Liver Biopsy: Ultrasonography Guidance is not Superior to the Blind Method

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Abstract

Aim: The aim of this study was to evaluate our experience with adequate liver biopsy samples and compare the complication rates of blind and US-guided biopsies, as well as to compare the histological yield of blind and US-guided biopsy specimens. Methods: We retrospectively analyzed 205 consecutive patients that underwent liver biopsies during a 12-month period. Liver biopsy was performed via the blind method in 152 patients, and via US-guidance in 53 patients. Biopsy specimens were evaluated according to length, presence of fragmentation, crush artifacts, adequacy for diagnosis, and the number of portal tracts and central veins. We also evaluated the rates of mortality and major life-threatening complications. Results: All the biopsy specimens were adequate for histological evaluation, except in 8 cases, of which 4 were in the blind biopsy group (2.63%) and 4 were in the US-guided biopsy group (7.54%) (P > 0.05). There were no statistically significant differences between the two groups in terms of the specimen fragmentation, or number of portal tracts and central veins in each specimen. Mean specimen length in the US-guided liver biopsy group was 12.58 ± 5.59 mm, and in the blind biopsy group 16.22 ± 9.91 mm (P < 0.005). There was no mortality or major complications in either of the two study groups. Conclusion: US-guided biopsy was not superior to blind biopsy, an unexpected result. Gastroenterologists/hepatologists should be encouraged to perform liver biopsies via the blind method.

Key words


Introduction

Percutaneous needle liver biopsy (LB) is an important procedure in the diagnosis of and assessment of the severity of liver diseases. Complete evaluation of patients with diffuse liver diseases requires clinical and laboratory examinations, and histopathological examination of liver tissue. Histopathological examination of liver tissue plays an important role in confirming the diagnosis of chronic hepatitis, assessing necro-inflammatory activity (grading), staging the severity of fibrosis, excluding other pathologies or associated diseases, and certifying the diagnosis of cirrhosis (if present) [1]. The first percutaneous LB was performed by Paul Ehrlich in Germany in 1883; however, the procedure required an intrahepatic phase as long as 15 minutes, making it impractical and unsafe. Sheila Sherlock described the percutaneous LB technique in 1945 and then Menghini reported a technique for the “1-second needle biopsy of the liver” in 1958, which has since become the most widely used technique [2, 3]. Since Menghini, the evolution of liver biopsy has been extensive. At present, percutaneous biopsies are performed primarily by gastroentero/hepatologists or by radiologists. A variety of approaches may be utilized for obtaining a liver tissue sample. These include a blind percutaneous biopsy after percussion of the chest wall, biopsy under ultrasonography (US) or CT guidance, intravascular tissue sampling via the hepatic vein, and intra-abdominal biopsy during laparoscopy or laparotomy. The choice of procedure is based on availability, personal preference, and the clinical status of the patient. Various needles are also available for use, depending on the approach and physician experience [4]. The aim of the present study was to evaluate our experience with adequate LB samples and to compare the complication rates of blind and US-guided biopsies, as well as the histological yield of blind and US-guided biopsy specimens.

Material and methods

We retrospectively analyzed 205 consecutive patients
that had underwent LB during a 12-month period. Liver biopsies were performed via the blind method using the Menghini technique in 152 patients, and via US-guidance with automated needles in 53 patients. All patients were informed about the indications and possible risks of the procedure and written informed consent was obtained from each patient at least one day prior to the procedure. In all, 99 patients had chronic HBV infection, 62 chronic HCV infection, 17 had unknown liver enzyme elevation, and the rest had other etiologies (e.g. primary biliary cirrhosis, autoimmune hepatitis).

No patient had clinical diagnosis of cirrhosis and all patients had well compensated liver diseases. Coagulation tests, including a complete blood count, prothrombin time, and partial thromboplastin time, were performed in every patient. Abnormal coagulation test results, use of medications with warfarin, acetylsalicylic acid, non-steroid anti-inflammatory drugs, or other antiplatelet agents one week prior to the procedure and the presence of ascites, infection or fever were considered contraindications for the procedure. To exclude other pathologies that contraindicate the blind biopsy procedure, the patients also underwent abdominal US. No patient had contraindications for liver biopsy. All the patients were hospitalized for 24 hours after the procedure. On the day of the procedure patients were encouraged to have a light breakfast. The procedure was explained in detail to every patient and each step of the procedure was announced. The present study was performed in accordance with the Declaration of Helsinki.

For blind biopsies the puncture site was localized via percussion and then anesthetized with 5 mL of 1% mepivacaine hydrochloride. The entire procedure was carried out in aseptic conditions. After making a small incision, the biopsy was performed via the transcostal approach using the Menghini technique with a 1.4 mm needle (Braun Hepafix Luer Lock 17 G/1.4 mm, Melsungen, Germany) in exhalation. Each procedure was performed by an experienced gastroentero/hepatologist.

For US-guided biopsy US guidance was performed using a Siemens Sonoline Adora 7.5-MHz linear transducer. A TruCore® 1 URO 18 G ’25 cm automated core biopsy needle was used. A GE (General Electric, USA) Logiq 5 expert US unit with a 3.6-MHz convex transducer was used to examine patients. Each procedure was performed in its entirety by an experienced radiologist.

The number of passes made for both biopsy methods depended on the physician’s suspicion that a specimen of adequate size would not be obtained, based on gross visual assessment. Biopsy specimens were placed in a formalin-filled container and sent to the pathology department for histological examination. All biopsy specimens were examined by the same pathologist specialized in liver pathology. Each specimen was examined to determine the adequacy of the sample, as well as for diagnosis and assessment of the severity of liver disease.

Biopsy specimens were evaluated in terms of length, presence of fragmentation, crush artifacts, adequacy for diagnosis, and the number of portal tracts and central veins. We also evaluated the rates of mortality and major life-threatening complications. Minor complications, such as postoperative pain, vasovagal reactions, and transient hypotension, were not evaluated.

### Statistical analysis

Statistical analyses were made using the Student’s t and chi square tests, with significance set at P < 0.05. Results were presented as the mean ± SD. Statistical calculations were performed using the SPSS version 10.0 statistical software (SPSS Inc., Chicago, IL, USA).

### Results

There were no statistically significant differences between the two groups in terms of age or sex. Both groups were comparable with respect to number of passes. Biopsy specimen characteristics are shown in the Table I. All the biopsy specimens were adequate for histological evaluation, except in 8 cases; 4 in the blind biopsy group (2.63%) and 4 in the US-guided biopsy group (7.54%) (P > 0.05).

In all, 13.81% of the patients in the blind biopsy group and 13.20% in the US-guided biopsy group were diagnosed with histopathologically proven cirrhosis (P > 0.05).

There were no statistically significant differences between the two groups in terms of the number of biopsy specimens, specimen fragmentation, or the number of portal tracts and central veins in each specimen. Mean length of

### Table I. Comparison of biopsy specimen characteristics between blind and US-guided procedures.

<table>
<thead>
<tr>
<th></th>
<th>Group</th>
<th>n</th>
<th>Mean</th>
<th>SD</th>
<th>SE Mean</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Length (mm)</td>
<td>Blind</td>
<td>152</td>
<td>16.22</td>
<td>9.91</td>
<td>0.80</td>
<td>0.0013</td>
</tr>
<tr>
<td></td>
<td>US-guided</td>
<td>53</td>
<td>12.58</td>
<td>5.59</td>
<td>0.77</td>
<td></td>
</tr>
<tr>
<td>Number of portal tracts</td>
<td>Blind</td>
<td>129</td>
<td>10.82</td>
<td>4.66</td>
<td>0.41</td>
<td>0.3967</td>
</tr>
<tr>
<td></td>
<td>US-guided</td>
<td>45</td>
<td>10.13</td>
<td>4.74</td>
<td>0.71</td>
<td></td>
</tr>
<tr>
<td>Number of central veins</td>
<td>Blind</td>
<td>45</td>
<td>7.36</td>
<td>3.21</td>
<td>0.48</td>
<td>0.0935</td>
</tr>
<tr>
<td></td>
<td>US-guided</td>
<td>19</td>
<td>5.74</td>
<td>4.04</td>
<td>0.93</td>
<td></td>
</tr>
<tr>
<td>Presence of fragmentation</td>
<td>Blind</td>
<td>152</td>
<td>0.25</td>
<td>0.57</td>
<td>0.05</td>
<td>0.4511</td>
</tr>
<tr>
<td></td>
<td>US-guided</td>
<td>53</td>
<td>0.32</td>
<td>0.64</td>
<td>0.09</td>
<td></td>
</tr>
</tbody>
</table>
US-guided LB specimens was significantly lower than of blind biopsy specimens (Table 1).

Neither mortality nor major complications (e.g. bleeding, pneumothorax, biliary peritonitis, and puncture of other organs) developed in both groups. Since minor complications were not recorded in the data and the present study was retrospective, we could not evaluate them. Nor could we evaluate the effect of the body mass index which could have affected the size of specimens.

**Discussion**

Percutaneous LB can be performed via two methods: blind and US-guided. The conventional percutaneous blind LB procedure is the simplest, quickest, and the most commonly performed approach in modern medical practice, and is very safe when performed by experienced hands.

Blind percutaneous LB has been performed for years and is still widely performed by gastroenterologists worldwide. US examination of the liver and bile ducts prior to the procedure provides important information about unknown mass lesions, and the anatomy of the liver and its relationship with adjacent organs. As such, all patients should be examined by US prior to the procedure. On the other hand, some advocate performing US examination only in selected patients, such as those with a history of upper abdominal surgery, those in whom the maximal hepatic dullness cannot be determined, and those suspected of having advanced cirrhosis with possible atrophy of the right lobe of the liver, based on clinical or laboratory results. It is known as “non real time sonographic guidance” [5, 6].

The most challenging aspect of the procedure is determining which method to use: 3/4 blind or US-guided. One study reported that complications cannot be avoided with the use of US prior to biopsy [7]. In a recent study that evaluated 222 consecutive biopsies, US was shown to be helpful in only 3.6% of patients in whom the biopsy site was marked by percussion [8]. The biopsy site marked by percussion changed in 13% of patients after US in another study, which led to abortion of the procedure in 4 patients [9]. In contrast, US guidance resulted in a lower complication rate and a higher diagnostic yield in two large studies [10, 11]. Similarly, Piccinino et al retrospectively evaluated 68,276 patients who underwent blind liver biopsies, and reported a 2.2% complication rate. Most complications were severe, including shock, pneumothorax, biliary peritonitis, and puncture of other organs (colon, kidney, lung) [12]. Fatal hemorrhages have also been reported following blind liver biopsies [13]. The American College of Radiology practice guidelines on percutaneous needle biopsy suggest a threshold for major complications, including a bleeding rate of 10%, infection rate of 2%, and peritonitis rate of 2% [14]. In contrast with other studies indicating that US-guided biopsy is associated with lower complication rates, neither mortality nor any life-threatening complications (e.g. bleeding, pneumothorax) developed following blind or US-guided liver biopsy procedures in the present study. This might be related to the fact that the patients evaluated in this study had well compensated liver disease and they also underwent abdominal US in order to evaluate contraindications for biopsy prior to the procedure. Another explanation for the absence of complications might also be related to the small number of patients included in this study. All biopsies were performed by experienced operators.

A biopsy specimen is considered to represent 1/50,000 of the total mass of the liver when it is 1-4 cm in length and 1.2-1.8 mm in diameter [15]. According to the British guidelines for LB, a biopsy specimen containing at least 6-8 portal triads is considered adequate [15]. Biopsy samples ≥ 2 cm in length and containing ≥ 11 portal tracts should be reliable for grading and staging chronic viral hepatitis [16, 17]. However, criteria for the adequacy of biopsy specimens vary according to the etiology of the liver disease. We accepted the specimen as adequate, when the length and the number of portal tracts were adequate to make diagnosis by the pathologist.

In the present study mean length of the samples obtained via blind biopsy was close to the length proposed in the literature, whereas that obtained via US-guidance was shorter. Nonetheless, the samples obtained with both methods were optimal with respect to the number of portal tracts. We did not observe any significant differences between blind and US-guided biopsy in terms of the number of portal tracts and central veins or sample fragmentation. Mean length was greater in blind biopsy samples than in US-guided biopsy samples and the difference was statistically significant.

The main drawbacks of LB as a diagnostic procedure are sampling and observation errors [18]. As LB involves only a part of the organ, the sample obtained may be inappropriate for evaluating a lesion heterogeneously distributed throughout the liver; therefore, increasing the length of the biopsy specimen can reduce the risk of the sampling error [16, 19, 20]. The length of the biopsy specimen, rather than the number of portal tracts, appears to be a relevant criterion for assessing the adequacy of a LB, especially as counting portal tracts is difficult in cases of septal fibrosis or cirrhosis. A 25-mm biopsy specimen is considered the optimal length for accurate evaluation, although 15 mm has also been considered sufficient in most studies. In our study, mean biopsy specimen length was 16.2 mm for blind biopsies and 12.8 mm for US-guided biopsies; the difference was statistically significant, which may have been due to differences between the needles. The needles used for blind biopsy allow tissue as long as the needle to be obtained; however, US-guided biopsy needles due to their characteristics 3/4 limit the length of tissue that can be obtained.

The diameter of the core is also important. Needles of 16-18 G have been shown to be much more useful for obtaining biopsy specimens suitable for accurate staging and grading of chronic liver disease, whereas fine needle biopsy, in which 20-22 G needles are used, has been shown to be inappropriate for this purpose [21]. We used needles...
of appropriate diameter in both techniques, which may explain why there was not a statistically significant difference between the two techniques with respect to adequacy for histopathologic examination.

Another important aspect of US-guided biopsy is its cost-effectiveness. Based on an economic analysis, the use of US for marking the biopsy site was reported to be cost-effective [22]. The use of US in order to avoid complications requiring hospitalization was also reported to be cost-effective [23]. Yet, there are no data about the cost-effectiveness of blind or US guided liver biopsy in Turkey. We, however, think that US guided LB is not cost effective because there were no complications requiring hospitalization in either of our biopsy groups.

The most important issue concerning LB should not be whether blind or US guided techniques are used; as there were no differences between blind and US-guided biopsy with respect to adequacy and complication rates in the present study, either technique can be used in any given patient in whom a LB is indicated. We recommend the use of US for marking the percutaneous biopsy site in obese patients in the following cases: when adequate localization by percussion cannot be achieved, when there is a suspicion of a focal lesion (e.g. hemangioma) in the liver, for less experienced operators, and when preferred by the operator.

Conclusion

There are no significant differences between blind biopsy and US-guided biopsy in terms of adequacy of biopsy samples or complication rates. Therefore, we advocate blind biopsy for patients in whom histopathologic examination of the liver tissue is necessary, following adequate preparation of the patient by experienced hands. Because US-guided biopsy was not superior to blind biopsy - an unexpected result - gastroentero/hepatologists should not hesitate to perform LB via the blind method.

Conflicts of interest

None to declare.

References