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# Predictive factors for early mortality after EUS-guided gastroenterostomy in malignant gastric outlet obstruction

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Key words
Endoscopy Upper GI Tract, Dilation, injection, stenting, Endoscopic ultrasonography, Intervention EUS, Pancreatobiliary (ERCP/PTCD), Strictures, Malignant strictures

**received** 17.6.2024
**accepted after revision** 15.11.2024
**accepted manuscript online** 18.11.2024

Bibliography
Endosc Int Open 2025; 13: a24749802
**DOI** 10.1055/a-2474-9802
**ISSN** 2364-3722

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Supplementary Material is available at https://doi.org/10.1055/a-2474-9802

## ABSTRACT

**Background and study aims** Endoscopic ultrasound-guided gastroenterostomy (EUS-GE) has recently emerged as a potential treatment option for malignant gastric outlet obstruction (mGOO), with a relatively long duration of patency and low rate of reintervention. Its intrinsic risk for serious adverse events and high procedure cost mandates careful patient selection beyond the common safety profiles. This study aimed to assess for predictors of early post-EUS-GE mortality.

**Patients and methods** We conducted a retrospective analysis of all patients with unresectable mGOO who underwent EUS-GE. Predictive factors for postoperative 30-day mortality with crude and adjusted hazard ratios were examined using univariate and multivariate penalized likelihood Firth logistic regression analyses.

**Results** Technical and clinical success was achieved in 96.7% and 93.1% of the patients, respectively. The 30-day mortality rate after the procedure was 11.7%, and no procedure complications were observed. The 30-day mortality group had a significantly low rate of initial clinical success (66.7% vs. 96.2%, $P = 0.007$). Univariate analysis identified significantly higher postoperative 30-day mortality in patients with poor baseline ECOG performance status scale (≥ 2) and ascites. Presence of grade 2 ascites was confirmed as an independent predictive factor in the multivariate analysis (adjusted hazard ratio 52.41, 95% confidence interval 1.55 to 1775.64, $P = 0.024$).

**Conclusions** EUS-GE should be carefully considered for patients with ascites which was an independent predictor for early mortality after procedure in mGOO, especially those with grade 2 or higher level of ascites.

## Introduction

Malignant gastric outlet obstruction (mGOO) is caused by any gastroduodenal or advanced pancreaticobiliary cancer, leading to severe malnutrition and quality of life (QoL) deterioration [1, 2]. Surgical gastrojejunostomy (SGJ) and endoscopic duodenal stenting are two well-established palliative treatment modalities for this condition. While SGJ typically provides longer symptom palliation than duodenal stenting, it is associated with higher surgery-related morbidity or mortality. Thus, treatment selection should be based on the patient's overall health, surgical risks, anticipated degree of recovery, and life expectancy after treatment [3, 4, 5, 6, 7, 8].

The recently introduced fully endoscopic creation of a gastrojejunal bypass, commonly referred to as endoscopic ultrasound-guided gastroenterostomy (EUS-GE), has been shown to result in more favorable short-term efficacy, longer duration of stent patency, and lower reintervention rates than duodenal stenting [9]. It appears that EUS-GE may offer the therapeutic advantages of both duodenal stenting and SGJ [10, 11, 12, 13, 14, 15, 16, 17]. Regarding overall survival (OS) outcome after EUS-GE, a previous study reported a survival rate of 65.9% at 6-month follow-up after EUS-GE, with the underlying malignancy being the primary cause of mortality. In another long-term analysis, 54.5% of patients with mGOO with clinical success after EUS-GE were deceased due to their primary cancer during a median follow-up of 162.5 days [18, 19]. On the other hand, there are insufficient data on early mortality after this procedure. By identifying putative preoperative factors associated with early post-procedure demise, it is possible to select patients who will most likely benefit from EUS-GE.

The present study aimed to identify preoperative clinical factors that would predict early post-EUS-GE mortality to minimize unnecessary EUS-GE procedures, given its cost and significant safety concern.

## Patients and methods

### Study design and patient selection

A retrospective analysis was conducted based on a prospectively collected database of patients who underwent EUS-GE with a lumen-opposing metal stent (LAMS) to treat symptomatic mGOO, where curative surgical resection was not feasible. Patients were diagnosed between October 2017 and October 2022 at Cedars-Sinai Medical Center (California, United States). Patients lost to follow-up within 30 days after the procedure were excluded from the final analysis. This retrospective study was approved by the Institutional Review Board (IRB No. 00000997), along with a waiver for written informed consent. This study complied with the ethical standards of the latest Declaration of Helsinki.

### LAMS placement

This study used a 15-mm × 10-mm or 20-mm x 10-mm electrocautery-enhanced AXIOS LAMS (Boston Scientific, Marlborough, Massachusetts, United States) to create the gastroenterostomy. All procedures were performed under general anesthesia by six experienced interventional endoscopists. Patients with coagulopathy (international normalized ratio [INR] ≥ 2), severe thrombocytopenia (platelet count < 50,000), distal small bowel obstruction, or grade 3 severe ascites were considered unfit for the procedure. Paracentesis was performed prior to the procedure on patients with a moderate amount of ascites. Patients were administered intravenous antibiotics (levofloxacin 500 mg and metronidazole 500 mg) pre-procedurally. The first step of the procedure was esophagogastroduodenoscopy (EGD) to examine the stricture and place a 7F nasobiliary catheter (Wilson Cook Medical, Inc., United States) distal to the duodenal obstruction site. A large-channel linear array echoendoscope (GF-UCT 180; Olympus, Tokyo, Japan) was inserted into the stomach to observe the optimally located jejunal loop. Most patients had the mixture infused into the small bowel via a water-immersion technique, in which at least 500 mL of sterile water, methylene blue, and radiopaque contrast media were injected through a 7F nasobiliary catheter in the prone position. In a small number of patients during the early phase, varying volumes of the mixture were used [18]. Finally, the LAMS was deployed using the freehand approach. Successful gastroenterostomy was confirmed by observing reflux of the methylene blue solution into the gastric lumen via the LAMS during endoscopy or by injecting a contrast agent from the stomach to the jejunum through the LAMS. The detailed standardized protocol for EUS-GE at this institution has been previously described [18].

### Data collection and outcome

Demographic, clinical, and post-procedure follow-up data were collected from electronic medical records of eligible patients. Covariates and demographic data for analysis included age, sex, race/ethnicity, weight, body mass index (BMI), Charlson comorbidity index (CCI), Eastern Cooperative Oncology Group (ECOG) performance status, type of primary disease, location of obstruction, administration of chemotherapy after procedure, staging, presence of peritoneal carcinomatosis or ascites, baseline laboratory findings including nutritional or systemic inflammatory markers, and procedure-related variables (adverse events [AEs], American Society for Gastrointestinal Endoscopy [ASGE] AE) grade [20], American Society of Anesthesiologists (ASA) grade, perioperative biliary drainage). Routine preoperative laboratory tests were performed immediately before EUS-GE in all patients. Ascites severity was categorized as grade 1 (a minimal layer of ascites in the gravity-dependent regions of the peritoneal and/or perihepatic cavity), grade 2 (the presence of fluid in the paracolic gutters), and grade 3 (sufficient ascites to displace the small bowel) based on the amount and distribution of ascites assessed by computed tomography (CT) of the abdomen and pelvis [21, 22]. Follow-up data included technical and clinical success, occurrence of recurrent obstruction and reintervention, death, cause of death, and duration of survival. The primary outcome was 30-day mortality following EUS-GE. Secondary outcomes included technical success rates, clinical success rates, procedure-related adverse events (AEs), recurrent obstruction and reintervention, and OS.

## Definitions

Technical success was defined as appropriate LAMS deployment in the correct position, as confirmed by endoscopy and/fluoroscopy. Successful placement of a second LAMS immediately following initial failure was also considered a technical success when accomplished in the same session. Clinical success was defined ability to tolerate a soft solid diet without symptoms 48 to 72 hours after technically successful EUS-GE. Oral food intake was assessed using the gastric outlet obstruction scoring system (GOOSS) [14]. GOOSS assigns a score of 0 in case of no oral intake, 1 for only liquids, 2 for soft solids, and 3 for low-residue or full diet, and currently is the most used score to assess for clinical symptoms of GOO and improvement post intervention. AEs were defined as events that occurred during or after EUS-GE, determined to be related to the procedure. Severity of AEs was classified according to the *grading* system proposed by the ASGE [20].

## Statistical analysis

Intention-to-treat (ITT) and per-protocol (PP) methods were used in this analysis. ITT analysis was based on the total cohort of patients and PP analysis was based on the group of patients with technically successful LAMS placement. Patient characteristics, procedure outcomes, survival outcome, and 30-day mortality were evaluated in the ITT population. Clinical success and reintervention due to stent dysfunction were evaluated by PP analysis.

Continuous variables were presented as mean (± standard deviation) or median (interquartile range). To compare 30-day survival and non-survival groups, categorical variables were analyzed using the Chi-square test or Fisher's exact test, whereas continuous variables were analyzed using the Mann-Whitney U test. Logistic regression analyses were conducted to elucidate clinical factors associated with 30-day post-procedure mortality. To mitigate bias associated with the small sample size, we employed Firth's penalized likelihood method, which offers a robust alternative to the traditional maximum likelihood logistic regression for analyzing rare events [23, 24]. Univariable logistic regression analysis was conducted to examine 30-day mortality or survival groups and potential confounders, including age, sex, CCI score (0–2, ≥ 3), ECOG performance score (0–1, ≥ 2), ASA score (0–3, ≥ 4), staging, peritoneal carcinomatosis, ascites, further systemic treatment, and procedure-related AEs. After univariate analyses, the association between the primary outcome and the study group was adjusted for potential confounders in the multivariate logistic regression analysis. Lack of multicollinearity among the variables was established by assessing the variance inflation factor, which was less than 2 before inclusion in the multivariable model [25]. Results are presented as odds ratios with 95% confidence intervals (CIs). All $P$ values were two-sided, and significance was set at $P \leq 0.05$. OS following EUS-GE was calculated from the time from the procedure to the time of death. If a patient was lost to follow-up or was alive at the end of the study, the last observation date was considered censored data using the Kaplan-Meier method. Statistical analyses were performed using SPSS software (version 27.0; IBM Corp.), SAS software (version 9.4; SAS Institute, Cary, North Carolina, United States), and GraphPad Prism software (version 9.4.1; GraphPad Software Inc.).

# Results

Of the 67 patients, 60 (34 males) with a median age of 69 years (interquartile range 64–78), excluding two patients with previous surgery and five patients who were lost to follow-up within 30 days, were included in the final analysis. ▶ **Table 1** shows demographic and baseline clinical characteristics of the patients. The most common etiology of malignancy causing GOO was pancreatic cancer (70%), followed by biliary (10%), and duodenal cancers (8.3%). Baseline GOOSS score was as follows. Of the 60 patients, 47 (78.3%) had a score of 1, while the rest had a score of 0. Technical success was achieved in 96.7% of all patients and clinical success was achieved in 93.1% of patients who demonstrated technical success. In our cohort, two cases of technical failure were observed, both of which were related to stent misplacement, and an over-the-scope clip was used for closure in such cases. In one case of stent misplacement, additional treatment for obstruction was not performed, and in the other case, a duodenal stent was used. In an additional three patients, despite initial stent misplacement, second LAMS insertion attempts done immediately as rescue treatment established gastroenterostomy after closure of the puncture site. Among the cases that achieved technical success, eight patients (13.8%) underwent reintervention for initial clinical failure (n = 1) or recurrent obstruction (n = 7) during the follow-up period. Percutaneous endoscopic gastrojejunostomy,

▶ **Table 1** Baseline demographic and clinical and characteristics at time of EUS-GE.

| | Patients (n = 60) | % |
|---|---|---|
| Age, mean (SD), range, y | 69.4 (10.8), 43–94 | |
| Sex ratio M:F | 1.31 | |
| Race/ethnicity (n, %) | | |
| White | 29 | 48.3 |
| Black | 6 | 10.0 |
| Hispanic | 10 | 16.7 |
| Asian | 14 | 23.3 |
| Native | 1 | 1.7 |
| Primary disease (n, %) | | |
| Pancreatic cancer | 42 | 70.0 |
| Biliary cancer | 6 | 10.0 |
| Duodenal cancer | 5 | 8.3 |
| Stomach cancer | 1 | 1.7 |
| Other origins | 6 | 10.0 |

EUS-GE, endoscopic ultrasound-guided gastroenterostomy; SD, standard deviation

stent unclogging, through-the-stent stenting, and balloon dilation were performed in five, one, one, and one patient, respectively. Fifty percent of these patients underwent reintervention within 1 month after EUS-GE.

Overall median survival duration after EUS-GE was 85 days (**Supplementary material Fig. 1**). Thirty-day mortality was observed in seven patients (11.7%). ▶**Table 2** summarizes demographic and baseline clinical characteristics of patients who survived less than and longer than 30 days. No significant differences in age, sex, race/ethnicity, and smoking and alcohol history were observed between the two groups. However, the 30-day mortality group had a higher proportion of overweight patients than the 30-day survival group. In addition, the proportion of patients with poor performance status, indicated by an ECOG score of 2 or higher, was identified to be significant in the 30-day mortality group (71.4% vs. 24.5%, $P = 0.011$). The two groups showed no difference in type of etiological diseases or stricture site. The 30-day mortality group tended to present cases with typical findings of peritoneal carcinomatosis on CT scan; however, no statistically significant difference was noted (42.9% vs. 15.1%, $P = 0.074$). The 30-day mortality group had a higher proportion of patients with ascites (85.7% vs. 24.5%, $P < 0.001$) than in the 30-day survival group. The proportion of patients with grade 1 ascites was 57.1% and 22.6% in the 30-day mortality and 30-day survival groups, respectively. In particular, the two groups demonstrated significant differences in the proportion of patients with grade 2 ascites (1.9% in the 30-day survival group vs. 28.6% in the 30-day mortality group). Other laboratory results, such as mean level of leukocyte, hemoglobin, blood urea nitrogen, prothrombin time-INR, and total bilirubin, were significantly different between the two groups. Representative cases from each group of patients with 30-day mortality and 30-day survival are displayed in ▶**Fig. 1**. Associations between 30-day mortality and various parameters associated with procedure outcomes are shown in ▶**Table 3**. Technical success was not significantly associated with 30-day mortality. The 30-day mortality group had a significantly low rate of initial clinical success (66.7% vs. 96.2%, $P = 0.007$). Other parameters, such as AE rates and severity grading, did not affect 30-day mortality. In addition, the two groups showed no significant difference in the rate of reintervention due to recurrent obstruction or initial clinical failure and rate of early reintervention within 1 month after EUS-GE.

▶**Table 4** displays risk factors for predicting 30-day mortality in univariate and multivariate penalized likelihood Firth logistic regression models. At the time of EUS-GE, poor performance status with ECOG score of 2 or higher and presence of ascites were associated with early poor outcomes. Multivariate analysis showed that ascites is a significant, independent predictive factor of 30-day mortality at the time of EUS-GE. Grades 1 and 2 ascites with hazard ratios of 7.19 (95% CI 0.72–71.43, $P = 0.11$) and 52.41 (95% CI 1.55–1775.64, $P = 0.024$), respectively, suggested that ascites of grade 2 or higher increased the risk of 30-day mortality (▶**Fig. 2**).

## Discussion

This single-center, retrospective study aimed to establish appropriate indications for palliation of mGOO. We identified cases of early mortality that occurred after performing palliative EUS-GE and investigated clinical factors to predict early postoperative mortality. Importantly, classification by ascites severity was identified as an independent factor associated with early mortality after EUS-GE in patients with mGOO.

Progression of malnutrition and cachexia in mGOO is expected to prolong hospitalization, significantly worsen QoL, weaken response to chemotherapy, and increase vulnerability to chemotherapy toxicity, and ultimately result in unfavorable OS. Hence, early intervention to relieve symptoms of malnutrition and cachexia in mGOO is vital [26]. However, it has been reported that life expectancy in these patients is very limited, raising the issue of which treatment modality is clinically appropriate and cost-effective [27].

Prior to introduction of EUS-GE, either SGJ or duodenal stenting had been used to palliate unresectable mGOO after weighing differences in intrinsic advantages and disadvantages of each treatment method against patient performance status and life expectancy. Of these two modalities, surgical bypass is generally favored if postoperative survival is expected for longer than 2 months and the performance status is good [3, 4, 8]. Now that EUS-GE is added as another minimally invasive treatment option, the management decision for mGOO has become more complex. Published data showed that EUS-GE was followed by lower postoperative morbidity and shorter length of hospital stay than SGJ, but with similar clinical success and recurrent obstruction rates, suggesting that EUS-GE may replace SGJ in most circumstances [28]. Moreover, in comparison with the duodenal stent group with higher reintervention rate, the EUS-GE group clearly showed more favorable stent patency at 3 months, presenting superior results in overall outcome in stent functions [11, 12]. This superiority was further confirmed by results of a recently reported multicenter randomized controlled trial [9]. Regarding safety concerns, no differences were found in the overall rate of AEs between EUS-GE and duodenal stenting, thus further negating a major perceived advantage of duodenal stenting over EUS-GE.

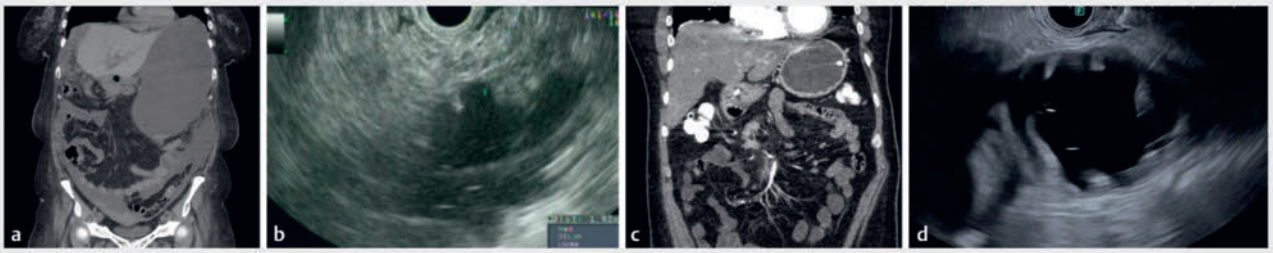
Nevertheless, there are real concerns over wide application of this new technique because complications, albeit rare, may require surgical revision. In addition, relative to duodenal stenting, it has a higher bleeding risk, longer procedure time, higher degree of technical difficulty, and steeper learning curve [13, 29, 30, 31]. Hence, like SGJ, EUS-GE may only be considered appropriate when sufficient life expectancy is anticipated and in the hands of adequately trained physicians.

Palliative treatment for end-stage cancer is generally performed on fragile patients on systemic therapy and the decision to choose a therapeutic modality can be made only after a comprehensive assessment process. Consequently, it is necessary to consider performance status in mGOO, cancer burden, life expectancy, and expected effect of palliative chemotherapy [27, 32]. If a very short life expectancy is anticipated, selecting less invasive and less expensive luminal stenting seems appro-

▶ **Table 2** Baseline clinical characteristics according to 30-day mortality.

| Variable | 30-day survival (n = 53) | 30-day mortality (n = 7) | *P* value |
|---|---|---|---|
| Age | | | |
| ▪ Mean (SD), years | 69.1 (11.1) | 71.1 (8.7) | 0.65 |
| ▪ ≥ 70 years (n, %) | 25, 47.2 | 3, 42.9 | 0.91 |
| Sex (n, %) | | | |
| ▪ Male | 30, 56.6 | 4, 57.1 | 0.98 |
| Race/ethnicity (n, %) | | | |
| ▪ White | 25, 47.2 | 4, 57.1 | 0.57 |
| ▪ Black | 5, 9.4 | 1, 14.3 | |
| ▪ Hispanic | 8, 15.1 | 2, 28.6 | |
| ▪ Asian | 14, 26.4 | 0 | |
| ▪ Native | 1, 1.9 | 0 | |
| BMI | | | |
| ▪ Underweight (n, %) | 11, 20.8 | 1, 14.3 | 0.001 |
| ▪ Normal (n, %) | 30, 56.6 | 0 | |
| ▪ Overweight (n, %) | 12, 22.6 | 6, 85.7 | |
| Smoking (n, %) | | | |
| ▪ Never | 35, 66.0 | 5, 71.4 | 0.81 |
| ▪ Former | 15, 28.3 | 2, 28.6 | |
| ▪ Current | 3, 5.7 | 0 | |
| Alcohol (n, %) | | | |
| ▪ Yes | 9, 17.0 | 1, 14.3 | 0.86 |
| Charlson comorbidity index | | | |
| ▪ Mild (n, %) | 8, 15.1 | 0 | 0.24 |
| ▪ Moderate (n, %) | 8, 15.1 | 0 | |
| ▪ Severe (n, %) | 37, 69.8 | 7, 100 | |
| ECOG performance status | | | |
| ▪ ECOG ≥ 2 (n, %) | 13, 24.5 | 5, 71.4 | 0.011 |
| ASA score | | | |
| ▪ ASA ≥ 4 (n, %) | 5, 9.4 | 1, 14.3 | 0.69 |
| Primary disease (n, %) | | | |
| ▪ Pancreatic cancer | 38, 71.7 | 4, 57.1 | 0.41 |
| ▪ Biliary cancer | 5, 9.4 | 1, 14.3 | |
| ▪ Duodenal cancer | 5, 9.4 | 0 | |
| ▪ Stomach cancer | 1, 1.9 | 0 | |
| ▪ Other origin | 4, 7.5 | 2, 28.6 | |
| Location of stricture (n, %) | | | |
| ▪ Distal stomach | 1, 1.9 | 0 | 0.53 |
| ▪ Bulb | 12, 22.6 | 3, 42.9 | |
| ▪ Second | 23, 43.4 | 3, 42.9 | |
| ▪ Third/fourth | 17, 32.1 | 1, 14.3 | |
| Staging (n, %) | | | |
| ▪ Locally advanced | 20, 37.7 | 1, 14.3 | 0.22 |
| ▪ Metastatic | 33, 62.3 | 6, 85.7 | |
| Peritoneal carcinomatosis (n, %) | 8, 15.1 | 3, 42.9 | 0.074 |
| Ascites (n, %) | | | |
| ▪ None | 40, 75.5 | 1, 14.3 | < 0.001 |
| ▪ Grade 1 | 12, 22.6 | 4, 57.1 | |
| ▪ Grade 2 | 1, 1.9 | 2, 28.6 | |
| Laboratory results, Mean (SD) | | | |
| ▪ Leukocyte ($\times 10^9$/L) | 8.2 (5.9) | 15.6 (10.0) | 0.007 |
| ▪ Hemoglobin (g/dL) | 10.7 (1.9) | 9.1 (1.1) | 0.03 |
| ▪ Platelet ($\times 10^9$/L) | 247.3 (113.2) | 268.4 (111.8) | 0.64 |
| ▪ BUN (mg/dL) | 15.8 (10.4) | 35.6 (27.6) | 0.001 |
| ▪ Creatinine (mg/dL) | 0.9 (0.6) | 1.3 (0.8) | 0.19 |
| ▪ AST (U/L) | 49.5 (69.5) | 87.9 (100.0) | 0.20 |
| ▪ ALT (U/L) | 59.1 (98.9) | 66.3 (74.6) | 0.85 |
| ▪ PT-INR | 1.17 (0.15) | 1.30 (0.16) | 0.045 |
| ▪ Total bilirubin (mg/dL) | 1.0 (1.2) | 1.9 (0.4) | 0.001 |
| ▪ Albumin (g/dL) | 3.2 (0.7) | 2.8 (0.6) | 0.17 |
| ▪ NLR ratio | 7.7 (8.3) | 15.2 (11.5) | 0.036 |
| ▪ PLR ratio | 281.7 (141.5) | 327.5 (141.4) | 0.42 |

ALT, alanine aminotransferase; AST, aspartate aminotransferase; ASA, American Society of Anesthesiologists; BMI, body mass index; BUN, blood urea nitrogen;
ECOG, Eastern Cooperative Oncology Group; NLR, neutrophil-to-lymphocyte ratio;
PLR, platelet-to-lymphocyte ratio; PT-INR, prothrombin time/international normalized ratio; SD, standard deviation.




▶ **Fig. 1** Representative cases from each group of patients with 30-day mortality (A,B) and 30-day survival (C,D). A 72-year-old male patient with gastric outlet obstruction due to invasion of the duodenal bulb by pancreatic cancer. This patient presented with severe grade of Charlson comorbidity index, accompanied by moderate-degree ascites. **a** Coronal image of the dilated stomach caused by stricture at the duodenal bulb on computed tomography scan. **b** Target jejunal limb identified under EUS. A 43-year-old male patient with obstruction of duodenal 4th portion by pancreatic cancer. No ascites was observed in this patient, and he had moderate grade of Charlson comorbidity index. **c** Coronal view of CT scan of the abdomen and pelvis showing marked dilatation of the proximal part of the duodenum and the entire stomach. **d** EUS showing distended fluid-filled proximal jejunal limb.

▶ **Table 3** Procedure outcomes according to 30-day mortality.

| Variable | 30-day survival (n = 53) | 30-day mortality (n = 7) | *P* value |
|---|---|---|---|
| Technical success (n, %) | 52, 98.1 | 6, 85.7 | 0.09 |
| Clinical success (n, %)* | 50, 96.2 | 4, 66.7 | 0.007 |
| GOOSS, Mean (SD)* | | | |
| ▪ Baseline | 0.81 (0.40) | 0.57 (0.54) | 0.43 |
| ▪ Post-treatment | 2.21 (0.67) | 1.57 (1.13) | 0.08 |
| Perioperative biliary drainage (n, %) | 14, 26.4 | 2, 28.6 | 0.90 |
| Adverse event (n, %) | 7, 13.2 | 1, 14.3 | 0.92 |
| ▪ Perforation due to misdeployment | 3, 5.7 | 1, 14.3 | |
| ▪ Minor bleeding | 3, 5.7 | 0 | |
| ▪ Pancreatitis | 1, 1.9 | | |
| ASGE AE grade (n, %) | | 0 | |
| ▪ I | 1, 1.9 | 0 | |
| ▪ II | 2, 3.8 | 0 | |
| ▪ IIIa | 3, 5.7 | 1, 14.3 | 0.52 |
| ▪ IIIb | 1, 1.9 | 0 | |
| Postoperative chemotherapy (n, %) | 36, 67.9 | 4, 57.1 | 0.57 |
| Reintervention (n, %) * | | | |
| ▪ Overall | 7, 13.5 | 1, 16.7 | 0.83 |
| ▪ Within 30 days | 3. 5.8 | 1, 16.7 | 0.36 |

*Results from per-protocol analysis
AE, adverse event; ASGE, American Society for Gastrointestinal Endoscopy; GOOSS, gastric outlet obstruction scoring system; SD, standard deviation.

priate despite the short duration of patency. Median time before stent dysfunction has been reported to be less than 2 months for duodenal stents, compared with more than 8 months for EUS-GE [13]. This showed that a duodenal stent can offer sufficient palliation in patients who are expected to have extremely early mortality, whereas EUS-GE may be more cost-effective when life expectancy is expected to be more than 2 months. Thus, predicting postoperative early mortality is crucial for selecting the treatment method, and identifying factors associated with postoperative early mortality would be helpful.

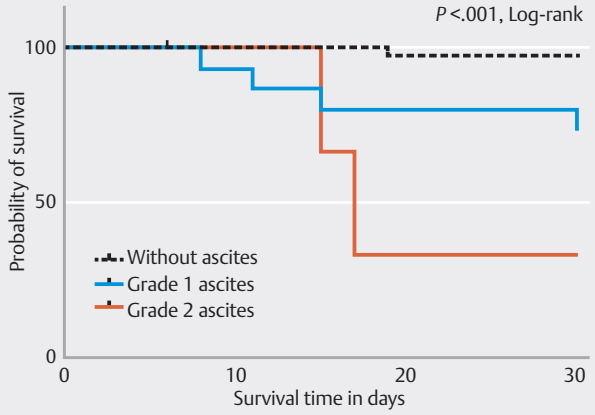
Our study found that, of all the patients who underwent EUS-GE, 11.7% died within 30 days after the procedure. Although this early mortality may be a natural progression of advanced-stage cancer, clinical deterioration due to direct or indirect effects of the procedure cannot be excluded. Our data revealed no association between the initial technical failure after EUS-GE and short-term mortality; however, clinical failure was associated with 30-day mortality. We examined various clinical factors that predispose patients to early mortality. Not surprisingly, ECOG performance status and presence of ascites appeared significantly associated with 30-day mortality. However, after adjustment, only presence of ascites was identified as an independent prognostic factor. Particularly, based on CT -determined ascites grading, it was possible to be more precise and identify the main risk to be grade 2 or higher ascites. It should be stressed that our pre-procedure protocol mandated therapeutic paracentesis before attempting EUS-GE in patients with clinically significant ascites.

A large amount of ascites is considered a contraindication to EUS-GE because it may distance the target bowel from the gastric wall, rendering the intestine excessively mobile for safe puncture and potentially inoculating the ascitic fluid, leading to bacterial peritonitis. It may also promote bowel separation and inhibit fixation of bowel loops after the procedure [33]. Large-volume ascites (whether secondary to malnutrition, peritoneal carcinomatosis, or mixed), may also indicate overall se-

▶ **Table 4** Univariable and multivariable penalized likelihood Firth logistic regression models that examined selected clinical factors as predictors of 30-day mortality after EUS-GE in malignant GOO.

| Covariate | | Univariate analysis | | | | Multivariate analysis | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | cHR | 95% CI | | P value | aHR | 95% CI | | P value | VIF |
| | | | Lower | Upper | | | Lower | Upper | | |
| Age | | 1.02 | 0.95 | 1.10 | 0.53 | | | | | |
| Sex | Male | 1.32 | 0.29 | 6.12 | 0.72 | | | | | |
| CCI | Severe | 7.69 | 0.38 | 153.90 | 0.18 | | | | | |
| ECOG score | ≥ 2 | 10.00 | 1.78 | 56.15 | 0.0089 | 6.62 | 0.95 | 46.04 | .056 | 1.14 |
| ASA score | ≥ 4 | 4.00 | 0.60 | 26.69 | 0.15 | | | | | |
| Staging | Metastatic | 4.38 | 0.50 | 38.26 | 0.18 | | | | | |
| Peritoneal carcinomatosis | | 3.30 | 0.66 | 16.63 | 0.15 | | | | | |
| Ascites | Grade 1 | 12.91 | 1.38 | 120.62 | 0.021 | 7.19 | 0.72 | 71.43 | .11 | 1.16 |
| | Grade 2 | 45.01 | 1.71 | 1186.18 | 0.018 | 52.41 | 1.55 | 1775.64 | .024 | 1.02 |
| Adverse event | | 1.09 | 0.12 | 10.24 | 0.94 | | | | | |
| Further systemic therapy | | 2.25 | 0.45 | 10.14 | 0.29 | | | | | |

aHR, adjusted hazard ratio; ASA, American Society of Anesthesiologists; CCI, Charlson comorbidity index; cHR, crude hazard ratio; CI, confidence interval; ECOG, Eastern Cooperative Oncology Group; EUS-GE, endoscopic ultrasound-guided gastroenterostomy; GOO, gastric outlet obstruction; VIF, variance inflation factor.




▶ **Fig. 2** Kaplan-Meier curve for 30-day survival according to severity of ascites in patients with EUS-GE. Thirty-day survival was more favorable in patients without ascites than in those with ascites, and was particularly unfavorable in those with grade 2 ascites (P < 0.001).

verity of disease and clinical condition, leading to overall earlier demise.

There is a lack of data about how ascites volume may affect results differently after the procedure. To date, two studies have reported on clinical outcomes after EUS-GE in ascites, with the first study presenting no difference in procedure outcomes even though there was a difference in median survival between the patient groups with and without ascites [34]. The second study revealed a higher rate of postoperative AEs, such as peritonitis and worsening ascites in the patients with ascites [35].

There are several valuable strengths to this study. First, 30-day early mortality, which can offer further evidence for treatment indication, was set as the primary endpoint. Because there are alternative treatments available, such as duodenal stenting, that may be effective in the short term, an analysis of early mortality is essential to explore clinical factors in choice of treatment modality based on remaining life expectancy. Second, the relationship between ascites and early mortality was analyzed by adjusting many confounding factors. Third, the results support that more objective ascites grading can be used as guidance in clinical practice. On the other hand, this study has several limitations. First, it was a single-center study. Second, the reliability of the analysis for confounding factors may be affected due to the small sample size. Third, because it was a retrospective study, no postoperative evaluation of ascites or systemic inflammatory condition was performed. Thus, a prospective comparative trial of EUS-GE and duodenal self-expanding metal stent in the patient group with an expected short life expectancy and grade 2 or higher ascites is warranted in the future.

## Conclusions

In conclusion, a 30-day mortality rate of 11.7% was observed in patients with unresectable mGOO who underwent EUS-GE. Among the factors that could be evaluated before the procedure, ascites was found to independently predict 30-day mortality, regardless of whether there was evidence of peritoneal carcinomatosis. Moreover, ascites with a grade 2 or higher de-

gree conferred a very high risk of early mortality and may deter performance of EUS-GE.

## Conflict of Interest

The authors declare that they have no conflict of interest.

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