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Contribution, Indications and Technical Realization of Ultrasound-guided Liver Biopsy

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Abstract: The liver biopsy (LB) still keeps some indications today, in spite of the progress of the non-invasive explorations. Several LB techniques have been studied. Some techniques use medical imaging. These techniques also differ in the material used to collect the hepatic sample. This study aimed to determine the current indications of LB, the interest using ultrasound guidance and an automatic device in order to improve its performance and its contribution to the diagnosis. This was a retrospective study including percutaneous LB performed under ultrasound guidance using automatic system equipped with a sharp needle. The study involved 50 patients with 26 diffuse liver diseases (DLD) and 24 focal liver lesions (FLL). The indications for DLD biopsy were dominated by suspicion of hepatic sarcoidosis, primary biliary cirrhosis and hepatic tuberculosis. FLL were dominated by the exploration of nodules or masses. The number of passes made was three in 96% of cases, otherwise it was four, with an average size of 1.3 cm for cores. DLD were dominated by chronic liver disease (42%), granulomatous hepatitis (23%), steatohepatitis (11%) and primary biliary cirrhosis (8%). FLL were dominated by secondary malignancies (46%) and primary malignant lesions (25%). For FLL, LB sensitivity, specificity, positive predictive value and negative predictive value were respectively 81%, 100%, 100% and 20%. LB confirmed 45% of DLD diagnoses, when they were well oriented by clinical and paraclinical data. The LB allowed to rectify the diagnosis in 54% of cases. When no initial diagnosis was suspected, LB enabled a specific diagnosis in 75% of cases. Major complications were void in our study. In conclusion, the use of ultrasound guidance and an automatic device with a sharp needle has increased the number of passes, improved the quality of sampling and reduced complications.

Keywords: Focal Liver Lesions, Diffuse Liver Disease, Biopsy, Ultrasound, Contribution

1. Introduction

The pathological examination of a fragment of liver obtained by liver biopsy (LB) remains essential for the etiological diagnosis and prognosis of many diffuse and focal liver diseases [1, 2]. Indeed, in the case of focal liver lesions,

the diagnostic challenge is twofold, to define the benignity or malignancy of a tumour and then determining the treatment to adopt. For diffuse liver diseases, indicating LB remains appropriate when a treatment decision or establishing a prognosis is likely to be modified by the results of the histopathological examination [2, 3]. LB keeps a place in the evaluation of liver fibrosis. All major liver and gastrointestinal society guidelines view LB as the gold standard for measuring liver fibrosis [4]. Noninvasive tests have not replaced liver biopsy but have clearly reduced the need for it. This change has greatly improved our aptitude to care for patients with liver diseases. However, Liver biopsy will continue to have a role in diagnosing some liver diseases, resolving indeterminate stages of fibrosis, and the choice of the adequate treatment [5].

LB is an invasive procedure that is not stripped of risk. The choice of the realization of this gesture under ultrasound has several advantages: allowing the screening of any anomalies that may contraindicate a blind biopsy, allows a first in-drawing, which reduces the frequency of bleeding complications by respiratory motion. Ultrasound can also follow the path of the needle which avoids complications related to accidental crossing of an adjacent organ. It remains a non-radiation means compared to the scanner and is a less invasive procedure compared to a surgical biopsy.

The objectives of our work were to determine the current indications of LB and the interest of using ultrasound guidance and an automatic device with a sharp 18-gauge needle to improve the performance of LB.

2. Materials and Methods

2.1. Study Design

It was a retrospective and descriptive study that was carried out at the internal medicine and gastroenterology departments of the Habib Thameur hospital and the gastroenterology department of the Nabeul regional hospital from 2012 to 2015.

2.2. Sample

This study included the liver biopsies indicated for patients followed by the three services elicited. We included LB of patients over 18 years-old with either focal liver lesion (FLL) at ultrasound imaging or homogeneous hepatomegaly with disturbed biological balance, an abnormal hepatic analysis without hepatomegaly, an extra-hepatic location of a disease providing diffuse liver disease (DLL), or an unclassified hepatopathy. Before the completion of each LB, the attending physician and the radiologist verify that there is no contraindication to this procedure.

2.3. Technique of the Liver Biopsy

A pre-biopsy coagulation profile (prothrombin time, cephalin-kaolin coagulation time, blood cell count with platelet count) was obtained in all patients. Before the completion of the LB, the attending physician and the radiologist verify that there is no contraindication to the realization of the LB. Local anaesthesia is performed by local infiltration plane by plane up to the hepatic capsule of a 1% lidocaine solution (10 mg/ml). The LB is performed using an automatic pistol equipped with a truCut® cutting needle, 18 gauge with an advance of 22 mm and ranging from 10 to 20 cm of single-use length, introduced in free hand technique, under continuous ultrasound control. The ultrasound system used is a LOGIQ E9® manufactured by General Electric Healthcare®, with a low-frequency curvilinear transducer (C1-5 MHZ). For focal lesions, at least 1 cm of healthy parenchyma should be interposed between the edge of the lesion and the liver capsule. Three passes are typically made. The radiologist visually checks the quality of the sample to decide if an additional one is necessary. Then, the sample was sent immediately to the pathology department. After the procedure, the patients were kept under observation in the department where the patient was being followed. At the slightest doubt of complication, a complement of explorations was made.

2.4. Statistics

All data was analysed using the software Statistical Package for Social Sciences (SPSS) trial version 23.0. Sensitivity is the proportion of people who LB positive for the suspected disease among those who have the disease. Specificity is the proportion of healthy patients known not to have the suspected disease, who will LB negative for it. The positive predictive value is the probability that the suspected disease is present when the LB is positive. The negative predictive value is the probability that the disease will not be present when the LB is negative.

3. Results

3.1. Characteristics of the Included Patients

Our study included 50 patients with diffuse liver disease in 26 cases and focal liver lesions in 24 cases. The average age was 43 years for diffuse liver damage and 60 for focal lesions. The sex ratio was 1.1 with a slight male predominance.

The clinical and laboratory abnormalities were essentially hepatomegaly and/or splenomegaly (50%) and abnormal liver tests (66%). Table 1 presents the main clinical and laboratory characteristics of patients with LB.

Table 1. *The clinical and biological characteristics of patients with LB.*

	Number of patients (N=50)	Percentage (%)
Fever	5	10
Impaired general condition	4	8
Jaundice	4	8

	Number of patients (N=50)	Percentage (%)
Hepatomegaly and/or splenomegaly	25	50
Abnormal liver analysis	33	66
Abnormal immunologic analysis	11/22	50
Positive viral hepatitis B or C	6/22	27

All patients had at least one abdominal imaging before LB. Forty patients had abdominal CT (80%), 34 abdominal ultrasonography (68%) and 7 biliary MRI (14%). Twenty-eight patients (56%) had two or three of these types of imaging.

3.2. Liver Biopsies Indications

Indications for LB were varied for DLD. Many origins were suspected: autoimmune origin (35%), granulomatous origin (23%), tumoral origin (15%), abnormal liver analysis (15%) and the suspicions of infectious liver diseases (12%). FLL biopsy indications were dominated by the exploration of nodules or masses.

3.3. Qualities of the Liver Biopsy Samples

Three passes were made in 96% of cases, otherwise it was four. The average size of the cores was 1.3cm [with extremes ranging 0.8-2.1cm]. Two samples did not contribute to diagnosis due to crush or delayed transfer.

3.4. Results and Contribution of the Liver Biopsy

For histologic findings DLD were varied, they were dominated by chronic liver disease with or without activity (42%), granulomatous hepatitis (23%), then steatohepatitis (11%) and primary biliary cirrhosis (8%). (table 2)

Table 2. *Histological result of diffuse liver diseases.*

Histological result	Number of patients (n=26)	Percentages (%)
Chronic liver disease with or without activity	11	42
Granulomatous hepatitis	6	23
Steatohepatitis	3	11
Primary biliary cirrhosis	2	8
Hepatic amyloidosis	1	4
Hepatic parenchyma with suspicious lymphoid cells	1	4
Overlap syndrome	1	4
Non contributory	1	4

For FLL, histological results were dominated by secondary malignancies (46%) and primary malignant lesions (25%). (table 3)

Table 3. *Distribution of histological results for focal liver lesions.*

Histological result	Number of patients (n=24)	Percentages (%)
Secondary malignant neoplasm	11	46
Primary malignancy	6	25
Non chronic liver disease	5	21
Tuberculous granulomatous hepatitis	1	4
Non contributory	1	4

For FLL, LB sensitivity was 81% and specificity was 100% with a positive predictive value of 100% and a negative predictive value of 20%.

To DLD, when the diagnosis was oriented by clinical and paraclinical data, LB confirmed the diagnosis in 45% of cases. The LB allowed to rectify the diagnosis in 54% of cases. When no initial diagnosis was suspected, LB enabled a specific diagnosis in 75% of cases.

3.5. Complications of the Liver Biopsy

Major complications are void in our study. They were minor, moderate abdominal pain in 8% of our cases.

4. Discussion

In our study, the clinical and paraclinical abnormalities were essentially hepatomegaly and/or splenomegaly and abnormal liver tests. Indications for LB were varied for DLD, they were essentially the suspicions of autoimmune origin and granulomatous origin. FLL biopsy indications were dominated by the exploration of nodules or masses. The number of passes made was usually three and the cores were of good length. For histologic findings DLD were varied, they were dominated by chronic liver disease with or without activity and granulomatous hepatitis. For FLL, histological results were dominated by secondary and primary malignancies. Our technique, to use an ultrasound guidance with an automatic biopsy device has allowed to have an excellent profitability for the LB with good sensibility, specificity and positive predictive value. Our technique was safe.

Our study included liver biopsies from different departments, internal medicine, rheumatology and gastroenterology. This allowed for a variety of indications for LB. Having a unique and experienced operator made the gesture very standardized. Our technique had a low failure

rate.

The limitations of our study were the retrospective character and the absence of a group of patients with a LB done via a different technique.

The indications of the LB according to literature can be for a diagnostic purpose, because certain diagnoses are based on histological evidence, or a prognostic goal such as the staging of a fibrosis, or to perform a lesion mapping as for systemic sarcoidosis, or for the search for a primitive of a hepatic metastasis.

In affluent countries, indications of LB have changed considerably in recent years due to the development of sensitive and specific non-invasive tests for the diagnosis of several chronic liver diseases [2].

In developed countries, the incidence of viral hepatitis is decreasing, so the indication of a liver biopsy for viral hepatitis in these countries is decreasing. This decrease is in contrast to the increase in indications for autoimmune and tumoral hepatopathy suspicions [6]. In some countries, some indications are rare or almost non-existent, such as post-transplant LB in countries where liver transplantation is not common. While in other countries, it is constantly increasing [3, 6, 7].

There is no consensus as to how to perform biopsies though there is heterogeneity in how it is being done. This disparity is more to personal habits, the operating performance of operators and local availability. [8]

In our work all LB were guided by ultrasound that allowed real-time monitoring of the progression of the needle to the liver parenchyma for DLD. For FLL, it allowed to interpose at least 1 cm of healthy parenchyma between the liver capsule and the edge of the lesion.

In literature, the needles used for transcutaneous liver biopsies are variable. Indeed, they can be suction (Menghini, Klaskin, Jamshidi) or cutting (Trucut, VimSilverman) and automatic or semi-automatic.

TruCut needles provide larger samples, less fragmented with portal spaces as opposed to Menghini needles [9, 10]. Manual TruCut type needles are more difficult to handle than the Menghini ones. Complications were more frequently observed with TruCut needles than with Menghini needles (3/1000 vs 1 / 1000) [11].

The use of automated cutting needles allowed to have the advantages of manual cutting needles without the inconvenience of handling. The quality of the samples is greater with automatic needle TruCut over manual needles.

The size of the needle varies from heavier 14G (2.1mm) to a smaller calibre 23G (0.8mm), a study on the LB focal small lesions showed that the use of larger gauge needles reduces the risk of false negatives at the highest price risks. 18G seems to be the best compromise [12]. In our work, sampling is always performed with automatic cutting 18 Gauge TruCut needles.

Several studies have shown that the risk of complications increases significantly after 2 biopsy passes. The prospective study of Perrault et al. showed that the percentage of complications, including pain, was 4% with one biopsy pass; this rate increased 2.5 times in case of 2 or 3 passes, and 3.3 with 4 passes or more [13]. A French national survey showed that the frequency of complications increased with the number of passes [3]. Similarly, the frequency of major complications increases with the number of passes [3, 13].

In our study, three passes were made for 48 patients (96%), an additional pass was performed in only two patients (4%), the ultrasound guidance and the use of an automatic pistol helped increase the number of passes without increasing the complication rate. The multiplicity of the number of passes can improve the representativeness of the biopsy specimen.

In several studies, decreased complication rate was correlated with the experience of the operator [3, 14, 15]. For Gilmore [16], the experience of the operator greatly affects the quality of biopsies. Chevallier et al. showed in a prospective study that the percentage of interpretable biopsies was not significantly modified by the operator was a "senior" or "junior" although core length and the number of portal spaces were lower for "junior" operators [16]. In our study all biopsies are performed by a senior and experimented radiologist. The quality of the histological specimen depends on both the type of needle used, its size and its mechanism, it determines the success of the LB which depends on the training of the radiologist and the experience of the pathologist [17]. According to several studies, the size of the sample and the number of portal spaces are quality criteria for a liver sample admitted for percutaneous biopsies. So, the shape of the needles has also its importance in the LB. Eskandari et al. demonstrated the superiority of the 19G and 20G needles over the SharkCore 22G needle, for the yield of complete portal tracts ($p < 0.001$ adjusted for multiplicity) [18].

The majority of biopsies obtained with sharp needles or suction is satisfactory in size [10]. However, TruCut needles provide larger, less fragmented samples, with portal spaces which is an advantage over Menghini needles [9]. It allows most often to diagnose cirrhosis [2, 19].

Generally, the size of the tissue sample obtained during a trans parietal LB varies between 1 and 3 cm in length and between 1.2 and 2mm in diameter, represents 1 / 50,000 of the total liver mass [20]. The size of a satisfactory LB is variously appreciated by pathologists, and varies with indication of the LB [14]. In case of diffuse disease, a sample of 15mm long is usually considered sufficient [8, 20-22]. French pathologists have recently recognized the need for a biopsy of a length of 1 cm minimum [23].

In case of fragmentation, it has been proposed to require a total length of a minimum of 1cm for a biopsy consists of 1 to 3 shards, and minimum 1.5cm from 4 fragments [23].

In the case of chronic liver diseases and in transplant patients, 6-8 portal spaces are desired. [22, 24]

For FLL, visually, quality sampling of the LB must have sharp edges and pale tumour contain a central area surrounded by two reddish areas non-tumour liver. In a series of one hundred nodules Borzio et al. showed that the accuracy of the LB intra nodular which was 67% amounted to 78% when it added an extra nodular pass [25].

Spycher et al [26] retrospectively reviewed 365 patients and 411 diagnoses were carried out before biopsy. Three hundred forty-seven diagnoses (84.4%) were confirmed by biopsy but in 8.8%, 6.8% and 10.5% the diagnosis was specified, changed or a diagnosis added, respectively. This review concluded a high diagnostic yield of the LB and a low mismatch between the pre biopsy diagnosis and final histological.

In a meta-analysis the sensitivity and specificity of the LB for the diagnosis of malignancy were respectively 92 and 100% [19]. However, the methodology for calculating the sensitivity varies widely in literature, making comparisons difficult. It depends on the inclusive and exclusive criteria of each study.

In our study, for FLL, we have kept the non-tumour histologies unconfirmed and non-diagnostic samples as false negatives, which reduces the diagnostic performance sensitivity of the LB is 81% and the specificity was 100%, thereby the sensitivity is slightly lower than reported in literature.

A non-randomized prospective study showed that the ultrasound-guided biopsies resulted significantly less pain than biopsy without imaging guidance (36.4% vs 47.3%) and pain measured on a visual analogue scale was significantly less intense [27].

Two randomized controlled prospective studies are available. Papini et al. have shown that the risk of complications was significantly reduced in the group of patients who had ultrasound-guided LB in the left lobe compared to patients who underwent biopsy Menghini needle in the right liver (0.6% vs respectively 4.1%) [28].

Lindor et al. have also shown in patients who had proposed an outpatient LB, the need for hospitalization was less frequent in the group that had a tracking ultrasound than in the group who underwent biopsy without tracking (0.5% vs 2.2%; $p < 0.05$) [29]. The pain was more common in the group who underwent biopsy without spotting (50.1% vs 37.4%; $p = 0.003$). Bleeding or hypotension were 2 times more frequent in the control group without ultrasound guidance (18 / 413 vs 9 / 423) although the difference was not statistically significant ($p = 0.07$). This study also showed that the frequency of complications did not differ by type of needle, however this rate was significantly lower in the case of ultrasound guidance.

According to a study by Piccinino the risk of complications was higher with TruCut system compared to suction needles [11].

In literature, a systematic ultrasound examination 24 hours after a biopsy can detect up to 23% of subcapsular or intrahepatic hematoma [30]. These are generally small and without hemodynamic consequence. They are usually treated symptomatically.

In a large sample study, 6613 LB, the rate of acute and delayed major adverse events was 0,7% [31]. Major complications reported in literature were intraperitoneal haemorrhage, haemobilia, infectious complications (cholangitis, bacteraemia), bile peritonitis secondary to biliary wound, pneumothorax, puncturing adjacent organs.

These complications seem significantly reduced by ultrasound guidance.

Several studies suggest that the risk of complications is higher in the case of non-imaging biopsies than when the LB is performed after ultrasound or with guidance. [3, 28, 29, 32]

5. Conclusion

LB is an invasive procedure, however indispensable in a number of clinical settings for diagnosis and correct treatment of diffuse and FLL. The suspicion of hepatic sarcoidosis, primary biliary cirrhosis and hepatic tuberculosis is still the main indication for liver biopsy. In many conditions and situations, percutaneous biopsy is the only option.

The use of ultrasound guidance and an automatic device with a sharp needle seems to be the most appropriate technique of the realization of the liver biopsy. This technique has increased the number of passes therefore improving the quality of sampling and reducing complications. We suggest the use of this technique and recommend the development of large-scale prospective studies to compare several techniques.

Conflict of Interest

The authors declare there are no conflicts of interest.

Authors' Contribution

FD, MS, IBH and SB: study design, data collection, data analysis, interpretation of results, preparation of manuscript; IR, DT and RJ: data analysis, interpretation of results, preparation of manuscript; HZ and EBB: data collection; DG, MHD, ACD and FB: data analysis, interpretation of results. All authors edited the manuscript and accepted its final form.

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