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EUS-guided liver biopsy: the optimal technique?

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Liver biopsy remains the gold standard for diagnosis of parenchymal liver disease. For decades, percutaneous liver biopsy (PLB) has been performed at bedside, based on percussion of the right hepatic lobe. Considered the gold standard, PLB now frequently employs image guidance, most commonly utilizing pre-biopsy ultrasound marking or real-time guidance. Transjugular liver biopsy (TJLB), performed by interventional radiologists, is ideal for patients with ascites, coagulopathy or obesity. In almost all cases, TJLB also samples the right hepatic lobe via the right hepatic vein given the anatomic access advantage.

EUS-guided liver biopsy (EUS-LB) has become an attractive option, particularly with the emergence of endo-hepatology, which can allow for variceal screening/management, elastography, direct portal pressure measurement, and liver biopsy in the same setting. EUS needles have evolved over the last 15 years, from fine-needle aspiration to spring-loaded biopsy to fine-needle biopsy (FNB). Current FNB needles with incorporated cutting surfaces allow for reliable core tissue acquisition. In the realm of liver histology, however, it is all dependent on the adequacy of the sample. The American Association for the Study of Liver Diseases (AASLD) defines an adequate liver biopsy sample as a 2- to 3-cm-long specimen containing at least 11 complete portal tracts (CPTs) [1]. This is concordant with the recommendation from the British Royal College of Pathology, requiring at least 2-cm-long specimen and >10 portal tracts [2]. Thus, EUS-LB needs to provide reliable samples to meet these standards.

In some institutions, EUS-LB has supplanted both PLB and TJLB as the preferred route for tissue acquisition. Compared to PLB and TJLB, EUS-LB is comparable for specimen adequacy and may be superior when bi-lobar samples are obtained [3]. Advantages of EUS-LB include decreased patient anxiety and increased patient satisfaction, as it is performed under sedation. In addition, real-time imaging is applied with Doppler analysis to avoid large blood vessels. The post-procedural monitoring time is shorter (typically 1 hour), and there is less post-procedure pain and lower complications rates compared to the other biopsy methods [4]. EUS-LB also provides the option for bi-lobar (right and left lobe) biopsies to decrease sampling error, particularly when assessing for non-alcoholic fatty liver disease (NAFLD), which can have a patchy distribution [5]. This is typically the current algorithm followed by most endosonographers: a single biopsy from both the right and left hepatic lobe. The question at hand is whether EUS-guided left lobe biopsies alone are adequate for diagnosis, as compared to right hepatic lobe or bi-lobar biopsies.

In this issue of Endoscopy International Open, Mithun et al [6] present a pilot study assessing the safety and accuracy of left-lobe EUS-LB compared to right-lobe and bi-lobar EUS-LB. Fifty patients underwent EUS-guided 22G FNB with a Franseen-tip needle from both the right and left lobe of the liver. Three blinded pathologists interpreted the specimens for adequacy and diagnosis. Biopsies were performed using the 'fanning' technique, with a dry 'slow-pull' withdrawal of the stylet. The median number of needle passes to achieve an aggregate specimen length of at least 2 cm was 2 for the left-lobe and 2.06 for the right-lobe. There was no significant difference in aggregate specimen length (LL: 2.31 ± 0.57 cm; RL 2.28 ± 0.69 cm; $P = 0.476$), number of CPTs (LL: 11.84 ± 6.71; RL: 9.58 ± 7.14; $P = 0.106$), and percentage of adequate specimens defined as length ≥ 2 cm + CPTs ≥ 11 (LL: 84 %; RL 76 %, $P = 0.3197$) between left-lobe and right-lobe biopsies. There was strong pa-

thology agreement between left-lobe and right-lobe biopsies (κ = 0.830), left-lobe and bi-lobar biopsies (κ = 0.878) and right-lobe and bi-lobar biopsies (κ = 0.903).

The endosonographers subjectively reported that right-lobe EUS-LB was more challenging compared to the left lobe. With regard to adverse events, one (2 %) serious complication of intraperitoneal bleeding requiring laparoscopy for hemostasis occurred in a patient who underwent three needle passes for EUS-LB of the right lobe. One additional minor intraprocedural bleed was reported following two needle passes to the right lobe that resolved spontaneously. The authors conclude EUS-LB from the left lobe may be safer, technically easier and sufficient to obtain a diagnosis compared to right-lobe or bi-lobar biopsy.

There are several aspects of this study that require critique. First, a 22G FNB needle was used for tissue acquisition. Currently, the preferred needle for EUS-LB is a 19G FNB needle, which demonstrates superior specimen adequacy and less tissue fragmentation compared to a 22G FNB needle or a 19G FNA needle [7–10]. Furthermore, the Franseen-tip appears to outperform the fork-tip in 19G FNB needle designs [10]. Likely due to the smaller needle gauge in this study, the mean number of CPTs was below the adequate level for right-lobe biopsy (9.58), and just at the adequate level (11.84) for left-lobe biopsies, leading to a higher rate of inadequate and compromised samples compared to 19G FNB studies. In addition, use of the smaller needle may have led to a higher number of passes required to obtain an adequate aggregate specimen length, resulting in the increased bleeding rate from right-lobe biopsies. The authors admit that the study was conceptualized in 2019 and implemented in 2020, when literature was not as definitive on the superiority of a 19G FNB needle. It is notable that the diagnostic rate in the study is comparable to those utilizing 19G needles.

A dry 'slow-pull' biopsy technique was used in this study. More recent literature suggests that a wet suction technique, where the stylet is removed and the needle primed with heparinized saline, is preferrable [11]. This can decrease blood clotting within the needle, allowing better tissue recovery and decreased fragmentation. The number of to and fro needle movements has also been evaluated; three actuations outperform a single needle actuation in regard to specimen adequacy, with a needle "throw" depth of at least 3 cm. However, two needle passes are required to reliably meet pathology criteria for tissue adequacy [12].

We agree that performing EUS-LB from the right hepatic lobe can be more challenging, and frankly, awkward at times. The echoendoscope is in a long position in the duodenal bulb, and frequently requires external rotation to adequately visualize the right lobe. EUS-LB from the left lobe is technically easier, as it is performed from the proximal stomach with the echoendoscope in a short, straight position.

Interestingly, 60 patients actually underwent EUS for the purpose of liver biopsy in this study. However, 10 patients (17 %) were not biopsied, and thus, were excluded for various reasons: intervening ascites, intervening large collateral vessels, small hepatic lobe, gallbladder in needle path, and failed duodenal intubation. This "failure rate" seems to be an outlier among EUS-LB studies, but is a reason to have additional indications for the endoscopic procedure, such as variceal screening/management, direct portal pressure management, and/or pancreatico-biliary evaluation.

The optimal technique for obtaining a liver biopsy is ultimately decided by resource availability and cost, as all three techniques (PLB, TJLB, EUS-LB) can obtain adequate specimens. In a cost-neutral world with unlimited resources, we feel EUS-LB would be the ideal technique given patient comfort, lower complication rate and ability to sample both hepatic lobes if needed. Unfortunately, Utopia does not exist, so liver biopsy technique will remain dependent upon local expertise and availability.

Regarding the optimal technique for EUS-LB, with current evidence, we feel it should be tailored to the individual patient and indication. If being performed to assess nonalcoholic fatty livery disease or nonalcoholic steatohepatitis, then likely bi-lobar biopsies should be performed to decrease sampling error due to regional variation [4]. For other indications, we suspect two biopsies from the left hepatic lobe would be sufficient, although yet proven. A Franseen-tip 19G FNB needle utilizing wet suction with at least 3 needle actuations appears to be optimal [10–12]. However, a modified one-pass, one actuation with a 7-cm "throw" yielded an adequate sample in all cases [10]. Common sense opines that one pass may be safer than two.

Mithun et al. raise the interesting question of whether EUS-LB from the left lobe alone suffices for diagnosis of parenchymal liver disease. Given limitations of this study, the question still remains. The number of biopsies, the number of needle actuations, and the needle "throw" depth are still worthy of study, to optimize technique for specimen adequacy. With the field of endo-hepatology in full motion, the time is right for a larger prospective multicenter study to address these questions, as EUS-LB is here to stay.

Competing interests

The authors declare that they have no conflict of interest.

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