

Semi-solid feeds may reduce the risk of aspiration pneumonia and shorten postoperative length of stay after percutaneous endoscopic gastrostomy (PEG)

Authors

Ezekiel Wong Toh Yoon¹, Kaori Yoneda², Kazuki Nishihara¹

Institutions

¹ Department of Internal Medicine (Gastroenterology), Hiroshima Kyoritsu Hospital, Hiroshima City, Japan

² Endoscopy Center, Hiroshima Kyoritsu Hospital, Hiroshima City, Japan

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Bibliography

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Corresponding author

Ezekiel Wong Toh Yoon, MD
Department of Internal
Medicine
Hiroshima Kyoritsu Hospital
2-20-20 Nakasu Asaminami-ku
Hiroshima City
Japan
Phone: +81-82-879-1111
easybs@hotmail.com

Background and study aims: Feeding-related adverse events after percutaneous endoscopic gastrostomy (PEG) such as aspiration pneumonia may result in prolonged hospitalization and postoperative mortality. This study evaluated the efficacy of using semi-solid feeds to reduce feeding-related adverse events and improve clinical outcomes.

Patients and methods: Patients who received PEG for enteral nutrition at our hospital between January 2014 and December 2015 were allocated to a postoperative feeding protocol that used either liquid feed or semi-solid feed. Baseline characteristics, postoperative feeding-related adverse events and clinical outcomes in the 2 groups were prospectively analysed and compared.

Results: One hundred and seventeen PEG patients (age range: 59–97 years, male: 53) were enrolled

with 72 patients given liquid feed and 45 patients receiving semi-solid feed. Baseline characteristics were similar in both groups. The semi-solid feed group experienced fewer incidence of feeding-related aspiration pneumonia (2.2% vs. 22.2%, $P < 0.005$) and shorter postoperative hospital length of stay (12.7 days vs. 18.8 days, $P < 0.01$). Significant differences were not observed in the frequency of peristomal infection (11.1% vs. 12.5%, $P = 0.82$), feeding-related diarrhea (2.2% vs. 12.5%, $P = 0.09$) and 30-day mortality rates (2.2% vs. 8.3%, $P = 0.25$).

Conclusions: Semi-solid feeding may reduce the risk of aspiration pneumonia and shorten postoperative hospital length of stay after PEG. Semi-solid feeds are safe to use and can be employed either as a first line feeding protocol or an alternative when liquid feeding is unsuccessful.

Introduction

Percutaneous endoscopic gastrostomy (PEG) is a minimally invasive procedure for long-term enteral tube feeding in patients with insufficient oral intake [1–3]. Although peristomal site infection is often noted as the most common adverse event (AE) after PEG tube placement, it is seldom life-threatening and considered a minor AE [4]. Feeding-related AEs have been identified as the main cause of death after PEG, with up to 50% of postoperative early mortality (30 days) being attributed to aspiration pneumonia [5,6]. This may be related to the persistence of gastroesophageal reflux (GER) of enteral feed after gastrostomy [7], even though PEG has been demonstrated to be superior to nasogastric tube feeding in terms of preventing GER [8,9].

Recently, elemental diet (monomeric feed) has been shown to reduce the incidence of aspiration pneumonia [10]. However, limitations such as high cost, high osmolality, and almost zero lipid content may be an obstacle to the general use of

this specialized feed. It has been more than a decade since semi-solid feeds were developed as an alternative to conventional liquid feeds to prevent feeding-related AEs [11,12]. Unfortunately, there is limited published literature on this topic despite the wide usage of this feeding method in Japan. Amidst the growing popularity of this method and the introduction of National Healthcare Insurance coverage for a semi-solid feed prescription, we initiated a semi-solid feed protocol along with our existing post-PEG feeding protocols in 2014. In this study (NCT02858596), we prospectively evaluated the safety and efficacy of using semi-solid feed compared to conventional liquid feed using clinical outcomes of interests such as the development of feeding-related AEs, postoperative hospital length of stay and mortality.

License terms



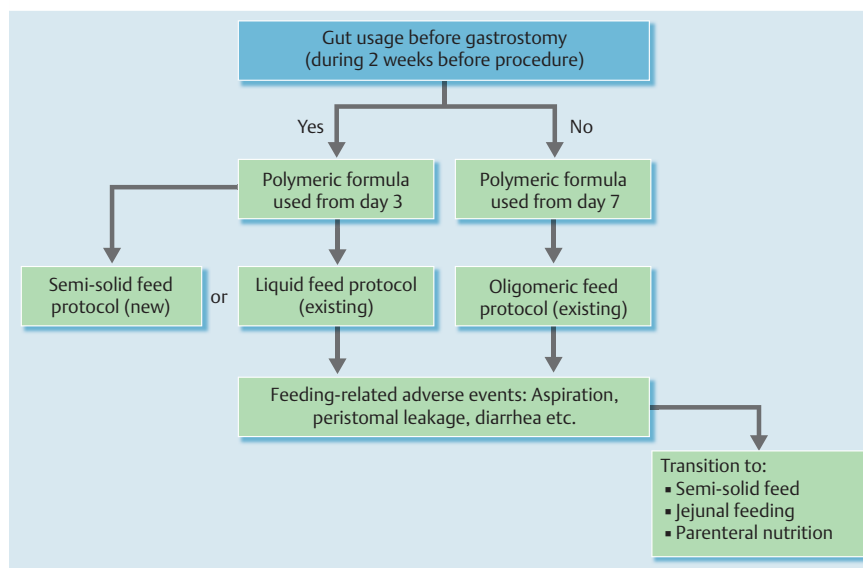


Fig. 1 Feeding protocols after percutaneous endoscopic gastrostomy (PEG) in Hiroshima Kyoritsu Hospital.

Patients and methods

Study design and patients

Patients who received PEG for enteral nutrition at our hospital between January 2014 and December 2015 with the usage of gut (oral or nasogastric feeding) during the 2 weeks prior to procedure were allocated to receive a feeding protocol using either liquid feed or semi-solid feed. Gastrostomy tube used was 20 Fr in size for all patients. Patient allocation depended on the attending physician ordering the procedure with most of the selection performed in a quasi-randomized manner. Patients with no recorded gut usage 2 weeks prior to PEG were given a slower feeding protocol starting with an oligomeric feed and not included in the study. This exclusion was to increase the homogeneity between the intervention (semi-solid feed) and control (liquid feed) groups in terms of baseline characteristics and protocol length. Likewise, procedure-related mortality cases (<1%) were also excluded because the feeding protocol assigned could not be sufficiently evaluated. **Fig. 1** summarizes the different postoperative feeding protocols used in our hospital.

The total amount and daily increment of tube feeding calories and water as well as the changes in parenteral nutrition used to supplement enteral feeding were the same for both the liquid feed and semi-solid feed groups. However, the increment in calories and water was stopped once daily requirements, as calculated by our nutrition support team, were reached. The characteristics and nutrient data of enteral feed used are shown in **Table 1**, with the major difference being the dynamic viscosity of the feeds. Liquid feeds were administered using gravity-controlled infusion (averaging 100 to 200 mL/hr) from a ready-to-hang bag whereas semi-solid feeds were injected directly into the stomach using a syringe via bolus infusion (5 to 10 minutes). For both groups, tube feeding was conducted intermittently according to meal times with gravity-controlled water administration (supplemented to match daily requirements) before infusion of feeds. After discharge, patients receiving semi-solid feed continue to receive the same type of prescription feed as currently covered by National Healthcare Insurance in Japan.

Data regarding baseline characteristics such as age, gender, comorbidities, and preoperative biomarkers (body mass index and blood laboratory markers collected on the day of procedure) as

Table 1 Characteristics and nutrient data of enteral feed used.

Characteristics per 100 kcal	Liquid feed ¹	Semi-solid feed ²
Total weight, g	100	66.7
Protein, g	4	4
Fat, g	2.8	2.2
Carbohydrate, g	14.5	16.1
Dietary Fiber, g	1	0.4
Water, ml	84.5	44
Dynamic viscosity, mPa·s (or cP)	5–10	20,000

¹ Meiji's Mei Balance 1.0 Z (Meiji Holdings Co., Ltd., Tokyo, Japan)

² PG Soft (Terumo Corporation, Tokyo, Japan)

well as postoperative findings such as laboratory biomarker changes at day 7 after the procedure, AEs (feeding-related aspiration pneumonia, diarrhea etc.) and clinical outcomes of interest (postoperative length of stay and mortality) were compared for the 2 groups studied. Feeding-related aspiration pneumonia was diagnosed using clinical symptoms, with confirmation through radiologic findings or detection of enteral feed in the patient's trachea aspirate. Peristomal infection was assessed 1 week after the procedure using a previously validated scoring system (Jain's infection score) by assigning a score for erythema (0 to 4), induration (0 to 3) and exudate (0 to 4) [13]. Infection was defined as development of pus or a combined infection score of 8 or more. Diarrhea was evaluated using the King's Stool Chart and feeding-related diarrhea was defined as an absolute daily fecal score of 15 or more after ruling out other causes such as drug-induced diarrhea or *Clostridium difficile* infection [14]. This study protocol was reviewed and approved by the ethics review committee of Hiroshima Kyoritsu Hospital. All patients, or their legal guardians, provided written informed consent for the procedures as well as enrollment in the study. The research was carried out in accordance with Japan's Ethical Guidelines for Epidemiological Research (2008) and the Declaration of Helsinki (2013).

Statistical analysis

Continuous variables are expressed as mean (standard deviation with range occasionally). Categorical variables are expressed as numbers (percentage). Comparisons for continuous variables were made using the Student *t*-test for normal data and the

	Liquid feed (n=72)	Semi-solid feed (n=45)	P value
Age, years, mean (SD, range)	81.0 (9.1, 59–97)	80.7 (8.3, 61–95)	0.76
Gender (male/female)	33/39	20/25	0.88
Comorbidities			
Stroke, n (%)	53 (73.6)	36 (80)	0.43
Antithrombotic therapy, n (%)	26 (36.1)	17 (37.8)	0.86
Dementia, n (%)	29 (40.3)	13 (28.9)	0.21
Neurodegenerative disorders, n (%)	11 (15.3)	7 (15.6)	0.97
Respiratory disorders, n (%)	35 (48.6)	19 (42.2)	0.50
Diabetes mellitus, n (%)	16 (22.2)	14 (31.1)	0.28
Pressure ulcer, n (%)	17 (23.6)	8 (17.8)	0.45
Malignancy, n (%)	11 (15.3)	5 (11.1)	0.52
Partial gastric resection, n (%)	2 (2.8)	1 (2.2)	1.00
Hiatal hernia (> moderate size), n (%)	2 (2.8)	2 (4.4)	0.64
Preoperative biomarkers			
Body mass index, kg/m ² , mean (SD)	17.9 (3.6)	18.0 (3.0)	0.67
Hemoglobin, g/dL, mean (SD)	11.6 (1.8)	11.3 (2.0)	0.52
Serum albumin, g/dL, mean (SD)	2.8 (0.5)	2.9 (0.6)	0.34
TLC, /μL, mean (SD)	1508 (863)	1532 (701)	0.61
C-reactive protein, mg/dL, mean (SD)	2.4 (2.9)	1.8 (2.7)	0.15
Total cholesterol, mg/dL, mean (SD)	152 (44)	151 (31)	0.82
Blood urea nitrogen, mg/dL, mean (SD)	23.7 (17.8)	22.8 (14.0)	0.75
PT-INR, mean (SD)	1.20 (0.23)	1.13 (0.11)	0.07

Table 2 Baseline characteristics of patients.

SD, standard deviation; TLC, total lymphocyte count; PT-INR, international normalized ratio of prothrombin time.

	Liquid feed (n=72)	Semi-solid feed (n=45)	P value
Biomarker changes at day 7			
Δ Hemoglobin, g/dL, mean (SD)	−0.6 (0.9)	−0.5 (1.2)	0.48
Δ C-reactive protein, mg/dL, mean (SD)	0.3 (3.8)	0.4 (3.2)	0.79
Δ Serum albumin, g/dL, mean (SD)	−0.1 (0.3)	−0.1 (0.4)	0.61
Δ Blood urea nitrogen, mg/dL, mean (SD)	−0.8 (8.9)	0.6 (7.8)	0.95
Adverse events			
Feeding-related aspiration pneumonia	16 (22.2)	1 (2.2)	<0.005
Peristomal infection	9 (12.5)	5 (11.1)	0.82
Jain's infection score, mean (SD)	1.5 (1.6)	1.2 (1.3)	0.24
Feeding-related diarrhea	9 (12.5)	1 (2.2)	0.09
Tube obstruction	0 (0)	0 (0)	N/A
Clinical outcomes			
Length of stay, days, mean (SD)	18.8 (13.4)	12.7 (7.5)	<0.01
In-hospital mortality	9 (12.5)	1 (2.2)	0.09
14-day mortality	3 (4.2)	1 (2.2)	1.00
30-day mortality	6 (8.3)	1 (2.2)	0.25
60-day mortality	9 (12.5)	2 (4.4)	0.20
90-day mortality	11 (15.3)	4 (8.9)	0.40
30-day readmission after discharge	3 (4.8)	0 (0)	0.05

Table 3 Postoperative clinical course of patients.

Values expressed as n (%) unless otherwise specified. N/A: Not applicable.

Mann-Whitney U test for non-parametric data. Tests for proportionality between groups were made using the chi-square test (or Fisher's exact test when indicated). Logistic regression and analysis of covariance were used to evaluate possible factors that may be associated with the development of feeding-related aspiration pneumonia and postoperative length of stay. The number needed to treat (and 95% confidence interval) for feeding-related pneumonia was also calculated. Statistical significance was defined as $P < 0.05$ and analysis was performed using XLSTAT2014 for Windows (Addinsoft Ltd., Paris, France).

Results



In total, 117 patients (age range: 59–97 years, male: 53) were included in the study. Seventy-two patients were given liquid feed protocols while 45 patients received semi-solid feed protocols. Baseline characteristics of patients (age, gender, comorbidities and preoperative biomarkers) are listed in **Table 2**. There were no significant differences at baseline, including the frequency of comorbidities that may affect gastric motility such as previous gastric resection and hiatal hernia (moderate size and above) between the 2 groups. Indications for PEG were primarily dysphagia secondary to neurologic impairments or insufficient oral intake

Table 4 Factors associated with postoperative length of stay (analysis of covariance).

Variable	β (95% CI) ¹	P value
Age	0.09 (-0.28 to 0.10)	0.35
Male gender	0.08 (-0.12 to 0.27)	0.43
Preoperative serum albumin	0.02 (-0.18 to 0.22)	0.84
Preoperative C-reactive protein	0.20 (0.01 to 0.40)	<0.05
Semi-solid feed protocol	-0.23 (-0.41 to -0.06)	<0.01

¹ Standardized coefficients with 95% confidence interval using all variables listed in table. (Model's adjusted $R^2=0.13$; $F_{5,111}=3.21$, $P<0.01$)

due to various underlying conditions as listed in the comorbidities section.

► **Table 3** summarizes the postoperative clinical course of patients after PEG tube placement. Laboratory biomarkers were collected on postoperative day 7 and changes from preoperative values were compared between the 2 groups, with no significant differences found. Overall, feeding-related aspiration pneumonia was the most common AE, followed by peristomal infection and feeding-related diarrhea. Compared to the Liquid feed group, the Semi-solid feed group had a significantly lower incidence of aspiration pneumonia (2.2% vs. 22.2%, $P<0.005$). Using logistic regression, after adjusting for preoperative C-reactive protein levels, patients in the Liquid feed group were more likely to develop feeding-related aspiration pneumonia compared to those in the Semi-solid feed group (Adjusted odds ratio 11.99, 95% CI: 1.51 to 95.08, $P<0.05$). After adjusting for preoperative serum albumin levels, the odds of developing aspiration pneumonia was also higher in the Liquid feed group (Adjusted odds ratio 12.51, 95% CI: 1.56 to 100.52, $P<0.05$). The calculated number needed to treat using semi-solid feed for feeding-related aspiration pneumonia was 5 patients (95% CI: 3 to 13). Although not statistically significant, there were fewer cases of feeding-related diarrhea in the Semi-solid feed group as well. The frequency of peristomal infection and the average infection scores were not significantly different between both groups. No tube obstruction was observed in either groups.

Postoperative length of stay was significantly shorter in the Semi-solid feed group (12.7 days vs. 18.8 days, $P<0.01$). There were also fewer deaths (in-hospital, 14-day, 30-day, 60-day and 90-day) in the Semi-solid feed group albeit not significantly different when compared to the Liquid feed group. After discharge, patients in the Semi-solid group also seemed less likely to be readmitted within the same month (0% vs. 4.8%, $P=0.05$). As shown in ► **Table 4**, analysis of covariance demonstrated that using semi-solid feed was associated with a shorter postoperative length of stay even after taking into account age, gender, preoperative serum albumin levels and preoperative C-reactive protein levels ($\beta -0.23$, 95%CI: -0.41 to -0.06, $P<0.01$).

Discussion

PEG has been established as a safe and simple procedure for long-term enteral tube feeding. Nevertheless, feeding-related AEs such as aspiration pneumonia from GER of gastric feed may impede the successful use of PEG and contribute to postoperative mortality. Although jejunal feeding may reduce GER, an additional procedure is required and pump-assistance may also be necessary for enteral nutrition [15]. In Japan, the use of semi-solid feed in PEG patients to reduce feeding-related AEs such as aspiration

pneumonia, peristomal leakage, and diarrhea is quite common. Semi-solid feed is considered to be more physiologic (swallowed food does not enter the stomach in the liquid form) and is reported in Japanese literature to reduce the incidence of GER, peristomal leakage, and diarrhea. Because it is given via bolus infusion, patients and care-givers are less restricted during feeding time, which may in turn contribute to a higher quality of life and lower incidence of pressure ulcers.

In an animal model of gastroesophageal reflux disease (GERD), use of semi-solid feed significantly reduced the frequency of GER during feeding and post-feeding periods [16]. In PEG patients, the efficacy of semi-solid feed in decreasing or inhibiting GER is not conclusive, with conflicting results being reported [17–19]. That may be due to differences in the dynamic viscosity of semi-solid feed used in various studies. A recent study also demonstrated that use of semi-solid feed was associated with fewer observational days with fever but the cause of fever in that study was not clearly defined [20].

This study showed that PEG patients with a postoperative feeding protocol using semi-solid feed had better clinical outcomes in terms of the frequency of feeding-related aspiration pneumonia and postoperative hospital length of stay. Fewer feeding-related AEs such as aspiration pneumonia in the Semi-solid feed group may have contributed to the shorter postoperative length of stay. Multivariate analysis also showed that using semi-solid feed had a positive effect on postoperative hospital length of stay, regardless of age, gender, and preoperative nutritional as well as inflammation status. Tube obstruction did not occur no matter which type of feed was used. The positive effect of using semi-solid feed also seemed to extend beyond discharge, as shown in the 30-day hospital readmission rates of both groups. Even with the reduction in aspiration pneumonia, significant improvement in mortality rates was not observed in the Semi-solid feed group. One possible explanation is that the attending physicians were free to change the type of feed when patients encountered feeding-related AEs. Further analysis revealed that 10 of 16 patients who had feeding-related aspiration pneumonia in the Liquid feed group changed to semi-solid feeding upon resuming enteral nutrition. Likewise, 4 of 9 patients who experienced feeding-related diarrhea in the Liquid feed group also had their feed changed to semi-solid type. This could be a reason why only postoperative length of stay (affected by AEs) was significantly different between the 2 groups.

Notable limitations of this study include the probability of selection bias (only quasi-randomized at best), which could explain why there were fewer patients enrolled in the Semi-solid group. The study also lacks long term follow-up data beyond 90 days (which is still in progress as an ongoing observational study). One potential disadvantage of using semi-solid feed is the requirement for additional water supplementation. As shown in ► **Table 1**, for the same amount of calories, semi-solid feed contains roughly half the water contained in a typical liquid feed. There is concern that administration of larger amounts of water may cause GER, resulting in aspiration. However, it has been demonstrated that gastric emptying is usually faster for water and liquid with lower caloric content [21].

Conclusion

This study demonstrated that using semi-solid feeds may reduce the risk of aspiration pneumonia and shorten postoperative hospital length of stay after PEG. These clinical outcomes may lead to a better quality of life for patients and lower medical costs. Large-scale randomized controlled trials are warranted to confirm this. Semi-solid feeds are safe to use and can be employed either as a first-line feeding protocol or an alternative when liquid feeding is unsuccessful.

Competing interests: None

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