EUS-guided gastroenterostomy vs. surgical gastrojejunostomy and enteral stenting for malignant gastric outlet obstruction: a meta-analysis

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ABSTRACT

Background and study aims Malignant gastric outlet obstruction (MGOO) is traditionally treated with surgical gastrojejunostomy (SGJ), which is effective but associated with high rates of morbidity, or endoscopic stenting (ES), which is less invasive but associated with significant risk of stent dysfunction and need for reintervention. Endoscopic ultrasound-guided gastroenterostomy (EUS-GE) provides a robust bypass without the invasiveness of surgery.

Methods We performed a systematic review and meta-analysis comparing EUS-GE to SGJ and ES for MGOO. Electronic databases were searched from inception through February 2022. A meta-analysis was performed with results reported as odds ratios (ORs) with 95% confidence intervals (CIs) using random effects models. Primary outcomes included clinical success without recurrent GOO and adverse events (AEs).

Results Sixteen studies involving 1541 patients were included. EUS-GE was associated with higher clinical success without recurrent GOO compared to ES or SGJ [OR 2.60, 95% CI1.58–4.28] and compared to ES alone [OR 5.08, 95% CI 3.42–7.55], but yielded no significant difference compared to SGJ alone [OR 1.94, 95% CI 0.97–3.88]. AE rates were significantly lower for EUS-GE compared to ES or SGJ grouped together [OR 0.34, 95% CI 0.20–0.58], or SGJ alone [OR 0.17, 95% CI 0.10–0.30] but were not significant different versus ES alone [OR 0.57, 95% CI 0.29–1.14].

Conclusions EUS-GE is the most successful approach to treating MGOO, exhibiting a lower risk of recurrent obstruction compared to ES, and fewer AEs compared to SGJ.

Introduction

Gastric outlet obstruction (GOO) is a clinical condition caused by a mechanical malignant blockage of the upper digestive tract at the level of the distal stomach, pylorus or duodenum. Often encountered in the context of advanced malignancy, it is associated with debilitating symptoms including intractable nausea and vomiting, inability to tolerate oral nutrition, abdominal pain and decreased quality of life [1]. In addition, these symptoms contribute in large part to malnutrition and poor functional status in this fragile patient population, which can lead to increased hospitalizations and delays in proposed chemotherapy treatments. The traditional treatment modality for this condition is surgical gastrojejunostomy (SGJ) which bypasses the obstruction. While this method is highly effective, it is invasive and, in turn, can be associated with high rates of morbidity [2]. Endoscopic stenting (ES) provides a less-invasive approach that is associated with lower risk of adverse events (AEs) and better short-term outcomes including shorter hospital length of stay [3]; however, it is associated with a significant risk of stent obstruction and increased need for reintervention [4].

Endoscopic ultrasound-guided gastroenterostomy (EUS-GE) is a novel modality that aims to endoscopically bypass the obstruction by connecting stomach to small bowel downstream from the pathology with a lumen-apposing metal stent (LAMS). Given its endoscopic approach, it may avoid the substantial morbidity of the surgical alternative while at the same time providing the durability of a complete enteral bypass. Early data suggest good efficacy and safety outcomes, yet comparative data contrasting EUS-GE to traditional modalities have been limited by small sample sizes [5].

We, therefore, conducted a systematic review and meta-analysis assessing the efficacy and safety of EUS-GE compared to both ES and SGJ for the treatment of malignant GOO.

Methods

This study protocol was prospectively registered with the PROSPERO international database (CRD42021265074). The Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) and Meta-analysis Of Observational Studies in Epidemiology (MOOSE) guidelines were followed (Supplementary Table 1, Supplementary Table 2) [6, 7].

Search strategy

The literature was systematically searched for studies that assessed EUS-GE for the treatment of GOO due to malignancy. MEDLINE, EMBASE and Web of Science databases were searched from inception through February 2022 using the following keywords: 1) endoscopic or EUS; 2) gastrojejunostomy or gastroenterostomy (see Search Strategy in Supplementary Table 3). Previously published reviews on the topic were hand searched and the references of included articles were checked for relevant articles. Abstracts from the following annual, international scientific meetings were searched going back five years: Digestive Disease Week, American College of Gastroenterology and United European Gastroenterology Week.

Inclusion and exclusion criteria

Studies were included if they compared EUS-GE to ES or SGJ in patients with malignant GOO. Randomized controlled trials as well as observational studies of retrospective or prospective cohorts were included.

Exclusion criteria were: non-English and non-French articles; non-human studies; case reports and studies with fewer than 10 participants; studies of EUS-GE using magnets; studies of EUS-GE using Natural Orifice Transluminal Endoscopic Surgery; studies regarding the treatment of concomitant gastric outlet and biliary obstruction.

Validity assessment, data abstraction and rating of evidence

Studies were independently assessed for inclusion by two authors (CSM and JB) with discrepancies resolved, as needed, by a third (YC). Study and baseline patient characteristics, duration of follow-up and outcomes of interest were abstracted. The Cochrane Risk of bias tool for randomized trials or the Risk of Bias In Non-randomized Studies of Interventions (ROBINS-I) tool were used to assess the risk of bias when appropriate [8, 9]. Prespecified confounding domains were: cancer type; presence of carcinomatosis; age. No important co-interventions that have the potential to lead to bias were prespecified.

Outcomes and study definitions

There were two prespecified primary outcomes: clinical success without recurrent GOO and AEs. The secondary outcomes were technical success and hospital length of stay. Clinical success was defined as the ability to tolerate at least a liquid diet post-procedure. Recurrent GOO was defined as recurrence of initial symptoms of nausea, vomiting and inability to tolerate oral intake after clinical success had initially been achieved. Adverse events were graded in accordance with the American Society of Gastrointestinal Endoscopy lexicon [10] and included infection, perforation, bleeding, leak, pancreatitis, and in-hospital mortality related to the index procedure. Studies that did not report on recurrent GOO or that expressed this outcome only as a combined figure with other AEs were excluded. Technical success was defined for EUS-GE and ES as adequate deployment of the stent as reported by the endoscopist; for SGJ it was defined as feasibility to perform gastrojejunostomy.

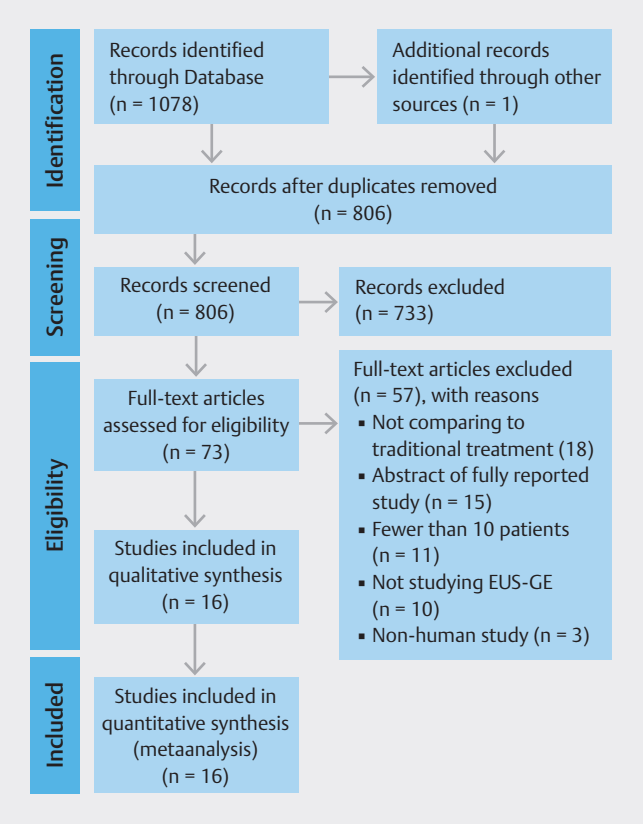
Statistical analysis

For all outcomes, effect sizes were calculated for EUS-GE compared to ES and SGJ combined with mean differences for continuous variables and odds ratios (ORs) for categorical variables. The DerSimonian and Laird method for random effect models was applied to all outcomes to determine corresponding overall effect sizes and their confidence intervals. Sensitivity analyses were performed using the Mantel-Haenszel method for fixed effects models when no statistical heterogeneity was noted.

Mean differences were handled as continuous variables using the inverse variance approach. Presence of heterogeneity across studies was defined using a Chi-square test of homogeneity with a 0.10 significance level. The Higgins I^2 statistic was calculated to quantify the proportion of variation in intervention effects attributable to between-study heterogeneity. Values of 0% to 40%, 30% to 60%, 50% to 90%, and 75% to 100% represent low, moderate, substantial, and considerable heterogeneity, respectively. Prediction intervals were calculated and added to the forest plots. The prediction interval calculates the 95% of where the effect size will be if a new study is randomly added to the meta-analysis [11]. For all comparisons publication bias was evaluated using funnel plots if at least three citations were identified. All statistical analyses were done using Revman 5.4 and Meta package in R version 2.13.0, (R Foundation for Statistical Computing, Vienna, Austria, 2008).

Sensitivity and subgroup analyses

Subgroup analyses using ES or SGJ as separate comparators were performed for all outcomes. Additional subgroup analyses were performed for primary outcome according to full publication status and continent of publication. Sensitivity analysis was performed adopting fixed effect models when appropriate. In addition, observational studies are subject to confounding and other forms of bias [12]. We, therefore, performed additional sensitivity analyses based on studies with low risk, moderate to serious risk, and critical risk of bias due to confounding, identified from the ROBINS-I risk of bias tool.



▶ **Fig. 1** PRISMA Diagram. From: *Page MJ, McKenzie JE, Bossuyt PM* et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ 2021; 372: n71.

Results

Study selection

The search yielded 1,078 citations (▶ **Fig. 1**). One study that resulted from the systematic search in abstract form was identified as a complete manuscript from hand searching [13]. After screening based on title and abstract, 73 articles were reviewed in full. Sixteen articles were included in the qualitative review [1, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27], all retrospective comparative studies. Eight were fully published articles [1, 13, 14, 15, 16, 17, 22, 27] and eight were abstracts [18, 19, 20, 21, 23, 24, 25, 26]. One study was excluded from quantitative analysis since data were reported per stent and not per patient [27]. The results of the literature search are summarized in the PRISMA diagram (▶ **Fig. 1**).

Risk of publication bias and heterogeneity and risk of bias

Publication bias was noted only for the outcomes of clinical success without recurrent GOO (Egger's $P = 0.04$; Begg's $P = 0.09$) and AEs (Egger's $P = 0.08$; Begg's $P = 0.04$). Moderate to substantial heterogeneity was noted for clinical success without recurrent GOO ($P < 0.01$; $I^2 = 60\%$). Adverse event rates reporting exhibited low to moderate heterogeneity ($P < 0.01$; $I^2 = 54\%$). No significant heterogeneity was noted for secondary outcomes. The ROBINS-I showed a low risk of bias due to confounding factors in six studies, moderate to critical in seven studies, and insufficient information was provided in the last three studies (Supplementary Fig. 1). Four studies were thought to have serious risk of bias in the selection of patient participations. All studies demonstrated moderate risk of bias in the classification of exposure or from intended interventions. Finally, the risk of bias was low due to missing data or measurement of exposure.

Patient and study characteristics

The main characteristics of the 16 included studies (n = 1541) [1, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27] are summarized in ▶ **Table 1**. These were conducted in Asia (India, Japan, Hong Kong), Europe (Belgium, Netherlands, Spain), and North America (United States). Studies were published between 2016 to 2022. Overall, 15 studies (n = 1,441) were included in the meta-analysis [1, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26]. Six [1, 13, 18, 20, 21, 26] (n = 494) compared EUS-GE to ES, seven [14, 15, 16, 17, 22, 23, 24] (n = 466) EUS-GE to SGJ, while two others [19, 25] (n = 481) described EUS-GE results versus both ES and SGJ. The average age of patients included ranged between 62 to 71 years. The percentage of female participants ranged between 32.3% and 64.3%. Eleven articles exclusively analyzed malignant GOO, whereas five articles also reported on a minority of patients with benign GOO. The etiology of malignant GOO was reported in 11 studies, with malignancies described as pancreatic, gastric, duodenal, biliary,

▶ **Table 1** Characteristics of studies included in systematic review.

Publication			Patients						Malignant GOO%		Cancer type		Carcinomatosis %		Follow-up, days***	
Author	Year	Country*	Groups	Age, y**	Female %	ITT	study	control	study	control	study (%)	control (%)	study	control	Study	control
Khashab et al ◊	2017	Japan	EUS-GE SGJ (a)	68.7	47.3	93	30	63	100	100	Pancreatic (56), Gastric (17.6), metastases (13), ampullary (6.7), biliary/GB (6.7)	Pancreatic (84.5) Ampullary (14), Duodenal (1.5)	43	11	115	196
Chen et al ◊	2016	Japan	EUS-GE ES	66.2	40.2	82	30	52	100	100	Pancreatic (56.7), Gastric (16.7), Metastases (13.3), Ampullary/duodenal (6.7), Biliary/GB (6.7)	Pancreatic (53.8), Metastases (19.2), Ampullary/duodenal (13.5), Biliary/GB (7.7), Gastric (5.8)	46.7	34.6	103	83
Bronswijk et al ◊	2021	Belgium	EUS-GE SGJ (b)	65.3	44	125	77	48	96.1	85.4	Pancreatic (48.1), Duodenal (14.3), Biliary/GB (11.7), Metastases (10.4), Gastric (9.1), Other (1.3)	Pancreatic (29.2), Duodenal (20.8), Gastric (10.4), Metastases (8.4), Biliary/GB (4.2), Ampullary (2.1)	26	33.3	76	122
Perez-Miranda et al ◊	2017	USA	EUS-GE SGJ (b)	70.3	38.9	54	25	29	68	100	NR	NR	NR	NR	56	269
Kouanda et al ◊	2021	USA	EUS-GE SGJ (a)	70.2	42.4	66	40	26	90	54	Pancreatic (72.2), Metastases (13.9), Biliary/GB (8.4), Ampullary (2.8), Duodenal (2.8)	Gastric (57.1), Pancreatic (21.4), Duodenal (7.1), Biliary/GB (7.1), Metastases (7.1)	11.1	42.9	98	166.5

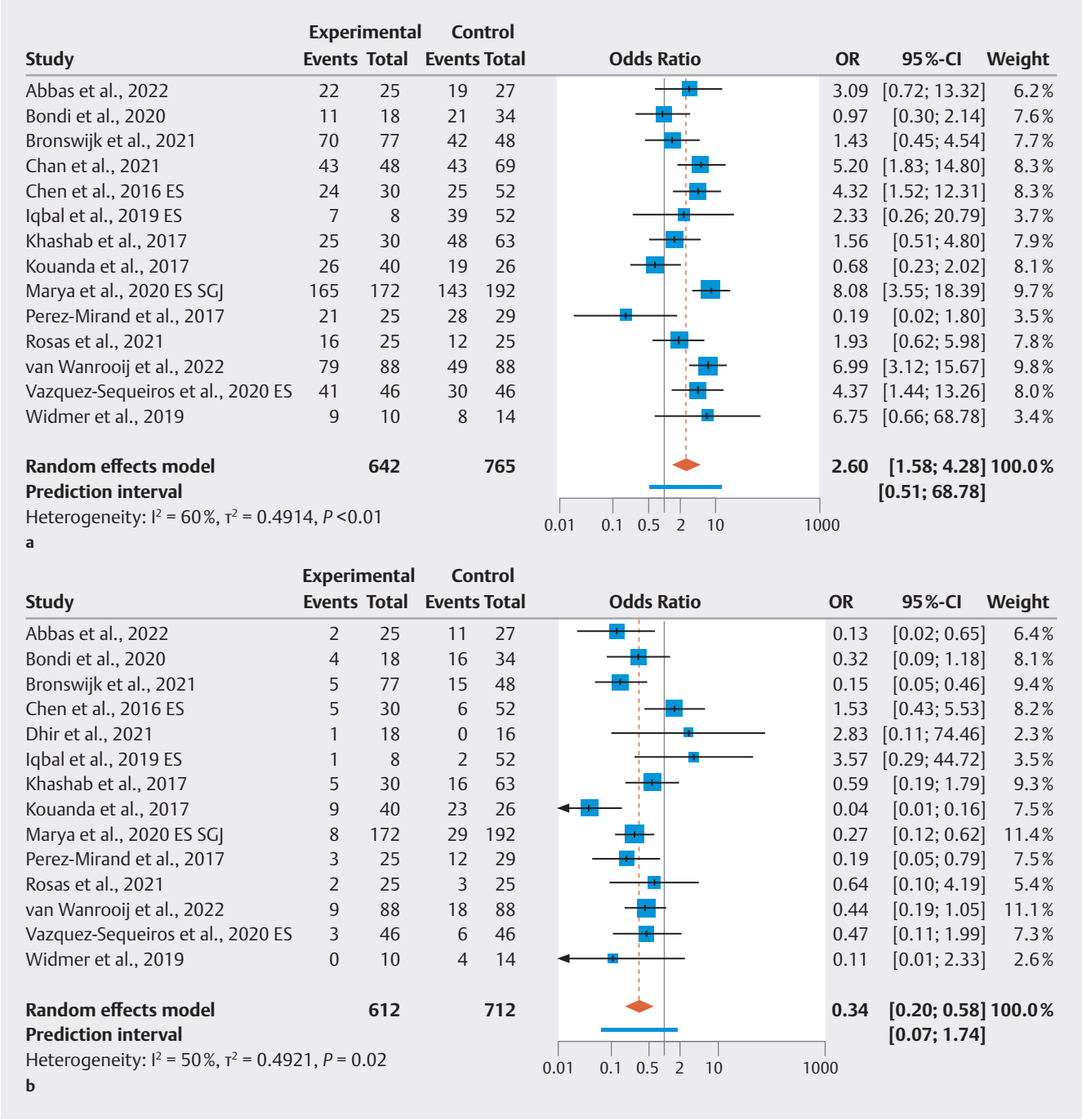
▶ **Table 1** (Continuation)

Publication			Patients						Malignant GOO%		Cancer type		Carcinomatosis %		Follow-up, days***	
Author	**Year**	**Country***	**Groups**	**Age, y****	**Female %**	**ITT**	**study**	**control**	**study**	**control**	**study (%)**	**control (%)**	**study**	**control**	**Study**	**control**
Vazquez-Sequeiros et al △	2020	Spain	EUS-GE ES	71.2	36.9	92	46	46	100	100	Pancreatic (61), Gastric (15), Biliary/GB (9), Metastases (9), Duodenal (6)	Pancreatic (61), Gastric (28), Biliary/GB (6), Duodenal (5)	NR	NR	76	91
Widmer et al △	2019	USA	EUS-GE SGJ (a/b)	65.9	58.3	24	10	14	100	100	Pancreatic (40), Metastases (30), Gastric (20), Duodenal (10)	Pancreatic (28.6), Duodenal (21.4), Metastases (21.3), Biliary/GB (14), Ampullary (7), Gastric (7)	NR	NR	90	240
Bondi et al △	2020	USA	EUS-GE SGJ	62.3	53.4	52	18	34	100	100	Metastases (33), Biliary/GB (28), Pancreatic (22), Gastric (11), Duodenal (6)	Pancreatic (32), Metastases (29), Gastric (24), Duodenal (12), Biliary/GB (3)	100	100	NR	NR
Marya et al △	2020	USA	EUS-GE ES/SGJ	62.4	43.7	364	172	153 (ES) 39 (SGJ)	79.7	88.2 (ES) 61.5 (SGJ)	NR	NR	11	11.7 (ES) 17.9 (SGJ)	234	61 (ES) 235 (SGJ)
Iqbal et al △	2019	USA	EUS-GE ES	68.4	48.3	60	8	52	92	92	NR	NR	NR	NR	NR	NR
Abbas et al △	2022	USA	EUS-GE SGJ	61.9	53.8	52	25	27	100	100	Other, pancreatic, billiary/GB, gastric	Pancreatic, gastric, biliary/GB, other	100	93	98	199
v. Wanrooij et al △	2022	Netherlands	EUS-GE ES	66.5	52.3	214	88	88	100	100	Pancreatic (46.7), other (18.7), biliary tract (14), gastric (11.2), duodenal (9.3)	Pancreatic (65.4), other (11.2), duodenal (9.3), gastric (7.5), biliary tract (6.5)	41.1	25.2	90.5	50

▶ **Table 1** (Continuation)

Publication			Patients						Malignant GOO%		Cancer type		Carcinomatosis %		Follow-up, days***	
Author	Year	Country*	Groups	Age, y**	Female %	ITT	study	control	study	control	study (%)	control (%)	study	control	Study	control
S.M Chan et al △	2021	Hong Kong	EUS-GE ES/SGJ	67.1	64.3	117	48	38 31	100	100	Other, pancreatic gastric	Gastric, pancreatc, other	NR	NR	51.5	163 48
Rosas et al △	2021	USA	EUS-GE ES	68.2	40	50	25	25	100	100	NR	NR	NR	NR	190	220
Dhir et al △	2021	India	EUS-GE ES	64.4	32.3	34	18	16	100	100	NR	NR	NR	NR	120	120
Ge et al ◊	2019	USA	EUS-GE ES	65.8	44	100	22	78	100	100	Metastases (40.9), Pancreatic (31.8), Biliary/GB (18.2), Duodenal (4.6), Gastric (4.6)	Pancreatic (51.3), Metastases (24.4), Biliary/GB (10.3), Gastric (10.3), Ampullary (2.6), Duodenal (1.3)	59.1	47.4	180	NR

ES, enteral stent; EUS-GE, endoscopic ultrasound-gastroenterostomy; GB, gallbladder; ITT, intention-to-treat; NR, not reported; SGJ, surgical gastrojejunostomy.
*Based on corresponding author
**Mean
***Median
(a): Open SGJ
(b): Laparoscopic SGJ
◊: Full manuscript
△: Abstract

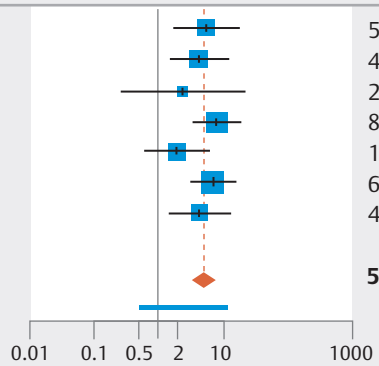


▶ **Fig. 2** **a** Clinical success without recurrent GOO. **b** Adverse events.

metastases or other. Nine studies reported on the presence of peritoneal carcinomatosis (ranging from 11% to 100%). Fourteen studies reported average follow-up times between 52 and 269 days.

Primary outcome

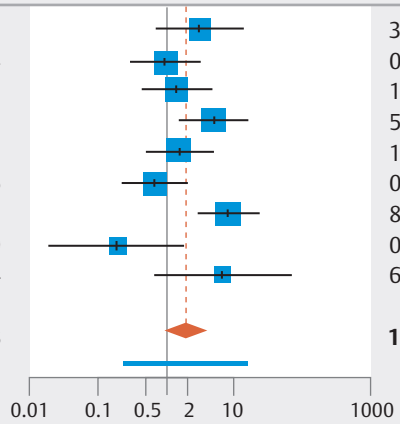
EUS-GE was associated with higher clinical success without recurrent GOO compared to ES or SGJ combined (OR, 2.60; 95% CI, 1.58–4.28) (▶ **Fig. 2a** and ▶ **Table 2**). Subgroup analysis also showed higher clinical success without recurrent GOO for EUS-GE compared to ES alone (OR, 5.08; 95% CI, 3.42–7.55), but yielded no statistically significant difference when compared to SGJ alone (OR, 1.94; 95% CI, 0.97–3.88) (▶ **Fig. 3**). Prediction interval remained significant for EUS-GE compared to ES alone, but not compared to ES or SGJ combined. EUS-GE was associated with significantly fewer AEs compared to ES or SGJ combined (OR, 0.34; 95% CI, 0.20–0.58) (▶ **Fig. 2b**). One study was excluded from this analysis as AEs were not specified and were presumed to include recurrent GOO [19]. On subgroup analysis, EUS-GE was associated with no statistically significant dif-



Study	Experimental Events	Experimental Total	Control Events	Control Total	OR	95%-CI	Weight
Chan et al., 2021	43	48	19	31	5.43	[1.68; 17.58]	11.3%
Chen et al., 2016 ES	24	30	25	52	4.32	[1.52; 12.31]	14.3%
Iqbal et al., 2019 ES	7	8	39	52	2.33	[0.26; 20.79]	3.3%
Marya et al., 2020 ES SGJ	165	172	114	153	8.06	[3.48; 18.66]	22.2%
Rosas et al., 2021	16	25	12	25	1.93	[0.62; 5.98]	12.2%
van Wanrooij et al., 2022	79	88	49	88	6.99	[3.12; 15.67]	24.0%
Vazquez-Sequeiros et al., 2020 ES	41	46	30	46	4.37	[1.44; 13.26]	12.7%
Random effects model		**417**		**447**	**5.08**	**[3.42; 7.55]**	**100.0%**
Prediction interval						**[0.03; 8.54]**	

Heterogeneity: $I^2 = 0\%$, $\tau^2 = 0$, $P = 0.51$

a



Study	Experimental Events	Experimental Total	Control Events	Control Total	OR	95%-CI	Weight
Abbas et al., 2022	22	25	19	27	3.09	[0.72; 13.32]	11.4%
Bondi et al., 2020	11	18	21	34	0.97	[0.30; 3.14]	12.4%
Bronswijk et al., 2021	70	77	42	48	1.43	[0.45; 4.54]	12.6%
Chan et al., 2021	43	48	24	38	5.02	[1.61; 15.63]	12.7%
Khashab et al., 2017	25	30	48	63	1.56	[0.51; 4.80]	12.8%
Kouanda et al., 2017	26	40	19	26	0.68	[0.23; 2.02]	13.1%
Marya et al., 2020 ES SGJ	165	172	29	39	8.13	[2.86; 23.07]	13.5%
Perez-Mirand et al., 2017	21	25	28	29	0.19	[0.02; 1.80]	6.3%
Widmer et al., 2019	9	10	8	14	6.75	[0.66; 68.78]	6.1%
Random effects model		**445**		**318**	**1.94**	**[0.97; 3.88]**	**100.0%**
Prediction interval						**[0.24; 15.43]**	

Heterogeneity: $I^2 = 61\%$, $\tau^2 = 0.6435$, $P < 0.01$

b

▶ **Fig. 3** Clinical success without recurrent GOO. **a** EUS-GE vs. ES. **b** EUS-GE vs. SGJ.

ference in AEs rates compared to ES alone (OR, 0.57; 95% CI, 0.29–1.14), and fewer AEs compared to SGJ alone (OR, 0.17; 95% CI, 0.10–0.30) (▶ **Fig. 4**). Prediction interval remained significant for EUS-GE compared to SGJ alone, but not compared to ES or SGJ combined.

Secondary outcomes

EUS-GE was associated with a significant decrease in technical success compared to ES or SGJ combined (OR, 0.32; 95% CI, 0.16–0.64) and compared to SGJ alone (OR, 0.17; 95% CI, 0.06–0.49); however, there was no statistically significant difference when compared to ES alone (OR, 0.44; 95% CI, 0.18–1.12) (▶ **Table 2**). Hospital length of stay was only reported in three studies with extractable data, two comparing EUS-GE to SGJ and one comparing EUS-GE to ES. There were no significant differences in lengths of hospital stay when comparing EUS-GE to ES or SGJ combined (mean difference (MD), 0.03; 95% CI, -2.31–2.36), or when compared to ES (MD, 1.80; 95% CI, -1.47–5.07) or SGJ (MD, -1.06; 95% CI, -3.75–1.63) alone.

Sensitivity and subgroup analyses

Among fully published studies, EUS-GE was associated with higher clinical success without recurrent GOO compared to SGJ or ES combined (OR, 3.51; 95% CI, 1.88–6.56) (▶ **Table 3**). Results were similar when assessing North American studies (OR, 2.28; 95% CI, 1.23–4.21) and European studies only (OR, 3.77; 95% CI, 1.51–9.42). There was no statistically significant difference found between the two groups in studies published as abstract only (OR, 1.91; 95% CI, 0.86–4.27). Results remained robust when including only low risk of confounding bias and there was no heterogeneity noted (OR, 3.51; 95% CI, 2.33–5.27), whereas no difference between the two groups was found for moderate to serious and critical risk of confounding bias (Supplementary Fig. 2).

Adverse events were significantly lower for EUS-GE compared to SGJ and ES combined when limiting the analysis to abstracts alone, as was also the case for North American studies. There were no significant differences identified when limiting the analysis to fully published articles or European studies. Results remained robust as well when including only low risk of

▶ **Table 2** Primary, secondary and subgroup analyses.

	N studies	N patients	OR or WMD (95% CI)	P value for heterogeneity	I^2
Primary outcomes					
Clinical success without recurrent GOO	14	1407	2.60 (1.58; 4.28)	< 0.01	60%
ES only	7	864	5.08 (3.42; 7.55)	0.51	0%
SGJ only	9	763	1.94 (0.97; 3.88)	< 0.01	61%
Adverse events	15	1441	0.34 (0.20, 0.58)	0.02	50%
ES only	8	937	0.57 (0.29; 1.14)	0.16	35%
SGJ only	9	763	0.17 (0.10; 0.30)	0.16	33%
Secondary outcomes					
Technical success	15	1441	0.32 (0.16; 0.64)	0.44	1%
ES only	8	898	0.44 (0.18; 1.12)	0.29	19%
SGJ only	9	763	0.17 (0.06; 0.49)	0.99	0%
Length of stay	3	227	0.03 (−2.31, 2.36)	0.30	18%
ES only	1	82	1.80 (−1.47, 5.07)	–	–
SGJ only	2	145	−1.06 (−3.75, 1.63)	0.41	0%

CI, confidence interval; ES, enteral stenting; GOO, gastric outlet obstruction; OR, odds ratio; SGJ, surgical gastrojejunostomy; WMD, weighted mean difference.

confounding bias and there was no heterogeneity (OR, 0.46; 95% CI, 0.28–0.75), whereas no difference between the two groups was found for moderate to serious and critical risk of confounding bias (Supplementary Fig. 3).

Significant heterogeneity precluded the performance of fixed effect models.

Discussion

EUS-GE has emerged as a promising modality for the treatment of malignant GOO. This approach exhibits two major potential benefits over the traditional modalities: Given the complete nature of the bypass of the obstruction created with a gastro-enteric anastomosis, EUS-GE may offer a more durable treatment compared to enteral stenting that traverses the tumor and is prone to recurrent obstruction. On the other hand, the endoscopic nature of the EUS-GE procedure, even if extraluminal, may offer significant safety advantages over a traditional surgical bypass. In the present systematic review and meta-analysis of 15 studies that included 1,441 patients, EUS-GE was associated with higher clinical success without recurrent obstruction and fewer AEs compared to the traditional treatments of GOO. Subgroup analysis showed higher clinical success without re-obstruction compared to traditional stenting, with no difference compared to surgical bypass. On the other hand, EUS-GE was associated with fewer AEs compared to SGJ, with no difference compared to ES. Taken together, these findings support the theoretical advantages of EUS-GE for the treatment of malignant GOO that results in a robust bypass while maintaining a safer, less-invasive approach. Indeed, recent European Society for Gastrointestinal Endoscopy guidelines have recommended EUS-GE be "performed in an expert setting, for malignant GOO, as an alternative to enteral stenting or surgery," as a strong recommendation based on low-quality evidence [28].

Despite the promising data presented herein, EUS-GE is not commonly utilized. This is likely due to its technically challenging nature relative to other interventional endoscopic procedures coupled with the lack of standardization of the technique, which has limited training and dissemination [29]. Furthermore, despite the reassuring safety data described above, there remains reasonable concern regarding the potential complication of stent misdeployment. For these reasons, the use of EUS-GE is presently limited mostly to high-volume, tertiary-care endoscopy centers.

The most feared complication of the EUS-GE procedure is stent misdeployment since the tract being created is extraluminal [30]. A recent international, multicentered study reported on outcomes and management of EUS-GE and found that stent misdeployment occurred in close to 10% of the 467 EUS-GE procedures, with surgery required in 11% of these and the remaining 89% managed by conservative or endoscopic means [31]. Most resulting AEs were graded as mild, although six cases were severe and one fatality occurred after an attempt at surgical repair.

Regarding factors that may contribute to stent misdeployment, the endoscopist's experience seems to play an important role. In the study by Ghandour et al [31], 73% of misdeployments occurred within the endoscopist's first 13 EUS-GE procedures. In a European multicentered cohort study of 45 EUS-GE procedures, most of the five misdeployments leading to techni-

▶ **Table 3** Additional sensitivity and subgroup analyses.

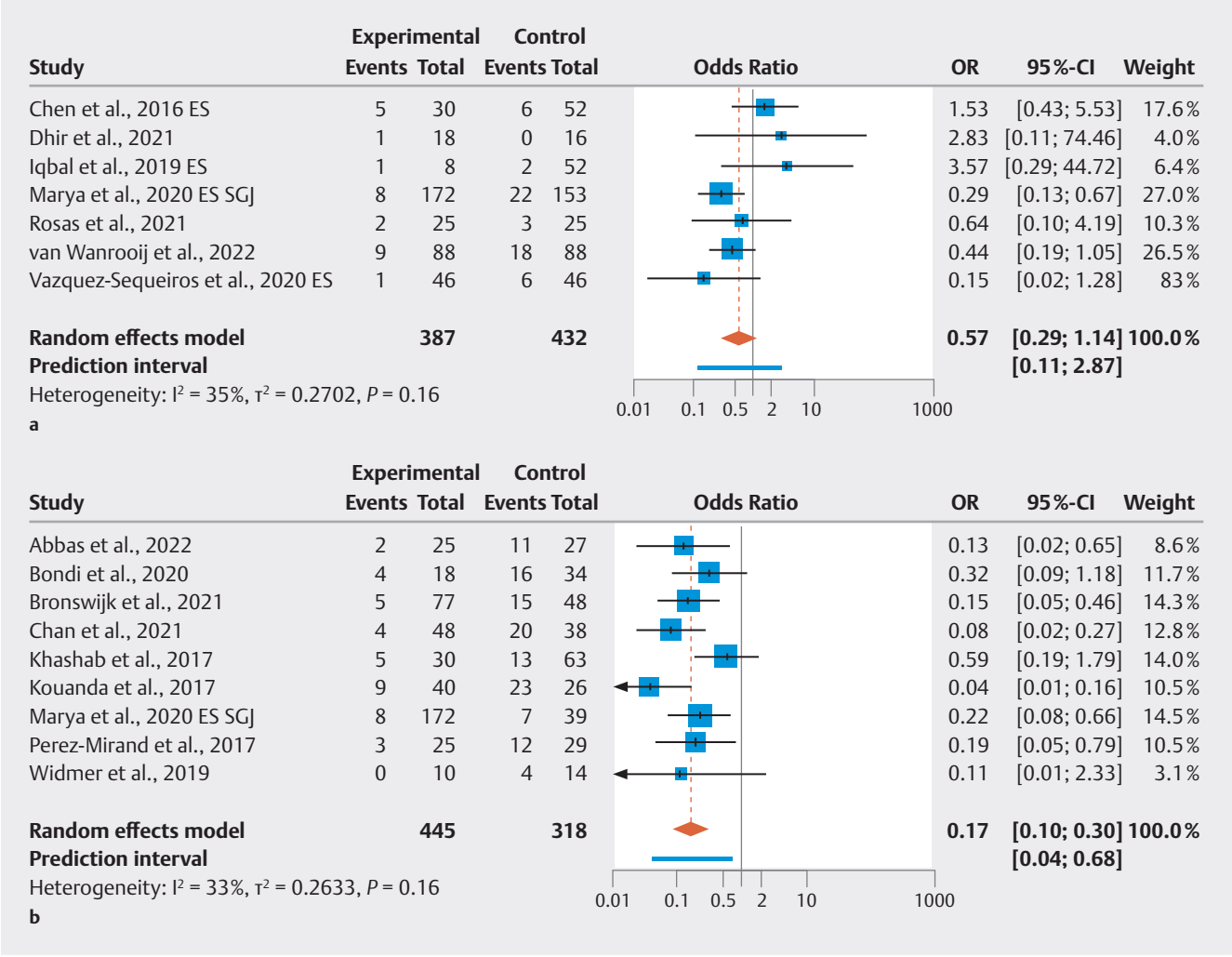
	No. studies	No. patients	Odds ratio (95% CI)	P value for heterogeneity	I^2
Clinical success without recurrent GOO					
Publication status					
Fully published article	7	759	3.51 (1.88, 6.56)	0.10	44%
Abstract	7	648	1.91 (0.86, 4.27)	< 0.01	69%
Continent					
North American	11	1014	2.28 (1.23, 4.21)	< 0.01	61%
Europe	3	393	3.77 (1.51, 9.42)	0.09	59%
Confounding bias					
Low risk of bias	6	643	3.51 (2.33; 5.27)	0.11	44%
Moderate to serious risk of bias	3	482	1.82 (0.34; 9.64)	< 0.01	88%
Critical risk of bias	3	166	1.38 (0.54; 3.53)	0.11	54%
Adverse events					
Publication status					
Fully published article	8	793	0.33 (0.08, 1.34)	0.13	42%
Abstract	7	648	0.26 (0.10, 0.64)	0.84	0%
Continent					
North America	11	1014	0.18 (0.07, 0.44)	0.86	0%
Europe	4	427	0.67 (0.19, 2.35)	0.26	25%
Confounding bias					
Low risk of bias	5	526	0.46 (0.28; 0.75)	0.11	47%
Moderate to serious risk of bias	3	482	0.16 (0.05; 0.54)	< 0.01	69%
Critical risk of bias	3	166	0.34 (0.06; 1.75)	0.08	61%

CI, confidence interval; GOO, gastric outlet obstruction.

cal failure happened at a single center early after introducing EUS-GE [32]. Indeed, a study of a single expert endoscopist's EUS-GE learning curve using cumulative sum curve analysis with mean procedure time as the target value suggested that 25 cases are necessary to become proficient, and 40 to achieve mastery [33]. Interestingly, in the study by Ghandour et al [31], 83% and 90% of stent misdeployments occurred prior to these suggested proficiency and mastery reference points, respectively. In terms of procedure-related factors, there has been a shift away from over-the-wire placement of the LAMS to form the gastroenterostomy, as the wire has been noted to push the small bowel away, potentially resulting in misdeployment [32, 34]. The risk of stent misdeployment highlights the need for further refinement and standardization of EUS-GE technique. It is also imperative that proper informed consent be obtained and that plans for salvage maneuvers are considered by the endoscopy team in advance. At the same time, our findings support the overall safety of EUS-GE compared to the traditional treatments of malignant GOO, with fewer total AEs compared to SGJ and no difference compared to ES.

Designated accessory devices will be essential for improvement of the EUS-GE procedure and its dissemination beyond the walls of the most expert centers. It should be noted that there are currently no approved dedicated devices for this complex procedure in North America. Even the LAMS, the stent universally used to form the gastroenterostomy, is off-label for this indication.

Although our results demonstrate better durability associated with EUS-GE compared to traditional ES, it is not clear whether EUS-GE allows for as robust a bypass as a surgical anastomosis. While EUS-GE has almost exclusively been studied using LAMS with a 15-mm diameter, 20-mm LAMS was recently developed. A retrospective study comparing EUS-GE using a 20-mm vs 15-mm LAMS demonstrated similar results with regards to technical success, clinical success and AEs; however, a higher proportion of patients in the larger LAMS group tolerated soft or complete diets [35]. Interestingly, the functional diameter of a SGJ anastomosis may not be more than 20 mm [36]. Current recommendations for patients with malignant GOO who have a life expectancy greater than 2 months favor SGJ over ES



▶ **Fig. 4** Adverse events. **a** EUS-GE vs. ES. **b** EUS-GE vs. SGJ.

given evidence of better long-term patency [37]. While our data suggest no difference in clinical success without recurrent GOO between EUS-GE and SGJ, high-quality prospective head-to-head studies with sufficient duration of follow-up are required to address this important comparison.

The current study is limited by mostly retrospective data and relatively small sample sizes of the included studies. There is clinical heterogeneity in the differences in EUS-GE technique used, as the procedure lacks standardization. Further heterogeneity is introduced by inclusion of both malignant and some benign GOO in patient selection. Observational studies are prone to confounding and other forms of bias. We assessed each study according to the ROBINS-I tool and performed sensitivity analyses for the primary outcomes by risk of bias due to confounding. Results demonstrated that the findings for both primary outcomes remain robust when including only studies at low risk for bias due to confounding. Furthermore, statistical heterogeneity was no longer present for these analyses, indicating that an important contribution to the heterogeneity found in the primary outcomes comes from studies that are higher risk for confounding. Lastly, the studies included were mainly performed in high-volume tertiary-care centers, which can impact the generalizability of these results to outside the most expert centers. Strengths of this meta-analysis include its a priori design with protocol registration and selection of primary endpoints that are both clinically most relevant as well as homogenous throughout individual studies.

Conclusions

In conclusion, our systematic review and meta-analysis show that EUS-GE is associated with higher clinical success without recurrent obstruction and fewer AEs compared to the traditional standard of care treatments of GOO. Further development of designated accessory devices and standardization of the technique are required to mitigate the technical challenges of this promising modality. High-quality randomized trials will also be needed to better characterize the role of EUS-GE in the treatment of malignant GOO.

Conflict of Interest

Alan Barkun is a consultant for Olympus Inc. Yen-I Chen is a consultant for Boston Scientific Inc. and president of Chess Medical. The remaining authors disclose no conflicts.

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