Therapeutic EUS: New tools, new devices, new applications

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ABSTRACT

Linear echoendoscopes with large instrument channels enable EUS-guided interventions in organs and anatomical spaces in proximity to the gastrointestinal tract. Novel devices and tools designed for EUS-guided transluminal interventions allow various new applications and improve the efficacy and safety of these procedures. New-generation biopsy needles provide higher histology rates and require less passes. Specially designed stents and stent insertion devices enable intra- and extra-hepatic bile and pancreatic duct stenting as well as gallbladder drainage. Currently, EUS-guided biliary drainage in obstructive jaundice due to malignant distal bile duct obstruction is feasible and safe when ERCP has failed. It might replace ERCP as first choice intervention in future. EUS-guided transmural stenting is regarded as the preferred intervention in the management of symptomatic peripancreatic fluid collections. Creating a new anastomosis between different organs such as gastrojejunostomy has also become possible with lumen-apposing stents. EUS-guided creation of a gastrogastrostomy is a promising novel technique to access the excluded stomach to facilitate conventional ERCP in patients with Roux-en-Y gastric bypass anatomy. The role of EUS in tumor ablation and targeted angiotherapy is also constantly expanding. In this review, we report on the newest developments of therapeutic EUS within the past 4 years.

Key words: Biliary drainage, peripancreatic collection, Roux-en-Y gastric bypass anatomy, targeted angiotherapy

INTRODUCTION

Diagnostic EUS has progressed in the last decade by advances in imaging techniques and introducing novel methods of tissue characterization based on the vascular structure and tissue stiffness. Contrast enhanced EUS has gained similar importance in characterization of hepatic and pancreatic masses comparable to cross-sectional imaging contrast techniques. Elastography has added another dimension to tissue characterization by adding the measurement of the stiffness.

Despite these improvements in imaging information, the main indication of EUS has shifted to therapeutic interventions, a similar phenomenon we have observed for ERCP which is nowadays only performed for therapeutic indications.

Noninvasive conventional imaging techniques such as computed tomography, magnetic resonance, and positron emission tomography have also improved allowing high-resolution images and contrast

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application. Noninvasive imaging has replaced EUS as the first modality for indications such as tumor staging or the assessment of the distal bile duct for choledocholithiasis.\(^1\)\(^,\)\(^2\) EUS still plays a role in the detection of distal bile duct stones when the magnetic resonance cholangiopancreatography was negative and the clinical suspicion remains as it has higher sensitivity.

On the other hand, the indications for endosonographic interventions are rapidly expanding. The instrument channel in curvilinear array echoendoscopes allows the use of various tools and devices (needles, forceps, stents, radiofrequency ablation [RFA], or microscopy probes) for transmural interventions. Beyond the EUS-guided drainage techniques in biliary and pancreatic disease, new techniques for tumor ablation or hemostasis have been developed. The development of lumen-apposing stents has enabled the option to create a new anastomosis between luminal organs.

The guidelines of the European Federation of Societies for Ultrasound in Medicine and Biology on interventional ultrasound have summarized the status quo in 2015,\(^3\)\(^-\)\(^5\) but many innovations have been reported since.

**METHODS**

In this review, we have focussed on the most recent literature (2015–2019) on therapeutic EUS and give an overview on established and emerging therapeutic EUS interventions. We have searched PubMed using the following singular and combined search terms: <EUS>; <endoscopic ultrasound>; <drainage>; <cholecystostomy>; <bile duct>; <pancreatic duct>; <peripancreatic collection>; <walled-off necrosis>; <malignant biliary obstruction>; <Roux-en-y gastric bypass anatomy>; <Fundal varix>; <pseudoeaneurysm>; <tumourablation>; <stent>; <coeliac block>; <neurolysis>; <anastomosis>; <tissue sampling>; <cytology>; <aspiration>; <biopsy>.

In the selection process, the authors favored randomized controlled multi-center studies over single-center randomized studies. If randomized studies were not available, controlled studies with large case numbers were cited, again preferring multi-center to single-center studies.

**Tissue sampling**

Apart from diagnostic sampling for tumor confirmation and classification, EUS-guided tissue acquisition is becoming also increasingly important for immunostaining, mutation analysis, and the prognosis of tumor behavior and therapy response allowing genetically based individualized risk stratification.\(^6\)

**FNA**

There is ongoing debate on whether suction techniques and needle caliber affect the diagnostic yield in fine-needle aspiration (FNA). In a randomized controlled study including 352 patients with pancreatic masses, 22G or 25G needles performed equally well. Use of suction increased specimen bloodiness and the passes required.\(^7\)

19G FNA needles performed equally well to 25G needles in a randomized multi-center study by Ramesh et al.\(^8\) in 100 patients with pancreatic head mass lesions, although the 19G needle produced more tissue cores. However, for the transduodenal approach, the randomized multi-center study by Laquière et al. including 125 patients demonstrated less technical success due to more difficult sampling using the 19G needle compared to the 22G needle.\(^9\)

In a multi-center study, the conventional suction technique has been compared to a new aspiration method with the slow withdrawal of the needle stylet to create a slight negative pressure. The diagnostic sensitivity or passes required did not differ between both suction methods.\(^10\)

For biliary tumors, EUS-FNA performs better than ERCP with brush cytology and intraductal forceps biopsy in diagnosing malignant biliary strictures.\(^11\) The superior sensitivity of EUS-FNA (73.6%) compared to ERCP brushings (56.5%) has also been confirmed in a multi-center study including 263 patients with suspected malignant biliary obstruction who underwent both procedures in the same session.\(^12\)

**FNB**

A recent meta-analysis concluded that there is no significant difference in the diagnostic yield whether an FNA or fine-needle biopsy (FNB) (using reverse bevel needles) has been used as long as rapid onsite evaluation by cytopathologist is available. Otherwise, FNB showed better diagnostic adequacy, which was
New-generation biopsy needles

Novel biopsy needles have been introduced with a special tip design to cut and keep the tissue. The fork-tip Sharkcore™ (Medtronic) has two, the Acquire™ needle (Boston Scientific) three opposing bevels. The first studies with the SharkCore™ needles demonstrate better tissue rates sufficient for histology with fewer needle passes not only compared to FNA needles[15-18] but also compared to the older generation biopsy needles with reverse bevels.[19,20]

The Acquire™ biopsy needle also obtained better tissue results than the conventional end-cut type needle for FNA.[21,22]

Comparing both new biopsy needles directly, the fork-tip biopsy needle (SharkCore™) and the Franseen tip biopsy needle (Acquire™), in a randomized study design including 50 patients, Bang et al. found no significant difference and excellent histology yields of >90% in just one pass for both needle types.[23]

A comparative study by Abdelfatah et al. with 97 patients in each group reported higher diagnostic yield (77%) for the fork-tip needle compared to the Franseen-needle (63%, P = 0.027).[24]

Through the needle forceps biopsy

A new disposable microbiopsy forceps has been developed with a 0.8-mm diameter; this minute biopsy forceps can be advanced through a 19G needle. Use of this forceps biopsy has shown promising results for assessing pancreatic cysts by obtaining cystic wall tissue [Table 1].[25-29] In a pilot study, tissue could also be obtained using a through-the-needle microforceps from solid pancreatic tumors with a good safety profile.[30]

EUS-GUIDED Pancreatic Fluid Drainage

Pancreatic pseudocysts

Acute pancreatitis is often complicated by (peri)-pancreatic fluid collections. According to the revised Atlanta classification,[31] we distinguish between acute peripancreatic fluid collections in interstitial edematous pancreatitis and acute necrotic collection located intra- or peripancreatic in necrotizing pancreatitis during the first 4 weeks, while later on, pseudocysts can develop after interstitial edematous pancreatitis and walled-off necrosis after necrotizing events.

Most pancreatic pseudocysts resolve spontaneously, but symptomatic enlarged and infected pseudocysts require drainage. Plastic stents are preferred as lumen-apposing metal stents give no added advantage but increase the costs significantly.[32-34]

Walled-off necrosis

Conventional plastic stents are often of limited use in the treatment of walled-off necrosis because the narrow lumen might become occluded by the thick necrotic debris. The development of large diameter lumen-apposing fully covered self-expanding metal stents has overcome problems of draining fluids of high consistency and avoids leakage along the newly created tract.[35] The saddle-shaped stent has double-walled flanges on both ends to anchor

| Table 1. Diagnostic yield and safety of through-the-needle microforceps biopsy in the evaluation of pancreatic cysts through EUS |
|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|
| Study           | n               | Technical success (%) | Diagnostic accuracy (%) | Adverse events | Comments |
| Mittal et al.[29] | 27              | 100               | 88.9               | None           | -               |
| Barresi et al.[23] | 56              | 100               | 83.9               | 9 (16%)        | Limited intracystic hemorrhage - 7 (12.5%) |
| Shakhatreh et al.[24] | 2               | 100               | 100                | None           | -               |
| Kovacevic et al.[27] | 31             | 87.1              | 71                 | 3 (9.7%)       | All adverse events - mild |
| Yang et al.[28] | 47              | 85.1              | 65                 | 2 (4.2%)       | One self-limited bleeding and one episode of mild pancreatitis |
| Nakai et al.[30] | 17              | 100               | 100                | None           | -               |

Data is in frequency and percentages
the position. The complete silicone cover and self-expanding radial forces avoid leakage along the tract. The stents are removable.

Fully covered metal stents can be inserted into the walled-off necrosis [Figure 1] under EUS-guidance only and without the need for fluoroscopy,[36,37] but it might be helpful to have access to X-ray when complications occur.

There is ongoing debate on whether lumen-apposing stents are superior to drainage with multiple plastic stents in the treatment of walled-off necrosis. Although lumen-apposing metal stents are very costly, a cost-analysis revealed that they are cost-effective[38] due to less procedures, higher efficacy,[39,40] and shorter hospital stay.[40] In some studies, more bleeding events have been observed using metal stents compared to plastic stents[41-43] and the recommendation is to extract metal stents after 3–4 weeks[41,44] to avoid eroding into vessels and pseudoaneurysm in or surrounding the pancreatic cavity. This is also advised by the European Society of Gastroenterology and Endoscopy which summarized the evidence for the endoscopic management of necrotizing pancreatitis in new guidelines.[45]

The large diameter of the lumen-apposing metal stents not only allows better spontaneous drainage of debris but also enables direct endoscopic necrosectomy through the stent if clinically required [Figure 2]. A large multi-center study from the United States concluded that direct endoscopic necrosectomy at the time of transmural stent placement results in earlier resolution of complex walled-off necrosis and reduced number of endoscopic sessions.[46] On the other hand, it could be shown that from 205 symptomatic walled-off necrosis, 75% resolved with stenting alone, whereas the rest required step-up approach including deblocking of the stent, nasocystic tube irrigation or direct endoscopic necrosectomy. Endoscopic necrosectomy was required only in 9.2%.[47]

EUS-guided drainage of infected pancreatic necrosis followed by endoscopic necrosectomy if required results in the less pancreatic fistula and shorter hospital stay than the surgical approach with percutaneous drainage followed by video-assisted retroperitoneal debridement if necessary.[48] Compared to open invasive surgical necrosectomy, EUS-guided endoscopic necrosectomy has clearly reduced the mortality in necrotizing pancreatitis.[49,50]

**EUS-GUIDED BILIARY DRAINAGE**

EUS-guided transmural biliary drainage (EUS-BD) has evolved as a helpful rescue tool after failed endoscopic retrograde cholangiography.[51-57] The biliary system can be accessed through the transgastric route into the intrahepatic ducts of the left liver lobe [Figure 3] or through the transduodenal route to the extrahepatic bile duct [Figure 4].

After accessing the bile duct from the duodenum or stomach, a guide wire can be advanced through the papilla to enable a rendez-vous technique and complete the BD in conventional ERCP techniques. Alternatively, plastic or metal stents (partially or fully covered) can be placed directly through the newly created tract to drain the bile. These stents can be placed antegrade transpapillary[58] or as transluminal stents creating a choledochoduodenostomy or hepaticogastrostomy.

The transhepatic or duodenal approach might be selected depending on the location of the malignant obstruction with similar technical success and safety.

Transgastric access to the intrahepatic system allows BD also in situations of gastric outlet obstruction or surgically altered anatomy (e.g., Billroth II, Whipple or Roux-en-Y).

Compared to percutaneous transhepatic biliary drainage (PTCD), EUS-BD has several advantages: The patients suffer less peri-interventional pain and less adverse events when treated by EUS-guided BD; they need less re-interventions, have better cosmesis without

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**Figure 1.** EUS-guided stent insertion for drainage of pancreatic fluid collections and EUS-guided insertion of a lumen-apposing stent to create a gastroenterostomy in gastric outlet syndrome.
external drainages that impair daily activities, and the hospital stay is shorter.\textsuperscript{[56,59-62]} The procedure can be performed during the same session of the failed ERCP. In centers with excellent expertise in EUS-BD, PTCD is not the treatment of choice after failed ERCP anymore.

Recent studies even point toward EUS-BD as first-line therapy in patients with distal malignant bile duct obstruction.\textsuperscript{[63,64]}

In a multi-center randomized clinical trial [Table 2], technical success was achieved in 93.8\% (60/64) for EUS-BD and 90.2\% (55/61) for ERCP ($P = 0.003$). Clinical success rates were 90.0\% (54/60) in EUS-BD and 94.5\% (52/55) in ERCP ($P = 0.49$). Complications rates were lower (6.3\% vs. 19.7\%, $P = 0.03$) including pancreatitis (0 vs. 14.8\%), re-intervention (15.6\% vs. 42.6\%), and higher stent patency (85.1\% vs. 48.9\%) were observed with EUS-BD. EUS-BD also had a better quality of life than ERCP after 3 months of the procedure.\textsuperscript{[65]} In two other randomized controlled studies including 30 patients and 67 patients with malignant biliary tract obstruction, respectively, EUS-BD was noninferior to transpapillary stenting using ERCP in clinical success rate.\textsuperscript{[66,67]}

The expertise of EUS-BD is limited to a few expert centers. Knowledge and expertise of the entire range of PTCD\textsuperscript{[68,69]} and EUS-BD techniques are required including (i) rendezvous techniques via the common bile duct or via the left liver lobe, (ii) antegrade transpapillary stent placement, or (iii) transmural stent application creating a choledochoduodenostomy or hepaticogastrostomy. The choice of techniques depends on the individual situation, proximal or distal malignant biliary obstruction, and various anatomic variations.

In future, EUS-guided BD might likely replace PTCD after failed ERCP access, but EUS-guided BD might
even become the first-line approach for BD instead of ERCP in malignant distal bile duct obstruction.

**Cholecystitis**

High-risk patients with acute cholecystitis who are unfit for cholecystectomy due to severe comorbidities usually undergo percutaneous drainage of the gallbladder or transpapillary cystic duct stenting through ERCP. In recent years, a EUS-guided approach has become an alternative treatment option creating a fistula tract between the gallbladder and the stomach or duodenum. EUS-guided drainage of the gallbladder has been attempted using plastic stents, nasobiliary drainage tubes, or self-expandable metal stents. The development of lumen-apposing fully covered metal stents (LAMS) has minimized the risk of bile leakage due to stent migration and nonadherence. These stents fix the gallbladder to the gastrointestinal wall.

Two meta-analysis including 226 patients and 189 patients concluded that EUS-guided LAMS placement for acute cholecystitis is highly successful (>90%) and acceptably safe in experts hands. Compared to percutaneous gallbladder drainage, the postoperative pain, length of hospital stay, and need for antibiotics are less. The technique is also helpful in patients with coagulopathy or ascites.

Patients who underwent percutaneous transhepatic gallbladder drainage but are unfit for surgical cholecystectomy can have conversion to a transgastric EUS-stent as long-term solution. Patients who underwent EUS-guided gallbladder drainage in the acute setting, can still have laparoscopic cholecystectomy later, should their clinical condition improve.

Compared to transpapillary stenting of the cystic duct, the EUS-guided drainage of the gallbladder appears safer, with higher technical and clinical success.

### EUS-GUIDED PANCREATIC DUCT DRAINAGE

Indications for the technically extremely challenging EUS-guided pancreatic duct drainage [Figure 5] might include pancreatic duct obstruction due to stones or strictures in chronic pancreatitis when ERCP has failed, a disconnected pancreatic duct, an inaccessible papilla due to surgically altered anatomy, or a postsurgical stricture at the pancreaticoenterostomy. In the hand of expert endoscopists, EUS-guided pancreatic drainage can be achieved through rendezvous through the papilla or by transmural stent insertion into the pancreatic duct, but the adverse event rate remains high (20%-55%). Even pancreateoscopy including electrohydraulic lithotripsy for pancreatic duct stones has become possible through EUS-guided transgastric access to the dilated pancreatic duct.

A new ultra-tapered mechanical dilator has been introduced to avoid bleeding complications that are often seen after electrocautery dilatation following the successful needle puncture of the pancreatic duct.
Usually, transgastric or transduodenal plastic stents are inserted, but recently, Oh et al. reported the successful long-term insertion of fully covered specially designed metal stents with antimigration features. The technical and clinical success rate was excellent (100%) in 25 patients with only mild adverse events in this single-center study.

An international multicenter study compared EUS-guided pancreatic duct drainage with enteroscopy-assisted endoscopic retrograde pancreatography after the Whipple surgical procedure. Technical (92.5%) and clinical success (87.5%) was higher in the EUS group compared to 20% and 23.1% in the ERCP group, respectively. Adverse events occurred more often (35%) in the EUS group but were mild.

**EUS-GUIDED CREATION OF NEW GASTRO-INTESTINAL ANASTOMOSIS**

**Gastroenterostomy for gastric outlet syndrome**

In recent years, novel methods for EUS-guided gastroenterostomy using the lumen-apposing metal stents [Figure 1] have been introduced to treat gastric outlet obstruction in benign and malignant diseases.

From the EUS position in the stomach, the distal part of the duodenum or a jejunal loop usually are adjacent to the gastric wall and can be reached with a needle to create a new gastroduodenotomy or gastrojejunostomy, respectively. However, the air content in the enteral loops impairs ultrasound imaging and the often collapsed status of the bowels render this puncture difficult and risky. To facilitate the enteral access and improve the ultrasound imaging, water-filling techniques with or without a balloon have been proposed.

If the obstruction can be passed by an endoscope or ultraslim endoscope, saline flushing through the scope can distend the small bowel. If a retrieval balloon can be placed across the stricture, the fluid-filled balloon can be targeted by EUS from the stomach to guide and ensure the intraluminal position before a wire is placed and coiled in the small bowel.

For the double-balloon technique, a special double-balloon enteric tube is used which allows fluid filling of the bowel segment between both inflated balloons. Over a previously placed wire into the jejunum, the balloons are positioned into the jejunum and distal duodenum, inflated and the interlaying bowel segment is filled with fluid or contrast to facilitate the EUS-guided puncture and stent deployment.

The lumen-apposing stents allow the fixation of the enteric wall to the gastric wall. The electrocautery system of the “hot-axios” (Axios-EC™) enables direct puncture of the duodenum or jejunum followed by direct stent deployment; this avoids the multiple steps of needle access, wire placement and changes of tools through the instrument channel for the enlargement of the tract which entails the risk of losing the position and access with subsequent risk of peritoneal leakage.

Compared to enteral stenting for malignant gastric outlet obstruction, EUS-guided gastroenterostomy seems to have similar clinical success and safety rate.

**Biliary drainage in altered anatomy**

Lumen-apposing stents placed under EUS and fluoroscopy guidance have also been used for the reversal of Roux-en-Y bariatric surgery. From the gastric pouch or the Roux-limb, the adjacent gastric remnant can be accessed and rejoined by placing a lumen-apposing stent. This reestablishes the continuity of the digestive tract [Figure 6].

In some patients with previous gastric bypass surgery who developed an indication for ERCP, the reconnection of the gastric pouch to the excluded gastric remnant by LAMS placement enabled the successful ERCP intervention allowing access to the duodenum through the newly placed gastrogastric stent.
A multi-center trial compared EUS-guided gastrogastrostomy-assisted ERCP (EUS-GG-ERCP) with double-balloon or single-balloon enteroscopy-assisted ERCP in patients with the Roux-en-Y gastric bypass anatomy. Thirty patients underwent EUS-GG-ERCP and 30 (50%) underwent enteroscopy-assisted ERCP. The technical success rate was significantly higher in the EUS-GG-ERCP versus the enteroscopy-ERCP group (100% vs. 60.0%, \( P < 0.001 \)). Procedure time was significantly less in patients who underwent EUS-GG-ERCP (49.8 min vs. 90.7 min, \( P < 0.001 \)). Following procedure, the median length of hospitalization was shorter in the EUS-GG-group (1 vs. 10.5 days, \( P = 0.02 \)). Both the groups had similar adverse events (10% vs. 6.7%, \( P = 1.0 \)).\[93\]

A similar technique placing a LAMS transmurally from the Roux-limb across to an adjacent jejunal loop as jejuno-jejunostomy has been successful to overcome a distal obstruction after a Roux-en-Y reconstruction.\[90,94\]

Randomized multi-center studies and long-term results for the use of LAMS for creation of new anastomosis in the gastrointestinal tract are still sparse, but the pilot studies from expert centers show promising results regarding clinical success and safety profile compared to the surgical alternatives.

**ABLATIVE TECHNIQUES**

EUS enables accurate positioning of needles or other tools in the tumor mass under real-time imaging. This allows precise delivery of energy, fiducial markers, and anti-tumor agents or radioactive seeds for tumor therapy and destruction of neoplastic tissue.\[95\] Fiducial placement using EUS has a high success rate and helps to plan stereotactic radiotherapy.\[96,97\]

Percutaneous tumor ablation using radiofrequency or ethanol injection is the standard treatment for liver tumors in patients unfit for surgery. EUS-guided ablative techniques using radiofrequency or ethanol injection have been employed in the treatment of not only cystic and solid pancreatic masses but also liver or adrenal lesions in patients who are not eligible for surgery.

For ethanol or macrogol injection in cystic pancreatic neoplasm, the complete resolution rate varies widely between 9% and 85%.\[98-104\] An additional infusion of the cyst with the chemotherapeutic agent paclitaxel seems to increase the complete resolution rate\[99,105-107\] and has shown long-term remission.\[109\]

A novel RFA probe has been developed for linear echoscopes which allows targeted tissue destruction by heating >45°C which induces protein degradation and irreversible cell injury. Feasibility studies in unresectable pancreatic cancer\[108,109\] and other solid pancreatic tumors\[110,111\] have been reported. Studies showing survival benefit are not yet available.

These techniques need further evaluation in prospective multicenter studies. Safety-related issues need to be carefully considered for patient selection. Adverse events of EUS-guided ablative techniques include abdominal pain, acute pancreatitis, vascular damage, and infection with abscess or fistula formation.

**EUS-GUIDED ANGIOThERAPY**

The standard management of acute bleeding or selective therapy in gastric fundal varices is endoscopic cyanoacrylate injection, but this can be complicated by re-bleeding or embolic events. EUS-guided injection of coils and cyanoacrylate or thrombin allows assessment of the variceal blood flow, selective targeting of the varices and monitoring of the obliteration results.\[112-117\] EUS can identify gastric varix even when the endoscopic view is obscured by blood and clots in the setting of acute bleeding\[118\] Direct visualization of the varix lumen with real-time imaging enables targeted injection to obliterate feeder vessels.
EUS-based hemostatic techniques combining endovascular coiling and cyanoacrylate injection seem to reduce complication rates such as re-bleeding and embolization due to improved obliteration.\textsuperscript{[119-123]}

Coils are made of metal alloy containing radially extending synthetic fibers, which start clot formation and hemostasis. Coils are 2–15 mm long and loops have diameter of 2–20 mm. Coils can be deployed through 22 G needle (0.018” coil) or 19 G needle (0.035” coil). The needle stylet is used to push and deploy the coil into varix.

A retrospective trial comparing EUS-guided coil deployment to EUS-guided cyanoacrylate injection showed similar rates of varix obliteration, number of sessions and re-bleeding rate over 17-month follow-up. Cyanoacrylate group had significantly higher adverse events (58% vs. 9%, \( P = 0.01 \)).\textsuperscript{[120]}

The hospital stay was longer in the cyanoacrylate group and coil deployment is more expensive. Although, in practice, it is not uncommon to inject cyanoacrylate immediately after coil deployment, which offers combined hemostasis effect of both modalities and reduces glue embolization rates.

Parastomal or rectal varices have also successfully been treated using similar EUS hemostasis techniques.\textsuperscript{[122-124]}

Transjugular intrahepatic portosystemic shunt plays a major role in the management of the chronic liver disease. It is used in cases of refractory ascites and refractory variceal bleed. EUS might offer an alternate approach to intrahepatic portosystemic shunt. So far, it has only been tried successfully in porcine models.\textsuperscript{[125]}

**COELIAC BLOCK**

EUS-guided coeliac plexus/ganglia neurolysis and block is widely practiced as pain management in palliative pancreatic cancer patients and in patients with chronic pancreatitis.

The neurolytic agent can be injected centrally at the base of the coeliac axis, bilaterally or directly into the coeliac ganglia.\textsuperscript{[72,126]} The coeliac ganglia can reliably be identified by EUS\textsuperscript{[127]} and selectively targeted for ethanol injection. However, the injected ethanol spreads beyond the targeted ganglion and high volume ethanol injection for diffuse coeliac plexus neurolysis is more likely to also reach unidentified ganglia.\textsuperscript{[128]}

Transient pain exacerbation, diarrhea, or hypotension can occur peri-procedural. Rare but serious major adverse events include retroperitoneal bleeding, ischemic complications, and abscess formation.

In a retrospective study including 123 patients with pancreatic cancer, the combination of coeliac plexus neurolysis with ethanol ablation of the tumor showed better pain relief and slightly improved survival compared to coeliac plexus neurolysis alone.\textsuperscript{[129]}

**CONCLUSION**

Therapeutic EUS is a fascinating rapidly expanding field and new techniques, tools, and applications are introduced every year. Many reports strongly indicate the technical feasibility and efficacy of EUS interventions in the hands of highly skilled endosonographers, but there is still a relative lack of randomized controlled multicenter studies. EUS is becoming the first line treatment modality for pancreatic fluid collections and gallbladder drainage.

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There are no conflicts of interest.

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