNRI was calculated as reported by Yamada et al<sup>8</sup>:  $GNRI = [14.89 \times \text{albumin (g/dL)}] + [41.7 \times (\text{weight/ideal$

$\text{body weight})]$ . Note that body weight/ideal body weight was higher than 1 when a subject's body weight exceeded his or her ideal body weight. The ideal body weight was calculated using height and a BMI of 22, which is reportedly associated with the lowest morbidity rate in the Asian population.<sup>9</sup> Hypertension was defined as a systolic blood pressure of 140 mm Hg or higher, and a diastolic blood pressure of 90 mm Hg or higher, or the current use of antihypertensive agents. Diabetes was defined as one of the following: fasting blood sugar level of 126 mg/dL or higher, nonfasting blood sugar level of 200 mg/dL or higher, a glycosylated hemoglobin level of 6.5% or higher, or the current use of insulin or oral hypoglycemic agents. Dyslipidemia was defined as a total cholesterol level of 220 mg/dL or higher, a high-density lipoprotein cholesterol level lower than 40 mg/dL for men and lower than 50 mg/dL for women, a triglyceride level of 150 mg/dL or higher, or medication with antidyslipidemia agents. The estimated glomerular filtration rate (eGFR) was calculated as previously described.<sup>10</sup> eGFR was expressed after body surface area adjustment. Proteinuria was defined as 1+ or more on a dipstick test. CKD was defined by proteinuria or eGFR lower than 60 mL/min. Functional independence measure (FIM) scores at admission and at discharge were recorded by trained therapists. FIM gain and FIM efficiency were also recorded.

### *Follow-Up*

Follow-up data were retrieved from clinical records or death certificates by personnel blinded to the anthropometric measurements, body composition, and laboratory assessments. Infection was defined as infectious diseases requiring admission, including pneumonia and urinary tract infection. Cardiovascular events were defined as acute coronary syndrome, heart failure, and stroke. Heart failure was defined upon admission as a result of new or worsening heart failure with New York Heart Association (NYHA) class II or higher. The follow-up began on the date of enrollment and finished at death from any cause or on September 31, 2016, whichever came first.

### *Statistical Analysis*

Results were expressed as means  $\pm$  standard deviations. Baseline characteristics between each group were compared using the Fisher exact test and the Mann-Whitney  $U$  test as appropriate. Univariate and multivariate Cox proportional hazards models were performed to determine the independent variables for the outcomes. The impact of GNRI at discharge on all-cause mortality, cardiovascular events, and infectious diseases was analyzed using Kaplan–Meier curves and log-rank tests. For the mortality analysis, the patients were censored at the time of death or at the last visit before September 31, 2016. For the event analysis (cardiovascular events or infectious diseases), the patients were censored at the first event

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