ENDOSCOPIC ULTRASOUND-GUIDED GASTROJEJUNOSTOMY VERSUS SURGICAL GASTROJEJUNOSTOMY AND ENTERAL STENTING FOR THE TREATMENT OF MALIGNANT GASTRIC OUTLET OBSTRUCTION: A SYSTEMATIC REVIEW AND META-ANALYSIS

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Background: Gastric outlet obstruction (GOO), often encountered in advanced malignancy, is associated with debilitating symptoms and decreased quality of life. Traditional management of this condition has been surgical gastrojejunostomy (SGJ) or enteral stenting (ES). While SGJ is highly effective, it is invasive and associated with high rates of morbidity. ES provides a less invasive approach with a lower risk of adverse events; however, it is associated with a significant risk of stent dysfunction with increased need for reintervention. Endoscopic ultrasound-guided gastrojejunostomy (EUS-GJ) is a novel modality in the management of GOO that aims to endoscopically bypass the obstruction with a lumen-apposing metal stent, with early studies suggesting good effectiveness and safety outcomes; but the data are limited.

Aims: To perform a systematic review and meta-analysis comparing the clinical outcomes of EUS-GJ to more traditional treatments of malignant GOO.

Methods: The study protocol was prospectively registered with the PROSPERO international database. The literature was systematically searched using MEDLINE, EMBASE and Web of Knowledge databases from inception through May 2021. Studies comparing EUS-GJ to ES or SGJ in patients with malignant GOO were included. Meta-analysis was performed with results reported as odds ratios (ORs) with 95% confidence intervals (CIs) using random effects models. The two primary outcomes of interest were clinical success without GOO recurrence and adverse events. Secondary outcome was technical success.

Results: Ten studies with a total of 1016 patients were included. EUS-GJ was associated with higher clinical success without GOO recurrence compared to SGJ or ES [OR: 2.19, 95% CI: 1.18-4.09, heterogeneity: P = 0.10; $I^2 = 59\%$]. Subgroup analysis showed higher clinical success without GOO recurrence compared to ES [OR: 5.31, 95% CI: 3.07-9.17], but no significant difference compared to SGJ [OR: 1.69, 95% CI: 0.76-3.72]. EUS-GJ was associated with fewer adverse events compared to SGJ and ES [OR: 0.28, 95% CI: 0.14-0.55] and compared to SGJ alone [OR: 0.20, 95% CI: 0.10-0.37], but no difference was noted when compared to ES alone [OR: 0.53, 95% CI: 0.15-1.87]. EUS-GJ was associated with decreased technical success compared to SGJ and ES [OR: 0.26, 95% CI: 0.09 – 0.75] and SGJ alone [OR: 0.14, 95% CI: 0.04-0.48]; however, there was no difference when compared to ES alone [OR: 0.43, 95% CI: 0.05-3.44].

Conclusions: EUS-GJ provides a robust bypass with lower risk of recurrent obstruction

compared to ES and fewer adverse events compared to SGJ. High quality prospective studies are needed to further characterize the role of EUS-GJ in the management of malignant GOO.

	EUS	GE	SGJo	rES		Odds Ratio	Odds Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI	M-H, Random, 95% CI
Bondi et al., 2020	11	18	21	34	11.2%	0.97 [0.30, 3.14]	
Bronswijk et al., 2021	70	77	42	48	11.3%	1.43 [0.45, 4.54]	
Chen et al., 2016 ES	24	30	25	52	12.1%	4.32 [1.52, 12.31]	
lqbal et al., 2019 ES	7	8	39	52	5.6%	2.33 [0.26, 20.79]	
Khashab et al., 2017	25	30	48	63	11.5%	1.56 [0.51, 4.80]	
Kouanda et al., 2017	27	40	17	26	12.1%	1.10 [0.39, 3.12]	
Marya et al., 2020 ES SGJ	165	172	143	192	13.9%	8.08 [3.55, 18.39]	
Perez-Mirand et al., 2017	21	25	28	29	5.4%	0.19 [0.02, 1.80]	
Vazquez-Sequeiros et al., 2020 ES	41	46	31	46	11.6%	3.97 [1.30, 12.09]	
Widmer et al., 2019	9	10	8	14	5.2%	6.75 [0.66, 68.78]	
Total (95% CI)		456		556	100.0%	2.19 [1.18, 4.09]	•
Total events	400		402				
7 AE Total							
7 AE Total	EUS-	GE	SGJ or	ES		Odds Ratio	Odds Ratio
7 AE Total Study or Subgroup	EUS- Events	GE Total	SGJ or Events	ES Total	Weight	Odds Ratio M-H, Random, 95% Cl	Odds Ratio M-H, Random, 95% Cl
7 AE Total Study or Subgroup Bondi et al., 2020	EUS- Events 4	GE Total 18	SGJ or Events 16	ES Total 34	Weight 10.8%	Odds Ratio M-H, Random, 95% Cl 0.32 (0.09. 1.18)	Odds Ratio M-H, Random, 95% Cl
7 AE Total Study or Subgroup Bondi et al., 2020 Bronswijk et al., 2021	EUS- Events 4 5	GE Total 18 77	SGJ or Events 16 15	ES Total 34 48	Weight 10.8% 12.2%	Odds Ratio M-H, Random, 95% Cl 0.32 [0.09, 1.18] 0.15 [0.05, 0.46]	Odds Ratio M-H, Random, 95% Cl
7 AE Total Study or Subgroup Bondi et al., 2020 Bronswijk et al., 2021 Chen et al., 2016 ES	EUS- Events 4 5 5	GE Total 18 77 30	SGJ or Events 16 15 6	ES Total 34 48 52	Weight 10.8% 12.2% 10.9%	Odds Ratio M-H, Random, 95% Cl 0.32 [0.09, 1.18] 0.15 [0.05, 0.46] 1.53 [0.43, 5.53]	Odds Ratio M-H, Random, 95% Cl
7 AE Total Study or Subgroup Bondi et al., 2020 Bronswijk et al., 2021 Chen et al., 2016 ES Ibal et al., 2019 ES	EUS- Events 4 5 5	GE Total 18 77 30 8	SGJ or Events 16 15 6 2	ES Total 34 48 52 52	Weight 10.8% 12.2% 10.9% 5.2%	Odds Ratio M-H, Random, 95% Cl 0.32 [0.09, 1.18] 0.15 [0.05, 0.46] 1.53 [0.43, 5.53] 3.57 [0.29, 44, 72]	Odds Ratio M-H, Random, 95% Cl
7 AE Total Study or Subgroup Bondi et al., 2020 Bronswijk et al., 2021 Chen et al., 2016 ES Iqbal et al., 2019 ES Khashab et al., 2017	EUS- <u>Events</u> 4 5 5 1 5	GE Total 18 77 30 8 30	SGJ or Events 16 15 6 2 16	ES Total 34 48 52 52 63	Weight 10.8% 12.2% 10.9% 5.2% 12.0%	Odds Ratio M-H, Random, 95% Cl 0.32 (0.09, 1.18) 0.15 (0.05, 0.46) 1.53 (0.43, 5.53) 3.57 (0.29, 44.72) 0.59 (0.19, 1.79)	Odds Ratio M-H, Random, 95% Cl
7 AE Total Study or Subgroup Bondi et al., 2020 Bronswijk et al., 2021 Chen et al., 2016 ES Iqbal et al., 2017 Knashab et al., 2017 Kouanda et al., 2017	EUS- Events 4 5 5 1 5 9	GE Total 18 77 30 8 30 40	SGJ or Events 16 15 6 2 16 23	ES Total 34 48 52 52 63 26	Weight 10.8% 12.2% 10.9% 5.2% 12.0% 10.1%	Odds Ratio M-H, Random, 95% Cl 0.32 [0.09, 1.18] 0.55 [0.05, 0.46] 1.53 [0.54, 3.553] 3.57 [0.29, 44.72] 0.59 [0.19, 1.79] 0.04 [0.01, 0.16]	Odds Ratio M-H, Random, 95% Cl
7 AE Total Study or Subgroup Bondi et al., 2020 Bronswijk et al., 2021 Chen et al., 2016 ES Iqbal et al., 2017 BS Khashab et al., 2017 Kouanda et al., 2017 Kouanda et al., 2017 Kouanda et al., 2017 Solution Solution Solution Brown et al., 2017 Solution Solution Brown et al., 2017 S	EUS- Events 4 5 5 1 5 9 8	GE <u>Total</u> 18 77 30 8 30 40 172	SGJ or <u>Events</u> 16 15 6 2 16 23 29	ES Total 34 48 52 52 63 26 192	Weight 10.8% 12.2% 10.9% 5.2% 12.0% 10.1% 14.2%	Odds Ratio M-H, Random, 95% Cl 0.32 [0.09, 1.18] 0.15 [0.05, 0.46] 1.53 [0.43, 5.53] 3.57 [0.29, 44.72] 0.59 [0.19, 1.79] 0.04 [0.01, 0.16] ← 0.27 [0.12, 0.62]	Odds Ratio M-H, Random, 95% Cl
7 AE Total Study or Subgroup Bondi et al., 2020 Bronswijk et al., 2021 Chen et al., 2019 ES Khashab et al., 2017 Kouanda et al., 2017 Marya et al., 2020 ES SGJ Perez-Mirand et al., 2017	EUS- Events 4 5 5 1 5 9 8 8 3	GE Total 18 77 30 8 30 40 172 25	SGJ or Events 16 15 6 2 16 23 29 12	ES Total 34 48 52 52 63 26 192 29	Weight 10.8% 12.2% 10.9% 5.2% 12.0% 10.1% 14.2% 10.1%	Odds Ratio M-H, Random, 95% Cl 0.32 [0.09, 1.18] 0.15 [0.05, 0.46] 1.53 [0.43, 5.53] 3.57 [0.29, 44.72] 0.59 [0.19, 1.79] 0.44 [0.01, 0.16] 0.27 [0.12, 0.62] 0.19 [0.05, 0.79]	Odds Ratio M-H, Random, 95% Cl
7 AE Total Study or Subgroup Bondi et al., 2020 Bronswijk et al., 2021 Chen et al., 2016 ES Iqbal et al., 2017 ES Knashab et al., 2017 Marya et al., 2020 ES SGJ Perez-Mirand et al., 2017 Varguez-Secueiros et al., 2020 ES	EUS- Events 4 5 5 1 5 9 8 3 3	GE Total 18 77 30 8 30 40 172 25 46	SGJ or Events 16 15 6 2 16 23 29 12 16	ES Total 34 48 52 52 63 26 192 29 46	Weight 10.8% 12.2% 10.9% 5.2% 12.0% 10.1% 14.2% 10.1% 10.7%	Odds Ratio M-H, Random, 95% CI 0.32 [0.09, 1.18] 0.15 [0.05, 0.46] 1.53 [0.43, 5.53] 3.57 [0.29, 44.72] 0.59 [0.19, 1.79] 0.04 [0.01, 0.16] 0.27 [0.12, 0.62] 0.19 [0.05, 0.79] 0.13 [0.04, 0.49]	Odds Ratio M-H, Random, 95% Cl
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