

Malignant Biliary Obstruction: Can EUS Replace ERCP?

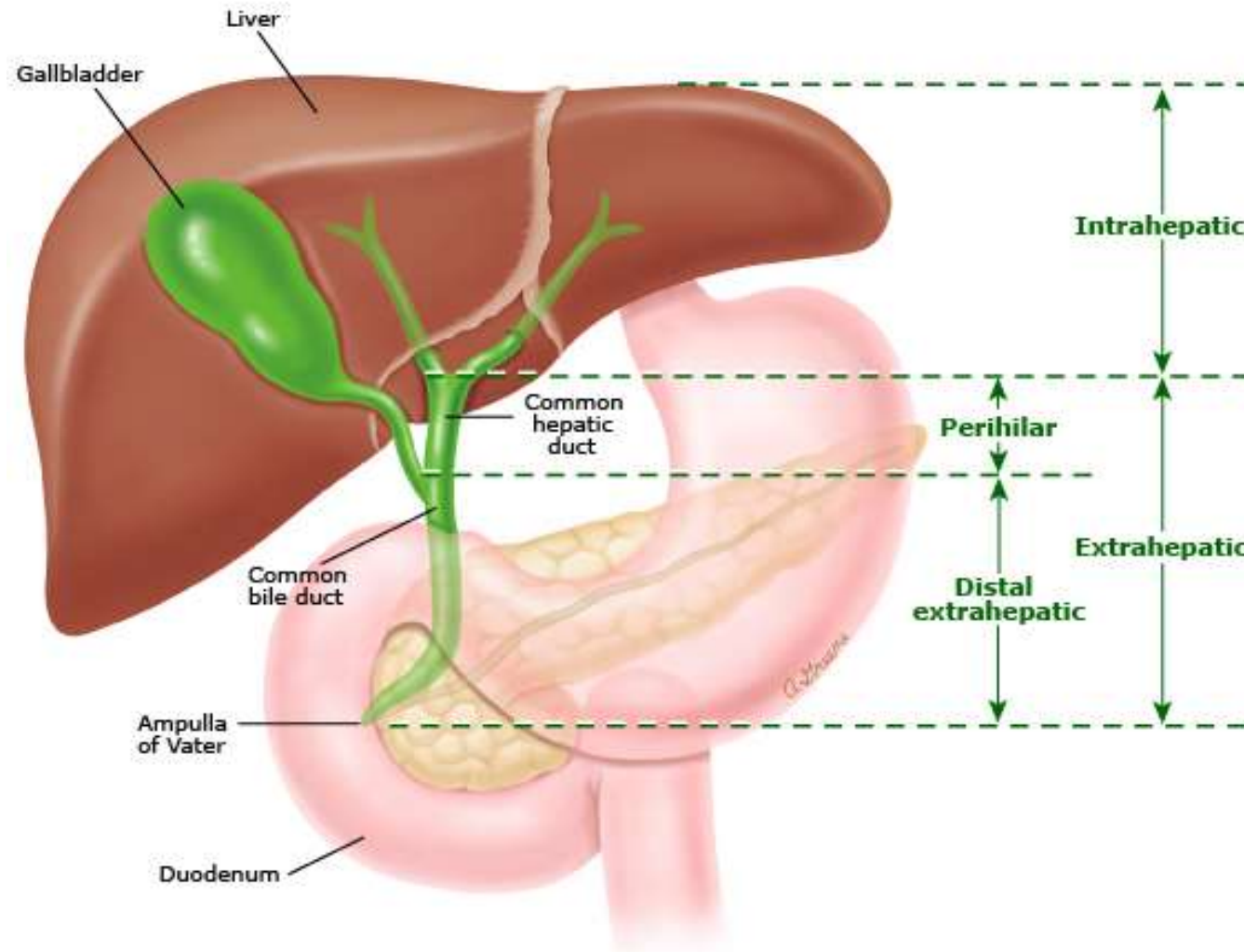
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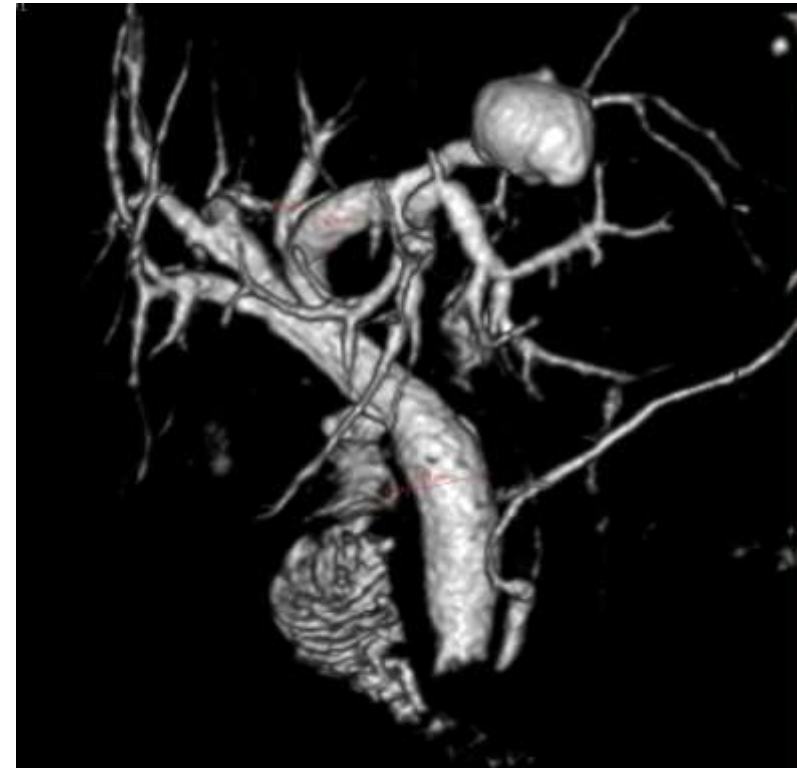
Hackensack Meridian
Hackensack University
Medical Center

Biliary Obstruction



Biliary Obstruction

Diagnosis	Patients, <i>n</i>	Percentage of total
Benign pathology		
Common bile duct stones	428	89.2
Chronic pancreatitis	22	4.6
Post-cholecystectomy stricture	17	3.5
Autoimmune pancreatitis	11	2.3
Primary sclerosing cholangitis	2	0.4
Malignant pathology		
Pancreatic ductal adenocarcinoma	200	36.6
Gallbladder cancer	146	26.7
Hilar cholangiocarcinoma	89	16.3
Metastatic disease with biliary obstruction	42	7.7
Distal cholangiocarcinoma	31	5.7
Ampullary adenocarcinoma	31	5.7
Duodenal adenocarcinoma	7	1.3



Garcia G, Wee N, et al.
HPB (Oxford) 2011 Jun;13(6):426-30

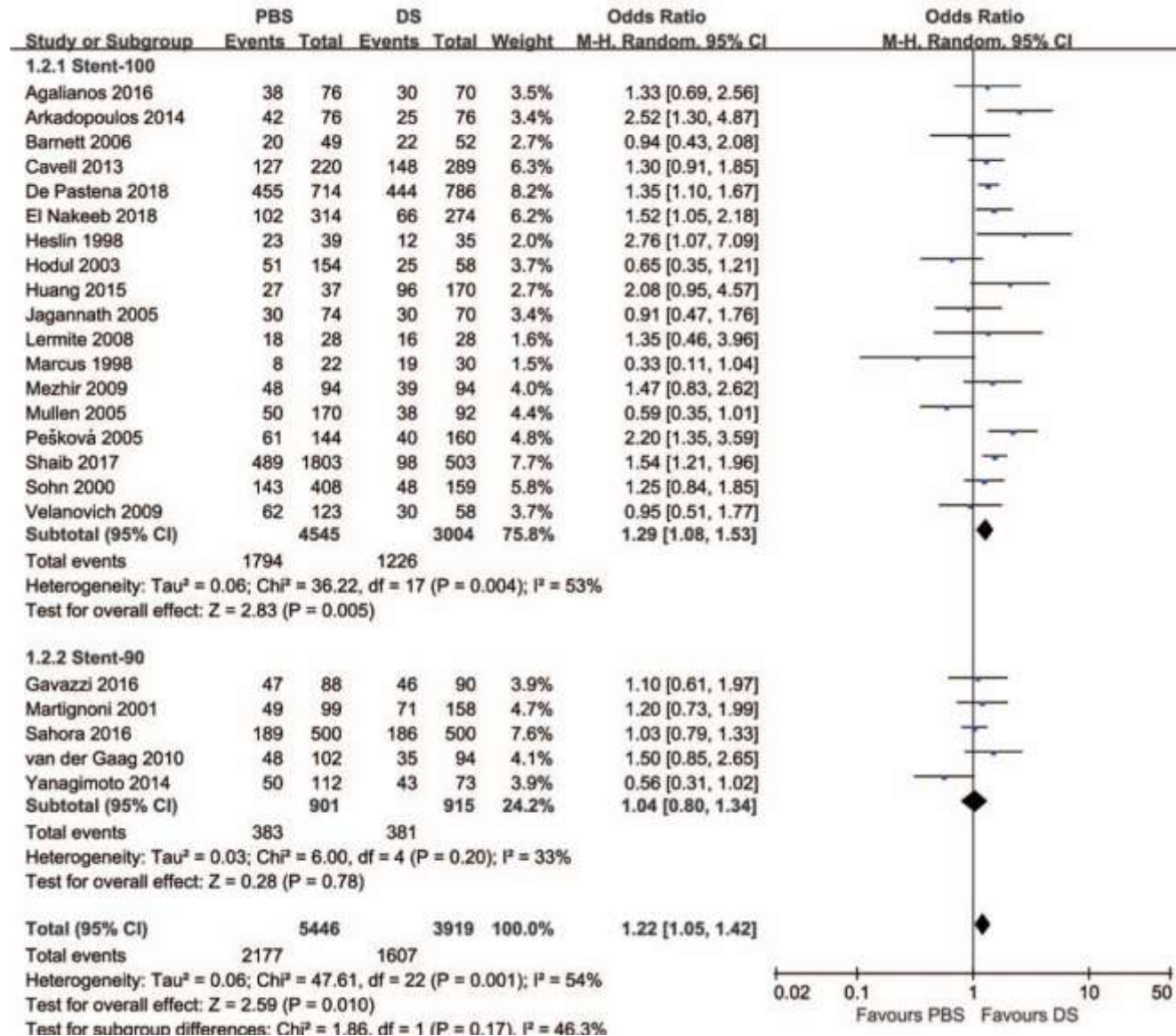
Malignant Biliary Obstruction

- 60-70% of pancreas cancers occur in the head of the pancreas
 - 70-80% of these present with malignant biliary obstruction
- It is important to fully evaluate these patients to rule out other common causes of liver dysfunction
 - Liver metastases
 - Other concomitant liver disease
 - Drug-induced

Malignant Biliary Obstruction

- **Many recent studies have demonstrated that if a patient has resectable pancreas cancer, then biliary obstruction should not be relieved pre-operatively**
- Exceptions include:
 - Cholangitis
 - Markedly elevated total bilirubin
 - Need for neoadjuvant chemotherapy
 - Delayed surgical scheduling

Resectable Malignant Biliary Obstruction



- The overall morbidity rate was significantly higher in the pre-op biliary stent (PBS) group than the direct surgery (DS) group (OR 1.22, 95% CI 1.05–1.42; *P* = .01)

Gong L et al.
 Medicine 99(42):p e22714, October 16, 2020

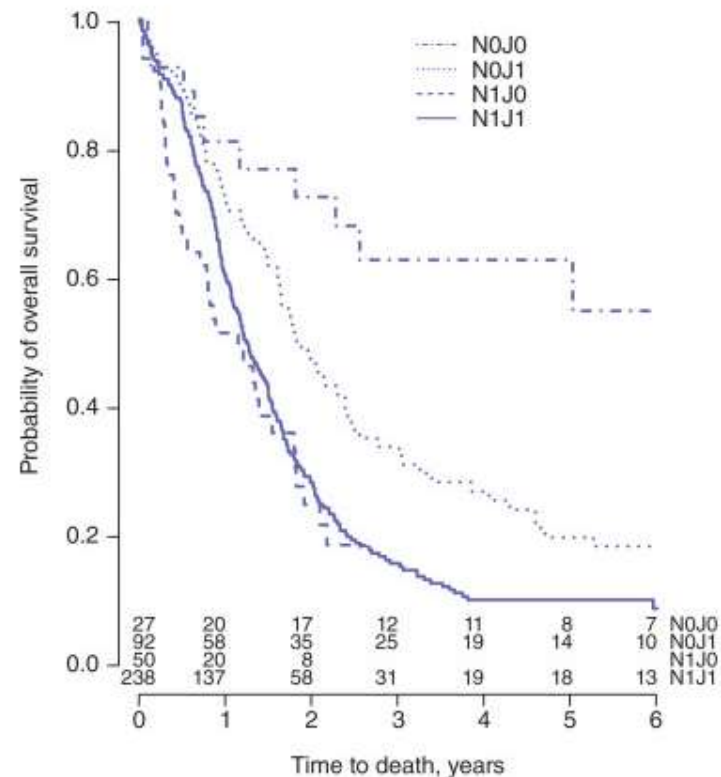
Why Is Jaundice So Bad Anyway?

- Complicates further management due to the risk of cholangitis
- Pruritis can be intolerable and compromise quality of life
- Contributes to overall malnutrition
- Significantly affects choice of chemotherapeutic agents
 - Pharmacokinetics of both nab-paclitaxel and gemcitabine are markedly altered
 - Toxicity of both increases
 - Both must have their dosages reduced
- Strongly associated with decreased survival

Why Is Jaundice So Bad Anyway?

- Multiple studies have shown that jaundice is a negative predictor of survival on univariate and multivariate analysis

Variables	HR (95% CI)	P-value ^a
Jaundice and node status		
Non-jaundiced, N0	1	
Non-jaundiced, N1	4.92 (2.01–12.05)	<0.001
Jaundiced, N0	3.01 (1.29–7.01)	0.011
Jaundiced, N1	4.02 (1.79–9.27)	0.001

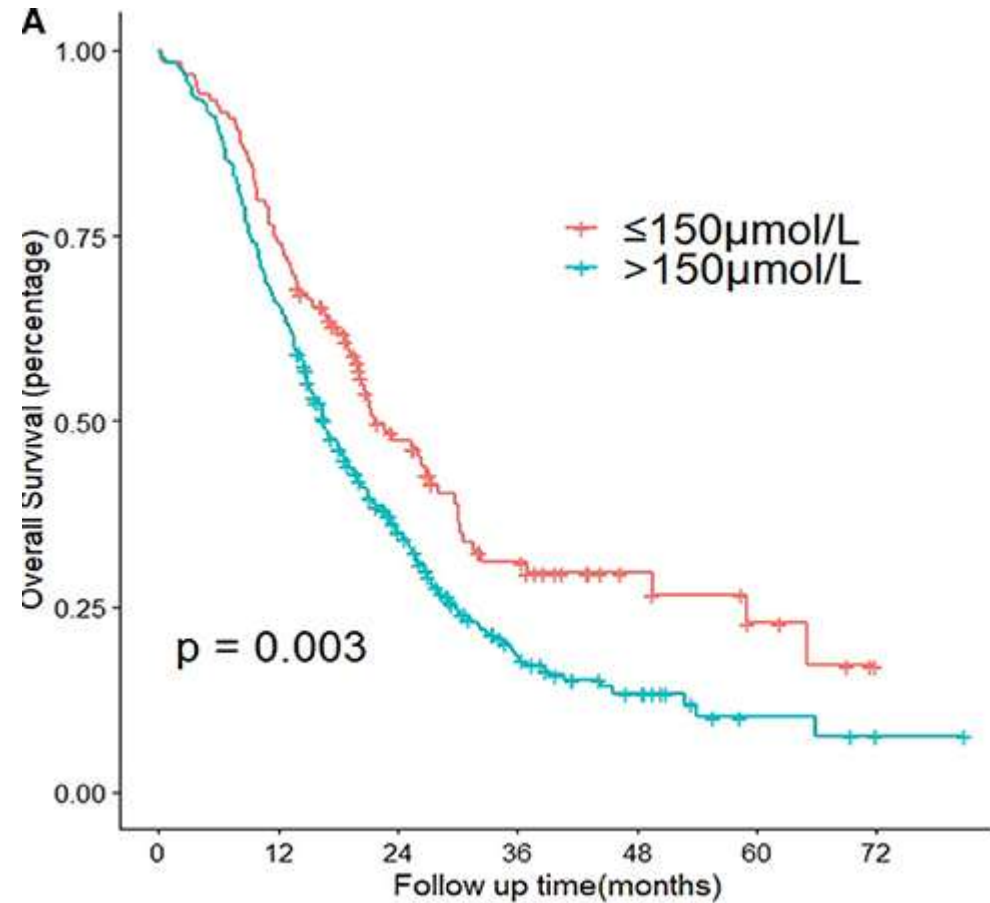


Strasberg S et al.
HPB 16 (2) Feb 2014

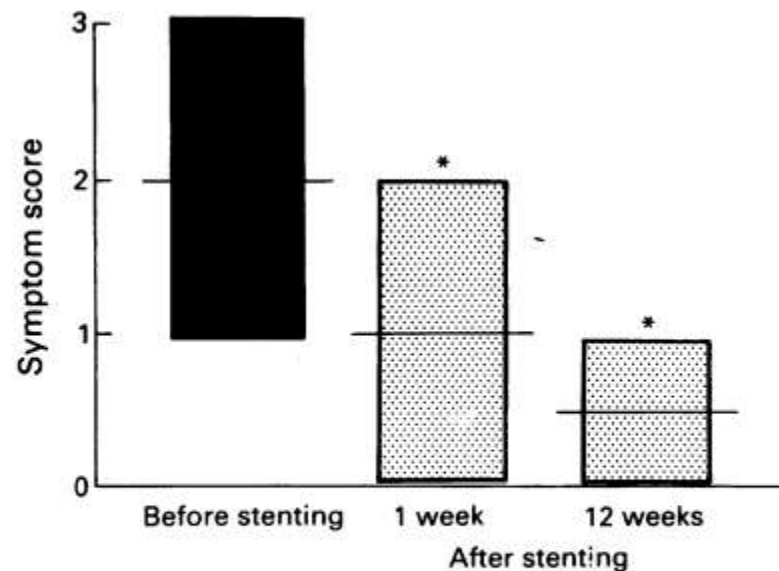
Why Is Jaundice So Bad Anyway?

- In fact, the higher the bilirubin, the worse the survival

Shen Z et al.
Front. Oncol., 16 September 2020



Relief Of Biliary Obstruction Has Been Shown To Dramatically Improve Quality Of Life



*Figure 1: Anorexia before stent insertion and at one and 12 weeks after stenting. Results are expressed as the median and interquartile range. * $p < 0.01$ compared with the score before stenting. There was no significant change between the one week and 12 week assessment.*

- Significant improvement in
 - indigestion
 - anorexia
 - nausea
 - pain
 - mood

Ballinger AB et al.
Gut 1994 Apr;35(4):467-70

Methods To Relieve Malignant Biliary Obstruction

- Percutaneous biliary drainage (PBD)
- ERCP
- EUS-guided ERCP
- EUS-only



Methods To Relieve Malignant Biliary Obstruction

- All are very effective
- Choice of one versus another currently may have much to do with the location of the obstruction and local clinical expertise
- EUS-guided approaches are likely to replace all others in the future

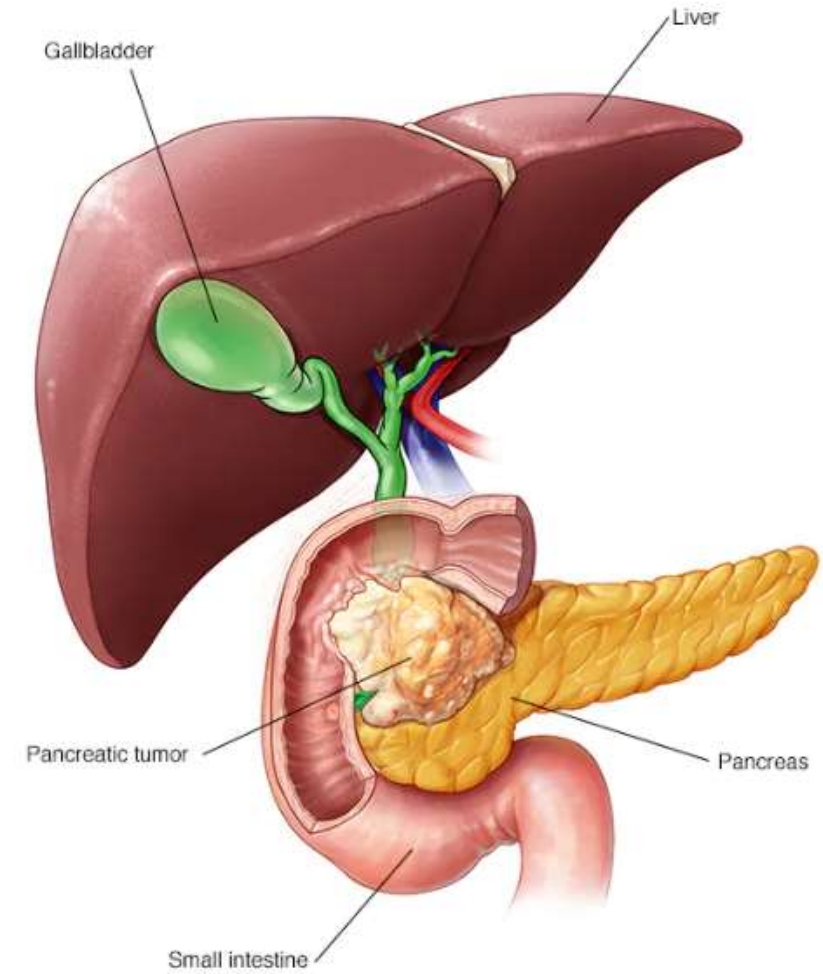
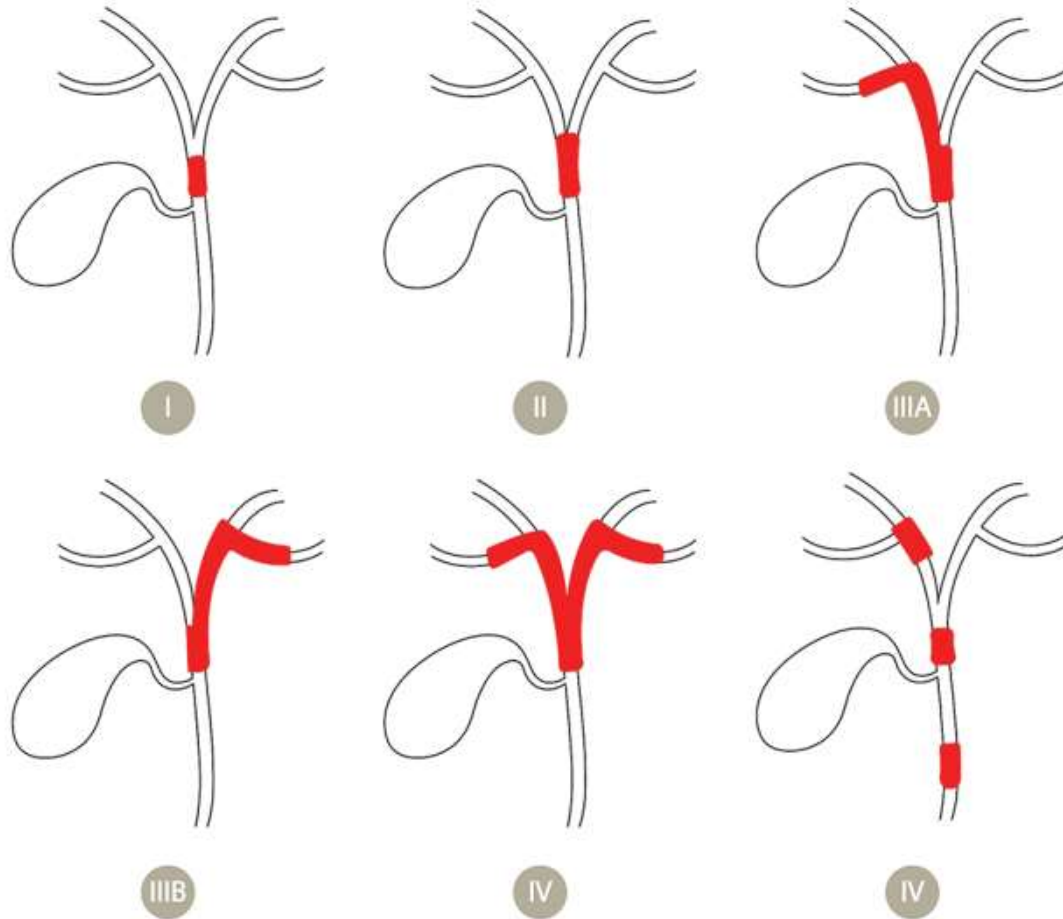
Effectiveness of biliary decompression

Parameters	Final drainage			Intention-to-treat		
	PTBD (n = 107)	ERBD/ENBD (n = 104)	<i>P</i> value	PTBD (n = 68)	ERBD/ENBD (n = 143)	<i>P</i> value
Initial bilirubin (mg/dL)	12.1 ± 6.7	10.3 ± 7.1	0.068	11.1 ± 6.2	11.2 ± 7.3	0.884
Final bilirubin (mg/dL)	4.4 ± 3.4	3.0 ± 3.0	0.002	4.0 ± 3.1	3.6 ± 3.4	0.370
Daily diminution of bilirubin ([mg/dL]/day)	0.7 ± 0.5	0.6 ± 0.4	0.049	0.7 ± 0.5	0.6 ± 0.4	0.041
Drainage duration (day)	14.2 ± 10.9	16.6 ± 11.5	0.121	13.2 ± 11.5	16.5 ± 11.0	0.049

PTBD, percutaneous transhepatic biliary drainage; ERBD, endoscopic retrograde biliary drainage;
ENBD, endoscopic naso-biliary drainage.

J Korean Med Sci. 2012 Apr;27(4):356-362.

Malignant Biliary Obstruction (MBO)



ERCP



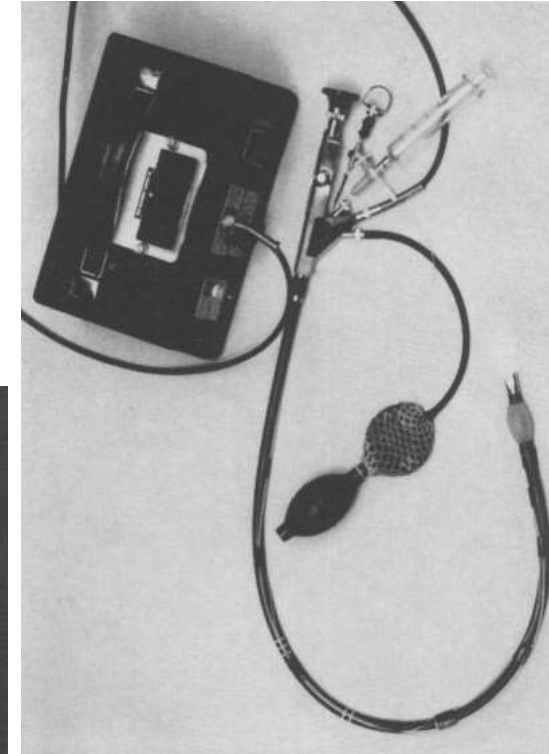
ERCP History

- First ERCP performed by William McCune and reported in 1968
- First ERCP series reported by Itaru Oi in 1970 and Peter Cotton in 1972

Endoscopic Cannulation of the Ampulla of Vater: A Preliminary Report

WILLIAM S. McCUNE, M.D., PAUL E. SHORB, M.D.,
HERBERT MOSCOVITZ, M.D.

*From the Department of Surgery, The George Washington University School
of Medicine, Washington, D. C.*



ERCP History

- First endoscopic sphincterotomy reported by Kawai and Classen independently in 1974
- First biliary stent placed by Soehendra in 1979

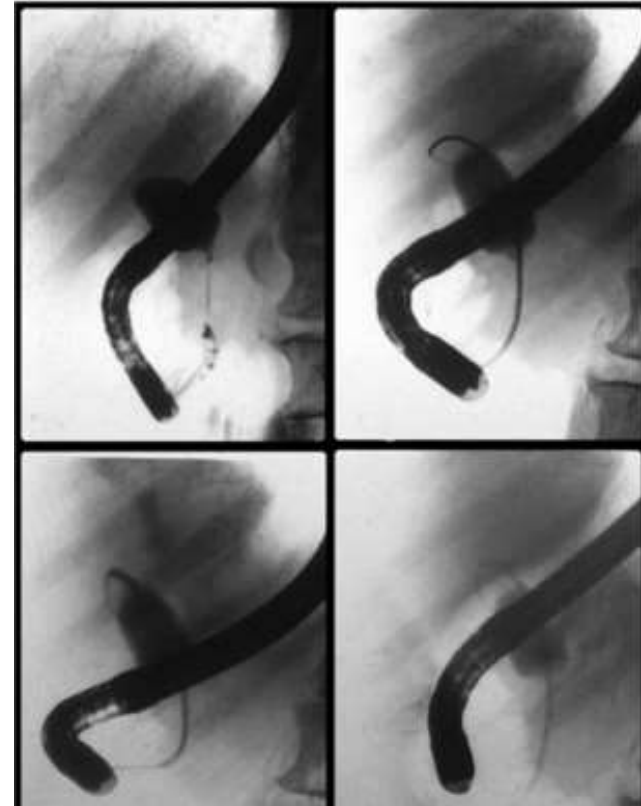
Dtsch. med. Wschr. 104 (1979), 206–207
© Georg Thieme Verlag, Stuttgart

Palliative Gallengangdrainage

Eine neue Methode zur endoskopischen Einführung eines inneren Drains

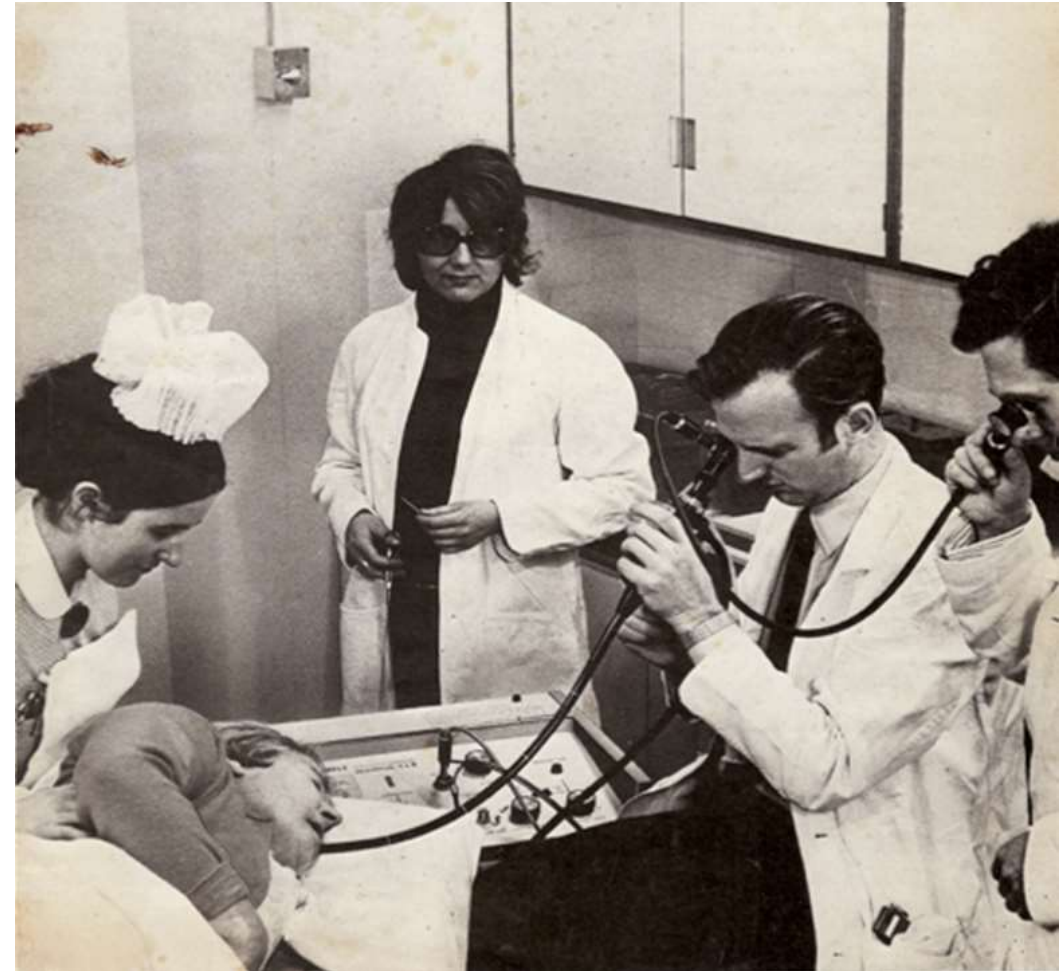
N. Soehendra und V. Reynders-Fredertx

Chirurgische Klinik und Poliklinik, Abteilung für Allgemeinchirurgie (Direktor: Prof. Dr. H. W. Schreiber)
der Universität Hamburg



ERCP History

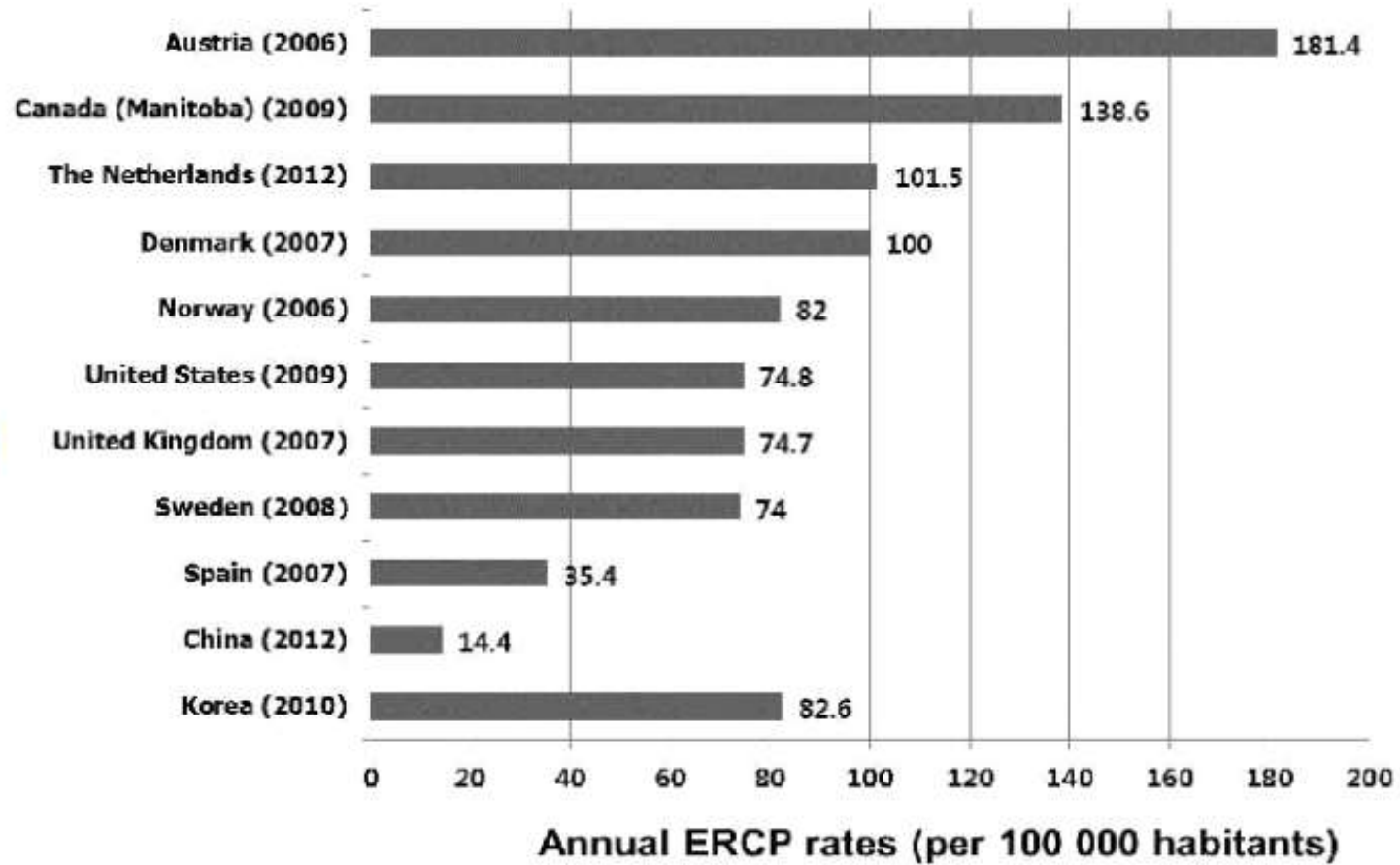
- “I performed many, many ERCPs in the 1970s, but it never occurred to me to take out stones.”
Peter Cotton, 40 Years Of Interventional ERCP-
Stories From The Pioneers 2014



ERCP

- Considered the **gold standard** for relieving malignant biliary obstruction
- Considered overall to be the riskiest high-volume endoscopic procedure currently performed
 - Complications can be severe or fatal
- **ERCP no longer has any role as a diagnostic procedure**
 - NIH Consensus Conference January 2002
 - Replaced by CT, MRI and EUS
- Volume is increasing throughout the world

ERCP



ERCP

► **Table 2** Use of ERCP from 2007 to 2016.

	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016
Total	148,179	162,609	162,419	167,943	170,931	161,685	160,714	160,100	155,695	156,874
Percentage	0.38%	0.41%	0.41%	0.43%	0.44%	0.44%	0.45%	0.45%	0.43%	0.44%

Temporal trend in use of ERCP from 2007 to 2016. The total number of patients is shown, as well as the respective percentage relative to the total number of discharges each year.

Kroner PT et al.
Endoscopy International Open 2020; 08: E761–
E769

ERCP

- Pancreatitis is the most common complication of ERCP (3.5-13%)
- In 90% of pancreatitis cases, severity is mild to moderate
- Infections occur in 1.4%
 - Cholangitis
 - Cholecystitis
- Bleeding complications occur in 1.3%
- Perforation occurs in 0.6%
- Procedure-related mortality is 0.3%

ERCP

► **Table 5** Occurrence of Post-ERCP pancreatitis from 2007 to 2016.

Year	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	Total
Total (percentage)	18,161 (12.3%)	21,623 (13.3%)	21,326 (13.3%)	21,824 (13.0%)	22,615 (13.2%)	21,250 (13.1%)	21,720 (13.5%)	21,590 (13.5%)	22,910 (14.7%)	25,804 (16.5%)	218,812 (13.6%)
Adjusted odds ratio (95% CI), P value	1.49 (1.39–1.60), <0.01										

Occurrence of post-ERCP pancreatitis in number and percentage of cases during the period from 2007 to 2016 as well as adjusted odds ratio, confidence interval and P value for 2016 versus 2007.

Kroner PT et al.
Endoscopy International Open 2020; 08: E761–E769

How Often Is ERCP Performed For MBO?

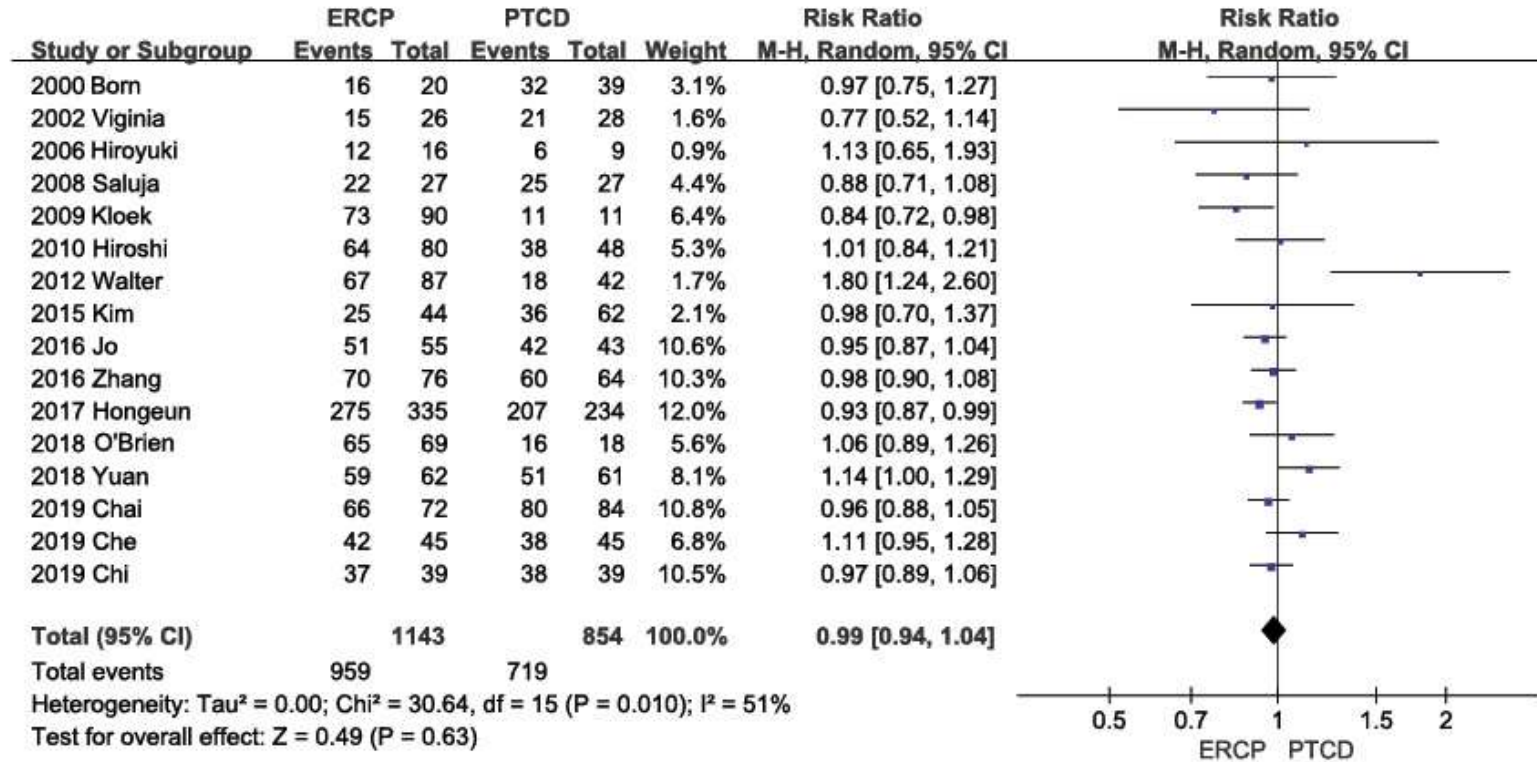
► **Table 3** Most common ERCP indications in 2016 compared to 2007.

Indication	2007	2016	Percent change
Choledocholithiasis (N = 499,339)	40.4%	30.2%	-10.2%
Acute biliary pancreatitis (N = 175,476)	13.9%	8.8%	-5.1%
Ascending cholangitis (N = 79,607)	4.1%	10.8%	+6.7%
Unspecified obstruction (N = 51,902)	5.8%	7.8%	+2.0%
Pancreatic head mass (N = 37,223)	2.5%	2.9%	+0.4%
Non-codable indication (N = 495,810)	33.3%	39.5%	+6.2%

Kroner PT et al.
Endoscopy International Open 2020; 08:
E761–E769

Is ERCP Effective For MBO? Is It Comparable To PBD?

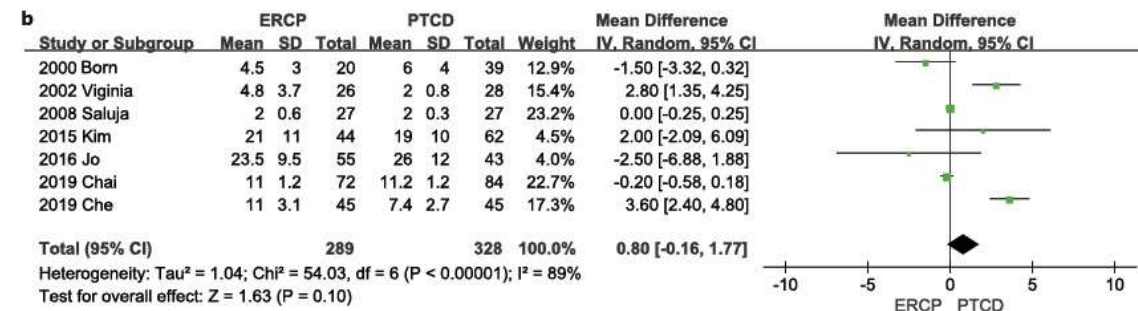
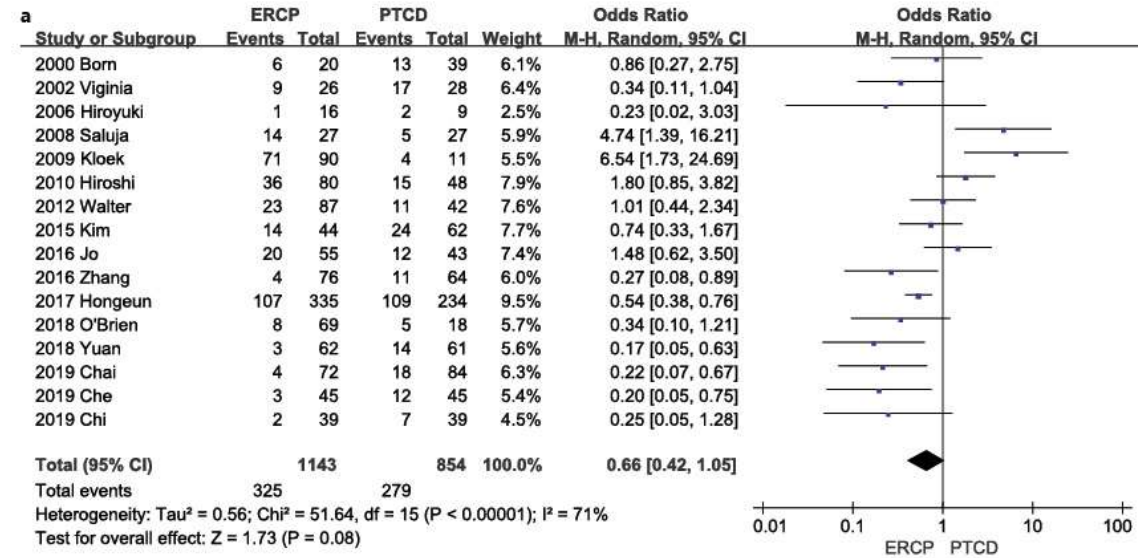
- Overall ERCP success rate was 85% vs. 83% for PBD



Pang L et al.
 Digestion Jan 2023

Is ERCP Effective For MBO? Is It Comparable To PBD?

- There were no significant differences between the two in total hospital stay or complication rates

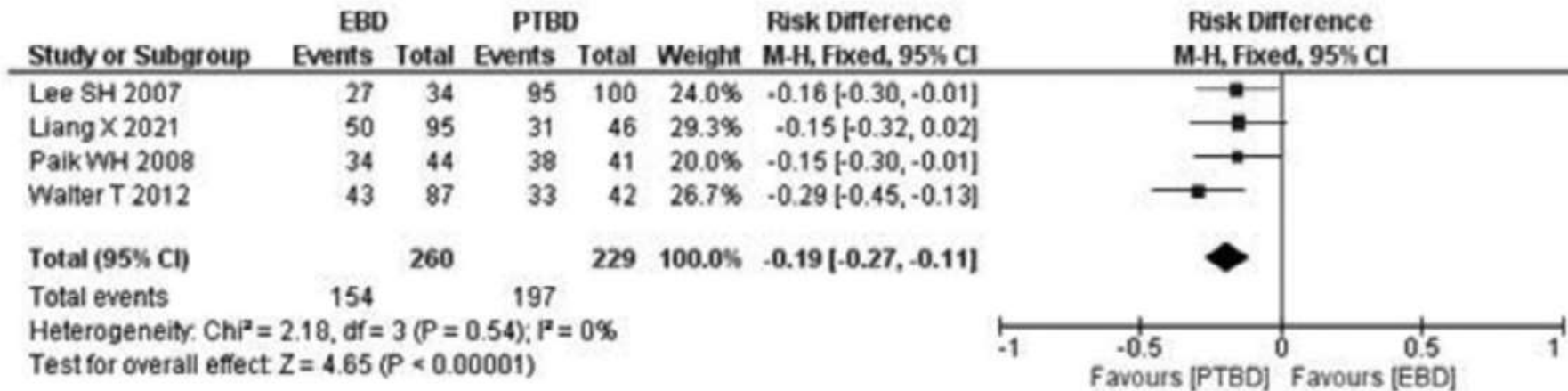


Pang L et al.
Digestion Jan 2023

How About MBO Due To Perihilar Cholangiocarcinoma?

- There was no statistical difference between the groups regarding: technical success, post-drainage bleeding, major post-drainage complications, and seeding metastases
- Percutaneous drainage had longer hospital stay but decreased rates of cholangitis

Clinical success in palliative PCCA



Moll CF et al.
 Clinics 78; 2023

EUS



EUS History

- First report of a ultrasonic endoscope was in 1980 by Eugene DiMagno from Mayo Clinic
- With it, mediastinal structures, liver and porta hepatis were readily imaged at 10 MHz



Methods and Devices

ULTRASONIC ENDOSCOPE

EUGENE P. DIMAGNO
PATRICK T. REGAN
DAVID A. WILSON

JAMES L. BUXTON
ROBERT R. HATTERY
JOSE R. SUAREZ

PHILLIP S. GREEN

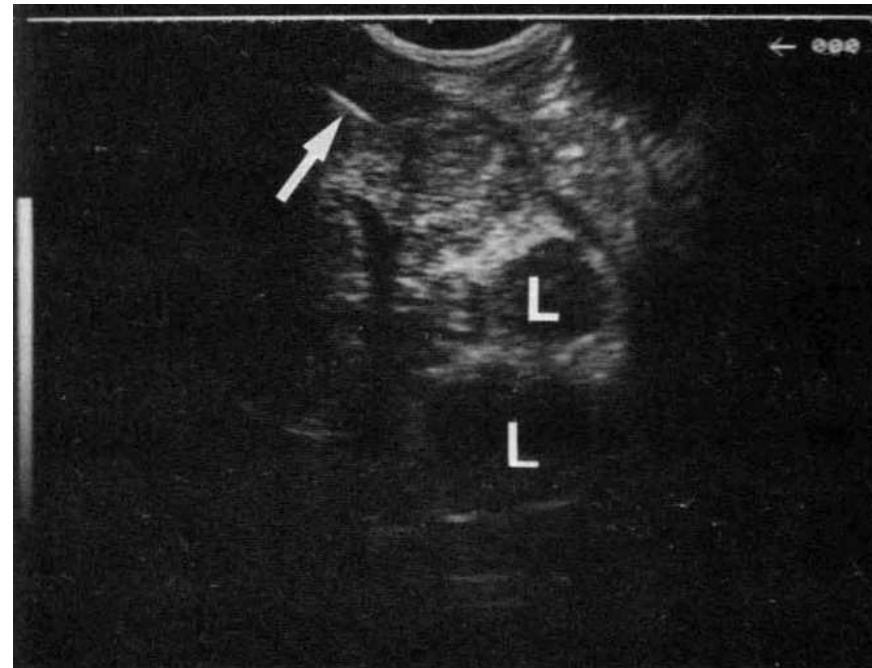
*Gastroenterology Unit and Department of Radiology, Mayo
Clinic and Mayo Foundation, Rochester, Minnesota 55901;
and Bioengineering Research Center, SRI International,
Menlo Park, California 94025*

EUS History

- Olympus marketed the first commercial echoendoscope in 1982
- Tio and Tytgat utilized the biopsy channel to complete the first EUS-guided biopsy in 1984
- For most of the 1980s, essentially only three physicians were performing diagnostic EUS in the world
 - Charles Lightdale in New York
 - Lok Tio in Amsterdam
 - Thomas Rosch in Munich

EUS History

- In 1988, Pentax/Hitachi marketed the first curvilinear echoendoscope and ushered in the era of needle-based therapy
- In 1992, Vilmann et al. published the first EUS/FNA of a pancreas mass using a 4 cm 24 gauge needle



As With ERCP, EUS Evolved Rapidly From Diagnostic To Therapeutic Indications

Procedure	Authors	Year	Reference
PFC drainage	Grimm, Binmoeller, Sohendra	1992	GIE 38:170-1
CPN	Wiersema	1996	GIE 44:656-62
Fine needle injection	Chang, Nguyen, Thompson	2000	Cancer 88:1325-35
Transluminal BD drain	Giovannini, Moutardier, Delpero	2001	Endoscopy 33:898-0
Pancreatogastrostomy	Francois, Giovannini, Deviere	2002	GIE 56:128-33
Pancreatic rendezvous	Bataille, Deprez	2002	GIE 55:740-3
Pelvic abscess drain	Giovannini, Moutardier, Delpero	2003	Endoscopy 35:511-4
Biliary rendezvous	Mallery, Matlock, Freeman	2004	GIE 59:100-7
Panc cyst ablation	Gan, Thompson, ... Brugge	2005	GIE 61:746-52
Brachytherapy	Lah, Kuo, Chang, Nguyen	2005	GIE 62:805-8
Fiducial placement	Pishvaian, Collins, ... Haddad	2006	GIE 64:412-7
GB drainage	Baron, Topazian	2007	GIE 65:735-7
Vascular therapy	Romero-Castro, Pellicer-Bautista	2007	GIE 66:402-7

If We Could See It, Then We Could Puncture It

- In 1996, Maurits Wiersema published the first series of EUS-guided cholangiography to rescue failed ERCP
- Successful cholangiography was reported in 8 out of 11 patients with no early or late complications

Endosonography-guided cholangiopancreatography

**Maurits J. Wiersema, MD, David Sandusky, RN, Roberta Carr, RN
Lisa M. Wiersema, MD, William C. Erdel, MD, Paul K. Frederick, MD**

Indianapolis, Indiana

If We Could See It, Then We Could Puncture It

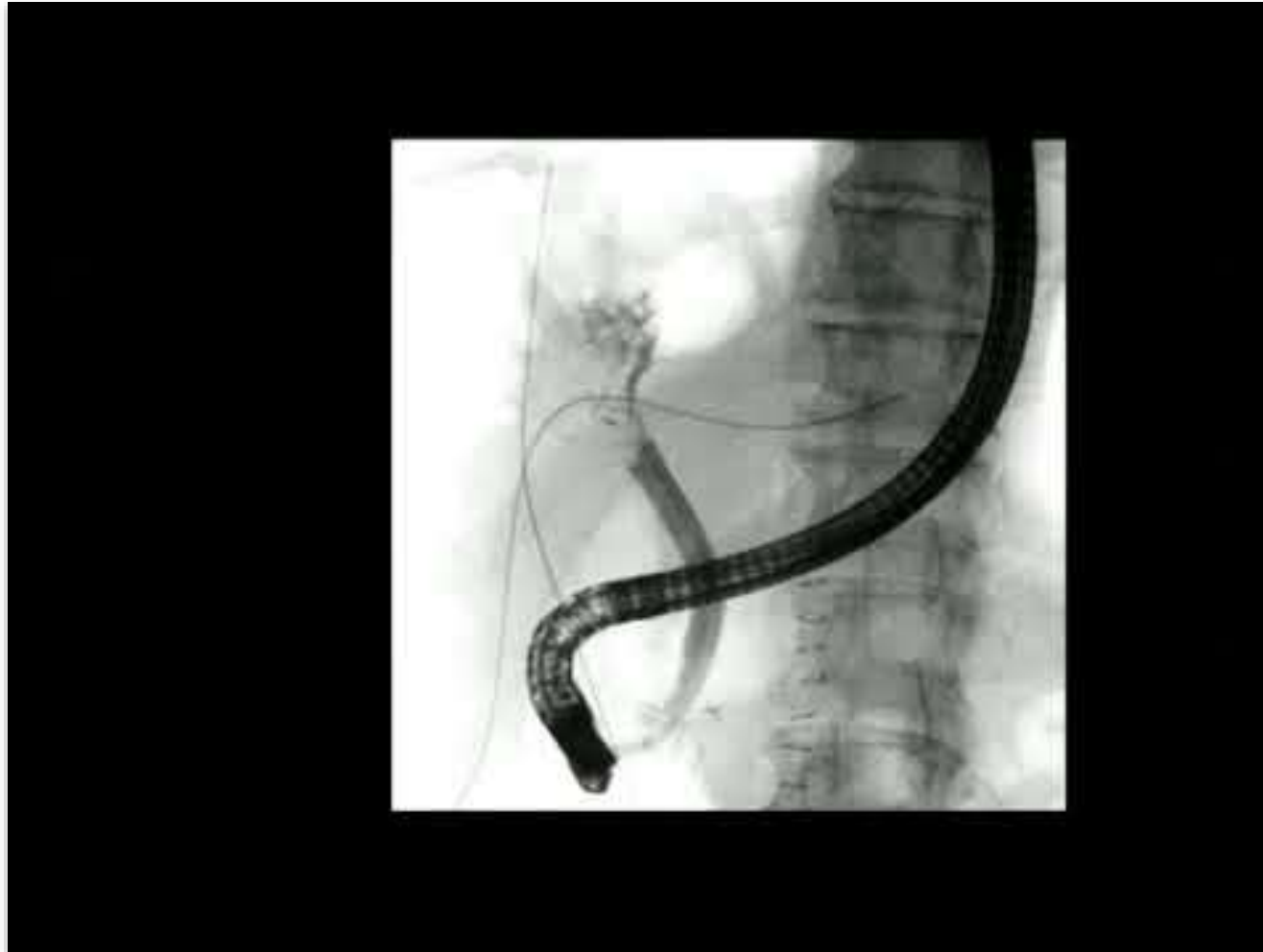
- This was followed by Giovannini et al. in 2001, Mallery et al. in 2004, and Kahaleh et al in 2005 all achieving biliary drainage by rendezvous technique

EUS-guided transhepatic cholangiography: report of 6 cases

Michel Kahaleh, MD, Pin Wang, MD, Vanessa M. Shami, MD, Jeffrey Tokar, MD, Paul Yeaton, MD

Charlottesville, Virginia

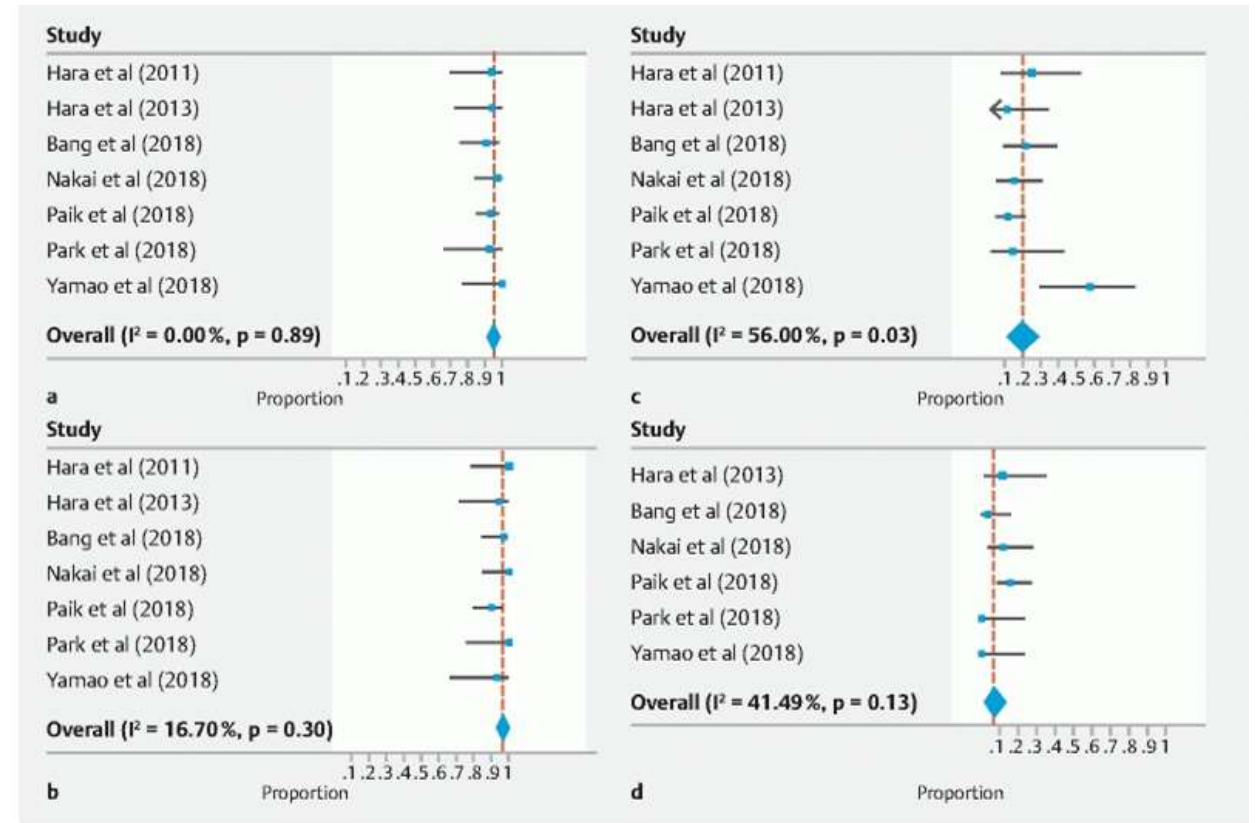
EUS-Guided Biliary Rendezvous For Failed ERCP



EUS-Guided ERCP (EUS-BD) Works

- Pooled technical success rate is 95% and rate of re-intervention is 7%
- Pooled adverse event rate is somewhat higher at 19%
 - Peritonitis
 - Cholangitis

Kathorn K et al.
Endosc Int Open 2019; 07(11): E1432-E1441



| Fig.2a Technical success rate for EUS-BD for treatment of distal malignant biliary obstruction. b Clinical success rate for EUS-BD for treatment of distal malignant biliary obstruction. c Serious adverse events for EUS-BD for treatment of distal malignant biliary obstruction d Rate of reintervention for EUS-BD for treatment of distal malignant biliary obstruction.]

EUS-Guided ERCP (EUS-BD) Works

Author (year)	Study design	Total no subjects	Type of EUS-BD	Type of stent used	Technical success EUS versus ERCP rate, % (n=#)	Clinical success EUS versus ERCP rate, % (n=#)	Total Adverse Events EUS-BD versus ERCP rate, % (n=#)
Tonozuka ⁷² (2013)	Single Centre, Retrospective	11 (8 EUS-BD; 3 ERCP)	EUS-CDS EUS-HGS EUS-CAS	FCSEMS	100 (8/8) vs 100 (3/3)	100 (8/8) vs 100 (3/3)	37.5 (3/8) vs 0
Hamada ⁷⁸ (2014)	Multicentre, Retrospective	20 (7 EUS-BD; 13 ERCP)	EUS-CDS EUS-HGS	SEMS Plastic	—	—	14 (1/7) vs 7.6 (1/13)
Dhir ⁷⁷ (2015)	Multicentre, Retrospective	208 (104 EUS-BD; 104 ERCP)	EUS-CDS EUS-AG	FCSEMS UCSEMS	93.3 (97/104) vs 94.2 (98/104)	89.4 (93/104) vs 91.3 (95/104)	8.7 (9/104) vs 8.7 (9/104)
Kawakubo ⁸⁰ (2016)	Single Centre, Retrospective	82 (26 EUS-BD; 56 ERCP)	EUS-CDS	PCSEMS	-	96.2 (25/26) vs 98.2 (55/56)	26.9 (7/26) vs 35.7 (20/56)
Bang ⁷⁵ (2018)	Single Centre, Prospective, RCT	67 (33 EUS-BD; 34 ERCP)	EUS-CDS	FCSEMS	90.9 (30/33) vs 94.1 (32/34)	97 (32/33) vs 91 (31/34)	21.2 (7/33) vs 14.7 (5/34)
Hamada ⁷⁹ (2018)	Multicentre, Retrospective	110 (20 EUS; 90 ERCP)	EUS-CDS EUS-HGS	FCSEMS PCSEMS UCSEMS	-	-	35% (7/20) vs 8.8% (8/90)
Paik ⁷³ (2018)	Multicentre, Prospective, RCT	125 (64 EUS-BD; 61 ERCP)	EUS-CDS EUS-HGS	Hybrid PCSEMS	93.8 (60/64) vs 90.2 (55/61)	90 (54/60) vs 94.5 (52/55)	10.9 (7/64) vs 39 (24/61)
Park ⁷⁴ (2018)	Single Centre, Prospective, RCT	28 (14 EUS-BD; 14 ERCP)	EUS-CDS	PCSEMS	92.8 (13/14) vs 100 (14/14)	92.8 (13/14) vs 100 (14/14)	0 vs 0
Yamao ⁸² (2018)	Multicentre, Retrospective	39 (14 EUS-BD; 25 ERCP)	EUS-CDS EUS-HGS	FCSEMS PCSEMS Plastic	100 (14/14) vs 56 (14/25)	92.9 (13/14) vs 52 (13/25)	57 (8/14) vs 32 (8/25)
Nakai ⁸¹ (2019)	Multicentre, Prospective	59 (34 EUS-BD; 25 ERCP)	EUS-CDS	FCSEMS PCSEMS	97 (33/34)	100 (34/34)	15 (5/34)

Canakis A, Baron TH
BMJ Open Gastro 2020;7:e000428

EUS-Guided ERCP (EUS-BD) Works

EUS-guided versus PTC drainage

Variable	EGBD (n=22)	PTBD (n=51)	P value
Mean pre-EGBD bilirubin (mg/dL)	15.8 ± 11.3	14.5 ± 8.8	0.64
Mean post-EGBD bilirubin (mg/dL)	1.3 ± 0.9	2.3 ± 1.1	0.004
Technical success,%	86.4	100	0.007
Clinical success, %	86.4	92.2	0.4
Adverse events (index procedure)	4 (18.2)	20 (39.2)	0.08
Adverse events (index procedure & reinterventions)	18.2	70.6	<0.001
Need for reintervention during follow-up, %	15.7	80.4	< 0.001

Khashab et al.
Dig Dig Sci 2015; 60(2): 557-65

The Problem With EUS-BD Is That It Still Involves ERCP

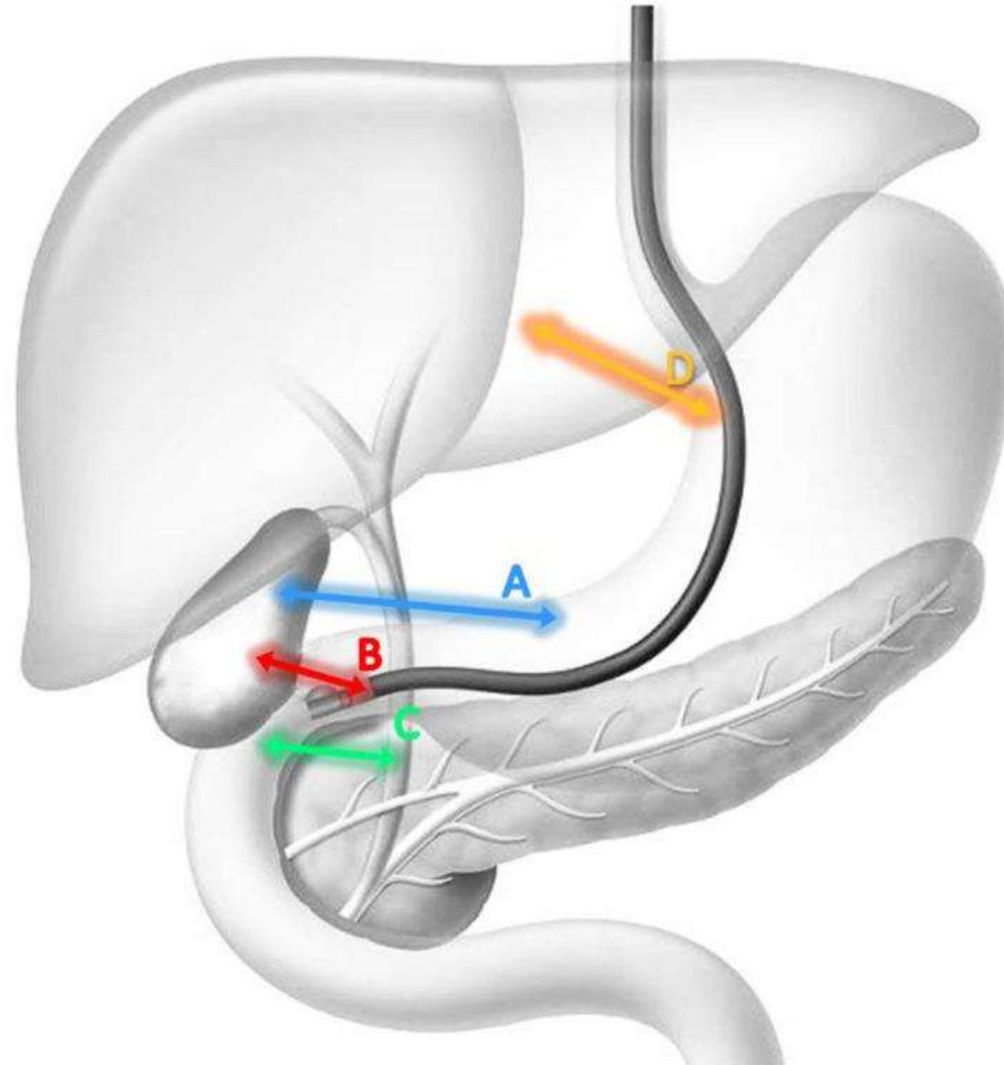
- At least similar complication rates to ERCP
- Suppose you can't even get to the ampulla?
 - Altered post-surgical anatomy
 - Malignant gastric or duodenal obstruction
- Are there any alternatives?

Surgically altered anatomy
Billroth-II gastrojejunostomy
Roux-en-Y gastric bypass
Hepaticojejunostomy
Gastric outlet obstruction
Duodenal invasion (types I and II)
High risk of post-ERCP pancreatitis

EUS-BD Alternatives

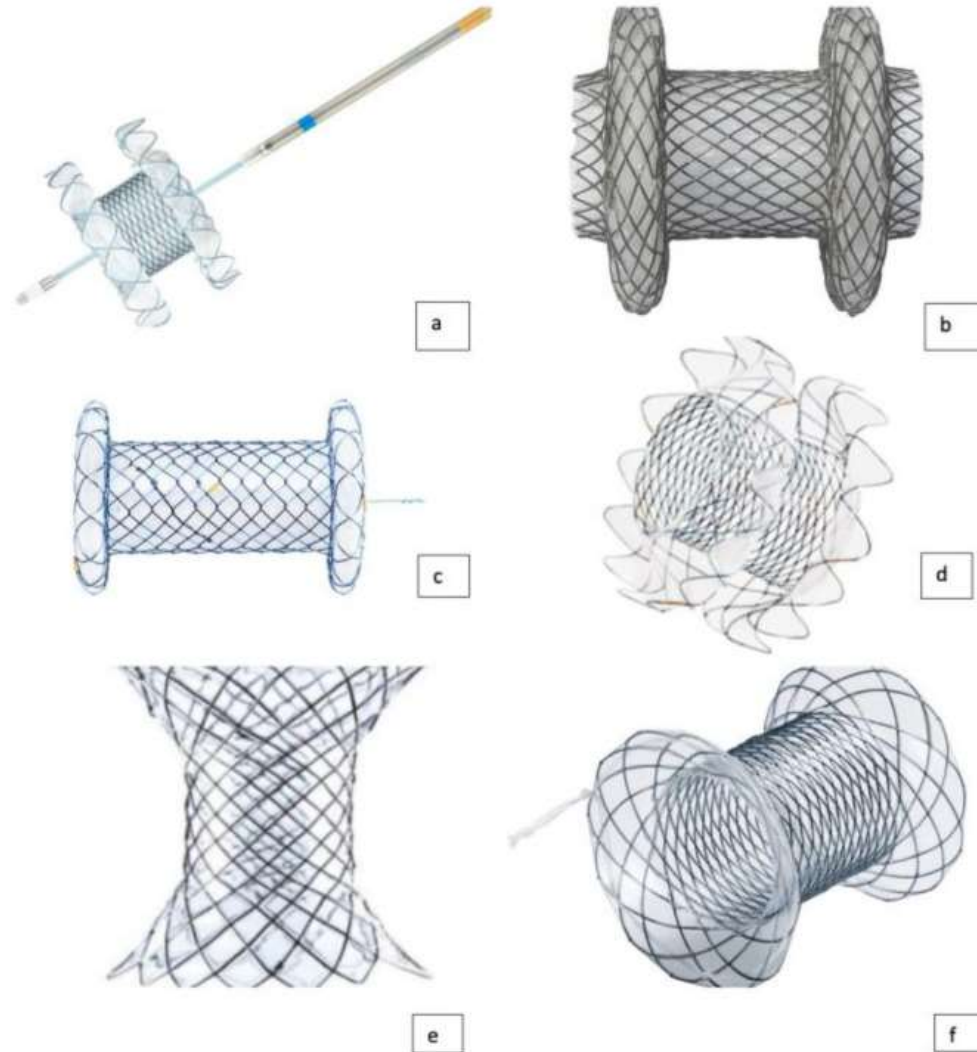
- EUS-guided choledochoduodenostomy (EUS-CD)
- EUS-guided hepaticogastrostomy (EUS-HG)
- EUS-guided cholecystogastrostomy
- These became much more feasible once covered metal stents became commercially available
 - Lumen Apposing Metal Stent (LAMS)

EUS-BD Alternatives



Clinically Available LAMS

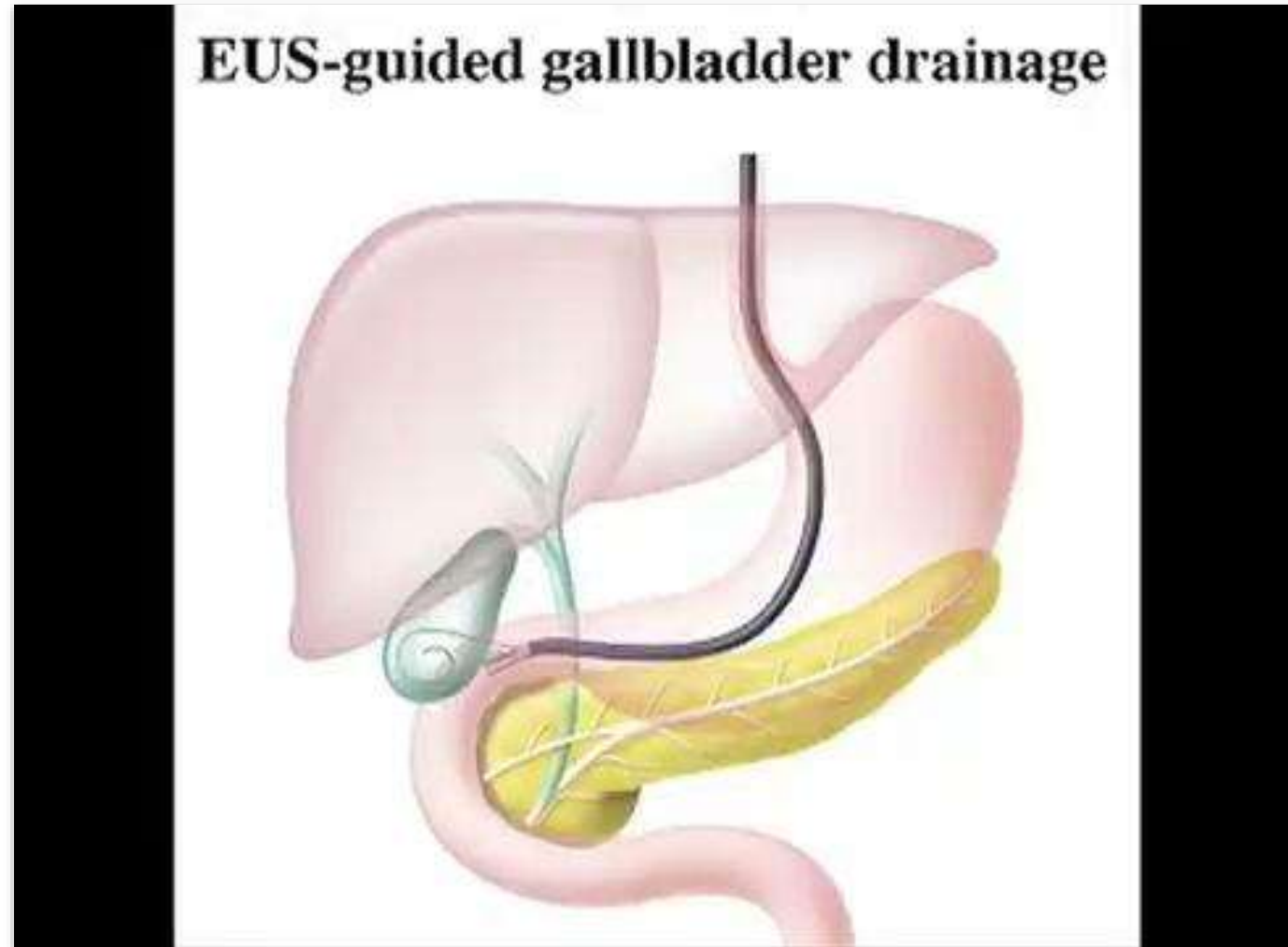
- LAMS were first described by Teoh and Binmoeller et al. in 2014 for gallbladder drainage
- They were rapidly used to connect other structures to the GI tract
 - Bile ducts
 - Collections
 - Other parts of the bowel



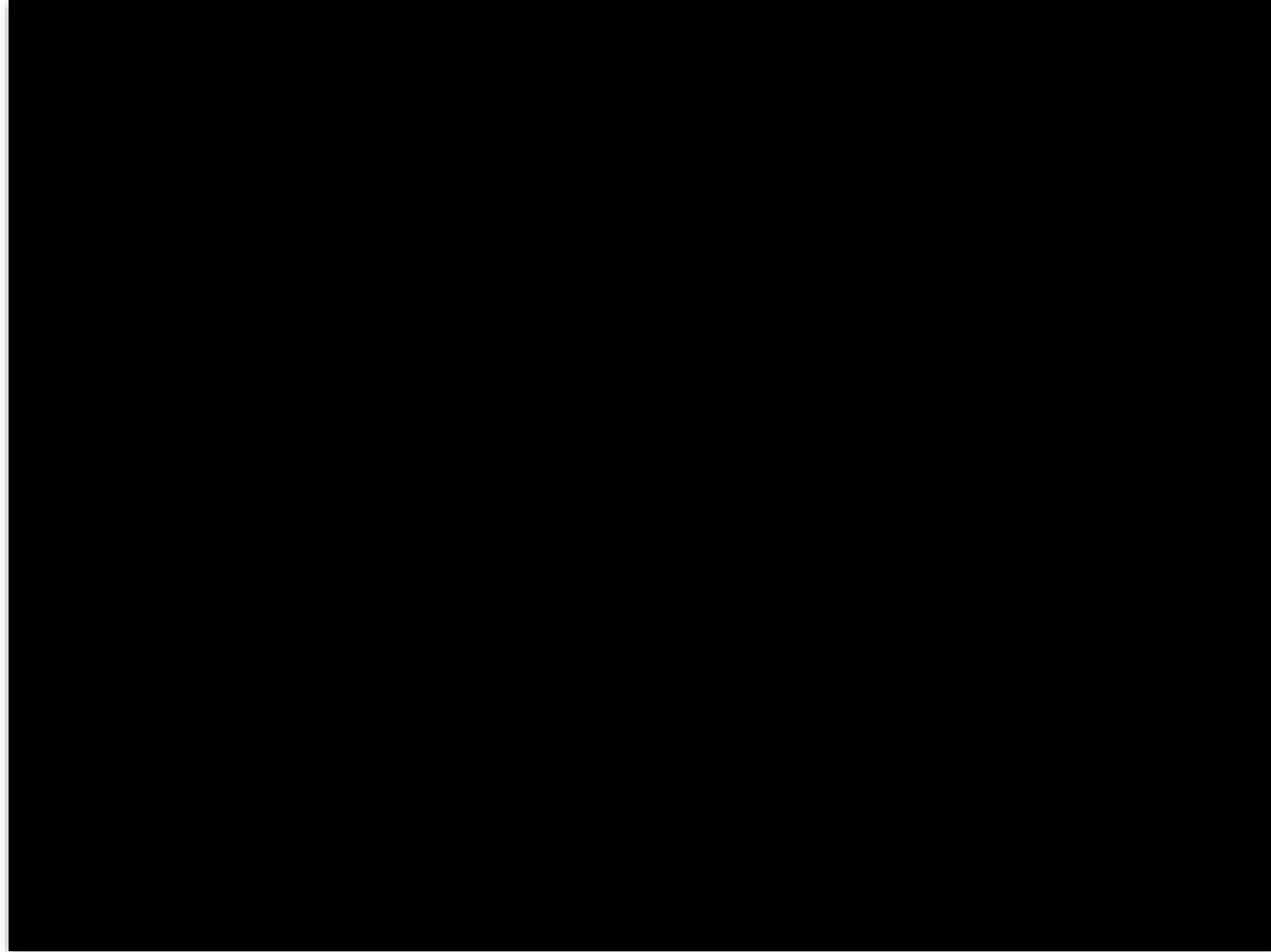
EUS-Guided Choledochoduodenostomy



EUS-Guided Cholecystogastrostomy



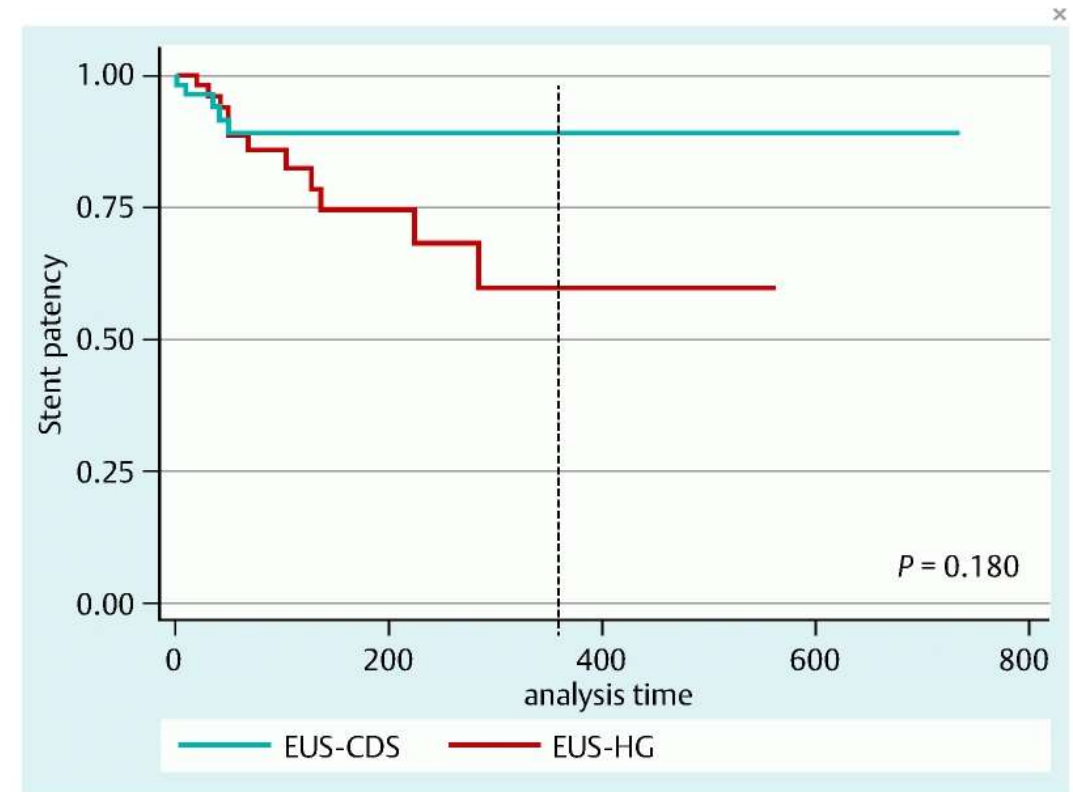
EUS-Guided Hepaticogastrostomy



Which Alternative Procedure Is Better? EUS-CD vs EUS-HG

- EUS-CD associated with shorter hospital stay, improved stent patency, and fewer procedure-related adverse events

Khasab M et al.
Endosc Int Open 2016; 04(02): E175-E181



| Fig.2 Kaplan-Meier plot estimates of the stent patency duration after EUS-CDS and EUS-HG. Dashed line represents probability of stent patency at 1 year: EUS-CDS 0.98 (96%CI: 0.76–0.96) vs EUS-HG 0.60 (95%CI: 0.35–0.78). Stent patency duration was not significantly different via log-rank test ($P=0.228$).|

Which Alternative Procedure Is Better? EUS-CD vs EUS-HG

- Adverse events were associated with the use of
 - Plastic stents
 - Non-coaxial cautery

Khasab M et al.
Endosc Int Open 2016; 04(02): E175-E181

Table 6
Multivariable analysis of predictors of adverse events after EUS-BD adjusting for EUS-BD route.

	Multivariable analysis	
	Odds Ratio (95%CI)	P value
Hepatogastrostomy	1.63 (0.56–4.74)	0.374
Plastic stenting	4.95 (1.41–17.38)	0.013
Non-coaxial electrocautery	3.95 (1.16–13.40)	0.027

EUS-BD, endoscopic ultrasound-guided biliary drainage

Which Alternative Procedure Is Better? EUS-CD vs EUS-HG

- Two other large reviews showed no difference in technical success
 - 92% in both groups
- They however did show a trend towards longer stent patency in EUS-CD patients
- Tyberg et al's metanalysis showed an increased complication rate of EUS-CD
 - 25/87 patients in the EUS-HG required stent revision (long-term success 71%)

Uemura RS et al.

J Clin Gastroenterol 2018 Feb;52(2):123-130

Tyberg A et al.

Endosc Ultrasound 2022 Jan-Feb;11(1):38-43

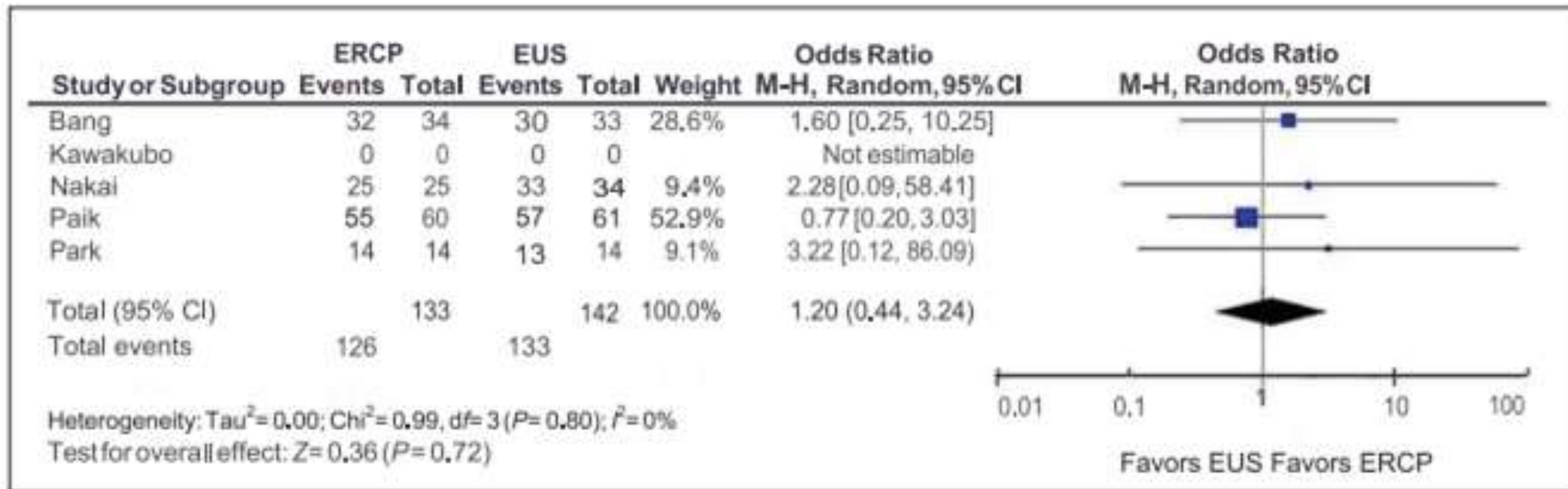
Primary EUS Drainage

- Most publications to date propose EUS-guided drainage only *after* failed ERCP (as an alternative to percutaneous biliary drainage)
- However, how about *never even considering ERCP in the first place?*



Primary EUS Drainage

- One metaanalysis showed comparable technical and clinical success with primary EUS-BD



Kakked G et al.

Endoscopic Ultrasound 9(5); Sept 2020

Primary EUS Drainage

- It also showed far less adverse events, especially pancreatitis, in the EUS-only group
- The rate of pancreatitis in the ERCP group was 9.5%, whereas in the EUS group it was 0%

Kakked G et al.

Endoscopic Ultrasound 9(5); Sept 2020

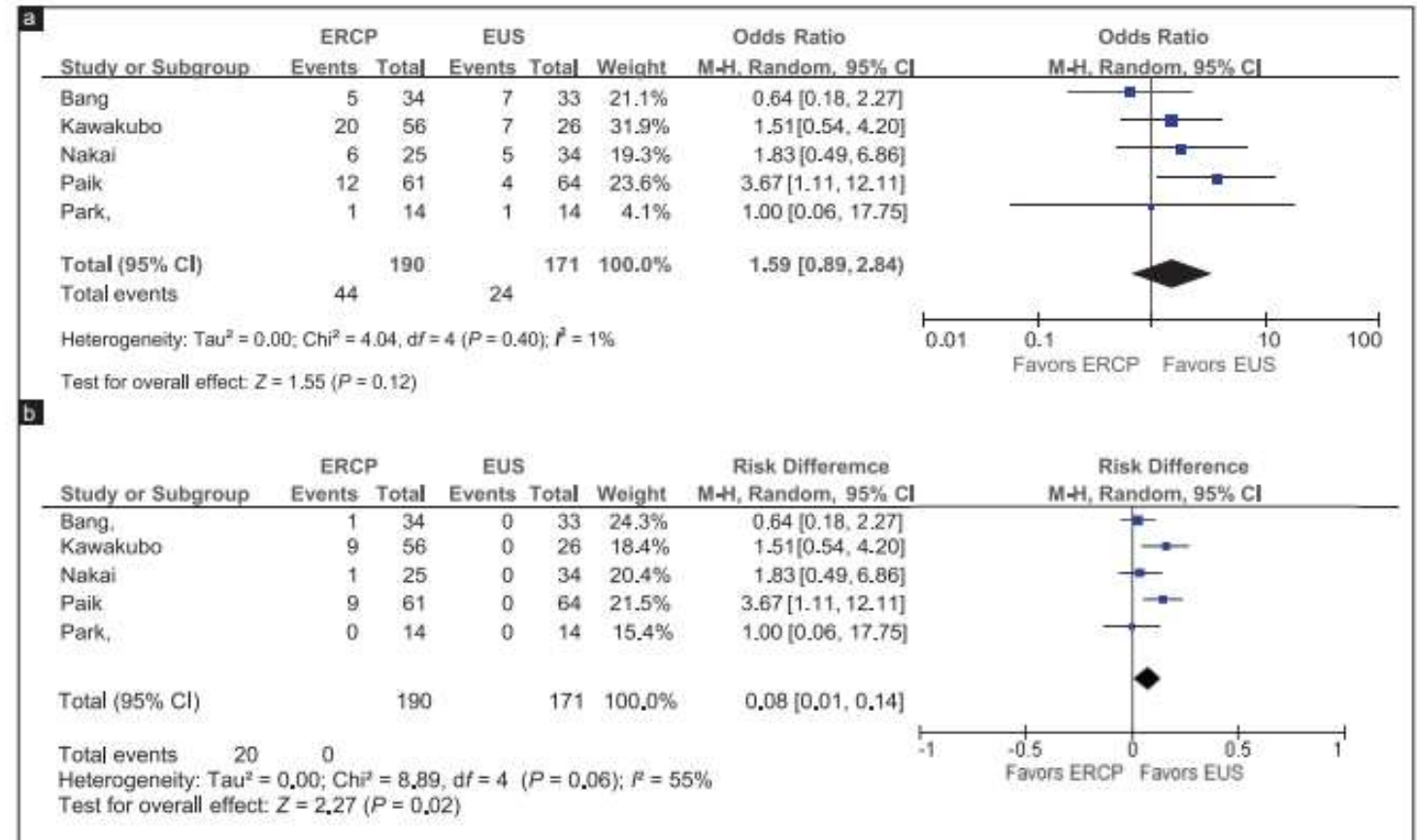


Figure 4. Adverse events. (a) Overall adverse events. (b) Procedure-related pancreatitis

So....Can We Come Up With An Algorithm?

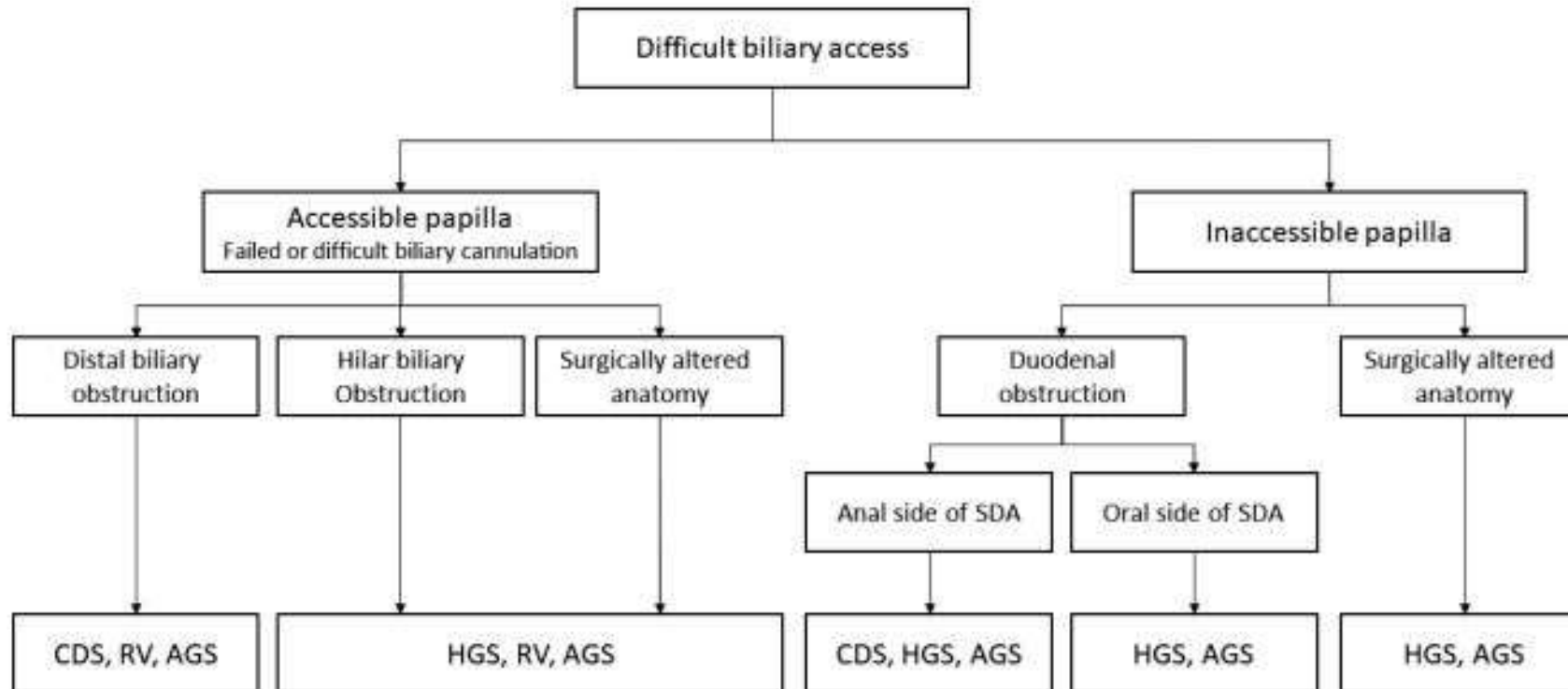


Fig. 3 Flowchart of selection of various EUS-BD procedures. *EUS* endoscopic ultrasound, *EUS-AGS* EUS-guided antegrade stenting, *EUS-CDS* EUS-guided choledochoduodenostomy, *EUS-HGS* EUS-guided hepaticogastrostomy, *EUS-RV* EUS-guided rendezvous technique, *SDA* supraduodenal angle

Paik WH
Curr Treat Options Gastro (2020)
18:188–199

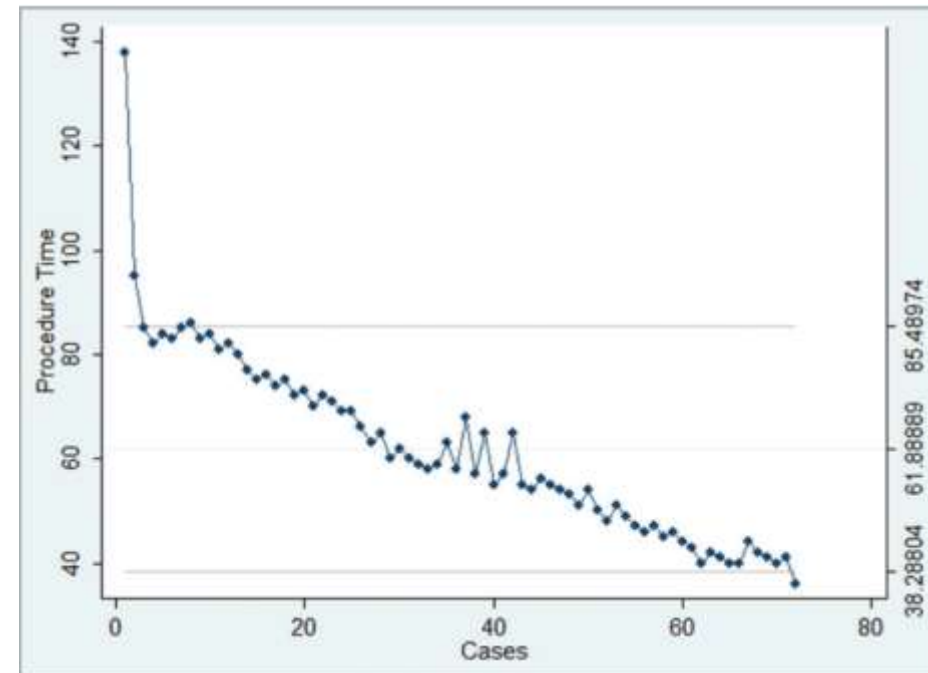
Can EUS-Only Approaches Truly Replace ERCP?

Pro	Con
Comparable efficacy to ERCP in expert hands	Steep learning curve
Longer stent patency	No dedicated devices for this
Less ERCP-type complications	Stent-related issues not fully resolved
Access to the bile duct regardless of anatomy	Not fully applicable to more benign disease

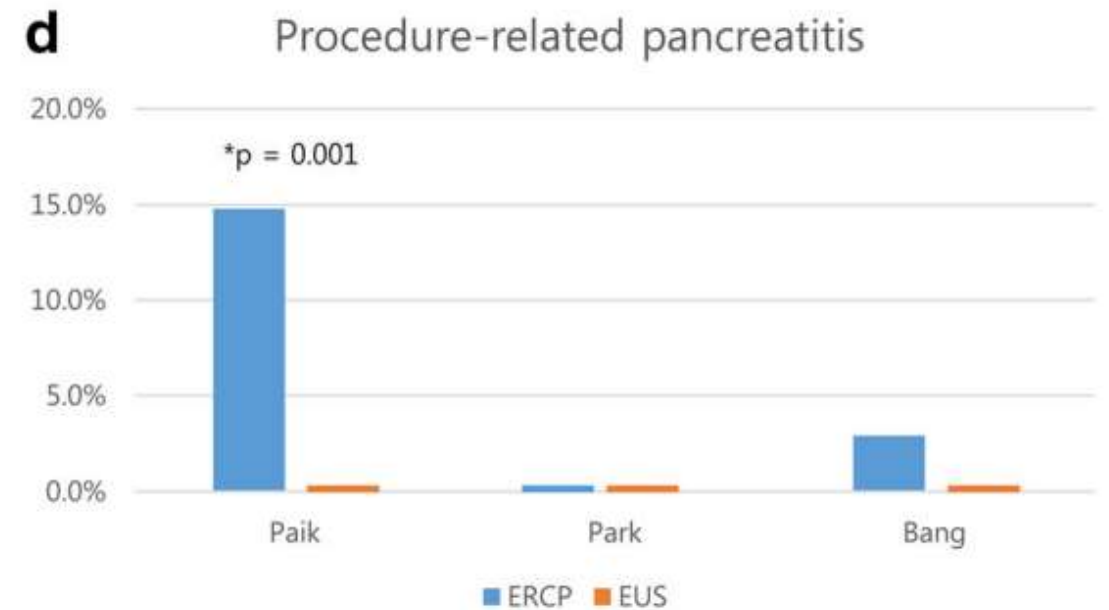
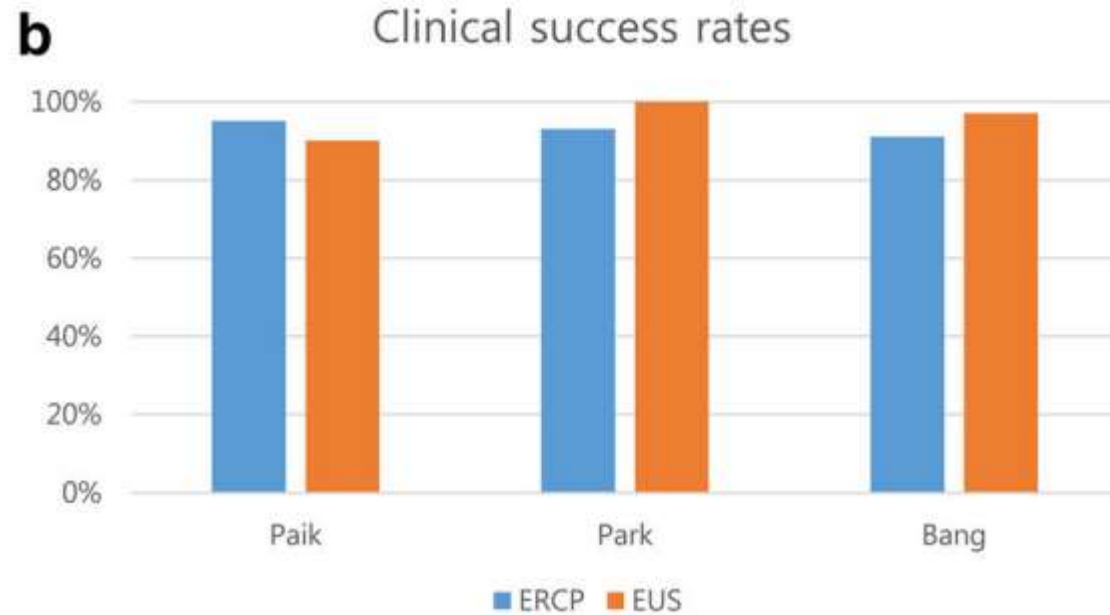
How Steep Is That Learning Curve By The Way

- A few studies have documented the steep learning curve of this highly technical skill
- It has been shown that skill starts to improve in a linear fashion after the first 32 cases and mastery is achieved after the first 100 cases

Tyberg A et al.
Endoscopic Ultrasound 9(6); Nov 2020



Can EUS Really Replace ERCP For Malignant Biliary Obstruction?



Can EUS Really Replace ERCP For Malignant Biliary Obstruction?

