Review Article

Recent developments in hepatopancreatobiliary EUS

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ABSTRACT

The last American College of Gastroenterology's (ACG) annual meeting was held in Philadelphia on October 5–10, 2018 and showcased a wide variety of the latest and upcoming research within the field of Gastroenterology. This article will present the advancements and research regarding endoscopic ultrasound (EUS) presented at this year's meeting with focus on hepatopancreatobiliary indications. Seventy studies related to EUS were presented; however, case reports and video forum presentations were excluded from this review. Many endosonographers investigated various aspects of EUS such as the tissue acquisition and diagnostic yields of fine-needle biopsies, the application of interventional EUS, and various novel techniques to advance the role of EUS. It would be very difficult to discuss all of the abstracts presented in details; however, we commend and encourage all endosonographers who presented at ACG to continue advancing research and development in EUS.

Key words: Drainage, EUS-guided biliary, EUS-guided fine-needle biopsy, EUS-guided FNA, EUS-guided liver biopsy, lauromacrogol ablation, pancreatic cystic lesions, radiofrequency ablation

EUS-GUIDED TISSUE ACQUISITION FOR SOLID LESIONS

Four strategies are currently available for tissue acquisition under EUS: Fine-needle aspiration (FNA), fine-needle biopsy (FNB), both, or FNA followed by FNB if the FNA samples are nondiagnostic. There were numerous studies that compared and analyzed the safety, efficacy, and diagnostic yield of EUS-FNA to EUS-FNB for the evaluation of solid lesions in the pancreas. Lindsey Temnykh *et al.*[1] presented a prospective study comparing these two tissue sampling methods in patients with solid lesions. The number of passes on average was significantly lower for EUS-FNB (2.9 vs. 3.8), and the number of adequate diagnostic specimens was higher in the EUS-FNB compared to the EUS-FNA group. Another study presented by Fareha Iqbal *et al.*[2] also investigated the two EUS sampling methods. The diagnostic yield for EUS-FNB was overall better than the EUS-FNA needles (96% *vs.* 86.2%). There was no difference in the diagnostic yield between the FNB needles (SharkCore, 96%; Acquire, 95%). These two studies both suggested that EUS-guided FNB has a better diagnostic yield and tissue acquisition capability than EUS-guided FNA.

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As we move toward the era of precision medicine, EUS-guided tissue acquisition may be essential for therapy guidance based on each individual cancer biology. Nadim Mahmud *et al.*[3] presented a retrospective study comparing EUS-FNA to EUS-FNB to analyze the degree of sufficient tissue acquisition for pancreatic tumor genotyping. The study included 167 patients, where 145 patients had EUS-FNA and 22 patients underwent FNB. EUS-FNB resulted in a higher proportion of patients with sufficient tissue samples compared to FNA (91% *vs.* 67%). Furthermore, FNB was more likely to obtain sufficient tissue from lesions located in the head and neck of the pancreas.

However, there is still no explicit consensus among endosonographers for which sampling means are superior in terms of efficacy, safety, and diagnostic results. At present, the choice between EUS-FNA and EUS-FNB is dependent on multiple factors, including endosonographer's preference, the presence of on-site cytopathology, institutional, or referring physician preference (e.g., obtain an instant diagnosis). Another important aspect to be considered is the need for undergoing endoscopic retrograde cholangiopancreatography (ERCP) with uncovered metal stenting post-EUS procedure in the same session. In this case, a diagnosis of malignancy is immediately required, and EUS-FNA with on-site cytopathologist interpretation is indicated.

PANCREATIC CYSTIC LESIONS

Diagnosis

Pancreatic cystic lesions (PCLs) have a varying range of malignant potential. The increase in the detection and clinical variability of pancreatic cysts has created a significant diagnostic and therapeutic challenge to physicians. It is of paramount importance to obtain an accurate differential diagnosis of PCLs to stratify the risks of malignant progression and decide the better clinical pathway for the patients that can comprise surgery or follow-up. Magnetic resonance imaging (MRI), computed tomography (CT), and EUS are the most widely used techniques for diagnosing PCLs. EUS diagnostic capability can be further improved by contrast-enhanced EUS (CE-EUS) that can, for example, differentiate a solidified mucin nodule from a true solid mural module based on enhancement pattern.

Lisen Zhong *et al.*[4] investigated the different imaging modalities used for PCLs diagnosis, specifically CE-EUS compared to MRI and CT. They revealed that CE-EUS had significantly greater accuracy in identifying PCLs than CT or MRI (92.3% *vs.* 76.9%, $P < 0.05$). However, the enhanced mode showed no difference between serous cystic neoplasms and mucinous cystic neoplasm.

Imaging modalities for PCLs give some guidance for the expected type of lesion, but the differential diagnosis between various PCLs still requires in most cases tissue confirmation with EUS-FNA.

At present, new microforceps are being introduced for PCLs sampling with the claim to have increased diagnostic yield. The Moray microforceps biopsy device is a disposable tissue acquisition device that can be passed through a 19G needle and it has been recently introduced to facilitate the EUS-guided biopsy of PCLs. Multiple studies have been published on the efficacy and safety of EUS-guided microforceps biopsy (EUS-MB). However, none are decisively conclusive since the postprocedure complication rate and diagnostic yield vary widely. Raina[5] presented a prospective pilot study to investigate the initial experiences of using the novel transneedle biopsy microforceps for sampling PCLs. A total of 44 patients were evaluated, half undergoing EUS-guided sampling with EUS-FNA or FNB and the other half using the novel Moray microforceps. A cyst diagnosis was made in 62% for the EUS-MB and 50% in the EUS-FNA group; however, these results did not reach statistical significance. Raina suggested that there is a trend toward increasing diagnostic yield with the EUS-MG for pancreatic cyst sampling, but it is not conclusive.

Valery Hrad *et al.*[6] presented their experience with EUS-guided MB in 37 patients with PCL. The procedure was high effective in making a diagnosis in cystic lesions, with 92% accuracy. Only two complications were recorded: mild acute pancreatitis and atrial fibrillation postprocedure.

Given the novelty of the method, further ongoing studies are expected to offer a better understanding of the safety profile, diagnostic accuracy, and reproducibility of this technique.

EUS-guided therapy

Surgical resection is the recommended treatment option for high-risk PCLs; however, not every patient is a viable candidate. Data on attempts to endoscopically ablate pancreatic cysts with alcohol and

chemotherapeutic agents under EUS guidance have been presented.

Emmanuel Ugbarugba *et al.*[7] conducted a meta-analysis on the treatment of EUS-guided pancreatic cystic ablation that analyzed the complete resolution (CR) rate and complication rate that resulted from this treatment. The most effective ablative agent was also investigated, comparing the CR rate between using ethanol or paclitaxel as the ablative agents in pancreatic cysts. The highest CR rate was observed when using both ethanol and paclitaxel as an ablative agent (66.4%) while ethanol alone produced a CR rate of 35.9%. Among the different types of PCLs, mucinous cystic neoplasms had the highest CR rate, whereas intraductal papillary mucinous neoplasms had relatively low CR rates no matter the ablative agent. The overall complication rate was 15.4%, with acute pancreatitis being the most common adverse event.

Other studies have been presented introducing new techniques such as combining radiofrequency ablation with lauromacrogol ablation to increase the treatment yield of ablation, but safety, efficacy, and optimum settings must be further investigated. The short-term data on efficacy of these techniques are promising, but we do need more long-term data before routine widespread application. A study presented by Chen Du *et al.*[8] studied the long-term follow-up of at least 12 months for patients who received EUS-guided lauromacrogol ablation for the treatment of PCLs. The effectiveness of this ablation treatment was determined by measuring tumor volume changes from repeated imaging obtained 3 months after procedure and every 6 months thereafter. The results showed CR in 53.8% of the patients, suggesting that EUS-guided lauromacrogol ablation can be effective. However, it should be noted that CR rate with this techniques was only about 50% with a single ablation session. Therefore, the authors recommended reablation after 5 months for cysts larger than 10 mm in diameter.

There is insufficient evidence to support the routine use of cyst ablation. In our opinion, EUS-guided ablation of PCLs is still experimental and should not be done outside a research protocol as its long-term efficacy and the clinical/survival benefit are yet to be determined. Furthermore, patients with cystic lesions may be at increased risk of pancreatic cancer at a site separate to the cyst due to field effect, and ablation does not remove the need for surveillance. Therapy and surveillance strategies for PCLs remain controversial. Clinical guidelines support decisions based on cyst features without consideration of patient characteristics, including extrapancreatic cancer-related factors. Our group[9] evaluated long-term outcomes to assess the behavior of pancreatic cysts in patients with historical or concomitant malignancies. We have shown that in in high-risk patients, comorbidities should be factored in with cyst features for surgical decision-making.

EUS-GUIDED LIVER BIOPSY

EUS-guided liver biopsy (EUS-LB) is evolving as a promising alternative method for sampling liver tissue over percutaneous or transjugular approaches. There are emerging data showing promise in terms of safety and tissue acquisition yield. The role of EUS-guided biopsy for focal liver lesions is well established, and at the moment, the utility of EUS-guided random biopsies for parenchymal liver diseases is becoming more popular with recent developments in FNB needles.

A meta-analysis presented by Anup Shah *et al.*[10] showed that EUS-LB in patients with suspected parenchymal liver disease can provide optimal samples with low adverse events rate (4%). Most commonly reported complications were bleeding (2.2%) and abdominal pain (4%).

Bulet *et al.* conducted another meta-analysis showing that EUS-parenchymal LB is a good alternative to other methods of liver sampling and using FNB needles with a slow-pull technique can provide better results. Harsh Patel *et al.*[11] compared the novel 22G FNB needle with the existing 19G FNA and FNB needles in 135 patients undergoing EUS-LB. They showed that 22G FNB needles provide clinically acceptable results, but the specimens appear to be highly fragmented, leading to inferior results compared to 19G needle platforms.

Moreover, the new specialized needles (nonTrucut) had higher rates of histologic diagnoses when compared to conventional Tru-cut needle, with potentially lower rate of adverse event, according to Singh Dhaliwal *et al.*[12]

EUS-GUIDED BILIARY DRAINAGE

ERCP is often the procedure of choice for drainage of biliary obstruction; however, this technique may not be feasible in all patients. Percutaneous transhepatic biliary drainage (PTBD) is another option but is associated

with high morbidity and postprocedural complications. EUS-guided biliary drainage (EUS-BD) has emerged as a technique for gaining biliary access when ERCP fails. Hingorani *et al.* presented a prospective analysis of 17 patients with biliary obstruction who failed ERCP and required EUS-BD. The procedure was technically successful in 13 patients while the remaining four received PTBD. There were no procedure-related complications, and clinical success (symptoms improvement, reduction of total bilirubin) was achieved in all patients. Therefore, they showed that EUS-BD is a technique that offers high clinical and technical success rates with low associated-adverse events rate.

Neil Vyas *et al.*[13] presented a retrospective study evaluating the safety and efficacy of EUS-BD when compared to PTBD. Eleven patients underwent EUS-guided stent placement for gall bladder drainage (GBD) while 11 patients received percutaneous cholecystostomy. The two cohorts were matched for age and gender. The study showed that the technical and clinical success of EUS-BD is as good as PTBD in patients who are high-risk surgical patients with acute cholecystitis. In addition, EUS-GBD is as safe as percutaneous GBD and it shows a trend for lower risk of recurrence of cholecystitis.

Hedjoudje[14] conducted a meta-analysis to evaluate the safety and efficacy of current procedures for EUS-BD. The meta-analysis of the available literature suggested that EUS-guided choledochoduodenostomy is a safer approach compared to EUS-guided hepaticogastrostomy, with a similar clinical and technical efficacy.

EUS-BD is indeed an emerging technique with promising safety and efficacy. However, there are no randomized control trials to support the best strategy for EUS-BD, and we believe that the best approach should be decided on a case-to-case basis according to the patient's anatomy and condition.

EUS-GUIDED NOVEL TECHNIQUES

Umar Hayat *et al.*[15] presented a novel technique for pancreaticogastrostomy consisting of EUS-guided puncture and opacification of the pancreatic duct (PD) with a 19G or a 22G needle, passage of 0.018 guidewire, creation of a transgastric fistula using an angioplasty balloon, and subsequent ductal decompression with a plastic endoprosthesis. It can be used as an alternative to surgery and/or conventional endoscopic techniques to drain the PD in cases of PD strictures, stenotic pancreaticodigestive tract anastomosis, and/or disconnected PD syndrome. Technical success was achieved in all five cases without any related complications.

CONCLUSION

This year's American College of Gastroenterology conference showcased EUSs greater involvement as an interventional subspecialty with a primary focus on tissue acquisition and EUS-guided therapies. Many novel tools and techniques were presented that have serious potential to shape treatment and management of GI pathologies. Further research and investigation into the concepts will improve the applications of EUS in routine clinical practice.

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Conflicts of interest
There are no conflicts of interest.

REFERENCES

1. Temnykh L, Rahal M, Zia Z, *et al*. An exclusive fine needle biopsy approach to sampling solid lesions under EUS guidance: A case-controlled study. *Am J Gastroenterol* 2018;113 Suppl 3:S435.
2. Iqbal F, Aditi A, Huang BL, *et al*. Diagnostic yield of a conventional endoscopic ultrasound-fine needle aspiration (EUS-FNA) and two endoscopic ultrasound-fine needle biopsy (EUS-FNB) needles: A single-center, retrospective study. *Am J Gastroenterol* 2018;113 Suppl 3:S442.
3. Mahmud N, Elhanafi S, Kochman ML, *et al*. Endoscopic ultrasound tissue acquisition for genomic analysis of pancreatic cancer using liquid next-generation sequencing. *Am J Gastroenterol* 2018;113:s13.
4. Zhong L, Chai N, Linghu E, *et al*. A prospective study on contrast-enhanced endoscopic ultrasound for differential diagnosis of pancreatic cystic neoplasms. *Am J Gastroenterol* 2018;113 Suppl 3:S48.
5. Raina A, Kantsevoy S. EUS-guided pancreatic cyst sampling with a novel trans-needle biopsy forceps: Initial experience in a pilot study. *Am J Gastroenterol* 2018;113 Suppl 3:S15.
6. Hrad V, Meidinger R, Peng HQ, *et al*. US-guided cyst wall biopsy is highly effective in definitive diagnosis of pancreatic cysts. *Am J Gastroenterol* 2018;113 Suppl 3:S40.
7. Ugbarugba E, Hart P, Cruz-Monserrate Z, *et al*. Endoscopic Ultrasound-guided ablation of pancreatic cystic neoplasms: A systematic review and meta-aanalysis. *Am J Gastroenterol* 2018;113 Suppl 3:S9-10.
8. Du C, Chai N, Linghu E, *et al*. EUS-guided lauromacrogol ablation for the treatment of pancreatic cystic neoplasms: Long-term follow-up of at least 12 months. *Am J Gastroenterol* 2018;113 Suppl 3:S48-9.
9. Coronel E, Abu-Sbeih H, Gonzalez GN, *et al*. Long-term outcome of mucinous pancreatic cystic lesions in cancer survivors or patients with extra-pancreatic malignancy. *Am J Gastroenterol* 2018;113 Suppl 3:S52.
10. Shah A, Martinez ICG, Valentin N, *et al*. Efficacy and safety of endoscopic ultrasound-guided liver biopsies in parenchymal liver diseases: A systematic review and meta-analysis. *Am J Gastroenterol* 2018; 113 Suppl 3:S565-6.

11. Patel H, Rush N, DeWitt JM, *et al*. 22G vs. 19G needles for EUS-guided transgastric liver biopsies for parenchymal disease: A comparative analysis. *Am J Gastroenterol* 2018;113 Suppl 3:S442.
12. Dhaliwal AJS, Cormier I, Jhand AS, *et al*. Efficacy of endoscopic ultrasonography-guided gastroenterostomy (EUS-GE) in gastric outlet obstruction (GOO): A systematic review and meta-analysis. *Am J Gastroenterol* 2018;113 Suppl 3:S449-50.
13. Vyas N, Aijaz S, Surkunalingam N, *et al*. Endoscopic ultrasound-guided gallbladder drainage is potentially a safer and efficacious treatment of choice in high-risk patients, as opposed to percutaneous transhepatic gallbladder drainage. *Am J Gastroenterol* 2018;113 Suppl 3:S441.
14. Hedjoudje A. Outcomes of endoscopic ultrasound-guided biliary drainage: A systematic review and meta-analysis. *Am J Gastroenterol* 2018;113 Suppl 3:S439.
15. Hayat U, Freeman M, Trikudanathan G, *et al*. A novel technique for endoscopic ultrasound-guided pancreaticogastrostomy: Duct access without cautery using angioplasty balloon. *Am J Gastroenterol* 2018;113 Suppl 3:S453.