REVIEW ARTICLE

LIVER BIOPSY - PAST, PRESENT AND FUTURE

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ABSTRACT

Percutaneous liver biopsy is widely used for the diagnosis and management of liver diseases. With the advancement in medical technology, there are now different approaches to performing liver biopsy, using various biopsy needles. This review highlights the differences between these various techniques. It re-examines in detail, the contraindications and complications of liver biopsy. Haemorrhage accounts for about 50% of all major complications and is the main cause of mortality. About 25% of complications are pulmonary in nature. The rest consists mainly of infective complications. Day case liver biopsy has been repeatedly shown to be safe in selected patients, but is underpractised. Routine practice of image-guided biopsy is advocated, even in the absence of discrete lesion. Medicine is constantly evolving. New indications for liver biopsy, eg of transplanted liver, are to be expected. Conversely, with the advent in other less invasive modalities of investigation, some indications will disappear from the list.

Keywords: *liver biopsy – review*

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INTRODUCTION

Nowadays, in the course of his training, most doctors would have learnt how to do a liver biopsy. With the advancement of other diagnostic modalities, such as endoscopic retrograde cholangiopancreatography (ERCP), angiography, computerised tomography (CT) and ultrasonography, the indications for liver biopsy have changed and may even have become fewer. Certainly the techniques have evolved and doctors now have a wide option of liver biopsy needles to choose from. The complications are now better recognised and the risks have decreased (Table I).

Table I – Incidence of liver biopsy complications and deaths over the years

Author	Year	Complication (%)	Mortality (%)
Terry[1]	1952	0.32	0.12
Zamcheck[2]	1953	not available	0.17
Lindner[3]	1967	not available	0.015
Piccinino[4]	1986	2.2	0.009
Froehlich[5]	1993	0.31	0.086
Chuah[6]	1994	0.56	0.052

The history of liver biopsy

The famous Paul Ehrlich was said to have performed the first liver biopsy in 1883[7]. But it was Schüpfer who, in 1907, published the first liver biopsy series[8]. He used the technique for the diagnosis of cirrhosis and hepatic tumours. However it was Huard[9] in France and Baron[10] in USA who popularise liver biopsy for general purposes in the 1930s. World War II saw a rapid increase in the use of liver biopsy to investigate the many cases of viral hepatitis amongst soldiers[11,12].

It was Iversen and Roholm who, in 1939, first proposed the transthoracic approach[11]. Tripoli and Fader[13] used a cutting mechanism for liver biopsy via the subcostal approach in 1941 which subsequently formed the basis for the Vim-Silverman needle[14]. In 1958, Menghini[15] described a suction technique using a needle which now bears his name.

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THE TECHNIQUES

Except in children[16], it is unnecessary to premedicate the patient before the biopsy as patient cooperation is desirable. There are pros and cons to allowing the patient a light breakfast. The gallbladder becomes contracted following a meal, hence minimising the chance of hitting it during the biopsy. However, the more cautious would prefer the patient to be fasted, in case they develop a complication requiring operative intervention.

Suction and non-suction techniques

The suction technique is based on the Menghini needle as opposed to the non-suction technique of the Vim-Silverman needle. Trucut needle is the most widely used disposable version of the latter[6]. The Menghini technique was thought to be safer because of its short intra-hepatic stage of about 0.1 s[15,17,18]. However a recent survey[6] has shown that the types of needles did not affect the complication and death rates significantly. This is not surprising as those well-trained in using the Trucut needle may execute the whole sequence of manoeuvres in less than a second, instead of the usual 5 to 10 seconds with the original Vim-Silverman needle. On the other hand, the suction technique does have the advantage of simplicity which lends itself to use in less cooperative patients, including children[16]. It has also been shown to be easier, quicker and cheaper[19]. The only drawback is that it may fail to procure adequate liver tissue from a tough cirrhotic liver[18] or obtain a fragmented sample only[19].

Fine needle aspiration biopsy and diameter of needles

"Fine", by convention, means an external diameter of less than 1 mm[20]. It has been shown to be safer[20,21]. However the specimen obtained is often inadequate for histology[22] and one may have to settle for cytologic study which is dependent on the skill of the histopathologist[17,23,24]. This method has been used successfully to biopsy liver neoplasms[17,18,23] which tend to bleed with conventional needles[5,25]. As for needles with an external diameter of greater than or equal to 1mm, the effect of needle size on complication rate is less clear-cut. Some authors suggest that complication rate may depend on needle size[3,26-29] while others do not think so[30-32].

Transjugular and plugged liver biopsy

Transjugular liver biopsy was first described by Rösch in 1973[33]. It is particularly suitable for patients with impaired coagulation and has proved safe and effective in some centres[34-36]. However it requires internal jugular vein cannulation, the use of intravenous contrasts with fluoroscopy and ECG monitoring. It is also more time-consuming than percutaneous biopsy. Fatal haemorrhage can still occur if the liver capsule is inadvertently perforated.

In 1984, percutaneous liver biopsy with plugging of the needle track with absorbable gelatin sponge was described[37]. This method has also been proven to be safe and effective[38]. In a head-to-head comparison of the above two methods[39], plugged liver biopsy yielded significantly larger biopsies but may be associated with an increased risk of haemorrhage (3.5% as opposed to 0 in the transjugular group). However this difference is not statistically significant.

Laparoscopic liver biopsy

This allows direct inspection of the liver surface prior to the biopsy. If this method is employed, a definite diagnosis is possible in nearly all cases[40,41]. Furthermore, it also allows direct compression of the biopsy site if bleeding is excessive. However it requires theatre time and the patient may need a general anaesthetic. In some diseases, capsular sampling may not be representative (eg primary biliary cirrhosis).

Image-guided liver biopsy

Nowadays, in the course of investigations leading up to a liver biopsy, most patients would have undergone some form of hepatic imaging. It has been shown that ultrasonography done before the biopsy and in cases with biopsy-related complications has significantly improved management and reduced the mortality[42]. Indeed, in recent years there has been a shift away from blind percutaneous biopsies towards image-guided biopsies using laparoscopy, ultrasonography and computerised tomography for accurate positioning of the needle[17]. The objective of image-guidance are: (i) to target the liver, (ii) to target a lesion, (iii) to avoid the gall bladder. Although advocated by the authors of a large-comparative series of 2,000 ultrasound-guided liver biopsies[43], two recent nationwide surveys[5, 6] did not show image-guided biopsies to be safer than blind percutaneous biopsies. Despite this, the tagetting of the liver should not be left completely to chance, even though it is a large and superficial organ. Furthermore there are anatomical variations to the position of the gall bladder. Those performing liver biopsies should be trained in ultrasonography of the hepato-biliary system. In a recent survey[6], a disproportionate number of gastroenterologists would choose image-guided biopsy for themselves even in the absence of discrete lesions. When it comes to offering image-guided biopsy to patients, one should not practise a double standard.

INDICATIONS FOR LIVER BIOPSY

These may include:

(i) chronic jaundice, in the absence of biliary system dilatation,
(ii) chronic hepatitis, including for pre- and post-interferon therapy assessment,
(iii) to help diagnose the cause of cirrhosis and portal hypertension,
(iv) drug-induced liver changes, eg due to methotrexate,
(v) alcoholic liver disease,
(vi) hepatomegaly and storage diseases,
(vii) assessment of systemic diseases, including infections and granulomatous diseases,
(viii) unexplained abnormal elevation in liver enzymes,
(ix) screening of families with hepatic diseases.

Before subjecting a patient to a liver biopsy, ask yourself the following questions:

(i) Will it change my management?
(ii) Will it change my approach to the patient?
(iii) Will it strengthen the suspected diagnosis?
(iv) Do the benefits outweigh the risks?

CONTRAINDICATIONS

The uncooperative patient

The patient must be able and willing to follow instructions, such as to stop breathing at the end of expiration just before and during the intrahepatic stage of the biopsy. Getting the patient to go through the breathing sequence prior to the biopsy may be helpful.

Ascites

Liver biopsy is contraindicated in cases of moderate to severe ascites. The liver is relatively more mobile in ascitic fluid hence making it more difficult to obtain tissue. It may also be more difficult to secure haemostasis in the presence of ascites. Attempts should be made to reduce the amount of ascites with diuretics or paracentesis prior to the biopsy.

Impaired coagulation

A recent survey[6] has suggested that patients' coagulation profile should not be compromised upon. Any attempts to correct the impaired coagulation should consist of giving 4 to 6 units of fresh frozen plasma over 1 or 2 hours and then repeated[44] after the procedure[45]. Coagulation defects in hepato-biliary disease are often accompanied by thrombocytopaenia and an elevated portal venous pressure[46]. Platelet transfusion may be given to cover liver biopsy[46]. However platelet function is more important than platelet count[47]. The initial nick of the skin may give an informal indication of the bleeding time[2]. Bleeding time may be prolonged in haematological malignancies by aspirin and cytotoxics. In such cases, if platelet count can be raised to above 60×10^9/L by platelet transfusion, the biopsy seems to be safe[48].

Two studies[49,50] have shown that peripheral blood coagulation indices correlate poorly with liver bleeding time following laparoscopic biopsy. Ewe proposed that the concentration of clotting factors within the liver and the mechanical compression of the needle tract by elastic tissue might play an important role[49].

Extrahepatic obstructive jaundice

Although liver biopsy has been shown to be safe in patients with extrahepatic obstructive jaundice[51], the possibility of bile leakage resulting in biliary peritonitis has been voiced by others[1,52]. Nowadays other modalities of investigation, such as ultrasonography, computerised tomography and ERCP can elucidate the causes of extrahepatic obstructive jaundice more accurately and safely. Liver biopsy in such cases merely confirms the presence of cholestasis and rarely indicates its cause and hence is unnecessary.

COMPLICATIONS

Pain

It should not be surprising that pain is actually the commonest complication. The incidence in various series ranged from 5% to 50%[10,53]. Pain may occur at the site of entry, in the right hypochondrium in the epigastrium or be referred to the right shoulder. It may occur during the procedure and persist thereafter but is usually transient. However a hepatic friction rub, if present, may last for several weeks.

Haemorrhage

Besides pain, the most common complication is haemorrhage[6].

It accounts for about 50% of all complications[6] and is the main cause of mortality[5] following liver biopsy. Most cases of fatal haemorrhage resulted from inadvertent perforation of distended portal or hepatic veins or aberrant arteries[2]. It may also occur as a result of a tear in the liver when the patient breathes deeply during the intrahepatic stage of the biopsy. Hence the importance of careful instruction of patients prior to the biopsy and patient cooperation during the procedure. Haemorrhage usually stops spontaneously and should be managed by blood transfusion. If bleeding is severe, surgery may be required. Laparotomy rate amongst patients who bled range from 6%[3] to 25%[1] (Table II). Selective angiography of the hepatic artery, besides establishing the diagnosis, also provides the opportunity for embolisation or balloon occlusion of the segmental artery involved.

Table II – Incidence of haemorrhage and laparotomy rates following liver biopsies

Author	Haemorrhage (%)	Laparotomy (%)
Terry[1]	0.2	0.05
*Lindner[3]	0.08	0.005
Froehlich[5]	0.14	not available
Chuah[6]	0.25	0.03

*denotes Menghini technique only

Pulmonary complications

The liver biopsy needle in the transthoracic approach tranverses the costophrenic angle below the reflection between the parietal and the visceral pleura. Therefore it is predictable that pneumothoraces and haemothoraces feature prominently in liver biopsy complications. Hydrothorax may also occur with the passage of ascitic fluid into the thorax through the puncture site on the diaphragm[2]. In a series of 68,276 biopsies, the incidence of pneumothorax was 0.35%[4]. In two recent national surveys conducted in the United Kingdom[6] and Switzerland[5], about 25% of the complications were pulmonary in nature. In one author's experience, when pneumothorax occurred, the symptoms were mild and the pulmonary collapse did not exceed 10%[17].

Peritonitis

This accounted for about 15% of adverse events in a recent survey[6]. In Lindner's series of 79,381 biopsies using the Menghini needle, all 12 deaths resulted from peritonitis[3]. It is most likely in the presence of extrahepatic cholestasis and probably reflects associated biliary sepsis.

Septicaemia

Transient bacteraemia has been reported in 5.8% to 13.5% of patients following liver biopsy[54,55], but septicaemia is rarer[56]. Fifty percent of the former are asymptomatic and in the latter, blood cultures usually grow *E. coli*[56]. Underlying cholangitis or malignancy should be suspected if septic shock occurs[57]. One reported case of liver abscess may have been complication of a prior liver biopsy[58].

Tumour seeding

Needle track seeding following liver biopsy of primary hepatocellular carcinoma and liver secondary from colorectal cancer have both been reported[59]. Although this complication is rare in the literature, it is well-documented[60,61]. Because of this risk, some authors recommend liver biopsy only for patients not amenable to surgical resection[59].

SPECIAL SITUATIONS

Day case liver biopsy

In the present age of health economics, clinicians have come under increasing pressure to perform a whole range of procedures on an outpatient basis[62]. One such procedure is liver biopsy. In 1978, Knauer calculated a minimal cost saving of US$153 per liver biopsy performed as outpatient[63]. Day case liver biopsy (DCLB) has been shown to be safe in a series of 829 patients from the Mayo Clinic[31]. In that series[31], 5.3% of the outpatients biopsied needed hospitalisation and complications tended to occur within the first 3 hours. Since then, several other series have reiterated the safety of DCLB[46,63-66] (Table III). However, it took the litigation-conscious American medical fraternity more than 10 years to formalise guidelines for outpatient percutaneous liver biopsy[67]. Even though clinicians are aware of its safety[11], DCLB remains underpractised. In Britain, < 5% of liver biopsies were performed as day cases[66] and only 11% of gastroenterologists offer DCLB routinely[11]. On the other hand, delayed haemorrhage has been reported to occur 3[63], 15[68] and even 30[69] days after liver biopsy. Therefore those practising DCLB should keep an open mind at all times to this possibility.

Table III – Safety of day case liver biopsies

Author	Year	No.	Complications (%)
Knauer[63]	1978	107	1
Perrault[31]	1978	829	5.3
Westaby[64]	1980	200	3
Judmaier[65]	1983	1221	0.02
Sherlock[46]	1984	55	0.5
Douds[66]	1993	145	0

Liver biopsy in children

Children are unlikely to cooperate with liver biopsy even if they are not sedated. Conversely sedation confers additional advantage by ensuring bedrest during and after the procedure. The Menghini technique does not involve an intricate sequence of manoeuvres and hence is more suitable for less cooperative patients, like children.

THE FUTURE

There is already a trend towards performing more image-guided DCLB rather than blind percutaneous biopsies and keeping the patients overnight. This trend is likely to continue with improvement in medical resources, such as the availability of ward ultrasound scanners, and the pressure to streamline services. Automatic biopsy gun devices, which can execute the whole intricate sequence of manoeuvres at the press of a trigger, are now available in the market and may gain popularity with time. With the advent of liver transplantation, there is now a need for distinction between graft rejection and other graft pathology. As for patients after bone marrow transplantation, liver biopsy is often helpful in differentiating viral hepatitis, drug-induced hepatitis and graft-versus-host disease. These 2 groups of patients usually have deranged coagulation profile and as such if liver biopsy is indicated, the plugged method, the transjugular or laparoscopic approach should be chosen. In the diagnosis of graft-versus-host disease, it may be safer to biopsy the gastrointestinal mucosa and skin first before embarking on a liver biopsy[16]. Medicine is constantly evolving and with it, liver biopsy techniques. New indications for liver biopsy are to be expected; conversely with the advent in other less invasive modalities of

investigation, some indications will disappear from the list.

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