

## Investigation and prediction of enteral nutrition problems after percutaneous endoscopic gastrostomy

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### Abstract

**AIM:** To investigate and predict enteral nutrition problems after percutaneous endoscopic gastrostomy (PEG).

**METHODS:** We retrospectively analyzed data for 252 out of 285 patients who underwent PEG at our hospital from 1999 to 2008. Enteral nutrition problems after PEG were defined as: (1) patients who required  $\geq 1$  mo after surgery to switch to complete enteral nutrition, or who required additional parenteral alimentation continuously; or (2) patients who abandoned switching to enteral nutrition using the gastrostoma and employed other nutritional methods. We attempted to identify the predictors of problem cases by using a logistic regression analysis that examined the patients' backgrounds and the specific causes that led to their problems.

**RESULTS:** Mean age of the patients was 75 years, and in general, their body weight was low and their overall condition was markedly poor. Blood testing revealed that patients tended to be anemic and malnourished. A total of 44 patients (17.5%) were diagnosed as having enteral nutrition problems after PEG. Major causes of

the problems included pneumonia, acute enterocolitis (often *Clostridium difficile*-related), paralytic ileus and biliary tract infection. A multivariate analysis identified the following independent predictors for problem cases: (1) enteral nutrition before gastrectomy (a risk reduction factor); (2) presence of esophageal hiatal hernia; (3) past history of paralytic ileus; and (4) presence of chronic renal dysfunction.

**CONCLUSION:** Enteral nutrition problems after PEG occurred at a comparatively high rate. Patient background analysis elucidated four predictive factors for the problem cases.

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**Key words:** Percutaneous endoscopic gastrostomy; Enteral nutrition; Complication, Risk factor; Predictor

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### INTRODUCTION

Percutaneous endoscopic gastrostomy (PEG) was first introduced by Gauderer *et al* in 1980<sup>[1]</sup>. Since that time, it has become one of the most useful and established enteral nutrition techniques performed at treatment centers. Compared to the use of a nasogastric tube, enteral nutrition using a PEG tube offers numerous advantages, including reduced laryngopharyngeal discomfort and a lower risk of aspiration lung disease<sup>[2,3]</sup>. When performing PEG, the associated risks must always be kept in mind. While various devices have been developed<sup>[4,5]</sup>, the frequency of adverse events is higher as compared to other nutritional methods, since PEG is based on a surgical technique<sup>[6-8]</sup>. Additionally, even

if PEG is successful, patients often encounter enteral nutrition problems after surgery. We investigated and analyzed the etiology of these problems in patients seen at our hospital.

## MATERIALS AND METHODS

### *Patients and gastrostomy*

Of the 285 patients who underwent PEG at our center from April 1999 to April 2008, we were able to statistically analyze the data for 252 subjects (157 males, 95 females). Our center admits many elderly patients who present poor general conditions in addition to having problems with ingesting food orally. PEG is primarily performed in the gastroenterology department after a request from a different department. After PEG is scheduled, upper gastrointestinal endoscopy is performed preoperatively in all cases, and abdominal computed tomography (CT) is carried out as needed in order to ascertain whether PEG can be done. If patients are taking anticoagulant or antiplatelet agents, a drug-free period is established, which depends on the type of drug being taken.

All patients in the present study underwent gastrostomy using the pull method<sup>[1]</sup>. With the exception of one patient, no sutures were used to fix the abdominal and gastric walls at the gastrostomy site. In general, antibiotics were administered intravenously for 3 d following PEG. Two days after surgery, lukewarm water was injected, followed by injection of enteral nutrients starting 4 d after the surgery. A switch to enteral nutrition using the PEG tube was initiated 7-10 d after surgery. At our clinical center, we have been using PEG clinical paths since June 2003.

### *Data analysis*

In the present study, patients were considered to have a problem with enteral nutrition after PEG if they met one of the following criteria: (1) patients who required  $\geq 1$  mo after surgery to switch to complete enteral nutrition, or who required additional parenteral alimentation continuously; or (2) patients who abandoned switching to enteral nutrition using the gastrostoma and employed other nutritional methods. The data on the patients' backgrounds and suspected reasons for their problems were collected and used for further analysis. To analyze the predictors among the problem cases, we chose 26 candidates that we believed could possibly have an influence on the postoperative enteral nutrition (Table 1). Binomial logistic regression analysis was performed using statistical software (SPSS Base 11.0j and SPSS Regression Models 9.0J; SPSS Japan Inc., Tokyo, Japan), with the presence or absence of enteral nutrition problems after PEG employed as the dependent variable. Since it was necessary to analyze numerous factors, univariate analysis was conducted to narrow down the candidates based on the significance probability ( $P < 0.1$ ). Independent predictors were determined by conducting multivariate analysis based on a step-down procedure that used likelihood ratios.

Subsequently, after subjects were grouped in relation to each predictor, problem characteristics were investigated.

## RESULTS

### *Patients' background factors*

Table 2 shows the background factors for the 252 patients. Mean age of the patients was 75 years (range, 38-99 years), with men making up approximately 60% of the group. As to the general physical conditions, body weight was low and overall condition was markedly poor. Blood testing revealed that the patients tended to be anemic and malnourished prior to gastrostomy. There were inflammatory reactions in many patients. Cerebrovascular disorders accounted for about 70% of the underlying diseases. Even though the majority of the patients had central nervous system diseases, disuse syndrome and senile dementia were also noted. PEG was performed for enteral nutrition in all patients.

### *Cases of enteral nutrition problems after PEG*

A total of 44 (17.5%) out of 252 patients exhibited enteral nutrition problems after PEG. There were 33 cases that met criterion (1), and three cases required continuous supportive parenteral alimentation. In 30 of these cases, the mean number of days required to switch to enteral nutrition was  $69 \pm 31$  (mean  $\pm$  SD) d (range 32-145 d). Eleven cases met criterion (2).

Table 3 shows causes of the enteral nutrition problems for each of the criteria. Although various events were confirmed, pneumonia, paralytic ileus, acute enterocolitis and biliary tract infection were the most frequently seen in both criterion groups. In the pneumonia and acute enterocolitis patients, aspiration pneumonia and *Clostridium difficile*-associated enteric disease (CDED) accounted for the majority of the cases, respectively. For criterion (2), aggravation of chronic renal dysfunction and heart failure were noted.

### *Statistical analysis*

In 252 patients, univariate analysis was performed for each of the 26 factors with the presence or absence of enteral nutrition problems after PEG used as the dependent variable (Table 1). Candidate predictors were narrowed down to the following: "enteral nutrition before gastrectomy"; "hemoglobin level the day before gastrostomy"; "albumin level the day before gastrectomy"; "presence of esophageal hiatal hernia"; "past history of paralytic ileus"; "past history of aspiration pneumonia"; and "presence of chronic renal dysfunction". A step-down procedure that employed likelihood ratios was used for the seven items subjected to multivariate analysis. The following four factors were identified as independent predictors for cases with enteral nutrition problems after PEG: (1) enteral nutrition before gastrectomy; (2) presence of esophageal hiatal hernia; (3) past history of paralytic ileus; and (4) presence of chronic renal dysfunction (Table 4). The sensitivity, specificity and overall accuracy using the prediction model were 30.0%, 97.0% and 85.8%,

Table 1 Potential factors and univariate analysis for each of the candidates

	Number of values	Significance probability	Odds ratio
Female sex	252	0.377	0.732
Age (yr)	245	0.377	1.007
Body mass index (weight <sup>2</sup> /height)	209	0.454	0.957
Performance status (ECOG scale)	252	0.996	0.999
Enteral nutrition before gastrectomy <sup>1</sup>	252	0.000	0.272
Alimentation by peripheral infusion before gastrectomy	252	0.983	1.014
Fever ≤ 48 h before gastrostomy (≥ 37.5°C)	243	0.188	1.874
Blood examination the day before gastrectomy			
White blood cell count (/μL)	240	0.718	1.000
Hemoglobin (g/dL) <sup>1</sup>	240	0.010	0.754
Albumin (g/dL) <sup>1</sup>	240	0.092	0.483
C-reactive protein (mg/dL)	238	0.295	1.110
Fasting blood sugar (mg/dL)	240	0.150	1.006
Presence of esophageal hiatal hernia <sup>1</sup>	252	0.002	4.076
Presence of gastric ulcer or erosive gastritis	252	0.170	1.800
Past history of gastrectomy	252	0.315	2.428
Past history of CDED	252	0.258	1.774
Past history of paralytic ileus <sup>1</sup>	252	0.012	5.204
Past history of cholecystitis or cholangitis	252	0.367	1.489
Presence of arteriosclerotic disorder	252	0.835	0.898
Past history of aspiration pneumonia <sup>1</sup>	252	0.037	2.014
Presence of chronic renal dysfunction <sup>1</sup>	252	0.003	13.205
Past history of urinary tract infection	252	0.958	0.975
Presence of diabetes mellitus	252	0.611	0.805
Rehabilitation before gastrectomy	252	0.416	0.612
Use of clinical paths	252	0.843	1.078
Duration of procedure (min)	199	0.553	1.016

<sup>1</sup>Items were used for the multivariate analysis.

Table 2 Patient background factors obtained on the day before PEG (mean ± SD)

	Patients with enteral nutrition problems after PEG	Patients without enteral nutrition problems after PEG
Number of patients	208	44
Sex (Male/female)	127/81	30/14
Age (yr)	75 ± 11 (range 38-99)	76 ± 9 (range 55-92)
Body mass index (weight <sup>2</sup> /height)	19.3 ± 3.1	18.8 ± 4.3
Performance status (EGOC scale)	3.6 ± 0.6	3.6 ± 0.5
Blood examination		
White blood cell count (/μL)	6550 ± 2105	6421 ± 1954
Hemoglobin (g/dL)	11.9 ± 1.7	11.1 ± 1.6
Albumin (g/dL)	3.3 ± 0.4	3.1 ± 0.3
C-reactive protein (mg/dL)	1.12 ± 1.51	1.40 ± 1.66
Fasting blood sugar (mg/dL)	105 ± 36	114 ± 36

respectively. After the deletion of unselected factors, the sensitivity and overall accuracy were improved.

### Investigation of each predictor

Table 5 summarizes the actual causes of the patients' problems for each predictor. Because enteral nutrition before gastrectomy is a risk reduction factor, we decided to investigate cases of parenteral alimentation before PEG. While pneumonia accounted for about 30% of the problems, paralytic ileus, acute enterocolitis and biliary tract infection were also noted. In the enteral nutrition group, blood albumin and hemoglobin levels prior to gastrectomy were significantly higher than those seen in parenteral alimentation group [mean ± SD; albumin level (g/dL): 3.3 ± 0.4 *versus* 3.1 ± 0.4,  $P < 0.001$ ; hemoglobin level (g/dL): 11.9 ± 1.7 *versus* 11.1 ± 1.6,  $P < 0.001$ ; unpaired *t*-test]. In cases with esophageal hiatal hernia,

pneumonia accounted for about 45% of the problems. In addition, the majority of these cases were caused by aspiration. On the other hand, in cases with a past history of paralytic ileus, the most frequent cause was a recurrence of ileus. Similarly, in cases with chronic renal dysfunction, an aggravation of chronic renal dysfunction accounted for about 30% of the cases.

## DISCUSSION

Although predictors for postoperative enteral nutrition problems can be used to determine indications for PEG, there are no studies that have specifically examined these factors. In the current study, most patients were elderly and suffering from cerebrovascular disorders or dementia, and their general condition was markedly poor. Due to long-term recumbency and undernutrition,

**Table 3** Causes of enteral nutrition problems after PEG

	No.	%
Cases that required $\geq$ 1 mo after surgery to switch to complete enteral nutrition, or that required additional parenteral alimentation continuously		
Pneumonia (aspiration pneumonia)	13 (8)	25
Paralytic ileus	8	15
Acute enterocolitis (CDED)	7 (5)	13
Biliary tract infection	5	10
Peritonitis	3	6
Urinary tract infection	3	6
Hemorrhagic gastric ulcer	1	2
Diarrhea	1	2
Drug-induced liver injury	1	2
Bacterial endocarditis	1	2
Aggravation of ASO	1	2
Stenosis of upper respiratory tract	1	2
Aggravation of chronic renal dysfunction	1	2
Cerebral infarction	1	2
Infection to central venous catheter	1	2
Sepsis	1	2
Convulsive seizure	1	2
Progression of hyponatremia	1	2
Fever (unknown origin)	1	2
Total	52	100
Patients that abandoned switching to enteral nutrition using the gastrostoma and employed other nutritional methods		
Pneumonia (aspiration pneumonia)	6 (6)	33
Paralytic ileus	2	11
Acute enterocolitis (CDED)	2 (1)	11
Biliary tract infection	2	11
Aggravation of chronic heart failure	2	11
Aggravation of chronic renal failure	2	11
Bleeding from fistula	1	6
Fever (unknown origin)	1	6
Total	18	100

ASO: Arteriosclerosis obliterans; CV: Central vein.

these patients had various infections. The current report presents useful information for gastroenterologists who perform PEG in patients with similar backgrounds.

The enteral nutrition problems that occurred after PEG were defined according to previously described criteria. We excluded cases in which there was switching to enteral nutrition within 1 mo after PEG, as we believe that there are few disadvantages for such patients. We also excluded cases where the reason for the problem was unclear, even if these patients required longer than 1 mo to switch to enteral nutrition.

Our results demonstrated that enteral nutrition problems after PEG occurred at a comparatively high rate. Although various causes were confirmed, few cases were determined to be a direct complication of PEG. For both of the inclusion criteria, pneumonia occurred most frequently, although enterocolitis, paralytic ileus and biliary tract infection were also noted. Aspiration pneumonia accounted for the majority of the pneumonia cases. We also noted that cerebrovascular disorders accounted for approximately 70% of the underlying diseases. It is possible that dysphagia may promote aspiration in these patients. In and by itself, paralytic ileus can cause enteral nutrition problems. Furthermore, it may also promote or aggravate aspiration pneumonia,

as bowel paralysis induces vomiting or gastrointestinal reflux<sup>[9]</sup>. In acute enterocolitis patients, CDED accounted for the majority of the cases. CDED is a drug (antibiotics)-induced enteric disease and we have previously reported that CDED can occur, with onset of the disease noted soon after the PEG procedure<sup>[10]</sup>. In this study, we confirmed that the CDED that occurred after PEG was able to interrupt enteral nutrition over a long period of time. In almost all cases of biliary tract infection, stones or sludge were noted in the gallbladder. Other studies have reported that when patients are switched to enteral nutrition from parenteral alimentation, there is an increase in choleresis, along with a sudden contraction of the gallbladder<sup>[11,12]</sup>. These events may promote obstruction and infection within the bile duct system.

We attempted to determine predictors for problem cases and our results indicated that only enteral nutrition before PEG was a risk reduction factor. Our analysis demonstrated there was a small but significant probability that preoperative enteral nutrition strongly inhibited enteral nutrition problems after PEG. As compared to parenteral alimentation, enteral nutrition offers the following advantages: (1) maintains a favorable and natural alimentation; (2) maintains gastrointestinal function; and (3) provides a check on the safety of enteral nutrition prior to the PEG procedure<sup>[13-15]</sup>. Actually, we noted that aspiration pneumonia after vomiting or gastrointestinal disorder occurred in cases of preoperative parenteral alimentation. In addition, there was one patient after the PEG procedure who was afflicted by a central-venous-catheter-caused infection. Our results also showed that blood albumin and hemoglobin levels prior to gastrectomy were significantly higher in the enteral nutrition group. Therefore, if parenteral alimentation cases are scheduled for PEG, the procedure should be performed after switching to enteral nutrition.

Among the three risk factors examined, the presence of an esophageal hiatal hernia had the strongest association with the enteral nutrition problems that are found after PEG. In these cases, pneumonia accounted for about 45% of the causes, with the majority of the pneumonia cases occurring due to aspiration. Previous studies have shown that aspiration is a complication of esophageal hiatal hernia and gastroesophageal reflux disease<sup>[16]</sup>. Recently, Kitamura *et al* reported that esophageal hiatal hernia was a risk factor for aspiration pneumonia after PEG<sup>[17]</sup>. Our results indicate that preoperative upper gastrointestinal endoscopy is important for predicting enteral nutrition problems after PEG. After PEG, the posture of patients with esophageal hiatal hernia needs to be evaluated during nutrition. In addition, in such situations, it may also be necessary to consider using half-solid enteral nutrients<sup>[18-20]</sup>. In patients with a past history of paralytic ileus, the recurrence of ileus accounted for about 40% of the causes. As chronic bowel dysfunction plays a role in the background of idiopathic paralytic ileus, its recurrence is not all that rare<sup>[21]</sup>. In such cases, a rapid increase of enteral nutrient

**Table 4 Predictors identified by multivariate analysis**

	Regression coefficients (B)	Standard error	Significance probability	Odds ratio
Enteral nutrition before gastrectomy	-1.369	0.397	0.000	0.248
Presence of esophageal hiatal hernia	1.728	0.512	0.001	5.629
Past history of paralytic ileus	1.634	0.773	0.035	5.123
Presence of chronic renal dysfunction	2.011	0.954	0.035	7.470

**Table 5 Causes of enteral nutrition problems after PEG with their respective predictors**

	No.	%
Parenteral alimentation before gastrectomy		
Pneumonia (aspiration pneumonia)	14 (11)	33
Paralytic ileus	6	14
Acute enterocolitis (CDED)	5 (4)	12
Biliary tract infection	2	9
Aggravation of chronic renal dysfunction	2	5
Fever (unknown origin)	2	5
Peritonitis	1	2
Bleeding from fistula	1	2
Diarrhea	1	2
Drug-induced liver injury	1	2
Aggravation of chronic heart failure	1	2
Aggravation of ASO	1	2
Urinary tract infection	1	2
Sepsis	1	2
Infection to central venous catheter	1	2
Convulsive seizure	1	2
Total	43	100
Presence of esophageal hiatal hernia		
Pneumonia (aspiration pneumonia)	8 (5)	44
Acute enterocolitis (CDED)	3 (2)	17
Paralytic ileus	2	11
Peritonitis	1	6
Aggravation of chronic heart failure	1	6
Stenosis of upper respiratory tract	1	6
Aggravation of chronic renal dysfunction	1	6
Cerebral infarction	1	6
Total	18	100
Past history of paralytic ileus		
Paralytic ileus	3	38
Biliary tract infection	2	25
Pneumonia (aspiration pneumonia)	2 (2)	25
Peritonitis	1	13
Total	8	100
Presence of chronic renal dysfunction		
Aggravation of chronic renal dysfunction	3	33
Aggravation of chronic heart failure	2	22
Pneumonia (Aspiration pneumonia)	2 (1)	22
Diarrhea	1	11
Fever (unknown origin)	1	11
Total	9	100

after PEG may be responsible for the recurrent paralytic ileus. When there is coadministration of enterokines activators or gradual increases of enteral nutrients, this may prevent such recurrences<sup>[22,23]</sup>. In cases with chronic renal dysfunction, an aggravation of renal dysfunction or heart failure accounted for about 60% of the causes. In most cases, there was an eventual discontinuation of the enteral nutrition after PEG. Therefore, in patients with poor renal function, the indication for PEG needs to be very carefully investigated. In addition, after performing PEG in such cases, it is necessary to finely control the infusions and medications by performing frequent blood

or X-ray tests.

Previous studies have reported that patients with diabetes or low body weight have a high frequency of complications<sup>[24,25]</sup>. However, body mass index, fasting blood sugar levels and the presence of diabetes mellitus were not identified as predictors of enteral nutrition problems after PEG. In the present study, most patients were elderly, displayed a markedly poor general condition and tended to be underweight, malnourished and anemic. A bias in patient background factors may also have affected our analysis. Based on the mean preoperative blood glucose levels, it is also quite possible that a stricter control of the diabetes could have suppressed an increased number of adverse events. Although our univariate analysis indicated that blood albumin and hemoglobin levels obtained on the day before PEG could be regarded as strong candidates, both were excluded by multivariate analysis. In the enteral nutrition group, blood albumin and hemoglobin levels obtained the day before gastrectomy were significantly higher than those found in the parenteral alimentation group. Therefore, the relevance of these factors may have affected our current analysis.

## CONCLUSION

Enteral nutrition problems after PEG occurred at a comparatively high rate. Analysis of patient background factors elucidated four predictors for these problem cases. Since characteristic causes exist for these respective predictors, it may be possible to analyze causal relationships and mechanisms of onset, thereby making it possible to devise several preventative methods.

## COMMENTS

### Background

Percutaneous endoscopic gastrostomy (PEG) has become one of the most useful and established enteral nutrition techniques. However, since PEG is based on a surgical technique and is mainly performed in elderly individuals with poor general conditions, the frequency of adverse events is higher compared to other methods of nutrition. Even if PEG is successful, patients often encounter enteral nutrition problems after surgery.

### Research frontiers

Although knowledge of predictors of postoperative enteral nutrition problems may provide useful information, there are no studies that have specifically examined such predictors. The authors investigated the etiology of these problems, and tried to predict enteral nutrition problems after PEG.

### Innovations and breakthroughs

The authors showed that enteral nutrition problems after PEG occurred at a comparatively high rate. Analysis of patient background factors elucidated the following four predictors for these problem cases: (1) enteral nutrition before gastrectomy; (2) presence of esophageal hiatal hernia; (3) past history of paralytic ileus; and (4) presence of chronic renal dysfunction.

### Applications

Predictors for postoperative enteral nutrition problems can be used to determine indications for PEG. Since specific causes exist for these predictors, it may be possible to analyze causal relationships and mechanisms of onset, thereby making it possible to devise several preventive methods.

### Peer review

This study reports a large number of patients with PEGs and identifies factors that seem to predict failure of enteral nutrition. This is likely to be of interest to readers and provides some novel data. In addition, the discussion gives some ideas about how to address individual patients with poor prognostic factors.

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