

東邦大学学術リポジトリ

Toho University Academic Repository

タイトル	Preprocedural control of nutritional status score and prediction of early death after percutaneous endoscopic gastrostomy
別タイトル	経皮内視鏡的胃瘻造設術の予後関連因子に関する検討
作成者（著者）	吉田, 有輝
公開者	東邦大学
発行日	2023.12.22
掲載情報	東邦大学大学院医学研究科 博士論文.
資料種別	学位論文
内容記述	主査：斉田芳久 / タイトル：Preprocedural control of nutritional status score and prediction of early death after percutaneous endoscopic gastrostomy / 著者：Yuki Yoshida, Iruru Maetani, Hiroaki Shigoka, Takahisa Matsuda / 掲載誌：JGH Open / 巻号・発行年等：7(7): 504-508, 2023 / 本文ファイル：出版社版 / This is the peer reviewed version of the following article: 【JGH Open,7,7】, which has been published in final form at DOI: 【10.1002/jgh3.12941】. This article may be used for non commercial purposes in accordance With Wiley Terms and Conditions for self archiving.
著者版フラグ	ETD
報告番号	32661乙第2984号
学位記番号	乙第2819号
学位授与年月日	2023.12.22
学位授与機関	東邦大学
DOI	info:doi/10.1002/jgh3.12941
メタデータのURL	https://mylibrary.toho-u.ac.jp/webopac/TD34443173

ORIGINAL ARTICLE

Preprocedural control of nutritional status score and prediction of early death after percutaneous endoscopic gastrostomy

Yuki Yoshida,*  Iruru Maetani,*  Hiroaki Shigoka* and Takahisa Matsuda† 

*Division of Gastroenterology and Hepatology, Department of Internal Medicine, Toho University Ohashi Medical Center and †Division of Gastroenterology and Hepatology, Department of Internal Medicine, Toho University Omori Medical Center, Tokyo, Japan

Key words

early mortality, percutaneous endoscopic gastrostomy, prognostic factor.

Accepted for publication 30 June 2023.

Correspondence

Yuki Yoshida, Division of Gastroenterology and Hepatology, Department of Internal Medicine, Toho University Ohashi Medical Center, 2-22-36 Ohashi meguro-ku, Tokyo 153-8515 Japan. Email: yuuki.yoshida@med.toho-u.ac.jp

Declaration of conflict of interest: All authors declare no conflict of interest.

Author contribution: Iruru Maetani and Hiroaki Shigoka substantially contributed to the study conceptualization. Iruru Maetani and Yuki Yoshida significantly contributed to data analysis and interpretation. Yuki Yoshida substantially contributed to the manuscript drafting. All authors critically reviewed and revised the manuscript draft and approved the final version for submission.

Introduction

In recent years, percutaneous endoscopic gastrostomy (PEG) has played an important role as a means of enteral nutrition in patients with feeding disorders, as happens following cerebrovascular disease. PEG is a minimally invasive procedure compared to surgical gastrostomy but has recognized complications that include mortality.^{1–4} Previous studies have identified certain pre-existing medical conditions and serological tests as prognostic factors for early mortality after PEG^{5–10}; however, these results have been inconsistent between studies. Other studies have reported that preoperative nutritional status is associated with prognosis in patients undergoing gastrointestinal surgery.^{11–15} Despite the inconsistent results of previous studies, the controlling nutritional status (CONUT) score,¹⁶ a relatively new nutritional index, has been reported to have utility as a predictor of prognosis following surgery for various diseases and cancers.^{13,14}

We therefore evaluated the CONUT score and other clinical parameters as risk factors for early mortality after PEG.

Abstract

Background and Aim: Percutaneous endoscopic gastrostomy (PEG) is often associated with early mortality. We therefore investigated factors associated with early death after PEG.

Methods: The present study comprised patients who had undergone PEG between April 2014 and March 2020. Patients were divided into two groups: an early mortality group who died within 1 month of PEG, and a non-mortality group whose clinical course could be followed for more than 1 month after the procedure. Patient background, hematological data, and procedural duration were compared between groups.

Results: Univariate analysis identified older age, high blood urea nitrogen (BUN), low prognostic nutritional index (PNI), and high controlling nutritional status (CONUT) score as factors associated with early death after PEG. In multivariate analysis, high CONUT score remained an independent prognostic factor ($P = 0.0035$).

Conclusion: A high CONUT score may be a prognostic factor for early mortality after PEG.

Methods

Subjects. This retrospective record review study comprised patients who had undergone PEG between April 2014 and March 2020. Patients were divided into two groups: The non-mortality group comprised patients who could be followed for more than 1 month after PEG, and the early mortality group comprised patients who died within 1 month of PEG. Patient background, hematological data, and procedural duration were compared between the groups. Eligibility criteria were patients with oral feeding difficulties and aged 20 years or older. Exclusion criteria were pharyngeal or esophageal obstruction, PEG for decompression, and post-gastrectomy patients. The present study was conducted with approval obtained in advance from the Ethics Committee of Toho University Ohashi Medical Center (approval number H22083-H22057). Information regarding the present study is available at the institution's website.

Table 1 Onodera's prognostic nutritional index (PNI)

$$\text{PNI} = 10 \times \text{Alb} + 0005 \times \text{TLC}$$

Alb, serum albumin (g/dl); TLC, total lymphocyte count (μl).

Endoscopic procedure. All procedures were performed by one responsible physician (YY) with the assistance of another physician. In those who were under antithrombotic medication, the decision to continue or interrupt such medication before PEG, the timing of interruption if any, and the use of heparin bridges were based primarily on Japanese guidelines that became available in Japan in 2012.¹⁷ In case of interruption, anti-thrombotic medications were resumed the day after PEG. All patients underwent PEG placement by the pull method using a One Step Button (24 Fr, 1.7–4.4 cm; Boston Scientific, Natick, MA, USA). Gastric wall fixation was not conducted in all cases. The catheter length was selected using a measuring device. All patients received a single dose of 1 g cefazolin if not receiving antibiotics for other reasons, with additional antimicrobial therapy administered in the event of systemic infection, including aspiration pneumonia or peritonitis. Patients with other complications were treated as appropriate.

Study design. Evaluated parameters included patient background such as age, sex, underlying diseases, serological tests, and PEG placement time. Serological data included white blood cell count, lymphocyte count, hemoglobin, platelets, albumin, blood urea nitrogen (BUN), C-reactive protein (CRP), and CRP/albumin ratio before PEG, based on previous reports.^{5–10} Serological results from blood samples taken on the day of PEG or the day before were used. In addition, the prognostic nutritional index (PNI) developed by Onodera *et al.*¹⁸ (Table 1) and the CONUT score¹⁶ (Table 2), which are based on serological results only, were used to evaluate nutritional status.

Statistical analyses. Nonparametric data are presented as median values. Fisher's exact test and the Mann–Whitney *U* test were used to compare factors between the two groups. For multivariate analysis, multiple logistic regression analysis was used. Prior to analysis, the multicollinearity of each independent variable was checked, and those with a correlation coefficient of 0.5 or more were excluded from each other. In all cases, *P*-values <0.05 were considered statistically significant. EZR Ver. 1.54 (Saitama Medical Center, Jichi Medical University, Saitama, Japan) was used for statistical analyses.

Table 2 Controlling nutritional status scores

Parameters	Normal	Mild	Moderate	Severe
Serum albumin (g/dl)	≥ 3.5	3.0–3.4	2.5–2.9	<2.5
Score	0	2	4	6
Total lymphocyte count (μl)	≥ 1600	1200–1599	800–1199	<800
Score	0	1	2	3
Total cholesterol (mg/dl)	≥ 180	140–179	100–139	<100
Score	0	1	2	3
Total score	0–1	2–4	5–8	9–12
Dysnutritional status	Normal	Mild	Moderate	Severe

Results

The study analysis comprised 100 patients who had undergone PEG and met the inclusion criteria during the study period. Of these, 93 were in the non-mortality group and 7 in the early mortality group. The causes of early mortality were aspiration pneumonia in three, sepsis in two, acute respiratory failure in one, and peritonitis in one. Early complications included aspiration pneumonia in three, sepsis in two, and wound infection in one in the early mortality group, whereas aspiration pneumonia in seven, sepsis in one, and wound infection in five in the non-mortality group. Patient age was significantly higher in the early mortality group ($P = 0.031$). BUN levels were significantly higher in the early mortality group ($P = 0.0275$). Lower PNI ($P = 0.0258$) and significantly higher CONUT score ($P = 0.00127$) were observed in the early mortality group (Table 3). Univariate analysis identified older age, high BUN, low PNI, and high CONUT score as factors associated with early death after PEG. A strong negative correlation was observed between CONUT scores and PNI ($R = -0.796$; $P < 0.001$). PNI was therefore excluded from the model of independent variables. Multivariate analysis using age, BUN, and CONUT showed that CONUT score was an independent prognostic factor (odds ratio [OR], 1.58; 95% confidence interval [CI], 1.04–2.40; $P = 0.0335$; Table 4).

Discussion

PEG was first reported in 1980 by Gauderer *et al.*¹⁹ Although PEG has been performed at many centers, as it is minimally invasive and easy to perform, PEG has a number of recognized complications including death. The mortality rate within 30 days of PEG is reportedly between 3.9 and 18%,^{5,20,21} and 7% in this study.

The results of the present study indicate that the CONUT score, which is a nutritional indicator, is associated with early mortality after PEG. The CONUT score is an objective screening test for malnutrition developed by de Ulíbarri *et al.* in 2005.¹⁶ Although there are many tools for nutritional assessment,^{22–25} these require the assessment of height, weight, weight change, and change in dietary intake. The utility of nutritional assessment tools is limited in patients undergoing PEG because of difficulties in measuring height and weight, let alone weight change. However, the PNI and CONUT score used in this study are objective scoring criteria that are solely based on serological data, with results

Table 3 Factors included in univariate analysis

	Early mortality group (n = 7)	Non-mortality group (n = 93)	P-value
Age	87 (86–88)	82 (74–86)	0.031*
Sex (male: female)	3:4	49:44	0.707
Procedure time (s)	540 (512.5–615)	540 (460.0–600.0)	0.267
Underlying disease			
Cerebrovascular disease	3	34	0.708
Dementia	1	14	1
Neurological disorders	1	21	1
Diabetes mellitus	3	15	0.108
White blood cell count (/μl)	5700 (5200–6200)	6200 (4700–7800)	0.612
Lymphocyte count (/μl)	858 (706–1340)	1302 (950–1668)	0.102
Serum albumin (g/dl)	2.4 (2.2–2.6)	2.9 (2.5–3.2)	0.0843
Hemoglobin (g/dl)	11.7 (9.6–11.95)	11.5 (10.3–12.70)	0.504
Platelet count (/μl)	172 000 (138 000–200 000)	226 000 (174 000–284 000)	0.0642
BUN (mg/dl)	25 (22.5–28.5)	18 (12–24.0)	0.0275*
CRP (mg/dl)	1.38 (0.665–1.525)	0.82 (0.200–2.310)	0.418
PNI	28.6 (28.4–30.7)	35.8 (31.1–39.9)	0.0258*
CONUT score	9 (8.5–9.5)	6 (4.0–8.0)	0.0127*
CRP/Alb ratio	0.55 (0.30–0.77)	0.27 (0.07–0.86)	0.292

*P < 0.05.

Data are represented as median (interquartile range).

Alb, serum albumin; BUN, blood urea nitrogen; CONUT, controlling nutritional status; CRP, C-reactive protein; PNI, prognostic nutritional index.

obtained from blood samples only. The CONUT score comprises serum albumin, lymphocyte count, and total cholesterol as variables, while the PNI uses serum albumin and lymphocyte count as variables. A strong negative correlation was observed between the PNI and CONUT score in the present study, which may be attributed to the inclusion of serum albumin and lymphocyte count in both criteria.

Previous studies have reported albumin, lymphocyte count, and total cholesterol as risk factors for death after PEG.^{8,9,26–29} Albumin is the most abundant protein in human serum and has been used for decades as an indicator of malnutrition in clinically stable patients.³⁰ Several studies have reported that albumin is a good predictor of surgical outcomes^{31,32}; however, the relative contributions of malnutrition and advanced disease to hypoalbuminemia was not clear in these studies. More recently, studies have reported that low serum albumin levels are not a reflection of malnutrition but rather the result of an underlying inflammatory response.³³ Lymphocyte counts have been posited to be low in malnourished patients due to reduced lymphocyte maturation. This finding can be considered an indication of malnutrition but it is not specific and its use as a diagnostic tool for malnutrition alone is limited, as immune status,

comorbidities, and severe stress responses may also have an impact on the nutritional status.³⁴ Total cholesterol reflects lipid metabolism. Low total cholesterol levels are associated with increased mortality; however, the sensitivity and specificity of total cholesterol levels for detecting malnutrition are considered low.³⁵ In the present univariate analysis, serum albumin levels and lymphocyte counts were lower in the early mortality group, although there were no significant differences between the two groups.

Previous studies have reported prognostic factors for early mortality after PEG (Table 5). Although no parameters have consistently been shown to be associated with early mortality after PEG, many studies reported inflammatory markers such as albumin and CRP as prognostic predictors.^{6,8–10,26} Inflammation, which may be caused by chronic disease or uncontrolled infection, is reported to be associated with poor prognosis. Poor nutritional status, such as anemia and high BUN, is also associated with poor prognosis.^{5,7} Although consistent results may not be obtained when a single parameter is assessed, new insights may be obtained by combining several parameters that reflect protein reserves, immune status, and lipid metabolism, as in the CONUT score. Although various internal and external factors contribute to early mortality after PEG that cannot be simply quantified, the results of the present study indicate that the CONUT score may have utility in identifying patients at risk of early mortality after PEG.

The limitations of the present study include its retrospective nature and the small sample size. Prospective studies comprising a larger number of cases are required to validate the results of the present study.

In conclusion, low nutritional status, particularly in cases with high CONUT scores, may be associated with early mortality

Table 4 Multivariate analysis of factors associated with early mortality

	Odds ratio	95% confidence interval	P-value
Age	1.08	0.949–1.240	0.2380
BUN	1.06	0.975–1.150	0.1750
CONUT score	1.58	1.040–2.400	0.0335*

*P < 0.05.

BUN, blood urea nitrogen; CONUT, controlling nutritional status.

Table 5 Factors reported to be associated with early mortality after percutaneous endoscopic gastrostomy

Source	Variables	OR (95% confidence interval)	P-value
Pih <i>et al.</i> ⁶	Platelet < 100 000	OR 14.294 (3.358–60.851)	0.000*
	CRP ≥ 5.00 mg/dl	OR 3.101 (1.021–9.414)	0.046*
Duzenli <i>et al.</i> ⁷	CRP/albumin ratio > 10.46	OR 6.670 (1.873–23.752)	0.003*
	Urea > 37.5 mg/dl	OR 3.783 (1.407–10.171)	0.008*
Gumaste <i>et al.</i> ⁸	Albumin	OR 0.4443 (0.2156–0.9159)	0.0288*
	Female	OR 0.2386 (0.1005–0.5663)	0.0012*
	Positive urine cultures	OR 2.5524 (1.0857–6.0006)	0.0325*
Onder <i>et al.</i> ⁹	Albumin ≥ 3.0 g/dl	OR 4.09 (1.08–15.5)	0.038*
Barbosa <i>et al.</i> ¹⁰	CRP ≥ 35.9 mg/dl	OR 1.008 (1.001–1.014)	0.029*
Lee <i>et al.</i> ²⁶	CRP > 21.5 mg/l	OR 8.55 (3.11–23.45)	<0.001*
	Serum albumin < 31.5 g/l	OR 3.01 (1.27–7.16)	0.012*
Lang <i>et al.</i> ²⁷	Serum albumin < 3 g/dl	OR 2.82 (1.34–5.96)	0.007*
	Diabetes mellitus	OR 2.44 (1.20–4.97)	0.014*
	Chronic obstructive pulmonary disease	OR 2.79 (1.26–6.14)	0.011*

*P < 0.05.

CRP, C-reactive protein; OR, odds ratio.

after PEG. Nutritional status should be assessed in patients considered candidates for PEG placement. Larger prospective studies are required to validate the results of the present study.

Acknowledgment

We thank all members of the Division of Gastroenterology and Hepatology, Department of Internal Medicine, Toho University Ohashi Medical Center.

Informed consent

Informed consent was obtained in the form of opt-out on the web site.

Data availability statement. The datasets used and/or analyzed during the current study are available from the corresponding author upon reasonable request.

References

- Ponsky JL, Gauderer MW. Percutaneous endoscopic gastrostomy: a nonoperative technique for feeding gastrostomy. *Gastrointest. Endosc.* 1981; **27**: 9–11.
- Shellito PC, Malt RA. Tube gastrostomy: techniques and complications. *Ann. Surg.* 1985; **201**: 180–5.
- Schurink CA, Tuynman H, Scholten P *et al.* Percutaneous endoscopic gastrostomy: complications and suggestions to avoid them. *Eur. J. Gastroenterol. Hepatol.* 2001; **13**: 819–23.
- Rahnemai-Azar AA, Rahnemai-Azar AA, Naghshizadian R, Kurtz A, Farkas DT. Percutaneous endoscopic gastrostomy: indications, technique, complications and management. *World J. Gastroenterol.* 2014; **20**: 7739–51.
- Lima DL, Miranda LE, da Penha MR *et al.* Factors associated with 30-day mortality in patients after percutaneous endoscopic gastrostomy. *JSLs.* 2021; **25**: e2021.00040.
- Pih GY, Na HK, Ahn JY *et al.* Risk factors for complications and mortality of percutaneous endoscopic gastrostomy insertion. *BMC Gastroenterol.* 2018; **18**: 101.
- Duzenli T, Ketenci M, Akyol T *et al.* Predictive factors of complications and 30-day mortality in patients undergoing percutaneous endoscopic gastrostomy: the utility of C-reactive protein to albumin ratio. *Acta Gastroenterol. Belg.* 2021; **84**: 283–8.
- Gumaste VV, Bhamidimarri KR, Bansal R, Sidhu L, Baum J, Walfish A. Factors predicting early discharge and mortality in post percutaneous endoscopic gastrostomy patients. *Ann. Gastroenterol.* 2014; **27**: 42–7.
- Onder A, Kapan M, Arikanoglu Z *et al.* Percutaneous endoscopic gastrostomy: mortality and risk factors for survival. *Gastroenterology Res.* 2012; **5**: 21–7.
- Barbosa M, Magalhaes J, Marinho C, Cotter J. Predictive factors of early mortality after percutaneous endoscopic gastrostomy placement: the importance of C-reactive protein. *Clin. Nutr. ESPEN.* 2016; **14**: 19–23.
- Qi Q, Song Q, Cheng Y, Wang N. Prognostic significance of preoperative prognostic nutritional index for overall survival and postoperative complications in esophageal cancer patients. *Cancer Manag. Res.* 2021; **13**: 8585–97.
- Xishan Z, Ye Z. The role of prognostic nutritional index for clinical outcomes of gastric cancer after total gastrectomy. *Sci. Rep.* 2020; **10**: 17373.
- Kuroda D, Sawayama H, Kurashige J *et al.* Controlling nutritional status (CONUT) score is a prognostic marker for gastric cancer patients after curative resection. *Gastric Cancer.* 2018; **21**: 204–12.
- Xiao Q, Li X, Duan B *et al.* Clinical Significance of Controlling Nutritional Status Score (CONUT) in evaluating outcome of postoperative patients with gastric cancer. *Sci. Rep.* 2022; **12**: 93.
- Nozoe T, Kimura Y, Ishida M, Saeki H, Korenaga D, Sugimachi K. Correlation of pre-operative nutritional condition with post-operative complications in surgical treatment for oesophageal carcinoma. *Eur. J. Surg. Oncol.* 2002; **28**: 396–400.
- de Ulíbarri JI, González-Madroño A, de Villar NG *et al.* CONUT: a tool for controlling nutritional status. First validation in a hospital population. *Nutr. Hosp.* 2005; **20**: 38–45.
- Fujimoto K, Fujishiro M, Kato M *et al.* Guidelines for gastroenterological endoscopy in patients undergoing antithrombotic treatment. *Dig. Endosc.* 2014; **26**: 1–4.
- Onodera T, Goseki N, Kosaki G. Prognostic nutritional index in gastrointestinal surgery of malnourished cancer patients. *Nihon Geka Gakkai Zasshi.* 1984; **85**: 1001–5.

- 19 Gauderer MWL, Ponsky JL, Izant RJ. Gastrostomy without laparotomy; a percutaneous technique. *J. Pediatr. Surg.* 1980; **5**: 872–5.
- 20 Limpas Kamiya KJ, Hosoe N, Takabayashi K *et al.* Factors predicting major complications, mortality, and recovery in percutaneous endoscopic gastrostomy. *JGH Open.* 2021; **5**: 590–8.
- 21 Cortez-Pinto H, Correia AP, Camilo ME, Tavares L, De Moura MC. Long-term management of percutaneous endoscopic gastrostomy by a nutritional support team. *Clin. Nutr.* 2002; **21**: 27–31.
- 22 Vellas B, Guigoz Y, Garry PJ *et al.* The mini nutritional assessment (MNA) and its use in grading the nutritional state of elderly patients. *Nutrition.* 1999; **15**: 116–22.
- 23 Kaiser MJ, Bauer JM, Ramsch C *et al.* Validation of the Mini Nutritional Assessment short-form (MNA-SF): a practical tool for identification of nutritional status. *J. Nutr. Health Aging.* 2009; **13**: 782–8.
- 24 Kondrup J, Rasmussen HH, Hamberg OL, Stanga Z. An ad hoc ESPEN Working Group. Nutritional risk screening (NRS 2002): a new method based on an analysis of controlled clinical trials. *Clin. Nutr.* 2003; **22**: 321–36.
- 25 Bouillanne O, Morineau G, Dupont C *et al.* Geriatric Nutritional Risk Index: a new index for evaluating at-risk elderly medical patients. *Am. J. Clin. Nutr.* 2005; **82**: 777–83.
- 26 Lee C, Im JP, Kim JW *et al.* Risk factors for complications and mortality of percutaneous endoscopic gastrostomy: a multicenter, retrospective study. *Surg. Endosc.* 2013; **27**: 3806–15.
- 27 Lang A, Bardan E, Chowers Y *et al.* Risk factors for mortality in patients undergoing percutaneous endoscopic gastrostomy. *Endoscopy.* 2004; **36**: 522–6.
- 28 Tominaga N, Shimoda R, Iwakiri R *et al.* Low serum albumin level is risk factor for patients with percutaneous endoscopic gastrostomy. *Intern. Med.* 2010; **49**: 2283–8.
- 29 Patita M, Nunes G, Grunho M, Santos CA, Fonseca J. Endoscopic gastrostomy for nutritional support in post-stroke dysphagia. *Nutr. Hosp.* 2021; **38**: 1126–31.
- 30 Cabrerizo S, Cuadras D, Gomez-Busto F, Artaza-Artabe I, Marín-Ciancas F, Malafarina V. Serum albumin and health in older people: review and meta-analysis. *Maturitas.* 2015; **81**: 17–27.
- 31 Kudsk KA, Tolley EA, DeWitt RC *et al.* Preoperative albumin and surgical site identify surgical risk for major postoperative complications. *J. Parenter. Enteral Nutr.* 2003; **27**: 1–9.
- 32 Gibbs J, Cull W, Henderson W, Daley J, Hur K, Khuri SF. Preoperative serum albumin level as a predictor of operative mortality and morbidity: results from the National VA Surgical Risk Study. *Arch. Surg.* 1999; **134**: 36–42.
- 33 Evans DC, Corkins MR, Malone A *et al.* The use of visceral proteins as nutrition markers: an ASPEN position paper. *Nutr. Clin. Pract.* 2021; **36**: 22–8.
- 34 Shenkin A, Cederblad G, Elia M, Isaksson B. Laboratory assessment of protein-energy status. *Clin. Chim. Acta.* 1996; **253**: S5–9.
- 35 Neaton JD, Blackburn H, Jacobs D *et al.* Serum cholesterol level and mortality findings for men screened in the multiple risk factor intervention trial. *Arch. Intern. Med.* 1992; **152**: 1490–500.