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Effect of early enteral nutrition on critical care outcomes in patients with acute ischemic stroke

Atsushi Mizuma[1], Shizuka Netsu[1], Masaki Sakamoto[2], Sachiko Yutani[1], Eiichiro Nagata[1] and Shunya Takizawa[1]

Abstract

Objective: Stroke-associated pneumonia (SAP) is a comorbidity of ischemic stroke related to clinical outcomes. Early enteral nutrition (EEN; within 48 hours) reduces the incidence of infection and length of intensive care unit (ICU)/hospital stay. The relationship between EEN and critical care outcomes, including SAP, in patients with ischemic stroke has been insufficiently studied.

Methods: We recruited 499 patients in this retrospective observational study. We evaluated SAP incidence within 14 days from admission. Patients were divided into an EEN group and a late EN group (LEN; start later than EEN). We compared groups regarding background and length of ICU/hospital stay.

Results: EN was started within 48 hours in 236 patients. SAP was diagnosed in 94 patients (18.8%), with most in the LEN group (28.1% vs. 8.5%). Median [interquartile range] lengths of hospitalization (22 [12–30] days vs. 35 [20–45] days) and ICU stay (4 [2–5] days vs. 6 [3–8] days) were longer in the LEN group. EEN reduced the incidence of SAP. By contrast, consciousness disturbance and worsening consciousness level increased the SAP incidence. Increased age and National Institutes of Health Stroke Scale score were associated with start of prolonged EN.

Conclusions: We found that EEN may reduce SAP risk.

[1]Department of Neurology, Tokai University School of Medicine, Isehara, Japan
[2]Department of Nursing, Tokai University Hospital, Isehara, Japan

Corresponding author:
Atsushi Mizuma, Department of Neurology, Tokai University School of Medicine, 143 Shimokasuya, Isehara, Kanagawa 259-1193, Japan.
Email: atushi.mizuma@gmail.com

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Introduction

Stroke-associated pneumonia (SAP) is a comorbidity in 20% of patients with acute ischemic stroke (IS),[1] and the development of SAP is associated with increased mortality.[2] Furthermore, early-onset pneumonia (within 72 hours of admission) accounts for 70% of SAP cases.[3] Hence, the timing of enteral nutrition (EN) requires caution and should be delayed in patients with acute IS who have dysphagia. Generally, dysphagia is considered an important risk factor of SAP, which is frequently detected (64%) using swallowing endoscopy within 10 days after the onset of acute IS.[4] Clinically, approximately half of patients with dysphagia develop SAP;[5] hence, early detection and treatment of dysphagia are important. In contrast, early EN (EEN; nutrition started within 48 hours) reportedly reduces the incidence of infection, such as bloodstream infections, and the length of stay in the intensive care unit (ICU) or the hospital.[6–8] However, the mortality rate and organ failure rate have not been clarified with respect to the efficacy of EEN.[8,9]

Previously, we reported the efficacy of early administration of drugs in patients with acute IS, especially cilostazole.[10] Recently, a late start of nutritional support (more than 7 days) has been related to poor clinical prognosis in patients with acute IS who have diabetes mellitus.[11] However, the relationship between EEN and SAP-related critical care outcomes in patients with acute IS has not been sufficiently studied. We hypothesized that EEN can contribute to improved outcomes in patients with acute IS. Thus, in this study, we investigated the introduction of EEN and its benefit according to stroke clinical subtype and severity.

Methods

Study design and ethical considerations

This was a retrospective observational study with participants selected from among 1511 consecutive patients with acute IS admitted to the Department of Neurology, Tokai University Hospital, between April 2009 and March 2014. This study was approved by the Institutional Review Board (IRB) of Tokai University (No. 14R-238). Information about this study was provided to patients via posters at our hospital. Written informed consent was obtained from all recruited patients or their family. The reporting of this study conforms to the STROBE guidelines.[12]

Patient population

The following inclusion criteria were used in the recruitment of study participants: patients admitted within a week after onset of IS and patients whose ischemic lesions were detected using magnetic resonance imaging (MRI). We excluded patients with severe stroke (National Institutes of Health Stroke Scale [NIHSS] score > 22), severe consciousness disturbance (eyes closed), mild stroke (NIHSS score < 4), comorbidity of aspiration pneumonia on admission occurring within

72 hours before starting EN, and discharge time <1 week. The included patients were classified into the following subtypes: atherothrombotic brain infarction, n = 97 (19.4%); cardiogenic embolism, n = 204 (40.9%); lacunar, n = 39 (7.8%); and other, n = 159 (31.9%). The diagnosis and classification of IS were according to the criteria of The Trial of Org 10172 in the Acute Stroke Treatment classification.[13] We collected information regarding the following patient characteristics: age, sex, clinical severity on admission (consciousness state, dysarthria, aphasia, and NIHSS score), worsening of consciousness level within 48 hours of admission, intervention by a speech–language–hearing therapist (ST) within 72 hours, atherosclerotic risk factors (hypertension, diabetes mellitus, and dyslipidemia), acute revascularization therapy (thrombolytic therapy and thrombectomy), MRI findings (infarct volume [small: maximum diameter ≤15 mm, large: larger than one-third the area of each vessel governing region, and medium: other], symptomatic hemorrhagic infarction (HI) [worsening of NIHSS score to ≥4], and site of ischemic lesion (middle cerebral artery [MCA], cortical branch or penetrating branch; anterior cerebral artery; watershed area; posterior cerebral artery; thalamus; brain stem; and cerebellum). We divided patients into two groups, an EEN group and a late EN group (LEN; nutrition start later than EEN). The timing of EN was decided by the attending clinician. We compared the two groups in terms of characteristics, incidence of SAP, and length of ICU/hospital stay. EN was defined as both oral nutrition and tubal feeding (TF). All details of recruited patients with IS were de-identified prior to the analysis.

Definition of aspiration pneumonia

We defined aspiration pneumonia as previously described[14]: (1) body temperature ≥37.5°C in two consecutive measurements or one measurement of 38.0°C; (2) white blood cell count >11,000/μL and chest infiltrates on radiography; and (3) exclusion of other diagnoses.

Primary and secondary outcomes

The primary end point was the incidence of SAP within 14 days of admission according to previous studies. The secondary end points were length of ICU or hospital stay.

Statistical analyses

Statistical analyses were performed using IBM SPSS 26.0 (IBM Corp., Armonk, NY, USA). To account for a lack of randomization, a propensity score-matched analysis was performed. Before matching, chi-square and Mann–Whitney *U* tests were used for categorical data. Propensity scores were developed using a logistic regression model including the following variables; age, disturbance of consciousness, NIHSS score on admission, hemiparesis, dysarthria, aphasia, worsening of clinical symptoms (consciousness level or dysarthria), and hemorrhagic infarction. We used multivariable logistic regression to assess the risk of SAP and start of prolonged EN after matching. All data were nonparametric data and are therefore expressed as median (interquartile range [IQR]). The significance level was set to $p < .05$.

Results

We included 499 patients (307 men and 192 women, mean age ± standard deviation, 73 ± 13 years) in this study. Of the total 449 patients, 236 started receiving EN within 48 hours (EEN group). Table 1 summarizes the patients' background and critical care outcomes. Patients in the LEN group were older than those in the EEN group (median [IQR] 76 years [70–80 years]

Table 1. Patient characteristics.

	EEN group				LEN group			
	Total (n = 236)	SAP+ (n = 20 [8.5%])	SAP− (n=216)	p value comparing SAP+ vs. SAP−	Total (n = 263 [28.1%]***)	SAP+ (n = 74)	SAP− (n = 189)	p value comparing SAP+ vs. SAP−
Age, years[1)]	74	76	73	<.05	76**	78	76	NS
Female, n [%][2)]	81 [34.3]	15 [75.0]	140 [64.8]	NS	111 [42.2]	51 [68.9]	101 [53.4]	<.05
Atherosclerotic risk factors, n [%][2)]								
Hypertension	155 [65.7]	11 [55.0]	144 [66.7]	NS	162 [61.6]	46 [62.2]	116 [61.4]	NS
Diabetes mellitus	69 [29.2]	8 [40.0]	61 [28.2]	NS	67 [25.5]	20 [27.0]	47 [24.9]	NS
Dyslipidemia	114 [48.3]	7 [35.0]	107 [49.5]	NS	111 [42.2]	25 [33.8]	86 [45.5]	NS
Disturbance of consciousness, n [%][2)]	4 [1.7]	0 [0.0]	4 [1.9]	NS	22 [8.4]**	14 [18.9]	8 [4.2]	<.001
NIHSS score on admission[1)]	7	10	7	NS	12***	13 [17.6]	11 [5.8]	<.05
Hemiparesis, n [%][2)]	196 [83.1]	19 [95.0]	177 [81.9]	NS	240 [91.3]**	68 [91.9]	172 [91.0]	NS
Dysarthria, n [%][2)]	162 [68.6]	14 [70.0]	148 [68.5]	NS	221 [84.0]***	63 [85.1]	158 [83.6]	NS
Aphasia, n [%][2)]	66 [28.0]	6 [30.0]	60 [27.8]	NS	97 [36.9]*	29 [39.2]	68 [36.0]	NS
Worsening of consciousness level, n [%][2)]	11 [4.7]	2 [10.0]	9 [4.2]	NS	36 [13.7]**	20 [27.0]	16 [8.5]	<.001
Symptomatic hemorrhagic infarction, n [%][2)]	2 [0.8]	1 [5.0]	1 [0.5]	<.05	17 [6.5]**	12 [16.2]	5 [2.6]	<.001
Revascularization treatment, n [%][2)]	18 [7.6]	3 [15.0]	17 [7.9]	NS	37 [14.1]	15 [20.3]	22 [11.6]	NS
Intervention by a ST within 48 hours, n [%][2)]	42 [17.8]	3 [15.0]	39 [18.1]	NS	40 [15.2]	12 [16.2]	28 [14.8]	NS
Length of hospitalization, days[1)]	22	35	22	<.01	35***	44	33	<.001
Length of ICU stay, days[1)]	4	5	4	NS	6***	8	6	<.001

EEN group vs. LEN group (total); *<.05, **<.01, ***<.001.

[1)] Mann-Whitney U test; [2)] chi-square test.

NIHSS, National Institutes of Health Stroke Scale; ST, speech–language–hearing therapist; SAP, stroke-associated pneumonia; ICU, intensive care unit; NS, non-significant.

vs. 74 years [71–85 years], $p < .01$). Regarding clinical features, patients in the LEN group showed greater severity than those in the EEN group, as follows: median [IQR] NIHSS score on admission (LEN vs. EEN, 12 [4–12] vs. 7 [6–18], $p < .01$), disturbance of consciousness (8.4% vs. 1.7%, $p < .01$), hemiparesis (91.3% vs. 83.1%, $p < .01$), dysarthria (84.0% vs. 68.6%, $p < .001$), aphasia (36.9 vs. 28.0%, $p < .05$), worsening of consciousness level (13.7% vs. 4.7%, $p < .01$), and symptomatic HI (symptomatic: 6.5% vs. 0.8%, $p < .01$).

At 14 days, SAP was diagnosed in 94 (18.8%) of the 499 patients. More patients had SAP in the LEN group than in the EEN group (28.1% vs. 8.5%, $p < .001$). When comparing patients with the presence or absence of SAP (SAP+ vs. SAP−), age (76 [68–79] vs. 73 [65–76], $p < .05$) and symptomatic HI (5.0% vs. 0.5%, $p < .05$) showed significant differences in the EEN group; in contrast, sex (female; 68.9% vs. 53.4%, $p < .05$), disturbance of consciousness (18.9% vs. 4.2%, $p < .001$), median [IQR] NIHSS score on admission (13 [8–15] vs. 11 [6–13], $p < .05$), worsening of consciousness level (27.0% vs. 8.5%, $p < .001$), and symptomatic HI (16.2% vs. 2.6%, $p < .001$]) showed significant differences in the LEN group.

The median [IQR] lengths of hospitalization (22 days [12–30 days] vs. 35 days [20–45 days], $p < .001$) and ICU stay (4 days [2–5 days] vs. 6 days [3–8 days], $p < .001$) were longer in the LEN group than in the EEN group. These trends were also observed in the LEN group for the presence of SAP (SAP+ vs. SAP−, hospitalization: 44 days [34–54 days] vs. 33 days [28–43 days], $p < .001$; ICU stay: 8 days [4–10 days] vs. 6 days [5–7 days]).

The patient distributions according to clinical subtype, infarct size, and site of infarction are shown in Figure 1. We found no significant differences, although cardiogenic embolism, large infarction, and cortical branch of the MCA infarction were more frequently observed in the LEN group.

The multivariate-adjusted associations of SAP with the start of prolonged EN among patients in the acute phase of IS are shown in Tables 2 and 3. Significant interactions were found between the incidence of SAP and increased age (per each 1 year), female sex, disturbance of consciousness, worsening of consciousness level, and EEN (Table 2). In particular, EEN was associated with a risk reduction of SAP, with odds ratio (OR) and (95% confidence interval [CI]) 0.37 (0.21–0.66); $p < .001$. By contrast, disturbance of consciousness (3.67, [1.48–9.06]; $p = .005$), and worsening of consciousness level (3.05, [1.53–6.11], $p = .002$) were risk factors for SAP. Significant interactions were also observed between the start of prolonged EN and increased age (per each 1 year), increased NIHSS score (per each 1 point), dysarthria, worsening of consciousness level, asymptomatic and symptomatic HI, and large-sized infarction (Table 3). In particular, older age (OR 1.02 [95% CI 1.00–1.04]; $p = .013$) and NIHSS score (OR, 1.14 [95% CI 1.09–1.19]; $p < .001$) were associated with the start of prolonged EN.

After propensity score matching, the LEN group still had higher NIHSS scores than the EEN group (Table 4). The median [IQR] lengths of hospitalization (25 days [18–38 days] vs. 39 days [26–56 days], $p < .001$) and ICU stay (5 days [3–7 days] vs. 7 days [5–11 days], $p < .001$) were also longer in the LEN group than in the EEN group. The multivariate-adjusted associations of SAP with the start of prolonged EN among patients in the acute phase of IS after matching are shown in Tables 5 and 6. Significant interactions were found between the incidence of SAP and increased age (per each 1 year: OR, 1.04 [95% CI 1.01–1.07]; $p < .05$) and EEN (Table 5).

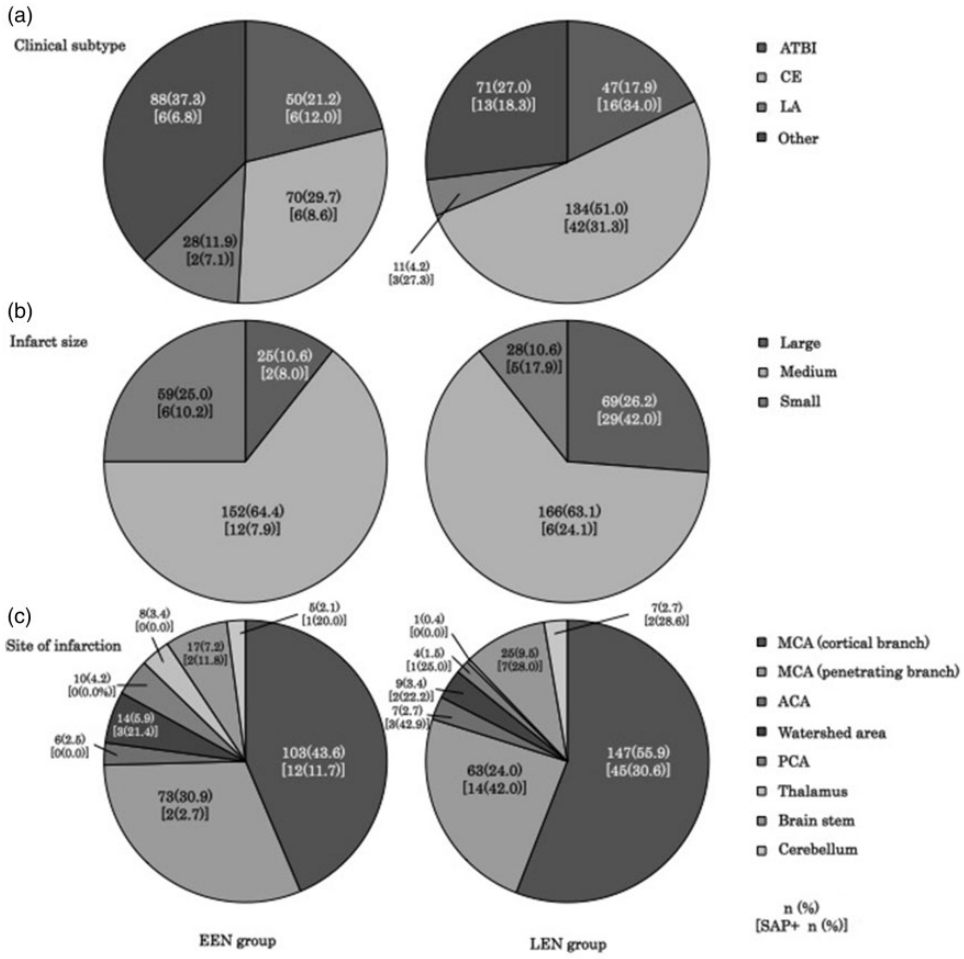

Figure 1. Patient distributions according to clinical subtype, infarct size, and infarction site.
(a) Distribution according to clinical subtype. CE was more frequently seen in the LEN group.
(b) Distribution according to infarct size. Large-sized infarction was more frequently seen in the LEN group.
(c) Distribution according to site of infarction. Cortical branch of MCA infarction was more frequently seen in the LEN group.
ATBI, atherothrombotic brain infarction; CE, cardiogenic embolism; LA, lacunar infarction; MCA, middle cerebral artery; ACA, anterior cerebral artery; PCA, posterior cerebral artery; EEN, early enteral nutrition; LEN, late enteral nutrition; SAP, stroke-associated pneumonia.

EEN was strongly associated with a reduced risk of SAP (OR, 0.31 [95% CI 0.15–0.63]; $p < .001$). Significant interactions were also observed between the start of prolonged EN and dysarthria, worsening of consciousness level, and cardiogenic cerebral infarction (Table 6). In particular, dysarthria (OR, 3.36 [95% CI 1.40–8.04]; $p < .01$) and cardiogenic cerebral infarction (OR, 4.00 [95% CI 1.35–11.84]; $p < .05$) were strongly associated with prolonged EN.

Table 2. Multivariate-adjusted associations for SAP in acute phase of ischemic stroke.

	Odds ratio	95% confidence interval	p value
Older age (each 1 year)	0.97	0.94–0.99	.004
Female sex	2.11	1.21–3.69	.008
Disturbance of consciousness	3.67	1.48–9.06	.005
Increased NIHSS score (each 1 point)	0.97	0.92–1.03	.367
Dysarthria	1.08	0.55–2.13	.817
Worsening of consciousness level	3.05	1.53–6.11	.002
Symptomatic HI	2.59	0.74–9.14	.138
MCA cortical infarction	1.35	0.79–2.31	.265
Cardiogenic cerebral infarction	0.73	0.41–1.30	.282
Large-sized infarction	1.71	0.96–3.05	.068
EEN	0.37	0.21–0.66	<.001
Early intervention by ST	1.29	0.66–2.52	.462

NIHSS, National Institutes of Health Stroke Scale; ST, speech–language–hearing therapist; HI, hemorrhagic infarction; MCA, middle cerebral artery; EEN, early enteral nutrition.

Table 3. Multivariate-adjusted associations for start of prolonged enteral nutrition in acute phase of ischemic stroke.

	Odds ratio	95% confidence interval	p value
Older age (each 1 year)	1.02	1.00–1.04	.013
Female sex	1.23	0.81–1.88	.328
Disturbance of consciousness	0.68	0.21–2.19	.514
Increased NIHSS score (each 1 point)	1.14	1.09–1.19	<.001
Dysarthria	0.48	0.29–0.77	.003
Worsening of consciousness level	0.42	0.19–0.92	.029
Symptomatic HI	0.73	0.14–3.94	.716
MCA cortical infarction	1.02	0.67–1.57	.925
Cardiogenic cerebral infarction	0.88	0.56–1.38	.563
Large-sized infarction	0.53	0.30–0.94	.030

NIHSS, National Institutes of Health Stroke Scale; HI, hemorrhagic infarction; MCA, middle cerebral artery.

Discussion

IS can often be complicated by aspiration pneumonia, especially in association with dysphagia, brainstem lesion, and higher stroke severity (including a high NIHSS score), and in patients receiving nutrition by TF.[5,15–18] The efficacy of EEN has been associated with a reduction in the incidence of infection and the length of ICU/hospital stay in several studies.[4,19] In contrast, the relevance of EEN and the risk of SAP-related clinical outcomes are unclear. In the present study, we clarified the associations of EEN and the incidence of SAP.

The main findings of this study involved the EEN safety, SAP risk reduction, and reduction in the length of ICU and hospital stay among patients with acute IS. We also found that increased age and NIHSS can contribute to the occurrence of SAP. Baseline NIHSS score has been reported to be a predictor of IS outcome.[20] However, EEN may independently contribute to improved IS outcomes with respect to SAP.

Table 4. Patients' characteristics after propensity score-matched analysis.

	EEN group				LEN group			
	Total (n = 69)	SAP+ (n = 20 [29.0%])	SAP− (n = 49)	p value comparing SAP+ vs. SAP−	Total (n = 119)	SAP+ (n = 74 [62.1%]**)	SAP− (n = 45)	p value comparing SAP+ vs. SAP−
Age, years[1)]	75	76	73	NS	78	78	78	NS
Female, n [%][2)]	21 [30.4]	5 [25.0]	16 [32.7]	NS	41[33.6]	23 [31.1]	17 [37.8]	NS
Atherosclerotic risk factors, n [%][2)]								
Hypertension	37 [53.6]	11 [55.0]	26 [53.1]	NS	71 [59.7]	45 [60.8]	26 [57.8]	NS
Diabetes mellitus	15 [21.7]	8 [40.0]	7 [14.3]	NS	29 [24.4]	20 [27.0]	9 [20.0]	NS
Dyslipidemia	33 [47.8]	7 [35.0]	26 [53.1]	NS	42 [35.3]	25 [33.8]	17 [37.8]	NS
Disturbance of consciousness, n [%][2)]	2 [2.9]	0 [0.0]	2 [4.1]	NS	16 [13.4]**	14 [18.9]	2 [4.4]	<.05
NIHSS score on admission[1)]	9	10	9	NS	12 **	13	10	<.05
Hemiparesis, n [%][2)]	60 [87.0]	19 [95.0]	41 [83.7]	NS	108 [90.8]	68 [91.9]	40 [88.9]	NS
Dysarthria, n [%][2)]	48 [69.6]	14 [70.0]	34 [69.4]	NS	102 [85.7]**	63 [85.1]	39 [86.7]	NS
Aphasia, n [%][2)]	21 [30.4]	6 [30.0]	15 [30.6]	NS	43 [36.1]	29 [39.2]	14 [31.1]	NS
Worsening of conscious level, n [%][2)]	7 [10.1]	2 [10.0]	5 [10.2]	NS	29 [24.4]	20 [27.0]	9 [20.0]	NS
Symptomatic HI, n [%][2)]	1 [1.4]	1 [5.0]	0 [0.0]	NS	12 [10.1]*	12 [16.2]	0 [0.0]	<.01
Revascularization treatment, n [%][2)]	8 [11.6]	3 [15.0]	5 [10.2]	NS	19 [16.0]	14 [18.9]	5 [11.1]	NS
Intervention by a ST within 48 hours, n [%][2)]	13 [18.8]	3 [15.0]	10 [20.4]	NS	15 [12.6]	12 [16.2]	3 [6.7]	NS
Length of hospitalization, days[1)]	25	35	23	NS	39***	44	31	NS
Length of ICU stay, days[1)]	5	5	5	NS	7***	8	5	<.05

EEN group vs. LEN group (total): *<.05, **<.01, ***<.001.

[1)] Mann-Whitney U test; [2)] chi-square test.

NIHSS, National Institutes of Health Stroke Scale; ST, speech–language–hearing therapist; SAP, stroke-associated pneumonia; HI, hemorrhagic infarction; ICU, intensive care unit; NS, non-significant.

Table 5. Multivariate-adjusted associations for SAP in acute phase of ischemic stroke after propensity score-matched analysis.

	Odds ratio	95% confidence interval	p value
Increased age (each 1 year)	1.04	1.01–1.07	.02
Female sex	1.67	0.81–3.46	.164
Disturbance of consciousness	3.62	0.85–15.45	.08
Increased NIHSS score (each 1 point)	1.03	0.96–1.10	.378
Dysarthria	0.69	0.29–1.66	.411
Worsening of consciousness level	1.13	0.35–3.64	.819
Symptomatic HI	4.69	0.89–24.70	.069
MCA cortical infarction	1.14	0.58–2.22	.707
Cardiogenic cerebral infarction	2.08	0.87–4.99	.100
Large-sized infarction	1.20	0.56–2.54	.644
EEN	0.31	0.15–0.63	<.001
Early intervention by ST	1.43	0.58–3.51	.438

NIHSS, National Institutes of Health Stroke Scale; ST, speech–language–hearing therapist; HI, hemorrhagic infarction; MCA, middle cerebral artery; EEN, early enteral nutrition.

Table 6. Multivariate-adjusted associations for start of prolonged enteral nutrition in acute phase of ischemic stroke after propensity score-matched analysis.

	Odds ratio	95% confidence interval	p value
Increased age (each 1 year)	1.39	0.66–2.94	.387
Disturbance of consciousness	0.47	0.09–2.39	.364
Increased NIHSS score (each 1 point)	0.98	0.91–1.05	.520
Dysarthria	3.36	1.40–8.04	.007
Worsening of consciousness level	0.42	0.19–0.92	.029
Symptomatic HI	1.71	0.31–9.42	.536
MCA cortical infarction	0.84	0.42–1.66	.606
Cardiogenic cerebral infarction	4.00	1.35–11.84	.012
Large-sized infarction	1.12	0.51–2.46	.781

NIHSS, National Institutes of Health Stroke Scale; HI, hemorrhagic infarction; MCA, middle cerebral artery.

Kudsk et al.[21] and Moore et al.[22] previously reported lowering of the merger rate of pneumonia and sepsis in patients receiving EEN compared with those receiving parenteral nutrition in perioperative management. Maintenance of systemic immune function and biological defense capabilities by preserving gastrointestinal function are expected with EEN. Our study findings showed that this effect of EEN can be expected not only in perioperative patients but also in those with acute IS. EEN combined with probiotics has been reported to improve the nutritional status of patients with IS via regulation of the intestinal flora and intestinal mucosal barrier function, which reduces the incidence of infectious complications and gastrointestinal motility disorders.[23] Hence, EEN might also reduce SAP risk in patients with acute IS by maintaining systemic immune function. In contrast, the associations of dysarthria and cardiogenic cerebral infarction are newly revealed. Although symptomatic HI was not associated with SAP, HI events should be considered

a complication in relation to EEN; a previous study reported that EEN was a risk factor of pneumonia in patients with subarachnoid hemorrhage.[24] Furthermore, the relevance of SAP and sex, arterial fibrillation, and dysphagia have been reported previously,[16,25] although these factors did not have an obvious relationship with SAP in our study. Grouping of patients according to the start time of EN and the limited NIHSS score ranges might be reflected in our results. The present results might have also been affected by the fact that dysphasia was not evaluated, owing to the retrospective nature of our study. A prospective study is necessary to evaluate dysphagia, which might affect the incidence of SAP in the EEN group, along with other factors (e.g., gastrointestinal motility function).

The start of prolonged EN was related to patient severity and risk factors of SAP; hence, EEN was considered carefully in high-risk patients. EEN within 48 hours has been reported to reduce the incidence of infection and length of ICU/hospital stay;[6] however, the incidence of SAP within 72 hours accounted for 70% of IS cases.[26] Moreover, early initiation of TF does not contribute to the improvement of clinical outcomes or reduced mortality in patients with IS and traumatic brain injury.[8,9,17,27,28] Hence, some patients with severe IS were excluded from our study. Evaluation of dysphagia with early intervention by an ST may more precisely distinguish the risk of SAP in severe cases so as to initiate EEN in some patients.

Our study has some limitations. The collected data were from a single center and the sample size was small, which could have underpowered the statistical analysis. Selection bias could also affect the results regarding improvement of outcomes in the EEN group, such as owing to judgment of the start time of EN by the attending physician, different characteristics in each group from a lack of randomization, and the exclusion of mild and severe cases according to NIHSS score. Details of interventions by STs and limitations of swallowing evaluations conducted by STs were unclear. Swallowing evaluation is essential in assessment of the effect of EEN.

In conclusion, EEN may reduce the risk of SAP events, except in certain severe cases. In the future, we aim to conduct a prospective study that includes swallowing evaluations and randomization of cases.

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Authors' Contributions

A. Mizuma wrote the manuscript and prepared the figures and tables. Data collection was performed by A. Mizuma, S. Netsu, M. Sakamoto, and S. Yutani. Data analysis was performed by A. Mizuma. E. Nagata and S. Takizawa developed the study design and revised the manuscript. All authors approved the final version of the manuscript.

Declaration of conflicting interest

The authors declare that there is no conflict of interest.

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ORCID iD

Atsushi Mizuma https://orcid.org/0000-0002-4548-6660

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