Advanced Endoscopy Updates

Chris M Hamerski MD

Assistant Professor of Medicine, UCSF

Director of Luminal Oncology, CPMC

Director, International Interventional Fellowship Program, CPMC

Interventional Endoscopy Services

California Pacific Medical Center, San Francisco, CA

San Francisco VA Medical Center

Outline

- Prevention of post-ERCP pancreatitis
- Endoscopic Sleeve Gastroplasty (ESG)
- Management of Gastric Outlet Obstruction
- Management of Acute Cholecystitis
- Altered anatomy ERCP
- Third Space Endoscopy
  - G-POEM
- Not discussed: EUS-RFA of pancreatic neoplasms, ESD, Endoscopic management of GERD, EUS-guided biliary access, EUS-guided variceal ablation, Cyst gastrostomy, necrosectomy…

Prevention of Post-ERCP Pancreatitis

- PEP occurs in 1-25%
  - Mortality rate: 0.3-0.6%
- Rectal indomethacin decreases PEP in high risk patients
  - Pancreatitis: 9.2% vs 16.9%
  - Moderate/severe pancreatitis: 4.4% vs 8.8%
- Pancreatic stents
  - Meta-analysis of 15 studies
    - 3.9% vs 10.4% PEP
  - Failed attempt at PD stent increases risk of PEP

Elmunzer et al. NEJM 2012
Fan et al. World J Gastro 2015
Freeman et al. GIE 2004

Prevention of Post-ERCP Pancreatitis

- Periprocedural IV hydration with Lactated Ringers
  - 3 cc/kg/hr during ERCP, 20 cc/kg bolus and 3 cc/kg/hr after ERCP
  - Small pilot study (62 patients total)
    - 0 vs 17% PEP
  - Larger RCT (n=150)
    - 5.3% vs 22.7% (p=0.002)
- Few studies have suggested benefit of sublingual nitrates (isosorbide dinitrate, glycerol trinitrate)
  - Smooth muscle relaxant -> may relax sphincter of Oddi
  - Nitrates -> nitric oxide -> dilation of microvascular vessels -> improved pancreatic blood flow

Buxbaumet al. CGH 2014
Chen et al. BMC Gastro 2010
Sotoudehmanesh et al. Am J Gastro 2014

Combination of Diclofenac and Sublingual Nitrates Is Superior to Diclofenac Alone in Preventing Pancreatitis After Endoscopic Retrograde Cholangiopancreatography

Takeshi Tomoda,[1] Hironari Kato,[1] Toru Ueki,[2] Yutaka Akimoto,[3] Hidenori Hata,[4] Masakuni Fujii,[5] Ryo Harada,[6] Tsuneyoshi Ogawa,[7] Masaki Wato,[8] Masahiro Takatani,[9] Minoru Matsubara,[10] Yoshinari Kawai,[11] and Hiroyuki Okada[1]

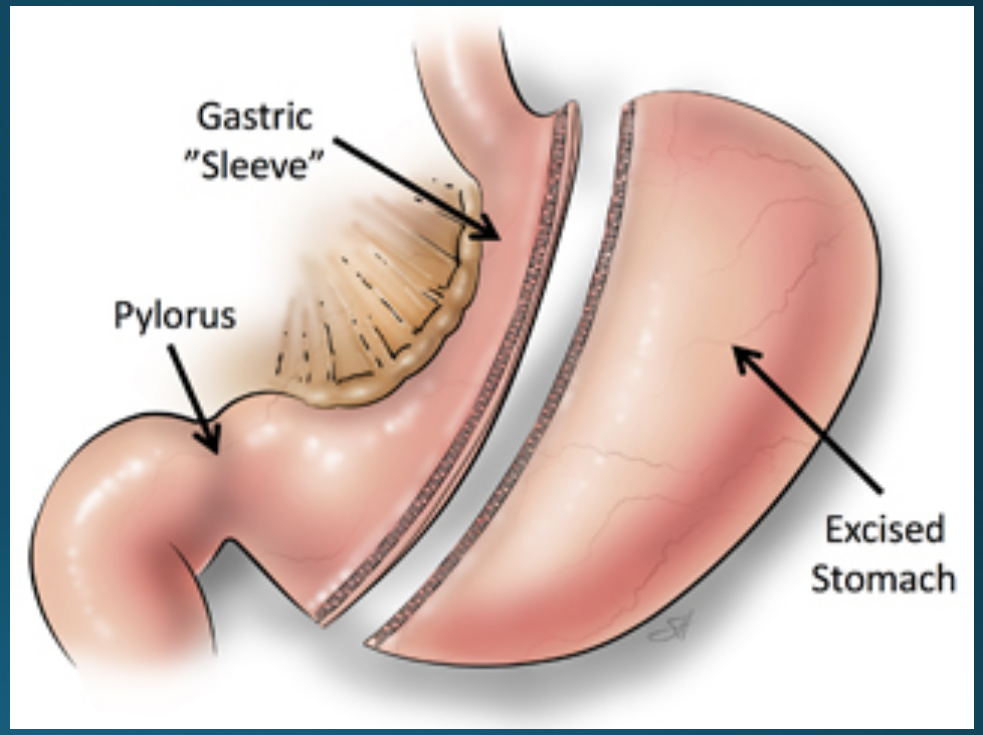
Gastroenterology 2019;156:1753–1760

- Multicenter RCT of 886 patients
  - Randomized to Diclofenac PR (50 mg within 15 minutes after ERCP) alone vs diclofenac plus 5 mg isosorbide dintrate SL 5 mins before ERCP

	Combination group	Diclofenac alone group	
	n = 444	n = 442	*P*
Post-ERCP pancreatitis in all patients, n (%)	25 (5.6)	42 (9.5)	.03
Mild	21 (4.7)	32 (7.2)	.12
Moderate	4 (0.9)	10 (2.3)	.12
Severe	0 (0)	0 (0)	
Post-ERCP pancreatitis in patients with no risk factor	1/155 (0.7)	3/142 (2.1)	.27
Post-ERCP pancreatitis in patients with risk factor	24/289 (8.3)	39/300 (13.0)	.08

Endoscopic Sleeve Gastroplasty

- Endoscopic alternative to sleeve gastrectomy
- Endoscopic suturing device reduces volume of the stomach by ~70%
  - Smaller gastric capacity
  - Slower transit through stomach
  - Hormonal changes
- 5 year data presented at DDW



Methods

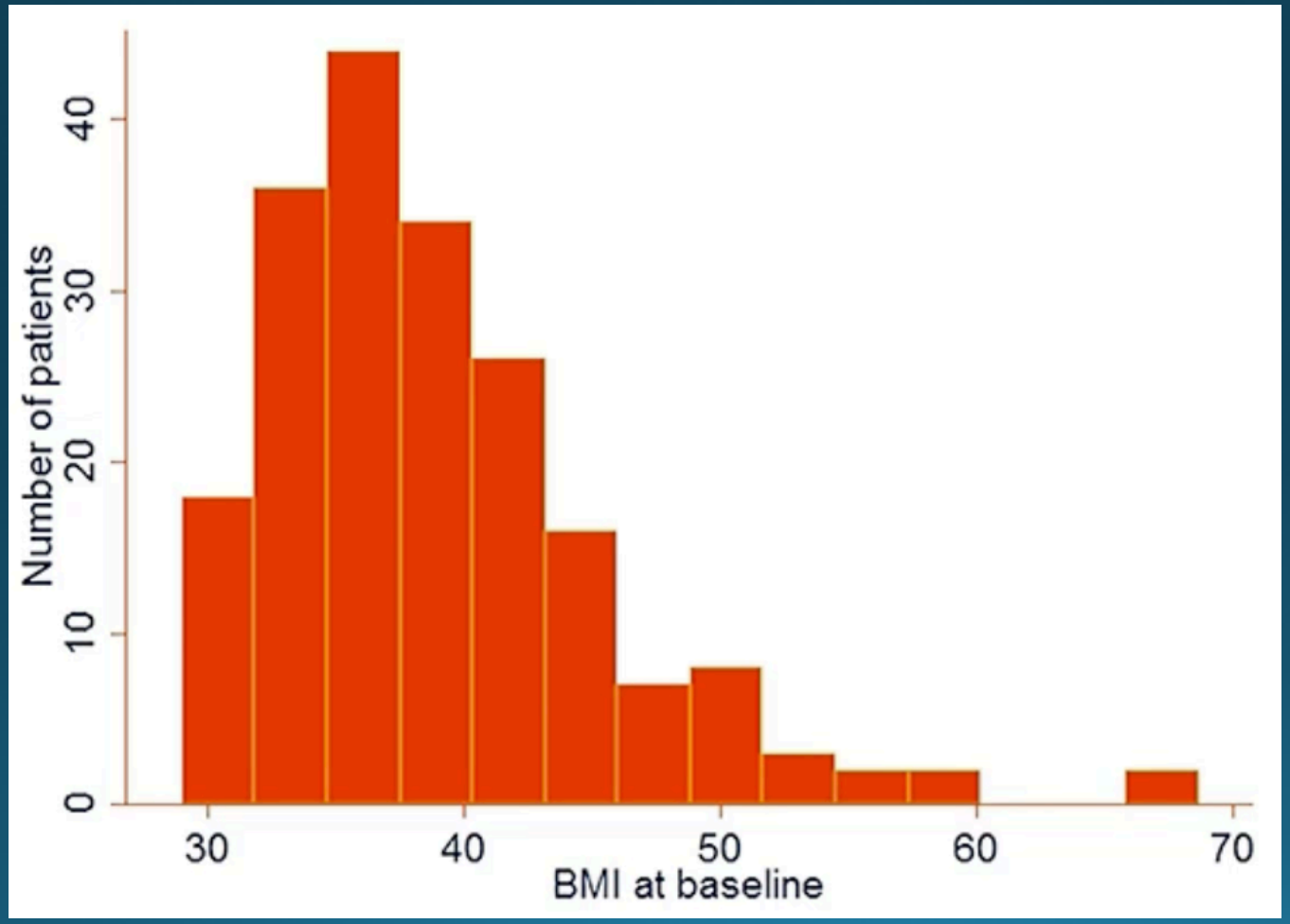
- 203 consecutive patients who underwent ESG between Aug 2013 and Oct 2018
  - BMI >30 kg/m^2
  - Failed noninvasive weight-loss measures
  - Not considered surgical candidates or refused surgery
  - Patients with prior bariatric procedures/surgeries were excluded

- Primary outcome: Percentage total body weight loss (%TBWL = [(Initial weight) – (Postop weight)] / (Initial weight) * 100)

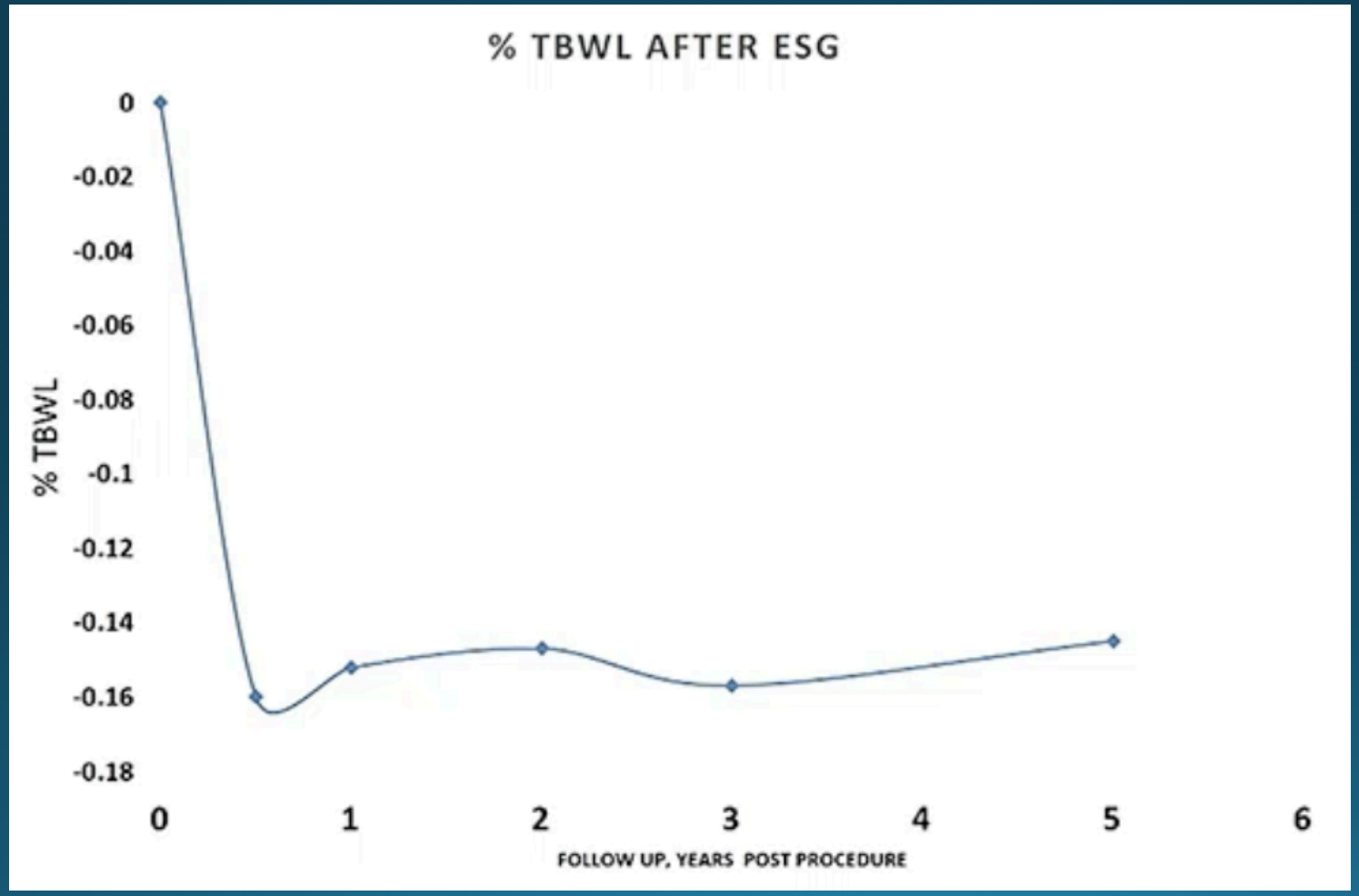
Baseline Characteristics

Characteristics	N=203
Age	46 ±13
Female	135 (67%)
BMI	39 ±7
Hgb A1C	5.6 ±1.5
Diabetes	57 (29%)
Elevated ALT	110 (54%)

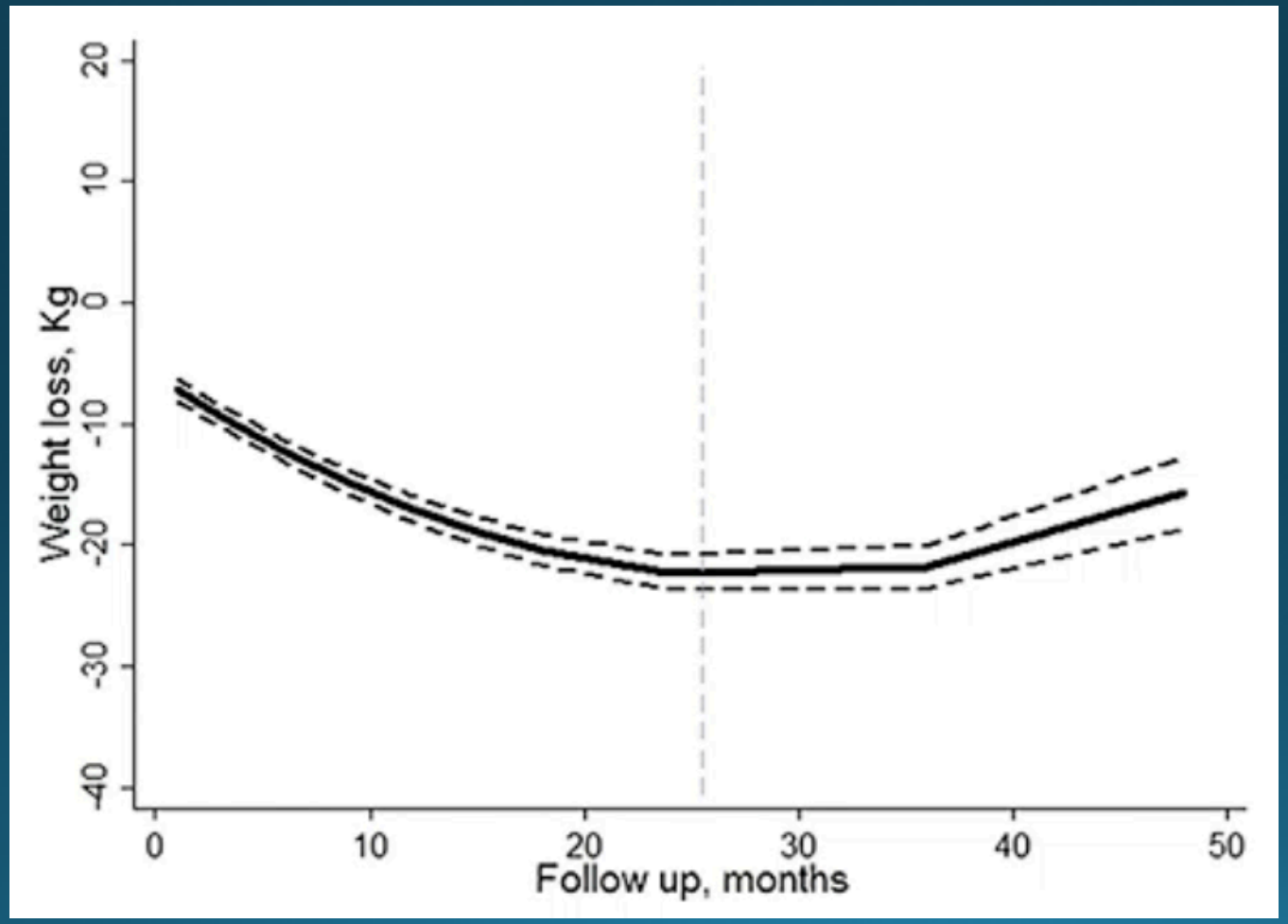
Baseline BMI Distribution



% TBWL After ESG



Maximum Weight Loss Achieved at 24 Months



Early Post-ESG Weight Loss Predicts Long Term Outcome

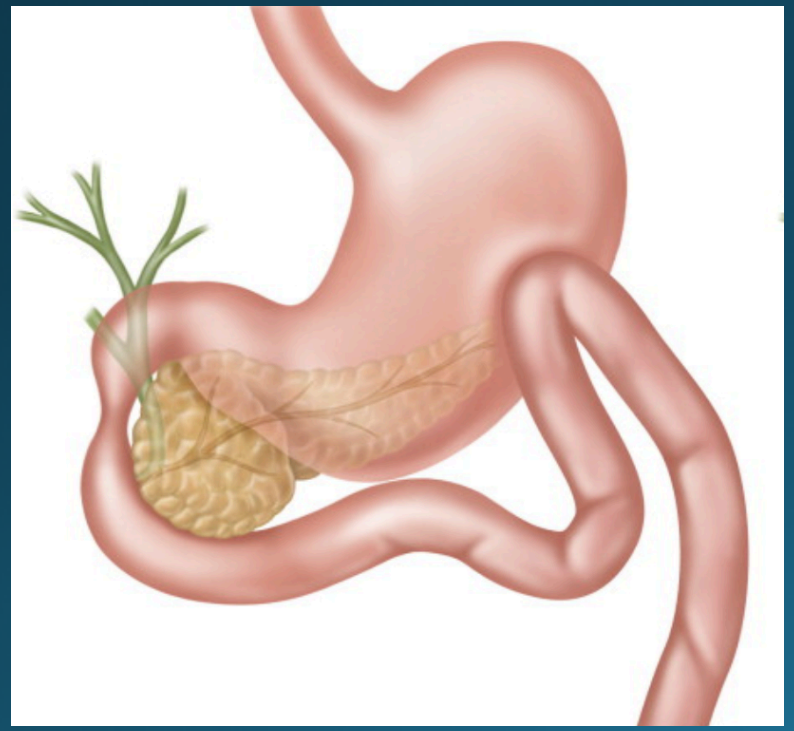
	Odds of %TBWL>10% at 24 months	95% CI	p-value
%TBWL at 3 months<10%	0.23	0.07-0.74	0.014
Age	0.96	0.91-1.02	0.154
Gender	2.09	0.61-7.18	0.24
Baseline BMI	1.06	0.97-1.16	0.202

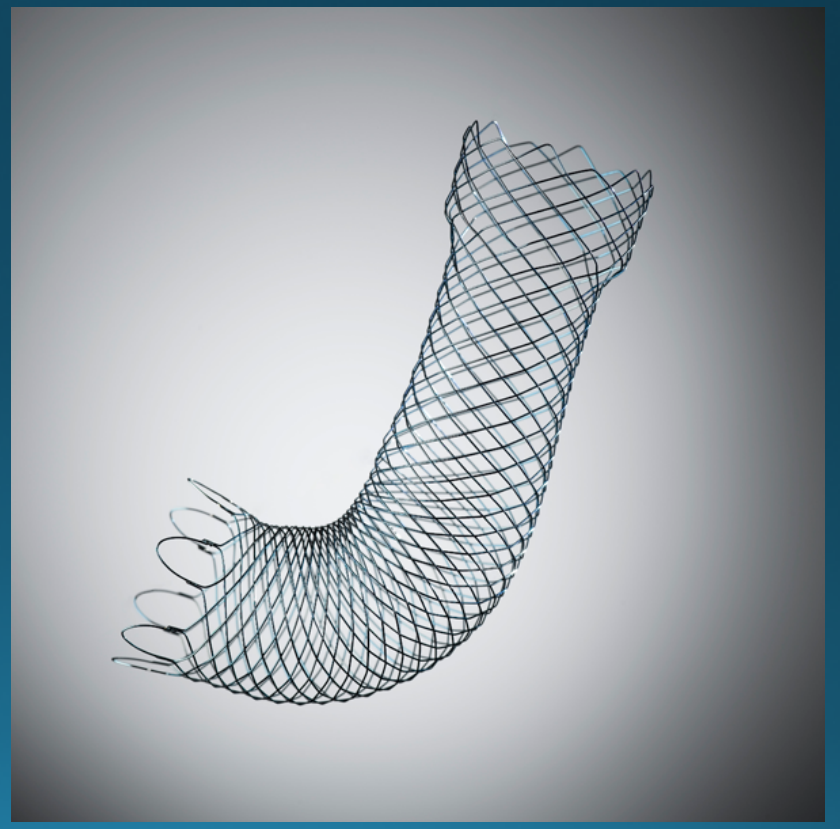
Adverse Events

- Serious adverse events <1%
  - 1 patient with perigastric inflammatory fluid collection that resolved with percutaneous drainage
  - 1 gastric perforation, managed with OTSC
- Minor side effects
  - Immediate post-procedural nausea and abdominal pain

Endoscopic Management of Gastric Outlet Obstruction (GOO)

- Malignant GOO
  - Surgery vs Enteral stenting





Enteral Stent vs Surgical GJ

- 2007 Systematic review
  - No difference in efficacy or complications
  - Stenting had shorter hospital stay, higher clinical success, faster relief of symptoms
  - Stenting required more frequent reintervention

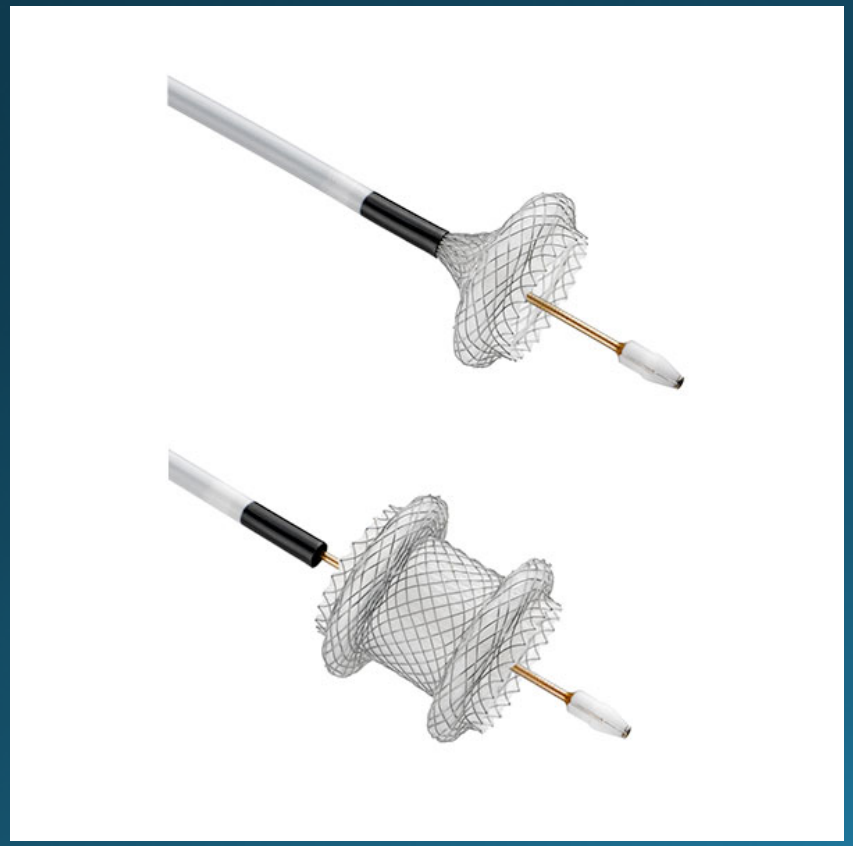
- 2009 RCT of 39 patients
  - Food intake improved more rapidly in stenting group
  - Long term relief worse in the stent group (50 vs 73 days)
  - Higher "complication rate" in stent group → stent occlusion requiring reintervention

Enteral Stenting for GOO

- 15-40% of enteral stent patients require reintervention
- Duodenal stent increases risk of biliary stent dysfunction (HR 2.0)
  - Mean biliary stent patency 64 days with duodenal stent vs 170 days w/o duodenal stent
- **Take home**: Enteral stenting faster at relieving obstruction with shorter hospitalization, but worse long term outcomes
- When life expectancy is
  - >6 months, surgical GJ is superior
  - <6 months, enteral stent is superior

EUS-Gastrojejunostomy

- Axios biflanged Lumen Apposing Metal Stent (LAMS)
  - EUS-guided stent deployment system with electrocautery enhanced tip



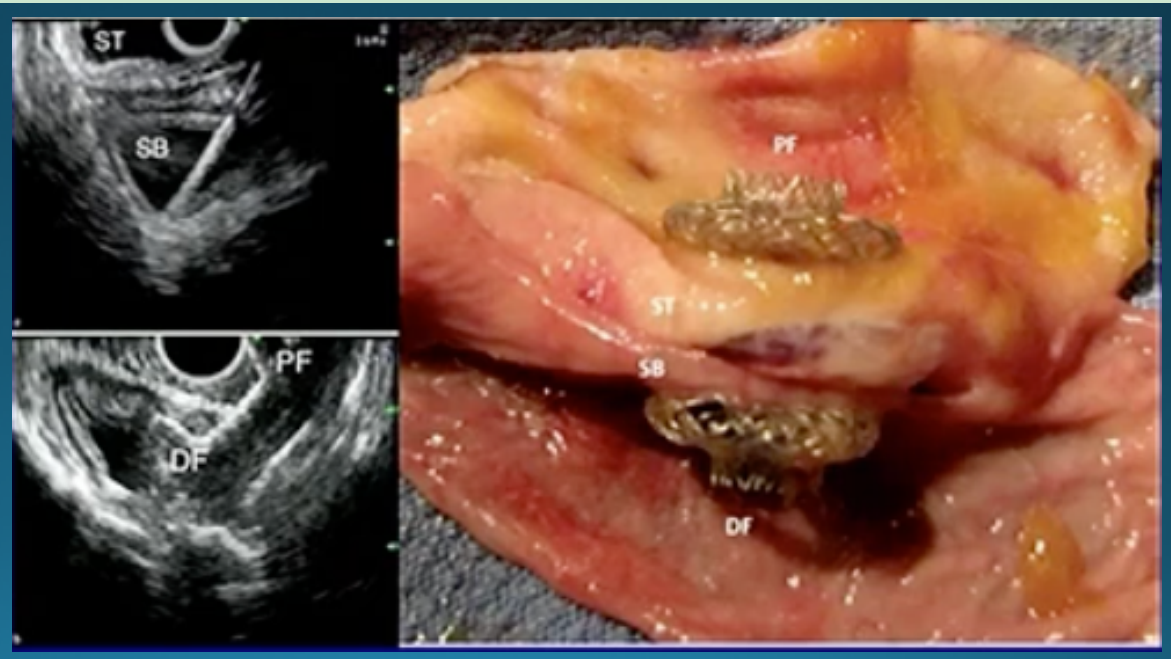
Endoscopic ultrasound-guided gastroenterostomy using novel tools designed for transluminal therapy: a porcine study

Endoscopy 2012

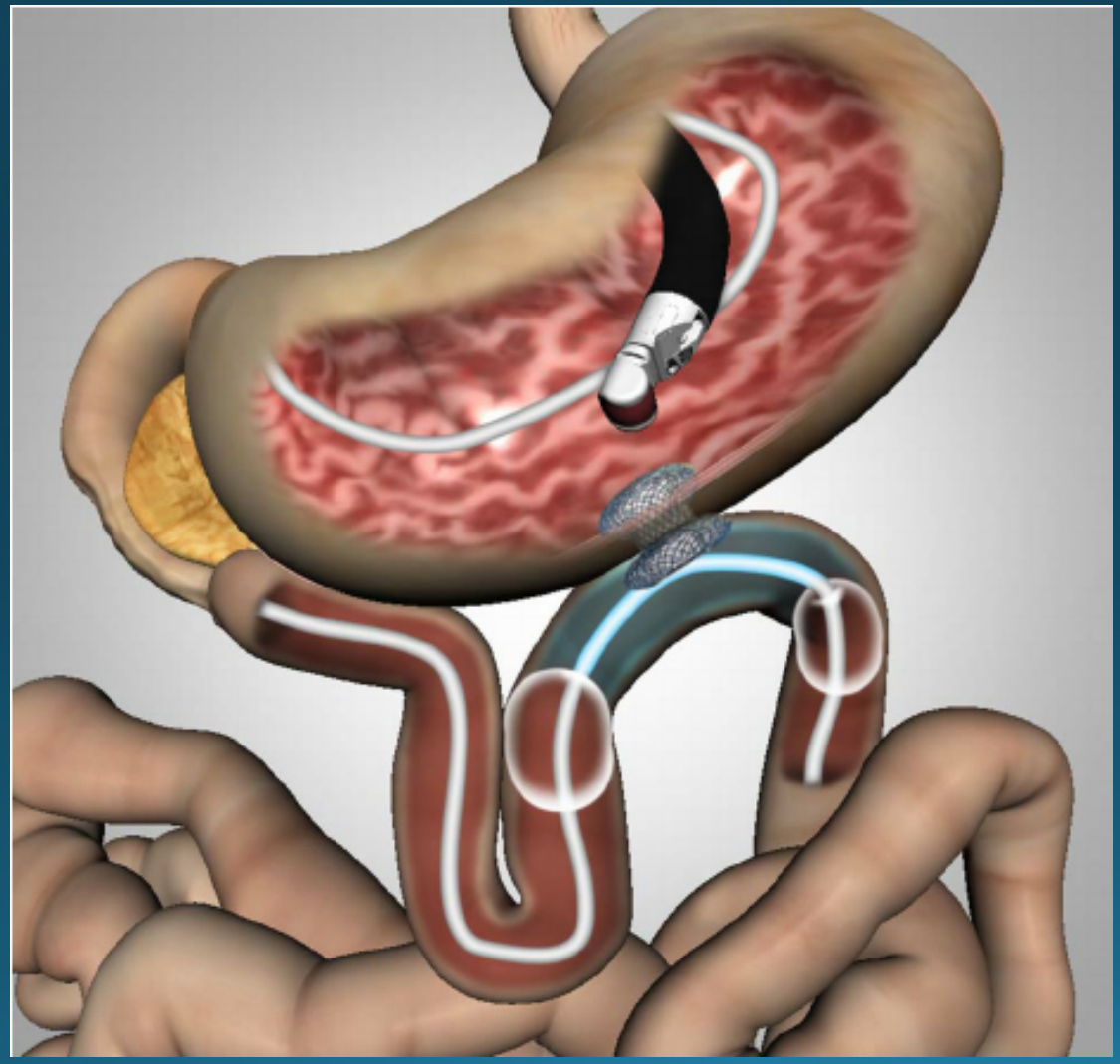
Authors K. F. Binmoeller, J. N. Shah

Institution Interventional Endoscopy Services, California Pacific Medical Center, San Francisco, California, USA

- Feasibility study in 5 pigs
- 100% technical success



EUS-Gastrojejunostomy



EUS-GJ Outcomes

- Data limited to case series (generally 10-30 patients)
  - 90% technical success, 90% clinical success
  - AEs: 10-15%; most managed endoscopically; 1 conversion to surgical GJ

Name of author	Number of patients	Clinical success %	Technical success %	Adverse event %
Khashab *et al.* (10)	10	90	90	0
Itoi (11)	20	90	90	2
Tyberg *et al.* (3)	26	85	92	11.5
Chen *et al.* (12)	30	83.3	86.7	10
Khashab *et al.* (1)	30	87	87	16

EUS-GJ Outcomes

- 2018 retrospective study of EUS-GJ (n=22) vs enteral stenting (n=78)
  - 100% technical success in both groups
  - Similar hospital stays
  - Higher stent failure requiring reintervention in ES group (32% vs 8%)
  - Higher adverse events in ES group (40% vs 21%)

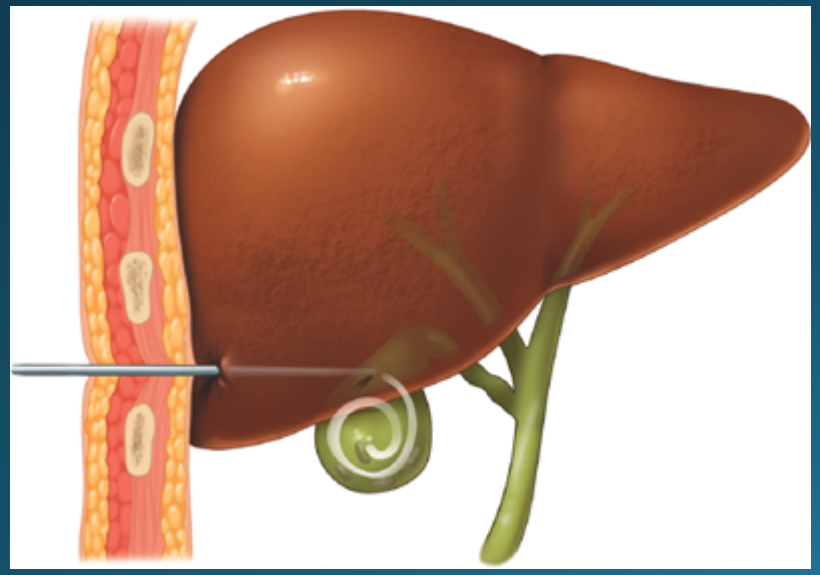
EUS-GJ

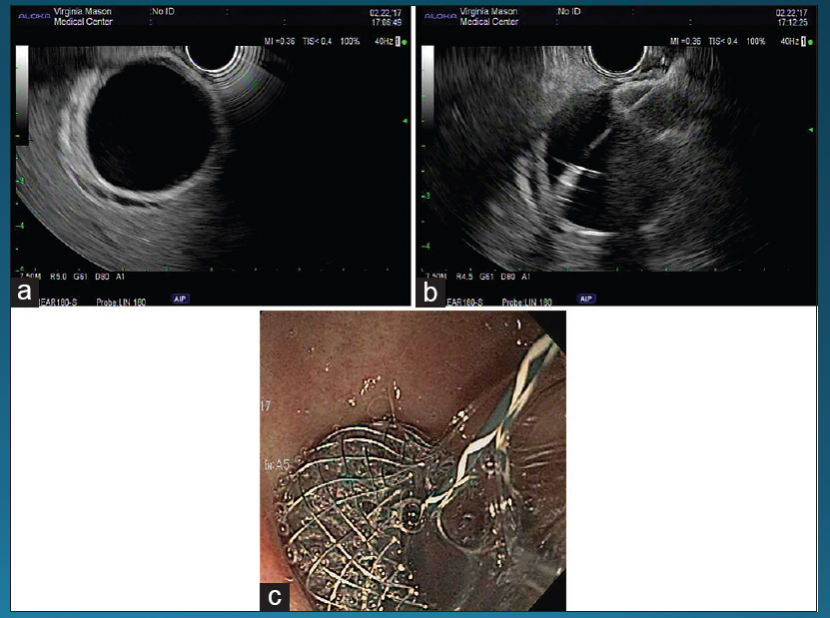
- Malignant biliary obstruction plus malignant enteral obstruction
  - Surgical double bypass (hepaticojejunostomy and gastrojejunostomy)
  - PTBD plus enteral stent
  - ”EAC” EUS-guided anterograde cholangiography w/ antegrade biliary stent plus enteral stent
  - EUS-guided choledochoduodenostomy plus enteral stent

  - EUS-guided choledochoduodenostomy plus EUS-GJ

Management of Acute Cholecystitis

- Typically managed surgically
- High risk patients have been managed with percutaneous cholecystotomy tube
- Retrospective studies have suggested EUS-guided gallbladder drainage (EUS-GBD) may be superior to percutaneous GB drainage (PT-GBD)





EUS-GBD vs PT-GBD

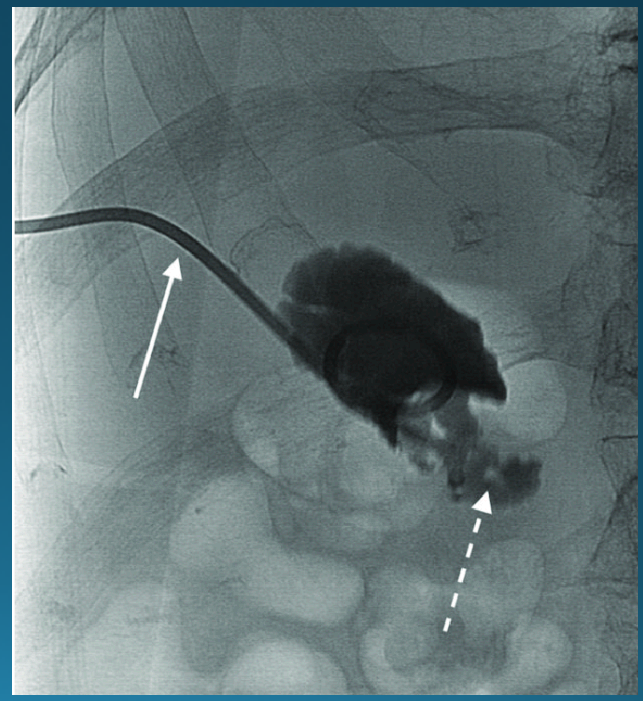
- Prospective multicenter RCT, 5 high volume centers
- Inclusion
  - >18 yo with acute cholecystitis
  - Deemed high risk for cholecystectomy or refused surgery
- Exclusion
  - Suspected gangrene or perforated GB
  - Previous GB drainage
  - Liver abscess
  - Altered anatomy of upper GI tract
  - Decompensated cirrhosis, portal HTN, varices
  - Coagulopathy
  - Pregnancy

Methods

- EUS-GBD
  - EUS puncture from stomach or duodenum (duodenum preferred)
  - Could use conventional method (19G needle -> guidewire -> LAMS or direct method with cautery enhanced system
  - 10 x 10 mm stent if stones <10 mm, otherwise 15 x 10 mm
  - GB stones removed when able
- PT-GBD
  - Experienced interventional radiologist
  - 8.5F pigtail drainage catheter, transhepatic preferred

Follow Up

- EUS-GBD
  - 1 month F/U cholecystoscopy
    - If stones cleared -> remove LAMS -> place 7F double pigtail stent
- PT-GBD
  - 1 month F/U cholecytogram
    - If patent cystic duct -> drain removed
    - If obstructed cystic duct -> long term PT-GBD

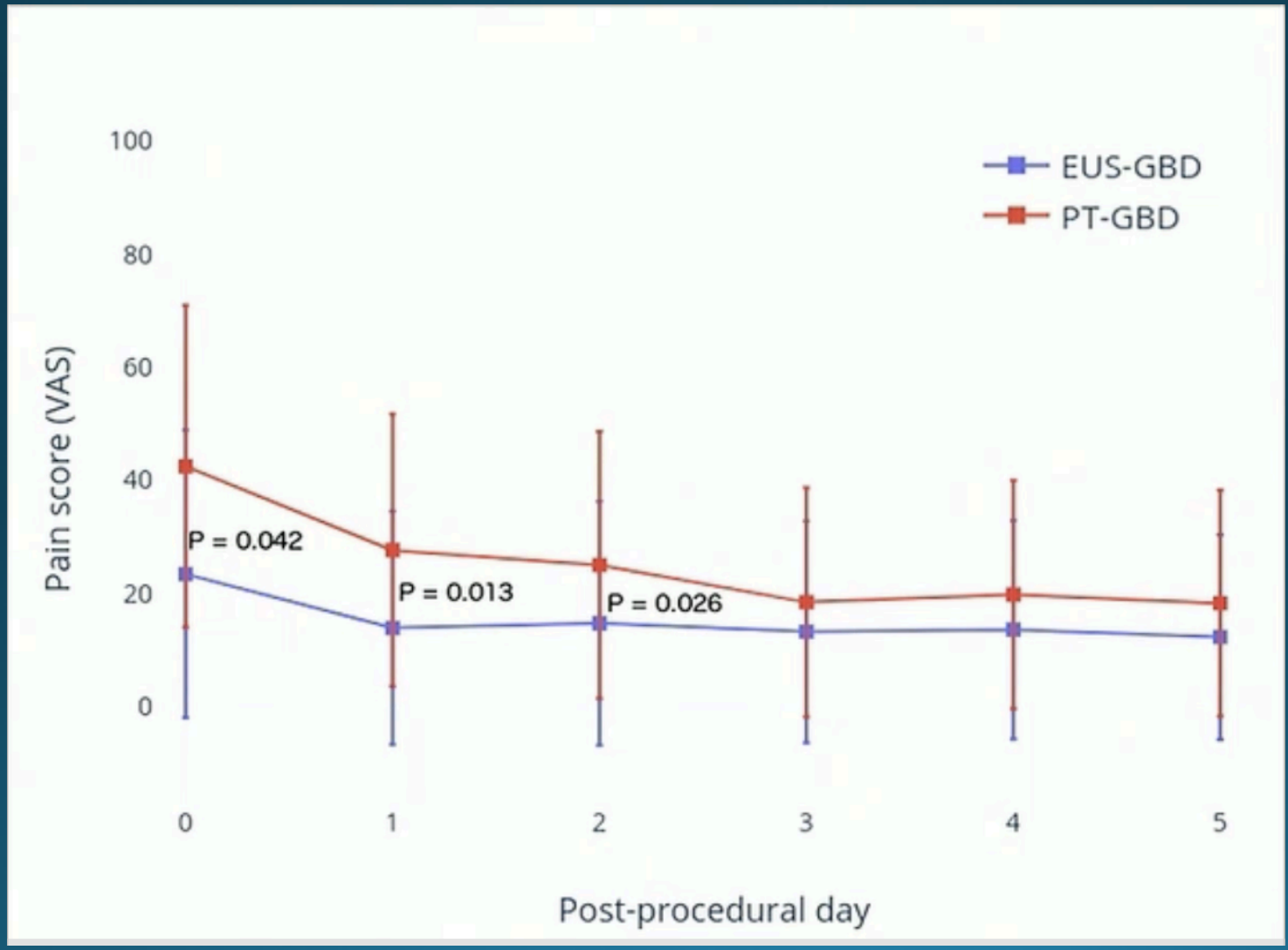


Clinical Outcomes

	EUS-GBD N = 39	PT-GBD N = 40	P-value
1-year adverse events (%)	10 (25.6)	31 (77.5)	< 0.001
Grading 1/2/3/4/5	1/1/6/0/2	13/6/8/0/4	
Recurrent acute cholecystitis (%)	1 (2.6)	8 (20)	0.029
Reinterventions after 30-days (%)	1 (2.6)	12 (30)	0.001
Reinsertion of PT-GBD	0	12	
Clearing blocked stent	1	0	
Unplanned admissions (%)	6 (15.4)	20 (50)	0.002
30-day adverse events (%)	5 (12.8)	19 (47.5)	0.001
Grading 1/2/3/4/5	0/1/2/0/2	6/4/5/0/4	
30-day mortality (%)	3 (7.7)	4 (10)	1
Technical success (%)	38 (97.4)	40 (100)	0.494
Clinical success (%)	36 (92.3)	37 (92.5)	1
Procedure time (minutes)	22.7 (13.0)	27.4 (12.0)	0.108
Hospital stay (days) *	8 (4 – 13)	9 (7 – 14)	0.181

	EUS-GBD N = 39	PT-GBD N = 40	P-value
30-day adverse events (%)	5 (12.8)	19 (47.5)	0.010
Tube dislodgement	0	15	
Blocked stent	2	0	
Perforation	1	0	
Multi-organ failure	0	1	
Pericholecystic collection	0	1	
Acute myocardial infarction	0	1	
Atrial fibrillation	1	1	
Pneumonia	3	1	
Acute renal failure	0	2	
Bleeding	0	1	
Decompensated liver cirrhosis	0	1	
Urinary tract infection	0	1	
1-year adverse events (%)	10 (25.6)	31 (77.5)	< 0.001
30-day adverse events	5	16	
Recurrent acute cholecystitis	1	8	
Tube dislodgement	0	18	
Blocked stent / tube	1	2	
Common bile duct stones requiring ERCP	3	1	

Post Procedural Pain Score



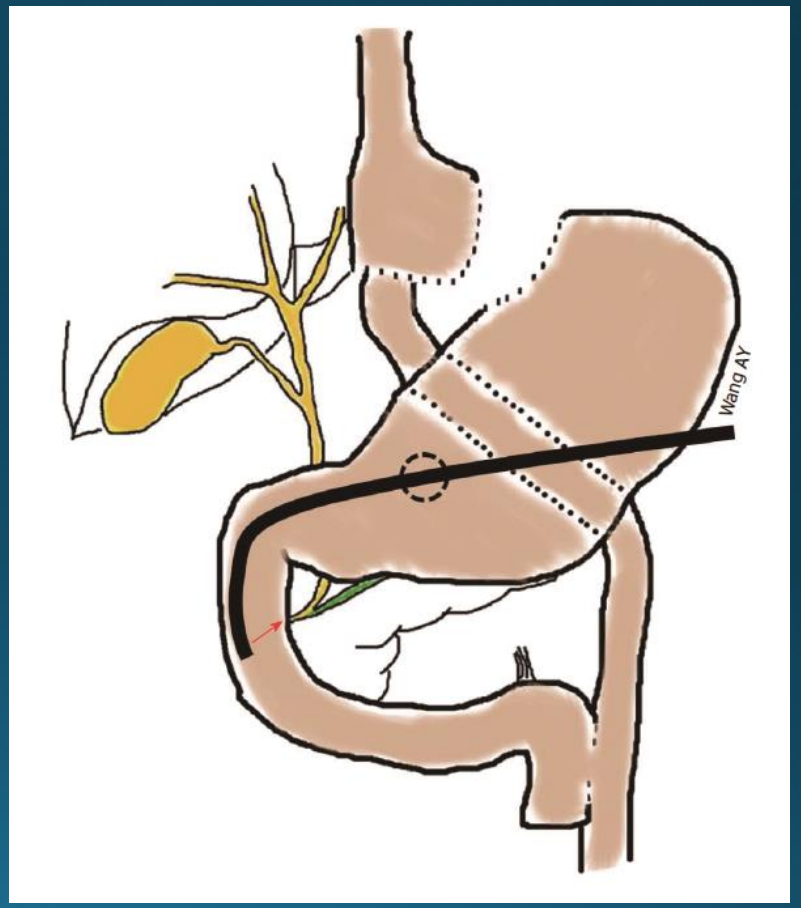
Conclusions

- EUS-GBD reduced 30-day and 1-year adverse events, post-procedure pain, recurrent acute cholecystitis, re-interventions and unplanned admissions

- EUS-GBD should be the procedure of choice in high risk surgical patients, provided expertise is available

Altered Anatomy ERCP

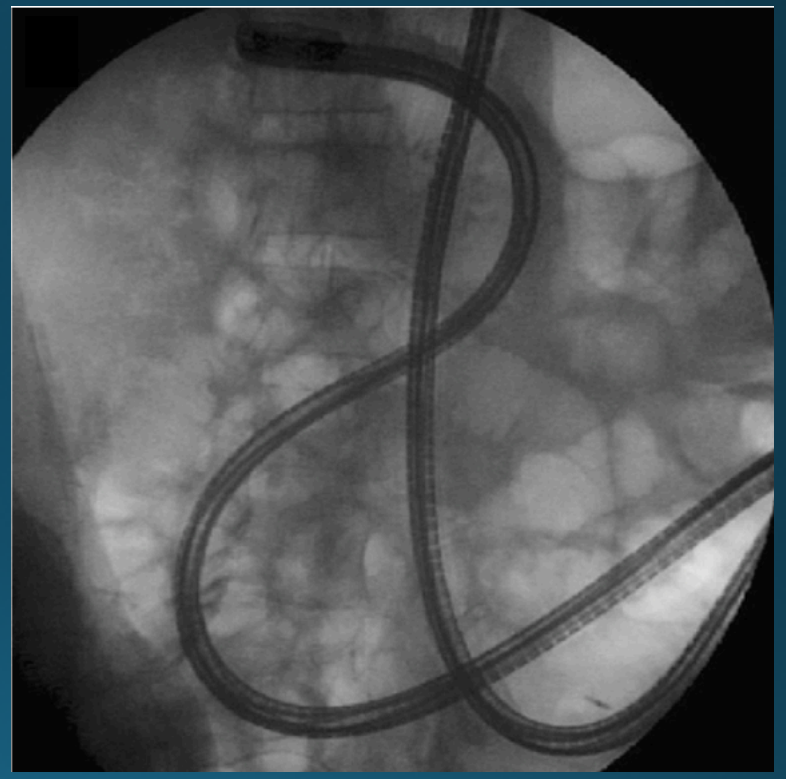
- Laparoscopic-Assisted ERCP
  - Timing issues
  - Sterility
  - Surgical complications/difficulties
    - Adhesions, co-morbidities
    - Requires large trocar (>15 mm)
    - 10% risk of lap-associated Aes
  - Difficult positioning



Abbas et al. GIE 2018
Wang et al World J Surg Proc 2014

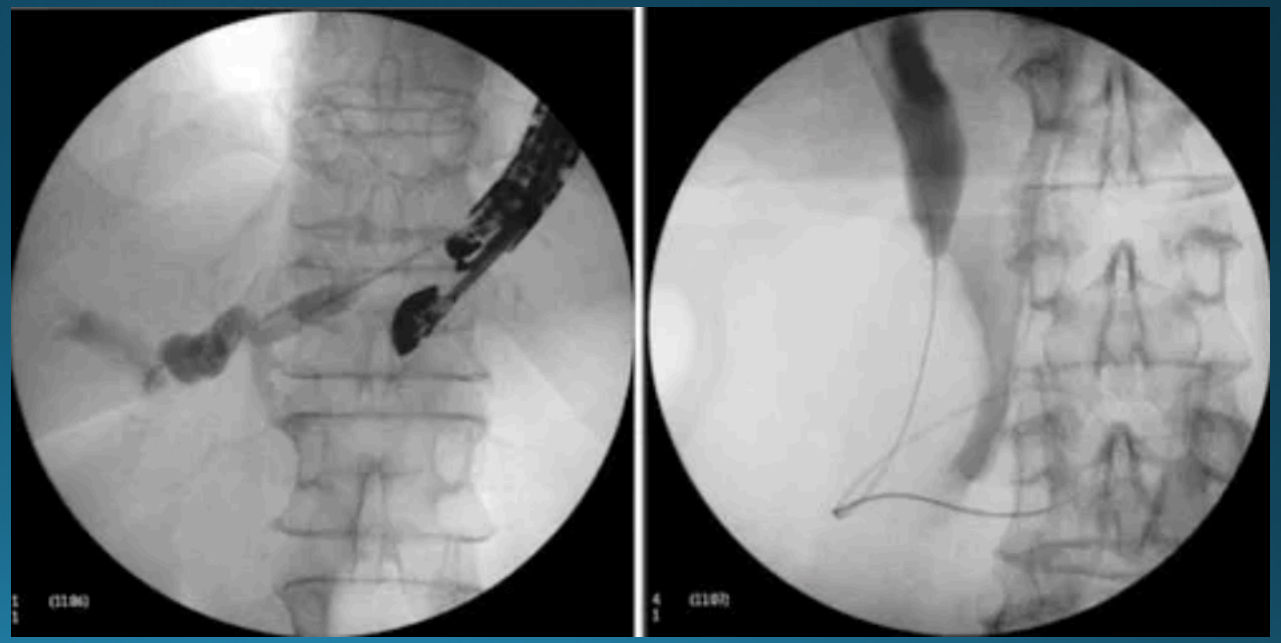
Altered Anatomy ERCP

- Deep enteroscopy
  - Time
  - Access (80-93% success accessing papilla)
  - Limited accessories
    - Cannulation rates 68-95%
- PEG tube
  - Requires deep enteroscopy into excluded stomach to place PEG
  - Tract matures in 4 weeks
  - Dilate mature tract (>12 mm)
  - ERCP through PEG tract



EUS to the Rescue!

- "EAC": EUS-guided anterograde cholangiography / EUS-guided ERCP
- Technique:
  - 19G transgastric-transhepatic puncture of left intrahepatic duct
  - Cholangiogram
  - Anterograde guidewire passage
  - Dilation of needle tract
  - Anterograde intervention
    - Balloon sphincteroplasty
    - Anterograde stone extraction
    - Anterograde stent placement
  - Long limb rendezvous if necessary



Anterograde EUS Outcomes

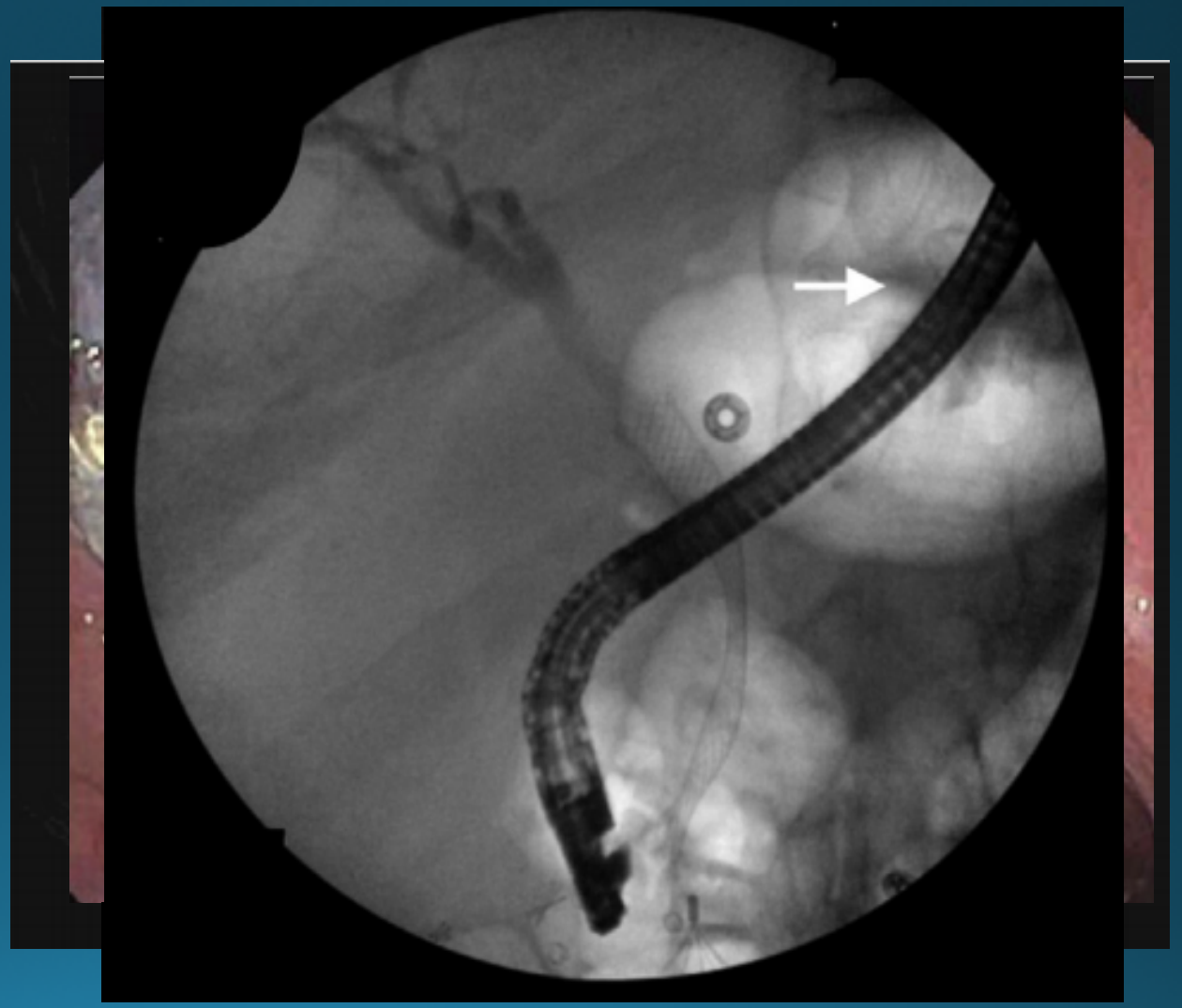
	Patients (n=37)
Technical Success (Hepatico-gastric/enteric fistula)	91.9%
Adverse Events (bile peritonitis)	8.1%
Clinical Success	91.9%
Procedure Time (range) One Stage Two Stage	 27.4 (22-35) 47.8 (14-84)

- Expert hands only

Mukai et al GIE 2019

EUS-Directed transGastric ERCP (EDGE)

- EUS-guided 19G needle puncture of excluded stomach
  - Transgastric or transjejujunal
- Water +/- contrast injected
- 15 mm or 20 mm LAMS placed
  - Secured in place?
- ERCP performed immediately or in 2-3 weeks
- LAMS removed
  - Fistula closure?



Laparoscopic vs Enteroscopy

- Systematic review of 22 case series
  - Cannulation rates
    - LA-ERCP: 96%
    - SBE-ERCP: 62%
    - DNE-ERCP: 82%
  - Complications:
    - LA-ERCP: 18%
    - SBE-ERCP: 10%
    - DBE-ERCP: 2%

Comparison between Enteroscopy-Based and Laparoscopy-Assisted ERCP for Accessing the Biliary Tree in Patients with Roux-en-Y Gastric Bypass: Systematic Review and Meta-analysis

Alberto Machado da Ponte-Neto[1,2] · Wanderley M. Bernardo[3] · Lara M. de A. Coutinho[1] · Iatagan Rocha Josino[1] Vitor Ottoboni Brunaldi[1] · Diogo T. H. Moura[1] · Paulo Sakai[1] · Rogério Kuga[1] · Eduardo G. H. de Moura[1]

LA-ERCP has higher success rate, but higher adverse events

Machado da Ponte-Neto et al. Obesity Surgery 2018

EUS-directed Transgastric ERCP (EDGE) Versus Laparoscopy-assisted ERCP (LA-ERCP) for Roux-en-Y Gastric Bypass (RYGB) Anatomy

A Multicenter Early Comparative Experience of Clinical Outcomes

	EGDE (n=29)	LA-ERCP (n=43)
Technical Success	96.5%	100%
ERCP success	96.5%	97.7%
Adverse Events	24%	19%
Procedure time, min	73	184
Length of stay, days	0.8	2.7

Kedia et al. J Clin Gastro 2019

An international, multicenter, comparative trial of EUS-guided gastrogastrostomy-assisted ERCP versus enteroscopy-assisted ERCP in patients with Roux-en-Y gastric bypass anatomy

Majidah Bukhari, MD,[1,6] Thomas Kowalski, MD,[2] Jose Nieto, MD,[3] Rastislav Kunda, MD,[4] Nitin K. Ahuja, MD,[1] Shayan Irani, MD,[5] Apeksha Shah,[2] David Loren, MD,[2] Olaya Brewer, MD,[1] Omid Sanaei, MD,[1] Yen-I Chen, MD,[1] Saowanee Ngamruengphong, MD,[1] Vivek Kumbhari, MD,[1] Vikesh Singh, MD,[1] Hanaa Dakour Aridi, MD,[1] Mouen A. Khashab, MD[1]

	EGDE (n=30)	e-ERCP (n=30)
ERCP Success	100%	60%
Procedure time, min	49.8	90.7
Adverse Events	6.7%	10%
Mean weight change, kg	-1.1	+0.07
Length of stay, days	1	10.5

Mukhari et al. GIE 2018

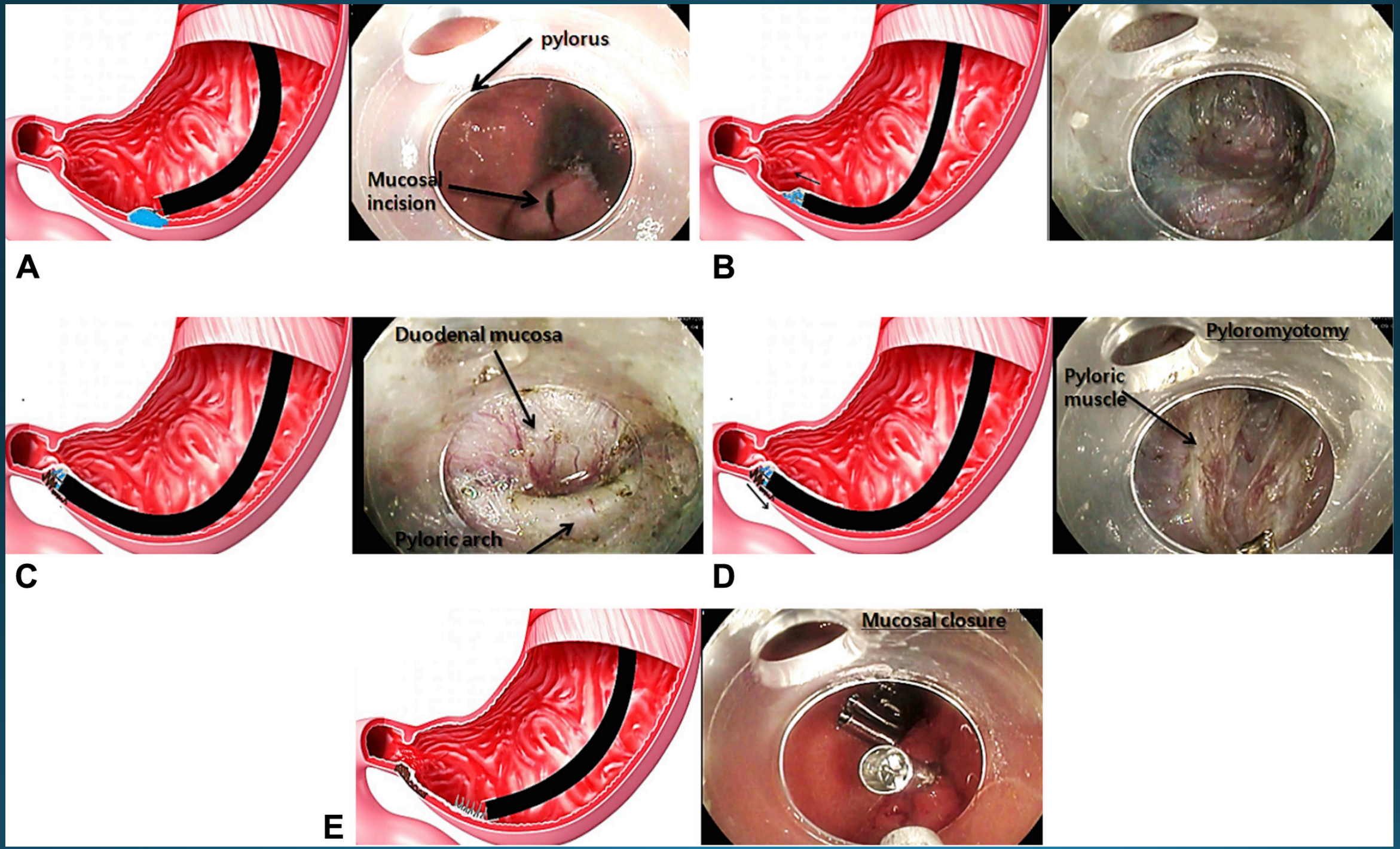
	Pros	Cons	Summary
Lap assisted	Widely available; requires little/no "extra" advanced endo skills	Difficulty with timing/coordination; High adverse events	Not first line May consider if pt also needs chole
PEG assisted	"Basic" endo skills	Time for tract to mature High AEs	Rarely used currently
Enteroscopy-assisted	Relatively low AEs; single session	Time consuming; access to DBE, low success rate	Can be used as first line when adv techniques not available
Antegrade EUS / EAC	Single session; allows for easy rendezvous if antegrade not successful	Requires advanced EUS skills; modest AE rates; stenting is problematic	Only for experienced hands in select indications
EDGE (LAMS-assisted)	Quicker, allows for use of duodenoscope; can allow for single session*	Requires advanced EUS skills; modest AE rates; may require 2nd ERCP	Becoming first line, especially if urgent ERCP not needed
Interventional Radiology	Less anesthesia; wide availability	Clinical success often low, modest AE rate	Reserved for rare select cases, or when interventional endoscopist not available

Third Space Endoscopy

Gastroparesis

- Difficult to treat
  - Large RCT in 2015: Only 28% clinical success at 48 weeks with standard treatment
- Gastric Per-Oral Endoscopic Myotomy (G-POEM)
  - Minimally invasive endoscopic treatment for refractory gastroparesis, introduced in 2013

Pasricha et al. Gastro 2015
Khashab et al. GIE 2013


pylorus
Mucosal incision
A
B
Duodenal mucosa
Pyloric arch
C
Pyloromyotomy
Pyloric muscle
D
E
Mucosal closure

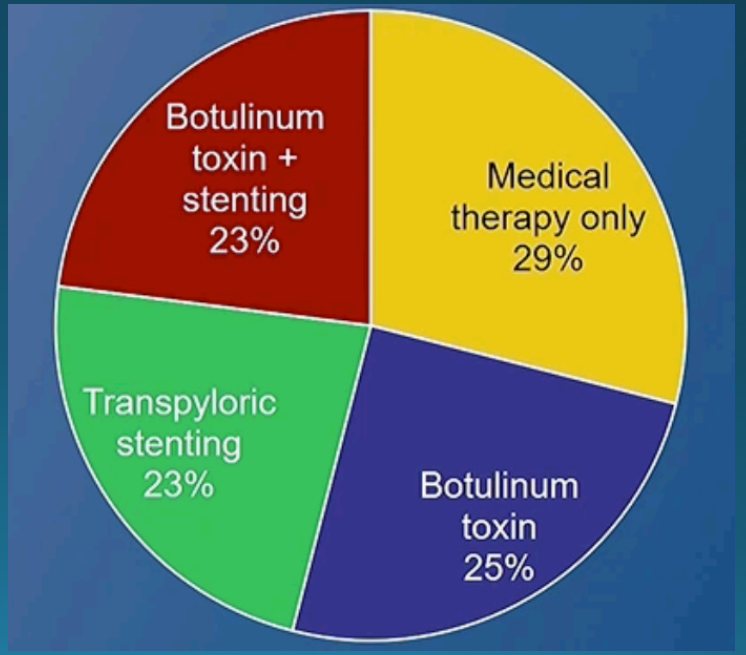
G-POEM: International Prospective Trial

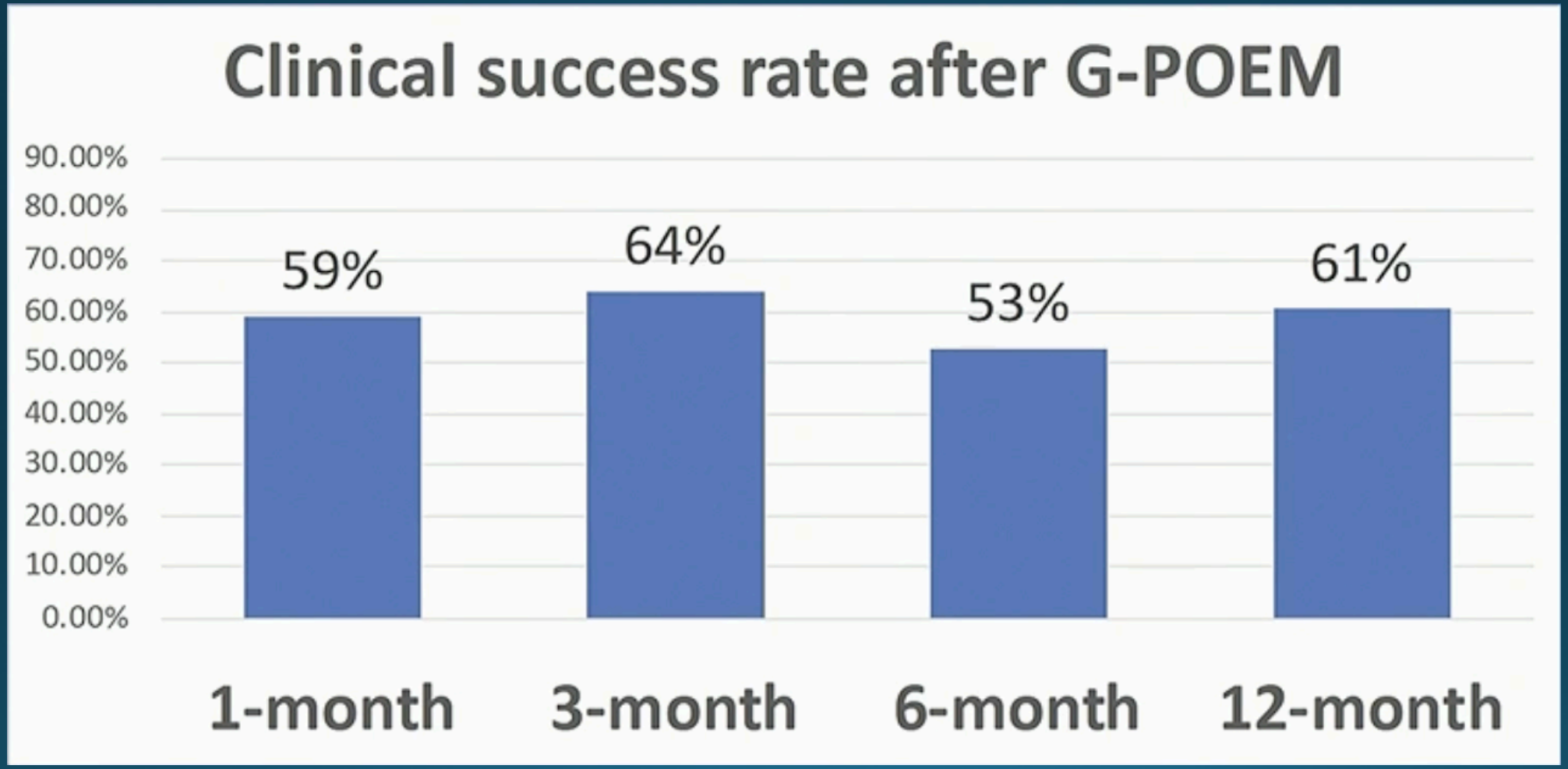
- 6 centers: Nov 2015 to May 2019
- Inclusion: Gastroparesis, refractory to standard medical therapy
- Exclusion: Prior gastric surgery
- Clinical success:
  - Decrease in Gastroparesis Cardinal Symptom Index
    - Postprandial fullness/early satiety
    - Nausea/vomiting
    - Bloating
  - Quality of life (SF-36)
  - Gastric emptying study

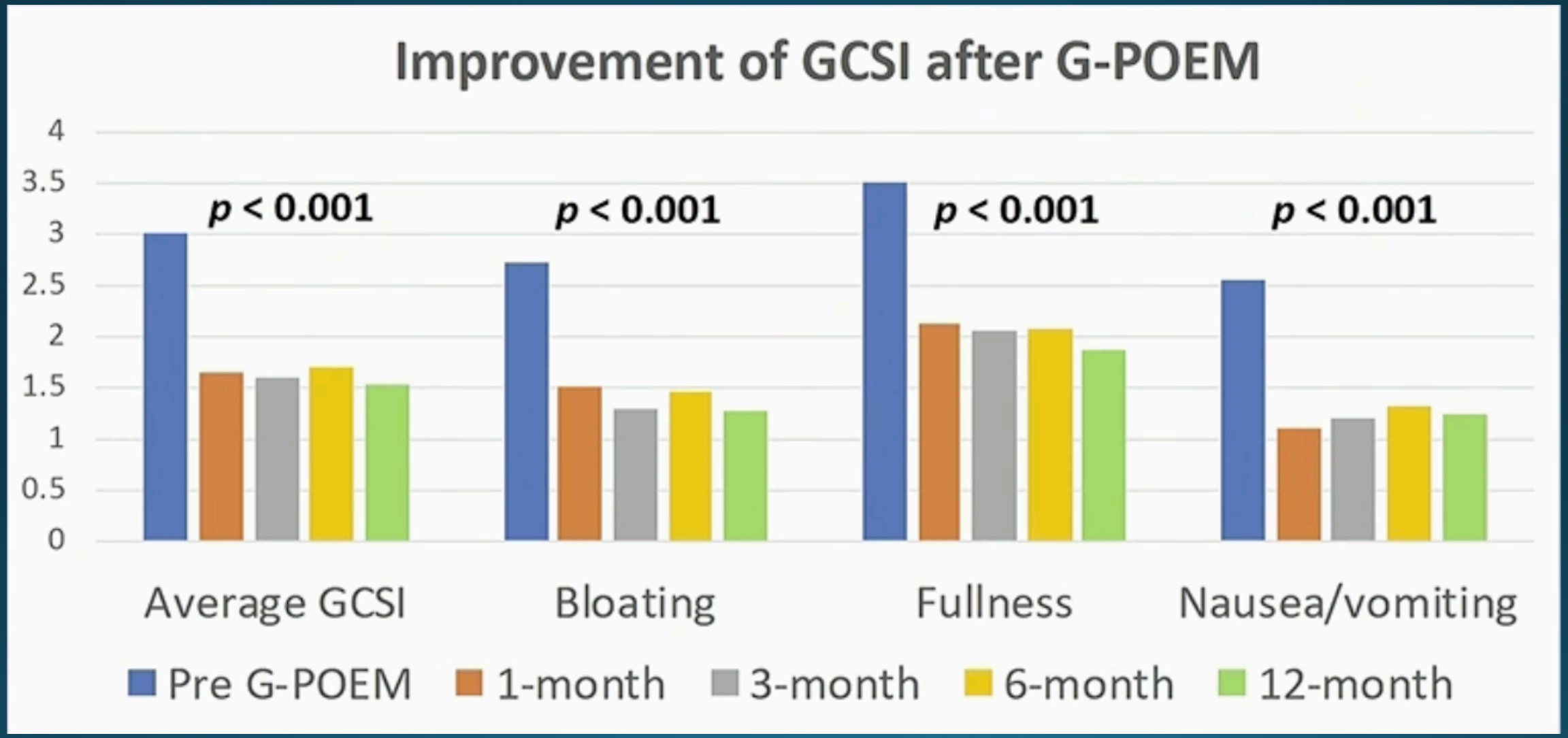
Vosoughi, Khashab et al DDW 2019

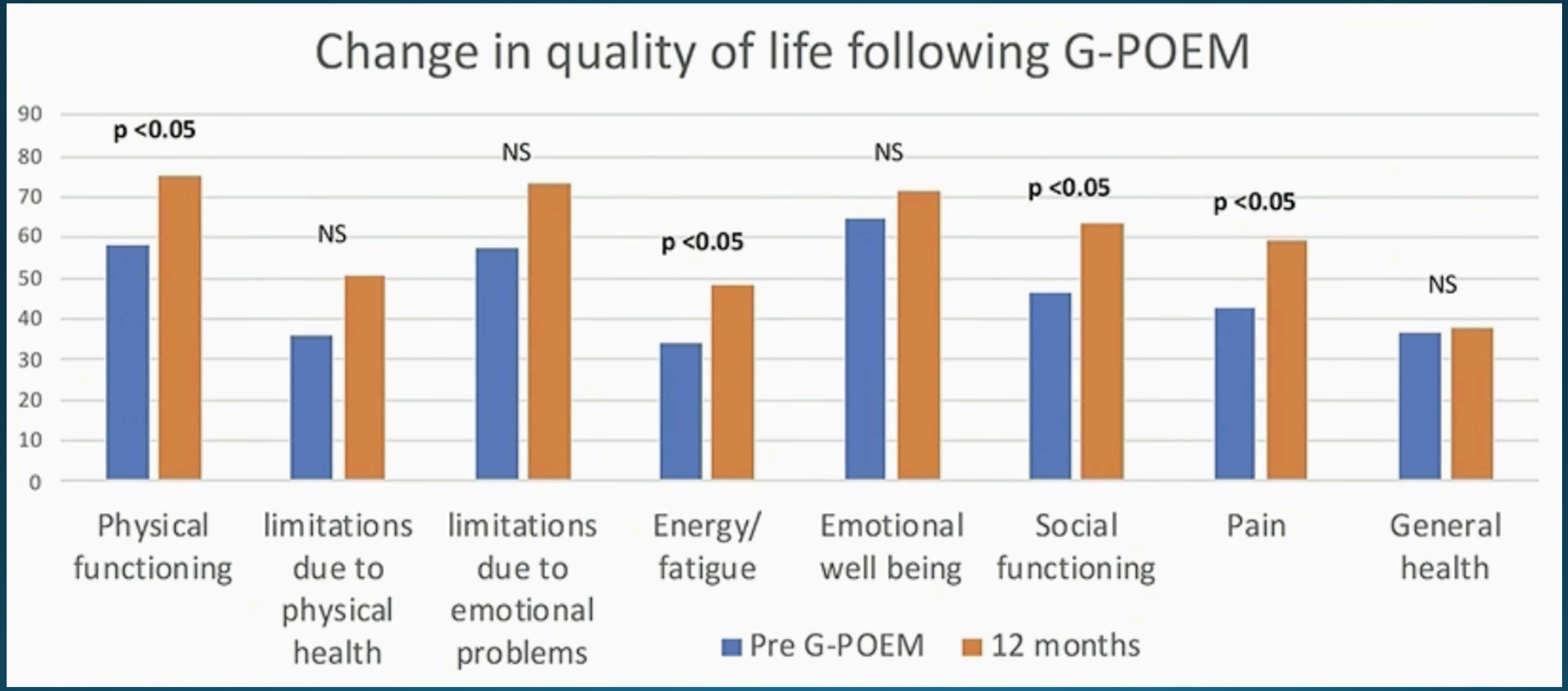
Results

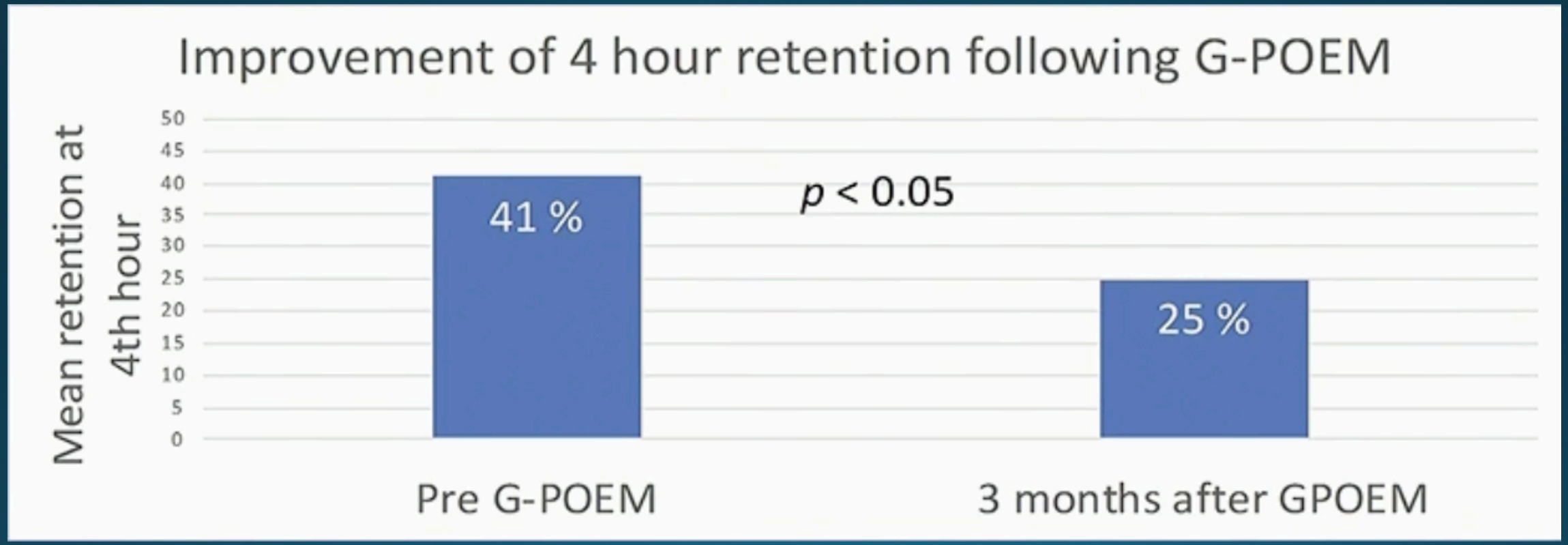
- 80 patients
  - 65% female
  - Mean age: 51
- Etiology: 24% DM, 36% post-surgical, 40% idiopathic
- Interventions prior to G-POEM:




Clinical success rate after G-POEM
90.00%
80.00%
70.00%
60.00%
50.00%
40.00%
30.00%
20.00%
10.00%
0.00%
59%
64%
53%
61%
1-month
3-month
6-month
12-month


Improvement of GCSI after G-POEM
4
3.5
3
2.5
2
1.5
1
0.5
0
p < 0.001
p < 0.001
p < 0.001
p < 0.001
Average GCSI
Bloating
Fullness
Nausea/vomiting
Pre G-POEM
1-month
3-month
6-month
12-month


Change in quality of life following G-POEM
90
80
70
60
50
40
30
20
10
0
p <0.05
NS
NS
p <0.05
NS
p <0.05
p <0.05
NS
Physical functioning
limitations due to physical health
limitations due to emotional problems
Energy/ fatigue
Emotional well being
Social functioning
Pain
General health
Pre G-POEM
12 months

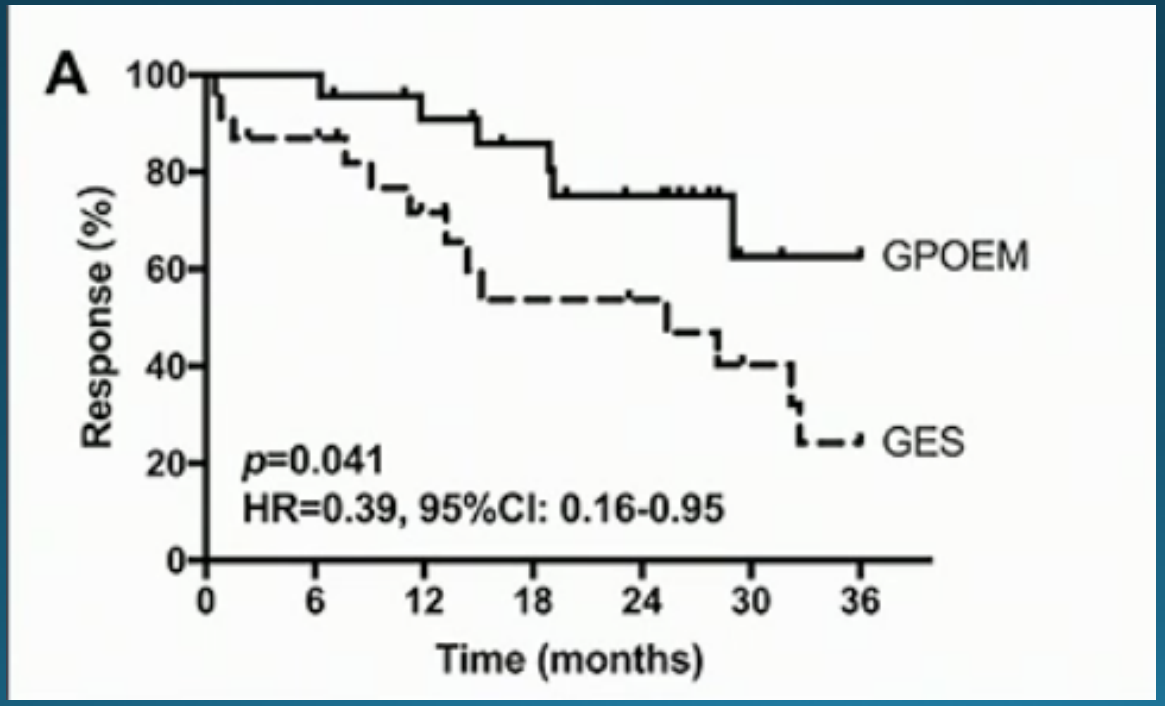

Improvement of 4 hour retention following G-POEM
Mean retention at 4th hour
50
45
40
35
30
25
20
15
10
5
0
41 %
p < 0.05
25 %
Pre G-POEM
3 months after GPOEM

Adverse event	Severity	Frequency (percent)	Treatment
Mucosotomy	Mild	2 (2.5%)	1 Stent placement 1 Endoscopic clipping
Symptomatic capnoperitoneum	Mild	3 (3.7%)	3 Drainage with syringe
Pneumonia	Moderate	1 (1.3%)	1 Antibiotic therapy

- Overall adverse events: 6/80 (7.5%)

G-POEM vs Gastric Electrical Stimulator

- Consecutive patients: G-POEM (n=23) or GES (n=23)
  - Matched by one-to-one propensity score
- Primary outcome: duration of clinical response



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Conclusions

- G-POEM has potential to become a frontline therapy for refractory gastroparesis
- Research needed to identify candidates likely to respond to G-POEM