

How to improve the quality of the tissue sample obtained by percutaneous liver biopsy

Review Article

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Abstract: The evaluation of liver lesions in patients with chronic hepatopathy is mandatory for assessing prognosis and sometimes for making treatment decisions. The liver biopsy (LB) is still considered the gold standard for the evaluation of chronic hepatopathy, despite the fact that noninvasive methods (serologic markers and transient elastography or real-time elastography) are being used more often. The quality of the hepatic tissue sample obtained at biopsy is important for the correct diagnosis. Usually, a liver specimen is considered to be adequate for pathological examination if it is no less than 20 mm and preferably more than 25 mm and if it includes 8 to 11 portal tracts. To improve the quality of the tissue sample obtained by percutaneous LB, we believe it is optimal for the operator to use the Menghini needle technique with two intrahepatic passages (specimens up to 4 cm in length can be obtained), to use echo guidance or ultrasonographic assistance, to have extensive personal experience (defined as having performed between 50 and 100 biopsies), and to assess the length of the tissue sample immediately after the LB, and, in the event the specimen is inadequate in length, to rapidly perform another passage.

Keywords: *Liver biopsy • Quality of the tissue sample • Biopsy needle*

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The evaluation of liver lesions in patients with chronic hepatopathy is mandatory in assessing the prognosis of chronic hepatitis or cirrhosis, of alcoholic and nonalcoholic liver diseases, as well as for making treatment decisions such as in cases of chronic hepatitis C and sometimes B.

The liver biopsy (LB) is still considered the gold standard for the evaluation of chronic hepatopathy, despite the fact that noninvasive methods (serologic markers and transient elastography or real-time elastography) are being used more often.

One problem is that the specimen obtained by LB represents roughly only 1/50,000 of the liver, and it is known that fibrosis is unevenly distributed throughout the liver. Another problem is in the relevancy of the specimen obtained by LB in terms of its dimension and the number of portal tracts (PT). Liver samples 1 to 4 cm (preferably at least 1.5 cm) in length are obtained by LB [1]. Usually, a specimen is considered to be adequate for pathological examination if it is longer than 25 mm and includes more than 8 PT [2] or, according to other authors, more than 11 PT [3].

Colloredo et al. [4] showed that the shorter the sample obtained by LB the greater the chance of underestimating the severity of fibrosis and necroinflammatory lesions. Other authors obtained the same results [5]. In a mathematical model created by Bedossa et al. [6], it was estimated that the assessment of a biopsy specimen only 25 mm in length can lead to diagnostic error in 25% of the cases and that the optimal size of the specimen must be at least 40 mm.

If the optimal size of the sample estimated by the mathematical model is 40 mm, the question is how often we obtain fragments this size in clinical practice. A multicentre study performed in France showed that the mean length of the fragment obtained by LB was 15 mm [7]. Another French study [7] showed that of the 323 liver biopsy specimens analyzed, 49 (15.2%) were considered to be uninterpretable by the pathologist. Another French study performed on 1,257 LB [7] showed that in 132 cases (10.5%) the samples were considered uninterpretable by the pathologist. So, considering the optimal length calculated by the mathematical model of Bedossa and the real-life data published in the French

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studies, the rate of diagnostic error can reach 30% to 40%, which we consider unacceptable.

The question is how to improve the liver sample size and thus increase the accuracy of the pathological examination, especially in a period when noninvasive methods for the evaluation of liver fibrosis are becoming increasingly accurate.

Many factors influence the performance of a percutaneous liver biopsy:

1. Type of biopsy needle;
2. Technical performance;
3. Performing LB with ultrasound assistance;
4. Experience of the operator.

Two types of biopsy needles are used for performing LB: cutting needles (Tru-Cut, Vim-Silverman) and suction needles (Menghini, Klatzkin, and Jamshidi). Some of the needles can be used to perform freehand LB, whereas some are automatic needles ("gun" type). Only a few published studies have aimed to determine whether the type of needle (suction or cutting) used for liver biopsy influenced the quality of the sample obtained.

In a Dutch study [8] that compared the standard automatic Tru-Cut needle with a new automatic biopsy gun (Acecut), the performance of the new needle was superior and more consistent with respect to tissue yield, but post-biopsy pain and post-biopsy use of analgesics were higher after use of the Acecut automatic biopsy gun. The authors concluded that the automatic Tru-Cut needle ("gun") offers an advantage, particularly for physicians with no or limited experience in performing liver biopsies.

Because of the construction of the Menghini modified needle and its technique (two passes in the liver in a very short time, which was described by Menghini in 1958), two samples, 2 cm each, can be obtained, so that the final liver specimen can reach 4 cm in length. TruCut needles for automatic devices are user-friendly. After passage through the abdominal wall to the surface of the liver, only a push of a button is needed to obtain a liver sample that is usually 20 mm long. This ease of technique is why, in the study of de Man et al. [8], improved results with respect to tissue yield were obtained with automatic needles and also why automatic Tru-Cut needles offer an advantage for physicians with no or limited experience in LB.

Some experience is needed for performing the Menghini technique, because the time that the needle is in the liver must be very short and because, for best results, usually two passages are performed. In a Romanian multicentre prospective study [9] on the influence of the needle type and the experience of operator on the sample size, we found that the specimens best suited for pathological examination were obtained by biopsy

with Menghini needles, with two intrahepatic passages, instead of a single passage. With this type of needle and two intrahepatic passages, the mean size of the biopsy specimen was 32.41 ± 8.08 mm, compared with the samples from other facilities obtained with the same type of needle, but with only one passage (8.53 ± 4.71 mm from one center and 19.98 ± 4.79 mm from another) ($p < 0.001$).

Only very few studies have addressed the safety of different types of needles (the risk of complications). In a retrospective study performed in 1986, Piccinino et al [10] showed that the rate of complications for the type of the needle used for biopsy was 3.5% for Tru-Cut and 1% for Menghini. This study was performed with an older type of Tru-Cut needle that did not involve use of a gun. So, on the basis of currently available information, the results of that study are probably inconclusive regarding a higher safety profile of either needle type.

In a study by Lindor et al. [11], the impact of use of manual Tru-Cut needles versus automatic needles for liver biopsy was evaluated, along with blind versus echo-guided technique. The mean length of the specimen was slightly greater when the echo-guided technique was used (1.7 cm vs. 1.6 cm, $p < 0.05$) and when automatic needles were used compared to manual Tru-Cut needles (1.7 cm vs. 1.5 cm, $p < 0.05$), but this finding did not seem to be clinically important.

An operator's extensive personal experience with one type of needle (defined as daily performance of liver biopsies, with an overall total of more than 100 procedures) may be the best predictor of success

Regarding ultrasound guidance in liver biopsy, echo-guided and echo-assisted techniques are available. With the Menghini method, echo-assistance is used (the location for LB is chosen via the ultrasound probe and the site is marked on the skin, but the biopsy is performed without actually visualizing the needle in the liver). With the "gun" technique, the LB is performed using real-time ultrasonography (the needle is seen during the intrahepatic passage). Concerning the safety of blind or echo-guided biopsy, Younossi et al. [12] showed that the complications occurred in 4% of the blind biopsies and in 2% of the echo-guided biopsies (thus proving the cost effectiveness of echo-guidance). Pasha et al. [13] found severe complications in 0.5% of the ultrasound-guided LB and in 2.2% of the blind biopsies ($p < 0.05$). The same authors showed that pain appeared more often (50% of the time) in the group undergoing blind biopsy, as compared to the group undergoing ultrasound-guided biopsy (37%) ($p = 0.003$).

Regarding operator expertise, as in every field of activity, experience is mandatory, but in medicine it is difficult to achieve, especially in invasive procedures.

Jensen [14] showed that the operator's experience and expertise are important in limiting the patient's anxiety and in minimizing the complications and, with the use of a biopsy gun, maximizing adequate sampling. In the study performed by de Man et al. [8], automatic Tru-Cut needles offered an advantage for physicians with no or limited experience performing liver biopsies.

In a study by our group [9], we found that the experience of the operator obtaining the biopsy influenced the quality of the sample. The mean length of the specimen obtained was greater in LB performed by more experienced operators (23.5 ± 11.6 mm) compared with biopsies performed by those who were less experienced (15.9 ± 9.8 mm) ($p < 0.001$). Also, considering that the length of the hepatic specimen must be no less than 20 mm and preferably 25 mm or more for adequate pathological assessment [2,3], our study showed that the specimens obtained by experienced operators were satisfactory, but those obtained by operators with less experience were inadequate (mean length, 15.9 mm).

In our opinion the liver biopsy should be performed by a clinical fellow only under the strict supervision of an attendant (to promptly correct every technical mistake); if the visual inspection of the liver sample reveals a specimen smaller than 2 cm (1.5 cm by the set standards in some centers), a new biopsy should be performed immediately by the senior. At the same time, we must be aware that performing more than one biopsy can increase the diagnostic value, but it may also have an effect on morbidity [15]. In a study by Riley [16] on 165 patients, when LB was performed by seniors in daily practice, a second biopsy was necessary in only

1.8% of cases. In a study by our group [17], if visual inspection of the specimen was made immediately after the procedure and, in the event the specimen was deemed inadequate, the LB was repeated in the same session, the percentage of uninterpretable liver biopsies was zero [18].

Recently, Poynard et al. [19] demonstrated that LB is not the gold standard for the evaluation of liver diseases, due at least in part to the insufficient length of the specimen obtained by LB or to the specimen's fragmentation. In another study by Poynard et al. [20] in which the LB was compared to FibroTest, the discordance between these two methods (in 18% of cases) was generated especially by the biopsy failure mostly due to the short length of the specimen. Thus, in order to maintain the liver biopsy as the gold standard, we must obtain adequate specimens in every LB. Otherwise, noninvasive modalities for the evaluation of liver fibrosis and activity that are non-operator-dependent can become more accurate than LB [21].

So, to improve the performance of percutaneous LB, we believe that the operator should use the Menghini needle technique with 2 intrahepatic passages (specimens 4 cm in length can be obtained); use echoguidance or ultrasonographic assistance; to have extensive personal experience (defined as having performed between 50 and 100 biopsies); assess the length of the tissue sample immediately after the biopsy and rapidly perform another passage, if the sample is visually inadequate.

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