Original Article

Emerging malnutrition during hospitalisation independently predicts poor 3-month outcomes after acute stroke: data from a Chinese cohort

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Objective: Questions exist regarding the causal relationship between malnutrition and stroke outcomes. This study aimed to determine whether nutritional status changes or malnutrition during hospitalisation could predict 3-month outcomes in acute stroke patients. **Methods**: During a 10-month period, patients who suffered their first stroke within 7 days after stroke onset were included in this prospective multi-centre study. The demographic parameters, stroke risk and severity factors, malnutrition risk factors and dysphagia were recorded. Nutritional status was assessed by 3 anthropometric and 3 biochemical indices. Changes in nutritional status were defined by comparing the admission values with the 2-week values. A Modified Rankin Scale score of 3-6 was defined as a poor outcome at the 3-month follow-up. Univariate and multiple logistic regression analyses were used to investigate the power of nutritional status changes in predicting poor patient outcomes. **Results**: Data from 760 patients were analysed. Poor outcomes were observed in 264 (34.7%) patients. Malnutrition prevalence was 3.8% at admission and 7.5% after 2-weeks in hospital, which could not predict 3-month outcome. Emerging malnutrition was observed in 36 patients (4.7%) during the 2-week hospitalisation period and independently predicted poor 3-month outcomes after adjusting for confounding factors (odds ratio 1.37, 95% confidence interval, 1.03-1.83). **Conclusions**: Emerging malnutrition during hospitalisation independently predicted poor 3-month outcomes in acute stroke patients in this study.

Key Words: malnutrition, deterioration, predict, outcome, acute stroke

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INTRODUCTION

Although different definitions of malnutrition have been used, studies have shown that malnutrition after stroke may affect and be associated with outcomes, including morbidity, length of hospital stay, mortality and functional short-term and long-term disability.[1-9] However, there is still a question regarding the causal relationship between malnutrition and stroke outcomes.[10]

Serial measurements of nutritional status may have identified an even stronger relationship between malnutrition and outcomes.[7] Trending hepatic protein measurements over time are considered to be of more clinical significance than a single measurement.[11] With increased length of hospitalisation, a patient with an adequate nutritional status may become at risk for malnutrition,[12] malnutrition may develop gradually over time,[13] and the prevalence of malnutrition may increase.[14] Braunschweig and colleagues observed that a greater percentage of patients who were normally nourished at admission experienced nutritional status declines during hospitalisation compared with patients who presented with moderate or severe malnourishment at admission.[15] Other studies have also indicated that nutritional status or nutritional indicators gradually decreased during hospitalisation.[1,4-6,16-18] Investigators have shown that declining in-hospital nutritional status was associated with increased hospital charges, long hospital stays and a greater likelihood of complications.[15] However, few studies have assessed the effect of deteriorating nutritional status during hospitalisation on functional stroke outcomes.

This study sought to investigate whether malnutrition or deteriorating nutritional status could independently predict poor 3-month clinical outcomes through the serial measurement of objective nutrition parameters, after adjusting for potential confounding factors.

METHODS

This prospective cohort multi-centre study was performed between March 5, 2007 and January 31, 2008 at eleven teaching hospitals in different parts of China. This project was approved by the multi-centre research ethics committee and the local research committee at each hospital.

Inclusion and exclusion criteria

Patients 18 years or older were consecutively included if they had had their first (ever) stroke within 7 days after onset. Stroke was defined according to the World Health Organization (WHO) criteria.[19] Subarachnoid haemorrhage was excluded. Patients who were discharged or died within 2 weeks after admission, who suffered from hepatic cirrhosis or renal inadequacy and required restricted protein intake, or who had malignant diseases were also excluded. Informed consent was obtained from each patient, a family member, or a legal guardian.

Data collection

The patients' demographic data were documented, including age, gender, education, socio-economic status, medical insurance, and living conditions (e.g., with family or care giver, alone, in a nursing home). Education was divided into two levels: high school or lower or university education or above. A patient's economic situation was indicated as having income or low income. Age was stratified into 3 levels: younger than 50 years old, 51-70 years old, and older than 70 years of age.

Stroke risk factors were also recorded, including hypertension (history of hypertension or hypertensive drug use), dyslipidemia (history of dyslipidemia or lipid-lowering drug use), atrial fibrillation (history of atrial fibrillation confirmed by at least 1 electrocardiogram or the presence of arrhythmia during hospitalisation), coronary heart disease (CHD), diabetes, current or previous smoking, and moderate or heavy alcohol consumption ($\geq$2 standard alcoholic beverages consumed per day). Stroke severity was assessed using the National Institutes of Health Stroke Scale (NIHSS),[20] with a score of >8 being identified as severe stroke.[21] A patient was classified as unconsciousness if he/she was somnolent, lethargic or in a coma.

On admission, data on malnutrition risk factors was collected and included, chronic obstructive pulmonary disease (COPD), stomach or duodenum ulcer, chronic gastritis, inflammatory bowel disease, bowel resection, biliary tract disease, chronic diarrhoea, hyperthyroidism and poor appetite or digestion function. During hospitalisation, complications were prospectively recorded, including fever, pulmonary and/or urinary tract infection, heart failure, and acute myocardial infarction. The use of enteral tube feeding or parenteral nutrition support was also documented.

Nutritional status changes

Nutritional status changes were divided into 4 categories: group 1 (normal), patients had normal nutritional status at admission and at week 2 in the hospital; group 2 (recovered), patients improved from malnourished at admission to normal at week 2 in the hospital; group 3 (deteriorated/emerging malnutrition), a patient's normal nutritional status at admission deteriorated to malnourished at week 2; and group 4 (abnormal), patients were malnourished at admission and at week 2.

Nutritional status was assessed at admission (within 72 hours after admission) and 2 weeks after admission. There were 3 anthropometric indicators (i.e., body mass index [BMI], mid-upper arm circumference [MUAC], and triceps skinfold thickness [TSF]) and 3 biochemical indicators (i.e., albumin, prealbumin, and haemoglobin).[1,3-6,17] Malnutrition was diagnosed when at least one indicator in each group was below the reference interval.[16] The criteria were as follows: BMI <18.5 kg/m^2, MUAC below the tenth percentile of the reference value for Chinese people (males <24.8 cm and females <23.2 cm), TSF below the tenth percentile of the reference value for Chinese people (males <7.47 mm and females <13.8 mm), serum albumin levels <35 g/L low haemoglobin count (males <120 g/L and females <110 g/L), and serum prealbumin levels that were less than each hospital's established criteria.

Body weight was measured using a portable bathroom scale (EB9872, Guangdong, China) for the ambulatory patients. Height was measured using a full-length stadiometer. For the immobile patients, the body weight and height reported by the patients (or their caregivers or next of kin) were recorded, according to the most recent measure before stroke onset. MUAC and TSF were measured with a flexible tape and a skinfold calliper that was accurate to 0.2 mm (Changshu Indicators Ltd., Changshu, China) as described by Davalos.[1] All anthropometric measurements were performed at one hospital by a single observer who was blinded to the objective of this study.

Dysphagia

Patients were evaluated at bedside by a speech-language pathologist or by a physician who was trained in dysphagia. A patient was diagnosed with dysphagia if he/she had two or more abnormal findings in the following areas: history of choking or coughing during eating or drinking, dysphonia or aphonia, drooling, dysarthria, difficulty with voluntary coughing, nasal regurgitation or a failed drinking test. The drinking test consisted of 3 swallows of 1 mL of room temperature water and an additional 3 swallows of 5 mL of water. Patients failed the test if they demonstrated choking, voice changes, delayed initial swallowing or ineffective swallowing. A patient was diagnosed with dysphagia if he/she was lethargic or in a coma.

Follow-up and outcomes

At 3 months after admission, Modified Rankin Scale (MRS) was measured during a telephone follow-up by a team of physicians who were unaware of the study protocol or objectives. Patients with MRS scores of 3-6 were identified as having a poor outcome.[22]

Statistical analysis

Univariate analysis was conducted using chi-squared or Fisher's exact test to investigate the association between possible variables associated with poor 3-month outcomes, such as age, gender, education, socio-economic status, living status, stroke type and severity (as indicated by NIHSS), stroke risk factors, dysphagia, malnutrition at admission and at 2 weeks, changes in nutritional status and malnutrition risk factors. Nutritional status changes were analysed against the poor outcomes using binary regression analysis, with significant confounding factors indicated by the univariate analysis mentioned above. The Wilcoxon test was used to compare the differences in the 6 nutritional status parameters between the admission and 2-week follow-up. The Kruskal-Wallis test was used to test the differences in the 6 nutritional status parameters between the 4 categories of status changes. All significance tests were evaluated at the 0.05 level of significance. Statistical analysis was performed using Statistical Analysis System (SAS), version 10.0.

Sample size determination

In previous studies, the prevalence of malnutrition has been reported as being between 8% and 49%.[1,2-7,15-17,20] We hypothesised that our sample would have a prevalence of 8%. If that estimate was accurate within 2%, and the 95% CI had a width of 4%, the estimated sample would be 757 patients.

RESULTS

A total of 1087 patients were screened, and 760 patients completed the nutritional assessment at admission and at 2 weeks. A total of 63 patients refused to participate in the study. Forty-nine patients had liver disease, tumours or renal diseases that prohibited protein intake. Fourteen patients had swallowing problems or decreased weight before their strokes. A total of 126 patients died or were discharged during the 2-weeks hospitalisation period. Two patients were diagnosed with renal diseases (with limited protein intake). Seventy-three patients were lost to follow-up or refused to participate in the follow-up. The patient distribution is illustrated in the Figure 1. The excluded patients were those with liver or renal diseases or tumour or those who had swallowing problems or decreased weight before stroke onset; the differences between the included and excluded patients are shown in Table 1. Malnutrition increased from 3.8% at admission to 7.5% at 2 weeks. Poor outcomes (MRS score 3-6) at 3 months were observed in 264 (34.7%) patients.

The number of patients in each nutritional status category were as follows: group 1 (normal), 695 patients had normal nutritional status at admission and at week 2; group 2 (recovered), 8 patients improved from malnourished to normal; group 3 (deteriorated/emerging malnutrition), 36 patients deteriorated from normal nutritional statuses to malnourished at week 2; and group 4 (abnormal), 21 patients were malnourished at admission and at week 2. Table 2 depicts the differences between the patients for the 4 nutritional status change categories.

Nutritional indicators changed differently between the 4 groups. In group1, excluding prealbumin, the other 5 nutritional indicators decreased significantly; this result was also observed for all of the patients in our study. Patients in group 2 improved slightly but not significantly for most of the 6 nutritional indicators; in group 3, all 6

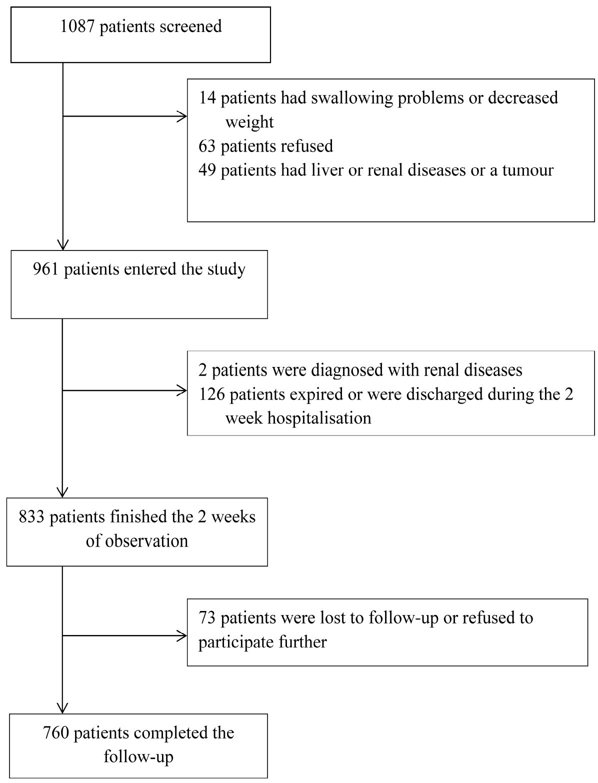

Figure 1. Flow chart of the patients who were included and excluded from this study

Table 1. The differences between the included and excluded patients

Factors	Patients included (% (n/total n))	Patients excluded (% (n/total n))	*p*
Unconsciousness	17.2 (130/756)	26.8 (70/261)	0.001
Intensive care unit	19.1 (145/760)	25.2 (66/262)	0.023
University education or above	17.1 (129/756)	11.5 (30/262)	0.018
Low income	7.3 (56/760)	9.9 (26/262)	<0.001
No insurance	19.7 (149/757)	30.6 (79/258)	0.001
Tube fed	13.3 (101/759)	24.2 (56/232)	<0.001
Infection	18.6 (141/760)	28.4 (65/229)	0.001
Died	1.4 (11/760)	9.5 (25/262)	<0.001
	Median (min-max)	Median (min-max)	
TSF	17.5 (2–52)	14.5 (4–38)	0.002

TSF: triceps skinfold thickness.

Table 2. The differences between the 4 nutritional status change groups

Factors	Changes in nutritional status (% (n/total n))				*p*
	Group 1 (normal)	Group 2 (recovered)	Group 3 (emerging)	Group 4 (abnormal)	
Age (years)					<0.001
<50	19.9 (138/695)	0 (0/8)	8.3 (3/36)	0 (0/21)	
51-70	47.1 (327/695)	50 (4/8)	19.4 (7/36)	23.8 (5/21)	
>70	33.1 (230/695)	50 (4/8)	72.2 (26/36)	76.2 (16/21)	
Female	33.5 (233/695)	25 (2/8)	47.2 (17/36)	66.7 (14/21)	0.005
CHD	20.3 (141/693)	0 (0/8)	41.7 (15/36)	38.1 (8/21)	0.016
COPD	2.3 (16/692)	0 (0/8)	11.1 (4/36)	4.8 (1/21)	0.016
Living alone or in nursing home	3.9 (27/691)	0 (0/8)	19.4 (7/36)	0 (0/21)	<0.001
Unconsciousness	15.4 (107/693)	0 (0/8)	51.4 (18/35)	25 (5/20)	0.000
Visuospatial neglect	5.6 (38/673)	0 (0/7)	23.5 (8/34)	14.3 (3/21)	0.001
Tube fed	11.9 (83/694)	12.5 (1/8)	41.7 (15/36)	9.5 (2/21)	<0.001
Parenteral nutrition	15.4 (107/694)	25 (2/8)	27.8 (10/36)	47.6 (10/21)	<0.001
Infection	16.4 (114/695)	37.5 (3/8)	47.2 (17/36)	33.3 (7/21)	<0.001
Heart failure	1.4 (10/694)	0 (0/8)	8.3 (3/36)	5 (1/20)	0.017
Acute myocardial infarction	0.3 (2/694)	0 (0/8)	0 (0/36)	5 (1/20)	0.011
NIHSS >8 at admission	39.9 (275/690)	37.5 (3/8)	75 (27/36)	52.4 (11/21)	<0.001
Dysphagia at 2 week	19.4 (135/695)	25 (2/8)	61.1 (22/36)	38.1 (8/21)	<0.001

CHD: coronary heart disease; COPD: chronic obstructive pulmonary disease; NIHSS: ational Institutes of Health Stroke Scale.

parameters decreased significantly; and in group 4, only TSF, BMI and haemoglobin decreased significantly.

The factors associated with poor 3-month outcomes following univariate analysis are shown in Table 3. Multiple regression analysis revealed that emerging malnutrition or deteriorated nutritional status could predict poor outcomes after adjusting for the confounding factors (OR 1.37, 95% CI, 1.03-1.83) (see Table 4).

DISCUSSION

The present study aimed to investigate the impact of nutritional status changes, particularly deterioration or emerging malnutrition, on 3-month functional outcomes in acute stroke patients. In four categories of nutritional status changes, emerging malnutrition showed an independently predictive value for poor 3-month outcomes in acute stroke patients; steady abnormal nutritional status throughout the 2-week hospitalisation period did not affect the regression equation. We didn't find malnutrition at admission or at 2-weeks could predict 3-month poor outcome, although malnutrition at 2-weeks was associated with poor outcome. This finding indicates that emerging malnutrition influenced 3-month outcomes more than malnutrition did at baseline,[5] or at any other time during hospitalisation. This study suggests that rather than focusing on patients who are nutritionally compromised at admission, it seems prudent to watch for deteriorating nutritional status during hospitalisation and to prevent nutritional decline.[15] For these patients, nutritional support may be more effective in preventing poor outcomes, although no differences were found in fatality, death or dependency with nutritional supplementation in a previous study.[23]

Older age, severe stroke and dysphagia could predict poor outcome in stroke patients. Unconsciousness is also an indicator of severity of stroke. Enteral tube feeding usually is the treatment of patients with dysphagia or unable to meet their nutritional requirements orally.[14] Table 4 indicated that after adjustment for these factors, emerging malnutrition still could predict 3-month outcome in this study, and parenteral nutrition support could improve the outcome of patients.

This study demonstrated the deterioration of nutritional status during a 2-week hospitalisation period. The prevalence of malnutrition increased from 3.8% at admission to 7.5% after 2-weeks in hospital. Nutritional indicators worsened to a certain extent. Previous studies have demon-strated the deterioration of nutritional status,[1,5,17] or of nutritional parameters,[4,6,16,18] during the hospitalisation of stroke patients. However, not all patients were under

Table 3. The factors associated with poor 3-month outcomes

Factors	3-month outcome (n)		OR	95% CI		*p*
	Good	Poor		Lower	Upper	
Age (years)			2.47	1.59	3.82	<0.001
≤50	102	39				
51-70	252	91				
≥71	142	134				
Gender			1.81	1.33	2.46	<0.001
Male	346	48				
Female	50	116				
Education			0.626	0.410	0.957	0.018
High school level or below	399	228				
University or above	95	34				
Atrial fibrillation			2.22	1.36	3.64	0.001
Yes	34	37				
No	451	221				
Smoking			0.628	0.458	0.860	0.004
Yes	222	89				
No	252	161				
Stroke type			1.52	1.13	2.22	0.008
Ischemic	389	184				
Haemorrhage	107	80				
Consciousness			6.44	4.25	9.77	<0.001
Alert	455	171				
Unconsciousness	38	92				
NIHSS at admission			9.22	6.54	13.0	<0.001
≤8	372	67				
>8	120	196				
NIHSS at 2-week			15.1	0.389	22.1	<0.001
≤8	429	86				
>8	58	176				
Dysphagia at admission			3.24	2.37	4.43	<0.001
Yes	362	120				
No	134	144				
Dysphagia at 2-week			5.50	3.80	7.96	<0.001
Yes	439	154				
No	57	110				
Changes in nutritional status			5.43	2.58	11.5	<0.001
Normal	470	225				
Recovered	10	11				
Emerging malnutrition	10	26				
Abnormal	6	2				
Malnutrition at 2-week			3.88	2.20	6.84	<0.001
Yes	476	227				
No	20	37				
Fever (yes/no)			4.16	2.91	5.95	<0.001
Yes	431	163				
No	65	99				
Infection			3.59	2.46	5.25	<0.001
Yes	439	180				
No	57	84				
Acute myocardial infarction			1.01	0.999	1.03	0.042
Yes	494	261				
No	0	3				
Enteral tube fed			7.21	4.48	11.6	<0.001
Yes	470	188				
No	26	75				
Parenteral nutrition			2.59	1.76	3.80	<0.001
Yes	436	194				
No	60	69				

NIHSS: National Institutes of Health Stroke Scale.

observation throughout these studies because patients were discharged gradually during the study periods. Furthermore, these studies did not investigate the impact of changes in nutritional status on outcomes. In a previous study, the authors also indicated that declines in nutritional status had affected outcomes. However, the subjects in their study were acute-care patients with possible heterogeneity in the disease categories and were diag- nosed malnutrition with subjective global assessment (SGA).[15]

The patients with emerging malnutrition were older, with more severe strokes and poor living conditions, and were more likely to be female compared with the patients

Table 4. The predictive factors for poor 3-month outcomes

Variables	OR	95% CI		*p*
		Lower	Upper	
Age ≥71years	1.70	1.31	2.21	0.000
NIHSS >8 at admission	6.77	4.55	10.1	0.000
Unconsciousness	2.63	1.51	4.57	0.001
Emerging malnutrition	1.37	1.03	1.83	0.031
Enteral tube fed	2.39	1.31	4.35	0.004
Parenteral nutrition	0.53	0.30	0.91	0.022

NIHSS: National Institutes of Health Stroke Scale.

in the other categories. Unfortunately, the swallowing and neurological functions of these patients with emerging malnutrition deteriorated during the 2 weeks in hospital (see Table 2), and they required more enteral tube feeding, although their swallowing function at admission did not differ from that of the patients in the other categories. These patients also had higher prevalences of COPD and CHD. Some of these factors above mentioned may be the risk factors of emerging malnutrition. As the risk factors of poor outcomes, older age and severe stroke (NIHSS >8) did not affect the predictive value of emerging malnutrition. Paying attention to and treating these factors may protect patients from newly emerging malnutrition. There was no difference in education, socio-economic status, or type of stroke between the nutritional status change categories.[14]

Our study had some limitations. First, albumin and prealbumin were used in this study to diagnose malnutrition, but they were not recommended as biomarkers for diagnosing malnutrition in the guidelines proposed by the Academy of Nutrition and Dietetics (Academy) and the American Society for Parenteral and Enteral Nutrition (ASPEN).[13] However, the proposed approach is a work in progress, and it requires validation before being used in routine clinical practice.[13] There is no universally accepted definition or gold standard for malnutrition, particularly for stroke patients.[11-13] This study excluded patients with liver, kidney and malignant diseases, which could have reduced the effects on the biomarkers. Subcutaneous fat and muscle mass and weight loss have long been used as biomarkers for malnutrition and are recommended by the Academy and the ASPEN.[13] This study selected at least one of these 3 anthropometry indicators to diagnose malnutrition in each patient, which may be one reason why the frequency of malnutrition in our study was relatively low compared with previous studies.[1,2-7,17,18,24] Second, for immobile patients, we did not obtain precise weight and height using tools such as the bed scale and the stadiometer. However, estimated BMI could be a useful tool for screening for malnutrition.[25] Third, this study may have excluded more severe patients who stayed in the hospital for <2 weeks or rejected study or follow-up participating. This exclusion may be one reason why the prevalence was lower than that in other studies. Fourth, our study was performed in east China. Considering our patients' specific cultures, dietary habits, and economic conditions, generalising our results to other populations should be carefully considered.

In conclusion, emerging malnutrition during hospitalisation independently predicted poor 3-month outcomes in acute stroke patients in this study. Closely monitoring nutritional status, particularly that of patients who are prone to malnutrition, may be important in improving patient outcomes.

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AUTHOR DISCLOSURES

No conflicts of interest were declared.

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Original Article

Emerging malnutrition during hospitalisation independently predicts poor 3-month outcomes after acute stroke: data from a Chinese cohort

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急性脑卒中患者住院期间新出现的营养不良独立预测3个月后的不良结局：来自一个中国人队列的数据

目的：营养不良和脑卒中结局之间的因果关系仍然存在疑问。本研究的目的是确定住院期间营养状态的变化或者营养不良能否预测急性脑卒中患者3个月后的结局。**方法：**在10个月期间，首次卒中7天内的患者纳入该前瞻性多中心研究。记录人口统计学参数、脑卒中危险因素和严重程度、营养不良的危险因素及是否有吞咽障碍。营养状态由3个人体测量学指标和3个生化指标来评估。营养状态的变化是对比入院时和住院2周时的6个指标的变化。3个月随访时改良的Rankin评分3-6分者认为是不良结局。单因素和多因素Logistic回归分析用于检测营养状态的变化对不良结局预测的力度。**结果：**共有760例患者的数据纳入分析，其中存在不良结局的有264（34.7%）例。入院时营养不良的患病率是3.8%，住院2周时是7.5%，而这均不能预测3个月后的结局。住院2周内新出现营养不良的患者有36例（4.7%），在纠正了混杂因素后仍可独立预测3个月后的结局（OR：1.37；95% CI：1.03-1.83）。**结论：**本研究中急性卒中患者住院期间新出现的营养不良可以独立预测3个月后的不良结局。

关键词：营养不良、恶化、预测、结局、急性卒中