Safety and adequacy of endoscopic ultrasound-guided random liver biopsy in comparison with transjugular and percutaneous approaches

ABSTRACT

Background and study aims Endoscopic ultrasound-guided liver biopsy (EUS-LB) is an accepted technique for tissue acquisition. Traditionally, random LB has been performed with percutaneous (PC-LB) and transjugular (TJ-LB) approaches. The purpose of this study was to compare the safety profile and efficacy of EUS-LB, PC-LB, and TJ-LB.

Patients and methods A retrospective analysis was performed at a tertiary academic medical center. Inclusion criteria for analysis were all adult patients who underwent EUS-LB since inception and TJ-LB/PC-LB over a 3-year span (June 2016 to June 2019). The primary outcome assessed was any adverse events. Secondary outcomes included technical success resulting in tissue acquisition and diagnostic adequacy of the sample for histologic analysis.

Results A total of 513 patients were included for analysis. There were 135 EUS-LB, 287 PC-LB, and 91 TJ-LB. The most common indication for LB was abnormal liver function tests. For the primary outcome, the rate of adverse events was low with reported (<1%). There were two in the EUS-LB group, two in the PC-LB group, and one in TJ-LB group, and this difference was not statistically significant (P=0.585). The technical success rate was 100% in each group. The rate of diagnostic adequacy was 100% in TJ-LB group and 99% in both EUS-LB and PC-LB groups. This difference was not statistically significant (P=1.000). The most common histologic finding was non-specific changes (33.7%) followed by non-alcoholic steatohepatitis (15.6%).

Conclusion In comparison with PC-LB and TJ-LB, EUS-LB has comparable safety profile, technical success rate, and diagnostic adequacy. EUS-LB should be considered as an option for random liver biopsy.

Introduction

Endoscopic ultrasound-guided liver biopsy (EUS-LB) is an established method for tissue acquisition of hepatic parenchyma for histologic analysis [1]. LB remains the gold standard for the diagnosis and staging of a variety of hepatic disorders [2]. Although non-invasive testing such as serologic markers, imaging modalities, and elastography have reduced the need for LB, histologic analysis remains necessary in a variety of clinically important situations. This includes but is not limited to diagnosis...
and response to therapy in auto-immune hepatitis, AMA-negative
primary biliary cholangitis, small-duct primary sclerosing
cholangitis, response therapy for chronic hepatitis B infection,
infiltrative disorders, and discerning simple steatosis from
non-alcoholic steatohepatitis (NASH) [3].

LB is most commonly performed using percutaneous (PC-LB)
and transjugular (TJ-LB) approaches. Limitations of the PC-LB
method include sampling error as only the right lobe is accessi-
ble for biopsy, pain, hemorrhage, and hematoma. Limitations of
TJ-LB approach include neck hematoma, vascular injury, ar-
terio-venous fistula, and intra-abdominal hemorrhage [4].

EUS fine-needle aspiration (FNA) and fine-needle biopsy
(FNB) have been routinely employed for targeting abnormal so-
lid and cystic liver lesions accessible from transgastric or trans-
duodenal approaches [5]. More recently, EUS-LB to diagnose
parenchymal liver disease has been shown to be as effective as
both PC-LB and TJ-LB approaches in terms of diagnostic yield
[6]. In addition, EUS-LB has the advantage of sampling multiple
segments of the liver. Finally, this technique has been shown to
have a favorable safety profile as a recent meta-analysis found
the pooled adverse event rate to be 2.3% [7].

Despite the increasing use of EUS-LB, there is a paucity of
data regarding the safety and efficacy in comparison with PC-
LB and TJ-LB approaches. The purpose of this study was to com-
pare the efficacy and safety profiles of EUS-LB, PC-LB, and TJ-LB.

Patients and methods

A retrospective analysis was performed at a tertiary academic
medical center. The study was approved by the institutional re-
view board and informed consent was waived given the ret-
rospective nature of the study. Inclusion criteria were all adult pa-
tients that underwent EUS-LB since inception of this procedure
at our institution (October 2013 to June 2019) and TJ-LB/PC-LB
over a 3-year span (June 2016 to June 2019). Exclusion criteria
included patients under 18 years old, patients with concern for
primary or secondary hepatic malignancy, or if the indication
for biopsy was a discrete imaging finding. The indications for
hepatic biopsy were recorded. Hepatobiliary pathology records
were utilized to create a patient database and they were strati-
fied according to type of modality used for random hepatic
biopsy. All biopsy specimens were assessed by expert liver pa-
thologists.

EUS-LB was performed by five experienced interventional
endoscopists. All EUS-LB were performed using a 19-gauge
needle (Expect FNA 2013 to 2017, Acquire FNB 2017 to 2019
Boston Scientific). The core sample was confirmed by the ther-
apeutic endoscopy team. The majority of specimens were ob-
tained from the left hepatic lobe via a transgastric approach.

The primary outcome assessed was any adverse events related
to EUS-LB, PC-LB, or TJ-LB. The definition of adverse event
(AE) was adopted from the International Organization of Stan-
dardization (ISO) and defined as “any untoward medical occur-
rence, unintended disease or injury, or untoward clinical signs”
[8]. These were considered related to the procedure if they oc-
curred within 30 days. Secondary outcomes included technical
success defined as sufficient tissue acquisition for histologic a-
alysis and diagnostic adequacy defined as ability to reach a
histopathologic diagnosis independent of number of portal
triads or fragmentation. Demographic data and the indication
for the procedures were all collected. The histologic findings
were collected.

The statistical analysis was performed by a professional sta-
tistician in the department of public health. All measures were
summarized by biopsy method using means and standard de-
viations for continuous measures and counts and percentages
for categorical measures. Mean ages were compared between
methods using an analysis of variance (ANOVA) model. Distri-
butions of patient sex, etiology, location, technical success, di-
agnostic adequacy, and the occurrence of adverse events were
compared between methods using either chi-square tests or
Fisher’s exact test, as appropriate. All analyses were performed
using STATA version 16.1 (StataCorp LLC, College Station,
Texas, United States).

Results

A total of 513 patients were reviewed and included for statisti-
cal analysis. There were 135 EUS-LB, 287 PC-LB, and 91 TJ-LB
patients. The mean age of each group was 53 years old for
EUS-LB, 52 years old for PC-LB, and 51 years old for TJ-LB. There
was an overall female preponderance at 52.4%. The most com-
mon indication for LB regardless of modality was abnormal liver
function tests (EUS-LB 89%, PC-LB 89%, TJ-LB 55%). The demo-
graphic data and indications for liver biopsy are summarized in
Table 1.

For the primary outcome, the total rate of AEs was low with
five reported (<1%). There were two events in the EUS-LB
group, two events in the PC-LB group, and one event in the TJ-
LB group. This difference was not statistically significant (P=
0.585). There was a single patient with 30-day mortality in the
EUS-LB group, however, this was determined to be unrelated to
the procedure. The technical success rate was 100% in each
group. The rate of diagnostic adequacy was 100% in TJ-LB
group and 99% in both EUS-LB and PC-LB groups. This differ-
ence was not statistically significant (P=1.000). The study out-
comes are summarized in Table 2. The most common histo-
logic findings were non-specific histologic changes (33.7%) and
NASH (15.6%). These results are summarized in Table 3.

In each cohort, a random sample of specimens was reviewed
by our hepato-pathologists and mean number of complete por-
tal tracts (CPT) and specimen lengths were assessed. The mean
number of CPT was higher in the EUS-LB group (19.7) than the
PC-LB (17.44) and TJ-LB (10.5) groups. This difference was sta-
tistically significant (P=0.0083). The mean specimen lengths
were greater in the EUS-LB group (3.47 cm) than the PC-LB
(2.92 cm) and TJ-LB (2.11 cm) groups. This difference was also
statistically significant (P=0.0163). These results are summarized
in Table 2.
Discussion

The acquisition of hepatic tissue via liver biopsy remains essential for the diagnosis, staging, and management of a variety of benign hepatic disorders [9, 10]. Traditionally, liver biopsy has been performed percutaneously often with ultrasound guidance or by interventional radiology using a transjugular approach [11, 12]. A recent alternative to these techniques is EUS-LB in a patient that is already undergoing an endoscopic procedure such as esophagogastroduodenoscopy or endoscopic ultrasound for an accepted indication, EUS-LB can be performed with minimal added procedure time or risk [13].

In this study, we found that the safety profile and diagnostic adequacy is comparable between EUS-LB, PC-LB, and TJ-LB. The overall rate of AEs was generally low in all procedure groups (< 1 %). A single patient in each group had post-procedural pain requiring intravenous analgesia and a patient in the PC-LB group had self-limited bleeding. One patient in the EUS-LB cohort experienced 30-day mortality, which was determined to be unrelated to the procedure.

Hepatic needle biopsy was first described by Paul Ehrlich in 1883 [14]. PC-LB is the most commonly used approach for tissue acquisition. The advantages include cost-effectiveness, limited equipment, and less technical skill required [13, 15]. Conversely, disadvantages of this method are sample bias given only the right lobe is accessible and procedure related pain [16]. TJ-LB is another commonly used modality for biopsy. Advantages of this technique include ability to perform hepatic venous pressure gradient measurements simultaneously and comparatively less complications [17, 18]. However, TJ-LB confers higher cost than PC-LB, requires more technical skill, and is more time-consuming [17, 19].

Levy et al first described using EUS-LB for hepatic tissue acquisition using a disposable 19G Trucut needle (EUS-TCB, QuickCore, Wilson-Cook) [20]. In their experience FNB was comparable to FNA for diagnostic adequacy and was found to require fewer passes. In addition, there is the added benefit of not requiring on-site cytology for tissue preparation as opposed to FNA. Subsequent studies using updated devices with both 19G and 22G FNB needles have shown excellent diagnostic ade-

<table>
<thead>
<tr>
<th>Measure</th>
<th>EUS (n=135)</th>
<th>Percutaneous (n=287)</th>
<th>Transjugular (n=91)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years; mean (SD)</td>
<td>53 (15)</td>
<td>52 (15)</td>
<td>51 (15)</td>
<td>0.54</td>
</tr>
<tr>
<td>Male; n (%)</td>
<td>49 (36)</td>
<td>145 (51)</td>
<td>50 (55)</td>
<td>0.007</td>
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<td>Etiology; n (%)</td>
<td></td>
<td></td>
<td></td>
<td>&lt;0.001</td>
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<tr>
<td>Abnormal LFT</td>
<td>120 (89)</td>
<td>254 (89)</td>
<td>50 (55)</td>
<td></td>
</tr>
<tr>
<td>Abnormal Imaging</td>
<td>9 (7)</td>
<td>5 (2)</td>
<td>3 (3)</td>
<td></td>
</tr>
<tr>
<td>Suspected adv fib Cirrhosis</td>
<td>3 (2)</td>
<td>4 (1)</td>
<td>17 (19)</td>
<td></td>
</tr>
<tr>
<td>Follow-up of chronic condition</td>
<td>3 (2)</td>
<td>22 (8)</td>
<td>21 (23)</td>
<td></td>
</tr>
</tbody>
</table>

LFT, liver function test.

<table>
<thead>
<tr>
<th>Measure</th>
<th>EUS (n=135)</th>
<th>Percutaneous (n=287)</th>
<th>Transjugular (n=91)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adverse events; n (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>133 (99)</td>
<td>285 (99)</td>
<td>90 (99)</td>
<td>0.507</td>
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<tr>
<td>Severe pain</td>
<td>1 (1)</td>
<td>1 (0)</td>
<td>1 (1)</td>
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<td>Bleeding</td>
<td>0 (0)</td>
<td>1 (0)</td>
<td>0 (0)</td>
<td></td>
</tr>
<tr>
<td>Mortality (within 30 days)</td>
<td>1 (1)</td>
<td>0 (0)</td>
<td>0 (0)</td>
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</tr>
<tr>
<td>Any adverse event; n (%)</td>
<td>2 (1)</td>
<td>2 (1)</td>
<td>1 (1)</td>
<td>0.585</td>
</tr>
<tr>
<td>Technical success; n (%)</td>
<td>135 (100)</td>
<td>287 (100)</td>
<td>91 (100)</td>
<td>–</td>
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<tr>
<td>Diagnostic adequacy; n (%)</td>
<td>134 (99)</td>
<td>284 (99)</td>
<td>91 (100)</td>
<td>1.000</td>
</tr>
<tr>
<td>Complete portal tracts; n</td>
<td>19.7 (10)</td>
<td>17.4 (9)</td>
<td>10.5 (10)</td>
<td>0.0083</td>
</tr>
<tr>
<td>Specimen length (cm); n</td>
<td>3.47 (10)</td>
<td>2.92 (9)</td>
<td>2.11 (10)</td>
<td>0.0163</td>
</tr>
</tbody>
</table>
Acuity and efficacy [21–23]. EUS-LB confers an advantage over other modalities of being able to obtain tissue from multiple segments of the liver, thus limiting sample error [24]. However, access to the right lobe via a transduodenal approach is technically more demanding than the left lobe via a transgastric approach [25]. Disadvantages of this approach are the cost and sedation related to the procedure. This is generally mitigated by performing this procedure in conjunction with an endoscopic procedure for another indication [21]. However, there remains a paucity of data regarding the safety profile and diagnostic adequacy of EUS-LB in comparison with other approaches.

This study has several strengths. First, this is a large cohort of EUS-LB patients in comparison with most previous studies with over 135 included for analysis. Second, EUS-LB was performed by five experienced endoscopists, thus improving generalizability. This study also has limitations. As with any retrospective study there is the potential of confounding from variables that were unable to be measured. In addition, there was incomplete documentation for the EUS-LB cohort in regard to which lobe was accessed and regarding which technique was utilized. This can be valuable information as previous studies have shown that biopsies from multiple hepatic segments may decrease sample bias [26]. All AEs were found retrospectively and thus there is the potential that they were not completely captured. Finally, there is a potential selection bias in patients that have undergone a liver transplant as these patients are under the care of a transplant hepatologist that may perform PC-LB over other approaches.

**Conclusion**

In conclusion, the results of this study show that EUS-LB is associated with low rate of AEs and high diagnostic adequacy in comparison with TJ-LB and PC-LB. EUS-LB should be considered as an option for acquisition of hepatic tissue for histologic analysis, especially if another endoscopic procedure is planned. Further prospective and potentially multicenter studies are warranted to validate these findings.

**Competing interests**

The authors declare that they have no conflict of interest.

**References**


