NYSGE
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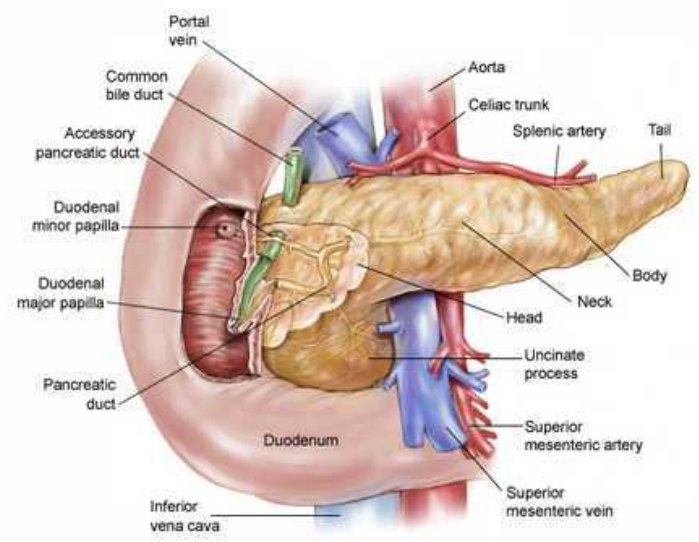
for Gastrointestinal Endoscopy

Best of DDW 2019

Pancreas



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CACTES
Center for Advanced Colonoscopy & Therapeutic Endoscopy as Mount Sinai

Agenda

- Acute pancreatitis
- Pancreatic cysts
- EUS-guided therapy

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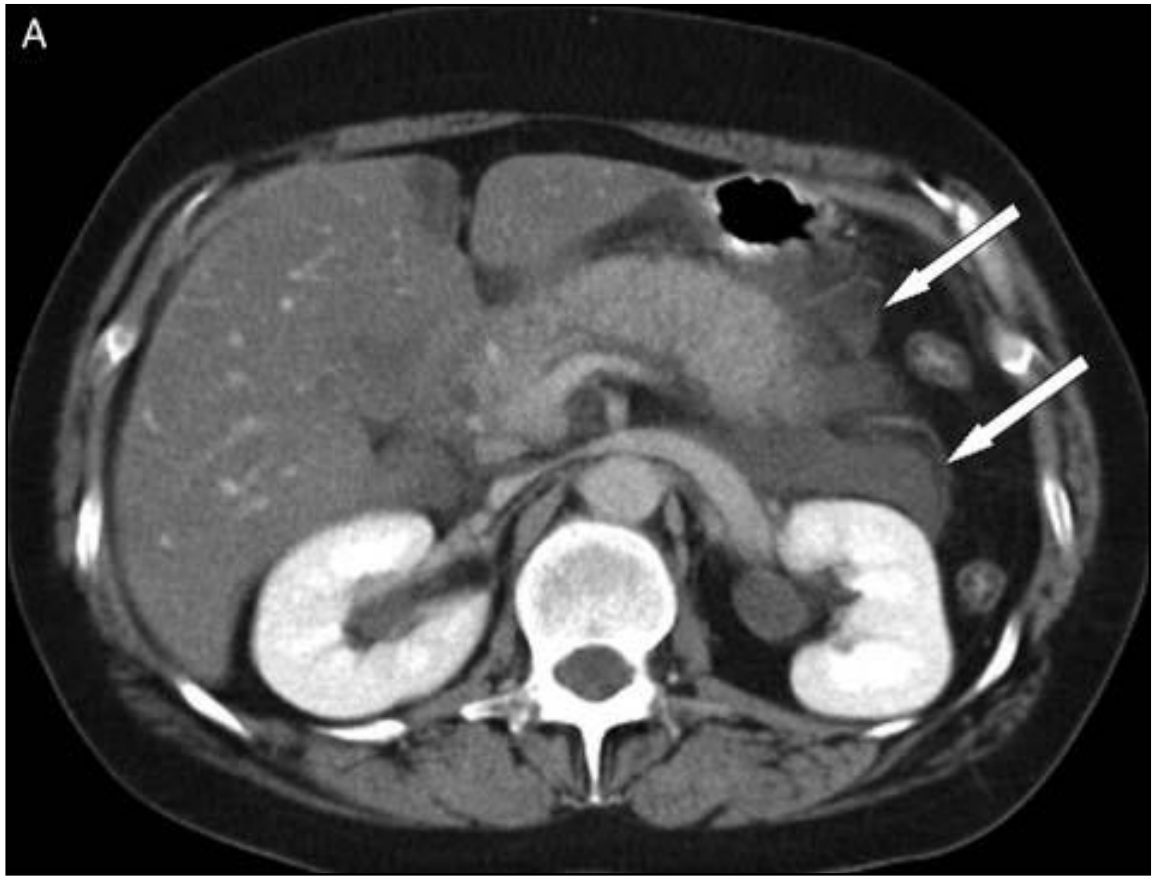
Acute Pancreatitis



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THE CLINICAL COURSE AND DIAGNOSTIC WORK-UP OF IDIOPATHIC ACUTE PANCREATITIS, A POST-HOC ANALYSIS OF A PROSPECTIVE MULTICENTER OBSERVATIONAL COHORT

AuthorBlock: *Nora D. Hallensleben[1,2], Devica S. Umans[3,2], Stefan A.W. Bouwense[4], Robert C. Verdonk[2], Marc Besselink[3], Jeanin E. Van Hooft[3], Marco J. Bruno[1]*

[1]Gastroenterology & Hepatology, Erasmus Medical Centre, Rotterdam, Netherlands; [2]Gastroenterology, St. Antonius Hospital, Nieuwegein, Netherlands; [3]Amsterdam Medical Centres, location AMC, Amsterdam, Netherlands; [4]Surgery, Radboud umc, Nijmegen, Netherlands;

- After standard diagnostic work-up, the etiology of acute pancreatitis remains unknown in up to 25% of cases, a condition referred to as idiopathic acute pancreatitis (IAP).

- Determining the etiology of pancreatitis is essential, as it may direct treatment in the acute phase of the disease and guide interventions to prevent recurrent pancreatitis.

- **AIM**

  - Explore the use of additional diagnostic modalities and their diagnostic yield to identify underlying etiologies in “presumed” IAP

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Work-Up of Idiopathic Acute Pancreatitis

- Between 2008 and 2015, patients with acute pancreatitis were registered prospectively in 15 Dutch hospitals.
- Patients who initially had a negative diagnostic work-up with regard to the etiology of their first episode of pancreatitis were labelled IAP.
- This initial work-up included:
  - personal history, family history, trans abdominal ultrasound, and laboratory tests (i.e. liver enzymes, calcium, triglycerides).
- Post-hoc analysis including the type and number of all additional diagnostic tests performed, the yield of these test to establish an etiological diagnosis, and recurrence rates of IAP.

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Results: Baseline characteristics

Characteristics	N = 191
Age in years – median (IQR[§])	61 (52-72)
Female sex - no. (%)	79 (41%)
Mild disease course[1]	135 (71%)
Follow-up time in years – median (IQR[§])	4 (3-6)

§ IQR = Interquartile range.
[1] Banks PA, Bollen TL, Dervenis C, et al. Classification of acute pancreatitis--2012: revision of the Atlanta classification and definitions by international consensus. *Gut*. 2013;62(1):102-111.

Dutch Pancreatitis Study Group

Results:
Baseline characteristics

	N = 191
Cholecystectomy prior to pancreatitis - no. (%)	19 (10%)
ALT[#] in U/L– median (IQR)	26 (21 – 37)
AST[&] in U/L – median (IQR)	26 (21 – 37)
Bilirubin in µmol/liter – median (IQR)	10 (7- 17)
Triglycerides in mmol/L (n=141) – median (IQR)	1.3 (0.8 – 1.7)
Calcium (n=179) in mmol/L – median (IQR)	2.3 (2.2-2.4)

[#]IQR = Interquartile range, [&]ALT= alanine transaminase, [&]AST= aspartate transaminase

Results:
Use and yield of diagnostic tests

- 176 out of 191 patients (92%) underwent one or more additional diagnostic tests
- In 64 patients an etiology was demonstrated (36%)

Results: Etiological factors

Etiological factor	No. (percentage) – n=176
Biliary disease	39 (22%)
Neoplasm - Pancreatic carcinoma - Ampullary carcinoma - Neuroendocrine tumor - IPMN	13 (7.4%) - 9 (5.1%) - 2 (1.1) - 1 (0.6%) - 1 (0.6%)
Autoimmune	6 (3.4%)
Chronic pancreatitis	5 (2.8%)
Pancreas divisum	1 (0.6%)

Results: Recurrence rate

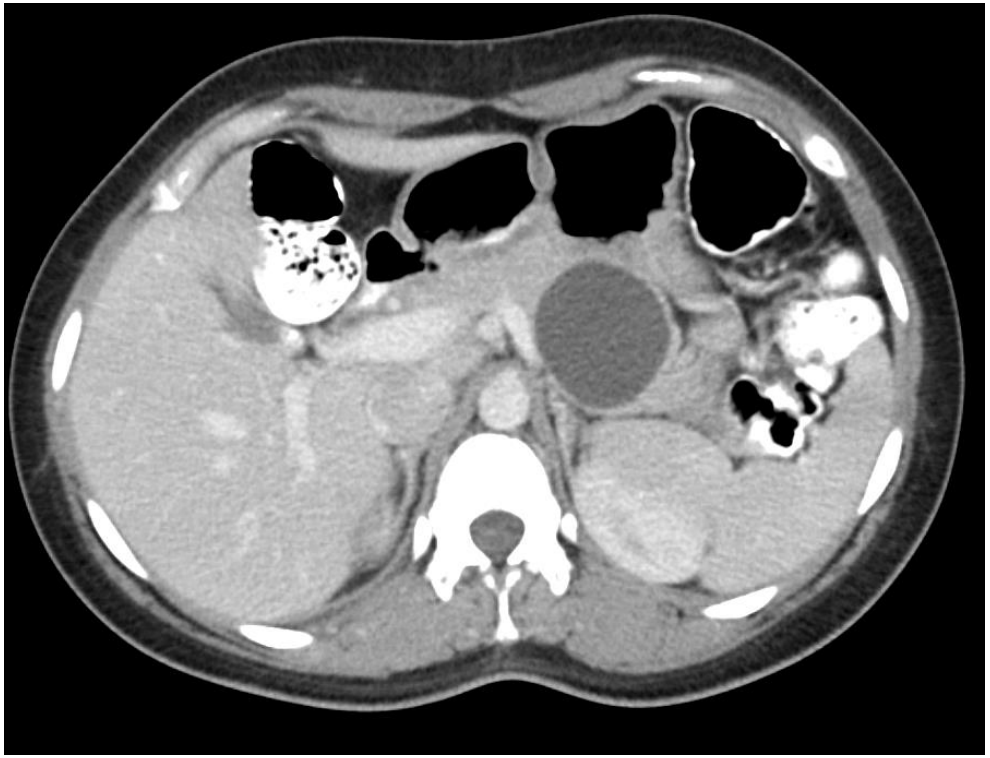
- 50 out of 191 patients had a recurrence (26%)
  - 26 patients had > 1 recurrence
  - Total of 101 recurrences
  - Median 2 recurrences per patient (IQR 1-2)

- Etiology was found in 27% of patients with a single episode vs 58% of patients with recurrent pancreatitis (p=0.00)

Conclusions

- Additional diagnostic work-up detects an etiology in one-third of patients
  - More than half biliary
  - 7% neoplasms
- EUS and MRI/MRCP have a high diagnostic yield (33-35%)
- Detection of etiology and subsequent treatment can prevent recurrences

Pancreatic Cysts



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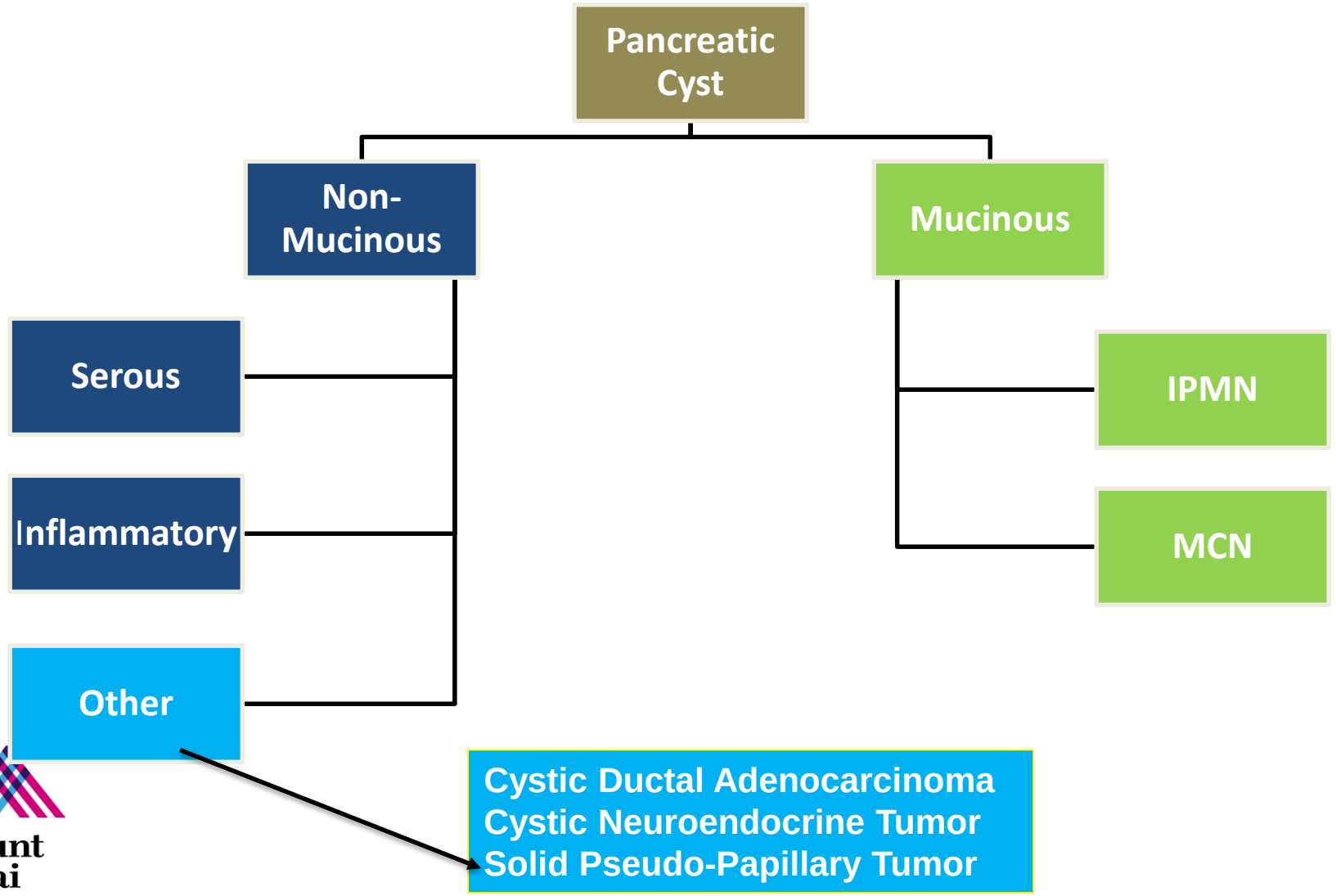
Differential Diagnosis



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Limitations of Current Diagnostic Testing in Distinguishing Pancreatic Cystic Neoplasms (Mucinous vs Non-Mucinous)

	Accuracy
Differentiate cyst type	
Contrast-enhanced CT	39-44.7%
MRI/MRCP*	39.5-50%

*MRCP has high sensitivity 96% for BD-IPMN

	Sensitivity	Specificity
Differentiate cyst type		
Cyst fluid CEA level	63%	93%
Cyst fluid cytology	54-67%	88-93%

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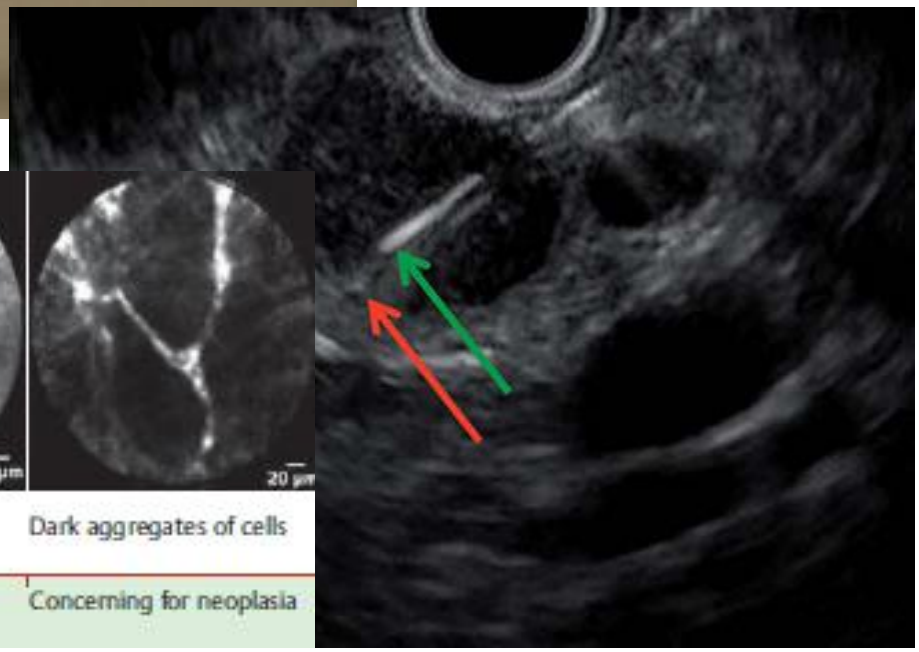
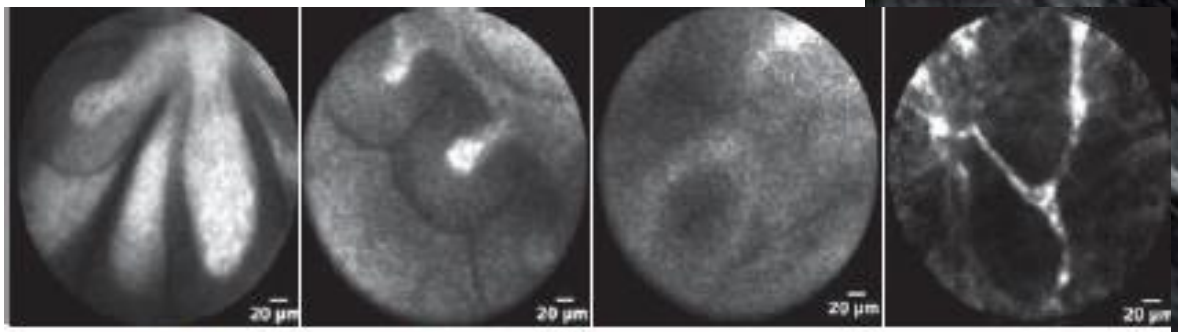
Jones MJ, et al. Pancreatology 2013
Tirkes T, et al. Abdom Imag 2014
de Jong K, et al. Endoscopy 2011
Thosani N, et al. Dig Dis Sci 2010
Thornton GD, et al. Pancreatology 2013
Ngamruengphong S, et al. Dig Liver Dis 2014
Suzuki R, et al. Pancreatology 2014

Needle-Based Confocal Laser Endomicroscopy (nCLE)





Finger-like papillary projections	Dark ring with white core	Gland-like or crypt-like structures	Dark aggregates of cells
Villous structure	Villous structure	Villous structure	Concerning for neoplasia

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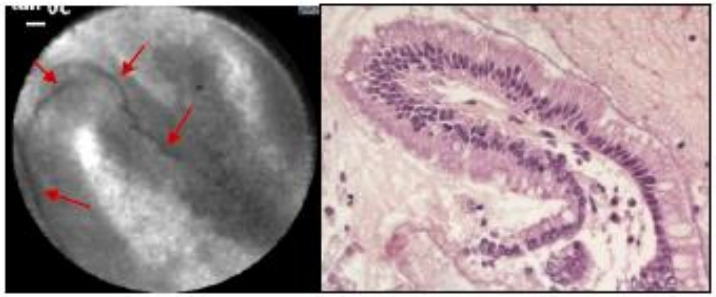
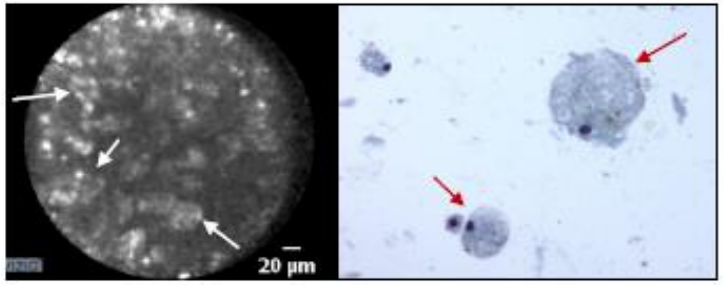
Konda VJ, et al. Endoscopy 2013.
Napolean B, et al. Endoscopy 2015.

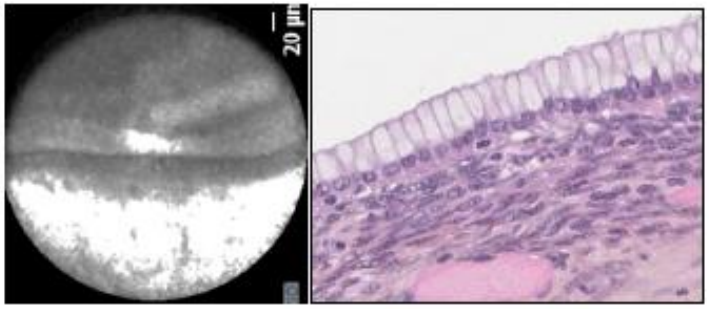
nCLE criteria for pancreatic CL diagnosis



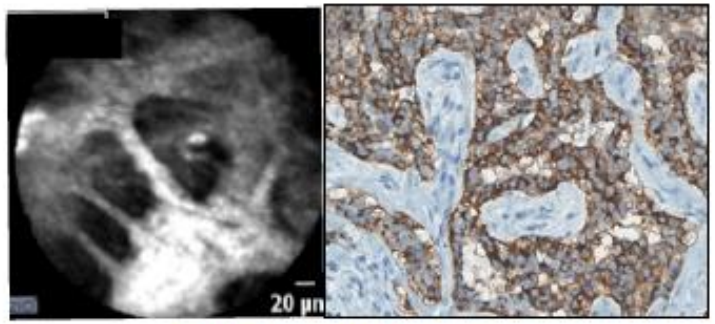
Papillae = IPMN



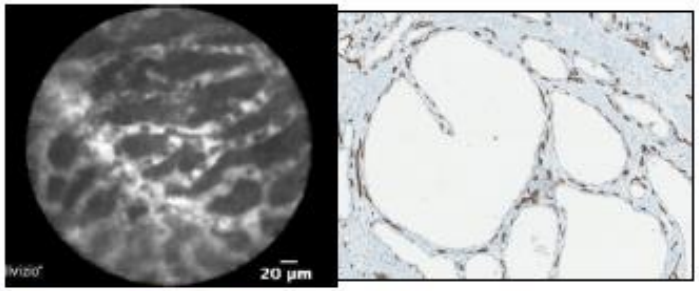
Field of bright, gray,black particules = PC



Epithelial border = MCN



Black cell clusters
with white fibrous areas and vessels = NEN

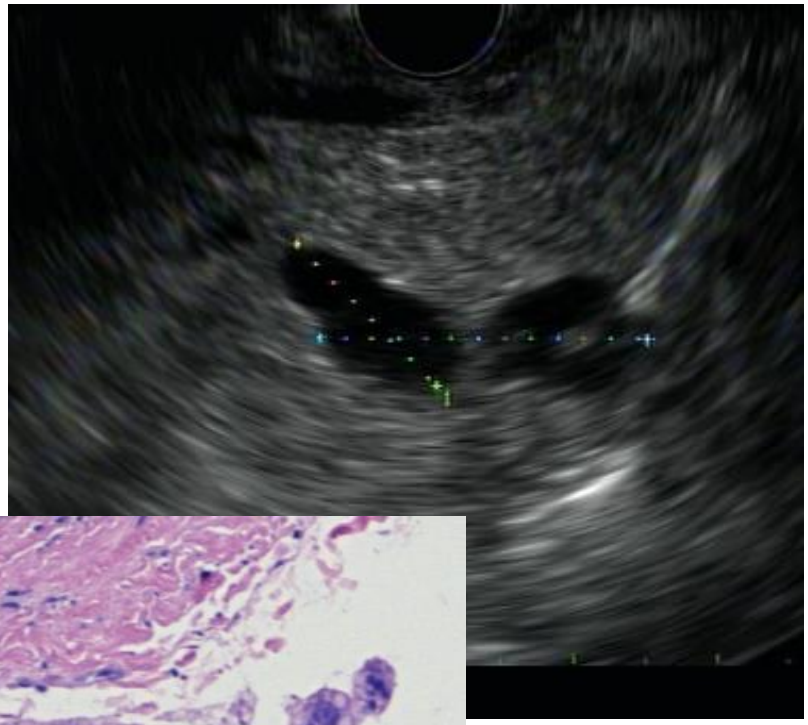


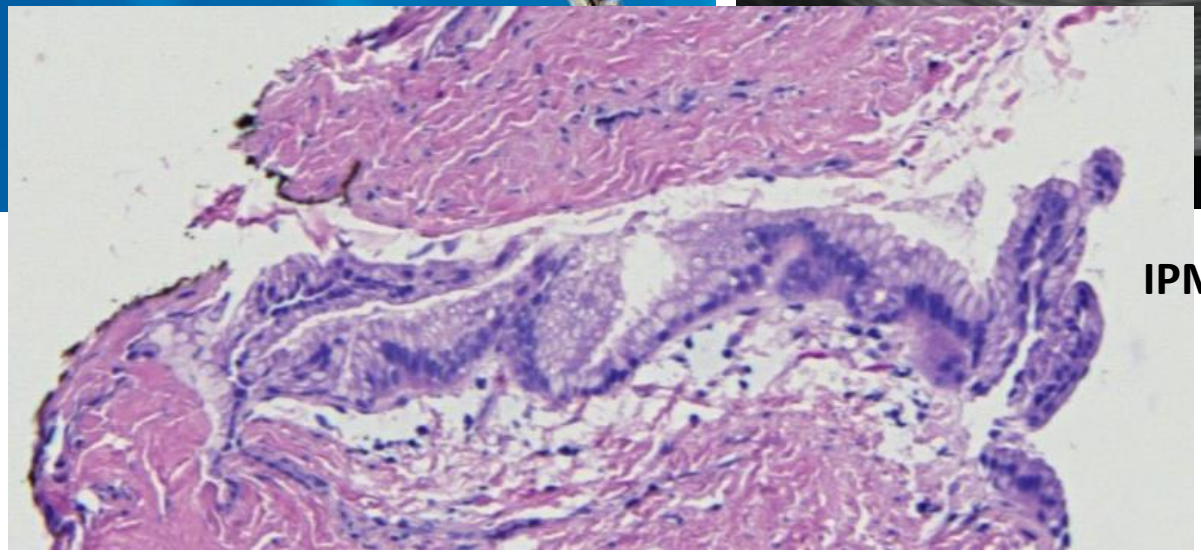
Superficial Vascular Network = SCA

Konda V.J. et al. Endoscopy 2013,
Napoléon B. et al. Endoscopy 2015,
Napoléon B et al. Surg Endosc 2016

Kadayifci A, et al Surg Endosc 2017
Krishna S et al WJG 2017

Through-The-Needle Microforceps





IPMN w/LGD (gastric type)

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EUS-GUIDED MICROFORCEPS BIOPSY AND NEEDLE-BASED CONFOCAL LASER ENDOMICROSCOPY SIGNIFICANTLY IMPROVE THE DIAGNOSTIC YIELD AND HAVE MAJOR IMPACT ON CLINICAL MANAGEMENT OF PANCREATIC CYSTIC LESIONS

Authors: Antonio R. Cheesman, MD[1], Hongfa Zhu, MD, PhD[2], Nikhil A. Kumta, MD, MS[1], Satish Nagula, MD[1], Christopher J. DiMaio, MD[1]

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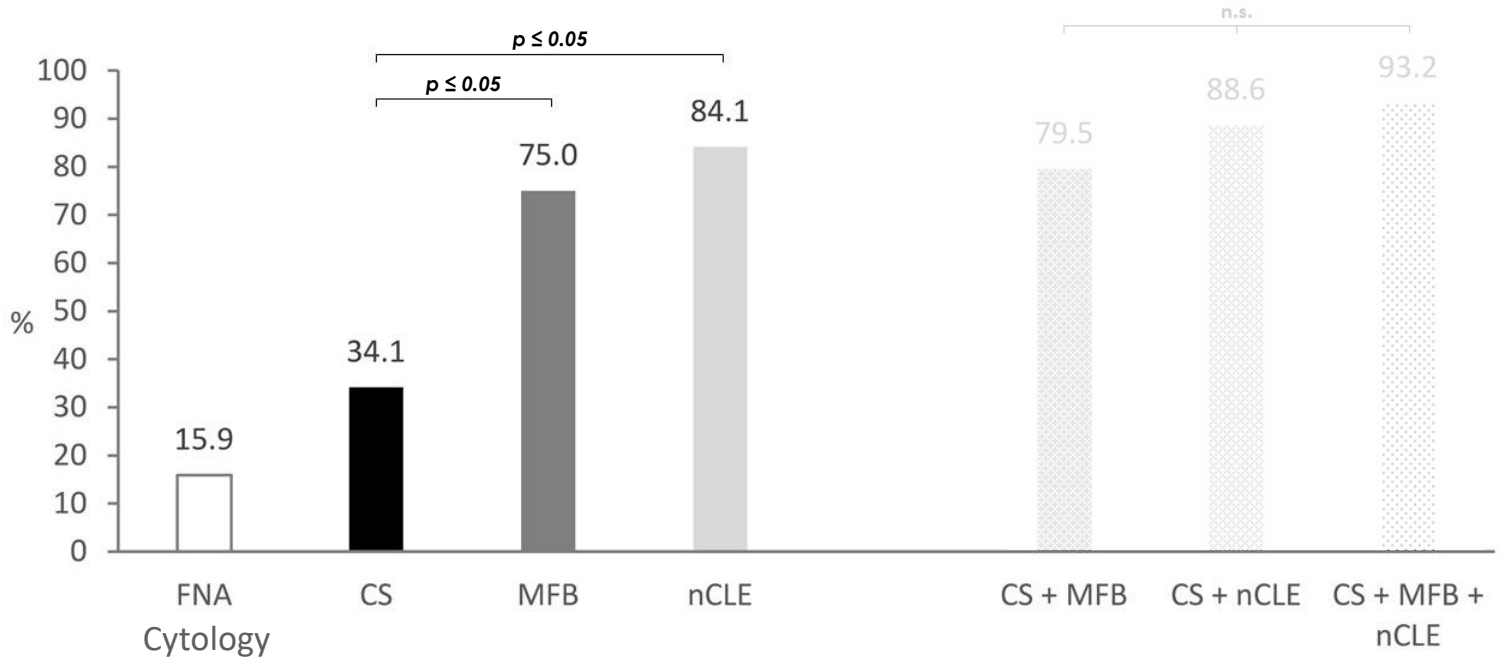
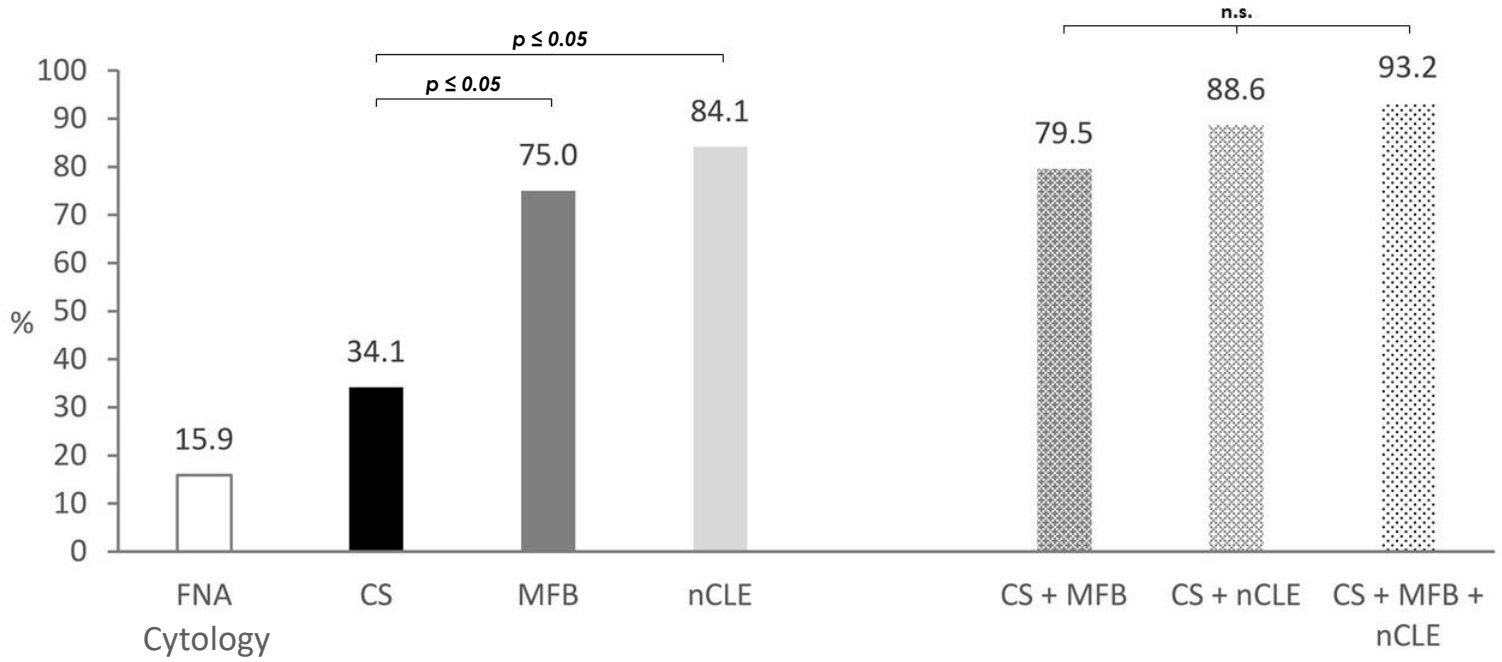
Diagnostic yield of FNA cytology, current standard, MFB and nCLE for PCLs



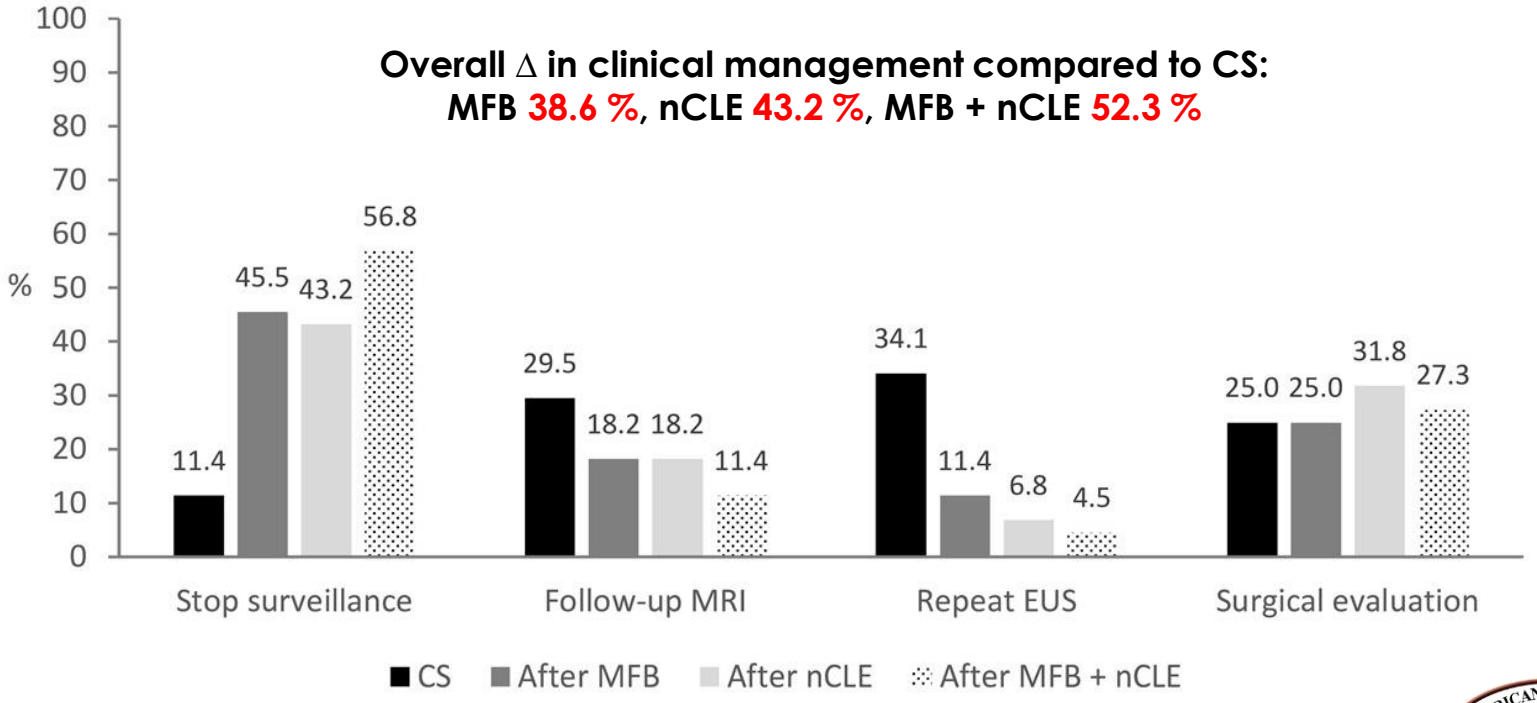
CS = Current standard

Diagnostic yield of FNA cytology, current standard, MFB and nCLE for PCLs



CS = Current standard

Clinical management of patient cohort based on current standard vs. MFB, nCLE and MFB/nCLE



CS = Current standard

Conclusions

- **Use of combined EUS-guided FNA, MFB and nCLE appears safe**
- **Diagnostic yield:**
  - **Current evaluation of PCLs including EUS-FNA is suboptimal** (34.1 %)
  - **Significant improvement with use of adjunct MFB** (79.5 %) **or nCLE** (88.6 %)
  - **No significant difference between either of these**
- **Clinical management**
  - **Significant changes in management from MFB** (38.6 %) **and nCLE** (43.2 %) **use**
  - **Reclassification of indeterminate lesions → discontinuation of surveillance**

Consider MFB or nCLE when performing EUS-FNA of PCLs

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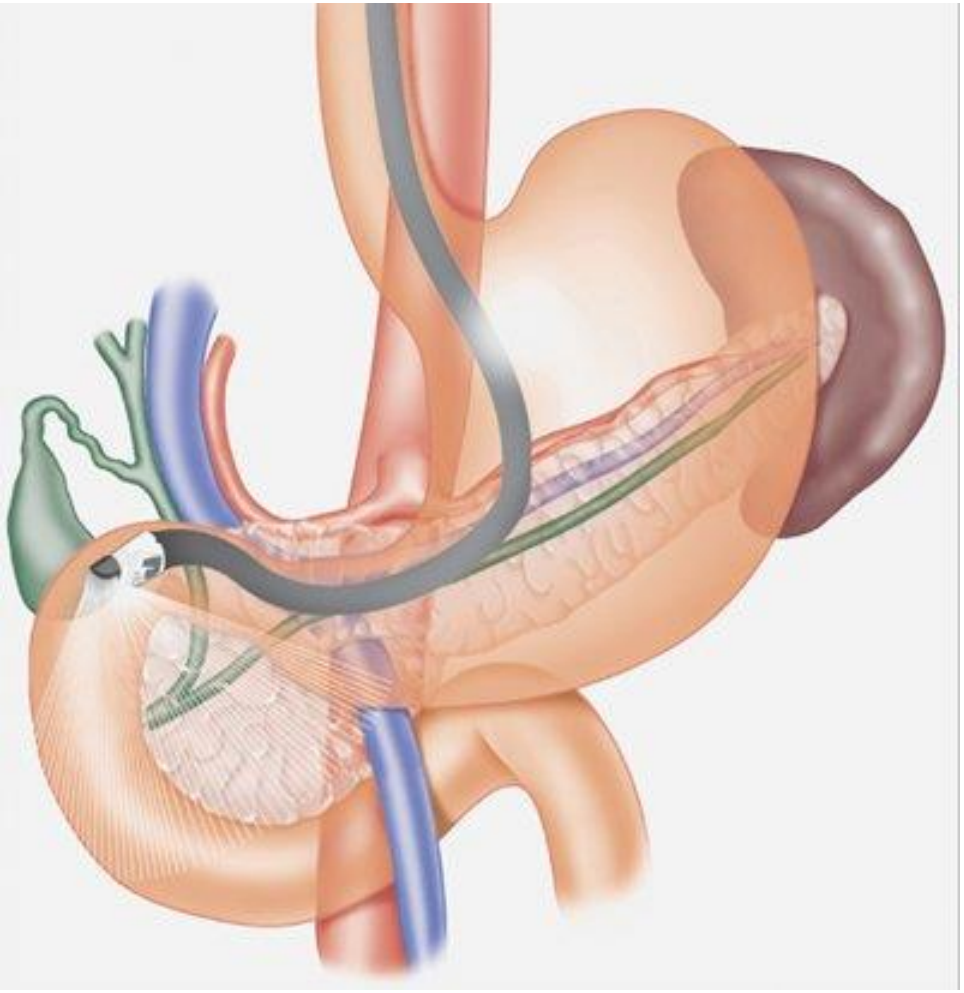
Therapeutic EUS



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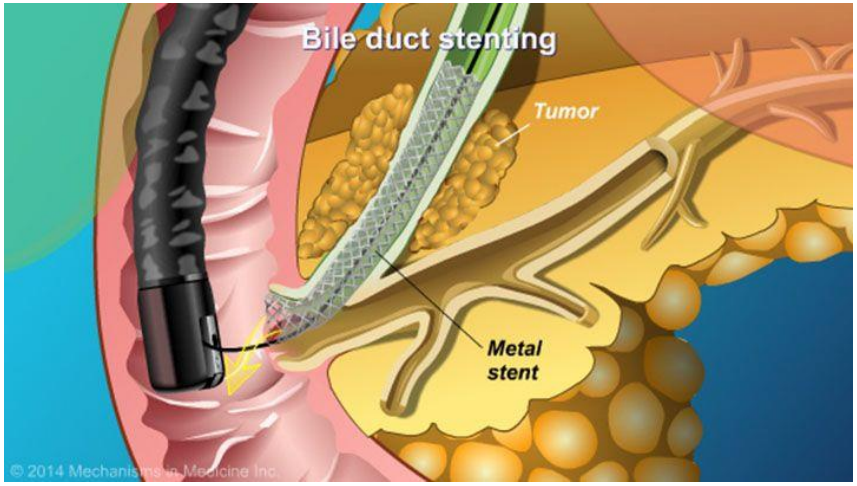
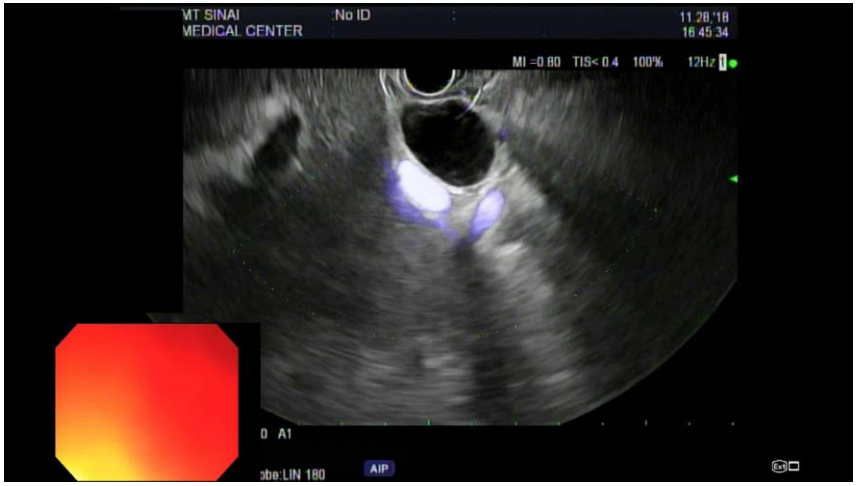
Drainage of Malignant Biliary Obstruction

ERCP/metal stent



EUS-guided biliary drainage



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Results

- 5 studies with 361 patients were included in meta-analysis and systematic review
- Comparable technical and clinical success in both groups.
- Comparable rates of adverse outcomes and reintervention rate.
- No difference in non-pancreatitis related adverse events.

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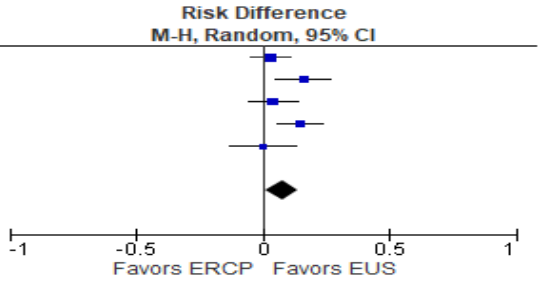
Results

Procedure-related pancreatitis

Study or Subgroup	ERCP Events	ERCP Total	EUS Events	EUS Total	Weight	Risk Difference M-H, Random, 95% CI
Bang,	1	34	0	33	24.3%	0.03 [-0.05, 0.11]
Kawakubo	9	56	0	26	18.4%	0.16 [0.05, 0.27]
Nakai	1	25	0	34	20.4%	0.04 [-0.06, 0.14]
Paik	9	61	0	64	21.5%	0.15 [0.06, 0.24]
Park,	0	14	0	14	15.4%	0.00 [-0.13, 0.13]
Total (95% CI)		**190**		**171**	**100.0%**	**0.08 [0.01, 0.14]**
Total events	20		0			

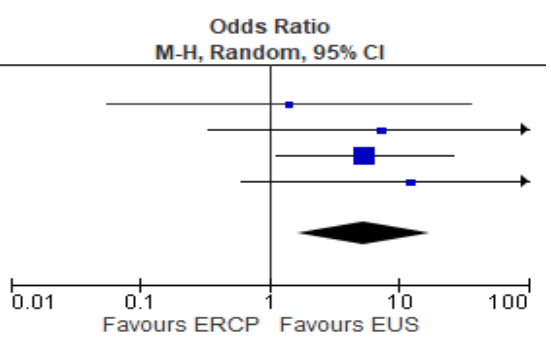
Heterogeneity: Tau² = 0.00; Chi² = 8.89, df = 4 (P = 0.06); I² = 55%
Test for overall effect: Z = 2.27 (P = 0.02)



Tumor overgrowth requiring reintervention

Study or Subgroup	ERCP Events	ERCP Total	EUS Events	EUS Total	Weight	Odds Ratio M-H, Random, 95% CI
Bang,	0	34	0	33		Not estimable
Kawakubo	1	56	0	26	13.4%	1.43 [0.06, 36.35]
Nakai	2	25	0	34	14.8%	7.34 [0.34, 159.92]
Paik	9	61	2	64	56.5%	5.37 [1.11, 25.94]
Park,	4	14	0	14	15.3%	12.43 [0.60, 256.66]
Total (95% CI)		**190**		**171**	**100.0%**	**5.35 [1.64, 17.50]**
Total events	16		2			

Heterogeneity: Tau² = 0.00; Chi² = 0.98, df = 3 (P = 0.81); I² = 0%
Test for overall effect: Z = 2.78 (P = 0.006)



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Conclusions

- EUS can potentially be used as an alternative to ERCP as the first line palliative modality for MBO.

- Larger studies are needed to assess the impact of EUS-BD in patients with resectable disease.

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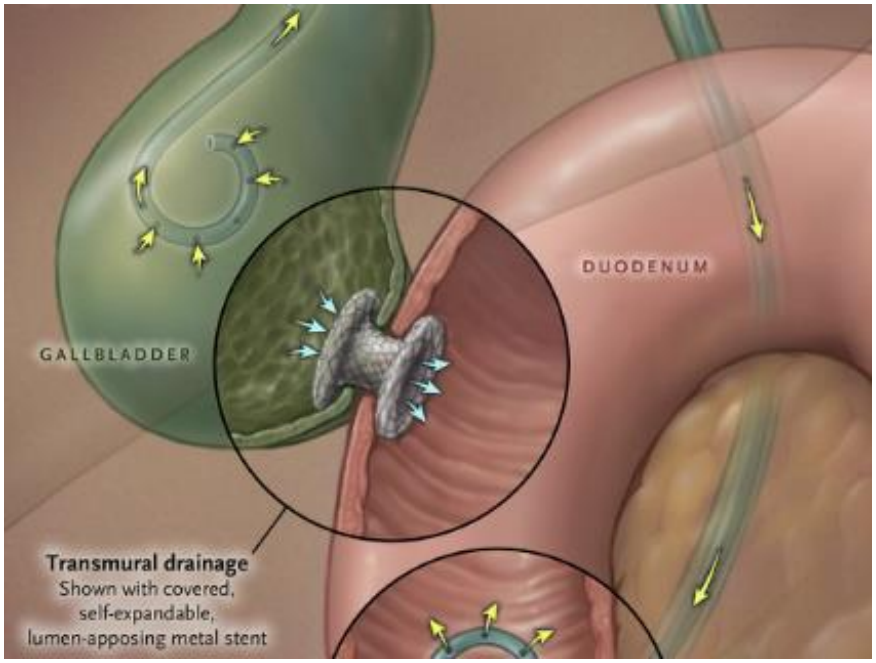
EUS-Guided Gallbladder Drainage



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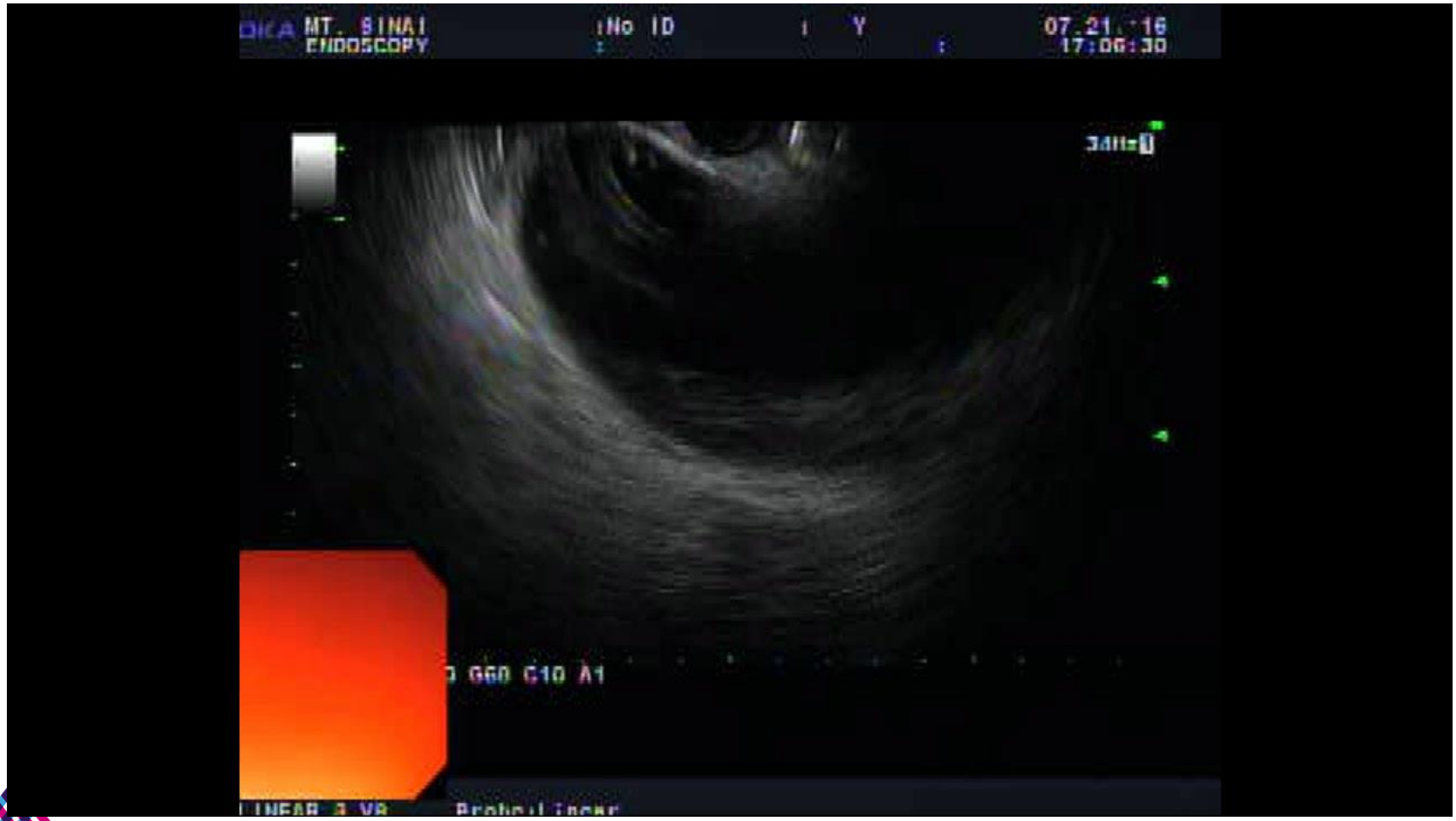
EUS-GB with LAMS



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Endosonography-guided gallbladder drainage reduced adverse events as compared to percutaneous cholecystostomy (PC) in patients suffering from acute cholecystitis that are at high risk for surgery. A randomized controlled trial (DRAC).

Teoh AY[1], Kitano M[2], Itoi T[3], Perez- Miranda M4, Ogura T[5], Chan SM[1], Serna-Huguera C[2], Omoto S[6], Torres-Yuste R[2], Tsuchiya T[3], Leung CH[1], Chiu PY [1], Ng EKW[1], Lau JYW[1]

[1]Department of Surgery, Prince of Wales Hospital, The Chinese University of Hong Kong, Hong Kong.
[2]Second Department of Internal Medicine, Wakayama Medical University School of Medicine, Japan.
[3]Department of Gastroenterology and Hepatology, Tokyo Medical University, Japan
[4]Department of Medicine, University Hospital Rio Hortega, Valladolid, Spain.
[5]Second Department of Internal Medicine, Osaka Medical College, Takatsuki, Japan
[6]Department of Gastroenterology and Hepatology, Kindai University, Japan

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EUS-Guided Gallbladder Drainage

- Hypothesis
  - EUS-guided gallbladder drainage (EUS-GBD) would reduce 1-year adverse events as compared to percutaneous gallbladder drainage (PT-GBD)

- Aim
  - To compare the outcomes of EUS-GBD vs PT-GBD in treatment of acute calculous cholecystitis in patients that are very high-risk for cholecystectomy

- Prospective, RCT

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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

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	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	

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Conclusions

- At 1 year, EUS-GBD reduced adverse events, recurrent acute cholecystitis, re-interventions and unplanned admissions.
- In the shorter term, it reduced 30-day adverse events, had lower post-procedural pain scores and analgesic requirements
- These findings support the use of this modality as a definitive treatment for acute cholecystitis in those patients that cannot receive cholecystectomy.
- EUS-GBD should be the procedure of choice in these patients provided that the expertise is available.

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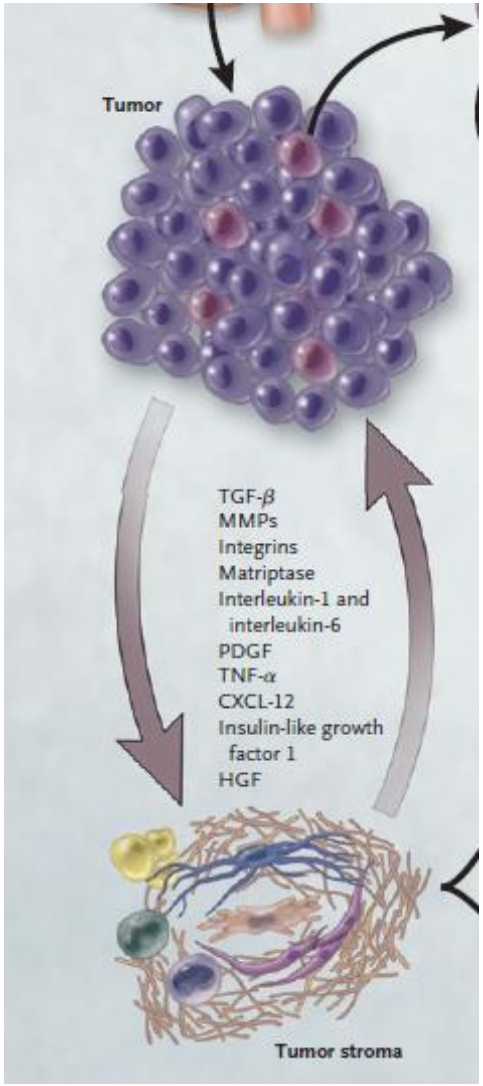
Pancreatic Cancer

- Current therapies…
  - Suboptimal
    - Dense stroma
    - Poorly vascularized
  - Systemic toxicity

- Potential solution…
  - Direct intra-tumoral therapy
  - High local concentrations
  - Minimize systemic toxicity



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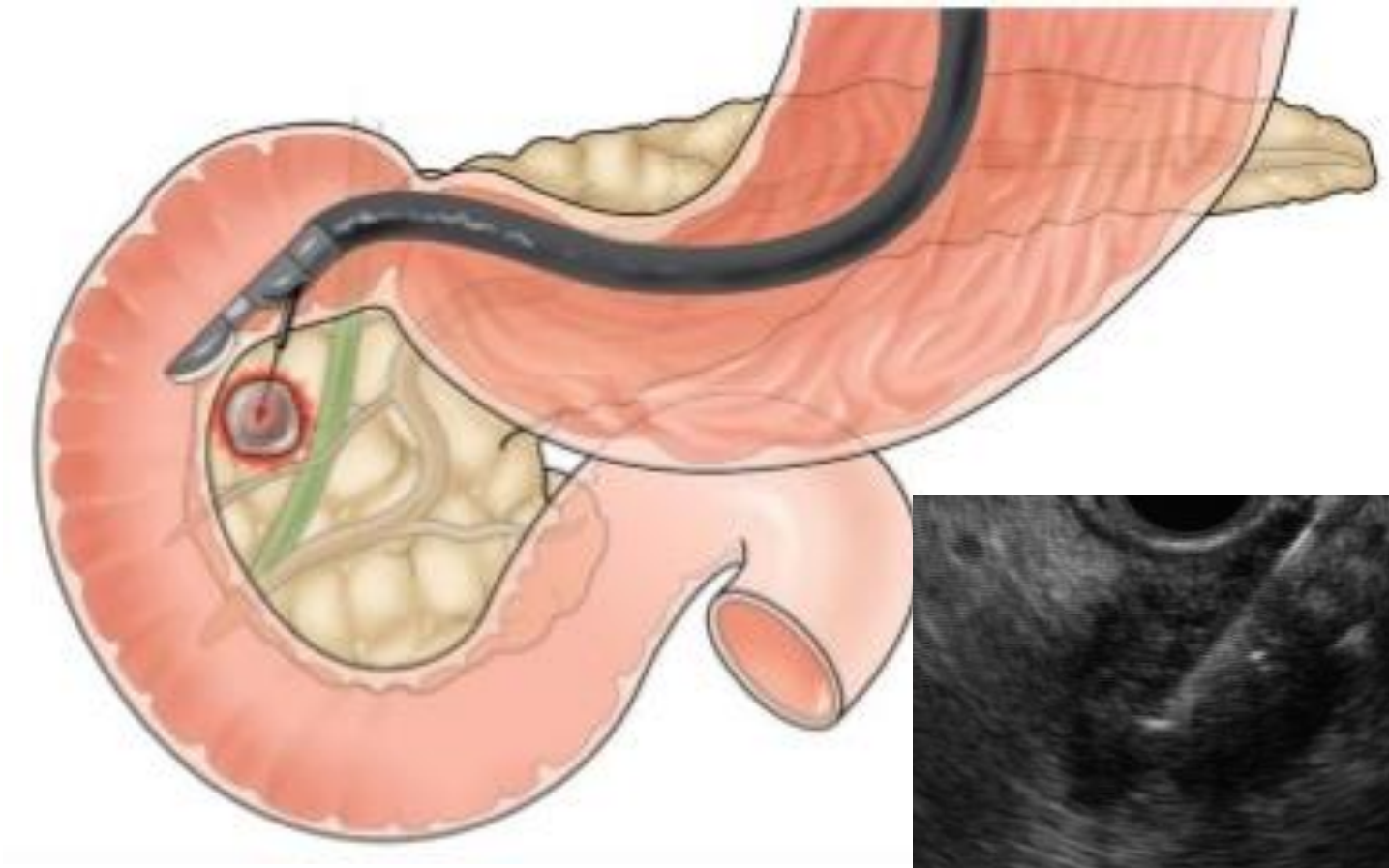
EUS-Guided Tumor Ablation



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EUS-GUIDED RADIOFREQUENCY ABLATION PLUS CHEMOTHERAPY VERSUS CHEMOTHERAPY ALONE FOR UNRESECTABLE PANCREATIC CANCER (ERAP): PRELIMINARY RESULTS OF A PROSPECTIVE COMPARATIVE STUDY

Pradermchai Kongkam[1,2], Kasenee Tiankanon[1], Arlyn R. Cañones[1], Thanawat Luangsukrerk[1], Dong Wan Seo[4], Chonnipa Nantavithya[3], Trirat Jantarattana[6], Virote Sriuranpong[5], Phonthep Angsuwatcharakon[1], Wiriyaporn Ridtitid[1], Pinit Kullavanijaya[1], Rungsun Rerknimitr[1]

Table 2. Outcomes of patients with pancreatic cancer receiving EUS-guided radiofrequency ablation plus chemotherapy (group A) versus chemotherapy alone (group B)

Parameters	Group A (RFA+CMT) (n = 10)	Group B (CMT) (n = 10)	p Value
Median of morphine equivalent analgesia dosage reduction (mg/day(range)) (n = 7)*	15 (0 to 60)	0 (-20 to 30)	.005
Median percentage of morphine equivalent analgesia dosage reduction (%(range)) (n = 7)*	50% (37.5 to 100)	0% (-100 to -42.9)	.007
Mean maximal diameter of target lesion before and after treatment (mm.)	63.1 ± 20.3 vs 66.4 ± 22.0 (p = NS)	53.0 ± 20.7 vs 59.2 ± 16.6 (p = 0.039)	N/A
Mean tumor volume before and after treatment (ml)	97.1 ± 70.1 vs 120.2 ± 65.4 (p = NS)	76.3 ± 77.0 vs 91.1 ± 83.6 (p = 0.014)	N/A
6-months survival rate	70%	70%	NS

Abbreviation: RFA = radiofrequency ablation, CMT = chemotherapy, vs = versus, NS = not significant *Patients underwent celiac plexus neurolysis were excluded.

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