

Role of Liver Biopsy in Evaluation of Fibrosis: Review Article

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ABSTRACT

Background: When determining the cause and severity of liver disease, a liver biopsy is still the gold standard. Experts in gastroenterology and hepatology or radiologists are the most common providers for percutaneous biopsies. The collection of liver tissue can be accomplished in several ways. Intravascular tissue sample through the hepatic vein, laparoscopy and laparotomy for intra-abdominal biopsy, and a blind percutaneous technique following percussion of the chest wall are all viable options. Availability, individual desire, and the needs of the patient inform which methods are used. Additionally, different needles might be used based on the treatment modality and the practitioner's level of expertise.

Objective: Assessment of possible role of liver biopsy in evaluation of fibrosis.

Methods: Liver biopsy, pediatrics, and fibrosis were all looked for in PubMed, Google scholar, and Science direct. References from relevant literature were also evaluated by the authors, but only the most recent or complete study from February 2013 to June 2021 was included. Due to the lack of sources for translation, documents in languages other than English have been ruled out. Papers that did not fall under the purview of major scientific investigations, such as unpublished manuscripts, oral presentations, conference abstracts, and dissertations, were omitted.

Conclusion: Sampling mistake, uncommon complications, and occasional patient worry are possible outcomes of the typically safe procedure known as liver biopsy, which is now the gold standard for assessing hepatic inflammation and fibrosis.

Keywords: Liver biopsy, Fibrosis, Pediatrics.

INTRODUCTION

Even when a sizable portion of the liver is damaged, the organ can recover to its pre-injury state and original design in a short period of time. However, chronic liver injury, which can be caused by a variety of factors, leads to ongoing tissue damage and a diminished ability to recover. This is characterized by a changed inflammatory infiltration and a chronic wound healing response. Parenchymal cells undergo necrosis and/or death and are subsequently replaced by extracellular matrix in response to chronic damage (ECM). In the liver, for example, the wound-healing process can become malignant if it leads to the gradual replacement of parenchyma by scar tissue and a distortion of the vascular architecture ⁽¹⁾.

Historically, liver biopsies served primarily as diagnostic tools. Liver biopsies and histological examination of the liver have always played an important role in clinical therapy, but this has only been more so as additional natural history data has been developed and several novel medicines for patients with liver disease have been introduced. In 2009, the three most common causes for a liver biopsy were diagnostic, prognostic (disease staging), and therapeutic (helping decide between several treatment options) ⁽²⁾.

A liver biopsy can be very helpful for patients who are experiencing strange symptoms. Liver histology can help determine if a patient with raised alanine aminotransferase levels, an elevated immunoglobulin G concentration, and/or a positive antinuclear anti-body titer has autoimmune hepatitis or nonalcoholic fatty liver disease. Patients with overlapping syndromes of PBC and autoimmune hepatitis (AIH), steatosis and

HCV, or hemochromatosis may also benefit greatly from liver histology ⁽³⁾.

Liver biopsies are expected to remain an important part of treating patients with diagnostic mysteries. Patients with suspected but unconfirmed liver illness or those with abnormal liver tests of unclear cause fall under this category. Patients with genetic illnesses such as Wilson disease, alpha-1 antitrypsin deficiency, glycogen storage diseases, and others are used as examples ⁽⁴⁾.

Patients who appear to have systemic disorders in which the liver plays a role may also benefit from liver histology for diagnostic purposes. Patients suspected of having hereditary hemorrhagic telangiectasia should have their livers examined microscopically only if absolutely required, and this should be done transvenously in tandem with a measurement of the portosystemic pressure gradient ⁽⁴⁾.

In addition to its diagnostic value, liver biopsies are also useful for predicting the development of portal hypertension complications and other related hepatic mortality or morbidity by identifying pre-cirrhotic stages of the illness, such as fibrosis. The importance of fibrosis evaluation in HCV prognosis has been highlighted by recent evidence. Histology is presently the gold standard for assessing factors including alcohol use, elevated hepatic iron content, and/or hepatic steatosis, which are all linked to a more rapid advancement of fibrosis in individuals with chronic HCV ⁽⁵⁾.

Patients with AIH may potentially benefit from prognostic information that may be gleaned from their liver histology, as it appears that those with cirrhosis

have a poorer prognosis than those without. At long last, there's hope that patients whose fibrosis is regressing will be spared the worst clinical effects. Therefore, histological study of liver fibrosis gives vital prognostic information ⁽⁵⁾.

The use of liver biopsies in the creation of therapeutic approaches is on the rise. The availability of effective new treatments for people suffering from a wide range of liver illnesses has contributed to this shift. For patients with preexisting hepatic affection, treatment may be determined by the specific histological lesion, in addition to a treatment plan being implemented when a diagnosis is obtained. Histologically advanced patients are typically the focus of treatment in the latter scenario. Histological study of the liver, for instance, can reveal the grade (degree of inflammation), which likely represents the severity of the continuing liver disease harm in HCV patients. Chronic HCV-induced liver disease patients who have low or no fibrosis may be advised to wait before beginning therapy ⁽⁶⁾.

Causes of abnormal liver tests that are not known:

When a complete history, physical exam, biochemical, serological, and imaging testing have failed to establish a diagnosis, a liver biopsy has long been recognized as a significant diagnostic adjuvant in the evaluation of abnormal liver tests of uncertain etiology. According to the literature, liver histology can provide a definitive diagnosis and alter patient care in specific cases ⁽⁷⁾.

A liver biopsy was performed on 354 patients with abnormal liver tests, and the histological findings were analysed. NAFLD was present in 64% of the biopsies, and Drug-induced liver damage, alcoholic liver disease, primary sclerosing cholangitis (PSC), amyloid and glycogen storage disease, and amyloidosis were among the additional diagnoses. According to liver biopsies, just 6% of people had a healthy liver, while 26% had fibrosis and 6% had cirrhosis. Liver biopsies resulted in changes in treatment for 18% of patients, and 3 families were sent to a genetic screening program for liver disease ⁽⁷⁾.

Cryptogenic cirrhosis:

Somewhere between 3 and 30% of cirrhotic individuals are diagnosed with cryptogenic cirrhosis, often known as cirrhosis of uncertain cause. Several potential factors contribute to the development of cryptogenic cirrhosis. These include silent or "burnt out" autoimmune hepatitis (AIH), nonalcoholic steatohepatitis (NASH), an undetected virus or alcoholism that isn't affecting daily life. NASH has been identified as a primary cause of cryptogenic cirrhosis based on comprehensive epidemiological data and well-documented serial biopsy studies demonstrating progression of previous histological NASH to cirrhosis without any continuing clear evidence of NASH. Some regions of Europe, however, have a higher prevalence of autoimmune illness as the underlying cause ⁽⁸⁾.

Liver transplantation:

The management of patients who have had orthotopic liver transplantation relies heavily on histological examinations of the transplanted organ. Allograft rejection, preservation or reperfusion injury, drug-induced liver injury (typically recurring), viral infection, and bile duct injury are all causes for concern following a liver transplant. Liver biopsies can be helpful in late-stage allograft dysfunction for a number of reasons, including excluding the possibility of the original disease returning ⁽⁸⁾.

Furthermore, it appears that histological assessment of the donor liver is crucial in evaluating the liver for transplantation at the very last minute. It is known that macrovesicular steatosis, (occult) fibrosis, and inflammation all contribute to poor graft function following liver transplantation in older recipients and those with chronic HCV liver disease. In the case of donor livers with questionable clinical histories, several experts recommend collecting tissue samples from at least two distinct locations ⁽⁹⁾.

Focal disease and mass lesions:

Focal liver disease (i.e. a lesion discovered by imaging) assessment with liver biopsy is controversial and challenging. There is a lot of visual overlap between benign and malignant lesions, which makes it difficult to tell which kind of lesion you're looking at while evaluating focal liver illness. In addition, the clinical context nearly always dictates when a liver biopsy is performed. A patient with a large lesion on their liver, for instance, has to have their underlying liver health assessed. Liver biopsies may be necessary for both patient types to arrive at a definitive diagnosis. At first, cross-sectional imaging may show signs of portal venous hypertension, including splenomegaly and intra-abdominal varices, and indicate that the liver has an irregular shape compatible with cirrhosis. Additionally, the existence of the lesion may cause the liver to swell ⁽²⁾.

Histological confirmation may enhance therapy by decreasing ambiguity, but the presence of HCC significantly alters the priority for liver transplantation, making it necessary to minimise false positive imaging scans. Lack of precision in addressing these issues likely contributes to the widespread variety seen in practice ⁽³⁾.

Preparation for liver biopsy:

The patient must be adequately prepped for a percutaneous liver biopsy before the procedure can begin. Measuring coagulation parameters, reviewing the patient's prescription list, and doing a thorough physical examination are all necessary. It is required to seek written agreement from the patient after thoroughly explaining the operation and any minor and significant issues that might arise. You can help your gallbladder empty and lower your risk of complications

by eating a light meal 2 to 3 hours before your surgery. Also, fasting the night before may be recommended to lessen the likelihood of aspiration in the event of vomiting while under conscious sedation. After the biopsy, the patient can relax in the right lateral decubitus position by having a vein accessed, ideally through the left arm. Intravenous fentanyl and midazolam are used to help patients relax, make it easier to undergo the treatment, lessen any discomfort they may have afterwards, and even induce amnesia if they have trouble remembering it. For most individuals, 50 ug of fentanyl and 2 mg of midazolam is sufficient to induce anesthesia without impairing their capacity to participate during the biopsy. It's possible that elderly individuals need less sedation ⁽¹⁰⁾.

Prebiopsy testing:

The patient's platelet count, prothrombin time (PT), international normalised ratio (INR), activated partial thromboplastin time (APTT), and/or cutaneous bleeding time are often measured at an appropriate period before the biopsy. It is suggested by some professionals that a blood type be established in advance, so that transfusions may be quickly arranged in the event of a serious injury or hemorrhage. Abnormal laboratory tests may need to be repeated closer to the time of biopsy, depending on the patient's unique clinical circumstances and local restrictions. The bleeding risk prediction tests are not widely supported by evidence ⁽¹⁰⁾.

Even while the frequency of more complex hemostatic disorders in patients undergoing biopsy, such as hyperfibrinolysis, is unknown and cannot be diagnosed by conventional diagnostics, it appears that 10%-15% of hospitalized patients with cirrhosis have this disease ⁽¹⁰⁾.

Management of medications:

Treatment with anti-platelet medicines before and after a liver biopsy is an essential consideration. Very little data exist to help guide management decisions regarding whether to stop these drugs (or if they should be stopped at all). It is generally agreed that these drugs should be stopped several to ten days before the surgery, while evidence from other regions in which invasive procedures are conducted (such as the prostate, kidney, breast, and gastrointestinal system) are scarce and inconsistent ⁽¹¹⁾.

The liver, on the other hand, is fundamentally different from these other organs (for example, it is very vascular), therefore information concerning the danger of a biopsy at other sites may not be applicable to the liver. Insufficient data exist to provide strong recommendations about the risk of bleeding in individuals treated with newer antiplatelet medications. Discontinuation of warfarin at least 5 days before to surgery is required and preoperative blood testing is optional. PT decisions need to be taken on a case-by-case basis ⁽¹¹⁾.

Liver biopsies are commonly performed on individuals who also have diabetes mellitus. Patients in this situation are encouraged to keep taking their antidiabetic medication. While oral medications typically pose no problems during the peribiopsy period and insulin dosage adjustments may be necessary if the patient had no preoperative intramuscular injections. There is a lack of information on when patients can resume taking drugs that were stopped before a liver biopsy, especially those that may raise the risk of bleeding. The risk of bleeding after a liver biopsy is highest in the first few hours following the surgery and gradually diminishes as time passes. However, delayed bleeding reports raise the possibility that clot breakdown takes place near the biopsy site ⁽¹¹⁾.

Liver biopsy methods in children:

The operator(s), assistant(s), emergency equipment (if necessary), and family members waiting for the patient's recuperation should all have ample space in the area designated for the liver biopsy. There is minimal evidence to support the use of conscious sedation or anxiolytic medication to assist patients relax during medical procedures, but the available data shows that they are safe when done ⁽¹²⁾.

- 1. Percutaneous biopsy.** This technique may be performed in three distinct ways: with palpation/percussion as a guide, with prerecorded images, or with live, streaming images. The traditional percutaneous procedure involves a transthoracic, palpation- and percussion-guided approach following local anaesthetic insertion. In patients with hepatomegaly that extends deep beyond the right costal margin, the subcostal technique has been used; however, this method is not suggested for use outside of a hospital setting without the assistance of imaging ⁽¹²⁾.
- 2. Transvenous (transjugular or transfemoral) biopsy.** There are a few niche cases when taking this tack makes sense. Patients with ascites, a hemostatic problem, a tiny hard cirrhotic liver and morbid obesity with a difficult-to-identify flank location, or in whom free and wedged hepatic vein pressure measures are further needed are all candidates for transvenous liver biopsy. The procedure is now standard since it has been thoroughly documented ⁽¹²⁾.
- 3. Surgical/laparoscopic biopsy.** When the liver is found to be aberrant in appearance, either before surgery is scheduled or during surgery itself, it is often necessary to resort to a surgical or laparoscopic technique. In this case, a biopsy can be taken using a standard needle instrument or by wedge resection. The closeness of the latter to the capsule has been questioned for leading to exaggerated fibrosis estimations. Abundant tissue may be sampled with a laparoscopic liver biopsy, and hemorrhage can be controlled in real time. This is a procedure best left to trained

professionals, and is usually done when the patient is unconscious. Importantly, the use of nitrous gas to create a pneumoperitoneum is so safe and effective that it permits the use of conscious sedation and the conduct of the surgery in specialised sections inside an endoscopic unit. Diagnostic accuracy for cirrhosis has been shown to be higher with laparoscopic biopsy than transthoracic percutaneous biopsy in the majority of trials comparing the two methods. This is likely due to the extra advantage of peritoneal examination during laparoscopic biopsy ⁽¹²⁾.

With the advent of new laparoscopic procedures, it may soon be possible to do a laparoscopic liver biopsy, which would potentially be both safe and inexpensive. The intriguing prospect that natural orifice transluminal endoscopic surgery (NOTES) procedures may be adapted for use in liver biopsies is real. Transgastric flexible endoscopic peritoneoscopy was used to systematically visualise the liver and perform a liver biopsy in a subset of morbidly obese patients for whom percutaneous biopsy was either technically challenging or carried an unacceptable risk of complication ⁽¹³⁾.

4. **Plugged biopsy.** Patients with coagulopathy and/or thrombocytopenia or a small cirrhotic liver have been proposed as candidates for whom the plugged biopsy may be safer than standard percutaneous biopsy due to a reduced risk of bleeding. In a plugged biopsy, the biopsy track is plugged with collagen or thrombin (or other materials) when the cutting needle is removed from the sheath while the patient's breath is still being held ⁽¹²⁾.

CONCLUSION

Sampling mistake, uncommon problems, and occasionally patient concern occur despite liver biopsy being usually safe and now being regarded the criteria standard for the assessment of hepatic inflammation and fibrosis.

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