



Trabajo Original

Epidemiología y dietética

Correlation between dysphagia and serum albumin levels and prognosis: a retrospective study

Correlación entre la disfagia y los niveles de albúmina sérica y el pronóstico: un estudio retrospectivo

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Abstract

Introduction: dysphagia is a common complication of stroke, and serum albumin is widely recognized as a strong prognostic marker of health and/or disease status. However, the correlation between dysphagia and serum albumin levels has not been established.

Objectives: to observe the correlation between dysphagia and serum albumin levels and prognosis in patients with stroke.

Methods: we performed a retrospective study of patients hospitalized between June 1, 2018, and June 1, 2022. A total of 1,370 patients were enrolled. The patients were divided into two groups: dysphagia and non-dysphagia. Binary logistic regression and multiple linear regression models were used to analyze the correlation between dysphagia, albumin, modified Rankin Scale (mRS), activities of daily living (ADL), and length of hospital stay (LOS).

Results: after adjusting for confounding factors, the risk of pneumonia in the dysphagia group was 2.417 times higher than that in the non-dysphagia group (OR = 2.417, 95 % CI: 1.902-3.072, $p = 0.000$). The risk of mRS ≥ 3 and modified Barthel index (MBI) < 60 in patients with dysphagia was 3.272-fold (OR = 3.272, 95 % CI: 2.508-4.269, $p < 0.001$) and 1.670-fold (OR = 1.670, 95 % CI: 1.230-2.268, $p < 0.001$), respectively; and the risk of hypoproteinemia was 2.533 times higher (OR = 2.533, 95 % CI: 1.879-3.414, $p = 0.000$). Stepwise linear regression showed that dysphagia was significantly correlated with lower albumin levels and higher mRS, lower ADL, and longer LOS in patients with stroke ($\beta = -0.220$, $\beta = 0.265$, $\beta = -0.210$, and $\beta = 0.147$, respectively; $p < 0.001$).

Conclusions: dysphagia in patients with stroke is associated with decreased albumin levels and has an impact on its prognosis.

Keywords:

Dysphagia. Stroke. Serum albumin. Prognosis.

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Ethics statement: because the study was retrospective in design and the extracted data did not involve patient privacy or sensitive information, the requirement for informed consent was waived.

Data sharing statement: the datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

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Resumen

Introducción: la disfagia es una complicación común del accidente cerebrovascular, y la albúmina sérica es ampliamente reconocida como un fuerte marcador pronóstico del estado de salud y/o enfermedad. Sin embargo, no se ha establecido la correlación entre la disfagia y los niveles de albúmina sérica.

Objetivos: observar la correlación entre la disfagia y los niveles de albúmina sérica y el pronóstico en pacientes con accidente cerebrovascular.

Métodos: realizamos un estudio retrospectivo de pacientes hospitalizados entre el 1 de junio de 2018 y el 1 de junio de 2022. Se inscribieron un total de 1.370 pacientes, los cuales fueron divididos en dos grupos: con disfagia y sin disfagia. Se utilizaron modelos de regresión logística binaria y de regresión lineal múltiple para analizar la correlación entre la disfagia, la albúmina, la escala de Rankin modificada (ERM), las actividades de la vida diaria (AVD) y el tiempo de estancia hospitalaria (TEH).

Resultados: después de ajustar por factores de confusión, el riesgo de neumonía en el grupo de disfagia fue 2,417 veces mayor que en el grupo sin disfagia (OR = 2,417, IC 95 %: 1,902-3,072, $p = 0,000$). El riesgo de ERM ≥ 3 y el índice de Barthel modificado (MBI) < 60 en pacientes con disfagia se multiplicó por 3,272 veces (OR = 3,272, IC 95 %: 2,508-4,269, $p < 0,001$) y 1,670 veces (OR = 1,670, IC 95 %: 1,230-2,268, $p < 0,001$), respectivamente; el riesgo de hipoproteinemia fue 2,533 veces mayor (OR = 2,533, IC 95 %: 1,879-3,414, $p = 0,000$). La regresión lineal por pasos mostró que la disfagia se correlacionó significativamente con niveles más bajos de albúmina y ERM más altos, AVD más bajos y TEH más prolongados en pacientes con accidente cerebrovascular ($\beta = -0,220$, $\beta = 0,265$, $\beta = -0,210$ y $\beta = 0,147$, respectivamente; $p < 0,001$).

Conclusiones: la disfagia en pacientes con accidente cerebrovascular se asocia a una disminución de los niveles de albúmina y repercute en su pronóstico.

Palabras clave:

Disfagia. Accidente cerebrovascular. Albúmina sérica. Pronóstico.

INTRODUCTION

Stroke is currently the second leading cause of human death, and motor dysfunction after stroke is the third leading cause of disability. Stroke affects approximately 25 % of the world's population, and patients often suffer from limb dysfunction, cognitive impairment, aphasia, sensory dysfunction, dysphagia, and other complications (1). The prevalence of dysphagia in stroke patients is approximately 8.1-80 % (2). Dysphagia often leads to serious complications. Studies have found that stroke patients with dysphagia have a 4- to 13-fold increased risk of death during hospitalization (2,3). Low serum albumin level is often considered as a marker of malnutrition. Low albumin is also strongly associated with adverse outcomes and death, and is widely recognized as a strong prognostic marker for health and/or disease states (4-6). The correlation between dysphagia and serum albumin levels has not been reported. Understanding the prognostic factors affecting stroke is of great significance for determining the rehabilitation goals of patients with stroke and formulating the best treatment plan. Therefore, we aimed to conduct a retrospective analysis of 1,370 patients with stroke and explore the complex relationship between dysphagia, serum albumin levels, and prognosis during hospitalization.

MATERIAL AND METHODS

RESEARCH OBJECTIVE AND DESIGN

Our study was designed retrospectively and included stroke patients diagnosed at the Rehabilitation Department of Weifang People's Hospital, Affiliated Hospital of Weifang Medical University, and Weifang Brain Hospital from June 1, 2018, to June 1, 2022. All patients met the diagnostic criteria of the "Chinese Guidelines for Diagnosis and Treatment of Acute Ischemic stroke 2018" (7). Patients were diagnosed with stroke using computed tomography (CT) or magnetic resonance imaging (MRI), with International Classification of Diseases codes I69 or I63. The in-

clusion criteria were as follows: no history of dysphagia or health conditions affecting swallowing and stable vital signs. Patients with a history of transient ischemic attack and subarachnoid hemorrhage were excluded because the hemorrhage in the subarachnoid space did not result in parenchymal hemorrhage. Patients hospitalized for > 180 days and those with missing data were excluded.

RESEARCH METHOD

Data collection was conducted by five researchers who underwent unified training and pre-collection. The hospital database was searched to obtain baseline patient data, including age, sex, type of health insurance (basic medical insurance for urban residents, urban employee basic medical insurance, or self-paying), type of stroke (supratentorial, infratentorial, or supratentorial + infratentorial), site of lesion, and Charlson Comorbidity Index (CCI). The CCI is a comorbidity scoring system based on the number and severity of diseases in patients that can effectively predict the risk of death from disease and is widely used in clinical practice (8).

OUTCOME

Given that previous studies used questionnaire screening or clinical bedside swallowing assessments, the actual incidence of dysphagia may have been underestimated. Video fluoroscopic swallowing study (VFSS), the gold standard for determining dysphagia, was used in this study to ensure the accuracy of the incidence of dysphagia. Dysphagia was diagnosed when patients had difficulty swallowing fluids or food, and a VFSS confirmed dysphagia in conscious patients with stable vital signs (9).

Serum total protein concentration 24 hours after admission to the Rehabilitation Department was the primary measurement used in this study. Blood samples were collected via brachial venipuncture, centrifuged, and sent to the laboratory for analysis.

Serum albumin concentration was measured once a week, and the mean value of serum albumin during hospitalization was recorded.

Modified Rankin Scale (mRS), activities of daily living (ADL), and length of hospital stay (LOS) were recorded at discharge. The mRS measures patients' neurological recovery following stroke, with a total score of 0-5, and an mRS score ≥ 3 indicates poor functional recovery (10). ADL was assessed using a modified Barthel index (MBI) scale to assess patients' ability to perform ADL. ADL < 60 indicates that patients cannot live independently and need to rely on others (11).

STATISTICAL ANALYSIS

We built the database using Microsoft Excel (version 17.0; Microsoft, Redmond, WA), and SPSS (version 16.0; IBM, Armonk, NY, USA) was used for data analysis. If measurement data conformed to normal distribution and homogeneity of variance, the t-test was used for comparison; if there was no accordance with normal distribution, the Mann-Whitney U test was used. Enumeration data were represented by the number of cases and percentages, and preliminary crosstabs were evaluated using the Chi-squared test or Fisher's exact test. Logistic regression and multiple linear regression models were employed to analyze the correlation between dysphagia and mRS, ADL, LOS, and hypo-proteinemia. Odds ratios (ORs) and corresponding 95 % confidence intervals (CIs) were calculated. To avoid the influence of insignificant independent variables on the regression equation,

the stepped-multiple linear regression method was used to analyze the correlation between measurement data and dysphagia.

STANDARD PROTOCOL APPROVAL, REGISTRATION, AND PATIENT CONSENT

This study was approved by the Ethics Committee of the Weifang Medical University (2022YX056). Because the study was retrospective and the extracted data did not involve patient privacy or sensitive information, the requirement for informed consent was waived.

RESULTS

A total of 1,370 patients were included in the study after excluding those with missing data and those who did not meet the inclusion criteria. The included patients had a mean age of 59.08 ± 2.121 years and comprised 903 men (65.91 %) and 467 women (34.09 %). Among them, 610 (44.52 %) and 760 (55.48 %) had hemorrhagic stroke and ischemic stroke, respectively. Of the 1,370 patients included in the study, 499 (36.42 %) had dysphagia. There were significant differences in age, lesion location, and CCI between the patients with and without dysphagia ($p < 0.05$). The median length of hospitalization was 26 days. Patient characteristics are presented in table I. Figure 1 shows the distribution of serum albumin, mRS, ADL, and length of hospital stay data between the two groups.

Table I. Comparison of baseline characteristics of patients

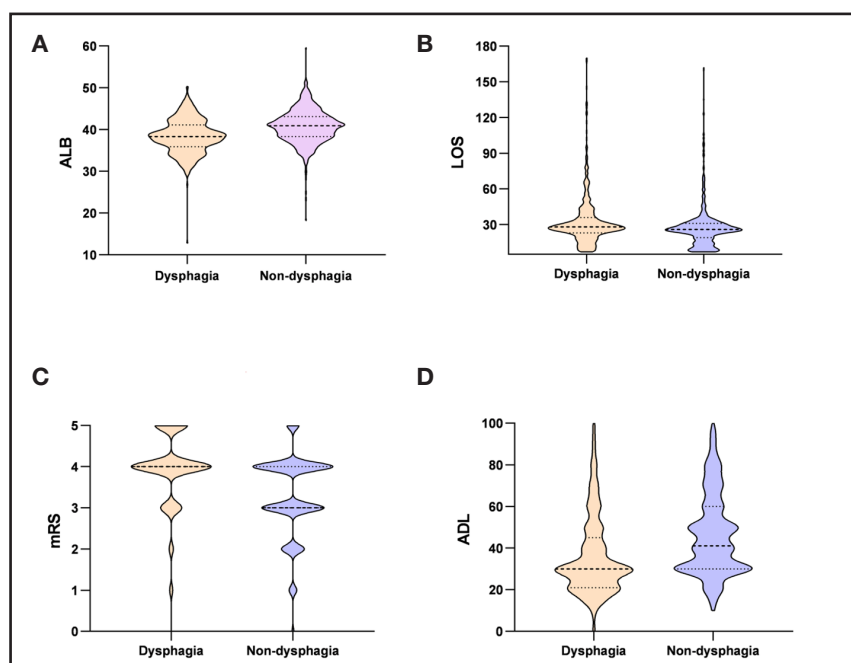
	Total	Non-dysphagia group	Dysphagia group	Statistics	<i>p</i>
Age (years)	59.08 \pm 2.121	56.79 \pm 12.544	61.63 \pm 10.161	t = 5.684	< 0.001
Sex, n (%)					
Male	903	587 (42.8)	316 (23.1)	$\chi^2 = 2.336$	0.126
Female	467	284 (20.6)	183 (13.5)		
Type of stroke, n (%)					
Hemorrhagic	610	374 (27.3)	236 (17.2)	$\chi^2 = 2.436$	0.119
Ischemic	760	497 (36.3)	263 (19.2)		
Site of lesion, n (%)					
Supratentorial	1,097	739 (53.9)	358 (26.1)	$\chi^2 = 50.518$	< 0.001
Infratentorial	157	60 (4.4)	97 (7.1)		
Supratentorial + infratentorial	116	72 (5.3)	44 (3.2)		
Type of health insurance, n (%)					
Basic medical insurance for urban residents	484	300 (21.9)	184 (13.4)	$\chi^2 = 2.661$	0.264
Urban employee basic medical insurance	824	536 (39.1)	288 (21.0)		
Self-paying	62	35 (2.55)	27 (2.0)		
CCI		1.75 \pm 1.691	2.10 \pm 1.801	t = 2.761	0.006

(Continues on next page)

Table I (Cont.). Comparison of baseline characteristics of patients

	Total	Non-dysphagia group	Dysphagia group	Statistics	p
Type of health insurance, n (%)					
Myocardial infarction	11	5 (0.36)	6 (0.44)	1.573	0.210
Congestive heart failure	28	15 (1.10)	13 (0.95)	1.236	0.266
Peripheral vascular diseases	46	25 (1.82)	21 (1.53)	1.751	0.186
Cerebrovascular disease	581	375 (27.4)	206 (15.03)	0.408	0.561
Dementia	259	166 (12.17)	93 (6.79)	0.037	0.848
Chronic obstructive pulmonary disease	41	26 (1.90)	15 (1.10)	0.000	0.983
Connective tissue disease	2	1 (0.07)	1 (0.07)	0.159	0.690
Peptic ulcer disease	15	8 (0.58)	7 (0.51)	0.587	0.407
Mild liver disease	24	15 (1.10)	9 (0.66)	0.012	0.912
Diabetes <i>mellitus</i> (without comorbidities)	412	267 (19.49)	145 (10.58)	0.384	0.535
Hemiplegia	1052	672 (49.05)	380 (27.74)	0.178	0.673
Moderate to severe chronic kidney disease	3	1 (0.07)	2 (0.14)	1.188	0.276
Diabetes <i>mellitus</i> (with comorbidities)	11	3 (0.21)	9 (0.66)	6.190	0.013
Solid tumor, leukemia, lymphoma	0	0	0		
Moderate to severe liver disease 15	76	54 (3.94)	22 (1.61)	1.942	0.163
Metastatic carcinoma 16	0	0	0		
Acquired immunodeficiency syndrome 17	0	0	0		
Albumin, g/l	39.76 ± 3.861	40.5289 ± 3.494	38.2945 ± 4.129	t = -7.843	< 0.001
Total protein, g/l	65.73 ± 5.432	66.5079 ± 6.2754	65.6883 ± 5.95155	t = -2.731	0.006
Pneumonia, n (%)					
No	626	472 (75.4)	154 (24.6)	$\chi^2 = 69.579$	< 0.001
Yes	744	399 (53.6)	345 (46.4)		
mRS	3.55 ± 0.979	4.04 ± 0.8190	3.54 ± 0.910	t = 7.717	< 0.001
ADL	42.42 ± 19.756	42.01 ± 18.671	34.38 ± 18.701	t = -5.473	< 0.001
LOS	29.39 ± 19.043	30.5518 ± 20.24542	34.1983 ± 22.79865	t = 2.270	0.023

CCI: Charlson Comorbidity Index; mRS: modified Rankin scale; ADL: activities of daily living; LOS: length of stay.

**Figure 1.**

Data distribution of serum albumin, mRS, ADL, and LOS in the dysphagia and non-dysphagia groups. A. Serum albumin level in the dysphagia group is lower than that in the non-dysphagia group (t = -7.843, SE = -0.285, 95 % CI: -1.674, -2.79). B. LOS in the dysphagia group is higher than that in the non-dysphagia group (t = 2.268, SE = 1.608, 95 % CI: 6.803-0.490). C. The mRS in the dysphagia group is higher than that in the non-dysphagia group (t = 7.723, SE = 0.064, 95 % CI: 0.625-0.371). D. ADL in the dysphagia group is lower than that in the non-dysphagia group (t = -5.473, SE = -1.393, 95 % CI: -4.888, -10.357).

MULTIPLE LOGISTIC REGRESSION OF DYSPHAGIA WITH PNEUMONIA, PROGNOSIS, AND HYPOPROTEINEMIA

After adjusting for confounding factors, the results of the Hosmer-Lemeshow test demonstrated that the model fit well with the actual situation and accurately reflects the relationships between variables. The dysphagia group exhibited a 2.417-fold higher risk of pneumonia compared to the non-dysphagia group (OR = 2.417, 95 % CI: 1.902-3.072, $p = 0.000$). Moreover, at discharge, patients with dysphagia had a 3.272-fold higher

risk of mRS Score ≥ 3 (OR = 3.272, 95 % CI: 2.508-4.269, $p < 0.001$) and a 1.670-fold higher risk of MBI < 60 (OR = 1.670, 95 % CI: 1.230-2.268, respectively; $p < 0.001$). Additionally, the risk of hypoproteinemia was 2.533 times higher (OR = 2.533, 95 % CI: 1.879-3.414, $p = 0.000$). Furthermore, the OR for hospitalization duration > 26 days was 1.457, with a 95 % CI of 1.136-1.868 and a p -value of 0.003.

The relevant variables and their assignments in the logistic regression are outlined in table II, while specific data can be found in table III. The forest plot illustrating the OR is depicted in figure 2.

Table II. Logistic regression main variables and assignment

Variable	Assignment
Age (years)	0 = ≤ 59 , 1 = 60-69, 2 = 70-79, 3 = 80~89, 4 = ≥ 90
Sex	0 = male, 1 = female
Type of stroke	0 = hemorrhagic, 1 = ischemic
Site of lesion	0 = supratentorial, 1 = infratentorial, 2 = supratentorial + infratentorial
Type of health insurance	0 = basic medical insurance for urban residents, 1 = urban employee basic medical insurance, 2 = self-paying
CCI	0 = no disease, 1 = acquired immunodeficiency syndrome; 2 = metastatic carcinoma; 3 = moderate to severe liver disease; 4 = solid tumor, leukemia, lymphoma; 5 = diabetes mellitus (with comorbidities); 6 = moderate to severe chronic kidney disease; 7 = hemiplegia; 8 = diabetes mellitus (without comorbidities); 9 = mild liver disease; 10 = peptic ulcer disease; 11 = connective tissue disease; 12 = chronic obstructive pulmonary disease; 13 = dementia; 14 = cerebrovascular disease; 15 = peripheral vascular diseases; 16 = congestive heart failure; 17 = myocardial infarction
Dysphagia	0 = non-dysphagia, 1 = dysphagia
Pneumonia	0 = non-pneumonia, 1 = pneumonia
mRS	0 = < 3 , 1 = ≥ 3
MBI	0 = ≥ 60 , 1 = < 60

CCI: Charlson Comorbidity Index; mRS: modified Rankin scale; MBI: modified Barthel index.

Table III. Multiple logistic regression of dysphagia with pneumonia, prognosis, and hypoproteinemia

	B	SE	Wald χ^2	OR	95 % CI	p
Pneumonia						
Before adjustment	0.975	0.118	67.765	2.650	2.101, 3.342	< 0.001
After adjustment*	0.882	0.122	52.031	2.417	1.902, 3.072	< 0.001
mRS ≥ 3						
Before adjustment	1.363	0.130	110.367	3.907	3.907, 5.038	< 0.001
After adjustment†	1.186	0.136	76.357	3.272	2.508, 4.269	< 0.001
MBI < 60						
Before adjustment	0.644	0.147	19.223	1.904	1.428, 2.539	< 0.001
After adjustment†	0.513	0.156	10.808	1.670	1.230, 2.268	0.001
ALB < 35 g/l						
Before adjustment	1.105	.147	56.385	3.020	2.263, 4.030	< 0.001
After adjustment‡	.929	.152	37.166	2.533	1.879, 3.414	< 0.001
LOS > 27d						
Before adjustment	0.540	0.114	22.605	1.716	1.373, 2.143	< 0.001
After adjustment§	0.376	0.127	8.808	1.457	1.136, 1.868	0.003

CCI: Charlson Comorbidity Index; mRS: modified Rankin scale; MBI: modified Barthel index; LOS: length of stay; ALB: albumin. *Adjusted for confounding factors including type of stroke (hemorrhagic) and age (380~89; ≥ 90). †Adjusted for confounding factors including type of stroke (hemorrhagic), age (80-89 years), and site of lesion (supratentorial, supratentorial + infratentorial). ‡Adjusted for confounding factors including pneumonia, age, and CCI (mild liver disease, moderate to severe chronic kidney disease, moderate to severe liver disease). §Adjusted for confounding factors including type of stroke (hemorrhagic), age (≤ 59), and type of health insurance (self-paying).

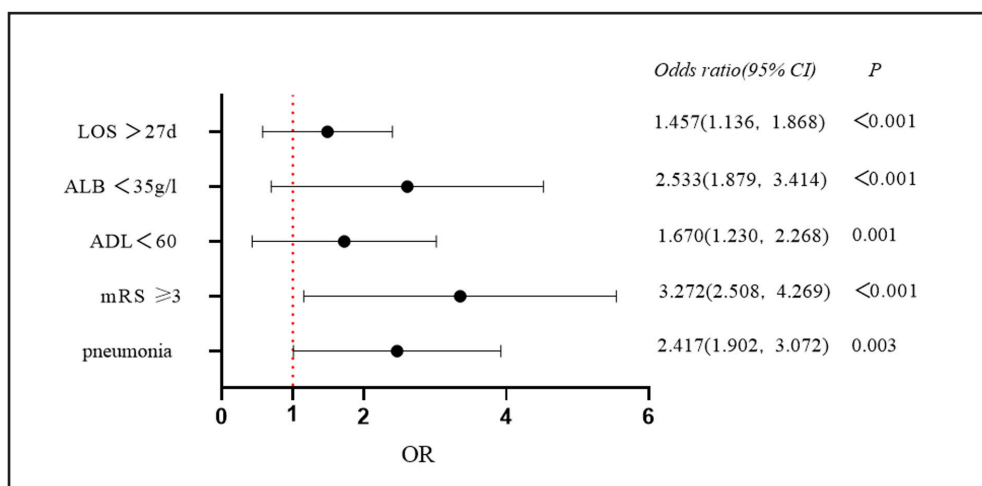


Figure 2.

Forest plot detailing the broad range of the odds ratio in patients with dysphagia with pneumonia, their prognosis, and hypoproteinemia.

Table IV. Stepwise multiple linear regression to analyze the associations between dysphagia and mRS, ADL, and LOS in patients with stroke

		Non-normalized coefficient		Normalization coefficient	t	p*	R	R ² _{adjust}	VIF	F	p†
		B	Standard error	Beta							
mRS‡	Constant	2.433	0.145		16.772	< 0.001					
	Dysphagia	0.540	0.053	0.265	10.128	< 0.001	0.627	0.395	1.108	41.876	< 0.001
ADL‡	Constant	64.275	2.965		21.679	< 0.001					
	Dysphagia	-8.634	1.088	-0.210	-7.937	< 0.001	0.496	0.378	0.903	39.941	< 0.001
LOS§	Constant	22.091	1.455		15.181	< 0.001					
	Dysphagia	5.808	1.099	0.147	5.283	< 0.001	0.354	0.209	0.998	12.492	< 0.001
Serum albumin¶	Constant	45.500	0.665		68.439	< 0.001					
	Dysphagia	-1.874	0.221	-0.220	-8.284	< 0.001	0.576	0.386	1.846	39.826	< 0.001
	Non-dysphagia										

CCI: Charlson Comorbidity Index; mRS: modified Rankin scale; LOS: length of stay; ADL: activities of daily living. *The independent variable (dysphagia) had a significant effect on the dependent variable. †The regression equation has statistical significance. ‡Adjusted for confounding factors including type of stroke (hemorrhagic) and age (80-89; ≥ 90 years). §Adjusted for confounding factors including type of stroke (hemorrhagic), age (80-89 years), and site of lesion (supratentorial, supratentorial + infratentorial). ¶Adjusted for confounding factors including pneumonia, age, and CCI (mild liver disease, moderate to severe chronic kidney disease, and moderate to severe liver disease).

MULTIPLE STEP LINEAR REGRESSION ANALYSIS OF DYSPHAGIA, PROGNOSIS, AND SERUM ALBUMIN

mRS, MBI, LOS, and serum albumin levels were utilized as dependent variables in the multiple stepwise regression analysis. The inclusion criteria for variables was set at $p < 0.05$, while the exclusion criterion was $p > 0.10$. Categorical variables were incorporated into the model as dummy variables. A multiple stepwise linear regression model was constructed, ensuring the

absence of multicollinearity among the variables, and confirming that the residuals followed a normal distribution. Importantly, each model's multiple linear regression equations exhibited statistical significance ($p < 0.001$). Our results showed that dysphagia was significantly associated with a higher mRS ($\beta = 0.265$), lower ADL ($\beta = -0.210$), and longer LOS ($\beta = 0.147$, $p < 0.001$) ($p < 0.05$). When considering serum albumin as the dependent variable, the correlation coefficient was $R = 0.576$. Further, the coefficient of determination was $R^2 = 0.386$, exceeding the threshold of 0.3, indicating a good fit of the model. Approximate-

ly 38.64 % of the variability in serum albumin levels could be accounted for by the variables included in the model. In addition, our results showed that dysphagia was significantly associated with lower serum albumin levels ($\beta = -0.221, p < 0.001$). In addition to dysphagia, several other factors, namely age, pneumonia, mild liver disease, moderate to severe chronic kidney disease, and moderate to severe liver disease, were identified as contributors to the variation in serum albumin levels among stroke patients. Further details are provided in table IV.

DISCUSSION

In this retrospective study, we reported the effects of dysphagia on serum albumin levels and the prognosis of patients with stroke. Dysphagia was associated with reduced serum albumin levels, higher mRS, lower ADL, and longer LOS.

Serum albumin is a multifunctional protein with several important physiological functions. A serum albumin level < 35 mg/l has long been considered as a strong prognostic marker of health and/or disease status, and is strongly associated with short-term death in patients (12). However, little is known about the correlation between dysphagia and serum albumin levels. In this study, albumin was used as an observational indicator, and dysphagia was found to be significantly associated with decreased albumin levels. Charlson comorbidities include a total of 17 diseases. The quantification of comorbidities based on the number and severity of the disease in the patient can be used to predict the risk of death from the disease (13). Patients' CCI scores were recorded along with their comorbidities, including 17 diseases, which were incorporated into the regression analysis as dummy variables. In order to ensure the meaningfulness of each variable in the regression model and to establish the independence of the association between dysphagia and serum albumin levels from other potential factors, a stepwise multiple near linear regression method was employed.

This method involved the gradual introduction of variables one by one into the model. After introducing a new variable, the previously selected variables in the regression model were individually tested, and those found to be insignificant were eliminated. This iterative process continued until no new variables were introduced, and no existing variables were deleted, thereby ensuring the meaningful inclusion of every variable in the regression model (14).

The regression coefficient R^2 in this study was 0.386, indicating that 38.6 % of the variability in serum albumin levels could be explained by the selected variables within the model. Notably, it was observed that dysphagia, age, pneumonia, mild liver disease, moderate to severe chronic kidney disease, and moderate to severe liver disease all influenced serum albumin levels in stroke patients. These factors impact albumin concentration through various mechanisms, including the absolute albumin synthesis rate, partial catabolic rate, albumin infiltration into extravascular ventricle, and exogenous albumin loss (15).

Stroke patients with dysphagia often have symptoms of choking, coughing, drooling, swallowing difficulty, and pain owing to the reduced safety and effectiveness of eating. Patients' willingness to eat is reduced, resulting in insufficient food intake. Stroke patients with swallowing disorders have a 2.425-fold increased risk of malnutrition (OR = 2.425, 95 % CI: 1.264-4.649, $p < 0.05$) (16-18). Albumin synthesis is associated with nutritional intake (19). When dysphagia results in a low intake of total calories and specific amino-acid reduction, liver parenchymal cells cannot obtain the required nutrients for albumin synthesis, thereby reducing albumin content in the body (4). Meanwhile, people with dysphagia can experience accidental aspiration of fluid, food, and saliva into the lungs, which increases the risk of developing pneumonia. Several studies have shown that inflammation is an important determinant of albumin concentration. When inflammation occurs, IL-6 activates C-reactive protein (CRP) and inhibits albumin synthesis, and CRP is negatively correlated with albumin levels (20,21). It is suggested that decreased serum albumin levels occur due to changes in vascular permeability induced by cytokines, leading to the diffusion of albumin into the extravascular fluid space. The above are two possible causes of reduced serum albumin caused by dysphagia.

Dysphagia also affects the prognosis of stroke patients. The MBI and mRS have been widely used in large-scale clinical trials and long-term prognostic studies of patients with stroke, and the MBI is scored based on the ability of patients to complete specific tasks in daily life (22,23). The score is positively correlated with independent ability, which can quantitatively assess the level of disability and degree of recovery of neurological function in patients with stroke (23). mRS was strongly correlated with the pathological indicators of stroke, and could reflect the differences in functional disability among patients with stroke (24). After adjusting for various confounding factors, it was observed that stroke patients with dysphagia faced a higher risk of poor functioning and dependence for ADL upon discharge from the hospital. Swallowing disorders in stroke patients can lead to inadequate food intake and increase the risk of malnutrition (16-18). Subsequently, poor nutritional status can further exacerbate the neuroinflammatory response and impede the recovery of brain injury by suppressing the expression of axonal terminal proteins (25). Furthermore, dysphagia-induced dehydration and malnutrition can contribute to muscle atrophy, compromised immune function, and overall decline in systemic function among patients. This, in turn, perpetuates a worsening cycle of patient functionality and negatively impacts prognosis (26,27).

The results of this study suggest that dysphagia and malnutrition are associated with decreased serum albumin levels and a poor prognosis. Despite the limitations and small study size, these findings further shed light on the link between dysphagia and poor prognosis. Thus, dysphagia can be used as a reference item for poor prognosis in patients with stroke. Reduced albumin levels may occur in stroke patients with dysphagia.

Several limitations of our study should be considered when interpreting our findings. A multicenter retrospective study design was not adopted, and the number of observational hospitals was

insufficient. Further studies with a larger sample size should be conducted using a strict study design to improve the accuracy of the results. Therefore, our findings, especially with respect to serum albumin levels, should be carefully interpreted and treated as exploratory data.

REFERENCES

- Hankey GJ. Stroke. *Lancet* 2017;389:641-54. DOI: 10.1016/S0140-6736(16)30962-X
- Banda KJ, Chu H, Kang XL, Liu D, Pien LC, Jen HJ, et al. Prevalence of dysphagia and risk of pneumonia and mortality in acute stroke patients: a meta-analysis. *BMC Geriatr* 2022;22:420. DOI: 10.1186/s12877-022-02960-5
- Altman KW, Yu GP, Schaefer SD. Consequence of dysphagia in the hospitalized patient: impact on prognosis and hospital resources. *Arch Otolaryngol Head Neck Surg* 2010;136(8):784-9. DOI: 10.1001/archoto.2010.129
- D'Angio RG. Is there a role for albumin administration in nutrition support? *Ann Pharmacother* 1994;28:478-82. DOI: 10.1177/106002809402800411
- Doweiko JP, Nompleggi DJ. Role of albumin in human physiology and pathophysiology. *JPEN J Parenter Enter Nutr* 1991;15:207-11. DOI: 10.1177/0148607191015002207
- Tayek JA. Albumin synthesis and nutritional assessment. *Nutr Clin Pract* 1988;3:219-21. DOI: 10.1177/0115426588003006219
- Chinese Society of Neurology, Chinese Stroke Society. Chinese guidelines for diagnosis and treatment of acute ischemic stroke. *Chin J Neurol* 2018;51:666-82.
- Charlson ME, Pompei P, Ales KL, MacKenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. *J Chronic Dis* 1987;40:373-83. DOI: 10.1016/0021-9681(87)90171-8
- Baijens LW, Clavé P, Cras P, Ekberg O, Forster A, Kolb GF, et al. European Society for Swallowing Disorders - European Union Geriatric Medicine Society white paper: oropharyngeal dysphagia as a geriatric syndrome. *Clin Interv Aging* 2016;11:1403-28. DOI: 10.2147/CIA.S107750
- Sulter G, Steen C, De Keyser J. Use of the Barthel index and modified Rankin scale in acute stroke trials. *Stroke* 1999;30:1538-41. DOI: 10.1161/01.STR.30.8.1538
- Mahoney FI, Barthel DW. Functional evaluation: the Barthel index. *Md State Med J* 1965;14:61-5.
- Goldwasser P, Feldman J. Association of serum albumin and mortality risk. *J Clin Epidemiol* 1997;50:693-703. DOI: 10.1016/S0895-4356(97)00015-2
- Fanali G, Di Masi A, Trezza V, Marino M, Fasano M, Ascenzi P. Human serum albumin: from bench to bedside. *Mol Aspects Med* 2012;33:209-90. DOI: 10.1016/j.mam.2011.12.002
- Johnson RA, Wichern DW. Applied multivariate statistical analysis. 3rd ed. London: Prentice Hall, Inc.; 1992. pp. 219-69.
- Rozga J, Piątek T, Małkowski P. Human albumin: old, new, and emerging applications. *Ann Transplant* 2013;18:205-17. DOI: 10.12659/AOT.889188
- Kim H, Suh Y. Changes in the dysphagia and nutritional status of patients with brain injury. *J Clin Nurs* 2018;27:1581-8. DOI: 10.1111/jocn.14226
- Foley NC, Martin RE, Salter KL, Teasell RW. A review of the relationship between dysphagia and malnutrition following stroke. *J Rehabil Med* 2009;41:707-13. DOI: 10.2340/16501977-0415
- Cichero JA, Altman KW. Definition, prevalence and burden of oropharyngeal dysphagia: a serious problem among older adults worldwide and the impact on prognosis and hospital resources. *Nestle Nutr Inst Workshop Ser* 2012;72:1-11. DOI: 10.1159/000339974
- Kirsch R, Frith L, Black E, Hoffenberg R. Regulation of albumin synthesis and catabolism by alteration of dietary protein. *Nature* 1968;217:578-9. DOI: 10.1038/217578a0
- Sullivan DH, Roberson PK, Johnson LE, Mendiratta P, Bopp MM, Bishara O. Association between inflammation-associated cytokines, serum albumins, and mortality in the elderly. *J Am Med Dir Assoc* 2007;8:458-63. DOI: 10.1016/j.jamda.2007.04.004
- Sullivan DH, Johnson LE, Dennis RA, Roberson PK, Heif M, Garner KK, et al. The interrelationships among albumin, nutrient intake, and inflammation in elderly recuperative care patients. *J Nutr Health Aging* 2011;15:311-5. DOI: 10.1007/s12603-010-0297-1
- Broderick JP, Adeoye O, Elm J. Evolution of the modified Rankin scale and its use in future stroke trials. *Stroke* 2017;48(7):2007-12. DOI: 10.1161/STROKEAHA.117.017866
- Huybrechts KF, Caro JJ. The Barthel Index and modified Rankin scale as prognostic tools for long-term outcomes after stroke: a qualitative review of the literature. *Curr Med Res Opin* 2007;23(7):1627-36. DOI: 10.1185/030079907X210444
- Harrison JK, McArthur KS, Quinn TJ. Assessment scales in stroke: clinimetric and clinical considerations. *Clin Interv Aging* 2013;8:201-11.
- Smith SE, Figley SA, Schreyer DJ, Paterson PG. Protein-energy malnutrition developing after global brain ischemia induces an atypical acute-phase response and hinders expression of GAP-43. *PLoS One* 2014;9(9):e107570. DOI: 10.1371/journal.pone.0107570
- Xu M, Pirtskhalava T, Farr JN, Weigand BM, Palmer AK, Weivoda MM, et al. Senolytics improve physical function and increase lifespan in old age. *Nat Med* 2018;24(8):1246-56. DOI: 10.1038/s41591-018-0092-9
- Patel DA, Krishnaswami S, Steger E, Conover E, Vaezi MF, Ciucci MR, et al. Economic and survival burden of dysphagia among inpatients in the United States. *Dis Esophagus* 2018;31(1):1-7. DOI: 10.1093/dote/dox131