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# Approach to liver biopsy

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#### INTRODUCTION

Histopathologic examination of liver tissue can provide qualitative information about the type and degree of injury and/or fibrosis [1,2]. Pertinent clinical information should be made available to the pathologist so that the histopathological findings can be interpreted in the clinical context [3].

A guideline from the American Association for the Study of Liver Diseases (AASLD) lists the following indications for liver biopsy [4]:

- Diagnostic evaluation of:
  - Focal or diffuse abnormalities on imaging studies
  - Parenchymal liver disease
  - Chronically (ie, greater than six months) abnormal liver tests of unknown etiology after a thorough, noninvasive evaluation
  - · Fever of unknown origin
- Staging of known parenchymal liver disease
- Development of treatment plans based on histologic analysis

This topic will discuss the approach to liver biopsy, with a focus on the percutaneous route. Our recommendations are generally consistent with the AASLD guidelines for liver biopsy

( table 1) [4]. The role of liver biopsy in the evaluation and management of specific liver diseases is discussed separately. (See individual topic reviews.)

Noninvasive diagnostic tests for evaluation of liver fibrosis are also discussed separately. (See "Noninvasive assessment of hepatic fibrosis: Overview of serologic tests and imaging examinations" and "Noninvasive assessment of hepatic fibrosis: Ultrasound-based elastography".)

#### **CHOOSING A ROUTE**

For most patients, percutaneous liver biopsy is the preferred approach because it is less invasive and less costly compared with other approaches (eg, transjugular liver biopsy). Nontargeted liver biopsies can be performed with or without image guidance. (See 'Role of image guidance for nontargeted biopsies' below.)

Other routes are used in specific settings:

- A transjugular liver biopsy is preferred for patients with coagulopathy, large-volume ascites, or a suspected vascular tumor. (See "Transjugular liver biopsy".)
- Fine needle aspiration (FNA) of the liver with image guidance is used to sample a focal liver lesion and provides a small number of cells for cytological examination; thus, it is not a complete tissue biopsy. (See 'Fine-needle aspiration biopsy' below.)
- Laparoscopic liver biopsy is used for staging disease in patients with intra-abdominal malignancy and is likely to have a higher diagnostic yield in patients with cirrhosis compared with percutaneous liver biopsy. However, it requires general anesthesia, which is associated with increased risk of complications and cost. (See 'Laparoscopic liver biopsy' below.)

#### **CONTRAINDICATIONS**

Absolute and relative contraindications to percutaneous liver biopsy based on expert consensus are listed in the table ( table 2).

#### PREPARATION OF THE PATIENT

Written, informed consent that has a detailed explanation of the major complications (including bleeding, bile peritonitis, pain, and internal organ injury) should be obtained. The patient should be informed of the indications for and alternatives to the procedure, and should be able to understand and cooperate with instructions before and during the procedure [4]. (See 'Contraindications' above.)

**Medications** — Medications known to prolong bleeding time (eg, clopidogrel, aspirin, nonsteroidal antiinflammatory drugs [NSAIDs], and alternative and complementary therapies such as *Ginkgo biloba* and fish oil) should be discontinued at least one week prior to the biopsy, if medically feasible.

Two options are reasonable in patients who inadvertently took aspirin or other NSAIDs in the week prior to the procedure: the procedure can be rescheduled, or it can be performed if a bleeding time immediately prior to the procedure is normal.

For patients at high risk for thromboembolic events who must remain on anticoagulation, a transjugular liver biopsy is an alternative. (See "Transjugular liver biopsy".)

Patients on an oral anticoagulant or those with a coagulopathy will require specific prebiopsy management (eg, stopping vitamin K antagonists such as warfarin and administration of fresh frozen plasma or platelet transfusions). The specific management will depend on the oral anticoagulant and the indication for anticoagulation (eg, in a patient receiving a vitamin K antagonist for atrial fibrillation, the vitamin K antagonist can typically be discontinued five days prior to the procedure, whereas a patient with a mechanical mitral valve may require bridge therapy) ( table 1) [4]. (See "Perioperative management of patients receiving anticoagulants".)

Recommendations for management of antiplatelet medications and anticoagulants have also been issued by the AASLD ( table 1) [4].

**Evaluation of coagulation status** — The clinical history should include details of personal or family history of excessive bleeding, and we obtain the following laboratory testing prior to liver biopsy [5]:

- Complete blood count
- Prothrombin time/international normalized ratio
- Partial thromboplastin time

**Approach to patients with abnormal coagulation studies** — In patients with a platelet count ≥60,000 per microliter, we proceed with percutaneous liver biopsy without specific

therapy to raise the platelet count. In patients with a platelet count <60,000 per microliter, we prefer a transjugular approach, but an alternative is to improve the platelet count (eg, thrombopoietin receptor agonists or platelet transfusion) in addition to addressing treatable comorbidities, and this is discussed separately. (See "Hemostatic abnormalities in patients with liver disease", section on 'Invasive procedures'.)

A guideline issued by the AASLD recommends considering treatment when the platelet count is less than 50,000 to 60,000 platelets per microliter, whether the biopsy is being performed percutaneously or transvenously ( table 1) [4].

The Society of Interventional Radiology guidelines suggest the following INR thresholds for performing procedures with high bleeding risk [6,7]:

- General population: INR ≤1.5 to 1.8
- Patients with chronic liver disease: INR <2.5

The preprocedure management of patients with chronic liver disease and elevated INR is discussed separately. (See "Hemostatic abnormalities in patients with liver disease", section on 'Laboratory abnormalities'.)

**Dietary recommendations** — We suggest that patients fast after midnight prior to liver biopsy, although some centers allow patients to eat a light breakfast. In patients with an intact gallbladder, a light breakfast containing a small amount of fat (such as butter or margarine) will empty the gallbladder and thereby may reduce the chance of injuring it during the biopsy.

**Sedation assessment** — Most patients can undergo percutaneous liver biopsy comfortably without sedation. Anxious patients can be offered premedication with a benzodiazepine [8]. Alternatively, some practitioners routinely give a benzodiazepine combined with opioid analgesia to all patients to enhance their comfort and in case sedation becomes necessary during the procedure, which is uncommon. The level of sedation should be carefully monitored so that patients can cooperate with breathing maneuvers.

#### SPECIAL PATIENT POPULATIONS

**Patients with chronic renal failure** — Patients with chronic renal failure on hemodialysis should have a liver biopsy on the day after dialysis, if possible. In addition, we administer desmopressin immediately prior to the procedure, even when coagulation studies (ie, prothrombin time and activated partial thromboplastin time) are normal [9], although whether

this is beneficial is unclear [10]. (See "Uremic platelet dysfunction" and "Gastrointestinal endoscopy in patients with disorders of hemostasis", section on 'Severe renal dysfunction'.)

We also obtain a bleeding time in patients with chronic renal failure, and if abnormal, we prefer a transjugular route for liver biopsy.

**Patients with inherited disorders of hemostasis** — A number of inherited disorders of hemostasis may increase the risk of bleeding with liver biopsy and require specific preventive measures. We suggest consultation with an expert in coagulation disorders before performing liver biopsy in these patients. (See "Gastrointestinal endoscopy in patients with disorders of hemostasis", section on 'Inherited disorders'.)

**Patients with sickle cell disease** — Serious complications, including bleeding and death, have been described in patients with acute hepatic disease, complicating sickle cell anemia, and suggesting that a percutaneous biopsy should be avoided in such patients [11]. (See "Hepatic manifestations of sickle cell disease".)

For patients with sickle cell disease who require liver evaluation beyond standard laboratory testing and imaging, we suggest a noninvasive assessment of liver fibrosis such as ultrasound-based elastography. (See "Noninvasive assessment of hepatic fibrosis: Overview of serologic tests and imaging examinations" and "Noninvasive assessment of hepatic fibrosis: Ultrasound-based elastography".)

**Patients with amyloidosis** — Amyloidosis is associated with an increased risk of bleeding. Several factors may contribute, including factor X deficiency, due to binding to amyloid fibrils; decreased synthesis of coagulation proteins in patients with advanced liver disease; and amyloid infiltration of blood vessel walls. (See "Overview of amyloidosis", section on 'Hematologic abnormalities'.)

As a general rule, the diagnosis of amyloidosis should be established by sampling tissue from the intestine, fat, kidney or bone marrow, rather than liver. Some case reports have suggested that patients with hepatic amyloidosis have an increased risk of bleeding and/or hepatic rupture following the biopsy, but this has not been consistently demonstrated [12,13]. (See "Gastrointestinal amyloidosis: Clinical manifestations, diagnosis, and management".)

#### PERCUTANEOUS NEEDLE BIOPSY

Immediately prior to the procedure, the patient's bladder should be empty because bed rest is required for at least three hours following the procedure.

**Choice of needle** — There are three categories of equipment used to obtain a percutaneous liver biopsy:

- Suction needles (Menghini needle, Klatskin needle, Jamshidi needle)
- Cutting needles (Vim-Silverman needle, Trucut needle)
- Spring-loaded cutting needles that have triggering mechanisms (eg, Microvasive, Bard Monopty)

We routinely use the spring-loaded needles because of ease of use. Others regularly use suction needles because, in general, they produce large specimens. Cutting needles, with the exception of the spring-loaded variety, require a relatively longer time in the liver during the biopsy, a factor that may influence the risk of bleeding [14]. Although not consistent, a greater risk of bleeding following a biopsy has been observed with larger-diameter needles [15]. If cirrhosis is clinically suspected, a cutting needle is preferred over a suction-type needle, as fibrotic tissue tends to be fragmented with the latter [4,16].

**Description of procedure** — With the patient in the supine position and right hand under the head, the point of maximum liver dullness (in both inspiratory and expiratory phases) is percussed over the right hemithorax at the mid-axillary line. The point of maximum liver dullness is usually between the sixth and ninth (usually eighth) intercostal spaces, and the site is marked. We then perform a bedside ultrasound to confirm the appropriateness of the biopsy site. If the point of maximum liver dullness is uncertain, ultrasound guidance is mandatory. Some operators use a 22 to 25 gauge spinal needle to help determine the depth that the needle needs to penetrate through the diaphragm before reaching the hepatic capsule.

Lidocaine (2 to 4 mL of a 2 percent solution) is injected over the upper border of the rib to avoid the intercostal vessels that traverse along the lower border of each rib. A small scalpel incision is made.

If a spring-loaded or automated needle is being used, the device is passed through the skin incision and the biopsy specimen is obtained with the patient holding his/her breath transiently in quiet, not forced, expiration phase.

If a biopsy needle that requires a suction technique is used, it is first attached to a 10 or 20 mL syringe containing 5 to 10 mL of sterile saline. A trocar can be used to create the tract. The biopsy needle is then passed through the incision until it reaches the peritoneal cavity. A small amount of saline is flushed into the peritoneal cavity to eliminate any fat tissue that may have entered the needle during the passage. With the patient holding his/her breath transiently in quiet, not forced, expiration phase, suction is applied and the biopsy is performed, minimizing

the time the needle is within the liver. A similar approach without saline flushing applies to cutting needles (eg, Trucut needle).

Role of image guidance for nontargeted biopsies — Most practitioners obtain liver imaging within one week prior to a non-targeted liver biopsy (ie, a liver biopsy that is not of a specific liver lesion, but is a representative sample of liver parenchyma). Ultrasonography or computed tomography (CT) identifies mass lesions and defines the anatomy of the liver and the relative positions of the gallbladder, lung, and kidney.

For non-targeted biopsies, the use of ultrasound marking prior to percutaneous biopsy is mandatory when adequate localization by percussion cannot be achieved. Ultrasound guidance can also be helpful for less experienced operators and in patients who are obese, have a history of prior upper abdominal surgery, or those who are suspected of having advanced cirrhosis with possible atrophy of the right lobe of the liver based upon clinical or laboratory grounds.

A guideline issued by the American Association for the Study of Liver Diseases (AASLD) recommends ultrasound marking before biopsy because of the potential to reduce complications, but does not consider it to be mandatory ( table 1) [4].

In a study of 165 consecutive outpatient liver biopsies, ultrasound imaging resulted in changing the biopsy site in 21 of 165 patients (13 percent) and led to abortion of the procedure in four patients [17]. Similarly, two large studies demonstrated a lower complication rate and a higher diagnostic yield using ultrasound guidance [18,19]. However, in a study that evaluated 222 consecutive non-targeted liver biopsies by a single operator, ultrasound was helpful in only 3.6 percent of the patients in whom the biopsy site had to be changed after it had been marked by the percussion technique [20].

Targeted liver biopsies are typically performed by an interventional radiologist who uses imaging studies (eg, ultrasound or CT scanning) to guide the biopsy. (See "Approach to the adult patient with an incidental solid liver lesion".)

**Post-biopsy care** — While the optimal post-procedure position has not been studied, we suggest positioning the patient in the right decubitus position for two hours followed by a supine position for an additional hour.

We monitor the patient's vital signs every 15 minutes for the first hour, every 30 minutes for two hours, and then hourly until discharge at four hours after biopsy. The minimal duration of observation that is safe has not been clearly established; an observation period as short as one hour has been described [21,22]. An observation period of two to four hours has been recommended in a guideline from the AASLD ( table 1) [4].

Written post-procedure instructions should be discussed with the patient before discharge. The patient is asked to report immediately any abdominal pain, fever, weakness, dyspnea, or bleeding and to avoid lifting more than 15 to 20 pounds for one week. (See 'Information for patients' below.)

#### **Complications**

**Overall rates and mortality** — The overall rate of serious complications following liver biopsy was approximately 1 percent in two series including 3000 to 6000 patients [23,24], while in another series of over 60,000 patients, overall mortality risk was estimated to be 0.2 percent [25]. Sixty percent of complications occur within two hours of the procedure, and in two studies including 6000 to 68,000 patients, 83 to 96 percent of complications occurred within 24 hours [15,24]. Approximately 2 to 3 percent of patients require hospital admission for management of complications; pain or hypotension are the predominant causes [26,27].

The risk of mortality appears to be higher in patients who undergo a biopsy of a malignant lesion [28]. Other factors associated with complications include more than two biopsy passes, platelet count ≤50,000 per microliter, and female sex [24]. Operator experience affected the risk of complications in some reports. In one study, a lower complication rate was observed when biopsies were performed by clinicians who did more than 50 biopsies a year [29].

**Pain** — Pain is the most common complication following percutaneous liver biopsy with approximately one-fourth of patients experiencing pain in the right upper quadrant or right shoulder [4]. The pain is usually dull, worse with inspiration, mild, and resolves completely within a few hours. We manage post-biopsy pain in patients who are hemodynamically stable with acetaminophen with codeine or meperidine.

Persistent or moderate to severe pain or hemodynamic instability is uncommon, and these patients should be further evaluated with laboratory testing and imaging (ie, complete blood count, ultrasound, or abdominal computed tomography [CT]) to look for evidence of bleeding or peritonitis.

**Bleeding** — The most common serious complication of liver biopsy is intraperitoneal hemorrhage, although hematoma and hemobilia can also occur. The incidence of severe bleeding that results in hemodynamic compromise or requires intervention has been reported following 0.01 to 0.5 percent of liver biopsies [4,24,30]. In a study of over 6600 image-guided liver biopsies, the incidence of hematoma requiring transfusion or angiographic intervention was 0.5 percent [24]. Bleeding usually becomes clinically apparent within three to four hours after the biopsy. Hypotension and/or tachycardia following a biopsy, particularly when associated with abdominal pain, are usually related to hemorrhage.

Three categories of bleeding have been recognized:

• Intraperitoneal hemorrhage - Intraperitoneal hemorrhage, which may result from laceration caused by deep inspiration during the biopsy or may be related to penetrating injury of a branch of the hepatic artery or portal vein. It can be recognized by the presence of free fluid in the peritoneal cavity on imaging tests. However, the presence of small amounts of free fluid without other clinical features of bleeding may be clinically insignificant [31].

In patients with suspected intraperitoneal hemorrhage, immediate arrangements for blood, platelets, and plasma should be made and a surgeon and interventional radiologist should be alerted. Subsequent management depends upon the type of bleeding and the clinical course. The administration of intravenous fluids and/or blood products may result in stabilization without the need for further intervention. Angiography with an attempt at embolization or surgical exploration is indicated if hemodynamic instability persists despite aggressive resuscitative measures.

• **Hematoma** - Small intrahepatic and/or subcapsular hematomas are usually asymptomatic, while large hematomas may cause pain, tachycardia, hypotension, or a delayed drop in hemoglobin and hematocrit. In one series, symptomatic, subcapsular hematomas were observed in only 3 of 12,750 biopsies (0.023 percent) [32]. A trial involving 51 patients who underwent biopsy with a suction needle technique found an overall incidence of 2.3 percent [33].

Conservative treatment is usually sufficient. Angiography is rarely required to embolize an arteriovenous fistula.

• **Hemobilia** - Hemobilia is the least common of the hemorrhagic complications. In a series of over 68,000 percutaneous liver biopsies, only four cases (0.006 percent) of hemobilia were identified [15]. Hemobilia usually presents with the classical triad of gastrointestinal bleeding, biliary pain, and jaundice. The bleeding is usually arterial in origin, but can be venous in patients with pre-existing portal hypertension. It can vary in severity from occult to life-threatening hemorrhage. Hemobilia can present acutely after simultaneous perforation of intrahepatic bile ducts and blood vessels, or, more commonly, in a delayed fashion from gradual erosion of a biopsy-induced hematoma or pseudoaneurysm into a bile duct. The mean interval from the time of biopsy to the onset of symptoms is approximately five days [34].

Hemobilia may resolve with supportive care, but ongoing or intermittent bleeding requires angiographic embolization or surgery. (See "Angiographic control of nonvariceal

gastrointestinal bleeding in adults", section on 'Embolization' and "Causes of upper gastrointestinal bleeding in adults", section on 'Hemobilia'.)

**Transient bacteremia** — Transient bacteremia has been observed in 6 to 14 percent of patients [9]. It is almost always inconsequential, but septicemia and shock can rarely occur in patients with biliary obstruction and cholangitis. The routine use of prophylactic antibiotics has not been recommended. (See "Primary sclerosing cholangitis in adults: Clinical manifestations and diagnosis", section on 'Complications of primary sclerosing cholangitis'.)

**Bile peritonitis** — Bile peritonitis is a complication of liver biopsy, particularly in patients with mechanical obstruction of the extrahepatic biliary system. In other patients, it may indicate perforation of the gallbladder [35]. Bile peritonitis should be suspected in patients who develop the abrupt onset of abdominal pain with peritoneal signs (typically within a few minutes of the biopsy), particularly when bile was aspirated through the biopsy needle. Symptoms range from mild to severe and may include fever, leukocytosis, ileus, and hemodynamic instability. For patients with suspected bile peritonitis, we obtain imaging with computed tomography scan. Treatment includes intravenous fluids, broad spectrum antibiotics, inpatient monitoring and surgical intervention in patients with clinical deterioration.

**Organ injury** — Pneumothorax (incidence of approximately 0.0078 percent) and hemothorax (incidence of approximately 0.063 percent) often resolve spontaneously and seldom require intervention with a chest tube [32]. Inadvertent perforation of other abdominal organs is usually well tolerated and does not require specific intervention [15].

**Other complications** — The risk of malignant needle-track seeding is a potential complication in patients suspected of having a malignancy. (See "Approach to the adult patient with an incidental solid liver lesion".)

Other rare complications after percutaneous liver biopsy include subcutaneous emphysema, pneumoperitoneum, pneumoscrotum, subphrenic abscess, carcinoid crisis, anaphylaxis after biopsy of an echinococcal cyst, and pancreatitis due to hemobilia.

**Limitations** — Limitations to liver biopsy include sampling variability and the subjective nature of the pathologist's interpretation [2,4]. Diagnostic accuracy of a liver biopsy may be affected by specimen size or by variable distribution of the disease throughout the liver parenchyma. In a study of 124 patients with chronic hepatitis C who underwent laparoscopic-guided liver biopsy, 41 patients (31 percent) had a difference by at least one histologic stage between right and left lobes [36]. (See "Histologic scoring systems for chronic liver disease".)

In a study of 51 patients with nonalcoholic fatty liver disease who underwent percutaneous liver biopsy with collection of two samples, six of the 17 patients (35 percent) with bridging fibrosis on one sample had mild or no fibrosis on the second sample [37].

#### FINE-NEEDLE ASPIRATION BIOPSY

Liver fine-needle aspiration biopsy (FNAB) is performed by an interventional radiologist under ultrasound or computed tomographic guidance, usually to sample a focal liver lesion (ie, targeted liver biopsy). Liver fine-needle aspiration biopsy is contraindicated in patients with underlying coagulopathy or if a safe access route to the lesion cannot be identified. (See "Approach to the adult patient with an incidental solid liver lesion", section on 'Biopsy'.)

**Complications** — Overall mortality related to fine-needle aspiration biopsy of the liver is low (0.008 to 0.031 percent). Bleeding is uncommon in patients without coagulopathy or a vascular lesion, such as a hemangioma [38]. Some studies suggest that seeding of the biopsy tract with malignant cells is rare (0.003 to 0.009 percent); a large review identified only three reported cases [39]. However, this figure could be an underestimation because the studies were retrospective and based upon mailed questionnaires. A much higher rate of malignant biopsy tract seeding was described in a review that focused on 43 patients who had undergone a preoperative biopsy for suspected hepatic metastases from colorectal cancer [40]. Evidence of dissemination related to the biopsy was observed in seven patients (16 percent).

The yield of cytological material obtained from fine-needle aspiration biopsy compares favorably with the final histologic diagnosis of surgical specimens [41]. However, negative cytology does not rule out malignancy.

#### **ENDOSCOPIC ULTRASOUND-GUIDED LIVER BIOPSY**

Endoscopic ultrasound (EUS)-guided liver biopsy is a reasonable alternative to percutaneous liver biopsy [42,43]. EUS-guided liver biopsy is safe and allows for sampling both the left and right lobes of the liver, although biopsy of the right lobe is technically more difficult. Limitations of EUS-guided liver biopsy include that it requires expertise in advanced endoscopy and increases overall cost (ie, endoscopy with anesthesia). Thus, the EUS approach has not been widely adopted in clinical practice. (See "Endoscopic ultrasound: Examination of the upper gastrointestinal tract".)

Parenchymal liver biopsy using EUS has been associated with good quality specimens (ie, adequate specimen length and complete portal tracts) [43-45]. In a systematic review of 23

studies including 1326 patients who underwent EUS-guided nontargeted liver biopsy, the overall diagnostic yield was 93 percent with a low rate of serious complications (1 percent) [44].

#### LAPAROSCOPIC LIVER BIOPSY

Laparoscopic liver biopsy is an alternative for patients with contraindications to percutaneous liver biopsy or who have other indications for laparoscopy [46,47]. However, its use has declined in favor of less invasive radiological procedures. When used, the yield of diagnostic laparoscopy is high. In one review, a definitive diagnosis was obtained in 93 percent of 1794 diagnostic laparoscopies [48]. A total of 31 complications were observed (2 percent), of which only eight were considered to be major.

# TRANSJUGULAR LIVER BIOPSY

Transjugular liver biopsy is discussed separately. (See "Transjugular liver biopsy".)

### **INFORMATION FOR PATIENTS**

UpToDate offers two types of patient education materials, "The Basics" and "Beyond the Basics." The Basics patient education pieces are written in plain language, at the 5<sup>th</sup> to 6<sup>th</sup> grade reading level, and they answer the four or five key questions a patient might have about a given condition. These articles are best for patients who want a general overview and who prefer short, easy-to-read materials. Beyond the Basics patient education pieces are longer, more sophisticated, and more detailed. These articles are written at the 10<sup>th</sup> to 12<sup>th</sup> grade reading level and are best for patients who want in-depth information and are comfortable with some medical jargon.

Here are the patient education articles that are relevant to this topic. We encourage you to print or e-mail these topics to your patients. (You can also locate patient education articles on a variety of subjects by searching on "patient info" and the keyword(s) of interest.)

• Beyond the Basics topics (see "Patient education: Liver biopsy (Beyond the Basics)")

#### SUMMARY AND RECOMMENDATIONS

• Indications – The indications for liver biopsy include (see 'Introduction' above):

- Diagnostic evaluation of abnormalities on imaging studies, parenchymal liver disease, chronically abnormal liver tests of unknown etiology, or fever of unknown origin.
- Staging of known parenchymal liver disease.
- Development of treatment plans based on histologic analysis.
- Contraindications Absolute and relative contraindications to percutaneous liver biopsy based on expert consensus are listed in the table ( table 2). (See 'Contraindications' above.)
- **Choosing a route** For most patients, percutaneous liver biopsy is the preferred approach because it is less invasive and less costly compared with other approaches (eg, transjugular liver biopsy). Nontargeted liver biopsies can be performed with or without image guidance. (See 'Choosing a route' above.)
- **Patient preparation** We obtain the following laboratory testing prior to liver biopsy (see 'Evaluation of coagulation status' above):
  - Complete blood count
  - Prothrombin time/international normalized ratio
  - Partial thromboplastic time

For patients with platelet count ≥60,000 per microliter, we proceed with percutaneous liver biopsy without specific therapy to raise the platelet count.

For patients with a platelet count <60,000 per microliter, we prefer a transjugular approach, but an alternative is to improve the platelet count (eg, thrombopoietin receptor agonists or platelet transfusion) in addition to addressing treatable comorbidities. (See 'Approach to patients with abnormal coagulation studies' above and "Hemostatic abnormalities in patients with liver disease".)

- **Equipment** There are three categories of equipment used to obtain a percutaneous liver biopsy:
  - Spring-loaded cutting needles that have triggering mechanisms (Microvasive)
  - Suction needles (Menghini needle, Klatskin needle, Jamshidi needle)
  - Cutting needles (Vim-Silverman needle, Trucut needle)

We routinely use the spring-loaded needles because of ease of use. Others regularly use suction needles because, in general, they produce large specimens. (See 'Choice of needle'

above.)

• Adverse events – The most common serious complication of liver biopsy is intraperitoneal hemorrhage, although hematoma and hemobilia can also occur. Other potential complications of liver biopsy include right upper abdominal pain, right shoulder pain, bile peritonitis or pneumothorax. (See 'Complications' above.)

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#### **GRAPHICS**

# American Association for the Study of Liver Diseases (AASLD) liver biopsy recommendations

#### Focal disease and mass lesions

Liver biopsy should be considered in patients in whom diagnosis is in question, and when knowledge of a specific diagnosis is likely to alter the management plan.

Liver histology is an important adjunct in the management of patients with known liver disease, particularly in situations where (prognostic) information about fibrosis stage may guide subsequent treatment; the decision to perform liver biopsy in these situations should be closely tied to consideration of the risks and benefits of the procedure.

#### Technical issues, contraindications, and complications

Prior to performance of liver biopsy, patients should be educated about their liver disease and about investigations other than liver biopsy (if any) that may also provide diagnostic and prognostic information.

Prior to performance of liver biopsy, patients must be carefully informed about the procedure itself including alternatives (as above), risks, benefits, and limitations; written informed consent should be obtained.

# **Management of medications**

Antiplatelet medications should be discontinued several to 10 days before liver biopsy, although there is uncertainty surrounding the need for their discontinuation. Management of specific compounds should be handled on a case-by-case basis, taking into account their clinical indications, as well as the potential bleeding risk associated with their use in the setting of liver biopsy.

Anticoagulant medications should be discontinued prior to liver biopsy. Warfarin should generally be discontinued at least five days prior to liver biopsy. Heparin and related products should be discontinued 12 to 24 hours prior to biopsy. In all patients, the risk of discontinuing anticoagulant medications must be weighed against the (potential) risk of bleeding during/after liver biopsy.

Antiplatelet therapy may be restarted 48 to 72 hours after liver biopsy.

Warfarin may be restarted the day following liver biopsy.

# Liver biopsy procedure

Performance of liver biopsy requires an adequate sized and dedicated physical space suitable for focused physician effort as well as safe patient recovery.

The use of sedation, preferably light sedation, is safe and does not lead to increased procedural risk.

Vital signs must be frequently monitored (at least every 15 minutes for the first hour) after liver biopsy.

The recommended observation time after biopsy is between two to four hours and will vary depending on local expertise and practice.

Ultrasound guidance with marking of the optimal biopsy site performed immediately preceding biopsy, by the individual performing the biopsy, is preferred, though not mandatory, because it likely reduces the risk of complications from liver biopsy.

#### **Contraindications**

Percutaneous liver biopsy with or without image guidance is appropriate only in cooperative patients, and this technique should not be utilized in uncooperative patients.

Uncooperative patients who require liver biopsy should undergo the procedure under general anesthesia or via the transvenous route.

In patients with clinically evident ascites requiring a liver biopsy, a transvenous approach is generally recommended, although percutaneous biopsy (after removal of ascites) or laparoscopic biopsy are acceptable alternatives.

Patients who require liver biopsy and who have a large vascular lesion identified on imaging should undergo the procedure using real-time image guidance.

The decision to perform liver biopsy in the setting of abnormal laboratory parameters of hemostasis should continue to be reached as the result of local practice(s) and consideration of the risks and benefits of liver biopsy because there is no specific PT-INR and/or platelet count cutoff at or above which potentially adverse bleeding can be reliably predicted.

# **Complications**

Those performing liver biopsy must be cognizant of multiple potential complications (including death) that may occur after liver biopsy and discuss these appropriately with their patients beforehand.

Platelet transfusion should be considered when levels are less than 50,000 to 60,000/mL (this applies whether one is attempting biopsy transcutaneously or transvenously).

The use of prophylactic or rescue strategies such as plasma, fibrinolysis inhibitors, or recombinant factors should be considered in specific situations, although their effectiveness remains to be established.

In patients with renal failure or on hemodialysis, desmopressin (DDAVP) may be considered, although its use appears to be unnecessary in patients on stable dialysis regimens.

Patients on chronic hemodialysis should be well dialyzed prior to liver biopsy, and heparin should be avoided if at all possible.

# **Radiological considerations**

Image-guided liver biopsy is recommended in certain clinical situations including in patients with known intrahepatic lesions (real-time imaging is strongly preferred) and in those with previous intraabdominal surgery who may have adhesions. Image-guided liver biopsy should also be considered in the following situations: patients with small livers that are difficult to percuss, obese patients, and patients with clinically evident ascites.

# **Pathological considerations**

Because diagnosis, grading, and staging of nonneoplastic, diffuse parenchymal liver disease is dependent on an adequate sized biopsy, a biopsy of at least 2 to 3 cm in length and 16-gauge in caliber is recommended.

It is recommended that if applicable, the presence of fewer than 11 complete portal tracts be noted in the pathology report, with recognition that diagnosis, grading, and staging may be incorrect due to an insufficient sample size.

If cirrhosis is suspected, a cutting rather than a suction needle is recommended.

In clinical practice, use of a simple (eg, Metavir or Batts-Ludwig) rather than complex (eg, Ishak) scoring system is recommended.

# Noninvasive alternatives to liver biopsy

Liver biopsy is currently a fundamentally important tool in the management of patients with liver disease, important for diagnosis as well as staging of liver disease and its use is recommended until clearly superior methodologies are developed and validated.

# Training for liver biopsy

Specific training for liver biopsy is essential and is recommended for those who perform it.

Liver biopsy should be taught to trainees by experts, highly experienced in the practice of liver biopsy and management of its potential complications.

Although the number of biopsies required to become adequately trained is unknown, it is recommended that operators perform at least 40 biopsies.

Training in percutaneous liver biopsy should include specific training in ultrasound interpretation of fundamental liver anatomy and other landmarks.

Image-guided liver biopsy should be taught to trainees by experts who themselves have adequate training and experience with the technique.

Data from: Rockey DC, Caldwell SH, Goodman ZD, et al. Liver biopsy. Hepatology 2009; 49:1017.

Graphic 67820 Version 2.0

# Contraindications to a percutaneous liver biopsy

Absolute	Relative
Inability of patient to cooperate with procedure	Morbid obesity
Significant coagulopathy or thrombocytopenia (unless corrected prior to the liver biopsy)	Ascites
	Hemophilia
NSAID use (including aspirin) within last 7 to 10 days	Infection within the right pleural cavity
Patient refusal to accept blood transfusion or inability to provide blood transfusion support	Infection below right hemidiaphragm
Suspected hemangioma, vascular tumor, or echinococcal cyst	Amyloidosis
Inability to identify an adequate biopsy site by percussion and/or ultrasound	
Extrahepatic biliary obstruction	

Adapted from: Bravo AA, Sheth SG, Chopra S. Liver biopsy. N Engl J Med 2001; 344:495.

Graphic 78374 Version 9.0

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