Manipal Journal of Medical Sciences

Volume 3 | Issue 2 Article 1

12-1-2018

Utility of endoscopic ultrasound in Hepato-Pancreatico-Biliary (HPB) diseases

Suresh Vasan Venkatachalapathy
Nottingham Digestive Diseases Centre (NDDC) and NIHR Nottingham Biomedical Research Centre (BRC), Nottingham University and Nottingham University Hospitals NHS Trust Queen's Medical Centre, Derby Road, Nottingham NG2 7UH, guru.aithal@nottingham.ac.uk

Andrew Baxter
Nottingham Digestive Diseases Centre (NDDC) and NIHR Nottingham Biomedical Research Centre (BRC), Nottingham University and Nottingham University Hospitals NHS Trust Queen's Medical Centre, Derby Road, Nottingham NG2 7UH, guru.aithal@nottingham.ac.uk

Guruprasad p. Aithal
Nottingham Digestive Diseases Centre (NDDC) and NIHR Nottingham Biomedical Research Centre (BRC), Nottingham University and Nottingham University Hospitals NHS Trust Queen's Medical Centre, Derby Road, Nottingham NG2 7UH, guru.aithal@nottingham.ac.uk

Review Article

Utility of endoscopic ultrasound in Hepato-Pancreatico-Biliary (HPB) diseases

Suresh Vasan Venkatachalapathy, Andrew Baxter, Guruprasad P Aithal*

Email: guru.aithal@nottingham.ac.uk

Abstract

Endoscopic Ultrasound (EUS) has been used to diagnose benign and malignant Hepato-Pancreato-Biliary (HPB) conditions for over 20 years. EUS allows close access to pancreas, gall bladder, left lobe of the liver and bile duct. In particular, it is possible to sample these and other retroperitoneal tissue safely. With the introduction of novel fork-tip and Franssen type cutting needles, the diagnostic yield has improved significantly to greater than 95%. Hence, it has become the investigation of choice for pancreatic pathology. Contrast Enhanced EUS (CE-EUS) may help differentiating malignant tumours from slow growing tumours such as neuroendocrine tumours and inflammatory lesions. In addition, linear EUS has been used in a wide range of therapeutic procedures such as drainage of pancreatic fluid collections, gall bladder empyema, biliary drainage, treatment of pancreato-biliary tumours and coeliac plexus block/neurolysis for pain control. In this review, we will review the diagnostic and therapeutic use of EUS in HPB conditions.

Key words: Endoscopic ultrasound, therapeutic EUS, tissue acquisition with EUS

Introduction

Intraluminal ultrasound was first used in 1956 for the diagnosis of rectal cancer and in 1976, with an ultrasound probe down the accessory channel of a therapeutic gastroscope, for investigation of a pancreatic lesion.[1,2] Development in endoscopic ultrasound (EUS) was rapid and was initially used as a diagnostic modality for identifying benign and malignant gastrointestinal (GI) condition. The invention of linear echoendoscope facilitated the endo-sonographer to acquire tissue from the lesions.

The EUS probes have either radial arrays (radial) or curvy linear arrays (linear). Radial echoendoscopes lack an accessory channel and their use is limited to imaging, whereas the linear endoscopes have a channel positioned, so that instruments advance in the same plane as the ultrasound image, allowing visualization of the area of interest and the instrument simultaneously and therefore opening up therapeutic interventions. There is no significant difference in imaging accuracy between either array.[3] Radial arrays are more commonly used in staging of luminal lesions and linear arrays are more commonly used to acquire tissue for histology and for therapeutic interventions.

Contrast enhanced EUS (CE-EUS) was first reported in 1997.[4] Intra-arterial CO_2 microbubbles and later with the advent of power doppler sonography and increasingly high frequency probes, venous infusion with novel contrast agents (Sonoview) has been used as adjuncts in the diagnosis of cystic and malignant lesions in pancreas. [5]

EUS has become an important tool and often aid in the therapeutic management of various Hepatico-Pancreato-Biliary conditions (HPB). The recent advances in the accessories have facilitated improvements in the therapeutic role of EUS. The advantages of EUS over other modalities are it provides safe GI access as opposed to percutaneous

Suresh Vasan Venkatachalapathy, Andrew Baxter, Guruprasad P Aithal

Nottingham Digestive Diseases Centre (NDDC) and NIHR Nottingham Biomedical Research Centre (BRC), Nottingham University and Nottingham University Hospitals NHS Trust Queen's Medical Centre, Derby Road, Nottingham NG2 7UH

*Corresponding Author

Manuscript received : 24/10/18
Revision accepted : 18/11/2018

How to cite this article: Venkatachalapathy S V, Baxter A, P Aithal G. Utility of Endoscopic Ultrasound in Hepato-Pancreatico-Biliary (HPB) Diseases. *MJMS*. 2018; 3(2): 38-46.

CT or ultrasound guided access (lower adverse event rate).[6] It provides close access to retroperitoneal structures such as pancreas, left adrenal, coeliac plexus, left lobe of the liver, gall bladder and lower biliary tract which enables the endo-sonographer to provide minimally invasive treatment which would have otherwise be treated with either surgery or interventional radiology.

EUS has a wide range of applications and in this article; we will limit our review to the diagnostic and therapeutic use of EUS in HPB conditions.

Choledocholithiasis

The prevalence of choledocholithiasis is 5-25% in patients undergoing Cholecystectomy for gall stone disease.[7] Ten percent of those patients who have gallstones may have stones in the bile duct.[8] Transabdominal ultrasound (USG) and computed tomography (CT) are less sensitive in diagnosing choledocholithiasis compared to EUS. The sensitivity of EUS in picking up choledocholithiasis is 96% as compared to 71 and 63% for CT and USG respectively.[9] EUS is marginally superior to magnetic resonance cholangio-pancreatogram (MRCP) for diagnosing small CBD stones and microlithiasis (accuracy 93.3% vs. 89%, NPV 97% vs. 87.8%).[10] Many centres have combined EUS and endoscopic retrograde cholangio-pancreatography (ERCP) procedures for suspected CBD stone disease. Patients will have EUS first and if there are CBD stones, will proceed to ERCP. A retrospective study on 206 patients demonstrated that such an approach is safe in elderly population.[11] The procedure can be done with conscious sedation. The procedure related complications and sedation related complications were not different to either ERCP or EUS done alone.[12]

Staging of pancreatic cancer and tissue acquisition

EUS can be used to assess the vascular invasion of the coeliac artery, superior mesenteric artery (SMA) and portal vein (PV) in patients with pancreatic cancer. In a recent study, the diagnostic accuracy of EUS in assessing SMA involvement was 87% and the PV involvement was 92%.[13] However, considering well described limitations of individual imaging modalities in the staging of pancreatic cancer, EUS is used to assist decision making in selected patients where staging from cross sectional imaging is equivocal and risks of an exploratory laparotomy with an intention to resect are deemed substantial.

Contrast enhanced EUS (CE-EUS) may help differentiating malignant tumours from slow growing tumours such as neuroendocrine tumours and inflammatory lesions. Normal tissue has a homogenous enhancement during the arterial phase. Ductal adenocarcinomas are hypo-enhancing, inflammatory lesions are iso or hyper-enhancing and neuroendocrine tumours show hyper-enhancement. A retrospective study involving 210 patients reported that the sensitivity, specificity and diagnostic accuracy of CE-EUS in differentiating pancreatic cancer from neuroendocrine tumours and mass forming pancreatitis was 83%, 87% and 84% respectively.[14] EUS elastography can be an added adjunct for differentiating malignant lesions from benign pancreatic lesions. Malignant lesions are likely to have higher stiffness compared to benign lesions. It is easier to demonstrate with new generation stacks. A retrospective study of 218 patients reported that the sensitivity, specificity, PPV and NPV for high stiffness in identifying malignancy was 84%, 67%, 56% and 89% respectively.[15] A prospective study on 62 patients reported that combining the CE-EUS and elastography improved the diagnostic accuracy to 92% in diagnosing pancreatic malignancies.[16]

The advantage of EUS over other imaging modalities is the opportunity for sampling to confirm the diagnosis. A recent meta-analysis on 828 patients on EUS guided fine needle biopsy (FNB) of pancreatic lesions reported a sensitivity of 85% and a specificity of 98%.[17] However, the new generation fork tip cutting needles may have a higher diagnostic yield compared to the conventional needles. A prospective study comparing the new needle and historic fine needle aspiration (FNA) samples reported a diagnostic yield of 96% vs. 88%.[18]Another case-control study reported similar histological yield for the fork tip needle (Figure 1) but with reduced number of passes compared to the FNA needle (95% vs. 59%, P=0.01).[19] A retrospective study on FNB needle showed that the sample was adequate in 90%

of the patients. The sensitivity and specificity for diagnosis was 93% and 100% respectively.[20]

Figure 1: Fork tip needle

Chronic pancreatitis (CP)

EUS allows close assessment of the structure and architecture of the pancreas providing information of pancreatic parenchyma, pancreatic duct (PD), calcification, cysts and strictures. It is more sensitive and has comparable specificity in diagnosing chronic pancreatitis than CT or MRI.[21] Parenchymal features of chronic pancreatitis notable on EUS include hyperechoic foci, stranding, lobularity, honeycombing (contiguous lobularity) and cyst formation. The ductal features of chronic pancreatitis are PD stones, dilatation of PD and side branches, irregular main PD contour and hyperechoic duct margins. Rosemount criteria are widely used to diagnose CP using EUS.[22] As these are based on a subjective assessment, there is an inter-observer variability which may be one of the limiting factors of EUS as a test in this scenario. A prospective study comparing EUS features against endoscopic pancreatic function test reported that the specificity and negative predictive value of CP was 100% if they have more than five EUS features of CP on EUS.[23]

EUS elastography may have a role as an adjunct to conventional EUS. Elastography assesses the strain in the tissue arising from compression. It can also be quantitatively assessed by calculating the strain ratio between the region of interest and reference area. A prospective study on 191 patients with CP showed a significant linear correlation between number of criteria and strain ratio ($r=0.813$; $P<0.0001$). The overall diagnostic accuracy for EUS-elastography in diagnosing CP was 91.1%.[24]

A prospective observational study on 115 patients with CP reported that there was a direct relationship between strain ratio and pancreatic exocrine insufficiency (PEI). The probability of PEI rose from 4.2% if their strain ratio was less than 2.5 to 93% and if their SR was greater than 5.5%.[25]

Drainage of pancreatic fluid collections

Pancreatic fluid collections (PFC) develop secondary to pancreatic duct injury and are classified in to acute peri-pancreatic fluid collections, acute necrotic collection, walled off necrosis (WON) and pseudocysts (PP).[26] Acute peri-pancreatic and acute necrotic collections develops within four weeks of the attack of pancreatitis and do not have well defined walls around the collection. They may not need any intervention unless they are infected and may resolve on its own. Walled off necrosis and pseudocysts develop after four weeks of the acute insult and are more organized and may take several weeks to months to resolve spontaneously. In symptomatic patients, these need to be drained.

In the past, symptomatic walled off necrosis and pseudocysts were drained either through surgical cyst gastrostomy or percutaneous drainage under CT or ultrasound guidance. EUS guided drainage of PFC was first reported in 1992.[27] The advantages of EUS were it allowed the endo-sonographers have close access to the collection, visualize the collection, avoid blood vessels and deploy stent under x-ray guidance. Since then, there have been many studies reporting EUS guided drainage with success rates of 80-100% and complication rates of 10-20%. [28-30]

A randomised controlled trial in 2013 comparing surgical cyst gastrostomy with EUS-cyst gastrostomy reported a reduced morbidity and length of stay associated with the EUS based approach.[31] The TENSION trial which compared surgical with endoscopic step up approach, reported reduced length of stay, reduced rate of pancreatic fistula formation and a significant reduction in costs with endoscopic step up approach even though superiority of the endoscopic step up group was not shown.[32] Hence, EUS guided drainage is increasingly used as first line treatment in the management of PFC.

The different types of stents used in the drainage of PFC include plastic double pigtail stents, fully covered self-expanding metal stents (FC-SEMS) and lumen apposing metal stents (LAMS). Plastic stents are as efficacious as metal stents (Figure 2) in the drainage of uncomplicated pseudocysts. However, they are less efficacious and have a high serious adverse event if the collection is infected or if it is a walled off necrosis.[33]A retrospective comparative study reported that double pigtail stents were the sole negative predictive factor in the drainage of walled off necrosis, on multivariate analysis.[33]

Although FC-SEMS are effective allowing for effective debridement, risk of stent migration between 10-20% remains an issue. Three retrospective studies reported a success rate of 80-94% for the drainage of PFC with a serious adverse event rate of 20%.[30,34,35]

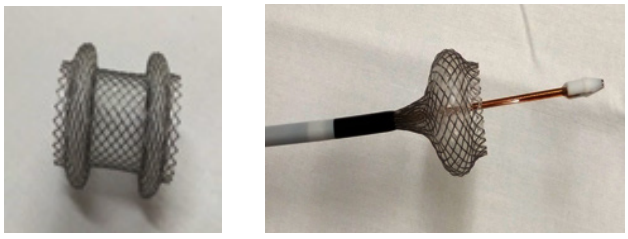

Figure 2: LAMS LAMS partially deployed

High rates of stent migration have led to increasing use of LAMS which were designed to reduce stent migration. Multiple studies have reported a technical success rate of 97-99%, clinical success rates of 91-94% reducing serious adverse event rates to 8-11% and stent migration rates to 5-7%. A recent retrospective study of 313 patients comparing plastic stents to two forms of metal stents in the drainage of WON reported that the mean number of endoscopic procedures (direct endoscopic necrosectomy) required for the resolution of the collections was significantly lower in the LAMS group compared to the FC-SEMS or plastic stent groups (2.2 vs. 3 vs. 3.6, respectively; P =0.04).[33]

Irrespective of the stent used, EUS guided drainage of PFC is minimally invasive, associated with reduced mortality, reduced morbidity, reduced length of stay in hospital and reduced SAE compared to surgical or radiological intervention.

Gall bladder drainage

The treatment of choice for acute cholecystitis is cholecystectomy, but in a small proportion of patients this may not be possible because of old age and comorbidities. The alternative treatment is radiologically guided percutaneous drainage of the gall bladder especially if they have gall bladder empyema. EUS guided gall bladder drainage was first reported in 2007 has advantages over percutaneous intervention. It does not require external drain and offer Transmural drainage in to the GI tract which is associated with reduced length of stay, fewer interventions and adverse events compared to percutaneous cholecystostomy or trans-papillary endoscopic cystic duct drainage.[41-43]A multi-centre prospective study assessing the long term efficacy of LAMS reported a technical success rate of 90% and clinical success rate of 96%.[44]

Biliary drainage

ERCP is the conventional mode of achieving biliary drainage when patients present with obstructive jaundice secondary to malignant biliary obstruction.

Table 1: Technical and clinical success rate of fully covered metal stent (FCSEMS) and lumen apposing metal stent (LAMS)

Author	Year	Stent type	Study design	Single centre/	Sample Size	Technical success %	Clinical success %	SAE %	Stent
Venkatachalapathy[36]	2018	LAMS	R	M	116	99	94	11.2	6.4
Siddiqui[37]	2016	LAMS	R	M	82	98.7	N/A	9.8	2.4
Sharaiha[38]	2016	LAMS	R	M	124	100	86.3	18.5	5.6
Rinninella[39]	2015	LAMS	R	M	93	98.7	92.5	5.3	N/A
Shah[40]	2015	LAMS	R	M	33	91	91	6.4	3.22
Vazquez-sequeiros[35]	2016	FCSEMS	R	M	211	97	85	25	5
Huggett[30]	2015	FCSEMS	R	M	19	100	N/A	26	20
Chandran[34]	2014	FCSEMS	R	M	47	98.1	76.6	24.2	18.5

R=Retrospective, P=Prospective, M= Multi-centre, S= Single centre

ERCP-guided biliary drainage is successful in 80-90% of cases, but selective bile duct cannulation may not be possible because of altered anatomy, duodenal obstruction, duodenal diverticulum, distorted ampulla, failed cannulation and *in situ* duodenal stents. Hence, in up to one in five patients biliary drainage may not be possible with ERCP.

Percutaneous transhepatic cholangiography (PTC) approach has a success rate of 88-98% in achieving biliary drainage; in those patients who had a failed ERCP. The major complication rate varies from 8-35% and a recent study from United Kingdom, using hospital episode statistics (HES) on 16,363 patients, reported inpatient mortality of 15%, 30-day mortality of 23.1% and a major complication rate of 35%.

EUS-BD (EUS biliary drainage or choledochoduodenostomy) was first described in 2001[45]and since then several studies have reported outcomes on EUS-guided biliary drainage in patients who had a failed ERCP. There are three modes one can establish biliary drainage. They are 1. Transduodenal route for distal CBD strictures (choledocho-duodenostomy), 2. Trans-gastric route for hilar strictures (hepatico-gastrostomy) and 3. EUS guided rendezvous especially for patients who have diverticulum or in those where the ampulla is not visible. Two systematic reviews and meta-analysis comparing EUS-BD and percutaneous approach; involving 9 studies (483 patients) and 6 studies (312 patients) reported that there was no difference in technical success between the two procedures but EUS BD was associated with better clinical success, lower re-intervention rate and reduced moderate to serious adverse event rate.[46,47]A multicentre randomized control trial comparing EUS-BD vs. ERCP showed marginally higher success rate, reduced adverse event rate(6.3% vs. 19.7%, P = 0.03) and reduced post procedure pancreatitis rate (0 vs. 14.8%) in the EUS-BD group.[48]

EUS guided coeliac plexus block/neurolysis

The advantages of EUS guided coeliac plexus neurolysis (CPN) over percutaneous approach are that accurate localization of coeliac plexus, clear definition of coeliac axis anatomy and the close proximity of the scope to the coeliac axis. This helps to place the needle (Figure 3) accurately and enhances the spread of injection. Three meta-analysis involving 803 patients reported that in patients with inoperable pancreatic cancer EUS-guided CPN alleviates pain in 70%–80% of patients at 8 weeks. The pain relief was higher in patients who received injections on both sides of coeliac artery.[49-51]

In patients with chronic pancreatitis, the pain relief was 50%–60% at 8 weeks. The main drawback of this treatment is that the pain relief is not permanent and it recurs after 8–12 weeks.

Figure 3: Coeliac plexus neurolysis needle with hole on the side

EUS guided treatment for pancreato-biliary tumours

EUS guided ablation of pancreatic cyst lesions have been reported in literature. Most of the case series used ethanol as an ablation agent. A recent prospective randomized control trial of 39 patients with mucinous cysts comparing alcohol vs. alcohol free (Normal saline) reported a successful ablation rate of 67 vs. 64% complete ablation rate at 6 months. Patients were randomly assigned to 1 of 2 groups that underwent EUS-guided pancreatic cyst lavage with either 80% ethanol (control) or normal saline (alcohol-free group). Cysts in both groups were then infused with an admixture of paclitaxel and gemcitabine. The serious adverse event rate was significantly lower in the alcohol free group.[52]

EUS guided radiofrequency ablation of solid and cystic lesions of the pancreas are being studied but they are not used outside the research studies. CyberKnife stereotactic radiotherapy has been used to treat pancreatic cancers. The radiographic

markers (Fiducial markers) are placed around the tumour to deliver direct beam radiation precisely over the target. As EUS allows close proximity to the lesion, it allows successful placement of these fiducials.[53]

Conclusion

In conclusion, endoscopic ultrasound can be used to diagnose and stage Hepato-Pancreato- Biliary diseases. As it allows the endo-sonographer to achieve close access the retroperitoneal organs, bile duct, liver and gall bladder, it is relatively safe in delivering minimally invasive treatments to the above organs.

References

1. Wild JJ, Reid JM. Diagnostic use of ultrasound. *Br J Phys Med.* 1956;Nov;19(11):248-57.
2. Lutz H, Rösch WJE. Transgastroscopic ultrasonography. 1976;8(04):203-205.
3. Stevens T, Zuccaro G, Jr., Dumot JA, et al. Prospective comparison of radial and linear endoscopic ultrasound for diagnosis of chronic pancreatitis. *Endoscopy.* 2009;41(10):836-841.
4. Hirooka Y, Naitoh Y, Goto H, Ito A, Taki T, Hayakawa T. Usefulness of contrast-enhanced endoscopic ultrasonography with intravenous injection of sonicated serum albumin. *Gastrointest Endosc.* 1997;46(2):166-169.
5. Alvarez-Sánchez M-V, Napoléon B. Contrast-enhanced harmonic endoscopic ultrasound imaging: Basic principles, present situation and future perspectives. *World Journal of Gastroenterology : WJG.* 2014;20(42):15549-15563.
6. Hsu MY, Pan KT, Chen CM, et al. CT-guided percutaneous core-needle biopsy of pancreatic masses: comparison of the standard mesenteric/ retroperitoneal versus the trans-organ approaches. *Clinical radiology.* 2016;71(6):507-512.
7. Everhart JE, Khare M, Hill M, Maurer KR. Prevalence and ethnic differences in gallbladder disease in the United States. *Gastroenterology.* 1999;117(3):632-639.
8. Petelin JBJSE, Techniques OI. Laparoscopic common bile duct exploration. 2003;17(11):1705-1715.
9. Sugiyama M, Atomi Y. Endoscopic ultrasonography for diagnosing choledocholithiasis: a prospective comparative study with ultrasonography and computed tomography. *Gastrointestinal endoscopy.* 1997;45(2):143-146.
10. De Castro VL, Moura EG, Chaves DM, Bernardo WM, Matuguma SE, Artifon EL. Endoscopic ultrasound versus magnetic resonance cholangiopancreatography in suspected choledocholithiasis: A systematic review. *Endoscopic ultrasound.* 2016;5(2):118-128.
11. Iles-Shih L, Hilden K, Adler DG. Combined ERCP and EUS in one session is safe in elderly patients when compared to non-elderly patients: outcomes in 206 combined procedures. *Dig Dis Sci.* 2012;57(7):1949-1953.
12. Che K, Muckova N, Olafsson S, Srikureja W. Safety of same-day endoscopic ultrasound and endoscopic retrograde cholangiopancreatography under conscious sedation. *World journal of gastroenterology.* 2010;16(26):3287-3291.
13. Bodea R, Seicean A, Vasile T, et al. Role of computer tomography and endoscopic ultrasonography in assessing portal and superior mesenteric vessels invasion in cephalo-pancreatic adenocarcinoma. *Annali italiani di chirurgia.* 2017;88:336-341.
14. Ishikawa T, Hirooka Y, Kawashima H, et al. Multiphase evaluation of contrast-enhanced endoscopic ultrasonography in the diagnosis of pancreatic solid lesions. *Pancreatology.* 2018;18(3):291-297.
15. Ignee A, Jenssen C, Arcidiacono PG, et al. Endoscopic ultrasound elastography of small solid pancreatic lesions: a multicenter study. *Endoscopy.* 2018.
16. Iglesias-Garcia J, Lindkvist B, Lariño-Noia J, Abdulkader-Nallib I, Dominguez-Muñoz

JE. Differential diagnosis of solid pancreatic masses: contrast-enhanced harmonic (CEH-EUS), quantitative-elastography (QE-EUS), or both? *United European Gastroenterology Journal*. 2017;5(2):236-246.

17. Yang Y, Li L, Qu C, Liang S, Zeng B, Luo Z. Endoscopic ultrasound-guided fine needle core biopsy for the diagnosis of pancreatic malignant lesions: a systematic review and Meta-Analysis. *Scientific reports*. 2016;6:22978.
18. Adler DG, Muthusamy VR, Ehrlich DS, et al. A multicenter evaluation of a new EUS core biopsy needle: Experience in 200 patients. *Endoscopic ultrasound*. 2018.
19. Kandel P, Tranesh G, Nassar A, et al. EUS-guided fine needle biopsy sampling using a novel fork-tip needle: a case-control study. *Gastrointest Endosc*. 2016;84(6):1034-1039.
20. Kasi M, Fernandez-Sordo JO, Kaye P, et al. PTH-028 A preliminary report on the feasibility and efficacy of the novel eus guided shark core fine needle biopsy. *Gut*. 2017;66(Suppl 2):A219-A219.
21. Issa Y, Kempeneers MA, van Santvoort HC, Bollen TL, Bipat S, Boermeester MA. Diagnostic performance of imaging modalities in chronic pancreatitis: a systematic review and meta-analysis. *European Radiology*. 2017;27(9):3820-3844.
22. Catalano MF, Sahai A, Levy M, et al. EUS-based criteria for the diagnosis of chronic pancreatitis: the Rosemont classification. *Gastrointest Endosc*. 2009;69(7):1251-1261.
23. Conwell DL, Zuccaro G, Purich E, et al. Comparison of endoscopic ultrasound chronic pancreatitis criteria to the endoscopic secretin-stimulated pancreatic function test. *Dig Dis Sci*. 2007;52(5):1206-1210.
24. Iglesias-Garcia J, Domínguez-Muñoz JE, Castiñeira-Alvariño M, Luaces-Regueira M, Lariño-Noia J. Quantitative elastography associated with endoscopic ultrasound for the diagnosis of chronic pancreatitis. *Endoscopy*. 2013;45(10):781-788.
25. Dominguez-Munoz JE, Iglesias-Garcia J, Castineira Alvarino M, Luaces Regueira M, Larino-Noia J. EUS elastography to predict pancreatic exocrine insufficiency in patients with chronic pancreatitis. *Gastrointest Endosc*. 2015;81(1):136-142.
26. 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.
27. Grimm H, Binmoeller KF, Soehendra N. Endosonography-guided drainage of a pancreatic pseudocyst. *Gastrointest Endosc*. 1992;38(2):170-171.
28. Binmoeller KF, Seifert H, Walter A, Soehendra NJGe. Transpapillary and transmural drainage of pancreatic pseudocysts. 1995;42(3):219-224.
29. Varadarajulu S, Rana SS, Bhasin DKJGEC. Endoscopic therapy for pancreatic duct leaks and disruptions. 2013;23(4):863-892.
30. Huggett MT, Oppong KW, Pereira SP, et al. Endoscopic drainage of walled-off pancreatic necrosis using a novel self-expanding metal stent. *Endoscopy*. 2015;47(10):929-932.
31. Varadarajulu S, Bang JY, Sutton BS, Trevino JM, Christein JD, Wilcox CMJG. Equal efficacy of endoscopic and surgical cystogastrostomy for pancreatic pseudocyst drainage in a randomized trial. 2013;145(3):583-590. e581.
32. van Brunschot S, van Grinsven J, van Santvoort HC, et al. Endoscopic or surgical step-up approach for infected necrotising pancreatitis: a multicentre randomised trial. *The Lancet*. 2018;391(10115):51-58.
33. Siddiqui AA, Kowalski TE, Loren DE, et al. Fully covered self-expanding metal stents versus lumen-apposing fully covered self-expanding metal stent versus plastic stents for endoscopic drainage of pancreatic walled-off necrosis: clinical outcomes and success. *Gastrointestinal endoscopy*. 2017;85(4):758-765.

34. Chandran S, Efthymiou M, Kaffes A, et al. Management of pancreatic collections with a novel endoscopically placed fully covered self-expandable metal stent: a national experience (with videos). *Gastrointestinal endoscopy*. 2015;81(1):127-135.

35. Vazquez-Sequeiros E, Baron TH, Pérez-Miranda M, et al. Evaluation of the short-and long-term effectiveness and safety of fully covered self-expandable metal stents for drainage of pancreatic fluid collections: results of a Spanish nationwide registry. *Gastrointestinal endoscopy*. 2016;84(3):450-457. e452.

36. Venkatachalapathy SV, Bekkali N, Pereira S, et al. Multicenter experience from the UK and Ireland of use of lumen-apposing metal stent for transluminal drainage of pancreatic fluid collections. *Endoscopy international open*. 2018;6(03):E259-E265.

37. Siddiqui AA, Adler DG, Nieto J, et al. EUS-guided drainage of peripancreatic fluid collections and necrosis by using a novel lumen-apposing stent: a large retrospective, multicenter US experience (with videos). *Gastrointestinal endoscopy*. 2016;83(4):699-707.

38. Sharaiha RZ, Tyberg A, Khashab MA, et al. Endoscopic therapy with lumen-apposing metal stents is safe and effective for patients with pancreatic walled-off necrosis. *Clinical Gastroenterology & Hepatology*. 2016;14(12):1797-1803.

39. Rinninella E, Kunda R, Dollhopf M, et al. EUS-guided drainage of pancreatic fluid collections using a novel lumen-apposing metal stent on an electrocautery-enhanced delivery system: a large retrospective study (with video). *Gastrointestinal endoscopy*. 2015;82(6):1039-1046.

40. Shah RJ, Shah JN, Waxman I, et al. Safety and efficacy of endoscopic ultrasound-guided drainage of pancreatic fluid collections with lumen-apposing covered self-expanding metal stents. *Clinical gastroenterology and hepatology : the official clinical practice journal of the American Gastroenterological Association*. 2015;13(4):747-752.

41. Teoh AYB, Serna C, Penas I, et al. Endoscopic ultrasound-guided gallbladder drainage reduces adverse events compared with percutaneous cholecystostomy in patients who are unfit for cholecystectomy. *Endoscopy*. 2017;49(02):130-138.

42. Irani S, Ngamruengphong S, Teoh A, et al. Similar efficacies of endoscopic ultrasound gallbladder drainage with a lumen-apposing metal stent versus percutaneous transhepatic gallbladder drainage for acute cholecystitis. *Clinical Gastroenterology & Hepatology*. 2017;15(5):738-745.

43. Khan MA, Atiq O, Kubiliun N, et al. Efficacy and safety of endoscopic gallbladder drainage in acute cholecystitis: Is it better than percutaneous gallbladder drainage? *Gastrointestinal endoscopy*. 2017;85(1):76-87. e73.

44. Walter D, Teoh AY, Itoi T, et al. EUS-guided gall bladder drainage with a lumen-apposing metal stent: a prospective long-term evaluation. *Gut*. 2016;65(1):6-8.

45. Giovannini M, Moutardier V, Pesenti C, Bories E, Lelong B, Delpero J. Endoscopic ultrasound-guided bilioduodenal anastomosis: a new technique for biliary drainage. *Endoscopy*. 2001;33(10):898-900.

46. Sharaiha RZ, Khan MA, Kamal F, et al. Efficacy and safety of EUS-guided biliary drainage in comparison with percutaneous biliary drainage when ERCP fails: a systematic review and meta-analysis. *Gastrointestinal endoscopy*. 2017;85(5):904-914.

47. Baniya R, Upadhaya S, Madala S, Subedi SC, Mohammed TS, Bachuwa G. Endoscopic ultrasound-guided biliary drainage versus percutaneous transhepatic biliary drainage after failed endoscopic retrograde cholangiopancreatography: a meta-analysis. *Clinical experimental gastroenterology*. 2017;10:67.

48. Paik WH, Lee TH, Park DH, et al. EUS-Guided Biliary Drainage Versus ERCP for the Primary Palliation of Malignant Biliary Obstruction:

A Multicenter Randomized Clinical Trial. *The American Journal of Gastroenterology*. 2018;113(7):987-997.

49. Yan BM, Myers RP. Neurolytic celiac plexus block for pain control in unresectable pancreatic cancer. *Am J Gastroenterol*. 2007;102(2):430-438.
50. Puli SR, Reddy JB, Bechtold ML, Antillon MR, Brugge WR. EUS-guided celiac plexus neurolysis for pain due to chronic pancreatitis or pancreatic cancer pain: a meta-analysis and systematic review. *Dig Dis Sci*. 2009;54(11):2330-2337.
51. Kaufman M, Singh G, Das S, et al. Efficacy of endoscopic ultrasound-guided celiac plexus block and celiac plexus neurolysis for managing abdominal pain associated with chronic pancreatitis and pancreatic cancer. *Journal of clinical gastroenterology*. 2010;44(2):127-134.
52. Moyer MT, Sharzehi S, Mathew A, et al. The Safety and Efficacy of an Alcohol-Free Pancreatic Cyst Ablation Protocol. *Gastroenterology*. 2017;153(5):1295-1303.
53. Sanders MK, Moser AJ, Khalid A, et al. EUS-guided fiducial placement for stereotactic body radiotherapy in locally advanced and recurrent pancreatic cancer. *Gastrointestinal endoscopy*. 2010;71(7):1178-1184.