ORIGINAL

Nutritional intervention improves prognosis of subarachnoid hemorrhage patients undergoing aneurysmal clipping : a retrospective study

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Abstract : Aneurysmal subarachnoid hemorrhage (SAH) is a serious clinical event associated with high mortality and, among survivors, serious morbidity. Maintaining the muscle volume in SAH patients is essential, as rehabilitation is often required after intensive care. In this study, we investigated whether proper nutritional administration improved clinical outcomes based on patients laboratory data and level of activities of daily living. This retrospective study was carried out on 250 consecutive SAH patients who underwent craniotomy within 72 hours of onset from February 2005 to June 2018. Finally, 75 patients with a BMI < 22 kg/m² were included. We compared postoperative energy and protein intake in relation to measures of biochemical parameters and modified Rankin Scale at discharge. Serum Alb concentrations at 25-35 hospital days was significantly improved by postoperative energy intake of ≥25 kcal/kg and protein intake of ≥0.8 g/kg per day beginning 3 days. High serum Alb concentrations at 25-35 hospital days following the start of this intake were independent factors for good prognosis. This study suggests that the minimum postoperative nutritional intake per day for SAH patients undergoing aneurysmal clipping is 25 kcal/kg of energy and 0.8 g/kg of protein. Higher serum Alb concentrations corresponded to improved long-term functional outcome. J. Med. Invest. 70 : 226-230, February, 2023

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INTRODUCTION

Aneurysmal subarachnoid hemorrhage (SAH) is the occurrence of bleeding within the subarachnoid space caused by a ruptured aneurysm (1). It is a severe clinical event associated with high mortality and severe morbidity among survivors (2). According to recent research, the overall crude global incidence of SAH across all study periods is thought to be 7.9 per 100,000 person-years (3). To prevent rebleeding, SAH patients need surgical treatment, such as aneurysmal clipping or endovascular coiling, within 72 hours of onset (4). Delayed cerebral ischemia, including cerebral vasospasm, is a frequent complication that typically occurs between 4 and 14 days after SAH onset (5). Therefore, patients are usually monitored in an intensive care unit (ICU) for 2 weeks after SAH onset (5). Proper nutrition to maintain muscle volume is crucial during this period, as half of patients need rehabilitation after being discharged from the ICU.

Malnutrition is present in 6% to 62% of patients in the acute phase of stroke onset (6). More specifically, undernutrition in this phase increases the likelihood of subsequent complications (7). Undernutrition also increases the risk of mortality, length of hospital stay, and healthcare costs (8). A low serum albumin (Alb) concentration, which is a classical biochemical parameter, is linked to increased disability and handicap during hospital stay (8). Therefore, preventing malnutrition is likely to improve clinical outcomes, appropriate nutritional intervention may improve clinical outcomes.

ICU admission induces ICU-acquired weakness, which is associated with functional disability and muscle dysfunction (9). Hermans *et al*. showed that ICU-acquired weakness aggravated morbidity and increased cost per patient, and resulted in higher mortality 1 year after ICU admission (10). To address such problems, many reports have focused on the effects of improved nutrition. A study by Park *et al*. indicated that protein supplementation prevented frailty in prefrail or frail elderly patients who were at risk of malnutrition (11). Thus, muscle atrophy is a critical clinical issue in the ICU context, and appropriate nutritional administration may help ameliorate the condition.

The aim of the present study was to determine an appropriate nutritional management strategy for the acute phase of SAH. To this end, we investigated whether nutritional intake improved the clinical outcome of patients with SAH.

METHODS

Study design and participant selection

We retrospectively reviewed the data of 250 consecutive SAH patients who received aneurysmal clipping at Seirei Hamamatsu General Hospital between February 2005 and June 2018. This study was approved by the Institutional Review Board for Human Studies at Seirei Hamamatsu General Hospital

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(approval number 2911). As previous research has indicated that low BMI (< 22 kg / m^2) increases the risk of mortality and decreases the likelihood of returning to living at home (12), we focused on patients with a BMI < 22 kg/m^2 (n = 75). The exclusion criteria in the initial cohort study were : the patients with a BMI ≥ 22 kg/m^2 (n = 61), missing biochemical data at 15–20 hospital days or 25–35 hospital days (n = 50), unclear medical records (n = 40), bodyweight missing at admission (n = 21), early death after admission (n = 2), and duplicate records (n = 1). The cut-off value for nutritional intake was based on the recommendations of the Society of Critical Care Medicine and the American Society for Parenteral and Enteral Nutrition that 80% of estimated or calculated goal energy and protein should be administered to critically ill patients (13). As healthy subjects need 30–40 kcal/kg of energy intake (14) and 1.0–1.5 g/kg of protein intake (15), the cut-off values for energy and protein were determined to be 25 kcal/kg and 0.8 g/kg, respectively.

Preoperatively, surgical clipping was performed within 72 hours of onset to prevent rebleeding. We performed the standard surgical clipping in all cases. Postoperatively, we managed intracranial pressure in the postoperative patients with Fisher groups 3 and 4 by placement of ventricular and cisternal drainage.

Logistic regression analysis was used to identify explanatory variables (serum Alb concentration at 25-35 hospital days, serum CRP concentration at 15-20 hospital days and World Federation of Neurosurgical Surgeons Scale (WFNSS)) independently associated with the modified Rankin Scale at discharge (mRS_d) score (4≤). This analysis was performed for parameters showing significant difference (serum Alb concentration at 25-35 hospital days, serum CRP concentration at 15-20 hospital days) and severity of SAH using the WFNSS.

Data collection

Medical records for past history (hypertension, diabetes, dyslipidaemia), alcohol consumption habits, smoking history, body measurements, laboratory data, nutritional intake, mRS_d score as an ADL, SAH severity, SAH type and complications were collected retrospectively. A registered nurse took past history, alcohol consumption habits, smoking history, and body measurements (weight and height) at admission. Body weight was measured using a bed-equipped weight scale and height using a measuring tape. SAH severity was assessed using the WFNSS (grade 1-5). ADL was assessed using the modified Rankin Scale (grade 0-6).

Laboratory data

Serum total protein (TP), serum Alb, serum cholinesterase (ChE), serum CRP concentrations were collected on the day of admission, and at 15–20 hospital days and 25–35 hospital days. The time ranges for data collection were due to variations in the scheduling of clinical examinations.

Nutritional intake

In many cases, we used enteral feeding (Oxepa™, Abbott, IL, USA) by a tube or oral before eating a hospital meal. Administrated volume of this enteral feeding was up to 750 mL (energy 1125 kcal, protein 47 g, lipid 68.6 g, carbohydrate 78.8 g) per day.

Postoperative nutritional intake (energy and protein) was calculated as the average intake on days 3, 4, and 5 after admission. The amount of energy and protein intake from enteral nutrition and parenteral nutrition were calculated based on the volume of enteral feeding or infusion. Therefore, caloric intake and protein intake were stable for 4 to 14 days postoperatively. Registered dietitians planned a master menu using a commercial meal planning application, and dietary intake volume was estimated visually by a registered nurse. The dietary intake volume was measured at 3 times a day. This percentage of dietary intake was then converted into the amount of energy and protein intake by registered dietitians.

Statistical analysis

Continuous variables are shown as mean ± standard deviation. To compare the two groups, an F-test was performed, followed by Student's t-test (equal variance) or Welch's test (different variance). To compare categorical data, Fisher's exact test was performed. Logistic regression analysis was performed to identify the relationships between variables. Dependent variable was mRS_d score (4 ≤), independent variables were WFNSS, serum Alb and serum CRP concentrations in the logistic regression analysis. All statistical analyses were performed using EZR

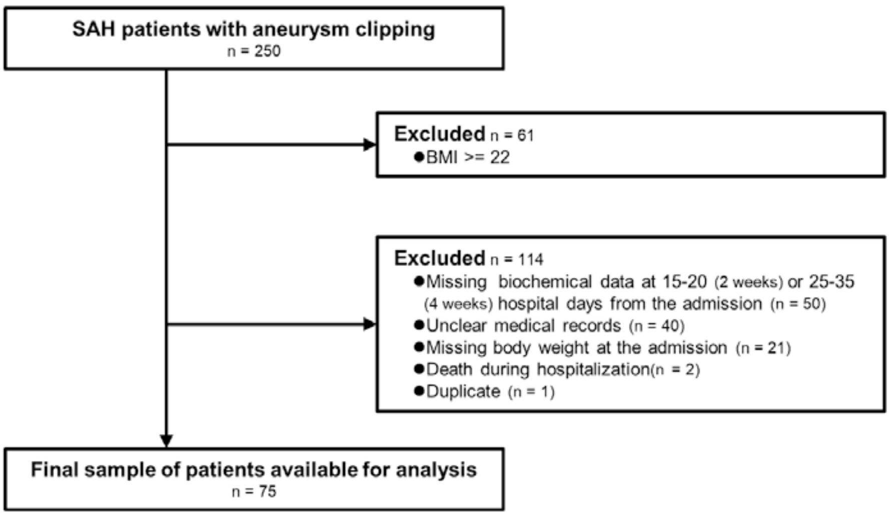

Figure 1. Patient enrollment, exclusion, and distribution
Two hundred and fifty patients undergoing aneurysmal clipping were enrolled in the study. We focused BMI < 22 kg/m^2 patients, we excluded 61 patients which are BMI ≥ 22 kg/m^2. One hundred and fourteen patients were initially excluded due to unclear medical records, death during admission, duplication, missing laboratory data at 15-20 hospital days or 25-35 hospital days, or missing bodyweight measurements at admission. Patients with BMI ≥ 22 kg/m^2 were separated for use as a comparison group.

software, version 1.41 (Saitama Medical Center, Jichi Medical University, Saitama, Japan) (16). For all results, the significance level was set at $p < 0.05$.

RESULTS

Patient characteristics

The characteristics of patients with BMI < 22 kg/m^2 are described in Table 1. There were 75 cases, with a mean age of 62 years, predominantly female (72%). Fifty-four (72%) patients were in the 1–3 range on the WFNSS.

Association between energy and protein intake and serum Alb concentration as nutritional status

Both energy intake of ≥ 25 kcal/kg and protein intake of ≥ 0.8 g/kg postoperatively was significantly associated with increased serum Alb concentration at the 25-35 hospital days in the BMI < 22 kg/m^2 patients (Table 2). In addition, protein intake of ≥ 0.8 g/kg was significantly associated with increased serum CRP concentration at the 15-20 hospital days.

Table 1. Baseline characteristics of patients with BMI < 22 kg/m^2

Variables	Group	Overall (n = 75)	Energy (kcal/kg) < 25 (n = 34)	Energy (kcal/kg) 25 ≤ (n = 41)	p	Protein (g/kg) < 0.8 (n = 18)	Protein (g/kg) 0.8 ≤ (n = 57)	p
Age		62 ± 12	64 ± 11	61 ± 13	0.195	65 ± 10	61 ± 12	0.225
Sex (%)	Male	21 (28.0)	10 (29.4)	11 (27)	1.000	2 (11.1)	19 (33.3)	0.079
	Female	54 (72.0)	24 (70.6)	30 (73)		16 (88.9)	38 (66.7)	
Alcohol (%)		31 (41.3)	13 (38.2)	18 (43.9)	0.646	5 (27.8)	26 (45.6)	0.272
Smoking (%)		25 (33.3)	11 (32.4)	14 (34.1)	1.000	4 (22.2)	21 (36.8)	0.390
Hypertension (%)		42 (56.0)	22 (64.7)	20 (48.8)	0.243	11 (61.1)	31 (54.4)	0.786
Diabetes (%)		13 (17.3)	9 (26.5)	4 (9.8)	0.071	7 (38.9)	6 (10.5)	0.011
Dyslipidaemia (%)		19 (25.3)	7 (20.6)	12 (29.3)	0.435	3 (16.7)	16 (28.1)	0.535
Location (%)	ACA	33 (44.0)	12 (35.3)	21 (51.2)	0.244	6 (33.3)	27 (47.4)	0.451
	ICA	25 (33.3)	11 (32.4)	14 (34.1)		6 (33.3)	19 (33.3)	
	MCA	15 (20.0)	10 (29.4)	5 (12.2)		5 (27.8)	10 (17.5)	
	VA-BA	2 (2.7)	1 (2.9)	1 (2.4)		1 (5.6)	1 (1.8)	
Hunt & Kosnik (%)	1	26 (34.7)	10 (29.4)	16 (39.0)	0.110	4 (22.2)	22 (38.6)	0.324
	2	18 (24.0)	5 (14.7)	13 (31.7)		3 (16.7)	15 (26.3)	
	3	14 (18.7)	9 (26.5)	5 (12.2)		5 (27.8)	9 (15.8)	
	4	15 (20.0)	8 (23.5)	7 (17.1)		5 (27.8)	10 (17.5)	
	5	2 (2.7)	2 (5.9)	0 (0.0)		1 (5.6)	1 (1.8)	
WFNSS (%)	1	34 (45.3)	13 (38.2)	21 (51.2)	0.210	6 (33.3)	28 (49.1)	0.212
	2	12 (16.0)	3 (8.8)	9 (22.0)		1 (5.6)	11 (19.3)	
	3	8 (10.7)	5 (14.7)	3 (7.3)		3 (16.7)	5 (8.8)	
	4	13 (17.3)	8 (23.5)	5 (12.2)		5 (27.8)	8 (14.0)	
	5	8 (10.7)	5 (14.7)	3 (7.3)		3 (16.7)	5 (8.8)	
Fisher (%)	1	0 (0.0)	0 (0.0)	0 (0.0)	0.238	0 (0.0)	0 (0.0)	0.076
	2	18 (24.0)	5 (14.7)	13 (31.7)		1 (5.6)	17 (29.8)	
	3	40 (53.3)	20 (58.8)	20 (48.8)		11 (61.1)	29 (50.9)	
	4	17 (22.7)	9 (26.5)	8 (19.5)		6 (33.3)	11 (19.3)	
SVS (%)		18 (24.0)	8 (23.5)	10 (24.4)	1.000	6 (33.3)	12 (21.1)	0.346
SIRS (%)		31 (41.3)	17 (50.0)	14 (34.1)	0.239	9 (50.0)	22 (38.6)	0.422
TP (g/dL)		7.2 ± 0.6	7.2 ± 0.6	7.1 ± 0.5	0.299	7.4 ± 0.7	7.1 ± 0.5	0.047
Alb (g/dL)		4.2 ± 0.3	4.1 ± 0.3	4.2 ± 0.3	0.976	4.1 ± 0.4	4.2 ± 0.3	0.723
ChE (U/L)		302 ± 59	289 ± 54	313 ± 62	0.098	290 ± 67	306 ± 57	0.339
CRP (mg/dL)		0.59 ± 2.16	0.75 ± 1.94	0.47 ± 2.35	0.584	0.83 ± 1.77	0.51 ± 2.28	0.588

Age, sex, past history (hypertension, diabetes, dyslipidaemia), alcohol consumption habits, smoking history, disease severity, disease type, complications, and laboratory data of SAH patients with BMI < 22 kg/m^2 taken on admission. There were no significant differences between the two nutritional intake groups in any parameter except for serum total protein levels in relation to protein administration. P-value was calculated using Student's t-test (comparison of two groups, equal variance), Welch's test (comparison of two groups, unequal variance), or Fisher's exact test (comparison of categorical data). Data are shown as the mean ± standard deviation. ACA, anterior cerebral artery ; ICA, internal carotid artery ; MCA, middle cerebral artery ; VA-BA, vertebral artery-basilar artery ; SVS, symptomatic vasospasm ; SIRS, systemic inflammatory response syndrome. TP, serum total protein concentration ; Alb, serum albumin concentration ; ChE, serum cholinesterase concentration ; CRP, serum C-reactive protein concentration.

Table 2. Changes in laboratory data in relation to energy intake (25 kcal/kg) and protein intake (0.8 g/kg) in patients with BMI < 22 kg/m^2

Variables		Energy intake (kcal/kg)			Protein intake (g/kg)		
		< 25	25 ≤	p	< 0.8	0.8 ≤	p
15-20 hospital days	TP (g/dL)	5.9 ± 0.7	5.6 ± 0.7	0.088	5.9 ± 0.4	5.7 ± 0.8	0.187
	Alb (g/dL)	2.8 ± 0.5	3.0 ± 0.5	0.246	2.8 ± 0.5	3.0 ± 0.5	0.222
	ChE (U/L)	170 ± 39	204 ± 64	0.076	171 ± 41	203 ± 64	0.104
	CRP (mg/dL)	4.3 ± 5.3	3.3 ± 4.0	0.366	5.7 ± 5.2	3.2 ± 4.2	0.045
25-35 hospital days	TP (g/dL)	6.3 ± 0.5	6.3 ± 0.6	0.932	6.3 ± 0.6	6.4 ± 0.5	0.422
	Alb (g/dL)	3.2 ± 0.5	3.5 ± 0.5	0.020	3.1 ± 0.5	3.4 ± 0.5	0.027
	ChE (U/L)	228 ± 50	257 ± 70	0.089	219 ± 48	251 ± 66	0.155
	CRP (mg/dL)	2.1 ± 3.8	1.0 ± 2.4	0.161	2.1 ± 3.7	1.3 ± 2.9	0.359

Participants were divided into two groups based on nutritional intake (25 kcal/kg of energy and 0.8 g/kg of protein). Serum CRP concentration at 15-20 hospital days were significantly improved by a protein intake of 0.8 g/kg or more. Serum Alb concentration at 25-35 hospital days were also improved by an energy intake of ≥ 25 kcal/kg and protein intake of 0.8 g/kg or more. P-values were calculated using Student's t-test (equal variance) or Welch's test (unequal variance). Data are shown as the mean ± standard deviation. TP, serum total protein concentration ; Alb, serum albumin concentration ; ChE, serum cholinesterase concentration ; CRP, serum C-reactive protein concentration.

Changes in mRS_d score as an ADL in relation to serum Alb concentration as nutritional status

To investigate the relationship between mRS_d score as an ADL and serum Alb concentration as nutritional status, logistic regression analyses were performed. As shown in Table 3, WFNSS and serum Alb concentrations at the 25-35 hospital days were independent variables for the mRS_d. Higher WFNSS and serum Alb concentrations associated with the high mRS_d score (4 ≤).

Table 3. Logistic regression analysis of variables associated with mRS_d score (4 ≤)

Variables	Odds ratio (95% confidence interval)	p
WFNS	1.49 (1.05-2.12)	0.0260
Alb (25-35 hospital days)	0.0684 (0.0185-0.253)	0.0001
CRP (15-20 hospital days)	1.02 (0.89-1.16)	0.8190

To investigate the effect of serum Alb concentration as nutritional status on mRS_d as an ADL, logistic regression analysis were performed. The independent variables for mRS_d score (4 ≤) was WFNSS value and serum Alb concentration at 25-35 hospital days. Higher WFNSS and serum Alb concentrations increased the risk of high mRS_d score (4 ≤). mRS_d, modified Rankin Scale at discharge ; WFNSS, World Federation of Neurological Surgeons Scale ; CRP, serum C-reactive protein concentration ; Alb, serum albumin concentration.

DISCUSSION

In our study, postoperative energy intake of ≥ 25 kcal/kg and protein intake of ≥ 0.8 g/kg per day beginning 3 days after admission improved serum Alb concentrations at 25-35 hospital days in SAH patients with BMI < 22 kg/m^2 undergoing aneurysmal clipping. Serum Alb concentration in these patients played an important role in ADL prediction on discharge from acute care hospital.

The present study also found that the biochemical nutritional parameters of participants with a BMI < 22 kg/m^2 were changed by nutritional intake. We hypothesize that this is due to their higher residual stores of muscle mass (protein) and fat (energy). The Global Leadership Initiative on Malnutrition suggests that malnutrition can be assessed based on low BMI (17). Moreover, previous research indicates that low BMI (< 22 kg/m^2) increases the risk of mortality and decreases the likelihood of returning to living at home (12). This suggests that low BMI increases the risk of malnutrition ; therefore, nutritional intervention is necessary for patients with BMI < 22 kg/m^2.

We also found that an energy intake of ≥ 25 kcal/kg and protein intake of ≥ 0.8 g/kg per day improved these patients' biochemical parameters. However, healthy individuals are widely considered to require 30-40 kcal/kg of energy intake (14) and 1.0-1.5 g/kg of protein intake per day (15). We hypothesize that this discrepancy is due to endogenous energy production, which reduces energy and protein demand. Previous studies have found that invasive surgery produces inflammatory mediators, and that the resulting inflammation induces gluconeogenesis and proteolysis (18). It has been estimated that an intake of 70% of targeted energy and protein significantly reduces the risk of mortality (19). Moreover, indirect calorimetry estimates energy expenditure is 25-30 kcal/kg at 3-5 hospital days in SAH patients (20). These reports suggest that postsurgical energy intake of ≥ 25 kcal/kg and protein intake of ≥ 0.8 g/kg per day may be optimal.

The present study has several limitations. We could not measure other nutritional status-related parameters, such as lymphocyte counts, and rapid turnover proteins, because the treatment data includes a long time ago. Our estimation of energy and protein intake was based on visual inspection by a registered nurse and is therefore subjective. However, this bias may have been moderated by the administration of enteral feeding products to almost all patients. We could not assess skeletal muscle mass (21) and cognitive ability (22), which are known to affect ADL. Although we collected the data continuously, the data was from a single faculty which limits the generalizability of our study. Logistic regression analysis utilizes limited variables based on significant differences were observed in restricted study patients (n = 75). Age, WFNSS, clinical improvement before aneurysm treatment, pupillary light reflex, intracerebral hematoma, modified Fisher grade are related to the outcome of SAH (23). These factors are not adjusted, generality of this study is limited. This study may also exhibit some bias related to unmeasured factors. Further research on these issues is needed.

CONCLUSION

To the best of our knowledge, this is the first investigation to reveal the relationship between nutritional intake and clinical outcomes in aneurysmal SAH patients. We have demonstrated that postsurgical energy intake of ≥ 25 kcal/kg and protein intake of ≥ 0.8 g/kg per day improves the serum Alb concentration of patients with BMI < 22 kg/m^2. Moreover, this improved serum Alb concentration predicts an improved level of ADL. Provision of appropriate energy and protein improves the prognosis of aneurysmal SAH patients.

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