How Can We Optimize Tools and Techniques for Endoscopic Ultrasound–Guided Liver Biopsy?

Itegbemie Obaitan

Mohammad A. Al-Haddad

Despite the advances in liver imaging, random parenchymal biopsies remain an essential tool for the diagnosis of acute and chronic liver diseases, providing an accurate assessment of disease severity and adding much valuable prognostication. For several decades, the percutaneous liver biopsy (P-LB) was the prevailing sampling method, but later this gave way to computed tomography and ultrasound-guided percutaneous biopsies, which became the gold standard. Other techniques, such as fluoroscopy-guided transjugular liver biopsies (TJ-LB) and surgically accrued (laparoscopic or open) Trucut biopsies evolved but are limited to niche clinical applications. Since the first report of endoscopic ultrasound (EUS)-guided liver biopsies (EUS-LB) more than a decade ago, a growing body of literature has supported the utilization of this novel technique because of its safety and the adequacy of the specimens provided.

Where Do We Stand Now?

Disruptive technologies typically bring about a significant departure from mainstream, widely accepted methods. In our opinion, EUS-LB could be considered a disruptive technology in liver sampling. In assessing whether an innovative technique is ready for widespread adoption, one ought to closely examine the evidence supporting its use. The first parameter to closely assess is feasibility. EUS allows generous visualization and access to both the right and left lobes of the liver through the transduodenal and transgastric approaches, respectively. In addition, upper endoscopy and EUS frequently are recommended to patients with potential parenchymal liver disease to rule out varices or assess for biliary stones or strictures based on increases in liver chemistry. In other patients with a suspicion for chronic liver disease, EUS may be recommended for a completely unrelated cause: such as to assess the pancreas or a subepithelial lesion. It is fair to say that EUS has passed the test of time and its widespread adoption in our practices is a testimony to the role it plays in diagnosing and staging various gastrointestinal pathologies.

The next parameter always should be a safety assessment. A recent meta-analysis by Mohan et al[1] with pooled data from 8 studies reported a 1.2% rate of postbiopsy hemorrhage and an overall 2.3% rate of adverse events, which is comparable with image-guided P-LB. At its basic principle, the technique of EUS-LB is not much different from a typical EUS-guided fine-needle aspiration (FNA), giving further credibility to the safety profile observed with this technique.

This is the author's manuscript of the work published in final edited form as:

Obaitan, I., & Al-Haddad, M. A. (2020). How Can We Optimize Tools and Techniques for Endoscopic Ultrasound-Guided Liver Biopsy? Clinical Gastroenterology and Hepatology: The Official Clinical Practice Journal of the American Gastroenterological Association, 18(5), 1025–1027. https://doi.org/10.1016/j.cgh.2020.01.026

Nevertheless, the challenge in assessing a novel technology resides in the ability to show superior outcomes associated with it over prevailing tools and methods. Earlier EUS literature previously has shown its benefits over conventional ultrasound and computed tomography imaging in detecting and sampling liver lesions. This leads to the assumption that EUS could acquire a biopsy with fewer limitations compared with the percutaneous approach including body habitus, and allowing shorter recovery time and avoiding additional invasive procedures such as venipuncture. The ability to conduct real-time ultrasound imaging during the entire sampling procedure is particularly attractive to endosonographers and is a safety net to avoid any vascular or biliary structures along the track of the needle. This also allows for accurately detecting and targeting discrete hepatic lesions if present. From what we have learned so far, EUS-LB is a potentially less morbid and painful procedure compared with P-LB, allowing faster and smoother recovery.

Lastly, but no less importantly, the question of specimen adequacy has to be attended to carefully. An adequate liver sample for pathology review as defined by the American Association for the Study of Liver Disease is the presence of 11 or more complete portal triads (CPTs).[2] A total sample length of 30 mm or more with minimal to no fragmentation also is ideal to enhance the quality of the specimen. It should be noted that this is more rigorous than suggested by some other Professional societies. For example, the Royal College of Pathologists in the United Kingdom deem a minimum of 6 CPTs and a total sample length of 10 mm as adequate for making a diagnosis.[3] Earlier studies describing the adequacy of EUS-LB were limited by the use of a single Trucut needle (19 Gauge Quick-Core; Cook Medical, Inc, Winston-Salem, NC), frequently associated with mechanical failures. Therefore, the reported diagnostic accuracy in these small prospective studies varied widely from 29%[4] to 100%,[5] despite using the same needle. Pineda et al[6] set out to compare the diagnostic samples obtained via EUS-LB with those obtained via the P-LB and TJ-LB in a larger study of 110 patients. EUS-guided liver biopsies using a non-Trucut traditional all-purpose 19G FNA device produced comparable results in terms of total specimen length and complete portal tracts (in some cases, better than) when compared with the conventional P-LB and TJ-LB techniques.

New Needle Technology and Sampling Techniques Drive the Field Forward

In our opinion, EUS-LB greatly benefited from the recent technological advancements and the launch of multiple dedicated EUS-guided fine-needle biopsy (FNB) devices with enhanced tip designs for maximal tissue accrual. Several studies have been devoted to comparing outcomes of EUS needles including the now out-of-favor Trucut EUS biopsy needle, traditional FNA platforms, and the more recently developed FNB needles. Eskandari et al[7] compared 6 needles ranging in size from 19G to 22G for sampling freshly harvested bovine liver. This study showed superior outcomes in the 19G and 20G needles compared with the smaller-bore 22G needles in terms of mean CPTs obtained. In a similar design, Schulman et al[8] tested 6 needle types on human cadaveric tissue and reported that the novel SharkCore 19 Gauge needle (Medtronic, Inc, Minneapolis, MN) was associated with the maximal number of CPTs. In a study dedicated to assessing 19G needles only, Nakanishi et al[9] from our center compared three 19G needles in 113 patients who underwent EUS-LB. A reverse-bevel (Procore; Cook Medical, Inc), and a Nitinol-based 19G needle (19 Expect Flexible; Boston Scientific, Natick, MA) performed well in regard to obtaining adequate CPTs and total sample lengths. In the same study, the EUS-LB cohort was compared with 2 other cohorts: P-LBs and TJ-LBs, including 100 patients in each group. The

Nitinol-based EUS needle samples were comparable with these 2 established modalities when the number of CPTs was considered, but this came at the cost of increased fragmentation, interfering with the ability to diagnose and/or stage liver disease in some cases. Specimen adequacy for diagnosis and staging of liver disease was 80%, 100%, and 98% for EUS, PC, and TJ biopsies, respectively. The difference in specimen adequacy was related primarily to tissue fragmentation of EUS-LBs rather than biopsy core length or numbers of CPTs.

Specimen fragmentation remains a significant limitation of EUS-LB (Figure 1). It can significantly compromise diagnostic accuracy but, despite its importance, it often is overlooked in EUS literature. There is currently no standardized method for the assessment and quantification of fragmentation. Factors that potentially could increase fragmentation include smaller-gauge needles (22G), needle-tip design (eg, FNA tips designed for suction vs FNB tips designed for cutting), extensive parenchymal fibrosis, the amount of blood clots in the sample, and the method of specimen expulsion from the needle. Prospective comparative studies are needed to answer many questions on how to minimize specimen fragmentation.

Beyond the needle design and size, the optimal EUS technique to sample the liver remains under intense study. Diehl et al[10] report using the fanning technique, a well-assessed FNA technique that involves several to-and-fro movements of the needle in the liver with slight variation in the access angle, allowing sampling of new areas of the lobe. Other techniques that are well described in the FNB literature include the slow pull technique, referring to a slow and staggered removal of the needle stylet during the actuations in the liver. Finally, a liver-specific technique that recently emerged relies on the negative pressure transmitted through a column of saline filling the hollow space of the needle, referred to as the “wet suction” technique. Although all the techniques are safe, it remains to be seen if a particular one provides specimens that are superior to the others. Several head-to-head trials are underway and we expect to have robust answers within the next few years.

Take-Home Message

EUS-guided liver biopsy has evolved over the years to become a safe and effective alternative to image-guided liver tissue sampling. The low incidence of adverse events coupled with a steep learning curve facilitated the increasing adoption of this technique by endosonographers at various practice settings. At the same time, we acknowledge several limitations to the mainstream utilization of this technique, including the need for sedation, associated costs and risks of endoscopy, and training required in EUS. Nevertheless, EUS-LB remains a very viable option for patients already scheduled for an EUS examination who could benefit from a liver biopsy. We expect a steady and continuous improvement in our ability to accrue intact and adequate pathologic specimens as the technology continues to evolve in this field.

Abbreviations used in this paper

CPT complete portal triad
EUS endoscopic ultrasound
FNA fine-needle aspiration
FNB fine-needle biopsy
P-LB percutaneous liver biopsy
TJ-LB transjugular liver biopsy

Reprint requests

Address requests for reprints to: Mohammad A. Al-Haddad, MD, Department of Gastroenterology and Hepatology, Indiana University School of Medicine, 702 Rotary Circle, Suite 225, Indianapolis, Indiana 46202. e-mail: moalhadd@ iu.edu; fax: (317) 948-8145.

Conflicts of interest

The authors disclose no conflicts.

References

1. Mohan BP, Shakhatreh M, Garg R, et al. Efficacy and safety of EUS-guided liver biopsy: a systematic review and meta-analysis. Gastrointest Endosc 2019;89:238–246 e3.
2. Rockey DC, Caldwell SH, Goodman ZD, et al. Liver biopsy. Hepatology 2009;49:1017–1044.
3. Fryer E, Wang LM, Verrill C, et al. How often do our liver core biopsies reach current definitions of adequacy? J Clin Pathol 2013;66:1087–1089.
4. Dewitt J, McGreevy K, Cummings O, et al. Initial experience with EUS-guided Tru-cut biopsy of benign liver disease. Gastrointest Endosc 2009;69:535–542.
5. Gleeson FC, Clayton AC, Zhang L, et al. Adequacy of endo-scopic ultrasound core needle biopsy specimen of nonmalignant hepatic parenchymal disease. Clin Gastroenterol Hepatol 2008;6:1437–1440.
6. Pineda JJ, Diehl DL, Miao CL, et al. EUS-guided liver biopsy provides diagnostic samples comparable with those via the percutaneous or transjugular route. Gastrointest Endosc 2016; 83:360–365.
7. Eskandari A, Koo P, Bang H, et al. Comparison of endoscopic ultrasound biopsy needles for endoscopic ultrasound-guided liver biopsy. Clin Endosc 2019;52:347–352.
8. Schulman AR, Thompson CC, Odze R, et al. Optimizing EUS-guided liver biopsy sampling: comprehensive assessment of needle types and tissue acquisition techniques. Gastrointest Endosc 2017;85:419–426.
9. Nakanishi Y, Mneimneh WS, Sey M, et al. One hundred thirteen consecutive transgastric liver biopsies for hepatic parenchymal diseases: a single-institution study. Am J Surg Pathol 2015; 39:968–976.
10. Diehl DL, Johal AS, Khara HS, et al. Endoscopic ultrasound-guided liver biopsy: a multicenter experience. Endosc Int Open 2015;3:E210–E215.

Figure 1. Examples of samples obtained by various needles and techniques highlighting the degree of fragmentation of the liver specimens. EUS-guided sampling as opposed to percutaneous or transjugular routes: (*A*) percutaneous needle; (*B*) transjugular needle; (*C*) 19G Quick-core needle (Cook Medical, Winston-Salem, NC); (*D*) 19G Procore needle; (*E*) 19G flexible Nitinol needle; and (*F*) 22G Franseen tip needle (Acquire, Boston Scientific Corp, Natick, MA).