Malnutrition in Acute Stroke Patients Stratified by Stroke Severity- A Hospital Based Study

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Abstract

- **Background:** Stroke results in high mortality with tremendous health care burden. Malnutrition is frequently observed in patients after stroke. This study was designed to explore the nutritional status in the acute stage of stroke aiming at exploring factors related to malnutrition after stroke.
- *Methods:* This was a hospital based, prospective, observational study recruiting cerebrovascular diseases patients hospitalized for acute management. Patients suffered from all kinds of cerebrovascular diseases hospitalized for management within 30 days after onset were consecutively recruited in the study hospitals. Stroke severity was evaluated by National Institutes of Health Stroke Scale, functional status by Barthel index, and global outcome by modified Rankin Scale. Cognitive function was evaluated by Mini-Mental State Examination. Nutritional status was assessed by Mini Nutritional Assessment (MNA), stratified by 1) adequate nutritional status, $MNA \ge 24$; 2) protein-calorie malnutrition, MNA < 17; 3) at risk of malnutrition, MNA between 17 and 23.5.
- *Results:* There were 231 cerebral infarction patients recruited at 13.5 days (25-75%: 5.0-17.0) after stroke onset with mild stroke severity 71.4% and severe 10.4% with nasogastric tube insertion in 14%. Malnutrition was identified in 12.1% with 54.1% at risk of malnutrition. Factor related to malnutrition was severe stroke severity with dependency. Patients with old age, hypertension, and diabetes mellitus tended to have malnutrition or risk of malnutrition.
- *Conclusion:* Nutritional status was poor in stroke patients across all stroke severities within weeks. Further longitudinal outcome studies to identify the poor outcome and the evolution of nutritional status are warranted.
- *Keywords:* Malnutrition/*complications; Prospective Studies; Stroke/*complications/*therapy; Treatment Outcome

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INTRODUCTION

Stroke results in high mortality rate with tremendous health care $burden^{(1,2)}$. One third of stroke survivors have partially to totally dependent activity of daily living⁽³⁾. Neurological deficits, such as dysphagia, have impact on the nutritional status with difficulties in adequate oral intake. Malnutrition is frequently observed in patients during the acute and rehabilitation phases of stroke associated with poor outcomes⁽⁴⁾. The prevalence of malnutrition after stroke varies widely among published reports⁽⁵⁾. Undernutrition was observed in the acute stage of stroke. Baseline undernutrition was reported to predict complications after stroke and 1-week undernutrition was reported to predict poor 3-month outcomes⁽⁴⁾. Also, the nutritional status might be at risk of deterioration rapidly within first few weeks after stroke⁽⁶⁾. Hence, nutritional evaluation at acute hospitalization and early recognition of patients at risk of malnutrition might be important for acute management⁽⁷⁻⁹⁾.

Causes of readmission and adverse events after stroke are from recurrent vascular diseases and infections^(10,11). There have been extensive studies investigated readmissions⁽¹²⁻¹⁴⁾ or mortality ⁽¹⁵⁻¹⁸⁾ after stroke. Further investigation and exploration of the nutritional status after stroke will spotlight better strategies for stroke management, and help to delineate the utilization patterns likely to change over time and in response to healthcare reform^(3,12-14,19-24).

Therefore, this study was designed to explore the nutritional status and related factors in the acute stage of stroke in a medical center in Taiwan, especially stratified by stroke severity.

METHODS

This was a hospital based, prospective, observational study recruiting cerebrovascular diseases patients hospitalized for acute management. This study was conducted in Department of Neurology of Chang Gung Memorial Hospital, Taiwan. The study protocols were approved by internal review board of the study hospitals (IRB 98-2700B, 99-2543C, 102-0355C) and granted by the study hospital.

Patients suffered from all kinds of cerebrovascular

diseases hospitalized for management within 30 days after onset were consecutively recruited in the study hospitals. All patients were screened by board certificated neurologists. Informed consent was obtained before study. Eligible patients were screened and surveyed during acute hospitalization or within 30 days after the stroke onset.

All variables of interests were pre-specified and obtained from interview of the patients or their family members using a structured questionnaire and chart review. Demographic data, including patient's age, gender, education, primary caregivers, and occupation, was collected.

Comorbidities were prespecified and collected from interview or chart review. Stroke severity was evaluated by National Institutes of Health Stroke Scale (NIHSS) (0-38, normal = 0), functional status by Barthel index (BI) (0-100, normal = 100), global outcome by modified Rankin Scale (mRS) (0-6, normal = 0). Cognitive function was evaluated by Mini-Mental State Examination (MMSE) (0-30, normal = 30).

Nutritional status was assessed by Mini Nutritional Assessment (MNA) (0-30, normal = 30)⁽²⁵⁾. It is an integrated and easily available method for evaluation of nutritional status, used to screen the elderly with risk of malnutrition. The MNA is composed of 18 items, including anthropometric measurements, a global assessment, a dietary questionnaire, and a subjective assessment with sensitivity 96%, specificity 98%, predictive value 97%, and reliability/validity more than 95%. The assessment is applicable to a variety of situation and only needs 10-15 minutes to accomplish evaluation; as a result, it was used to quickly screen the patients with malnutrition in order to give early nutritional supplement^(26, 27). The sum of the MNA score distinguishes between elderly patients with: 1) adequate nutritional status, $MNA \ge 24$; 2) protein-calorie malnutrition, MNA < 17; 3) at risk of malnutrition, MNA between 17 and 23.5^(25,28-30).

Laboratory test was advised but not mandatory in this study, including albumin (3.5-5.0 gm/deci-liter) and preablbumin 20-40 milligram/deci-liter)⁽³¹⁾. The blood urea nitrogen (BUN) and creatinine (Cr) were obtained within seven days of stroke onset. The BUN/Cr ratio ≥ 20 is one of the common laboratory tests that is typically indicative of pre-renal azotemia and dehydration status. Recent studies reported that an elevated BUN/Cr ratio in acute

stroke patients is associated with poor outcome at 30 days, and BUN/Cr ratio higher than 15 may be a novel predictor of stroke-in-evolution^(32,33).

All kinds of outcome events with rehospitalization or serious events assessed by investigators were recorded.

All analyses would be performed by SPSS 22 (IBM Corp. Released 2013. IBM SPSS Statistics for Windows, Version 22.0. Armonk, NY: IBM Corp.). For comparison of outcomes, patients were classified as favorable or poor outcomes. Pearson Chi Square test and one-way ANOVA were used for comparison of mean. Finally, multinomial logistic regression was used for adjusting the confounding factors. A probability value of P< 0.05 was considered significant.

RESULTS

As an investigator initiated study, due to restrain from

 Table 1. Characteristics of patient (n=231)

the funding, the study period was from April 2010 till April 2014.

There were 231 cerebral infarction patients recruited at 13.5 days (25-75%: 5.0-17.0) after stroke onset. The mean age at stroke onset was 64.3 ± 11.1 years and 62.3%male. Hypertension was documented in 64.8%, diabetes in 46.5% and hyperlipidemia in 41.9% with mean Body Mass Index (BMI) 25.2 ± 3.7 (25-75%: 22.8-27.3). Obesity defined as BMI>27 was recognized in 31.9% patients. There were 71.4% mild stroke patients and 10.4% severe stroke patients with nasogastric tube insertion in 14%patients. (Table 1)

During the initial evaluation at acute hospitalization, according to MNA, malnutrition was identified in 12.1% of study patients and 54.1% at risk of malnutrition (Table 2). Factor related to the risk of malnutrition was severe stroke severity with dependency defined as mRS more than two (p<0.001). Patients with old age, hypertension,

Characteristics	Ν	(%)	Median	(25-75%)
Age	64.3	±11.1	64.0	(57.0-73.0)
≥65	115	(49.8)		
Sex				
Male	144	(62.3)		
History				
Hypertension	150	(64.8)		
Diabetes mellitus	107	(46.5)		
Hyperlipidemia	97	(41.9)		
NG	32	(14.0)		
NIHSS	5.8	±7.5	3.0	(1.0-8.0)
Mild (0-6)	165	(71.4)		
Moderate (7-15)	42	(18.2)		
Severe (16-38)	24	(10.4)		
BI	62.4	±38.6	70.0	(30-100)
Mild (95-100)	104	(45.0)		
Moderate (65-90)	25	(10.8)		
Severe (0-60)	102	(44.2)		
mRS				
0	11	(4.8)		
1	78	(33.8)		
2	25	(10.8)		
3	22	(9.5)		
4	70	(30.3)		
5	25	(10.8)		
BMI				
≤20	14	(7.3)	19.4	(18.3-19.9)
20-24	69	(36.0)	22.5	(21.2-23.4)
24-27	60	(31.2)	25.5	(24.7-26.4)
≥27	49	(25.5)	29.2	(27.7-31.6)
MMSE	22.0	±8.5	25.0	(17.0-28.0)

NG: naso-gastric tube, NIHSS: National Institutes of Health Stroke Scale, BI: Barthel index, mRS: modified Rankin Scale, BMI: body mass index, MMSE: Mini-Mental State Examination

		Good nutrition	Risk of malnutrition	Malnutrition	
	Total	$(MNA \ge 24)$	$(17 \le MNA < 23.5)$	(MNA<17)	Р
		N=78 (33.8%)	N=125 (54.1%)	N=28 (12.1%)	
Age, yrs	64.3 ± 11.1	62.6 ± 11.3	64.7 ± 11.0	66.9 ± 11.3	.180
≥65	115 (49.8)	34 (43.6)	63 (50.4)	18 (64.3)	.168
Sex, male	144 (62.3)	51 (65.4)	77 (61.6)	16 (57.1)	.719
History					
Hypertension	147 (64.8)	43 (56.6)	82 (66.7)	22 (78.6)	.092
Diabetes mellitus	105 (46.5)	28 (36.8)	62 (50.8)	15 (53.6)	.115
Hyperlipidemia	95 (41.9)	37 (48.7)	49 (39.8)	9 (32.1)	.253
NG	31 (14.0)	6 (8.0)	14 (11.8)	11 (40.7)	.001
NIHSS	5.8 ± 7.5	2.8 ± 4.3	5.8 ± 7.0	14.1 ± 9.9	<.001
Mild (0-6)		68 (87.2)	90 (72.0)	7 (25.0)	<.001
Moderate (7-15)		8 (10.3)	25 (20.0)	9 (32.1)	
Severe (16-38)		2 (2.6)	10 (8.0)	12 (42.9)	
BI	62.4 ± 38.6	84.2 ± 26.0	59.7 ± 37.0	13.3 ± 24.3	<.001
Mild (95-100)		56 (71.8)	47 (37.6)	1 (3.6)	<.001
Moderate (65-90)		7 (9.0)	17 (13.6)	1 (3.6)	
Severe (0-60)		15 (19.2)	61 (48.8)	26 (92.9)	
mRS					<.001
0	11 (4.8)	7 (9.0)	4 (3.2)	0 (0)	
1	78 (33.8)	35 (44.9)	43 (34.4)	0 (0)	
2	25 (10.8)	13 (16.7)	12 (9.6)	0 (0)	
3	22 (9.5)	8 (10.3)	12 (9.6)	2 (7.1)	
4	70 (30.3)	11 (14.1)	47 (37.6)	12 (42.9)	
5	25 (10.8)	4 (5.1)	7 (5.6)	14 (50.0)	
Measurement					
BMI	25.2 ± 3.7	26.7 3.7	24.7 ± 3.6	23.5 ± 2.8	<.001
Waist	90.5 ± 12.3	92.9 ± 11.8	89.4 ± 13.0	89.1 ± 9.4	.129
Hip	96.9 ± 9.9	99.2 ± 9.1	96.2 ± 10.3	93.5 ± 9.3	.022
TSF	18.2 ± 11.2	19.6 ± 10.0	18.7 ± 11.8	12.4 ± 9.6	.015
MAC	28.7 ± 3.5	30.1 ± 3.2	28.1 ± 3.4	27.4 ± 3.3	<.001
Laboratory test					
ALB	4.0 ± 1.0	4.3 ± 1.5	3.9 ± 0.5	3.5 ± 0.5	.001
Abnormal		9 (11.8)	21 (18.1)	10 (40.0)	.007
PAB	26.3 ± 7.6	27.3 ± 7.5	26.5 ± 7.6	22.1 ± 6.8	.017
Abnormal		17 (23.6)	22 (19.8)	8 (36.4)	.238
BUN	17.0 ± 18.0	17.7 ± 26.5	14.9 ± 8.2	22.7 ± 23.1	
Cr	1.0 ± 0.7	0.9 ± 0.3	1.0 ± 0.6	1.3 ± 1.4	

Table 2. Characteristics of patients categorized by MNA

MNA: Mini Nutritional Assessment, NG: naso-gastric tube, NIHSS: National Institutes of Health Stroke Scale, BI: Barthel index, mRS: modified Rankin Scale, BMI: body mass index, TSF: triceps skinfold, MAC: mid-arm circumference, ALB: albumin, PAB: prealbumin, BUN: blood urea nitrogen, Cr: creatinine

and diabetes mellitus tended to have malnutrition or risk of malnutrition, but these factors did not reach statistical significance (Table 3, 4).

The average albumin and prealbumin level was 4.0 ± 1.0 g/L and 26.3 ± 7.6 g/dL with abnormal in 18.4% and 22.9%, respectively. Mean albumin and prealbumin was 3.5 ± 0.5 and 3.9 ± 0.5 at risk of malnutrition and 40.0%

and 36.4% malnutrition patients (p= .007, p= .238), respectively.

The BUN/Cr ratio higher than 15 was identified in 59.8% of acute stroke patients. Sixty-nine percent of patients with dysphagia (with nasogastric tube placement) had poor hydration, which was noted in 57% of patients without dysphagia (p=.274, OR=1.67, 95% CI 0.66-4.19).

Measurement	MNA	BMI	Waist	Hip	TSF	MAC	ALB	PAB
NIHSS								
Mild (0-6)	22.6 ±3.3	25.6 ± 3.8	90.9 ±11.3	96.8 ±9.7	17.8 ± 10.9	29.1 ±3.5	4.1 ±1.1	27.2 ± 7.6
Moderate (7-15)	19.6 ±4.1	24.7 ±3.3	91.3 ±9.1	97.1 ±10.3	19.4 ± 12.0	27.8 ±3.2	3.7 ±0.4	25.0 ± 6.9
Severe (16-38)	17.2 ±5.1	23.9 ± 3.2	86.7 ±20.9	97.4 ±11.2	18.7 ±11.5	27.5 ± 3.6	3.6 ±0.6	22.5 ± 7.4
Р	< .001	.079	.289	.968	.720	.024	.012	.020
BI								
Mild (95-100)	23.8 ±2.8	25.5 ± 4.0	90.0 ±11.5	95.9 ±9.6	14.2 ± 7.5	28.9 ± 3.4	4.3 ±1.4	29.1 ±6.9
Moderate (65-90)	21.5 ±2.9	25.3 ±3.5	89.4 ±9.5	96.7 ±7.2	25.5 ± 12.1	30.0 ±3.9	3.9 ± 0.5	27.2 ± 5.9
Severe (0-60)	19.2 ±4.1	24.9 ± 3.5	91.3 ±13.6	98.0 ± 10.7	20.5 ± 12.5	28.3 ± 3.4	3.7 ±0.4	23.2 ± 7.5
Р	< .001	.456	.679	.316	< .001	.080	< .001	< .001
mRS								
0	23.3 ±3.3	25.5 ± 4.9	88.6 ±12.5	96.8 ±12.7	15.8 ±9.3	29.4 ± 2.6	4.1 ±0.4	29.4 ±6.1
1	23.4 ±2.7	25.4 ±3.9	89.3 ±11.7	94.4 ±8.8	13.6 ±7.3	28.5 ± 3.7	4.4 ±1.6	29.4 ± 7.6
2	23.9 ±2.9	25.4 ± 4.0	92.6 ±11.1	98.9 ± 10.9	18.0 ± 10.3	29.3 ±3.1	4.0 ±0.5	28.2 ± 5.5
3	21.6 ±3.5	26.2 ± 3.6	87.2 ±19.2	100.5 ± 7.8	26.8 ± 12.5	30.7 ±3.2	3.9 ± 0.5	23.5 ± 6.7
4	19.7 ±3.6	25.0 ± 3.5	91.9 ± 10.2	97.3 ±9.0	21.2 ± 12.5	28.5 ± 3.4	3.7 ± 0.4	24.7 ±7.4
5	17.5 ±5.5	24.0 ± 3.0	92.0 ± 13.0	98.8 ±13.4	18.7 ±11.6	27.3 ±3.3	3.6 ±0.4	20.2 ± 6.4
Р	< .000	.463	.518	.103	< .000	.042	.002	< .000

Table 3. Correlation of stroke severity to BMI, MNA, Prealbumin and Albumin

NIHSS: National Institutes of Health Stroke Scale, BI: Barthel index, mRS: modified Rankin Scale, MNA: Mini Nutritional Assessment, BMI: body mass index, TSF: triceps skinfold, MAC: mid-arm circumference, ALB: albumin, PAB: prealbumin

Table 4. Correlation between variables in patients in baseline

	MNA	BMI	Waist	Hip	TSF	MAC	ALB	PAB
MNA	1	0.268**	0.103	0.161*	0.163*	0.255**	0.235**	0.219**
BMI		1	0.569**	0.660**	0.271**	0.715**	0.120	0.081
Waist			1	0.616**	0.070	0.383**	0.016	-0.049
Hip				1	0.325**	0.573**	0.101	-0.064
TSF					1	0.378**	-0.089	-0.135
MAC						1	0.201**	0.099
ALB							1	0.324**
PAB								1

MNA: Mini Nutritional Assessment, BMI: body mass index, TSF: triceps skinfold, MAC: mid-arm circumference, ALB: albumin, PAB: prealbumin

By using the multinomial logistic regression with age, hypertension, and diabetes mellitus controlled, as compared to patients with good nutrition, patients with malnutrition and at risk of malnutrition tended to have mRS>2 with p <0.001 and p=0.001, respectively.

DISCUSSION

Within 30 days (25-75%: 5.0-17.0) after stroke onset, there were 12.1% and 54.1% patients in our study suffered from malnutrition and at risk of malnutrition, respectively. Patients suffered from severe stroke severity with dependency tended to have poor nutrition. Patients with old age, hypertension, and diabetes mellitus tended to have risk of malnutrition.

The high incidence of malnutrition in severe stroke patients was as expected. However, 21.4% in moderate stroke severity patients suffered from malnutrition was an unexpected finding. In our study, among mild and moderate stroke severity patients, there were 54.5% and 59.5% patients at risk of malnutrition, respectively. The high incidence of patients at risk of malnutrition justified the follow up of our patients for further adverse events.

Nutrition is an important issue but lack of effective intervention in stroke management. There is no universally accepted definition of malnutrition or a gold standard for nutritional status assessment. The use of a wide assortment of nutritional assessment tools may have contributed to the wide range of estimates of malnutrition. In addition to the MNA, some markers may have relations to the patient's nutritional status, such as serum levels of albumin, prealbumin, and transferrin.⁽³⁴⁾ Albumin has a relatively long half-life, approximately 14–20 days, and has been thought as a marker of chronic nutritional status. Prealbumin, also known as transthyretin, and transferrin both have shorter half-life (2–3 days and 8–10 days, respectively), and may reflect patient's nutritional status more rapidly.⁽³¹⁾ However, these factors are affected by many non–nutrition factors, such as the coexisted inflammation or infection which were frequently encountered in stroke patients with dysphagia or comorbidities. As a result, findings of our study need to be justified with caution.

In our study, the MNA was used to assess the patient's nutritional status. At admission, 12.1% of the included patients were malnourished, 54.1% of the patients were at risk of malnutrition, and 33.8% of the patients were well nourished. The frequency of malnutrition falls within the range of 6.1% to 62% from one systematic review of 18 studies⁽³¹⁾. The variation of rate of malnutrition from studies may attribute to the different nutritional assessment methods and the definitions of malnutrition, differences in the timing of assessment, comorbid medical conditions, and stroke severity.

Concerning the BMI, there is no clear definition on BMI criteria for malnutrition among the elderly. The cutoff points of BMI less than 18.5 Kg/m² or 20 Kg/m² and weight loss more than 5% during the last 1-6 months are suggested to identify the patients with malnutrition, and BMI of less than 24 Kg/m² for the elderly patients with risk of malnutrition^(35,36). In our study, the mean BMI was 23.5, 24.7, 26.7 Kg/m² among patients identified as malnutrition, with risk of malnutrition and well-nourished, respectively.

Preexisting malnutrition is common in the hospitalized patients, however, the exact prevalence of preexisting malnutrition in stroke patients is currently uncertain. Many clinical conditions are associated with increased risk of malnutrition, such as the presence of comorbidities, polypharmacy, impaired functional status of daily living, or feeding difficulties. The elderly patients are particularly influenced. Diabetes mellitus and a history of stroke increased the risk for malnutrition on admission by 58 and 71%, respectively⁽³⁷⁾. In our study, BMI less than 20 was identified in 7.3% patients, hypoalbumin 17.3% and hypoprealbumin 20.3%. These patients might be at malnutrition before stroke. There was no uniformly accepted cut-off value of prealbumin that was regarded as abnormal or malnourished, the value of 15 or 17 mg/dL could also be accepted^(31,38). Six percent of our patients had prealbumin level less than 15 mg/dL, if this data could be more exact to reflex baseline malnutrition status might need clinical correlation.

Recent studies reported that an elevated BUN/Cr ratio in acute stroke patients may play an important role in poor outcome at 30 days and stroke-in-evolution, and the ratio was significantly greater in patients with dysphagia than in those without⁽³¹⁻³³⁾. The BUN/Cr ratio higher than 15 was identified in 59.8% of acute stroke patients, which was similar to one previous study $(53\%)^{(31)}$. The patients with dysphagia had poorer hydration status overall; however, which did not differ significantly from that observed in patients without dysphagia. Because second test of BUN or Cr at discharge was not designed in our study, the comparison of the change of BUN/Cr ratio at admission and discharge was not available.

By using the multinomial logistic regression, patients with malnutrition tended to have higher incidence of mRS>2. The association of malnutrition with stroke severity was so evident that no malnutrition was found in patients with mRS 0-2. This might be happened by chance with small sample size and might be from the limitation of the assessment tool; however, the poor nutrition in severe stroke patients might be supported partly from our results. The positive association of stroke severity and malnutrition might be as expected as part of the items of MNA and might be impacted directly by the neurological deficits resulted from stroke. Our finding might be suggestive of the impact of stroke in the malnutrition in acute stage of stroke irrespective to the baseline nutritional status.

Our study had the limitation which might be attributed to the method used for nutritional assessment. There is no universally accepted definition of malnutrition or a gold standard for nutritional status assessment. We used MNA as the major method to assess the nutritional status of patients in the acute stage of stroke. Three of 18 items (food intake, weight loss, and psychological stress or acute disease) in the MNA was assessed for the status over the past 3 months, therefore, the result partially reflexed the nutritional status during the past 3 months. We found that the patients with severe stroke severity with dependency tended to have poor nutrition, which did not indicate that malnutrition was the outcome related to the stroke event, instead, this result might remind the clinician of the importance of strategic nutritional support in the poststroke care.

In conclusion, from our study, nutrition status was poor in stroke patients across all stroke severities within weeks. Further longitudinal outcome studies to identify the poor outcome and the evolution of nutritional status are warranted.

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