

Gastrointestinal Endoscopy

Laparoscopic versus EUS-guided Gastroenterostomy for Gastric Outlet Obstruction: An International Multicentre Propensity Score-Matched Comparison.

--Manuscript Draft--

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Abstract:	<p>Background and aims</p> <p>In the management of gastric outlet obstruction (GOO), EUS-guided gastroenterostomy (EUS-GE) seems safe and more effective than enteral stenting. However, comparisons to laparoscopic gastroenterostomy (L-GE) are scarce. Our aim was to perform a propensity score-matched comparison between EUS-GE and L-GE.</p> <p>Methods</p> <p>An international, multicentre retrospective analysis was performed of consecutive EUS-GE and L-GE procedures in 3 academic centers (Jan-2015 to May-2020), using propensity score-matching in order to minimize selection bias. A standard maximum propensity score difference of 0.1 was applied, also considering underlying disease and oncological staging.</p> <p>Results</p> <p>Overall, 77 patients were treated with EUS-GE and 48 patients with L-GE. By means of propensity score-matching, 37 patients were allocated to both groups, resulting in 74 (1:1) matched patients.</p>

Technical success was achieved in 35/37 EUS-GE-treated patients (94.6%) vs. 100% in the L-GE group (p=0.493). Clinical success, defined as eating without vomiting or GOO Scoring System ≥ 2 , was achieved in 97.1% and 89.2% respectively (p=0.358). Median time to oral intake (1 (IQR 0.3-1.0) vs. 3 (IQR 1.0-5.0) days, p<0.001) and median hospital stay (4 (IQR 2-8) vs 8 (IQR 5.5-20) days, p<0.001) were significantly shorter in the EUS-GE group. Overall adverse events (AEs) (2.7% vs. 27.0%, p=0.007) and severe AEs (0.0% vs. 16.2%, p=0.025) were identified more frequently in the L-GE group.

Conclusion

For patients with GOO, EUS-GE and L-GE showed almost identical technical and clinical success. However, reduced time to oral intake, shorter median hospital stay and lower rate of adverse events suggest that the EUS-guided approach might be preferable.

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Editor-in-chief

Leuven, February 15th 2020

Gastrointestinal endoscopy

Dear prof. Wallace

RE: Response to reviewers

We hereby thank the editors for considering our revised manuscript entitled, **“Laparoscopic versus EUS-guided Gastroenterostomy for Gastric Outlet Obstruction: An International Multicentre Propensity Score-Matched Comparison”** for publication in *Gastrointestinal Endoscopy*.

Secondly, we would like to again express our gratitude towards the reviewers for providing their constructive criticism. Please find a point-by-point answer to Reviewer 1 underneath.

Based on these comments we have adapted the manuscript: changes have been **highlighted in light blue** for the convenience of the reader.

Response to Reviewer #1:

At this time, please check your submitted Disclosure and Attestation form carefully to ensure that it is complete and accurate for ALL authors. GIE takes this very seriously; please be sure all authors have disclosed all conflicts of interest.

Reviewer #1: The study by Bronswijk encourages the endosonographer to perform gastroenterostomy under EUS.

However, there are a few description on the surgical procedures.

Major

1. please mention the size of surgical gastrojejunostomy. It is important factor for endosonographers or device company to improve the LAMS in the future.

Response: All laparoscopic gastrojejunostomies were performed using 60mm blue Echelon staplers (Johnson & Johnson, New Brunswick, New Jersey, USA) or 60mm Endo GIA universal staplers (Medtronic Ltd., Dublin, Ireland), with additional staplers and sutures covering the staple line as needed. During construction of the gastro-enteric anastomosis, a 36 French nasogastric tube was temporarily placed through the defect in the majority of cases, in an effort to maintain and confirm patency while stapling or suturing. These considerations were revised in the *Methods*-section. These procedures

were performed by expert academic gastrointestinal surgeons specifically credentialed to perform these procedures.

The development of a LAMS is governed by the ability to pass the device along the working channel of the endoscope as well as the ability to deploy the device endoscopically. There will be a trade-off between size of the stent on the one hand, and the functionality of the device on the other hand. As our data have indicated, we have shown that size does matter and that the 20mm Axios stent performed better than the 15mm stent. However it is conceivable, given the constraints of design, that larger diameter stents will be cumbersome to place and not necessarily aid in better gastric emptying.

2. Surgical GE showed higher AE rate comparing to EUS-GE. The ratio of surgical GE looks higher than general outcome. Why? How about experience of surgeons? PI describe that in the result and discussion.

Response: Thank you for the in-depth appraisal of our comparative analysis. Indeed, a higher rate of adverse events was seen in the L-GE group, compared to EUS-GE in the overall cohort (6.5% vs. 31.3%, $p < 0.001$), as well as in the propensity score-matched cohort (2.7% vs. 27%, $p = 0.007$). However, when comparing surgical adverse event rates to the other available studies in this field as well as to the general published literature, we see that our overall surgical adverse event rate is even lower than the study by Perez-Miranda, et al. (41% surgical adverse events vs. 31.3% in our study- doi: 10.1097/MCG.0000000000000887) and similar results when compared with the comparative trial by Mouen Kashab, et al. (25% vs. 31.3% in our study - doi: 10.1055/s-0043-101695). This suggests that the superior safety outcomes of EUS-GE observed in our analysis were not due to inferior performance of the surgical comparator group. These comparisons were added to the *Discussion*-section.

Respectfully,

Schalk Van der Merwe, MD PhD

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Leuven, November 20th, 2020

Dear professor Michael B. Wallace

Editor in Chief – Gastrointestinal Endoscopy

Dear (co-)editors,

We hereby would like to submit our original manuscript entitled '**Laparoscopic versus EUS-guided Gastroenterostomy for Gastric Outlet Obstruction: An International Multicentre Propensity Score-Matched Comparison**', by Michiel Bronswijk et al. for publication in *Gastrointestinal Endoscopy* as an *Original Article*.

In the management of gastric outlet obstruction (GOO), EUS-guided gastroenterostomy (EUS-GE) has been gaining ground. However, there is still uncertainty regarding the place of EUS-GE in daily clinical practice, due to a lack of data comparing this technique to laparoscopic gastroenterostomy (L-GE) in patients stratified according to potential confounders, such as oncological staging and pre-procedural fragility.

We therefore performed a propensity score-matched analysis, comparing EUS-GE with LGE, using a large multicentre international cohort.

There are two reasons why we think that our paper is a great fit for *Gastrointestinal Endoscopy*. First, our study is one of the largest original cohorts of EUS-GE. And second, using this large international multicentre cohort, the current study represents the first propensity score-matched analysis comparing EUS-GE with L-GE. While awaiting high-quality prospective confirmation, these findings may guide gastroenterologists, oncologists and surgeons in therapeutic decision making in the context of GOO.

We thank you for taking our work into consideration and hope that our study merits publication in *GIE*.

Yours sincerely,

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Laparoscopic versus EUS-guided Gastroenterostomy for Gastric Outlet Obstruction: An International Multicentre Propensity Score-Matched Comparison.

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Author statement

MB was responsible for study design, data collection, statistical analysis and drafting of the manuscript. GV and RvW acted as local lead investigators, collected data, aided in data interpretation and critically revised the final versions of the manuscript. JJ, BT, FD and MGB were responsible for the surgical procedures and revised the final manuscript. GV, HvM, WL, RV, PF and RvW performed the EUS procedures and revised the final version of the manuscript. AL aided in data interpretation and revised the final versions of the manuscript. SVDM was responsible for data interpretation, provided critical insights into study design, performed EUS procedures and critically revised the final version of the manuscript.

Conflict of interest:

Michiel Bronswijk received grants from Taewoong, Takeda and Prion Medical. Hannah van Malenstein holds a consultancy agreement with Boston-Scientific. Schalk Van der Merwe holds the Cook chair in Interventional endoscopy and holds consultancy agreements with Cook, Pentax and Olympus. Wim Laleman co-chairs the Boston-Scientific Chair in Therapeutic Biliopancreatic Endoscopy with Schalk Van der Merwe and has consultancy agreements with Boston Scientific and Cook. Marc G. Besselink received grants for investigator initiated studies from Ethicon, Medtronic and Intuitive. Rogier P. Voermans received a research grant and consultancy fees from Boston Scientific.

The remaining authors declared no potential conflicts of interests regarding the current paper.

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Abstract

Background and aims:

In the management of gastric outlet obstruction (GOO), EUS-guided gastroenterostomy (EUS-GE) seems safe and more effective than enteral stenting. However, comparisons to laparoscopic gastroenterostomy (L-GE) are scarce. Our aim was to perform a propensity score-matched comparison between EUS-GE and L-GE.

Methods:

An international, multicentre retrospective analysis was performed of consecutive EUS-GE and L-GE procedures in 3 academic centers (Jan-2015 to May-2020), using propensity score-matching in order to minimize selection bias. A standard maximum propensity score difference of 0.1 was applied, also considering underlying disease and oncological staging.

Results:

Overall, 77 patients were treated with EUS-GE and 48 patients with L-GE. By means of propensity score-matching, 37 patients were allocated to both groups, resulting in 74 (1:1) matched patients.

Technical success was achieved in 35/37 EUS-GE-treated patients (94.6%) vs. 100% in the L-GE group ($p=0.493$). Clinical success, defined as eating without vomiting or GOO Scoring System ≥ 2 , was achieved in 97.1% and 89.2% respectively ($p=0.358$). Median time to oral intake (1 (IQR 0.3-1.0) vs. 3 (IQR 1.0-5.0) days, $p<0.001$) and median hospital stay (4 (IQR 2-8) vs 8 (IQR 5.5-20) days, $p<0.001$) were significantly shorter in the EUS-GE group. Overall adverse events (AEs) (2.7% vs. 27.0%, $p=0.007$) and severe AEs (0.0% vs. 16.2%, $p=0.025$) were identified more frequently in the L-GE group.

Conclusion:

For patients with GOO, EUS-GE and L-GE showed almost identical technical and clinical success. However, reduced time to oral intake, shorter median hospital stay and lower rate of adverse events suggest that the EUS-guided approach might be preferable.

Keywords

Gastric outlet syndrome, laparoscopic gastrojejunostomy, endoscopic ultrasound, LAMS.

Introduction

1
2 Gastric outlet obstruction (GOO), defined by a mechanical obstruction of the duodenum, pylorus or antrum, may result from
3 various diseases. The underlying aetiology has shifted from mainly peptic ulcer disease in the past, to predominantly
4 malignant causes at present^{1,2}. In the most recent cohorts, GOO was caused by underlying malignancy in up to 85% of
5 patients, the majority of which could be attributed to pancreatic cancer^{3,4,5,6,7}. On the other hand, peptic ulcer disease and
6 chronic pancreatitis are still the most prevalent causes of benign GOO^{8,9}. Consequences of GOO, such as nausea, vomiting,
7 anorexia, need for nasogastric tube decompression and subsequent loss of body mass, may further aggravate this complex
8 clinical entity, increasing morbidity, reducing quality of life and significantly influencing tolerability and efficacy of oncological
9 treatments¹⁰. Before the advent of endoscopic ultrasound-guided gastroenterostomy (EUS-GE), management of GOO mainly
10 relied on surgical gastroenterostomy, the standard of care for many years^{11,12}. Since the late nineties, placement of metal
11 enteral stents was found to provide higher efficacy regarding early re-initiation of oral intake, as well as reduce hospital stay
12 and major adverse events (AE)¹¹, albeit at the expense of more recurrent obstructive symptoms due to stent dysfunction^{13,14}.
13 Since 2012, EUS-GE has found its way from initial animal studies, into daily practice of tertiary centres^{15,16}. This EUS-guided
14 approach has become a minimally invasive alternative for patients with both benign or malignant GOO^{3,4} and demonstrated
15 higher clinical success and lower need for re-interventions compared to enteral stenting^{5,17}. There is still uncertainty regarding
16 the place of EUS-GE in daily clinical practice, due to a lack of data comparing this technique to the current reference standard,
17 laparoscopic gastroenterostomy (L-GE), in patients stratified according to potential confounders, such as oncological staging
18 and pre-procedural fragility¹⁸⁻²⁰.

19 Our aim was to perform a propensity score-matched comparison of EUS-GE to L-GE, using a large retrospective international
20 multicentre cohort.
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Methods

Patients and study design

A retrospective analysis was performed of all consecutive L-GE and EUS-GE procedures performed for GOO at the Amsterdam University Medical Centers, location AMC and VUmc (the Netherlands), IRCCS San Raffaele Scientific Institute Milan (Italy) and University Hospitals Leuven (Belgium) between January 2015 and May 2020. For both procedures, identical variables were extracted from patients' electronic medical charts. Inclusion criteria consisted of: (1) symptomatic GOO, (2) endoscopic or radiological confirmation of benign or malignant gastro-duodenal stenosis and (3) treatment with EUS-GE or L-GE. Considering the surgical procedures, only strictly "pure" laparoscopic gastroenterostomies were eligible for inclusion, as to minimize confounding effects of adjunctive procedures, such as metastasectomy, hepatico-enterostomy or cholecystectomy, often performed simultaneously. Each patient gave his or her consent with regards to the procedure. This study was furthermore approved by the central Institutional Review Board (study identifier: s64254) at the University Hospitals Leuven and at each participating center.

Endpoints

Technical success was defined as the successful creation of a gastro-enteric anastomosis by use of the initially chosen technique (see below for technical considerations). If additional approaches or techniques had to be involved or additional self-expandable metal stents (SEMS) were needed, this was regarded as a technical failure.

Food intake grading was defined using the GOO Scoring System (GOOSS) (0= no intake, 1= liquid only, 2= soft solids, 3= almost full diet, 4= full diet)^{21,22}; symptomatic GOO was defined as a GOOSS of 0. In concordance with previous work⁷, clinical success was defined as eating without vomiting or a GOOSS of ≥ 2 and was ascertained by evaluation of the electronic patient file, where this parameter is recorded as part of standard practice. Regarding safety, the ASGE lexicon for adverse events was used to stratify AE in mild, moderate, severe or fatal events²³.

Secondary endpoints were: hospital stay, weight change after 2 months, gastroenterostomy dysfunction, distal obstruction rates, 'time to oral intake' and 'time to full diet' (GOOSS of 4). For EUS-GE procedural time was extracted from the endoscopic electronic reporting system. For L-GE, procedural time was retrieved by revision of the anaesthesiology report, exactly stating the beginning and the end of the procedure. Gastroenterostomy dysfunction was defined as recurrence of obstructive symptoms (GOOSS < 1) after former clinical success, with confirmation of recurrent GOO by endoscopy or imaging studies. Mechanical obstructions located downstream the GE site, without signs of EUS-GE or L-GE dysfunction, were annotated as 'distal obstructions', but not registered as GE dysfunction.

Procedure: the Wireless EUS-gastroenterostomy Simplified Technique (WEST)

All EUS-GE are performed under deep sedation with propofol or general anaesthesia, using a electrocautery-enhanced lumen apposing metal stent (LAMS) and the Wireless EUS-gastroenterostomy Simplified Technique (WEST) as previously described, under prophylactic antibiotic therapy (Video)^{24,25}.

After a 7Fr nasobiliary catheter or enteral feeding tube is placed, through the gastric or duodenal stenosis into the jejunum, water is infused in the targeted loop of small bowel (Figure 1, upper left panel). Using a combination of fluoroscopy and EUS-guided identification of the catheter (Figure 1, upper middle panel) the dilated jejunal or enteric loop is accessed using the biflanged electrocautery-enhanced LAMS (Hot-Axios; Boston Scientific, Marlborough, MA, USA). Following successful intraluminal access to the small bowel, the distal flange is deployed under endosonographic guidance; the device is then

1 retracted (Figure 1, upper right panel), favouring apposition of the gastric and enteric wall and allowing the opening of the
2 proximal flange inside the endoscope channel (Figure 1, lower left panel); the device is finally pushed outside the working
3 channel together with a careful scope retraction, resulting in deployment of the proximal flange into the gastric lumen.
4 Afterwards, successful deployment is confirmed by either EUS (Figure 1, lower left panel), direct endoscopic visualisation
5 (Figure 2) or, if needed, combined with fluoroscopy and contrast injection (Figure 1, lower middle panel).
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7 8 *Procedure: Laparoscopic gastroenterostomy:* 9

10 Following CO₂-insufflation (12-15 mmHg intra-abdominal pressure) by a Veress needle or by open introduction, 4-5 trocars
11 are introduced: one camera port around the umbilicus and 3 to 4 trocars at different positions in the upper abdomen. Next,
12 Treitz' ligament is identified and two electrocautery incisions are made, one in the dorsal or anterior gastric wall and one in
13 the jejunum. An anterior, dorsal latero-lateral or side-to-side isoperistaltic gastroenteric anastomosis is constructed. The exact
14 location of the gastroenteric anastomosis, with regards to Treitz' ligament, varies from 30cm to 60cm. During the surgical
15 approach a 60mm blue Echelon stapler (Johnson & Johnson, New Brunswick, New Jersey, USA) or 60mm Endo GIA universal
16 stapler (Medtronic Ltd., Dublin, Ireland) is used depending on the preference of the surgeon, with additional staplers and
17 sutures covering the staple line as needed. During construction of the gastroenteric anastomosis, a 36 French nasogastric
18 tube is temporarily placed through the defect in the majority of cases, in an effort to maintain and confirm patency while
19 stapling or suturing. Anti-traction sutures are used when appropriate. If not in place before the surgical procedure, a
20 nasogastric tube is inserted afterwards and the patient remained on nil per mouth. In this study we only included "pure" L-GE
21 for comparison to EUS-GJ and excluded procedures were adjunctive treatments, such as cholecystectomy,
22 hepaticojejunostomy or metastasectomy were performed. All surgical procedures were performed by gastrointestinal
23 surgeons with extensive experience in laparoscopic gastrointestinal surgery, operating in high-volume academic centres.
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31 32 *Statistical analysis*

33 Categorical variables were reported as frequencies (%) and Fisher's test was used to compare these variables. Continuous
34 variables were reported as medians and interquartile range (IQR) or means \pm standard deviation (SD). Student's *t* test and
35 Mann-Whitney *U* test were used for comparing continuous variables as appropriate. Differences in outcomes are shown as
36 odds ratio (OR) and 95% confidence interval (CI). Kaplan-Meier curves were used for overall post-procedural survival analysis,
37 whereas the log-rank test was used for corresponding comparisons. Furthermore, learning curve effect was evaluated by
38 comparing the initial 50% of procedures with the second half of EUS-GE procedures in each centre. A multiple logistic
39 regression was performed to identify predictors of clinical failure: age, gender, pancreatic cancer, presence of ascites or
40 peritoneal carcinomatosis, use of 15mm LAMS and balloon dilation, as well as learning curve were used as variables. P-values
41 <0.05 were considered statistically significant.
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48 A propensity score-matched analysis was performed in an effort to minimize selection bias. Age, sex, underlying disease,
49 corresponding disease stage, presence of ascites and presence of peritoneal carcinomatosis were used as variables. The
50 aforementioned variables were selected based on: (1) analysis of previous literature and (2) significant differences between
51 the two groups after univariate analysis. In four previously published studies, which performed a multivariate analysis,
52 peritoneal carcinomatosis and ascites were identified as factors associated with clinical and technical failure respectively^{3,4,7,26}
53 A standard maximum propensity score difference of 0.1 was admitted for matching.
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55 SPSS version 26.0 (IBM, Chicago, IL, USA) was used for matching and statistical analysis, whereas Graphpad Prism version
56 9.0.0 for Windows (Graphpad Software, San Diego, CA, USA) was used for the Kaplan-Meier curves and survival analysis.
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Results

Overall, we identified 126 patients, one of whom was excluded due to missing data, resulting in a total of 77 patients (62%) who underwent EUS-GE and 48 patients (38%) undergoing L-GE.

Baseline characteristics are shown in Table 1. Ascites (22.1% vs. 4.2%, $p=0.009$) and pancreatic cancer-induced GOO (48.1% vs. 29.2%, $p=0.037$) were significantly more frequent in the EUS-GE group, whereas underlying benign disease was identified significantly less (3.9% vs. 14.6%, $p=0.044$) when compared to L-GE-treated patients (Table 1). Technical success (94.8% (95% CI: 87.0-98.4) vs. 100% (95% CI: 91.2-100.0), $p=0.297$) was similar when comparing both groups, while a trend towards higher per-protocol clinical success amongst EUS-GE-treated patients was observed (97.3% (95% CI: 90.0-99.8) vs. 87.5% (95% CI: 74.9-94.5), OR 5.07 (95% CI: 0.98-26.28), $p=0.057$) (Table 2).

Overall, 15mm and 20mm LAMS were utilized in 11 and 64 patients respectively, with higher clinical success rates (81.8% (95% CI: 51.2-96.0) vs. 100% (95% CI: 93.0-100.0) respectively, $p=0.021$) and a trend towards shorter median hospital stay (5 days (2.8-11) vs. 4 days (2.0-11), $p=0.054$) when 20mm LAMS were utilized. Intraprocedural balloon dilation of the central part of the LAMS immediately after its placement was performed in 26% of patients and did not affect efficacy outcomes (Supplementary Table 1). Although two primary clinical failures occurred in patients in whom 15mm LAMS were used without dilation, multivariate analysis did not identify any significant independent risk factors for clinical failure (Supplementary Table 2). Overall AEs (6.5% (95%CI: 2.5-14.7) vs 31.3% (95% CI: 19.9-45.4), OR 0.15 (95% CI: 0.05-0.46), $p<0.001$), and severe AEs (2.6% (95% CI: 0.2-9.5) vs 18.8% (95%CI: 10.0-32.2), OR 0.12 (95% CI: 0.03-0.59), $p=0.007$) occurred significantly less frequently in EUS-GE versus L-GE treated patients (Table 2).

Propensity score-matched analysis

By means of propensity score matching, 37 patients were allocated to each group, resulting in a total of 74 (1:1) matched patients (Figure 3). The propensity score-matched cohort revealed an overall mean age of 66.5 ± 11.8 years, 44.6% were female, 36.5% had underlying pancreatic cancer, with 31.1% and 6.8% of patients exhibiting peritoneal carcinomatosis and ascites. Underlying benign disease was present in four (5.4%) patients. Baseline comparisons between EUS-GE and L-GE-treated patients are shown in Table 3. No significant differences between both study groups were identified.

Efficacy

In the propensity score-matched EUS-GE group, two technical failures occurred, due to inability to advance the nasobiliary catheter through the stenosis. This resulted in a technical success rate of 94.6% (35 out of 37 patients, 95% CI: 81.4-99.4), compared to 100% (95% CI: 88.8-100.0), $p=0.493$) amongst L-GE-treated patients (Table 4). Clinical success rates by means of intention to treat analysis (91.9% (95% CI: 78.0-97.9) vs. 89.2% (95% CI: 74.7-96.3), $p=1.000$), as well as per-protocol analysis were comparable (97.1% (95% CI: 84.2-100.0) vs. 89.2% (95% CI: 74.7-96.3), $p=0.358$), with primary non-functional surgical gastroenterostomy in three L-GE-patients. Procedure time (46 minutes (IQR 37.5-80.0) vs. 85 minutes (73.0-110), $p<0.001$), median time to oral intake (1 day (IQR 0.3-1.0) vs. 3 days (IQR 1.0-5.0), $p<0.001$) and median time to full diet (2 days (IQR 1.0-3.8) vs. 9 days (IQR 4.0-23), $p<0.001$) were significantly shorter in the EUS-GE group.

After a median follow-up of 77 days (IQR 27-160) in the EUS group and 123 days in the surgical group (IQR 32-262), gastroenterostomy dysfunction rates (none in both groups) did not differ. With two-months' weight change available in 51.4% and 56.8% of patients treated with EUS-GE and L-GE respectively, no significant differences were detected (-0.3kg (IQR -2.4-1.1) vs. 0kg (IQR -3.0-0.7), $p=0.159$).

Safety and postoperative outcomes

1 The overall number of AEs in the propensity score-matched cohort was lower amongst EUS-GE treated patients (2.7% (95%
2 CI: 0.01-15.1) vs. 27% (95% CI: 15.2-43.1), OR 0.07 (95% CI: 0.01-0.62), p=0.007) (Table 4). Most AEs in the L-GE group (6 out
3 of 10) were severe, mainly consisting of anastomotic leaks (n=4, 10.8%) or bleeding (n=2, 5.4%), necessitating surgical
4 reintervention in three patients (8.1%), while no severe AEs were registered among EUS-GE treated patients (0.0% (95% CI:
5 0.0-11.2) vs. 16.2% (95% CI: 7.3-31.5), OR 0.07 (95% CI: 0.00-1.19), p=0.025). Mild (2.7% in each group) and moderate AE
6 rates (0.0% (95% CI: 0.0-11.2) vs. 8.1% (95% CI: 2.1-22.0), p=0.240) were similar in both groups. In two L-GE patients,
7 endoscopic reinterventions was deemed necessary in the context of postoperative bleeding and placement of a trans-
8 anastomotic stent to treat a dysfunctional surgical anastomosis.
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14 A significantly shorter median hospital stay (4 days (IQR 2.0-8.0) vs. 8 days (IQR 5.5-20), p<0.001) was observed amongst EUS-
15 GE-treated patients. Survival analysis did not reveal a significant difference in post-procedural survival in the matched cohort,
16 nor in the overall cohort (Figure 4).
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Learning Curve Assessment

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21 When comparing the first to the second half of both the overall and propensity score-matched EUS-GE cohorts
22 (Supplementary Table 3), no significant differences were found in terms of safety and efficacy.
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Discussion

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2 In the current analysis, we performed the first propensity score-matched comparison between EUS-GE and L-GE. We found
3 that EUS-GE achieved similar technical and clinical success, with significantly lower overall and severe AEs, faster resumption
4 of oral intake and earlier discharge compared to L-GE. Whilst the EUS-GE technical and clinical success rate was in line with
5 previously published studies^{3-9,27}, we observed that technical success depended mainly on the ability to pass a nasobiliary
6 catheter through the stenosis. Furthermore, amongst all technical variables, only LAMS calibre might have some influence on
7 clinical outcome, although this was not confirmed by multivariate analysis.
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11 The paucity of published comparative data makes it difficult to identify a well-defined place for EUS-GE in the management
12 of patients with GOO, especially compared to the more established techniques such as surgery and enteral stenting. Only a
13 single large multicentre retrospective study comparing open gastroenterostomy to EUS-GE has been published so far⁷. The
14 authors reported lower AEs compared to the open surgical approach, at the cost of a lower, but not statistically significant,
15 technical success rate. Surprisingly, length of hospital stay amongst both groups was similar. One can speculate whether this
16 was related to the limited experience available at the time, which may have influenced clinical decisions regarding timing of
17 discharge and general post-EUS-GE management. In our cohort, most patients were discharged after a median of 4 days (IQR
18 2.0-8.0) compared to 8 days (IQR 5.5-20) in the L-GE group, which may have an impact on health care costs and quality of life. We
19 chose to compare our EUS-GE cohort with laparoscopic surgery, as it has proven superior to open surgery, in and outside the
20 context of gastroenterostomy, showing lower morbidity and earlier recovery compared to open surgery, making the L-GE
21 approach the most desired comparator¹⁸. One previous multicentre retrospective analysis evaluated the efficacy and safety of
22 EUS-GE compared to L-GE, this study only included 25 patients undergoing EUS-GE and did not correct for potential
23 confounding factors or bias¹⁹. The authors demonstrated increased safety and lower costs using EUS-GE, while retaining
24 similar efficacy to L-GE, even if they detected a non-significant difference in technical success in favour of L-GE¹⁹.
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28 The surgical adverse event rate observed in our study (31.3%), was similar to those reported by Perez-Miranda, et al (41%)¹⁹
29 and Kashab, et al (25%)⁷, suggesting that the superior safety outcomes of EUS-GE observed in our analysis were not due to
30 inferior performance of the surgical comparator group. Furthermore, when comparing surgical adverse events rates in
31 historical cohorts of surgical palliative gastroenterostomy, similar²⁸⁻³⁰ or higher³¹⁻³³ adverse event rates were seen when
32 compared to the current analysis.
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41 When considering previous comparisons of EUS-GE with enteral stenting, limited evidence suggests that the latter is
42 associated with a lower rate of clinical success and higher rates of stent failure requiring re-intervention^{5,17}. These findings
43 have been confirmed in studies comparing enteral stenting with surgical gastroenterostomy, suggesting that enteral stenting
44 should be considered in the context of very limited life expectancy only^{13,34}.
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49 There are some issues when comparing previous EUS-GE data with our current analysis. First, several techniques have been
50 described for performing EUS-GE, which include the endoscopic ultrasonography-guided double-balloon-occluded
51 gastrojejunostomy bypass (EPASS)-technique, natural orifice transluminal endoscopic surgery (NOTES), rendez-vous methods
52 including balloon-assisted gastroenterostomy, and the direct or 'free-hand'-techniques^{7,35-37}. These techniques have been
53 interchangeably used throughout several studies^{3,4,7,8,19}, complicating reliable direct comparisons of results. Secondly, several
54 previous papers have published overlapping study cohorts, rendering data interpretation somewhat complicated^{4,19,20,35,38}.
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56 Third, the use of different LAMS with a limited number of studies also including cases where Niti-S Spaxus LAMS (Taewoong
57 Medical Co. Ltd., Ilsan, Korea) were used instead of the Hot-Axios^{3,7,26}. Regarding different EUS-GE approaches, a comparative
58 study has shown that the direct method achieves similar technical and clinical success, with a similar safety profile when
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1 compared to balloon-assisted EUS-GE³. However, in the context of the direct method, procedure time was more than twice
2 shorter (35.7 vs. 89.9min, p<0.001), thus suggesting the direct technique as the preferred method. In all of our patients, only
3 the Wireless EUS-gastroenterostomy Simplified Technique (WEST) was used, indicating that there is no need for a 19G
4 'finder'-needle, as has been described in the direct technique, or a guidewire and balloon in order to perform EUS-GE safely
5 and effectively^{3,24,25}. We recommend against inflating the targeted loop of small bowel by water or contrast injection using a
6 19-gauge needle, such as in the setting of EUS-directed transenteric ERCP (EDEE)³⁹, an approach which may carry a higher
7 theoretical risk of puncturing a more distal enteric loop or even the colon. We do recommend using the most straightforward
8 technique available, in an effort to reduce the number of additional accessories requiring exchange, which in our opinion
9 carries an increased risk of adverse events by complicating positioning, visualisation and, as time passes, reduction in small
10 bowel distention.

11 While the usefulness of EUS-GE in malignant disease has been reported in various studies, the evidence of this procedure in
12 benign disease has been increasing since only recently^{5,7,17}. Doubts concerning LAMS patency and long-term results have led
13 to restricted use in benign diseases. In 2020, James et al. published their series on EUS-GE in benign disease, revealing that
14 surgery was averted in 83.3% of patients and regression of the benign stricture allowed for LAMS removal in the majority of
15 patients over time⁹. Together with long-term follow-up data published in 2019⁵, which showed a 15% recurrence rate after a
16 median follow-up time of 169 (malignant disease) and 319.5 days (benign disease), we can conclude that especially in
17 patients with malignant disease GOO, recurrence is an issue. In our current propensity score-matched analysis
18 gastroenterostomy dysfunction did not occur at all, although two cases of distal enteric obstruction, due to metastatic
19 peritoneal disease, were identified in the EUS-GE group, compared to one in the L-GE-group.

20 In comparison to various other studies, where there was no mention of the incidence of ascites^{3,4,6-9,17,19}, 21% of our patients
21 underwent EUS-GE despite the presence of ascites, without any significant related AEs. Although ascites has been regarded as
22 a strict contraindication for EUS-GE, these results, together with a retrospective analysis in 2019⁵, suggest that patients with
23 mild or localized ascites can be considered for EUS-GE without risking leakage or subsequent peritonitis, provided that there
24 is no tense ascites and that the LAMS trajectory is not compromised due to fluid interference.

25 *Limitations and strengths:*

26 Several limitations of the current study should be addressed. First, the retrospective nature of this analysis might have
27 inadvertently introduced some bias. Secondly, due to the study design, a certain degree of missing data was identified, most
28 especially in the context of body weight evolution. Third, generalizability of our data might be an issue, as all endoscopists
29 were highly trained and operating in high-volume settings.

30 We have tried to address some of these limitations in our study design. We included a propensity score-matched design,
31 correcting for the selected variables to limit selection bias. These specific variables were chosen as they were differently
32 distributed amongst the two treatment groups, whilst potentially influencing technical and clinical success, as well as 'time to
33 oral intake', 'time to full diet', overall survival and gastroenterostomy dysfunction rates. One of the disadvantages of
34 propensity score-matching, is the dependence on the matching criteria. We therefore included various variables as to provide
35 a stringent matching process. To reduce larger treatment effects and higher degrees of bias of single centre studies, we
36 involved three different tertiary referral centres recruiting similar patients and all performing EUS-GE using the WEST
37 approach^{24,25}. Finally, with 77 patients in whom EUS-GE was performed, our study is one of the largest published original
38 cohorts of EUS-GE, and the largest study to date to compare EUS-GE with L-GE.

1 In conclusion, this study suggests that in patients with gastric outlet syndrome, EUS-GE and L-GE provide almost identical
2 technical and clinical success rates. Lower time to oral intake, shorter hospital stay and a lower rate of adverse events
3 prudentially suggest that EUS-GE should be the preferred approach in patients with GOO. While awaiting high-quality
4 prospective confirmation, these findings should guide gastroenterologists, oncologists and surgeons in considering EUS-GE
5 for treating GOO, especially in the setting of malignancy, where patients will benefit from the least invasive technique with
6 the highest expected efficacy.
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11 Acknowledgements

13 None
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Figure legend

Figure 1. Stepwise approach to the Wireless EUS-gastroenterostomy Simplified Technique (WEST).

Upper left: Fluoroscopic image, placement of a 7Fr nasobiliary catheter or enteral feeding tube through the gastric or duodenal stenosis into the jejunum. Confirmation of the distal position by contrast opacification.

Upper middle: Endoscopic ultrasound image, showing distention of the targeted loop of small bowel after infusion of water.

Upper right: Using a combination of fluoroscopy and EUS-guided identification of the catheter, the dilated jejunal or enteric loop is accessed using the biflanged electrocautery-enhanced LAMS, after which the distal flange is deployed under endosonographic guidance. The device is then retracted onto the gastric wall.

Lower left: Endoscopic ultrasound image, after compressing the gastric and enteric wall, as well as deployment of the proximal flange inside the endoscope channel, the device is finally pushed outside the working channel together with a careful scope retraction, resulting in deployment of the proximal flange into the gastric lumen.

Lower middle: Fluoroscopic evaluation after LAMS release, showing the successful deployment of the LAMS between the stomach and small bowel.

Lower right: Endoscopic view, after recannulation with a diagnostic catheter.

Figure 2. Direct endoscopic visualisation of successful gastroenterostomy.

Figure 3. Study flowchart.

Figure 4. Post-procedural survival analysis.

Tables

Table 1. Overall baseline characteristics.

Variable	EUS-GE (n=77)		L-GE (n=48)		P value
Age (years), mean ± SD	65	±12.3	66	±11.6	0.478
Female, n (%)	36	(46.8%)	19	(39.6%)	0.432
Median follow up duration, days (IQR)	76	(36-136)	122	(35-274)	0.057
Primary disease					
Pancreatic cancer	37	(48.1%)	14	(29.2%)	0.037
Biliary/gallbladder cancer	9	(11.7%)	2	(4.2%)	0.149
Gastric cancer	7	(9.1%)	5	(10.4%)	0.807
Duodenal cancer	11	(14.3%)	10	(20.8%)	0.341
Breast cancer	2	(2.6%)	2	(4.2%)	0.463
Colorectal cancer	2	(2.6%)	1	(2.1%)	1.000
NET	1	(1.3%)	0	(0.0%)	0.384
Ampullary cancer	0	(0.0%)	1	(2.1%)	0.384
NSCLC	3	(3.9%)	1	(2.1%)	1.000
Benign disease	3	(3.9%)	7	(14.6%)	0.044
Disease stage					
Local invasion	25	(32.5%)	13	(27.1%)	0.555
Liver metastases	8	(10.4%)	9	(18.8%)	0.193
Peritoneal metastases	8	(10.4%)	10	(20.8%)	0.122
Diffuse metastatic	19	(24.7%)	9	(18.8%)	0.512
Disease manifestations					
Ascites	17	(22.1%)	2	(4.2%)	0.009
Peritoneal carcinomatosis	20	(26.0%)	16	(33.3%)	0.420

Table 2. Overall outcomes.

	EUS-GE (n=77)		L-GE (n=48)		OR (95% CI), P value
Efficacy					
Technical success, n (%)	73	(94.8%)	48	(100%)	0.17 (0.01-3.20), 0.297
Clinical success, n (%)	71	(92.2%)	42	(87.5%)	1.69 (0.51-5.58), 0.534
Per protocol clinical success, n (%)	71	(97.3%)	42	(87.5%)	5.07 (0.98-26.28), 0.057
Median time to oral intake, days (IQR)	1	(0-1)	3	(1-5)	<0.001
Full diet tolerability, n (%)	32	(41.6%)	19	(39.6%)	1.16 (0.56-2.44), 0.854
Median time to full diet, days (IQR)	2	(1-4)	8	(4-21)	<0.001
Gastroenterostomy dysfunction, n (%)	1	(1.3%)	0	(0.0%)	1.90 (0.08-47.64), 1.000
Median time to dysfunction, days (IQR)	243	N/A	N/A	N/A	N/A
Distal obstruction, n (%)	8	(10.4%)	1	(1.3%)	5.45 (0.66-45.02), 0.151
Median time to distal obstruction, days (IQR)	34	(18-138)	13	N/A	N/A
Safety					
Overall adverse events, n (%)	5	(6.5%)	15	(31.3%)	0.15 (0.05-0.46), <0.001
Mild, n(%)	2	(2.6%)	1	(2.1%)	1.25 (0.11-14.21), 1.000
Post-procedural fever, n (%)	2	(2.6%)	0	(0.0%)	3.21 (0.15-68.35), 0.523
Moderate, n(%)	1	(1.3%)	5	(10.4%)	0.11 (0.01-1.00), 0.106
Sepsis, n (%)	1	(1.3%)	0	(0.0%)	1.90 (0.08-47.64), 1.000
Need for re-endoscopy, n (%)	0	(0.0%)	4	(8.3%)	0.06 (0.00-1.21), 0.020
Severe, n(%)	2	(2.6%)	9	(18.8%)	0.12 (0.03-0.59), 0.007
Intra-peritoneal LAMS deployment, n (%)	2	(2.6%)	N/A	N/A	N/A
Anastomotic leak, n (%)	N/A	N/A	3	(6.3%)	N/A
Anastomotic bleeding, n (%)	N/A	N/A	2	(4.2%)	N/A
Surgical re-intervention, n (%)	N/A	N/A	3	(6.3%)	N/A
Fatal, n(%)	0	(0.0%)	0	(0.0%)	1.000
Other					
Median procedure duration, min (IQR)	51	(36 - 79.8)	95	(75 - 118)	<0.001
Median hospital stay, days (IQR)	4	(2 - 10.5)	8	(5 - 20)	<0.001
Median weight change after 2 months, kg (IQR)	-1	(-4.0 - 1.1)	-0,4	(-4.2 - 0.8)	0.390
Median post-procedural survival, days (IQR)	103	(44 - 252)	147	(68 - 335)	0.246

Abbreviations: CI: confidence interval, EUS-GE: Endoscopic ultrasound-guided gastroenterostomy, IQR: interquartile range, LGE: laparoscopic gastroenterostomy, N/A: not applicable, OR: odds ratio.

Table 3. Matched cohort: baseline characteristics.

Variable	EUS-GE (n=37)		L-GE (n=37)		P value
Age (years), mean ± SD	66.5	±12.5	66.4	±11.1	0.954
Female, n(%)	18	(48.7%)	15	(40.5%)	0.640
Median follow up duration, days (IQR)	77	27-160	123	32-262	0.105
Primary disease					
Pancreatic cancer	15	(40.5%)	13	(35.1%)	0.811
Biliary/gallbladder cancer	5	(13.5%)	2	(5.4%)	0.430
Gastric cancer	5	(13.5%)	5	(13.5%)	1.000
Duodenal cancer	6	(16.2%)	8	(21.6%)	0.768
Benign disease	2	(5.4%)	2	(5.4%)	1.000
Breast cancer	1	(2.7%)	1	(2.7%)	1.000
Colorectal cancer	2	(5.4%)	0	(0.0%)	0.493
NET	1	(2.7%)	0	(0.0%)	1.000
Ampullary cancer	0	(0.0%)	1	(2.7%)	1.000
NSCLC	1	(2.7%)	1	(2.7%)	1.000
Disease stage					
Local invasion	15	(40.5%)	12	(32.4%)	0.630
Liver metastases	6	(16.2%)	8	(21.6%)	0.768
Peritoneal metastases	6	(16.2%)	7	(18.9%)	1.000
Diffuse metastatic	8	(21.6%)	6	(16.2%)	0.768
Disease manifestations					
Ascites	3	(8.1%)	2	(5.4%)	1.000
Peritoneal carcinomatosis	10	(27.0%)	13	(35.1%)	0.616

Table 4. Matched cohort: outcome comparisons.

	EUS-GE (n=37)		L-GE (n=37)		OR (95% CI), P value
Efficacy					
Technical success, n (%)	35	(94.6%)	37	(100%)	0.19 (0.01-4.08), 0.493
Clinical success, n (%)	34	(91.9%)	33	(89.2%)	1.37 (0.29-6.62), 1.000
Per protocol clinical success, n (%)	34/35	(97.1%)	33	(89.2%)	4.12 (0.44-38.83), 0.358
Median time to oral intake, days (IQR)	1	(0.3-1.0)	3	(1.0-5.0)	<0.001
Full diet at discharge, n (%)	21	(56.8%)	14	(37.8%)	2.16 (0.85-5.46), 0.162
Median time to full diet, days (IQR)	2	(1.0-3.8)	9	(4.0-23)	<0.001
Gastroenterostomy dysfunction, n (%)	0	(0.0%)	0	(0.0%)	1.000
Distal obstruction, n (%)	2	(5.4%)	1	(2.7%)	2.06 (0.18-23.72), 1.000
Safety					
Overall adverse events, n (%)	1	(2.7%)	10	(27.0%)	0.07 (0.01-0.62), 0.007
Mild, n(%)	1	(2.7%)	1	(2.7%)	1.000
Moderate, n(%)	0	(0.0%)	3	(8.1%)	0.13 (0.01-2.64), 0.240
Endoscopic reintervention	0	(0.0%)	2	(5.4%)	0.19 (0.01-4.08), 0.493
Severe, n(%)	0	(0.0%)	6	(16.2%)	0.07 (0.00-1.19), 0.025
Surgical reintervention	0	(0.0%)	3	(8.1%)	0.13 (0.01-2.64), 0.240
Anastomotic leak	0	(0.0%)	4	(10.8%)	0.10 (0.01-1.91), 0.115
Anastomotic bleed	0	(0.0%)	2	(5.4%)	0.19 (0.01-4.08), 0.493
Fatal, n(%)	0	(0.0%)	0	(0.0%)	1.000
Other					
Median procedure duration, min (IQR)	46	(37.5-80)	85	(73.0-110)	<0.001
Median hospital stay, days (IQR)	4	(2.0-8.0)	8	(5.5-19.5)	<0.001
Median 2-months' weight change, kg (IQR)	-0,3	(-2.4-1.1)	0	(-3.0-0.7)	0.159
Median post-procedural survival, days (IQR)	96	(41.5-248)	152	(43.5-282)	0.317

Abbreviations: CI: confidence interval, EUS-GE: Endoscopic ultrasound-guided gastroenterostomy, IQR: interquartile range, LGE: laparoscopic gastroenterostomy, N/A: not applicable, OR: odds ratio.

Supplementary tables

Supplementary table 1. Sub-analysis comparing 15mm and 20mm LAMS efficacy and outcomes with or without balloon dilation.

Variable:	15mm LAMS (n=11)		20mm LAMS (n=64)		P-value
Technical success, n (%)	11/11	100%	62/64	96.9%	1.000
Clinical success*, n (%)	9/11	81.8%	62/62	100%	0.021
Median time to oral intake, days (IQR)	1	(0-1)	1	(0-1)	0.826
Full diet tolerability, n (%)	6	54.5%	45	70.3%	0.314
Median time to full diet, days (IQR)	2	(1-3)	2	(1-4)	0.099
Overall adverse events, n (%)	1	9.1%	4	6.5%	0.558
Gastroenterostomy dysfunction, n (%)	0	0.0%	1	1.6%	1.000
Median time to dysfunction, days (IQR)	N/A	N/A	243	N/A	N/A
Median hospital stay, days (IQR)	5	(2.8-11)	4	(2.0-11)	0.054
Median weight change after 2 months, kg (IQR)	-1.4	(-5.2-0.6)	-1	(-4.0-1.1)	0.430
Variable:	With LAMS dilation (n=20)		Without LAMS dilation (n=55)		P-value
Technical success, n (%)	20/20	100%	53/55	96.4%	1.000
Clinical success*, n (%)	20/20	100%	51/53	96.2%	1.000
Median time to oral intake, days (IQR)	1	(0-1)	1	(0-1)	0.153
Full diet tolerability, n (%)	10	50.0%	39	70.9%	0.107
Median time to full diet, days (IQR)	2.5	(1-4)	2	(2-8)	0.254
Overall adverse events, n (%)	1	5.0%	4	7.3%	0.579
Gastroenterostomy dysfunction, n (%)	1	5.0%	0	0.0%	1.000
Median time to dysfunction, days (IQR)	243	N/A	N/A	N/A	N/A
Median hospital stay, days (IQR)	5	(2.0-11)	4	(2.0-11)	0.022
Median weight change after 2 months, kg (IQR)	-1.4	(-5.1-0.7)	-1	(-4.0-1.1)	0.849

Abbreviations: IQR: interquartile range, LAMS: lumen-apposing metal stent, kg: kilogram, N/A: not applicable.

*: per-protocol analysis.

Supplementary table 2. Multivariate analysis of variables in EUS-GE clinical failure.

Variable	OR	95% CI	P-value
Age	0.98	0.90-1.03	0.532
Gender, female	2.95	0.46-11.18	0.132
Pancreatic cancer	3.14	0.69-20.22	0.115
Ascites	8.39	1.29-375.4	0.104
Peritoneal carcinomatosis	2.65	0.44-28.94	0.305
15mm LAMS	2.45	0.14-14.09	0.332
Balloon dilation	0.11	0.01-0.72	0.059
Learning curve, first 50%	1.30	0.37-15.49	0.726

Supplementary table 3. Learning curve assessment: comparison between first and second half of the EUS-GE cohorts.

	First 50% (n=18)		Second 50% (n=19)		P-value
Propensity score-matched EUS-GE cohort:					
Technical success, n (%)	17/18	94.4%	18/19	94.7%	1.000
Clinical success, n (%)	17/18	94.4%	17/19	89.5%	1.000
Per protocol clinical success, n (%)	17/17	100%	17/18	94.4%	1.000
Overall adverse events, n (%)	1	5.6%	1	5.3%	1.000
Median procedure duration, min (IQR)	51	(34-84)	46	(40-83)	0.719
	First 50% (n=38)		Second 50% (n=39)		P-value
Overall EUS-GE cohort:					
Technical success, n (%)	37/38	97.4%	36/39	92.3%	0.615
Clinical success, n (%)	37/38	97.4%	34/39	87.2%	0.200
Per protocol clinical success, n (%)	37/37	100%	34/36	94.4%	0.240
Overall adverse events, n (%)	3	7.9%	3	7.7%	1.000
Median procedure duration, min (IQR)	49	(36-78)	52	(33-83)	0.719

Abbreviations: EUS-GE: Endoscopic ultrasound-guided gastroenterostomy, IQR: interquartile range.

Laparoscopic versus EUS-guided Gastroenterostomy for Gastric Outlet Obstruction: An International Multicentre Propensity Score-Matched Comparison.

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Abstract

Background and aims:

In the management of gastric outlet obstruction (GOO), EUS-guided gastroenterostomy (EUS-GE) seems safe and more effective than enteral stenting. However, comparisons to laparoscopic gastroenterostomy (L-GE) are scarce. Our aim was to perform a propensity score-matched comparison between EUS-GE and L-GE.

Methods:

An international, multicentre retrospective analysis was performed of consecutive EUS-GE and L-GE procedures in 3 academic centers (Jan-2015 to May-2020), using propensity score-matching in order to minimize selection bias. A standard maximum propensity score difference of 0.1 was applied, also considering underlying disease and oncological staging.

Results:

Overall, 77 patients were treated with EUS-GE and 48 patients with L-GE. By means of propensity score-matching, 37 patients were allocated to both groups, resulting in 74 (1:1) matched patients.

Technical success was achieved in 35/37 EUS-GE-treated patients (94.6%) vs. 100% in the L-GE group ($p=0.493$). Clinical success, defined as eating without vomiting or GOO Scoring System ≥ 2 , was achieved in 97.1% and 89.2% respectively ($p=0.358$). Median time to oral intake (1 (IQR 0.3-1.0) vs. 3 (IQR 1.0-5.0) days, $p<0.001$) and median hospital stay (4 (IQR 2-8) vs 8 (IQR 5.5-20) days, $p<0.001$) were significantly shorter in the EUS-GE group. Overall adverse events (AEs) (2.7% vs. 27.0%, $p=0.007$) and severe AEs (0.0% vs. 16.2%, $p=0.025$) were identified more frequently in the L-GE group.

Conclusion:

For patients with GOO, EUS-GE and L-GE showed almost identical technical and clinical success. However, reduced time to oral intake, shorter median hospital stay and lower rate of adverse events suggest that the EUS-guided approach might be preferable.

Keywords

Gastric outlet syndrome, laparoscopic gastrojejunostomy, endoscopic ultrasound, LAMS.

Introduction

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Gastric outlet obstruction (GOO), defined by a mechanical obstruction of the duodenum, pylorus or antrum, may result from various diseases. The underlying aetiology has shifted from mainly peptic ulcer disease in the past, to predominantly malignant causes at present^{1,2}. In the most recent cohorts, GOO was caused by underlying malignancy in up to 85% of patients, the majority of which could be attributed to pancreatic cancer^{3,4,5,6,7}. On the other hand, peptic ulcer disease and chronic pancreatitis are still the most prevalent causes of benign GOO^{8,9}. Consequences of GOO, such as nausea, vomiting, anorexia, need for nasogastric tube decompression and subsequent loss of body mass, may further aggravate this complex clinical entity, increasing morbidity, reducing quality of life and significantly influencing tolerability and efficacy of oncological treatments¹⁰. Before the advent of endoscopic ultrasound-guided gastroenterostomy (EUS-GE), management of GOO mainly relied on surgical gastroenterostomy, the standard of care for many years^{11,12}. Since the late nineties, placement of metal enteral stents was found to provide higher efficacy regarding early re-initiation of oral intake, as well as reduce hospital stay and major adverse events (AE)¹¹, albeit at the expense of more recurrent obstructive symptoms due to stent dysfunction^{13,14}. Since 2012, EUS-GE has found its way from initial animal studies, into daily practice of tertiary centres^{15,16}. This EUS-guided approach has become a minimally invasive alternative for patients with both benign or malignant GOO^{3,4} and demonstrated higher clinical success and lower need for re-interventions compared to enteral stenting^{5,17}. There is still uncertainty regarding the place of EUS-GE in daily clinical practice, due to a lack of data comparing this technique to the current reference standard, laparoscopic gastroenterostomy (L-GE), in patients stratified according to potential confounders, such as oncological staging and pre-procedural fragility¹⁸⁻²⁰.

Our aim was to perform a propensity score-matched comparison of EUS-GE to L-GE, using a large retrospective international multicentre cohort.

Methods

Patients and study design

A retrospective analysis was performed of all consecutive L-GE and EUS-GE procedures performed for GOO at the Amsterdam University Medical Centers, location AMC and VUmc (the Netherlands), IRCCS San Raffaele Scientific Institute Milan (Italy) and University Hospitals Leuven (Belgium) between January 2015 and May 2020. For both procedures, identical variables were extracted from patients' electronic medical charts. Inclusion criteria consisted of: (1) symptomatic GOO, (2) endoscopic or radiological confirmation of benign or malignant gastro-duodenal stenosis and (3) treatment with EUS-GE or L-GE. Considering the surgical procedures, only strictly "pure" laparoscopic gastroenterostomies were eligible for inclusion, as to minimize confounding effects of adjunctive procedures, such as metastasectomy, hepatico-enterostomy or cholecystectomy, often performed simultaneously. Each patient gave his or her consent with regards to the procedure. This study was furthermore approved by the central Institutional Review Board (study identifier: s64254) at the University Hospitals Leuven and at each participating center.

Endpoints

Technical success was defined as the successful creation of a gastro-enteric anastomosis by use of the initially chosen technique (see below for technical considerations). If additional approaches or techniques had to be involved or additional self-expandable metal stents (SEMS) were needed, this was regarded as a technical failure.

Food intake grading was defined using the GOO Scoring System (GOOSS) (0= no intake, 1= liquid only, 2= soft solids, 3= almost full diet, 4= full diet)^{21,22}; symptomatic GOO was defined as a GOOSS of 0. In concordance with previous work⁷, clinical success was defined as eating without vomiting or a GOOSS of ≥ 2 and was ascertained by evaluation of the electronic patient file, where this parameter is recorded as part of standard practice. Regarding safety, the ASGE lexicon for adverse events was used to stratify AE in mild, moderate, severe or fatal events²³.

Secondary endpoints were: hospital stay, weight change after 2 months, gastroenterostomy dysfunction, distal obstruction rates, 'time to oral intake' and 'time to full diet' (GOOSS of 4). For EUS-GE procedural time was extracted from the endoscopic electronic reporting system. For L-GE, procedural time was retrieved by revision of the anaesthesiology report, exactly stating the beginning and the end of the procedure. Gastroenterostomy dysfunction was defined as recurrence of obstructive symptoms (GOOSS < 1) after former clinical success, with confirmation of recurrent GOO by endoscopy or imaging studies. Mechanical obstructions located downstream the GE site, without signs of EUS-GE or L-GE dysfunction, were annotated as 'distal obstructions', but not registered as GE dysfunction.

Procedure: the Wireless EUS-gastroenterostomy Simplified Technique (WEST)

All EUS-GE are performed under deep sedation with propofol or general anaesthesia, using an electrocautery-enhanced lumen apposing metal stent (LAMS) and the Wireless EUS-gastroenterostomy Simplified Technique (WEST) as previously described, under prophylactic antibiotic therapy (Video)^{24,25}.

After a 7Fr nasobiliary catheter or enteral feeding tube is placed, through the gastric or duodenal stenosis into the jejunum, water is infused in the targeted loop of small bowel (Figure 1, upper left panel). Using a combination of fluoroscopy and EUS-guided identification of the catheter (Figure 1, upper middle panel) the dilated jejunal or enteric loop is accessed using the biflanged electrocautery-enhanced LAMS (Hot-Axios; Boston Scientific, Marlborough, MA, USA). Following successful intraluminal access to the small bowel, the distal flange is deployed under endosonographic guidance; the device is then

1 retracted (Figure 1, upper right panel), favouring apposition of the gastric and enteric wall and allowing the opening of the
2 proximal flange inside the endoscope channel (Figure 1, lower left panel); the device is finally pushed outside the working
3 channel together with a careful scope retraction, resulting in deployment of the proximal flange into the gastric lumen.
4 Afterwards, successful deployment is confirmed by either EUS (Figure 1, lower left panel), direct endoscopic visualisation
5 (Figure 2) or, if needed, combined with fluoroscopy and contrast injection (Figure 1, lower middle panel).
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8 *Procedure: Laparoscopic gastroenterostomy:*

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10 Following CO₂-insufflation (12-15 mmHg intra-abdominal pressure) by a Veress needle or by open introduction, 4-5 trocars
11 are introduced: one camera port around the umbilicus and 3 to 4 trocars at different positions in the upper abdomen. Next,
12 Treitz' ligament is identified and two electrocautery incisions are made, one in the dorsal or anterior gastric wall and one in
13 the jejunum. An anterior, dorsal latero-lateral or side-to-side isoperistaltic gastroenteric anastomosis is constructed. The exact
14 location of the gastroenteric anastomosis, with regards to Treitz' ligament, varies from 30cm to 60cm. During the surgical
15 approach a 60mm blue Echelon stapler (Johnson & Johnson, New Brunswick, New Jersey, USA) or 60mm Endo GIA universal
16 stapler (Medtronic Ltd., Dublin, Ireland) is used depending on the preference of the surgeon, with additional staplers and
17 sutures covering the staple line as needed. During construction of the gastroenteric anastomosis, a 36 French nasogastric
18 tube is temporarily placed through the defect in the majority of cases, in an effort to maintain and confirm patency while
19 stapling or suturing. Anti-traction sutures are used when appropriate. If not in place before the surgical procedure, a
20 nasogastric tube is inserted afterwards and the patient remained on nil per mouth. In this study we only included "pure" L-GE
21 for comparison to EUS-GJ and excluded procedures were adjunctive treatments, such as cholecystectomy,
22 hepaticojejunostomy or metastasectomy were performed. All surgical procedures were performed by gastrointestinal
23 surgeons with extensive experience in laparoscopic gastrointestinal surgery, operating in high-volume academic centres.
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31 *Statistical analysis*

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33 Categorical variables were reported as frequencies (%) and Fisher's test was used to compare these variables. Continuous
34 variables were reported as medians and interquartile range (IQR) or means \pm standard deviation (SD). Student's *t* test and
35 Mann-Whitney *U* test were used for comparing continuous variables as appropriate. Differences in outcomes are shown as
36 odds ratio (OR) and 95% confidence interval (CI). Kaplan-Meier curves were used for overall post-procedural survival analysis,
37 whereas the log-rank test was used for corresponding comparisons. Furthermore, learning curve effect was evaluated by
38 comparing the initial 50% of procedures with the second half of EUS-GE procedures in each centre. A multiple logistic
39 regression was performed to identify predictors of clinical failure: age, gender, pancreatic cancer, presence of ascites or
40 peritoneal carcinomatosis, use of 15mm LAMS and balloon dilation, as well as learning curve were used as variables. P-values
41 <0.05 were considered statistically significant.
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48 A propensity score-matched analysis was performed in an effort to minimize selection bias. Age, sex, underlying disease,
49 corresponding disease stage, presence of ascites and presence of peritoneal carcinomatosis were used as variables. The
50 aforementioned variables were selected based on: (1) analysis of previous literature and (2) significant differences between
51 the two groups after univariate analysis. In four previously published studies, which performed a multivariate analysis,
52 peritoneal carcinomatosis and ascites were identified as factors associated with clinical and technical failure respectively^{3,4,7,26}
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54 A standard maximum propensity score difference of 0.1 was admitted for matching.
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57 SPSS version 26.0 (IBM, Chicago, IL, USA) was used for matching and statistical analysis, whereas Graphpad Prism version
58 9.0.0 for Windows (Graphpad Software, San Diego, CA, USA) was used for the Kaplan-Meier curves and survival analysis.
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Results

Overall, we identified 126 patients, one of whom was excluded due to missing data, resulting in a total of 77 patients (62%) who underwent EUS-GE and 48 patients (38%) undergoing L-GE.

Baseline characteristics are shown in Table 1. Ascites (22.1% vs. 4.2%, $p=0.009$) and pancreatic cancer-induced GOO (48.1% vs. 29.2%, $p=0.037$) were significantly more frequent in the EUS-GE group, whereas underlying benign disease was identified significantly less (3.9% vs. 14.6%, $p=0.044$) when compared to L-GE-treated patients (Table 1). Technical success (94.8% (95% CI: 87.0-98.4) vs. 100% (95% CI: 91.2-100.0), $p=0.297$) was similar when comparing both groups, while a trend towards higher per-protocol clinical success amongst EUS-GE-treated patients was observed (97.3% (95% CI: 90.0-99.8) vs. 87.5% (95% CI: 74.9-94.5), OR 5.07 (95% CI: 0.98-26.28), $p=0.057$) (Table 2).

Overall, 15mm and 20mm LAMS were utilized in 11 and 64 patients respectively, with higher clinical success rates (81.8% (95% CI: 51.2-96.0) vs. 100% (95% CI: 93.0-100.0) respectively, $p=0.021$) and a trend towards shorter median hospital stay (5 days (2.8-11) vs. 4 days (2.0-11), $p=0.054$) when 20mm LAMS were utilized. Intraprocedural balloon dilation of the central part of the LAMS immediately after its placement was performed in 26% of patients and did not affect efficacy outcomes (Supplementary Table 1). Although two primary clinical failures occurred in patients in whom 15mm LAMS were used without dilation, multivariate analysis did not identify any significant independent risk factors for clinical failure (Supplementary Table 2). Overall AEs (6.5% (95%CI: 2.5-14.7) vs 31.3% (95% CI: 19.9-45.4), OR 0.15 (95% CI: 0.05-0.46), $p<0.001$), and severe AEs (2.6% (95% CI: 0.2-9.5) vs 18.8% (95%CI: 10.0-32.2), OR 0.12 (95% CI: 0.03-0.59), $p=0.007$) occurred significantly less frequently in EUS-GE versus L-GE treated patients (Table 2).

Propensity score-matched analysis

By means of propensity score matching, 37 patients were allocated to each group, resulting in a total of 74 (1:1) matched patients (Figure 3). The propensity score-matched cohort revealed an overall mean age of 66.5 ± 11.8 years, 44.6% were female, 36.5% had underlying pancreatic cancer, with 31.1% and 6.8% of patients exhibiting peritoneal carcinomatosis and ascites. Underlying benign disease was present in four (5.4%) patients. Baseline comparisons between EUS-GE and L-GE-treated patients are shown in Table 3. No significant differences between both study groups were identified.

Efficacy

In the propensity score-matched EUS-GE group, two technical failures occurred, due to inability to advance the nasobiliary catheter through the stenosis. This resulted in a technical success rate of 94.6% (35 out of 37 patients, 95% CI: 81.4-99.4), compared to 100% (95% CI: 88.8-100.0), $p=0.493$) amongst L-GE-treated patients (Table 4). Clinical success rates by means of intention to treat analysis (91.9% (95% CI: 78.0-97.9) vs. 89.2% (95% CI: 74.7-96.3), $p=1.000$), as well as per-protocol analysis were comparable (97.1% (95% CI: 84.2-100.0) vs. 89.2% (95% CI: 74.7-96.3), $p=0.358$), with primary non-functional surgical gastroenterostomy in three L-GE-patients. Procedure time (46 minutes (IQR 37.5-80.0) vs. 85 minutes (73.0-110), $p<0.001$), median time to oral intake (1 day (IQR 0.3-1.0) vs. 3 days (IQR 1.0-5.0), $p<0.001$) and median time to full diet (2 days (IQR 1.0-3.8) vs. 9 days (IQR 4.0-23), $p<0.001$) were significantly shorter in the EUS-GE group.

After a median follow-up of 77 days (IQR 27-160) in the EUS group and 123 days in the surgical group (IQR 32-262), gastroenterostomy dysfunction rates (none in both groups) did not differ. With two-months' weight change available in 51.4% and 56.8% of patients treated with EUS-GE and L-GE respectively, no significant differences were detected (-0.3kg (IQR -2.4-1.1) vs. 0kg (IQR -3.0-0.7), $p=0.159$).

Safety and postoperative outcomes

1 The overall number of AEs in the propensity score-matched cohort was lower amongst EUS-GE treated patients (2.7% (95%
2 CI: 0.01-15.1) vs. 27% (95% CI: 15.2-43.1), OR 0.07 (95% CI: 0.01-0.62), p=0.007) (Table 4). Most AEs in the L-GE group (6 out
3 of 10) were severe, mainly consisting of anastomotic leaks (n=4, 10.8%) or bleeding (n=2, 5.4%), necessitating surgical
4 reintervention in three patients (8.1%), while no severe AEs were registered among EUS-GE treated patients (0.0% (95% CI:
5 0.0-11.2) vs. 16.2% (95% CI: 7.3-31.5), OR 0.07 (95% CI: 0.00-1.19), p=0.025). Mild (2.7% in each group) and moderate AE
6 rates (0.0% (95% CI: 0.0-11.2) vs. 8.1% (95% CI: 2.1-22.0), p=0.240) were similar in both groups. In two L-GE patients,
7 endoscopic reinterventions was deemed necessary in the context of postoperative bleeding and placement of a trans-
8 anastomotic stent to treat a dysfunctional surgical anastomosis.
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14 A significantly shorter median hospital stay (4 days (IQR 2.0-8.0) vs. 8 days (IQR 5.5-20), p<0.001) was observed amongst EUS-
15 GE-treated patients. Survival analysis did not reveal a significant difference in post-procedural survival in the matched cohort,
16 nor in the overall cohort (Figure 4).
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Learning Curve Assessment

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21 When comparing the first to the second half of both the overall and propensity score-matched EUS-GE cohorts
22 (Supplementary Table 3), no significant differences were found in terms of safety and efficacy.
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Discussion

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2 In the current analysis, we performed the first propensity score-matched comparison between EUS-GE and L-GE. We found
3 that EUS-GE achieved similar technical and clinical success, with significantly lower overall and severe AEs, faster resumption
4 of oral intake and earlier discharge compared to L-GE. Whilst the EUS-GE technical and clinical success rate was in line with
5 previously published studies^{3-9,27}, we observed that technical success depended mainly on the ability to pass a nasobiliary
6 catheter through the stenosis. Furthermore, amongst all technical variables, only LAMS calibre might have some influence on
7 clinical outcome, although this was not confirmed by multivariate analysis.
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11 The paucity of published comparative data makes it difficult to identify a well-defined place for EUS-GE in the management
12 of patients with GOO, especially compared to the more established techniques such as surgery and enteral stenting. Only a
13 single large multicentre retrospective study comparing open gastroenterostomy to EUS-GE has been published so far⁷. The
14 authors reported lower AEs compared to the open surgical approach, at the cost of a lower, but not statistically significant,
15 technical success rate. Surprisingly, length of hospital stay amongst both groups was similar. One can speculate whether this
16 was related to the limited experience available at the time, which may have influenced clinical decisions regarding timing of
17 discharge and general post-EUS-GE management. In our cohort, most patients were discharged after a median of 4 days (IQR
18 2.0-8.0) compared to 8 days (IQR 5.5-20) in the L-GE group, which may have an impact on health care costs and quality of life. We
19 chose to compare our EUS-GE cohort with laparoscopic surgery, as it has proven superior to open surgery, in and outside the
20 context of gastroenterostomy, showing lower morbidity and earlier recovery compared to open surgery, making the L-GE
21 approach the most desired comparator¹⁸. One previous multicentre retrospective analysis evaluated the efficacy and safety of
22 EUS-GE compared to L-GE, this study only included 25 patients undergoing EUS-GE and did not correct for potential
23 confounding factors or bias¹⁹. The authors demonstrated increased safety and lower costs using EUS-GE, while retaining
24 similar efficacy to L-GE, even if they detected a non-significant difference in technical success in favour of L-GE¹⁹.
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28 The surgical adverse event rate observed in our study (31.3%), was similar to those reported by Perez-Miranda, et al (41%)¹⁹
29 and Kashab, et al (25%)⁷, suggesting that the superior safety outcomes of EUS-GE observed in our analysis were not due to
30 inferior performance of the surgical comparator group. Furthermore, when comparing surgical adverse events rates in
31 historical cohorts of surgical palliative gastroenterostomy, similar²⁸⁻³⁰ or higher³¹⁻³³ adverse event rates were seen when
32 compared to the current analysis.
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42 When considering previous comparisons of EUS-GE with enteral stenting, limited evidence suggests that the latter is
43 associated with a lower rate of clinical success and higher rates of stent failure requiring re-intervention^{5,17}. These findings
44 have been confirmed in studies comparing enteral stenting with surgical gastroenterostomy, suggesting that enteral stenting
45 should be considered in the context of very limited life expectancy only^{13,34}.
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49 There are some issues when comparing previous EUS-GE data with our current analysis. First, several techniques have been
50 described for performing EUS-GE, which include the endoscopic ultrasonography-guided double-balloon-occluded
51 gastrojejunostomy bypass (EPASS)-technique, natural orifice transluminal endoscopic surgery (NOTES), rendez-vous methods
52 including balloon-assisted gastroenterostomy, and the direct or 'free-hand'-techniques^{7,35-37}. These techniques have been
53 interchangeably used throughout several studies^{3,4,7,8,19}, complicating reliable direct comparisons of results. Secondly, several
54 previous papers have published overlapping study cohorts, rendering data interpretation somewhat complicated^{4,19,20,35,38}.
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56 Third, the use of different LAMS with a limited number of studies also including cases where Niti-S Spaxus LAMS (Taewoong
57 Medical Co. Ltd., Ilsan, Korea) were used instead of the Hot-Axios^{3,7,26}. Regarding different EUS-GE approaches, a comparative
58 study has shown that the direct method achieves similar technical and clinical success, with a similar safety profile when
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1 compared to balloon-assisted EUS-GE³. However, in the context of the direct method, procedure time was more than twice
2 shorter (35.7 vs. 89.9min, $p < 0.001$), thus suggesting the direct technique as the preferred method. In all of our patients, only
3 the Wireless EUS-gastroenterostomy Simplified Technique (WEST) was used, indicating that there is no need for a 19G
4 'finder'-needle, as has been described in the direct technique, or a guidewire and balloon in order to perform EUS-GE safely
5 and effectively^{3,24,25}. We recommend against inflating the targeted loop of small bowel by water or contrast injection using a
6 19-gauge needle, such as in the setting of EUS-directed transenteric ERCP (EDEE)³⁹, an approach which may carry a higher
7 theoretical risk of puncturing a more distal enteric loop or even the colon. We do recommend using the most straightforward
8 technique available, in an effort to reduce the number of additional accessories requiring exchange, which in our opinion
9 carries an increased risk of adverse events by complicating positioning, visualisation and, as time passes, reduction in small
10 bowel distention.
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15 While the usefulness of EUS-GE in malignant disease has been reported in various studies, the evidence of this procedure in
16 benign disease has been increasing since only recently^{5,7,17}. Doubts concerning LAMS patency and long-term results have led
17 to restricted use in benign diseases. In 2020, James et al. published their series on EUS-GE in benign disease, revealing that
18 surgery was averted in 83.3% of patients and regression of the benign stricture allowed for LAMS removal in the majority of
19 patients over time⁹. Together with long-term follow-up data published in 2019⁵, which showed a 15% recurrence rate after a
20 median follow-up time of 169 (malignant disease) and 319.5 days (benign disease), we can conclude that especially in
21 patients with malignant disease GOO, recurrence is an issue. In our current propensity score-matched analysis
22 gastroenterostomy dysfunction did not occur at all, although two cases of distal enteric obstruction, due to metastatic
23 peritoneal disease, were identified in the EUS-GE group, compared to one in the L-GE-group.
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30 In comparison to various other studies, where there was no mention of the incidence of ascites^{3,4,6-9,17,19}, 21% of our patients
31 underwent EUS-GE despite the presence of ascites, without any significant related AEs. Although ascites has been regarded as
32 a strict contraindication for EUS-GE, these results, together with a retrospective analysis in 2019⁵, suggest that patients with
33 mild or localized ascites can be considered for EUS-GE without risking leakage or subsequent peritonitis, provided that there
34 is no tense ascites and that the LAMS trajectory is not compromised due to fluid interference.
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39 *Limitations and strengths:*

40 Several limitations of the current study should be addressed. First, the retrospective nature of this analysis might have
41 inadvertently introduced some bias. Secondly, due to the study design, a certain degree of missing data was identified, most
42 especially in the context of body weight evolution. Third, generalizability of our data might be an issue, as all endoscopists
43 were highly trained and operating in high-volume settings.
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47 We have tried to address some of these limitations in our study design. We included a propensity score-matched design,
48 correcting for the selected variables to limit selection bias. These specific variables were chosen as they were differently
49 distributed amongst the two treatment groups, whilst potentially influencing technical and clinical success, as well as 'time to
50 oral intake', 'time to full diet', overall survival and gastroenterostomy dysfunction rates. One of the disadvantages of
51 propensity score-matching, is the dependence on the matching criteria. We therefore included various variables as to provide
52 a stringent matching process. To reduce larger treatment effects and higher degrees of bias of single centre studies, we
53 involved three different tertiary referral centres recruiting similar patients and all performing EUS-GE using the WEST
54 approach^{24,25}. Finally, with 77 patients in whom EUS-GE was performed, our study is one of the largest published original
55 cohorts of EUS-GE, and the largest study to date to compare EUS-GE with L-GE.
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1 In conclusion, this study suggests that in patients with gastric outlet syndrome, EUS-GE and L-GE provide almost identical
2 technical and clinical success rates. Lower time to oral intake, shorter hospital stay and a lower rate of adverse events
3 prudentially suggest that EUS-GE should be the preferred approach in patients with GOO. While awaiting high-quality
4 prospective confirmation, these findings should guide gastroenterologists, oncologists and surgeons in considering EUS-GE
5 for treating GOO, especially in the setting of malignancy, where patients will benefit from the least invasive technique with
6 the highest expected efficacy.
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11 Acknowledgements

13 None
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Figure legend

Figure 1. Stepwise approach to the Wireless EUS-gastroenterostomy Simplified Technique (WEST).

Upper left: Fluoroscopic image, placement of a 7Fr nasobiliary catheter or enteral feeding tube through the gastric or duodenal stenosis into the jejunum. Confirmation of the distal position by contrast opacification.

Upper middle: Endoscopic ultrasound image, showing distention of the targeted loop of small bowel after infusion of water.

Upper right: Using a combination of fluoroscopy and EUS-guided identification of the catheter, the dilated jejunal or enteric loop is accessed using the biflanged electrocautery-enhanced LAMS, after which the distal flange is deployed under endosonographic guidance. The device is then retracted onto the gastric wall.

Lower left: Endoscopic ultrasound image, after compressing the gastric and enteric wall, as well as deployment of the proximal flange inside the endoscope channel, the device is finally pushed outside the working channel together with a careful scope retraction, resulting in deployment of the proximal flange into the gastric lumen.

Lower middle: Fluoroscopic evaluation after LAMS release, showing the successful deployment of the LAMS between the stomach and small bowel.

Lower right: Endoscopic view, after recannulation with a diagnostic catheter.

Figure 2. Direct endoscopic visualisation of successful gastroenterostomy.

Figure 3. Study flowchart.

Figure 4. Post-procedural survival analysis.

Tables

Table 1. Overall baseline characteristics.

Variable	EUS-GE (n=77)		L-GE (n=48)		P value
Age (years), mean ± SD	65	±12.3	66	±11.6	0.478
Female, n (%)	36	(46.8%)	19	(39.6%)	0.432
Median follow up duration, days (IQR)	76	(36-136)	122	(35-274)	0.057
Primary disease					
Pancreatic cancer	37	(48.1%)	14	(29.2%)	0.037
Biliary/gallbladder cancer	9	(11.7%)	2	(4.2%)	0.149
Gastric cancer	7	(9.1%)	5	(10.4%)	0.807
Duodenal cancer	11	(14.3%)	10	(20.8%)	0.341
Breast cancer	2	(2.6%)	2	(4.2%)	0.463
Colorectal cancer	2	(2.6%)	1	(2.1%)	1.000
NET	1	(1.3%)	0	(0.0%)	0.384
Ampullary cancer	0	(0.0%)	1	(2.1%)	0.384
NSCLC	3	(3.9%)	1	(2.1%)	1.000
Benign disease	3	(3.9%)	7	(14.6%)	0.044
Disease stage					
Local invasion	25	(32.5%)	13	(27.1%)	0.555
Liver metastases	8	(10.4%)	9	(18.8%)	0.193
Peritoneal metastases	8	(10.4%)	10	(20.8%)	0.122
Diffuse metastatic	19	(24.7%)	9	(18.8%)	0.512
Disease manifestations					
Ascites	17	(22.1%)	2	(4.2%)	0.009
Peritoneal carcinomatosis	20	(26.0%)	16	(33.3%)	0.420

Table 2. Overall outcomes.

	EUS-GE (n=77)		L-GE (n=48)		OR (95% CI), P value
Efficacy					
Technical success, n (%)	73	(94.8%)	48	(100%)	0.17 (0.01-3.20), 0.297
Clinical success, n (%)	71	(92.2%)	42	(87.5%)	1.69 (0.51-5.58), 0.534
Per protocol clinical success, n (%)	71	(97.3%)	42	(87.5%)	5.07 (0.98-26.28), 0.057
Median time to oral intake, days (IQR)	1	(0-1)	3	(1-5)	<0.001
Full diet tolerability, n (%)	32	(41.6%)	19	(39.6%)	1.16 (0.56-2.44), 0.854
Median time to full diet, days (IQR)	2	(1-4)	8	(4-21)	<0.001
Gastroenterostomy dysfunction, n (%)	1	(1.3%)	0	(0.0%)	1.90 (0.08-47.64), 1.000
Median time to dysfunction, days (IQR)	243	N/A	N/A	N/A	N/A
Distal obstruction, n (%)	8	(10.4%)	1	(1.3%)	5.45 (0.66-45.02), 0.151
Median time to distal obstruction, days (IQR)	34	(18-138)	13	N/A	N/A
Safety					
Overall adverse events, n (%)	5	(6.5%)	15	(31.3%)	0.15 (0.05-0.46), <0.001
Mild, n(%)	2	(2.6%)	1	(2.1%)	1.25 (0.11-14.21), 1.000
Post-procedural fever, n (%)	2	(2.6%)	0	(0.0%)	3.21 (0.15-68.35), 0.523
Moderate, n(%)	1	(1.3%)	5	(10.4%)	0.11 (0.01-1.00), 0.106
Sepsis, n (%)	1	(1.3%)	0	(0.0%)	1.90 (0.08-47.64), 1.000
Need for re-endoscopy, n (%)	0	(0.0%)	4	(8.3%)	0.06 (0.00-1.21), 0.020
Severe, n(%)	2	(2.6%)	9	(18.8%)	0.12 (0.03-0.59), 0.007
Intra-peritoneal LAMS deployment, n (%)	2	(2.6%)	N/A	N/A	N/A
Anastomotic leak, n (%)	N/A	N/A	3	(6.3%)	N/A
Anastomotic bleeding, n (%)	N/A	N/A	2	(4.2%)	N/A
Surgical re-intervention, n (%)	N/A	N/A	3	(6.3%)	N/A
Fatal, n(%)	0	(0.0%)	0	(0.0%)	1.000
Other					
Median procedure duration, min (IQR)	51	(36 - 79.8)	95	(75 - 118)	<0.001
Median hospital stay, days (IQR)	4	(2 - 10.5)	8	(5 - 20)	<0.001
Median weight change after 2 months, kg (IQR)	-1	(-4.0 - 1.1)	-0,4	(-4.2 - 0.8)	0.390
Median post-procedural survival, days (IQR)	103	(44 - 252)	147	(68 - 335)	0.246

Abbreviations: CI: confidence interval, EUS-GE: Endoscopic ultrasound-guided gastroenterostomy, IQR: interquartile range, LGE: laparoscopic gastroenterostomy, N/A: not applicable, OR: odds ratio.

Table 3. Matched cohort: baseline characteristics.

Variable	EUS-GE (n=37)		L-GE (n=37)		P value
Age (years), mean ± SD	66.5	±12.5	66.4	±11.1	0.954
Female, n(%)	18	(48.7%)	15	(40.5%)	0.640
Median follow up duration, days (IQR)	77	27-160	123	32-262	0.105
Primary disease					
Pancreatic cancer	15	(40.5%)	13	(35.1%)	0.811
Biliary/gallbladder cancer	5	(13.5%)	2	(5.4%)	0.430
Gastric cancer	5	(13.5%)	5	(13.5%)	1.000
Duodenal cancer	6	(16.2%)	8	(21.6%)	0.768
Benign disease	2	(5.4%)	2	(5.4%)	1.000
Breast cancer	1	(2.7%)	1	(2.7%)	1.000
Colorectal cancer	2	(5.4%)	0	(0.0%)	0.493
NET	1	(2.7%)	0	(0.0%)	1.000
Ampullary cancer	0	(0.0%)	1	(2.7%)	1.000
NSCLC	1	(2.7%)	1	(2.7%)	1.000
Disease stage					
Local invasion	15	(40.5%)	12	(32.4%)	0.630
Liver metastases	6	(16.2%)	8	(21.6%)	0.768
Peritoneal metastases	6	(16.2%)	7	(18.9%)	1.000
Diffuse metastatic	8	(21.6%)	6	(16.2%)	0.768
Disease manifestations					
Ascites	3	(8.1%)	2	(5.4%)	1.000
Peritoneal carcinomatosis	10	(27.0%)	13	(35.1%)	0.616

Table 4. Matched cohort: outcome comparisons.

	EUS-GE (n=37)		L-GE (n=37)		OR (95% CI), P value
Efficacy					
Technical success, n (%)	35	(94.6%)	37	(100%)	0.19 (0.01-4.08), 0.493
Clinical success, n (%)	34	(91.9%)	33	(89.2%)	1.37 (0.29-6.62), 1.000
Per protocol clinical success, n (%)	34/35	(97.1%)	33	(89.2%)	4.12 (0.44-38.83), 0.358
Median time to oral intake, days (IQR)	1	(0.3-1.0)	3	(1.0-5.0)	<0.001
Full diet at discharge, n (%)	21	(56.8%)	14	(37.8%)	2.16 (0.85-5.46), 0.162
Median time to full diet, days (IQR)	2	(1.0-3.8)	9	(4.0-23)	<0.001
Gastroenterostomy dysfunction, n (%)	0	(0.0%)	0	(0.0%)	1.000
Distal obstruction, n (%)	2	(5.4%)	1	(2.7%)	2.06 (0.18-23.72), 1.000
Safety					
Overall adverse events, n (%)	1	(2.7%)	10	(27.0%)	0.07 (0.01-0.62), 0.007
Mild, n(%)	1	(2.7%)	1	(2.7%)	1.000
Moderate, n(%)	0	(0.0%)	3	(8.1%)	0.13 (0.01-2.64), 0.240
Endoscopic reintervention	0	(0.0%)	2	(5.4%)	0.19 (0.01-4.08), 0.493
Severe, n(%)	0	(0.0%)	6	(16.2%)	0.07 (0.00-1.19), 0.025
Surgical reintervention	0	(0.0%)	3	(8.1%)	0.13 (0.01-2.64), 0.240
Anastomotic leak	0	(0.0%)	4	(10.8%)	0.10 (0.01-1.91), 0.115
Anastomotic bleed	0	(0.0%)	2	(5.4%)	0.19 (0.01-4.08), 0.493
Fatal, n(%)	0	(0.0%)	0	(0.0%)	1.000
Other					
Median procedure duration, min (IQR)	46	(37.5-80)	85	(73.0-110)	<0.001
Median hospital stay, days (IQR)	4	(2.0-8.0)	8	(5.5-19.5)	<0.001
Median 2-months' weight change, kg (IQR)	-0,3	(-2.4-1.1)	0	(-3.0-0.7)	0.159
Median post-procedural survival, days (IQR)	96	(41.5-248)	152	(43.5-282)	0.317

Abbreviations: CI: confidence interval, EUS-GE: Endoscopic ultrasound-guided gastroenterostomy, IQR: interquartile range, LGE: laparoscopic gastroenterostomy, N/A: not applicable, OR: odds ratio.

Supplementary tables

Supplementary table 1. Sub-analysis comparing 15mm and 20mm LAMS efficacy and outcomes with or without balloon dilation.

Variable:	15mm LAMS (n=11)		20mm LAMS (n=64)		P-value
Technical success, n (%)	11/11	100%	62/64	96.9%	1.000
Clinical success*, n (%)	9/11	81.8%	62/62	100%	0.021
Median time to oral intake, days (IQR)	1	(0-1)	1	(0-1)	0.826
Full diet tolerability, n (%)	6	54.5%	45	70.3%	0.314
Median time to full diet, days (IQR)	2	(1-3)	2	(1-4)	0.099
Overall adverse events, n (%)	1	9.1%	4	6.5%	0.558
Gastroenterostomy dysfunction, n (%)	0	0.0%	1	1.6%	1.000
Median time to dysfunction, days (IQR)	N/A	N/A	243	N/A	N/A
Median hospital stay, days (IQR)	5	(2.8-11)	4	(2.0-11)	0.054
Median weight change after 2 months, kg (IQR)	-1.4	(-5.2-0.6)	-1	(-4.0-1.1)	0.430
Variable:	With LAMS dilation (n=20)		Without LAMS dilation (n=55)		P-value
Technical success, n (%)	20/20	100%	53/55	96.4%	1.000
Clinical success*, n (%)	20/20	100%	51/53	96.2%	1.000
Median time to oral intake, days (IQR)	1	(0-1)	1	(0-1)	0.153
Full diet tolerability, n (%)	10	50.0%	39	70.9%	0.107
Median time to full diet, days (IQR)	2.5	(1-4)	2	(2-8)	0.254
Overall adverse events, n (%)	1	5.0%	4	7.3%	0.579
Gastroenterostomy dysfunction, n (%)	1	5.0%	0	0.0%	1.000
Median time to dysfunction, days (IQR)	243	N/A	N/A	N/A	N/A
Median hospital stay, days (IQR)	5	(2.0-11)	4	(2.0-11)	0.022
Median weight change after 2 months, kg (IQR)	-1.4	(-5.1-0.7)	-1	(-4.0-1.1)	0.849

Abbreviations: IQR: interquartile range, LAMS: lumen-apposing metal stent, kg: kilogram, N/A: not applicable.

*: per-protocol analysis.

Supplementary table 2. Multivariate analysis of variables in EUS-GE clinical failure.

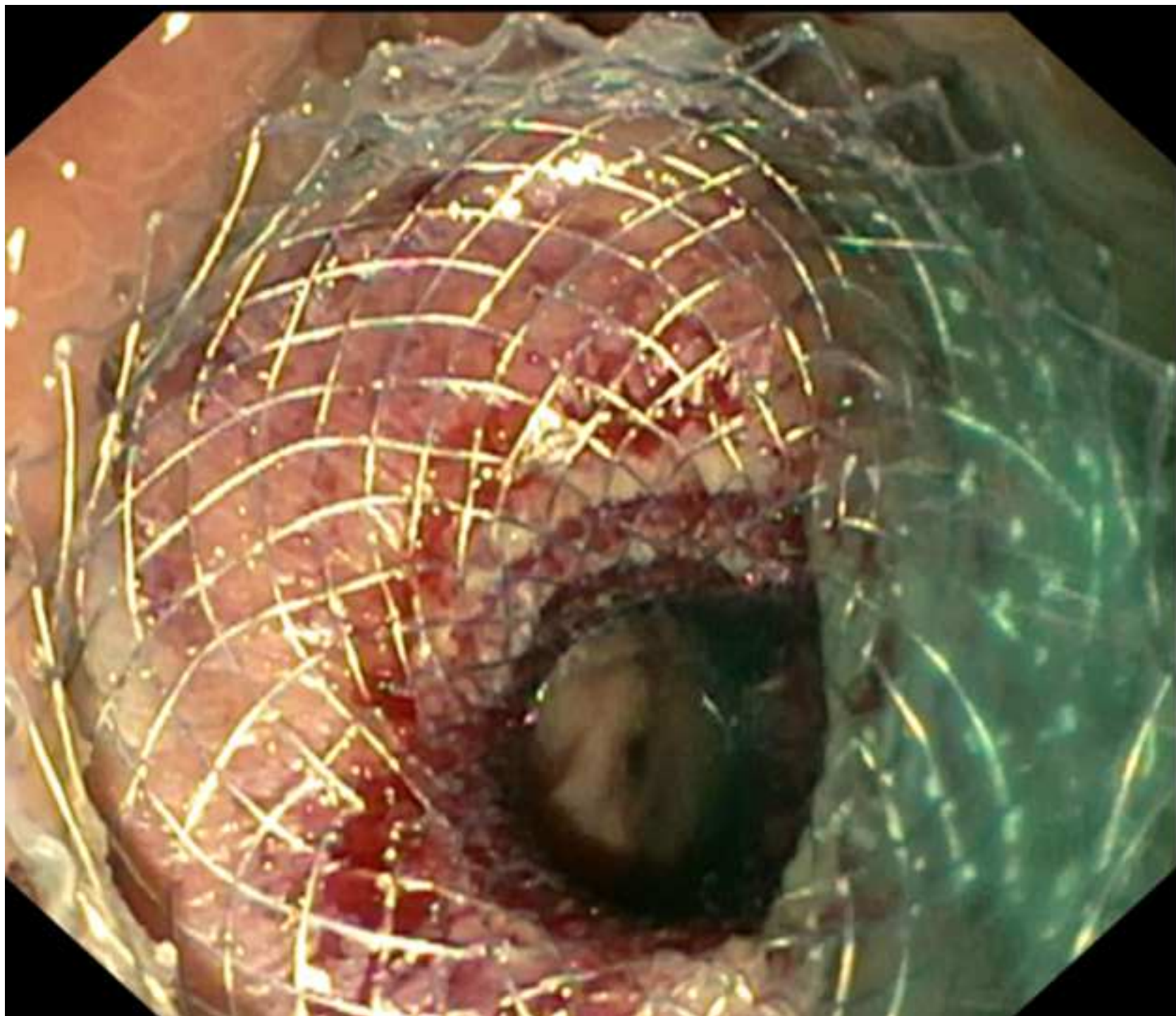
Variable	OR	95% CI	P-value
Age	0.98	0.90-1.03	0.532
Gender, female	2.95	0.46-11.18	0.132
Pancreatic cancer	3.14	0.69-20.22	0.115
Ascites	8.39	1.29-375.4	0.104
Peritoneal carcinomatosis	2.65	0.44-28.94	0.305
15mm LAMS	2.45	0.14-14.09	0.332
Balloon dilation	0.11	0.01-0.72	0.059
Learning curve, first 50%	1.30	0.37-15.49	0.726

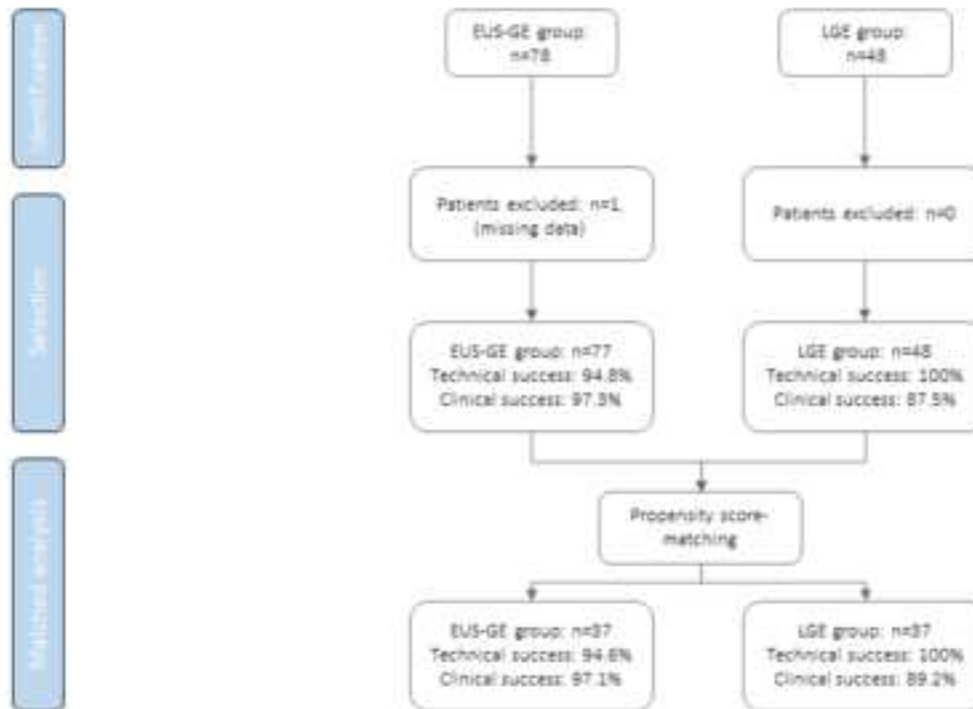
Supplementary table 3. Learning curve assessment: comparison between first and second half of the EUS-GE cohorts.

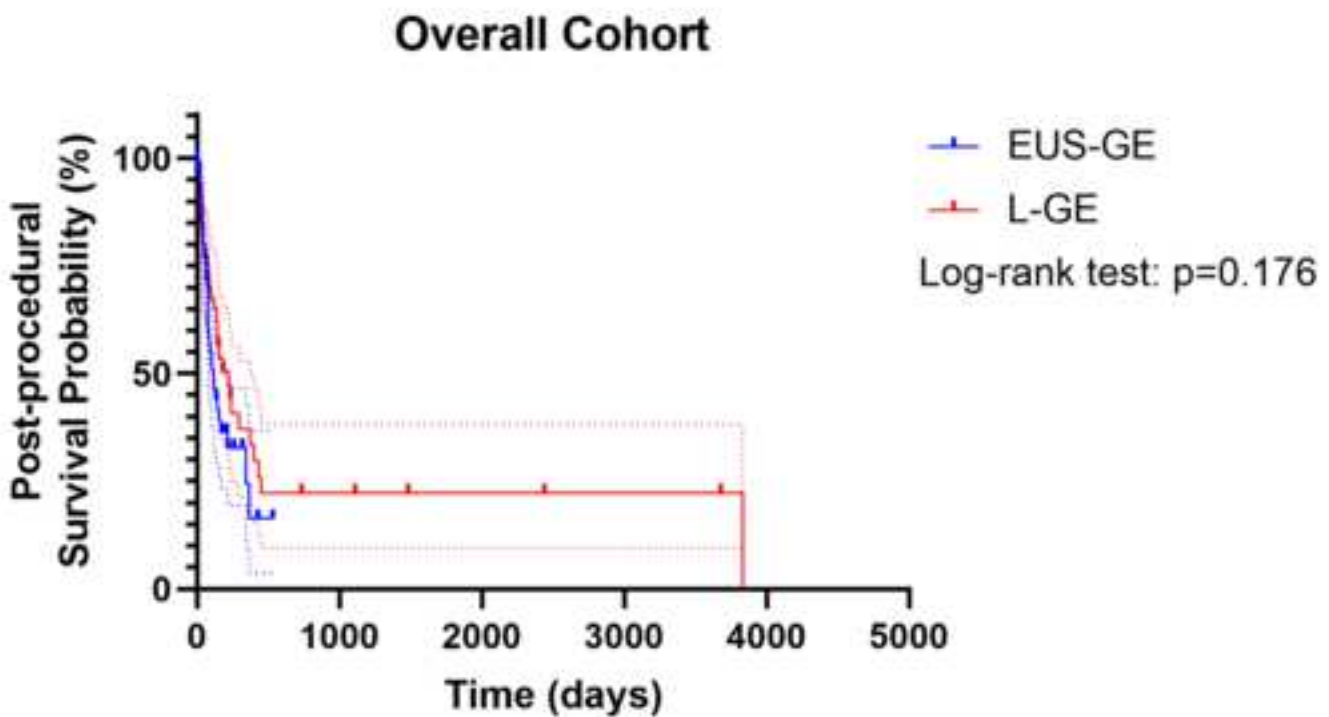
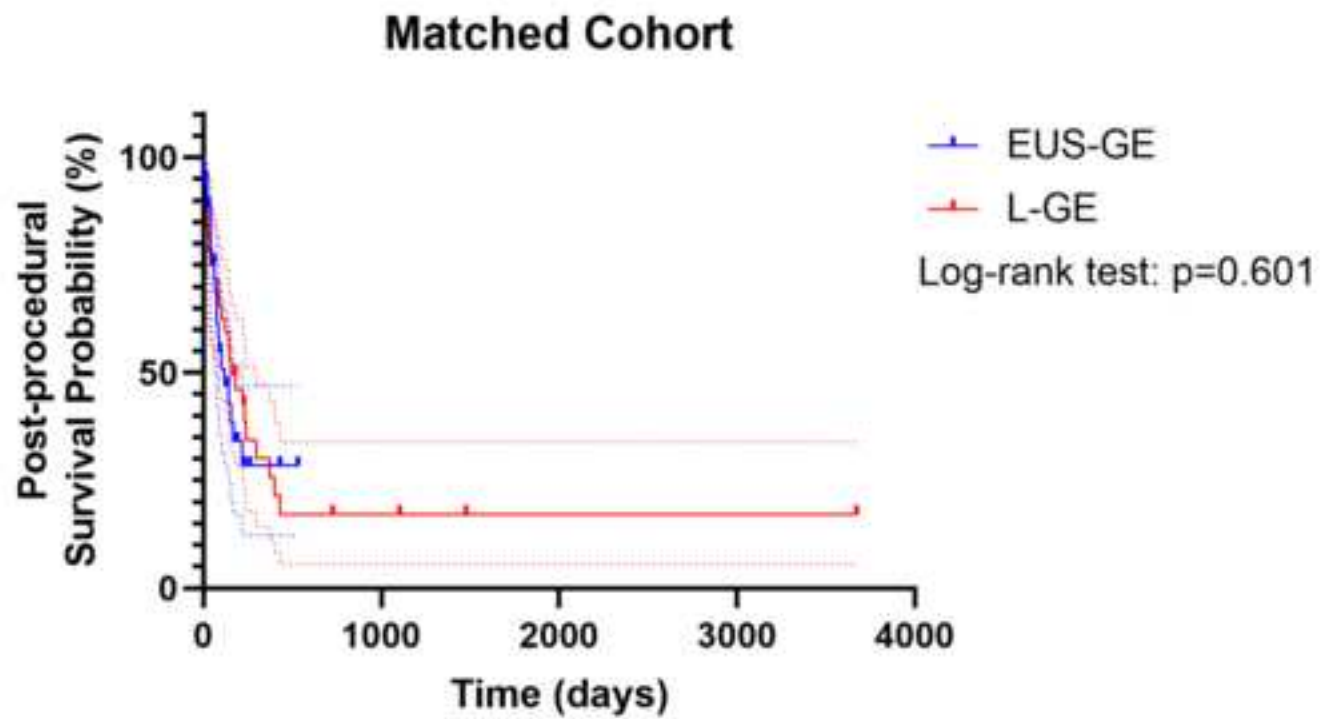
	First 50% (n=18)		Second 50% (n=19)		P-value
Propensity score-matched EUS-GE cohort:					
Technical success, n (%)	17/18	94.4%	18/19	94.7%	1.000
Clinical success, n (%)	17/18	94.4%	17/19	89.5%	1.000
Per protocol clinical success, n (%)	17/17	100%	17/18	94.4%	1.000
Overall adverse events, n (%)	1	5.6%	1	5.3%	1.000
Median procedure duration, min (IQR)	51	(34-84)	46	(40-83)	0.719
Overall EUS-GE cohort:	First 50% (n=38)		Second 50% (n=39)		P-value
Technical success, n (%)	37/38	97.4%	36/39	92.3%	0.615
Clinical success, n (%)	37/38	97.4%	34/39	87.2%	0.200
Per protocol clinical success, n (%)	37/37	100%	34/36	94.4%	0.240
Overall adverse events, n (%)	3	7.9%	3	7.7%	1.000
Median procedure duration, min (IQR)	49	(36-78)	52	(33-83)	0.719

Abbreviations: EUS-GE: Endoscopic ultrasound-guided gastroenterostomy, IQR: interquartile range.









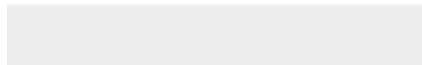
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Laparoscopic versus EUS-guided Gastroenterostomy for Gastric Outlet Obstruction: An International Multicentre Propensity Score-Matched Comparison.

Abbreviations:

AE: adverse event

ASGE: American society gastrointestinal endoscopy

CI: confidence interval

EUS: endoscopic ultrasound

EUS-GE: EUS-guided gastroenterostomy

GOO: gastric outlet obstruction

IQR: interquartile range

LAMS: lumen-apposing metal stent

L-GE: laparoscopic gastroenterostomy

OR: odds ratio

SD: standard deviation

SEMS: self-expandable metal stents

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	<p>Have you included IRB information in your article? If not, please explain why. Do not merely put NA or your article will be returned for a fuller explanation.</p> <p>Comments: Yes, we've included this in the <i>Methods</i>-section.</p>
	<p>Please list here the DATE of IRB approval for your study.</p> <p>Date of approval: August 6th 2020. Central IRB: University Hospitals Leuven.</p>
	<p>Proof of registration for randomized clinical trials, including registration number and dates of when patients were enrolled, when trial was registered, and when the trial was started, is required before subject enrollment; have you included this information?</p> <p>No, this was a retrospective study. No trial registration was therefore required.</p>



Journal CME Conflict of Interest: Disclosure and Attestation

Lead Author: Michiel Bronswijk, MD

Article: **Laparoscopic versus EUS-guided Gastroenterostomy for Gastric Outlet Obstruction: An International Multicentre Propensity Score-Matched Comparison.**

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