Accepted Manuscript

Endoscopy International Open

Endoscopic Ultrasound Gastroenterostomy versus Duodenal Stenting for Malignant Gastric Outlet Obstruction: A Cost-Effectiveness Study

Daryl Ramai, Richard Nelson, Nathorn Chaiyakunapruk, Andrew Ofosu, John C Fang.

Affiliations below.

DOI: 10.1055/a-2509-7671

Please cite this article as: Ramai D, Nelson R, Chaiyakunapruk N et al. Endoscopic Ultrasound Gastroenterostomy versus Duodenal Stenting for Malignant Gastric Outlet Obstruction: A Cost-Effectiveness Study. Endoscopy International Open 2024. doi: 10.1055/a-2509-7671

Conflict of Interest: The authors declare that they have no conflict of interest.

Abstract:

Background

Enteral stenting has been traditionally employed for managing malignant gastric outlet obstruction. However, concerns regarding high reintervention rates have brought into question its cost-effectiveness.

Endoscopic ultrasound-guided gastroenterostomy (EUS-GE) with a lumen-apposing metal stent (LAMS) provides an alternative to luminal stenting. The goal of this study was to assess the cost-effectiveness of EUS-GE relative to duodenal stenting.

Methods

A decision analysis was performed to analyze costs and survival in patients with unresectable or metastatic gastric outlet obstruction. The model was designed with two treatment arms: self-expanding metal stent (SEMS) placement and EUS-GE with LAMS. Costs were derived from Medicare reimbursement rates (US\$) while effectiveness was measured by quality-adjusted life years (QALYs). The primary outcome measure was the incremental cost-effectiveness ratio (ICER). Probabilistic sensitivity analyses were performed.

Results

Endoscopic stenting resulted in an average cost of \$22,748 and 0.31 QALYs while EUS-GE cost \$32,254 and yielded 0.53 QALYs which yielded a difference of \$9,507 in cost and 0.23 in QALY. EUS-GE was found to be a cost-effective strategy over duodenal stenting (ICER, \$41994/QALY) at a willingness-to-pay (WTP) of \$100,000/QALY. In 10,000 Monte-Carlo simulations, EUS-GE was favored 62% of the time. Using a tornado diagram, the model was most sensitive to the probability of mortality in patients with duodenal stents compared with EUS-GE.

Conclusions

In patients with malignant gastric outlet obstruction, EUS-GE is a cost-effective palliative intervention compared to duodenal stenting.

Corresponding Author:

Dr. Daryl Ramai, Brigham and Women's Hospital, Gastroenterology, Hepatology, and Endoscopy, Boston, United States, dramai@bwh. harvard.edu

Affiliations:

This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.



Daryl Ramai, Brigham and Women's Hospital, Gastroenterology, Hepatology, and Endoscopy, Boston, United States Richard Nelson, University of Utah Health, Division of Epidemiology, Salt Lake City, United States Nathorn Chaiyakunapruk, University of Utah Health, Division of Pharmacology, Salt Lake City, United States Andrew Ofosu, University of Cincinnati, Gastroenterology and Hepatology, Cincinnati, United States John C Fang, University of Utah Health, Gastroenterology, Salt Lake City, United States

This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.



Endoscopic Ultrasound Gastroenterostomy versus Duodenal Stenting for Malignant Gastric Outlet Obstruction: A Cost-Effectiveness Study

ABSTRACT

Background

Enteral stenting has been traditionally employed for managing malignant gastric outlet obstruction. However, concerns regarding high reintervention rates have brought into question its cost-effectiveness. Endoscopic ultrasound–guided gastroenterostomy (EUS-GE) with a lumen-apposing metal stent (LAMS) provides an alternative to luminal stenting. The goal of this study was to assess the cost-effectiveness of EUS-GE relative to duodenal stenting.

Methods

A decision analysis was performed to analyze costs and survival in patients with unresectable or metastatic gastric outlet obstruction. The model was designed with two treatment arms: self-expanding metal stent (SEMS) placement and EUS-GE with LAMS. Costs were derived from Medicare reimbursement rates (US\$) while effectiveness was measured by quality-adjusted life years (QALYs). The primary outcome measure was the incremental cost-effectiveness ratio (ICER). Probabilistic sensitivity analyses were performed.

Results

Endoscopic stenting resulted in an average cost of \$22,748 and 0.31 QALYs while EUS-GE cost \$32,254 and yielded 0.53 QALYs which yielded a difference of \$9,507 in cost and 0.23 in QALY. EUS-GE was found to be a cost-effective strategy over duodenal stenting (ICER, \$41994/QALY) at a willingness-to-pay (WTP) of \$100,000/QALY. In 10,000 Monte-Carlo simulations, EUS-GE was favored 62% of the time. Using a tornado diagram, the model was most sensitive to the probability of mortality in patients with duodenal stents compared with EUS-GE.

Conclusions

In patients with malignant gastric outlet obstruction, EUS-GE is a cost-effective palliative intervention compared to duodenal stenting.

Accepted Manuscript

INTRODUCTION

Malignant gastric outlet obstruction (GOO) is a condition secondary to mechanical obstruction characterized by post-prandial abdominal pain, abdominal distension, nausea and vomiting. In the past, these cases were treated with surgery. However, endoscopic duodenal stenting has become the current standard treatment for malignant GOO in patients with limited life expectancy. However, duodenal stenting is prone to stent dysfunction, stent migration, and stent occlusion. To this end, patients may require stent revision and possibly readmission to the hospital.

More recently, endoscopic ultrasound-guided gastroenterostomy (EUS-GE) has been used as a novel approach to treating malignant GOO and appears to have clinical benefit over duodenal stenting. Sánchez-Aldehuelo et al. looked at 158 patients (79 duodenal stenting and 79 EUS-GE) with GOO and showed that EUS-GE group had improved stent patency when compared with those patients undergoing duodenal stenting (92.23% vs 80.6%, P = .033) [2].

A meta-analysis (of 16 studies and 1541 patients) compared surgery, duodenal stenting, and EUS-GE [1]. The authors reported that EUS-GE was associated with higher clinical success without recurrent GOO compared to duodenal stenting or surgical gastroenterostomy (SGE) [odds ratio (OR) 2.60, 95% CI 1.58–4.28] and compared to duodenal stenting [OR 5.08, 95% CI 3.42–7.55]. Adverse events were superior to surgery and comparable to duodenal stenting. A recent prospective propensity score matched study showed that EUS-GE patients experienced higher and faster clinical success (100% vs. 75.0%, p=0.006), reduced recurrences of obstruction (3.7% vs. 33.3%, p=0.007) and a trend towards shorter time-to-chemotherapy [3].

A randomized clinical trial of 97 patients (48 EUS-GE group and 49 duodenal stenting group) showed that reintervention within 6 months was 4% in the EUS-GE group versus 29% in the duodenal stent group [risk ratio (RR) 0·15, 95% CI 0·04–0·61, p=0·0020) [4]. Stent patency was longer in the EUS-GE group than the duodenal stent group (log-rank p<0·0001). Furthermore, the study found that gastric outlet obstruction score (GOOS) at 1-month was significantly higher in the EUS-GE group than the duodenal stent group [2.41 versus 1.91, p=0.012], with similar rates of adverse events (p=1.00) [4].

Overall, the current literature suggests that EUS-GE may offer superior clinical advantages over duodenal stenting related to stent patency. The duodenal stenting approach carries a higher risk of stent occlusion with need for repeat procedure or stenting and/or hospital readmission. However, EUS-GE has not been widely adopted, particularly due to the ease of placing a duodenal stent over the complexity of EUS-GE [5]. While there is a growing body of evidence in support of EUS-GE, a cost-effectiveness analysis is needed to assess the economic impact of these two competing strategies.

The goal of this study was to analyze the cost-effectiveness of duodenal stenting and EUS-GE for the treatment of malignant GOO.

METHODS

Study design

This was a cost-effectiveness analysis simulating a base-case scenario of a patient undergoing endoscopic management with either EUS-GE or duodenal stenting for malignant GOO. The analysis was performed using the US healthcare payer perspective. The sample population for the study is represented by an adult with malignant GOO and the model was used to compare the cost-effectiveness of these two strategies.

Simulation model

We constructed a Markov simulation model with a monthly cycle length in accordance with guidelines of the Panel on the Cost-Effectiveness in Health and Medicine [6] and reported in accordance with CHEERS 2022 [7]. The model incorporated procedural mortality, technical success, stent patency, stent occlusion, and management of occluded stents [**Figure 1**].

Cost definitions

Direct costs of each treatment modality were obtained from hospital institutional level pricing, see Table 1. Pricing included the cost of endoscopy, duodenal stent, lumen apposing metal stent (LAMS), anesthesia, recovery, and accessories. A blended cost analysis was used to combine the probability cost for procedures with no adverse events and major adverse events (which includes stent occlusion / dysfunction) necessitating the need for repeated intervention [8]. Base-case point estimates of cost were varied by at least 50% for the sensitivity analysis. The costs were reported as 2024 USD.

Probability definitions

Probability values were expressed as percentages to facilitate their integration into the model. This was obtained by calculating the incidence of an adverse event, such as stent occlusion, represented as a

percentage of events compared to the percentage of occurrences without the adverse event. In selecting the most appropriate studies for our analysis, we adhered to a hierarchy of evidence, prioritizing sources that provided the highest level of reliability extracted from the existing literature by searching PubMed, using keywords related to GOO, duodenal stent, EUS-GE, occlusion, adverse events, technical success, and mortality. In order of hierarchy, priority was placed on systematic reviews and meta-analyses [9], multicenter studies [2], and observational prospective studies [3]. Probability estimates were varied by at least 50% for the deterministic sensitivity analysis.

Utility values of health states

Utility values, an overall assessment of well-being on a scale of 0 (death) to 1 (perfect health without disability), reflect the severity of disability in health states. We derived utility values that were specific for patients' long-term health state from published literature [10,11].

Outcome and statistical analysis

The primary outcome of the study was the incremental cost-effectiveness ratio (ICER) which was calculated by dividing the difference in cost between the 2 comparison strategies by the difference in QALYs between the 2 strategies. Cost-effectiveness was determined by comparing the ICER to a willingness-to-pay (WTP) threshold of \$100,000/QALY. Our model had a time horizon of 12 months following the index procedure. A series of sensitivity analyses were performed to determine the robustness of our findings. Monte-Carlo probabilistic sensitivity analysis (PSA) was performed with10,000 iterations assuming beta distributions for probability and utility parameters and gamma distribution for cost parameter. All analyses were conducted using TreeAge Pro 2023 (R 2.0 TreeAge Software Inc., Boston, MA).

RESULTS

Base-case analysis

In the base-case analysis, endoscopic management of GOO with duodenal stenting was associated with a cost of \$22,748 and 0.31 QALYs per patient, whereas an EUS-GE was associated with a cost of \$32,254 and 0.53 QALY (Table 2). The cost difference was \$9,507 and the QALY difference was 0.23. EUS-GE was found to be a cost-effective strategy over duodenal stenting (ICER = \$41,994/QALY) at a WTP of \$100,000.

Sensitivity analyses

Results from our deterministic sensitivity analyses are presented in **Figure 2** as a tornado diagram and depict how much the ICER changes across the range of values for each input parameter. The model was most sensitive to the probability of mortality in patients with duodenal stents compared with EUS-GE. Results from our PSA are presented as cost-effectiveness acceptability curves in **Figure 3**. In these analyses, EUS-GE was the optimal strategy in 62% of iterations at a WTP threshold of \$100,000/QALY.

DISCUSSION

There is growing clinical evidence to suggest that EUS-GE should be the preferred modality for treating malignant GOO as EUS-GE can reduce the frequency of reintervention, improve luminal patency, and result in better patient-reported eating habits compared with duodenal stenting [2,3,4].

Our study assessed the cost-effectiveness between these two treatment modalities. Using a decision analytic model, we found that EUS-GE was a cost-effective strategy for treating patients with malignant gastric outlet obstruction when compared to duodenal stenting using a WTP of \$100,000/QALY.

A survey of endosonographers (n=60) found that there is wide variability in clinical practice with over half of participants (62%) indicating that the procedure is technically challenging [13]. Interestingly, 89.7% of participants thought that EUS-GE could be useful in their daily clinical practice, with 100% concluding that this procedure should be performed in referral centers. To this end, it is recommended that EUS-GE be performed by expert endoscopists [14, 15]. Large population-level studies are needed to assess changing practice patterns in the US and other regions.

Our deterministic sensitivity analysis showed that the model was most sensitive to mortality in patients undergoing duodenal stenting. The exact mechanism for this is unclear. However, patients undergoing duodenal stenting had longer times to chemotherapy [2] and had worse gastric outlet obstruction scores [11] compared to EUS-GE patients which could have a bearing on overall mortality. It should be noted that in very ill patients with limited life expectancy (~ 1 month), duodenal stenting may be reasonable and cost effective with less procedural risk, particularly in centers where EUS-GE expertise is not available.

It is unclear exactly how many procedures (either endoscopic or surgical) related to GOO are performed each year. A prior report indicated that as many as 2000 operations were performed annually for GOO in the United States in the 1990s [16]. However, this is likely an underestimate with the rise in pancreatic cancer incidence along with other malignancies and the increased number of patients than can be treated less invasively with either duodenal stenting or EUS-GE. Using the number of operative cases performed, compared with duodenal stenting, EUS-GE would add an additional incremental cost of \$2 million dollars. However, this higher upfront cost would ultimately have cost savings when the cost of stent failure, hospital readmission, and days of life lost is considered.

Although economic evaluations like this one can be a useful way of quantifying an intervention's cost against its benefits, they have several limitations. As with any modeling exercise, there is uncertainty in the values of the input parameters. Regarding the inputs for stent failure, we performed an extensive literature review and gave priority to data from meta-analyses, but there is inherent heterogeneity in these data. In the absence of meta-analyses, priority was given to data from multicenter and/or prospective studies. However, significant differences in study populations and study design can introduce bias. To account for that, we performed sensitivity analyses across a wide range of probabilities and cost inputs.

Another limitation was that we only included direct health care costs related to the initial hospitalization for GOO and may not have accounted for outpatient follow-up costs or additional health care costs. However, from our experience at an academic tertiary care hospital, follow ups in this population is usually limited when compared to benign chronic diseases. Furthermore, given the similarities between both modalities, follow-up would also be treated similarly. Additionally, given the higher luminal failure rates with stenting vs. EUS-GE these unaccounted-for costs would likely be higher for duodenal stenting, making EUS-GE even more cost-effective. On the contrary, our model did not account for stent misdeployment and treatment for salvaging these events. Despite these limitations, we believe this analysis to be reflective of real-world experience as we utilized actual hospital level pricing accounting for endoscopy, anesthesia, and recovery. However, it should be kept in mind that the use of LAMS for this purpose remains off-label use.

In conclusion, based on recommendations from prospective and randomized studies [2, 7], and our costeffectiveness analysis results, we suggest the utilization of EUS-GE in treating patients with GOO where the expertise is available. Further studies should focus on barriers to adopting this therapeutic approach across different clinical practices and real-world data on costs modeled here. Furthermore, future costeffective studies may assess if EUS-GE is cost-effective in treating benign conditions.

References

1. Miller C, Benchaya JA, Martel M, et al. EUS-guided gastroenterostomy vs. surgical gastrojejunostomy and enteral stenting for malignant gastric outlet obstruction: a meta-analysis. Endosc Inter Open 2023;1:E660-72.

- Sánchez-Aldehuelo R, Iñigo JC, Moreno BM, et al. EUS-guided gastroenterostomy versus duodenal selfexpandable metal stent for malignant gastric outlet obstruction: results from a nationwide multicenter retrospective study (with video). Gastrointest Endosc 2022;96:1012-20.
- Vanella G, Dell'Anna G, Capurso G, et al. EUS-guided GastroEnterostomy for management of malignant Gastric Outlet Obstruction: a prospective cohort study with matched comparison with Enteral Stenting. Gastrointest Endosc 2023;98:337-347
- 4. Teoh AYB, Lakhtakia S, Tarantino I, et al. Endoscopic ultrasonography-guided gastroenterostomy versus uncovered duodenal metal stenting for unresectable malignant gastric outlet obstruction (DRA-GOO): a multicentre randomised controlled trial. Lancet Gastroenterol Hepatol 2024;9:124-132.
- 5. Ramai D, Facciorusso A, Crinò SF, et al. EUS-guided gastroenteric anastomosis: A first-line approach for gastric outlet obstruction? Endosc Ultrasound 2021;10:404-405.
- Sanders GD, Neumann PJ, Basu A. et al. Recommendations for conduct, methodological practices, and reporting of cost-effectiveness analyses: Second Panel on Cost-effectiveness in Health and Medicine. JAMA 2016;316:1093-1103
- Husereau D, Drummond M, Augustovski F, et al. Consolidated Health Economic Evaluation Reporting Standards 2022 (CHEERS 2022) Statement: Updated Reporting Guidance for Health Economic Evaluations. Value Health. 2022;25:3-9.
- 8. Forbes N, Coelho-Prabhu N, Al-Haddad MA, et al. Adverse events associated with EUS and EUS-guided procedures. Gastrointest Endosc. 2022;95:16-26.
- 9. Krishnamoorthi R, Bomman S, Benias P, et al. Efficacy and safety of endoscopic duodenal stent versus endoscopic or surgical gastrojejunostomy to treat malignant gastric outlet obstruction: systematic review and meta-analysis. Endosc Int Open. 2022;10:E874-E897.
- Garcia-Alonso FJ, Chavarria C, Subtil JC, et al. Prospective multicenter assessment of the impact of EUSguided gastroenterostomy on patient quality of life in unresectable malignant gastric outlet obstruction. Gastrointest Endosc. 2023;98:28-35.
- 11. Schmidt C, Gerdes H, Hawkins W, et al. prospective observational study examining quality of life in patients with malignant gastric outlet obstruction. Am J Surg. 2009;198:92-9.
- Canakis A, Irani SS. Endoscopic Treatment of Gastric Outlet Obstruction. Gastrointest Endosc Clin N Am. 2024;34:111-125.
- 13. Tarantino I, Sinagra E, Binda C, et al. Perceived feasibility of endoscopic ultrasound-guided gastroenteric anastomosis: an italian survey. Medicina. 2022;58:532.
- 14. Mangiavillano B, Repici A. EUS-guided gastro-enteral anastomosis for the treatment of gastric outlet obstruction: is the end of the enteral stent? Expert Rev Gastroenterol Hepatol. 2022;16:587-589.
- 15. Conti Bellocchi MC, Gasparini E, Stigliano S, et al. Endoscopic Ultrasound-Guided Gastroenterostomy versus Enteral Stenting for Malignant Gastric Outlet Obstruction: A Retrospective Propensity Score-Matched Study. Cancers (Basel). 2024;16:724.

 Gibson JB, Behrman SW, Fabian TC, et al. Gastric outlet obstruction resulting from peptic ulcer disease requiring surgical intervention is infrequently associated with Helicobacter pylori infection. J Am Coll Surg. 2000;191:32-37.

Table 1: Baseline input parameters comparing duodenal stenting and endoscopic ultrasound gastroenterostomy (EUS-GE) for malignant gastric outlet obstruction (GOO).

| Parameters | Base case | Sensitivity Analysis | Monte- Carlo Distributio n | References | |
|------------------------------|-------------|----------------------|-------------------------------------|------------|--|
| Periprocedural Mortality | | | | | |
| Duodenal Stent | 0.008 | 0.004 | Beta | [8] | |
| EUS-GE | 0.017 | 0.009 | | | |
| Stent Failure (1 Month) | | | | | |
| Duodenal Stent | 0.095 | 0.047 | Beta | [2] | |
| EUS-GE | 0.031 | 0.015 | | | |
| Mortality (1 Month) | | | | | |
| Duodenal Stent | 0.082 | 0.041 | Beta | [3,4] | |
| EUS-GE | 0.015 | 0.008 | | | |
| Utilities / QALY | | | | | |
| Duodenal Stent | 0.49 | | Beta | [9,10] | |
| EUS-GE | 0.57 | | | | |
| Cost of Duodenal Stenting | | | | | |
| Guidewire | \$595.53 | | | | |
| Extraction Balloon | \$1,288.72 | | | | |
| Duodenal Stent | \$8,918.99 | | | | |
| Anesthesia - first 30 mins | \$1,345 | | | | |
| Anesthesia - additional time | \$4,512 | | | | |
| Recovery | \$917 | | | | |
| Endoscopy - 15 mins | \$2,956 | | | | |
| Endoscopy - additional time | \$2,398 | | | | |
| Total costs | \$22,931.24 | \$11,465.62 | Gamma | | |
| Cost of EUS-GE | | | | | |
| Guidewire | \$595.53 | | | | |
| Extraction Balloon | \$1,288.72 | | | | |

| AXIOS with electrocautery delivery | \$16,790.94 | | |
|---------------------------------------|-------------|-----------------|----------------------|
| Anesthesia - first 30 mins | \$1,345 | | |
| Anesthesia - additional time | \$4,512 | | |
| Recovery | \$917 | | |
| Endoscopy - 15 mins | \$3,619 | | |
| Endoscopy - additional time | \$3,744 | | Table 2: |
| Total costs | \$32,812.19 | \$16,406.10 Gam | ma Detailed Analysis |

of ICER of duodenal stenting and endoscopic ultrasound guided gastroenterostomy (EUS-GE).

| | Cumulative Cost | Incremental Cost | QALY | Incremental Effectiveness | ICER |
|----------------|-----------------|---------------------|------|------------------------------|----------|
| Duodenal Stent | \$22,748 | | 0.31 | | |
| EUS-GE | \$32,254 | \$9,507 | 0.53 | 0.23 | 41994.16 |

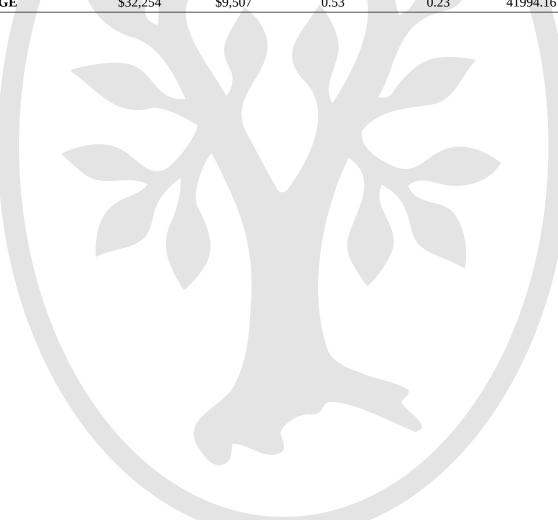


Figure legends:

Figure 1: Decision tree. Shown is the simulation model used to estimate costs, clinical outcomes, and quality-adjusted life-years of patients undergoing duodenal stenting or EUS-GE for malignant gastric outlet obstruction (GOO). Panel A shows the two interventions — duodenal stenting and EUS-GE — and health states of the patients, and Panel B shows the three categories of subsequent clinical events: mortality at one month, survival, stent patency, and stent failure. The blue square indicates the decision node, the point at which a treatment strategy is chosen; the blue encircled letter "M" indicates the Markov node, with branches indicating the health states in transition every 1 month; the green circle indicates the chance node, after which there is a probability of the occurrence of each event; and the red triangle indicates the terminal node, the end of a pathway within a 12-month cycle.

Figure 2: Tornado diagram showing the model is sensitive to the probability of mortality in patients with duodenal stents and the failure of duodenal stents compared with endoscopic ultrasound gastroenterostomy (EUS-GE). WTP, willingness to pay; ICER, incremental cost-effectiveness ratio.

Figure 3: Scatter plot of probabilistic sensitivity analysis. The incremental cost-effectiveness scatter plot for each of the 2 studied treatment strategies showing the iterations occurring either above (duodenal stenting) or below (EUS-GE) the willingness-to-pay (WTP) threshold of \$100,000/quality-adjusted life-year (QALY), with the oval showing the 95% CI. This visually represents what was found in the cost-effectiveness acceptability curve.

