HHS Public Access

Author manuscript

Curr Opin Gastroenterol. Author manuscript; available in PMC 2024 February 18.

Published in final edited form as:

Curr Opin Gastroenterol. 2020 May ; 36(3): 184–191. doi:10.1097/MOG.0000000000000621.

The utility of liver biopsy in 2020

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Abstract

Purpose of review—Over the past decade, imaging modalities and serological tests have emerged as important tools in the evaluation of liver diseases, in many cases supplanting the use of liver biopsy and histological examination. Nonetheless, the accuracy and diagnostic value of these methods may not always be conclusive and the assessment of liver histology often remains the gold standard for diagnostic evaluation. The purpose of this review is to summarize the current role of liver biopsy in contemporary hepatology practice.

Recent findings—Technical factors were found to influence the diagnostic value of liver biopsy and histological examination of the liver, including specimen number and size (preferably ≥3 nonfragmented specimens of >20 mm in length), needle diameter (1.6 mm Menghini), number of passes (mean 2.5), imaging-guidance, and operator experience. Liver biopsy was demonstrated to be diagnostically valuable in the evaluation of persistently abnormal liver tests of unclear cause, with histology pointing to a specific diagnosis in 84% of patients. Although coagulation abnormalities continue to be an important concern when performing liver biopsy, their influence on complication risk remains unclear. Implementation of less stringent preprocedural coagulation thresholds decreased preprocedural transfusions without increasing the bleeding rate. Serious complications associated with percutaneous liver-biopsy (PLB) and transjugular liver-biopsy are similar, but pain appears to be more common with PLB.

Summary—Histopathological evaluation continues to be fundamentally important in assessing hepatic disease, and liver histology remains the most accurate approach to assess fibrosis and assign prognosis.

Keywords

fibrosis; liver enzymes; liver mass; percutaneous liver biopsy; transjugular liver biopsy

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Contributors: A.K., review concept and design; acquisition of data and literature review; drafting of the article; critical revision of the article for important intellectual content. D.R., review concept and design; acquisition of data and literature review; drafting of the article; critical revision of the article for important intellectual content; supervisory efforts.

Conflicts of interest

There are no conflicts of interest.

INTRODUCTION

Histological evaluation of liver tissue is a critical element in the evaluation of liver diseases [1]. Historically, the primary value of liver biopsy was for diagnostic purposes. With the recognition that certain histologic features – such as the presence of inflammation (i.e. in autoimmune liver disease) or fibrosis (for many diseases) is important prognostically, liver biopsy (and histological analysis of the liver; for the purposes of this review, it is implied that the term 'liver biopsy' implies concomitant histological analysis) has become more than simply a diagnostic tool. However, with improvements in laboratory testing and imaging techniques, noninvasive assessments have started to emerge, reducing the need for liver biopsy [2]. Moreover, certain noninvasive tests may be effective for liver disease staging [3]. Nonetheless, histopathologic evaluation of liver disease remains essential in certain clinical situations [2,4,5].

INDICATIONS FOR LIVER BIOPSY

Currently, experienced clinicians and the American Association for the Study of Liver Disease (AASLD) consider liver biopsy for establishing diagnosis, evaluation and staging of underlying liver disease, and directing management based on the underlying histology [1] (Table 1).

APPROACHES TO LIVER BIOPSY

Different techniques can be used to obtain hepatic tissue, including the following: percutaneous liver biopsy (PLB), transjugular liver biopsy (TJLB), endoscopic ultrasound-guided liver biopsy (EUS-LB), and laparoscopic (surgical) biopsy [1,6▪▪]. At the current time, image-guided liver biopsy is the preferred approach (over palpation or percussion guided), and is considered the clear approach of choice in patients with prior abdominal surgery, a liver mass, obesity, or ascites [1]. There are a number of nuances associated with the different liver biopsy approaches (Table 2), and important differences between PLB and TJLB (Table 3) [7,8]. A recently published study [6▪▪] suggested that EUS-LB may be superior to PLB, as EUS-LB can easily sample both right and left lobes, may be done with more precise localization (and hence fewer sampling error and a lower complication rate), and has a shorter recovery time. Of note, EUS-LB had a comparable diagnostic yield to PLB, requires advanced training, and is associated with greater procedural cost than PLB [6▪▪].

Contraindications for both PLB and TJLB include infected hepatic tissue and significant extrahepatic biliary tract obstruction. Other contraindications exist for PLB, in particular, PLB should not be performed in an uncooperative patient. Vascular lesions (such as hemangioma) and hydatid cysts are considered to be relative contraindications to liver biopsy, though the evidence suggesting that biopsy of a hydatid cyst is dangerous is limited. TJLB is generally preferred over PLB in patients with coagulopathy, although the risk of bleeding among patients undergoing TJLB is likely to be similar to those undergoing PLB [9▪]. In terms of overall complications of TJLB and PLB, only pain was more likely to occur in patients undergoing PLB, after matching for disease severity [9▪]. It is probably not

necessary to consider one liver biopsy approach to be superior to the other – rather their use should be individualized based on patient specific details.

In terms of obtaining liver tissue, adequate specimen size is crucial for accurate histological interpretation and limiting the possibility of sampling error. A typical liver biopsy samples approximately one fifty-thousandth of the liver volume [4]. It has been shown that more reliable histological interpretation is made when at least three nonfragmented specimens of sufficient size are obtained [10]. It was hypothesized that biopsy specimens measuring at least 10 mm usually reflect the grade and stage of liver fibrosis (e.g. chronic hepatitis C) reliably, and that longer specimens only do slightly improve the diagnostic accuracy [11]. However, it was suggested that for a PLB specimen to be accurately diagnostic, it has to be greater than 15 mm in length with more than five complete portal tracts (CPTs) [4,12]. These criteria has been modified to greater than 20 mm in length with more than 11 CPTs to accurately establish the diagnosis, especially in the era where more detailed evaluation of the fibrotic hepatic tissue is needed [1,11,13]. It has been reported that liver biopsy specimens of at least 10 mm in length reliably reflect the grade of necroinflammatory activity and the stage of fibrosis, and that a little improvement in diagnostic accuracy is obtained with longer specimens [11]. Another study suggested that the size of the biopsy needle influences the number of portal tracts, concluding that 1.6 mm Menghini needles proved better specimens with higher number of CPTs as compared with 1.4 mm Menghini needles [14]. The quality of specimen obtained from ultrasound-guided versus nonultrasound-guided liver biopsy was evaluated in a systematic review [15], where 5392 specimens from ultrasound-guided procedures were compared with 1369 specimens from blind biopsy procedures. Ultrasound-guided biopsy specimens were longer than those obtained blindly (20.5 vs. 14.4 mm; $P = 0.021$). Nevertheless, ultrasound-guided biopsy specimens did not contain significantly more CPTs than specimens from non-ultrasound-guided biopsy procedures (8.3 vs. 5.3; $P = 0.13$) [15]. TJLB typically utilizes a smaller gauge needle than PLB, and is thus generally considered to provide inferior specimens as the tissue obtained is often smaller and more prone to fragmentation [4]. Studies comparing PLB to TJLB have shown that PLB more frequently yields a diagnostic specimen than TJLB, nevertheless, both methods were associated with a high success rate and a low incidence of complications, even in patients with coagulopathy [16]. Interestingly, a prospective comparative study demonstrated that TJLB is less painful, and therefore, better tolerated than PLB [7]. Another comparative study [8] evaluated the role of TJLB vs. plugged-PLB in patients with contraindications to ordinary PLB; in 329 patients, TJLB and plugged-PLB were similar in terms of quality of tissue samples [8]. In pediatric patients with liver disease, the safety of PLB vs. TJLB was comparable, even in the setting of coagulopathy [17]. A systematic review of PLB and TJLB showed that 1389 TJLB specimens were evaluated (mean, 2.5 passes per patient); the mean ± SD length was 13.5 ± 4.5 mm (13 of 15 studies), and the mean ± SD SD number of CPTs was 6.8 ± 2.3 [15]. The review suggested that recent improvements in TJLB techniques offer the possibility of safely obtaining ideal liver biopsy samples with a reduced likelihood of complications.

LIVER BIOPSY COMPLICATIONS

Despite being considered to be well tolerated when performed by experienced operators, a small proportion of liver biopsies result in complications (Table 4) [4,18–21]. As might be expected, major complications are much less common than minor complications.

There is great controversy about the importance of technical factors and the risk of liver biopsy complications; these include the number of passes, needle size, ultrasound guidance, and operator experience. A 10-year retrospective analysis [22] evaluated biopsy complications in relation to number of liver passes. Overall, 102 (5.6%) complications were observed, pain was reported in 74% of this group and bleeding was reported in 33%. Having two biopsy passes did not appear to be associated with an increased risk of complications compared with one biopsy pass, whereas having three or more biopsy passes was associated with increased risk. In a literature review of 34 studies, needle size (cutting biopsy vs. fine needle aspiration, $P < 0.001$) and the presence of a patent track on postbiopsy ultrasound ($P < 0.001$) were associated with postbiopsy bleeding [23▪]. However, in this study, the number of needle passes was not a risk factor of bleeding [23▪]. In a study of different needles sizes in more than 15 000 biopsies, there was no significant difference in bleeding rate associated with needle gauge ($P = 0.88$) [24]. Operator experience has also been postulated to be an important factor associated with complication rate. Several studies have reported that the rate of complications after liver biopsy diminished significantly when the procedure was carried out by experienced hepatologists [25]. In contrast, it was also been reported that the risk of complications is not increased when performed by inexperienced compared with experienced operators [18]. However, this finding may be biased, given that the 20% of the HALT-C biopsies not performed by experienced hepatologists were supervised by experienced faculty. Moreover, the HALT-C trial excluded patients with advanced liver disease (Child Pugh ≥7), a PC < 50 000/μl, or serum creatinine greater than 1.5 mg/dl, which all might have influenced the risk of complications [18]. Finally, similar postbiopsy complications rates have been reported for gastroenterologists and interventional radiologists [26].

PAIN AFTER LIVER BIOPSY

Pain after performance of a liver biopsy is generally accepted to result from injury to the liver capsule, as the capsule is innervated, whereas the hepatic parenchyma is not. The capsule clearly responds to stretch, and thus pain should be considered symptomatic of stretching of the capsule – typically by a hematoma. Overall, pain is the most commonly reported complication. Despite being the most common complication, severe pain (defined as that requiring re-evaluation) occurred in 78 (2.3%) of 3357 biopsies performed in one study between 1978 and 2015 [27].

A study graded the intensity of pain expected before the procedure compared with the pain experienced during the procedure, and evaluated the correlation between biopsy-induced pain and the patient's emotional status [28]. In this study, a visual analogue scale (VAS) was used before and after the procedure to grade the degree of pain expected, and the degree of the pain experienced, respectively. The mean VAS score for expected pain before

the procedure was 60+/−20 and for the pain experienced during the procedure was 22+/−16 ($P < 0.0001$). Hence, the authors concluded that informing and educating patients about the procedure and their disease is likely to diminish expected pain [28]. It has been demonstrated in the literature that prophylactic tramadol and lorazepam was well tolerated and reduced pain. Available literature suggests that light sedation is well tolerated and does not increase procedural risk [1].

RISK OF HEMORRHAGE

Hemorrhage is the most common major complication after liver biopsy. Although bleeding of any kind has been reported to occur in up to 11% of patients [23▪], major bleeding and transient hypotension have been reported much less commonly – in 1–2% of patients undergoing PLB [23▪]. Intraperitoneal hematoma requiring blood transfusion has been reported to occur in 0.5% of liver biopsies [19]. Interestingly, the use of image guidance for liver biopsy appears to reduce the rate of overall complications, including bleeding [1].

The exact mechanism(s) underlying an increased risk of bleeding is not entirely clear [19]. Female sex has been suggested to be associated with higher risk of bleeding [19]. Cirrhosis is risk factor for fatal bleeding after liver biopsy [4]. Furthermore, in a study of 2740 liver biopsies performed at 10 study sites between 2000 and 2006, showed that 0.5% of chronic hepatitis C patients with advanced fibrosis experienced potentially serious bleeding after liver biopsy; and that the risk increased significantly in patients with platelet count 60000/ml or less [18]. Whether focal hepatic lesions are a risk factor for aggressive bleeding following biopsy remains controversial [19]. In addition, it was recognized that the higher the number of the liver capsule punctures, the greater the risk of hemorrhage (>1–4) [19]. Other factors associated with increased risk of bleeding in liver biopsy included advanced age, ascites, bleeding disorders, amyloidosis, renal failure, and blind technique [23▪]. Furthermore, it has been suggested that the larger the gauge of needle, the higher the rate of complications [29].

The impact of either an elevated international normalized ratio (INR) or low platelet count on the risk of bleeding after liver biopsy is still controversial. The HALT-C trial identified a relationship between the platelet count and bleeding risk; the risk of bleeding was 0.2% when the platelet count exceeded 150,000/ml, 0.6–0.7% with a platelet count between 150,000 and 61,000/ml, and 5.3% with a platelet count 60,000/ml or less [18]. Similarly, in another study, an INR greater than 1.5 appeared to correlate with an increased risk of postbiopsy bleeding [24]. However, in a retrospective review of 1846 PLBs, it was reported that an INR 2.0 or less and platelet count at least 25 000 ml did not increase the rate of hemorrhagic complications [30▪▪]. Further it found that using these cutoffs resulted in a significant reduction in the use of preprocedural fresh frozen plasma and platelet transfusion. A literature review published by O'Connor *et al.* [31] suggested changing parameters for interventions to an INR of 2.0 and platelets of 25 000 μL. Current AASLD guidelines recommend considering treatment when the platelet count is less than 50 000–60 000 μL [1]. It has been suggested that data do not exist to support a specific cutoff for INR as a valid indicator of bleeding risk in cirrhosis patients. Current Society of Interventional Radiology (SIR) guidelines suggest that for the general population, INR should be 1.5–1.8 or less, whereas for patients with chronic liver disease INR should be less than 2.5 [32,33▪▪].

Another highly controversial topic surrounds when to re-start anticoagulation or antiplatelet therapy after liver biopsy. Although data addressing this issue are lacking. It has been suggested that anticoagulant therapy should be avoided for some period of time after PLB [34]. Intravenous heparin should be resumed first, and warfarin added subsequently. Time intervals are not well defined. Limited data are emerging to suggest that single-agent antiplatelet medication is likely to be well tolerated in patients undergoing liver biopsy. For example, the incidence of bleeding complications in patients who had taken aspirin within 10 days of solid organ biopsy in 15 181 patients was 0.6% (18 of 3195), and it did not differ significantly when compared with patients who had not taken aspirin (0.4%; 52 of 11 986; $P = 0.34$) [24]. The incidence of bleeding among patients undergoing liver biopsy was 0.5%, which is consistent with the incidence of bleeding in patients who are not on antiplatelet therapy prior to liver biopsy procedure [19].

MISCELLANEOUS COMPLICATIONS

The literature indicates that PLB carries a minimal risk of tumor seeding (0.76%) [1,35], with risk being slightly higher among patients with hepatocellular carcinoma (HCC) (3%). Other minor and less commonly seen complications include: bacterial translocation and transient bacteremia 9.6–14%, biliary peritonitis (primarily seen in patients with extrahepatic obstruction), organ injury (pneumothorax: 0.0078% and hemothorax: 0.063%) [36], and less commonly perforation of an intra-abdominal organ [37].

HOSPITALIZATION FOLLOWING LIVER BIOPSY

Approximately 1% of patients require hospitalization for complications after a liver biopsy [38]. The median direct cost of a hospitalization for complications was $4579 (range $1164–29 641) [20]. Pain and bleeding induced hemodynamic instability are the most common indications for hospital admission following liver biopsy [4,20]. Postbiopsy follow-up for potential complications remains a great concern for the physicians. Interestingly, the majority of severe bleeding occurs within 2–4 h postbiopsy [1]. Hence, the recommended observation time after biopsy is between 2 and 4 h [1]. Nevertheless, a review of 3806 liver biopsies of noncirrhotic patients reported that 12 patients (0.32%) suffered hemorrhagic complications 4–12 h after the biopsy [39]. Similarly, it was reported that 60% of liver biopsy complications develop within the first 2 h, whereas 90% develop within 24 h [19].

VALUE OF LIVER BIOPSY IN THE DIFFERENTIAL DIAGNOSIS OF LIVER DISEASE

Liver biopsy remains the most specific test to assess the nature and severity of different liver diseases. Histological evaluation of the liver is used primarily now in three settings as follows: evaluation of abnormally elevated liver enzymes, evaluation and staging of hepatic fibrosis, and evaluation of radiologically undiagnosed focal liver masses.

LIVER BIOPSY IN THE EVALUATION OF ABNORMAL LIVER FUNCTION TESTS

Abnormal liver tests are common in the US population (at approximately 8%) and are even more common in patients who present to general internal medicine clinic [40▪]. Further in one study, abnormal liver tests in the general population could not be explained by obvious disorders, such as alcohol consumption, viral hepatitis, or hemochromatosis [41]. Therefore, liver biopsy is often performed in asymptomatic patients with unexplained liver test elevations.

In a prospective assessment of the value of liver biopsy in the evaluation of abnormal liver function tests (LFTs), the most common explanation was nonalcoholic steatohepatitis (NASH) followed by drug-induced liver injury [42]. In another study, including 401 patients presenting for unexplained LFTs abnormalities, chronic hepatitis (defined as progressive inflammatory process characterized by lymphocytic inflammation and fibrosis) was the most common histological diagnosis (115/401, 29%), and viral hepatitis C was the most common clinical contributor (48/401, 12%). Liver biopsy showed normal histology in 54 patients (13%) and failed to establish the diagnosis in 12 patients (3%). Hence, it was concluded that liver biopsy for evaluation of unexplained liver tests identified a cause for the liver disease in 84% of patients [43▪]. In an effort to determine whether prebiopsy laboratory variables are able to predict biopsy results, liver tests (elevated by ≥2 upper limit normal) for each diagnosis were compared to evaluate their sensitivity, specificity, positive and negative values. Unfortunately, none of the obtained values of different specific liver tests were predictive of an underlying histological or clinical diagnosis.

In patients with normal or almost normal histology, it is often unclear as to whether or not histological findings are clinically meaningful. In a study evaluating diagnoses after an ‘almost normal liver biopsy’ including primarily patients with simply abnormal liver tests, it was reported that a diagnosis was eventually made in 72% of patients (70/97) after a median follow-up of 4.3 years [44]. The most likely diagnoses included the following: systemic autoimmune inflammatory condition (18%), vascular/ischemic disease (13%), metabolic syndrome (11%), and drug reactions (8%). On the other hand, in a study of 81 patients with elevated liver enzymes and a histologically normal liver, 70 of whom were followed up for 8 years, 52 patients (70%) had no features of clinical progression, whereas the diagnosis of fatty liver disease (whether alcoholic or nonalcoholic) or autoimmune hepatitis (3 patients only) was made in 20% of patients [45]. The majority of the patients did not develop evidence of chronic liver disease during the follow-up period. Additionally, a recent review concluded that for the nearly normal liver biopsy in an asymptomatic patient with elevated transaminase levels, patients are unlikely to develop any liver disease [46].

LIVER BIOPSY IN EVALUATION OF FIBROSIS/CIRRHOSIS

Liver histology plays an integral role in evaluating the severity of fibrosis/cirrhosis. This is critical as the severity of fibrosis has been well established as a prognostic indicator for a variety of liver diseases [47]. There is an extensive body of evidence examining hepatic histological examination for fibrosis and comparing histology to noninvasive approaches;

review of this literature is beyond the scope of this review. In brief, while a number of advances have been made in noninvasive assessment techniques (with a variety of blood tests, and imaging modalities), and despite the limitations of liver biopsy (especially with potential sampling error), liver biopsy and histological evaluation of the liver are still considered a gold standard.

Another evolving area for assessment of fibrosis is in assessing fibrosis regression. The underlying process incorporates the switch in the inflammatory media, elimination or regression of activated hepatic stellate cells, and degradation of extracellular matrix [47]. Extensive data, in a number of different liver diseases, indicate that fibrosis regresses – typically when the underlying cause of liver disease is treated [48]. For an instance, a recent review on fibrosis reversal after hepatitis C virus elimination concluded that not only fibrosis but also cirrhosis (to some extent), undergo reversion/reversal following successful hepatitis C virus eradication [49▪]. Similarly, there is growing evidence that antiviral treatment of hepatitis B virus is associated with hepatic fibrosis reversal [50,51].

LIVER BIOPSY IN EVALUATION OF FOCAL HEPATIC MASSES

Multiphasic – cross-sectional imaging with contrast [computerized tomography (CT) and MRI] are currently the standard method for evaluation of focal hepatic lesions on the basis of the tumor vasculature and other radiological features. In the majority of patients, particularly those with hepatocellular carcinoma, a specific diagnosis of the liver mass can be established and hence liver biopsy is not commonly needed [5]. For lesions not having typical imaging features of hepatocellular cancer, liver biopsy is most often appropriate. For example, the international consensus group for hepatobiliary malignancies has recommended liver biopsy for evaluation of such lesions [52]. In a study of liver biopsies performed for patients with radiologically atypical HCC, the authors reported that the first biopsy was positive in 43/60 (70%) of patients for HCC and that the follow-up biopsies established the diagnosis in the rest of the patients [53]. A retrospective analysis of patients who underwent endoscopic ultrasound-guided fine needle biopsy (EUS-FNB) for the pathological diagnosis of hepatic solid masses found that the sensitivity and specificity of EUS-FNB were 89.7 and 100%, respectively [54].

CONCLUSION

Liver biopsy continues to be a highly reliable and valuable test for diagnostic evaluation of liver disease. It is particularly helpful in patients with unexplained elevation of liver tests, for grading/staging of fibrosis before and after treatment, and evaluation of radiologically undiagnosed liver masses. Liver biopsy should be considered to be well tolerated whenever performed by a skilled operator and the patient is closely monitored after the procedure.

REFERENCES AND RECOMMENDED READING

Papers of particular interest, published within the annual period of review, have been highlighted as:

▪ of special interest

■■ of outstanding interest

1. Rockey DC, Caldwell SH, Goodman ZD, et al. Liver biopsy. Hepatology 2009; 49:1017–1044. [PubMed: 19243014]
2. Cadranel JF, Nousbaum JB, Gouillou M, Hanslik B. Major changes in the number and indications of liver biopsy for chronic liver diseases over one decade in France. Eur J Gastroenterol Hepatol 2016; 28:e26–e32. [PubMed: 27340896]
3. Rockey DC, Bissell DM. Noninvasive measures of liver fibrosis. Hepatology 2006; 43(2 Suppl 1):S113–S120. [PubMed: 16447288]
4. Bravo AA, Sheth SG, Chopra S. Liver biopsy. New Engl J Med 2001; 344:495–500. [PubMed: 11172192]
5. Tapper EB, Lok ASF. Use of liver imaging and biopsy in clinical practice. New Engl J Med 2017; 377:756–768. [PubMed: 28834467]
6. Shah AR, Al-Hanayneh M, Chowdhry M, et al. Endoscopic ultrasound guided liver biopsy for parenchymal liver disease. World J Hepatol 2019; 11:335–343. [PubMed: 31114638] ■■This review highlighted the current state of endoscopic ultrasound-guided liver biopsy (EUS-LB). Current evidence suggests that EUS-LB allows a targeted approach of focal lesions and may also provide less sampling variability in heterogeneous parenchymal disorders. Advantages of EUS-LB include easier access to both lobes of liver and improved diagnostic accuracy in heterogeneous parenchymal diseases as well as detecting multiple focal lesions. Procedure and recovery times are shorter with less reliance on patient cooperation. Additionally, the use of Doppler assistance helps avoid blood vessels reducing risk of hemorrhage.
7. Procopet B, Bureau C, Métivier S, et al. Tolerance of liver biopsy in a tertiary care center: comparison of the percutaneous and the transvenous route in 143 prospectively followed patients. Eur J Gastroenterol Hepatol 2012; 24:1209–1213. [PubMed: 22668874]
8. Atar E, Ben Ari Z, Bachar GN, et al. A comparison of transjugular and plugged-percutaneous liver biopsy in patients with contraindications to ordinary percutaneous liver biopsy and an 'in-house' protocol for selecting the procedure of choice. Cardiovasc Intervent Radiol 2010; 33:560–564. [PubMed: 19908088]
9. Sasso R, Khalifa A, Guimaraes M, Rockey DC. Is the transjugular liver biopsy approach safer than the percutaneous liver biopsy approach? (Abstract). Hepatology 2019; 70(S1):454A. [PubMed: 31245881] ■The study reviewed 1300 consecutive liver biopsies done over a 4-year period in a single center and described complications occurring from TJLB and PLB. It demonstrated that only pain was more common with PLB, with other complications being similar. Interestingly, the main predictors for performing TJLB were prolonged INR and activated partial thromboplastin time, and suspicion of underlying cirrhosis or portal hypertension.
10. Cholongitas E, Quaglia A, Samonakis D, et al. Transjugular liver biopsy in patients with diffuse liver disease: comparison of three cores with one or two cores for accurate histological interpretation. Liver Int 2007; 27:646–653. [PubMed: 17498250]
11. Schiano TD, Azeem S, Bodian CA, et al. Importance of specimen size in accurate needle liver biopsy evaluation of patients with chronic hepatitis C. Clin Gastroenterol Hepatol 2005; 3:930–935. [PubMed: 16234033]
12. Cholongitas E, Quaglia A, Samonakis D, et al. Transjugular liver biopsy: how good is it for accurate histological interpretation? Gut 2006; 55:1789–1794. [PubMed: 16636018]
13. Colloredo G, Guido M, Sonzogni A, Leandro G. Impact of liver biopsy size on histological evaluation of chronic viral hepatitis: the smaller the sample, the milder the disease. J Hepatol 2003; 39:239–244. [PubMed: 12873821]
14. Sporea I, Gherhardt D, Popescu A, et al. Does the size of the needle influence the number of portal tracts obtained through percutaneous liver biopsy? Annal Hepatol 2012; 11:691–695.
15. Cholongitas E, Senzolo M, Standish R, et al. A systematic review of the quality of liver biopsy specimens. Am J Clin Pathol 2006; 125:710–721. [PubMed: 16707372]
16. Hardman RL, Perrich KD, Silas AM. Single-institution results of image-guided nonplugged percutaneous versus transjugular liver biopsy. Cardiovasc Intervent Radiol 2011; 34:369–375. [PubMed: 20963589]

17. Tulin-Silver S, Obi C, Kothary N, Lungren MP. Comparison of Transjugular liver biopsy and percutaneous liver biopsy with tract embolization in pediatric patients. J Pediatr Gastroenterol Nutr 2018; 67:180–184. [PubMed: 29509634]

18. Seeff LB, Everson GT, Morgan TR, et al. , HALT–C Trial Group. Complication rate of percutaneous liver biopsies among persons with advanced chronic liver disease in the HALT-C trial. Clin Gastroenterol Hepatol 2010; 8:877–883. [PubMed: 20362695]

19. Boyum JH, Atwell TD, Schmit GD, et al. Incidence and risk factors for adverse events related to image-guided liver biopsy. Mayo Clin Proc 2016; 91:329–335. [PubMed: 26837481]

20. Myers RP, Fong A, Shaheen AA. Utilization rates, complications and costs of percutaneous liver biopsy: a population-based study including 4275 biopsies. Liver Int 2008; 28:705–712. [PubMed: 18433397]

21. West J, Card TR. Reduced mortality rates following elective percutaneous liver biopsies. Gastroenterology 2010; 139:1230–1237. [PubMed: 20547160]

22. Chi H, Hansen BE, Tang WY, et al. Multiple biopsy passes and the risk of complications of percutaneous liver biopsy. Eur J Gastroenterol Hepatol 2017; 29:36–41. [PubMed: 27556687]

23. Midia M, Odedra D, Shuster A, et al. Predictors of bleeding complications following percutaneous image-guided liver biopsy: a scoping review. Diagnostic and interventional radiology (Ankara, Turkey) 2019; 25:71–80. [PubMed: 30644369] ■In this review, several risk factors (patient, operator, and procedure-related) were identified to be associated with an increased risk of postbiopsy bleeding. Patient-related risk factors included patient age (>50 years or <2 years), inpatient status (8/12 vs. 4/12, $P < 0.001$), comorbidities and/or concurrent diagnoses, and coagulation status (rate of bleeding was 3.3% for INR 1.2–1.5 vs. 7.1% for INR >1.5, $P < 0.001$). There was no consensus on the impact of operator experience (>200 biopsies/year vs. <50/year) on postbiopsy bleeding rates. Procedure-related risk factors included needle size (cutting biopsy vs. fine needle aspiration, $P < 0.001$) and the presence of a patent track on postbiopsy ultrasound ($P < 0.001$).

24. Atwell TD, Smith RL, Hesley GK, et al. Incidence of bleeding after 15,181 percutaneous biopsies and the role of aspirin. AJR Am J Roentgenol 2010; 194:784–789. [PubMed: 20173160]

25. Bedossa P, Carrat F. Liver biopsy: the best, not the gold standard. J Hepatol 2009; 50:1–3. [PubMed: 19017551]

26. Anania G, Gigante E, Piciucchi M, et al. Liver biopsy: Analysis of results of two specialist teams. World J Gastrointest Pathophysiol 2014; 5:114–119. [PubMed: 24891983]

27. Takyar V, Etzion O, Heller T, et al. Complications of percutaneous liver biopsy with Klatskin needles: a 36-year single-centre experience. Aliment Pharmacol Ther 2017; 45:744–753. [PubMed: 28074540]

28. Akay S, Karasu Z, Noyan A, et al. Liver biopsy: is the pain for real or is it only the fear of it? Digest Dis Sci 2007; 52:579–581. [PubMed: 17211704]

29. Shankar S, van Sonnenberg E, Silverman SG, Tuncali K. Interventional radiology procedures in the liver. Biopsy, drainage, and ablation. Clin Liver Dis 2002; 6:91–118. [PubMed: 11933598]

30. Kitchin DR, Del Rio AM, Woods M, et al. Percutaneous liver biopsy and revised coagulation guidelines: a 9-year experience. Abdom Radiol (NY) 2018; 43:1494–1501. [PubMed: 28929196] ■■This study revealed that implementation of less stringent preprocedural platelet count (≥25 000 μL) and INR (INR ≤2.0) requirements did not lead to increased rates of bleeding after biopsy, and led to a significant decrease in the use of preprocedural FFP and platelet transfusions. Additionally, prebiopsy platelet transfusion also did not appear to have an effect on bleeding in patients with decreased platelet counts.

31. O'Connor SD, Taylor AJ, Williams EC, Winter TC. Coagulation concepts update. Am J Roentgenol 2009; 193:1656–1664. [PubMed: 19933661]

32. Davidson JC, Rahim S, Hanks SE, et al. Society of Interventional Radiology Consensus Guidelines for the Periprocedural Management of Thrombotic and Bleeding Risk in Patients Undergoing Percutaneous Image-Guided Interventions-part i: review of anticoagulation agents and clinical considerations: endorsed by the Canadian Association for Interventional Radiology and the Cardiovascular and Interventional Radiological Society of Europe. J Vasc Intervent Radiol 2019; 30:1155–1167.

33. Patel IJ, Rahim S, Davidson JC, et al. Society of Interventional Radiology Consensus Guidelines for the periprocedural management of thrombotic and bleeding risk in patients undergoing percutaneous image-guided interventions-part ii: recommendations: endorsed by the Canadian Association for Interventional Radiology and the Cardiovascular and Interventional Radiological Society of Europe. J Vasc Interv Radiol 2019; 30:1168.e1–1184.e1. [PubMed: 31229333] ■■This study presents guidelines around transfusion in patients with specific laboratory abnormalities in patients with chronic liver disease. The guidelines suggest that in patients with chronic liver disease undergoing an invasive procedure, adjusting INR and platelet count transfusion thresholds higher and lower, respectively, than in the general population is optimal – so as to minimize unnecessary transfusions.
34. Scott DA, Netchvolodoff CV, Bacon BR. Delayed subcapsular hematoma after percutaneous liver biopsy as a manifestation of warfarin toxicity. Am J Gastroenterol 1991; 86:503–505. [PubMed: 1849346]
35. De Paepe K, Bonne L, Fotiadis N, et al. Complications and seeding risk after percutaneous liver biopsy in an oncological setting. J Clin Oncol 2018; 36(4_suppl):246-.
36. Van Thiel DH, Gavaler JS, Wright H, Tzakis A. Liver biopsy. Its safety and complications as seen at a liver transplant center. Transplantation 1993; 55:1087–1090. [PubMed: 8497887]
37. Piccinino F, Sagnelli E, Pasquale G, Giusti G. Complications following percutaneous liver biopsy. A multicentre retrospective study on 68,276 biopsies. J Hepatol 1986; 2:165–173. [PubMed: 3958472]
38. Firpi RJ, Soldevila–Pico C, Abdelmalek MF, et al. Short recovery time after percutaneous liver biopsy: should we change our current practices? Clin Gastroenterol Hepatol 2005; 3:926–929. [PubMed: 16234032]
39. Huang J-F, Hsieh M-Y, Dai C-Y, et al. The incidence and risks of liver biopsy in noncirrhotic patients: an evaluation of 3806 biopsies. Gut 2007; 56:736–737.
40. Schreiner AD, Moran WP, Zhang J, et al. Evaluation of liver test abnormalities in a patient-centered medical home: do liver test patterns matter? J J Investig Med 2018; 66:1118–1123. ■The study demonstrated that abnormal liver tests were pervasive in a primary care clinic, and in addition that a substantial number of did not have follow-up testing. Higher proportions of patients with multiple liver test abnormalities had repeat testing compared with those with individual abnormalities. The data raise the possibility that many liver diseases go undiagnosed in primary care.
41. Clark JM, Brancati FL, Diehl AM. The prevalence and etiology of elevated aminotransferase levels in the United States. Am J Gastroenterol 2003; 98:960–967. [PubMed: 12809815]
42. Skelly MM, James PD, Ryder SD. Findings on liver biopsy to investigate abnormal liver function tests in the absence of diagnostic serology. J Hepatol 2001; 35:195–199. [PubMed: 11580141]
43. Khalifa A, Sasso R, Rockey DC. Value of liver biopsy in evaluating abnormal liver function tests (Abstract). Hepatology 2019; 70(S1):512A. ■The study demonstrated that histological investigation of unexplained liver tests led to a specific histological and clinical diagnosis in 84% of patients, suggesting that liver biopsy is extremely valuable in this patient population. In addition, the authors found that individual LFTs (or liver test patterns) were not predictive of the underlying liver abnormality and were not useful in establishing histological or clinical diagnosis.
44. Czeczok TW, Van Arnam JS, Wood LD, et al. The almost-normal liver biopsy: presentation, clinical associations, and outcome. Am J Surg Pathol 2017; 41:1247–1253. [PubMed: 28614198]
45. Strasser M, Stadlmayr A, Haufe H, et al. Natural course of subjects with elevated liver tests and normal liver histology. Liver Int 2016; 36:119–125. [PubMed: 26256590]
46. Ettel MG, Appelman HD. Approach to the liver biopsy in the patient with chronic low-level aminotransferase elevations. Arch Pathol Lab Med 2018; 142:1186–1190. [PubMed: 30281363]
47. Rockey DC. Translating an understanding of the pathogenesis of hepatic fibrosis to novel therapies. Clin Gastroenterol Hepatol 2013; 11:224.e1–231.e5. [PubMed: 23305825]
48. Rockey DC, Bell PD, Hill JA. Fibrosis — a common pathway to organ injury and failure. New Engl J Med 2015; 372:1138–1149. [PubMed: 25785971]
49. Rockey DC. Fibrosis reversal after hepatitis C virus elimination. Curr Opin Gastroenterol 2019; 35:137–144. [PubMed: 30865043] ■The review highlights that in the era of direct-acting antiviral

(DAA) regimen, successful eradication of hepatitis C virus (HCV) infection is almost guaranteed (with a cure rate of nearly 100%) and that after HCV eradication, there is significant regression/reversal in hepatic fibrosis. There is even reversion of cirrhosis in some patients following successful HCV treatment.

50. Marcellin P, Gane E, Buti M, et al. Regression of cirrhosis during treatment with tenofovir disoproxil fumarate for chronic hepatitis B: a 5-year open-label follow-up study. Lancet 2013; 381:468–475. [PubMed: 23234725]
51. Buti M, Fung S, Gane E, et al. Long-term clinical outcomes in cirrhotic chronic hepatitis B patients treated with tenofovir disoproxil fumarate for up to 5 years. Hepatol Int 2015; 9:243–250. [PubMed: 25788199]
52. Pathologic diagnosis of early hepatocellular carcinoma: a report of the international consensus group for hepatocellular neoplasia. Hepatology 2009; 49:658–664. [PubMed: 19177576]
53. Forner A, Vilana R, Ayuso C, et al. Diagnosis of hepatic nodules 20 mm or smaller in cirrhosis: prospective validation of the noninvasive diagnostic criteria for hepatocellular carcinoma. Hepatology 2008; 47:97–104. [PubMed: 18069697]
54. Chon HK, Yang HC, Choi KH, Kim TH. Endoscopic ultrasound-guided liver biopsy using a core needle for hepatic solid mass. Clin Endosc 2019; 52:340–346. [PubMed: 31302987]

KEY POINTS

- Liver biopsy and visualization of liver histology remains an important element in the clinical assessment and management for patients with liver disease.
- Liver biopsy and histologic assessment of the liver is used now for diagnostic purposes, to stage the severity of disease (especially fibrosis), and to investigate liver mass lesions.
- Advances in noninvasive assessment of fibrosis have curtailed the need for liver biopsy, particularly in patients in two specific categories – very early or advanced disease.
- Although invasive in nature, liver biopsy should be considered well tolerated when performed by an experienced operator, and informing and educating patients about the procedure may diminish the magnitude of the most common complication (pain).
- Despite the currently available literature, many questions still require further research (e.g. risks associated with coagulopathy, thrombocytopenia, and when to re-start anticoagulation or antiplatelet therapy following liver biopsy, for example).

Table 1.

Common indications for liver biopsy

Diagnosis	Evaluation of abnormal liver function tests in association with inconclusive serological workup or when suspecting DILI Establishing a suspected diagnosis of any of multiple parenchymal liver diseases (e.g. NAFLD, NASH, viral hepatitis, autoimmune hepatitis, metabolic liver diseases, etc.) Evaluation of fever of unknown origin Evaluation of the liver in infiltrative systemic diseases Evaluation of intrahepatic masses detected on imaging
Prognosis	Grading and staging of parenchymal liver diseases (extent of necroinflammatory activity, fibrosis stage) Evaluation of the donor liver pretransplantation Investigation of the liver posttransplantation (e.g. for rejection, recurrence of original liver disease, etc...)
Management	Treatment planning based on histopathological findings Evaluation of the efficacy of the current treatment plan

DILI, drug-induced liver iLnjury; NAFD, nonalcoholic fatty liver disease; NASH, nonalcoholic steatohepatitis.

Curr Opin Gastroenterol. Author manuscript; available in PMC 2024 February 18.

Table 2.

Indications and contraindications of different liver biopsy approaches

	PLB	TJLB	Surgical liver biopsy
	Indications PLB is the current preferred approach in standard clinical situations (less invasive and cost effective)	–Coagulopathy	–Staging of liver cancer
		–Small cirrhotic liver	–Ascites of undetermined cause
		–Ascites	–Peritoneal disease
		–Suspected vascular hepatic mass	–Evaluation of hepatic mass
		–Evaluation of HVPG and/or hepatic venography	–Unexplained hepatosplenomegaly
		–Failure of PLB, or refused PLB	
Contraindications	–Infected hepatic tissue	–Infected hepatic tissue	–Medical illness precluding safe performance of the procedure
	–Significant extrahepatic tissue biliary obstruction	–Significant extrahepatic tissue biliary obstruction	
	–Uncooperative patient	–Medical illness precluding safe	
	–Suspected vascular tumor (e.g. hemangioma)	performance of the procedure	
	–Morbid obesity		
	–Severe ascites		
	–Infection of the right pleura or hemidiaphragm		

PLB, percutaneous liver biopsy; TJLB, transjugular liver biopsy.

Table 3.

Comparison between percutaneous liver biopsy and transjugular liver biopsy

	PLB	TJLB
Localization	May be image-guided or ‘blind’ (using physical exam to localize)	Localization with fluoroscopy is not as accurate
Technical factors	Shorter (mean 10 min), may have radiation (CT-guided) exposure	Longer (mean 22 min), radiation exposure
Diagnostic yield and accuracy	Higher diagnostic yield because of parenchymal image guidance, and typically larger needle caliber (18 gauge or higher)	Comparatively, less diagnostic accuracy because a smaller needle caliber is used
Cost	Lower cost	Higher cost
Complications	Pain is more commonly reported than with TJLB	Bleeding risk is comparable with PLB
Coagulopathy	Lower threshold for correction (INR: 1.5; platelets: ≤50 000–70 000)	Higher threshold for correction (INR: 1.7–1.9; platelets: ≤50 000)
Other	Useful for evaluation of hepatic masses	Useful to measure HVPG and assess hepatic vascular structures

HVPG, hepatic venous pressure gradient; INR, international normalized ratio; PLB, percutaneous liver biopsy; TJLB, transjugular liver biopsy.

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Table 4.

Complications of liver biopsy

Complication	Incidence
Pain (right upper quadrant)	0.05–84%
Severe pain (pain requiring re-evaluation)	up to 2.3%
Hemorrhagic complications (bleeding of any kind)	11%
Major bleeding and transient hypotension	1–2%
Intraperitoneal hematoma requiring blood transfusion	0.5%
Hemobilia	0.18–0.49%
Hemothorax	0.063%
Tumor seeding	0.76%
Tumor seeding in patients with HCC	up to 3%
Bacterial translocation and transient bacteremia	9.6–14%
Pneumothorax	0.0078%
Mortality	0.001–0.2%

The frequencies given are estimates based on the literature reviewed in the text. HCC, hepatocellular carcinoma.