

Timing and Outcomes of Percutaneous Endoscopic Gastrostomy After Ischemic Stroke

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Abstract

Background: Guidelines recommend using percutaneous endoscopic gastrostomy (PEG) for dysphagia after 2 weeks of stroke onset. We aimed to study the impact of PEG timing on outcomes in patients with ischemic stroke.

Methods: In this retrospective study of patients with ischemic stroke and PEG between 2014 and 2019, early PEG was defined as PEG tube placed within 14 days of stroke and late PEG after 14 days. Outcomes of 30-day mortality, PEG-related complications, and functional swallow recovery were compared between early and late PEG. Logistic regression model assessed factors associated with PEG timing.

Results: The median time of PEG tube placement after stroke was 10.9 days. Of the 161 included patients, 60.9% had early PEG, and its associated patient factors were nursing facility discharge (adjusted odds ratio (OR): 3.4, confidence interval (CI): 1.48 - 7.82) and infection (OR: 0.32, CI: 0.139 - 0.178). Late PEG had 3.27 times greater odds of swallowing recovery, but mortality and complications were not significantly different between early and late PEG.

Conclusions: Skilled nursing facility disposition and lack of infection were predictors of early PEG, constituting the majority of PEG placed for ischemic stroke-related dysphagia. Although better odds of swallowing recovery were seen with late PEG, likely implicating better patient selection, overall, the timing of PEG tube placement did not impact short-term mortality and complications.

Keywords: Percutaneous endoscopic gastrostomy; Ischemic stroke; Dysphagia; Early PEG; Late PEG

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Introduction

The reported long-term outcomes in patients who receive percutaneous endoscopic gastrostomy (PEG) for stroke-related dysphagia are poor [1, 2], with 2-year mortality as high as 65% and only 14% alive with the regained ability to eat after 2 years of hospitalization. Furthermore, PEG during the index stroke admission is also an independent predictor of 30- and 60-day hospital readmissions [1, 3]. Hence, in patients with dysphagia due to acute stroke, careful patient selection is essential for PEG tube placement, which is, after all, an invasive procedure that is not risk-free [4, 5].

The incidence of dysphagia after acute stroke is greater than 60% [6]. Typically, a nasogastric tube (NGT) or nasoduodenal tube is used initially to administer medications and nutrition, and a PEG is placed later in those with prolonged dysphagia [7]. Regarding timing, the American Stroke Association (ASA) and American Heart Association (AHA) guidelines suggest NGT feeding until 2 - 4 weeks after stroke onset and consider PEG afterward [8]. However, in practice, the PEG tube placement rates in acute ischemic strokes vary widely across US hospitals, and most PEG tube placement happens earlier than the recommended guidelines [9-11]. However, there is a knowledge gap on the factors associated with early vs. late PEG tube placement timing relative to stroke onset and its impact on patient outcomes. The significance of the patient selection criterion is particularly relevant in the widely prevailing heterogeneity in the timing of PEG tube placement in patients with ischemic stroke [12].

We aimed to assess the impact of the timing of PEG tube placement relative to stroke onset on outcomes in patients with dysphagia from an acute ischemic stroke. The primary outcome was 30-day mortality. Secondary outcomes were PEG-related complications and functional swallowing recovery. We also aimed to assess factors associated with the timing of PEG tube placement in patients with acute ischemic stroke.

Materials and Methods

We conducted a retrospective single-center cohort study of all adult patients admitted for an acute ischemic stroke who received a PEG between 2014 and 2019. The study population was limited to ischemic strokes without including hemorrhagic stroke, as the neurological outcomes of hemorrhagic

stroke are very different compared to ischemic stroke [13]. Inclusion criteria were patients with acute ischemic stroke with a PEG placed for dysphagia during the same hospital admission. In our study, early PEG was defined as PEG placed within 14 days of ischemic stroke onset, and late PEG was defined as PEG placed at or 14 days after the ischemic stroke. We used 14 days from stroke onset to classify the timing of PEG, based on the ASA guidelines that recommend choosing NGT for 2 - 3 weeks after stroke. Additionally, this definition was used in a previous study that evaluated the trends of PEG tube timing in stroke patients [3, 8]. We compared outcomes between the patients who received early and late PEG. The primary outcome of our study was 30-day mortality. Secondary outcomes included PEG-related complications and functional swallowing recovery. The complications related to PEG included minor (tube dislodgement, PEG wound leakage, and wound infection) and major complications (peritonitis, gastric perforation, and significant bleeding). Functional swallowing recovery was defined as the ability to independently consume a pre-stroke oral diet and have PEG removed at follow-up visits. Partial recovery was defined as oral intake along with supplemental PEG tube feeding.

International Classification of Disease, Ninth Revision, and Clinical Modification (ICD-9-CM) codes of 434.xx and International Classification of Disease, Tenth Revision, and Clinical Modification (ICD-10-CM) codes of I63.xx were used to identify all cases of ischemic stroke in the study period. In addition, the PEG procedure during the hospital stay was identified by the procedure order (PEG tube placement, AN plc G tube Perc) and the ICD-10-CM of Z 93.1. In addition, medical records were reviewed, and the presence of ischemic stroke was verified based on documentation in the clinical progress notes and findings on diffusion-weighted imaging (DWI) on the brain magnetic resonance imaging (MRI). Among the confirmed patients with ischemic stroke, only those PEG placed due to dysphagia after the index stroke in the same admission were included (Fig. 1), and the rest were excluded.

Patient demographics, comorbidities, stroke-related vascular risk factors, and characteristics were abstracted from medical records. For comorbidity assessment, we utilized the Charlson Comorbidity Index (CCI), an index associated with outcomes and mortality in patients with ischemic stroke [14]. Based on diabetes mellitus, congestive heart failure, chronic obstructive pulmonary disease, chronic kidney disease, malignancies, peripheral vascular disease, and dementia, the CCI score was calculated to categorize them into three groups: mild (CCI score 1 - 2), moderate (CCI score 3 - 4), and severe (CCI score > 5). In addition, mechanical ventilation, tracheostomy status, and infections, including sepsis, pneumonia, urinary tract infections, and complications after PEG tube placement, were collected. The mean follow-up period of our study was 5.4 months. The study was conducted in accordance with the approval of the institutional review board in compliance with all the applicable institutional ethical guidelines for the care, welfare and use of animals.

Data analysis

The data were analyzed to estimate 30-day mortality (primary outcome), PEG-related complications, and functional swal-

low recovery after PEG removal (secondary outcomes). Data were described using descriptive statistics, and non-parametric methods were employed when data were not normally distributed. Continuous data were compared between groups with two-group *t*-tests or Wilcoxon rank-sum (Mann-Whitney) test as appropriate. The Chi-square test compared categorical data. Logistic regression was used to study the effect of PEG timing on dichotomous outcomes of 30-day mortality, PEG-related complications, and swallowing recovery. Clinical factors associated with early compared to late PEG tube placement were identified by univariable analysis with an alpha of 0.2 cut-offs, followed by multivariable logistic regression analysis. A backward stepwise selection method was implemented for variable selection, and statistical significance was defined as an alpha of 0.05, with two-sided alternative hypotheses. Data were analyzed using STATA® Version 17 (StataCorp, College Station, TX).

Results

Distribution and demographics

A total of 6,418 ischemic stroke patients were identified based on ICD codes (Fig. 1). Of these, 268 (4.2%) were identified as having PEG. Of the 268 patients, 70 were excluded after chart review as they did not have an ischemic stroke. Of the 198 patients with confirmed ischemic stroke and PEG, 37 were excluded as they had PEG placed before the ischemic stroke for dysphagia unrelated to the stroke. The final cohort comprised 161 patients with ischemic stroke and gastrostomy tubes placed after the index stroke.

The incidence of gastrostomy tubes in patients with ischemic stroke was 2.54%. Overall, the median time of PEG tube placement after ischemic stroke was 10.9 days (interquartile range (IQR): 7.6 - 17.9). Of them, 60.9% ($n = 98$) had an early PEG with a median duration of 8.4 days (IQR: 6.2 - 11.8) (Fig. 2). The clinical characteristics of the cohort and a comparison between the two groups of early and late PEG are shown in Table 1. The two groups had no significant difference in patient demographics, clinical features, comorbidities, and stroke severity based on National Institute of Health Stroke Scale (NIHSS) scores (16 vs. 17; $P = 0.968$). However, early PEG was associated with a significantly shorter length of stay (mean 15.8 vs. 20.11; $P = 0.029$).

The association of the timing of PEG with primary and secondary outcomes

The overall 30-day mortality of the cohort was 6.8% ($n = 11$). The 30-day mortality was not significantly different between early and late PEG (7.14% vs. 6.35%, $P = 0.558$) (Table 2). The functional swallow recovery rate in the cohort was 26.7% ($n = 43$), and it was significantly higher in the late PEG compared to early PEG at a mean follow-up of 5.4 months (36.51% vs. 20.41%, respectively; $P = 0.024$). In the multiple logistic regression model, those patients with late PEG had 3.27 times greater odds of swallowing recovery and PEG removal

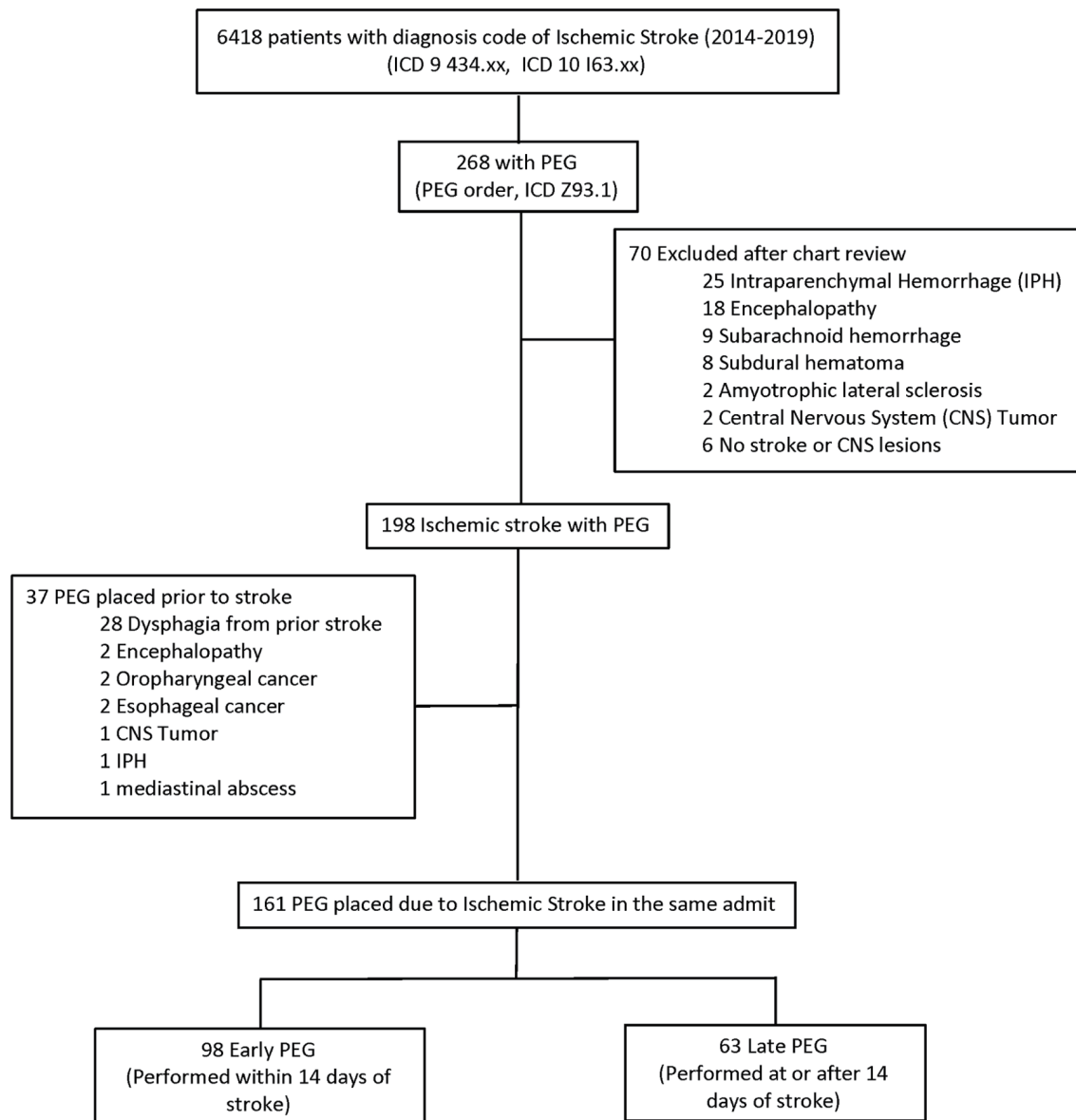


Figure 1. Distribution of the cohort.

after adjusting for covariates, including age, gender, race comorbidities, and stroke severity (adjusted OR: 3.27; 95% CI: 1.22 - 8.74; $P = 0.02$). A low NIHSS score was the other factor that predicted swallowing recovery with PEG removal in this model (Table 3).

There were no significant differences in overall PEG-associated complications between late PEG and early PEG (3.2% vs. 9.2%; $P = 0.204$). Our study had two major PEG-related complications (1.24%): one case of PEG malposition in the transverse colon and one case of gastric wall necrosis at the gastrostomy tube site that required partial gastric resection. The minor PEG-related complications included four dislodged gastrostomies, one G-tube leakage, one G-tube clog, and one G-tube malposition, most requiring PEG tube replacement. In addition, 75.8% of patients in the cohort were on uninter-

rupted antiplatelet (100 aspirin + 9 dual antiplatelet therapy with aspirin and clopidogrel) or anticoagulation therapy ($n = 13$ including intravenous heparin drip held 6 h prior to procedure; enoxaparin and apixaban with morning of procedure dose held). No direct PEG procedure-related gastrointestinal bleeding was observed in our cohort.

Patient factors associated with the timing of PEG tube placement

In order to evaluate the factors associated with the timing of PEG relative to stroke onset, we performed a univariate followed by multivariable regression analysis (Table 4). After adjusting for age, sex, comorbidities, intubation, tracheostomy

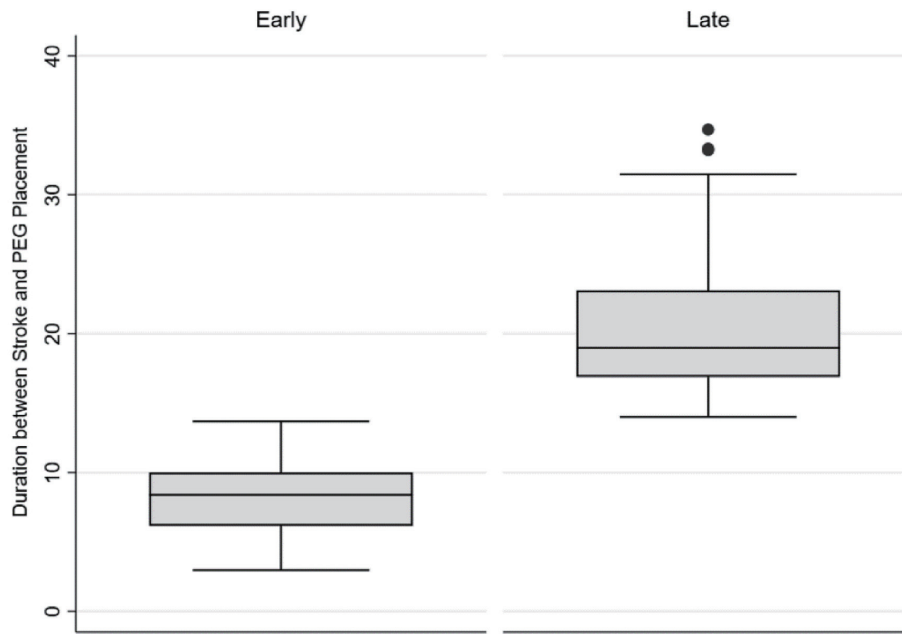


Figure 2. Distribution of median time from stroke to PEG in early vs. late PEG. PEG: percutaneous endoscopic gastrostomy.

Table 1. Patient Demographics and Comorbidities in the Early and Late PEG Groups

Characteristics	n	All PEG	Early PEG (n = 98)	Late PEG (n = 63)	P-value
Age, years, median (IQR)	161	66 (63 - 75)	67 (56 - 77)	65 (50 - 72)	0.055
Age, years, N (%)					0.464
< 65		74 (45.9)	43 (43.9)	31 (49.2)	
65 - 75		51 (31.7)	29 (29.6)	22 (34.9)	
75 - 85		28 (17.4)	20 (20.8)	8 (12.7)	
> 85		8 (4.9)	6 (6.1)	2 (3.17)	
Gender, male, N (%)		99 (61.5)	56 (57.1)	43 (68.2)	0.157
Race/ethnicity, N (%)					0.871
Non-Hispanic White		89 (55.3)	52 (53.1)	37 (58.7)	
Hispanic		37 (22.9)	23 (23.5)	14 (22.2)	
Black		16 (9.9)	11 (11.2)	5 (7.9)	
Other		19 (11.8)	12 (12.2)	7 (11.1)	
Comorbidities, N (%)	161				0.351
CCI score: 1 - 2		34 (21.1)	23 (23.5)	11 (17.5)	
CCI score: 3 - 4		71 (44.1)	45 (45.9)	26 (41.3)	
CCI score: > 5		56 (34.8)	30 (30.6)	26 (41.3)	
Atrial fibrillation, N (%)		62 (38.5)	38 (38.8)	24 (38.1)	0.931
Mechanical ventilation, N (%)		83 (51.5)	46 (46.9)	37 (58.7)	0.144
Tracheostomy, N (%)		38 (23.7)	25 (25.77)	13 (20.63)	0.456
Hospital length of stay, mean (SD)		17.4 (12.9)	15.8 (1.4)	20.11 (14.8)	0.029
Stroke characteristics					
NIHSS, median (IQR)	120	16.5 (7 - 23.5)	16 (7 - 24)	17 (7 - 23)	0.968

CCI: Charlson Comorbidity Index; IQR: interquartile range; PEG: percutaneous endoscopic gastrostomy; SD: standard deviaton; NIHSS: National Institute of Health Stroke Scale.

Table 2. Primary and Secondary Outcomes in the Early and Late PEG Groups

Characteristics	Early PEG (n = 98)	Late PEG (n = 63)	P-value
30-day mortality	7 (7.14)	4 (6.35)	0.558
PEG-related complications, N (%)	9 (9.18)	2 (3.17)	0.204
PEG removal and functional swallow recovery			
PEG removed, N (%)	20 (20.41)	23 (36.51)	0.024
PEG present, partial swallow recovery, N (%)	10 (10.20)	8 (12.7)	0.624
PEG dependent, N (%)	46 (46.94)	26 (41.27)	0.48

PEG: percutaneous endoscopic gastrostomy.

Table 3. Univariable and Multivariable Logistic Regression Model for PEG Removal and Swallowing Recovery

Patient characteristics	Univariable			Multivariable		
	Odds ratio	95% CI	P-value	Odds ratio	95% CI	P-value
Age, years	0.97	0.95 - 0.99	0.08	-	-	-
Male gender (compared to females)	0.70	0.34 - 1.47	0.35	-	-	-
Late PEG (compared to early PEG)	2.24	1.10 - 4.56	0.03	3.27	1.22 - 8.74	0.02
Hispanic race (compared to white)	0.56	0.15 - 2.12	0.39	-	-	-
Black race (compared to white)	0.57	0.22 - 1.45	0.2	-	-	-
Other race (compared to white)	1.41	0.50 - 3.99	0.51	-	-	-
NIHSS	0.95	0.91 - 0.99	0.04	0.95	0.89 - 0.99	0.045
CCI score: 3 - 4 (compared to 1 - 2)	0.82	0.35 - 1.95	0.66	-	-	-
CCI score > 5 (compared to 1 - 2)	0.35	0.13 - 0.95	0.04	-	-	-
Palliative care	0.22	0.05 - 0.99	0.48	-	-	-

Dash (-) indicates that the variable was included in the multivariable model but was not statistically significant. CCI: Charles Comorbidity Index; CI: confidence interval; NIHSS: National Institute of Health Stroke Scale; PEG: percutaneous endoscopic gastrostomy.

Table 4. Univariable and Multivariable Logistic Regression Model Assessing the Association Between Early PEG and Patient Factors

Patient characteristics	Univariable			Multivariable		
	Odds ratio	95% CI	P-value	Odds ratio	95% CI	P-value
Age, years	1.08	0.99 - 1.04	0.07	-	-	-
Male gender (compared to females)	1.6	0.83 - 3.13	0.16	-	-	-
Race	1.07	0.81 - 1.43	0.61	-	-	-
CCI score	0.73	0.47 - 1.13	0.16	-	-	-
NIHSS	0.99	0.96 - 1.03	0.92	0.95	0.90 - 0.99	0.02
Speech therapy evaluation	0.69	0.31 - 1.53	0.36	-	-	-
Tracheostomy status	1.33	0.62 - 2.85	0.46	-	-	-
Intubation status	0.62	0.33 - 1.18	0.16	-	-	-
All infection	0.54	0.28 - 1.01	0.06	0.32	0.14 - 0.73	0.007
Hospice (compared to home/acute rehabilitation)	1.89	0.42 - 8.6	0.41	-	-	-
SNF (compared to home/Acute rehabilitation facility)	2.69	1.37 - 5.28	0.004	3.4	1.48 - 7.8	0.004

Dash (-) indicates that the variable was included in the multivariable model but was not statistically significant. CCI: Charles Comorbidity Index; CI: confidence interval; NIHSS: National Institute of Health Stroke Scale; PEG: percutaneous endoscopic gastrostomy; SNF: skilled nursing facility.

status, and length of stay, those discharged to a skilled nursing facility after an ischemic stroke had 3.4 times higher odds of receiving an early PEG tube placement (adjusted odds ratio (OR): 3.4, confidence interval (CI): 1.48 - 7.82, $P = 0.004$) than those discharged to home or acute rehabilitation. In addition, those with infection during the ischemic stroke-related hospital stay (including sepsis from any cause, pneumonia, and urinary tract infection) had lower odds of having an early PEG (adjusted OR: 0.32, CI: 0.139 - 0.178, $P = 0.007$).

Discussion

The incidence of PEG tube placement for dysphagia after an acute ischemic stroke was 2.54% in our cohort. The majority (60.9%, $n = 63$) had an early PEG within 2 weeks of acute ischemic stroke. Disposition to a skilled nursing facility from the stroke hospital admission was associated with 3.4 times higher odds of receiving an early PEG. In addition, sepsis and infection during the stroke hospital admission were associated with 0.32 times lower odds of early PEG. Although late PEG had higher odds of functional swallowing recovery and PEG removal at follow-up, we did not find significant differences in the 30-day mortality and PEG-related complications between early and late PEG groups. Our results suggest that patients who received PEG after 14 days were adequately prepared for PEG construction.

A PEG tube was placed at a median of 10.9 days after the stroke. The distribution of early vs. late PEG in our study is aligned with the previously reported discrepancy between guidelines and practice trends in PEG tube placement across the USA. However, our late PEG rate of 39% is higher than that reported in previous studies. For example, a state inpatient database study on PEG after an acute stroke had a 14% prevalence of late PEG [9], and another study utilized National Inpatient Sample (NIS) data to study PEG timing in patients with ischemic stroke, where greater than 50% PEG happened within a week of admission [10]. Differences in dysphagia assessments of speech pathologists [15], physicians overestimating PEG benefits, and lack of awareness of late PEG benefits among providers are some of the speculated factors associated with varied PEG practices of nationwide hospitals after stroke [10, 11, 16].

In our study, discharge to a skilled nursing facility was associated with early PEG tube placement. Previous studies have speculated that policies of skilled nursing homes and their preferences for accepting PEG due to potential NGT dislodgement might contribute to early PEG tube placement [17]. Consistent with this association are findings of a nationwide survey study of speech pathologists that system pressures for early discharge influenced 35% of their recommendations for PEG tube placement [15]. Whether the disposition to skilled nursing influenced the decision for early PEG tube placement within 2 weeks of acute stroke and whether this practice, to facilitate early discharge to a skilled nursing facility, might over-select patients for the PEG procedure remains to be investigated further. Incorporating a multidisciplinary approach with the palliative care team while focusing on patient care

goals in PEG tube placement, using a nasal bridle in patients who temporarily need NGT to recover swallowing or wish not to get a PEG due to their poor prognosis, and improving education among providers and the nursing homes are some of the proposed solutions [18, 19]. The validated objective tools such as the validated Sheffield Gastrostomy Scoring System (SGSS) and predictive swallowing score to predict swallowing recovery in those with dysphagia from ischemic strokes are important clinical tools that can help clinicians and family members in identifying those who would benefit from a feeding tube [20-22]. In addition, in our study, we found that those with infections including pneumonia, urinary tract infections, and sepsis during the stroke hospitalization had lower odds of receiving an early PEG, likely reflecting that these patients were sicker from non-stroke-related issues that delayed the PEG tube placement decision. In comparison, a previous study that looked at factors associated with PEG timing found older age and large stroke volume to be associated with early PEG, placed within a week of stroke [10].

Although the 30-day mortality rate between early and late PEG in our study was not significantly different, the findings of more significant swallowing recovery followed by PEG removal support the guideline recommendations of PEG timing in stroke. In order to manage dysphagia after stroke in the first 2 - 3 weeks, the guidelines recommend placing an NGT [8], which helps appropriate patient selection for PEG in stroke by limiting its use to those with persistent dysphagia. A possible explanation for our findings of greater odds of swallowing recovery in the late PEG group may be attributed to better patient selection based on the independent association of swallowing recovery with NIHSS score. In addition, the effect of intense speech therapy services that this group had more access to, as those with late PEG were frequently discharged to an acute rehabilitation facility, might have played a role. Finally, dependency on PEG caused by its early placement might negatively impact swallowing recovery. Similar to our study, the authors of the FOOD randomized controlled trial found that more patients in the early PEG group remained PEG dependent at follow-up, in contrast with the NGT group, in which only 30% of patients randomized to NGT feeding ended up receiving PEG later [23]. With no difference in the two groups, the rate of post-PEG complications was 6.8%, which is similar to the reported rate in the literature [4]. Interestingly, our cohort did not have any direct PEG-related bleeding complications, despite 75.8% of patients being on peri-procedural antiplatelet or anticoagulation therapy. This is consistent with findings of recent studies, including a meta-analysis of 12 studies that included 8,471 patients, where antiplatelet therapy did not increase the risk of bleeding after PEG [24].

Here we review the literature on the outcomes of PEG after an ischemic stroke based on the timing of its placement. The PEG vs. NGT arm trial of multicenter randomized controlled FOOD trial studied the effect of the route of the enteral tube and timing on outcomes and found that early PEG in a week of stroke was associated with an increased borderline significance of the absolute risk of death [23]. A recent large observational study of patients that included both ischemic stroke and intracerebral hemorrhage found that gastrostomy and jejunostomy tubes placed within week 1 of stroke had sig-

nificantly greater 30-day mortality than those placed after 5 weeks. However, a severe disability with a modified Rankin Scale (MRS) of 4 - 5 at discharge was also noted in these late tube placement survivors. Unlike our study, patients who died after early PEG more commonly had dementia, advanced age, and greater stroke severity [25]. Another observational study of 154 patients did not show any difference in 30-day mortality similar to our results, although the authors considered early PEG as those placed within 7 days of stroke [26]. On the contrary, a systemic review that evaluated the effectiveness and safety of PEG as opposed to NGT in adults with dysphagia, not limited to stroke, found that PEG had lower chances of intervention failure. There was no significant difference in mortality between the two groups. The evidence, however, was of low quality [27].

Our study has several limitations. First, it is a retrospective study. Second, there might be residual confounding even after matching factors such as stroke severity, medical comorbidities, and age that could have affected our study results. Third, we acknowledge a loss to follow up with both groups in evaluating and comparing swallowing recovery between early and late PEG. However, this was non-differential as the baseline characteristics between the two groups were not statistically different. Lastly, we could not capture and adjust for the mRS in all the patients. Despite these weaknesses, we believe our study findings are significant in the context of varied PEG practices and will aid provider in decision-making on the placement of PEG in acute ischemic stroke.

In conclusion, consistent with current PEG practice patterns in the USA, most PEG tubes were placed within 2 weeks of stroke. Disposition to a skilled nursing facility and lack of infection during hospitalization were significant predictors of early PEG tube placement. Despite greater odds of swallowing recovery with less PEG dependency at follow-up in the late PEG group, no differences in 30-day mortality and post-PEG complications were seen between early and late PEG groups. Our results suggest that patients who received a late PEG after 14 days were adequately prepared for PEG construction. In the current era of widely varied PEG timing practices across the USA, with the potential influence of the health care system, education on the timing of PEG among providers and facilities might standardize the management of acute stroke-related dysphagia.

Acknowledgments

None to declare.

Financial Disclosure

None to declare.

Conflict of Interest

None to declare.

Informed Consent

Given the retrospective nature of the study, informed consent was waived.

Author Contributions

Shoma Bommena: conceptualization; investigation; methodology; validation; visualization; writing - initial draft and revisions. Pooja Rangan: methodology; statistical analysis. Joyce Lee-Iannotti: methodology; review and editing. Wahid Wassef: methodology; review and editing. Rakesh Nanda: conceptualization, methodology; review, and editing.

Data Availability

Any inquiries regarding supporting data availability of this study should be directed to the corresponding author.

Abbreviations

AHA: American Heart Association; ASA: American Stroke Association; CCI: Charlson Comorbidity Index; DWI: diffusion-weighted imaging; ICD: International Classification of Diseases; MBS: modified barium swallow; MRI: magnetic resonance imaging; NGT: nasogastric tube; NIHSS: National Institute of Health Stroke Scale; PEG: percutaneous endoscopic gastrostomy

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