

A retrospective analysis of 1.011 percutaneous liver biopsies performed in patients with liver transplantation or liver disease: ultrasonography can reduce complications?

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Abstract. – OBJECTIVE: In the last decades, liver biopsy was the reference procedure for the diagnosis and follow-up of liver disease. Aim of present retrospective analysis was to assess the prevalence of complications and risk factors after Percutaneous Liver Biopsy (PLB) performed for diagnosis and staging in patients with chronic liver disease and for monitoring the graft in liver transplanted patients

PATIENTS AND METHODS: Data were collected from a total of 1.011 PLB performed with the Menghini technique between January 2004 and December 2014 at the Hepatology and Transplant Units of the University of Rome Tor Vergata. The indications for biopsy were: follow-up of liver transplantation, chronic Hepatitis B Virus (HBV) or Hepatitis C Virus (HCV), with or without Human Immunodeficiency Virus (HIV) and alcohol-related liver disease. Our patients were divided into two groups according to the biopsy indication: follow-up of liver transplantation (Group A) and chronic liver disease (Group B). All the procedures were performed in Day Hospital regimen. After the biopsy, patients remained in bed for about 4-6 hours. In the absence of complications, they were then discharged on the same day.

RESULTS: The most frequent complication after biopsy was pain (Group A n. 57, 8.8%; Group B n. 105, 29.0%), hypotension as a result of a vasovagal reaction resolved spontaneously (Group A n. 7, 1.1%; Group B n. 6, 1.7%), and intrahepatic bleeding resolved with conservative therapy (Group A n. 1, 0.2%; Group B n. 6, 1.7%). Two cases of pneumothorax in the Group A (0.3%) were treated with a chest tube. Other complications did not have a significant impact. Also, we did not observe statistically significant differences in patients who underwent PLB with-out and with ultrasound guidance.

CONCLUSIONS: Liver biopsy is not a replaceable tool in diagnosis and follow-up of several

chronic liver diseases. The Menghini technique with the percutaneous trans costal approach, might be preferred because less traumatic and related with a low occurrence of minor and major complications.

According to our case load and comparing our findings with the previous published data, we speculate that ultrasound guidance is not crucial in the prevention of major complications.

Key Words:

Liver biopsy, Biopsy needle, Liver transplantation, Liver disease, Ultrasonography.

Introduction

Liver biopsy is a fundamental procedure in the diagnosis of liver disease in order to obtain the histological picture of several conditions and monitor their course. Furthermore, liver biopsy allows to evaluate the liver parenchyma after transplantation. Among the various methods, Percutaneous Liver Biopsy (PLB) sec. Menghini^{1,2} is certainly less traumatic for the needle small size and for a very rapid time of execution.

The aim of this retrospective study is to analyze the results of 1.011 PLB, performed with the Menghini technique in liver transplantation recipients (Group A) and in patients with chronic liver disease (Group B), and to compare our results with the most representative of the literature. We discuss about indications, advantages and disadvantages, complications and risk factors in relation to different biopsy procedures, with particular attention to the use of ultrasound guidance.

Patients and Methods

Between January 2004 and December 2014, at the Liver and Transplant Units of the University of Rome "Tor Vergata", 1.011 PLB were performed to assess the state of health of the hepatic parenchyma. Patients were divided in two groups based on specific indications: Group A, patients after Orthotopic Liver Transplantation (OLT) and Group B, patients with chronic liver disease (non-OLT). In our retrospective analysis, we paid specific attention to the procedures. Thus, the results show a discrepancy between the number of patients and the number of performed procedures because some transplanted patients underwent to numerous biopsies, not to a single one like those with liver disease. The mean age was calculated at the time of the first procedure.

The indications for biopsy are showed in Table I.

All patients signed their consent after being informed about the procedure and the possible risks and complications. The biopsy was always performed in the Day Hospital regimen.

The exclusion criteria for our analysis were considered: (1) Hemoglobin < 8.0 g/dl; (2) International Normalized Ratio (INR) > 2; (3) Platelets Count < 40.000/ μ l; (4) Other coagulation disorders; (5) Ascites; (6) Dilatation of the intrahepatic bile ducts. The patients with platelets < 40.000/ μ l (15 procedures), subjected to platelet transfusion

prior to biopsy, were not included in this study. Moreover, patients undergoing liver biopsy for acute rejection after liver transplantation or for serious complications were always hospitalized and, therefore, were not considered.

At the time of convening, the patients taking anticoagulants were asked to discontinue therapy at least 3 days before the examination. Before starting the procedure or in the days before, all patients underwent an abdominal ultrasound to exclude any anatomical or pathological conditions, that could represent a contraindication to the procedure. Also before the biopsy, all patients were subjected to blood sample tests, to evaluate coagulation and blood count parameters.

PLB with intercostal access was performed by the standard technique described by Menghini^{1,2}, using the appropriate automatic needle (16 gauge in diameter and 15 cm in length). The patient was placed supine, slightly turned to the left and right arm behind his head. By the percussion we delimited the upper margin of the liver and by the palpation the bottom margin. Then we identified the most suitable point for the biopsy, generally located in the intercostal space corresponding to the point of intersection between the anterior axillary line and the transverse line that passes on the xiphoid process. Local anesthesia was performed by infiltration of Ropicavaine 10 mg/ml. After practicing a small skin incision of about 2-3 mm in the set point, the needle was in-

Table I. Indications for liver biopsy.

Indications	Biopsies n.	Patients n.	Males n.	Females n.	Mean age (\pm SD)
OLT Follow-up	649	319	230	89	52.1 \pm 12.4
HCV chronic liver disease	130	127	94	33	35.2 \pm 14.3
HBV chronic liver disease	64	62	49	13	41.5 \pm 14.8
Alcohol related liver disease	49	47	24	23	53.1 \pm 18.1
HIV/ HBV or HCV coinfection	44	44	32	12	26.2 \pm 9.2
HBV/HCV chronic liver disease	40	39	28	11	41.6 \pm 11.2
Liver Enzymes elevation	13	13	6	7	48.7 \pm 7.9
NASH	8	8	5	3	42.6 \pm 8.7
Autoimmune hepatitis	4	4	2	2	37.5 \pm 12.3
HBV/HDV chronic liver disease	2	2	–	2	47
HCV/Autoimmune	2	2	1	1	45
Primary biliary cirrhosis	2	2	–	2	48
HBV/NASH	1	1	1	–	18
Wilson disease	1	1	–	1	39
Primary sclerosing cholangitis	1	1	1	–	40
Metastasis	1	1	–	1	54
Total	1.011	673	473	200	

OLT = Ortotopic Liver Transplantation; HCV = Hepatitis C Virus; HBV = Hepatitis B Virus; HIV = Human Immunodeficiency Virus; NASH = Non Alcoholic Steatohepatitis; HDV = Hepatitis Delta Virus.

serted through the intercostal space along the costal margin top to prevent accidental injury to the intercostal artery. In full expiration and apnea, the surgeon proceeded, with a rapid maneuver, to the puncture of the liver and biopsy by suction. The hepatic frustule was usually 1 mm in diameter and approximately 20-30 mm in length. It was preserved in formalin and sent to the histologist evaluation. We performed a pressure dressing on the point of incision and was also applied a bag of ice. After the procedure, the patient remained in bed for about 4-6 hours. Before discharge, they proceeded to check vital signs and a blood sampling to assess any changes. In the absence of complications, the patient was then discharged.

Statistical Analysis

The statistical analysis was performed with the Statistical Package for the Social Science Windows version 1.7 (SPSS Inc., Chicago, IL, USA). Descriptive statistics for quantitative variables were the mean and Standard Deviation (mean \pm SD). The comparison was performed with the Fisher's exact test for categorical variables. $p < 0.05$ was considered statistically significant.

Results

The post-biopsy pain was the most frequent minor complication. In a total of 162 cases (Group A n. 57, 8.8%; Group B n. 105, 29.0%) the administration of mild analgesic (Paracetamol) was necessary. Only in 21 cases the persistence of pain, mostly in anxious patients, has required further administration of Ketorolac or Tramadol. In 4 cases it was necessary precautionary hospitalization for 48 hours, during which the symptoms regressed so that the patient was regularly discharged. In 1 case the painful symptom was associated with an increase of

amylase and lipase blood levels. The patient was hospitalized for 7 days and subjected to medical therapy until normalization of values, occurred after 5 days.

We observed, in a total of 13 cases (Group A n. 7, 1.1%; Group B n. 6, 1.7%), a vasovagal reaction with transient hypotension, resolved spontaneously.

The intrahepatic bleeding occurred overall in 7 cases (Group A n. 1, 0.2%; Group B n. 6, 1.7%), but it has never been necessary surgical treatment. These patients were hospitalized, as a precautionary measure, and monitored by abdominal ultrasound and blood samples. The bleeding, however, was not serious, with spontaneous resolution after 48-72 hours.

In 2 cases we observed a pneumothorax, reduced in a few days with a chest tube. Both patients were smokers with emphysema. Probably the biopsy needle has through the phrenic angle cost injuring some emphysematous air bubble.

We reported only 1 case of hemothorax in liver-transplanted patient for potus related cirrhosis, who had already been subjected to 7 follow-up graft biopsies in previous years without any complication. In addition, this patient underwent regular hemodialysis for chronic renal failure. At the time of discharge from the day hospital, blood parameters were normal. The bleeding was manifested late after 48 hours, subsequently to the routine hemodialysis, and the surgery was necessary (performed in another hospital) to stop bleeding due to accidental injury of an intercostal vessel (Table II).

We have never been observed other complications reported in the literature, such as choleperitoneum, intestinal perforation, sepsis or hematuria. In our cases are not described death related to the procedures.

Frustule fragmentation occurred in a total of 105 cases (Group A n. 79, 12.2%; Group B n. 26, 7.2%) but has not proceeded to a further sam-

Table II. Prevalence of complications after liver biopsy.

Complication	Biopsies (n. 1.011)	Group A OLT (n. 649 biopsies)	Group B non OLT (n. 362 biopsies)
Pain	162 (16.0%)	57 (8.8%)	105 (29.0%)
Hypotension	13 (1.3%)	7 (1.1%)	6 (1.7%)
Intrahepatic bleeding	7 (0.7%)	1 (0.2%)	6 (1.7%)
Pneumothorax	2 (0.2%)	2 (0.3%)	–
Hemothorax	1 (0.1%)	1 (0.2%)	–
Pancreatitis	1 (0.1%)	1 (0.2%)	–

pling since, however, the amount of hepatic parenchyma was considered adequate for histological evaluation.

In 42 cases (4.2%) it was necessary to repeat the procedure, and in 14 cases (1.4%) even a third time because the sample was less than 15 mm and therefore not satisfactory for histological examination.

In a total of 50 cases, it was performed the biopsy under ultrasound guidance. Between these, 21 patients in Group B underwent liver biopsy under ultrasound guidance because the procedure had been unsuccessful previously in other centers. So were performed with ultrasound guidance a total of 23 biopsies in Group A and 27 in Group B. The complications observed in Group A (OLT) were 66 in total (10.5%) without ultrasound guidance and 4 (17.4%) with ultrasound guidance. In Group B (non-OLT) we observed 106 complications in total (31.6%) without ultrasound guidance and 10 (37.4) with ultrasound guidance.

Fisher's exact test analysis (Group A 0.2980 and Group B 0.6685, calculated on total complications and comparing the two groups with and without ultrasound guidance, 5% confidence interval, χ^2 0.05, $1 = 3.841$) shows a no significant difference for all variables in both groups (Table III).

Discussion

Liver biopsy is used by more than a century for the diagnosis and monitoring of liver diseases. Paul Ehrlich performed the first liver biopsy in 1883 in Germany, but it was risky because it required a run time of 15 minutes approximately. In 1958 Menghini devised and published an

innovative method, the "One-second needle biopsy of the liver". In subsequent years, this technique has been modified and improved mainly thanks to the introduction of syringes and needles devices¹⁻³.

Despite the growing enthusiasm for using the non-invasive methods (imaging or serological markers) for the assessment of liver damage, the histological evaluation of liver parenchyma is still crucial in several clinical setting: (1) In patients with unknown liver damage in which the non-invasive methods have failed to make a diagnosis; (2) in the staging of potentially progressive liver disease (i.e. Non-Alcoholic Steatohepatitis) in which differentiate "benign" form to advanced stages, could help to set the correct patient managing and follow-up; (3) monitoring the increasing liver-transplanted patient^{4,5}.

The liver biopsy will always play a role in the management of the patient with a diagnostic dilemma: patients with a specific liver disease, patients with abnormal liver tests of unknown etiology or with systemic disease in which the liver appears to be involved⁶⁻¹⁹.

The British Society of Gastroenterology²⁰, the American College of Gastroenterology²¹ the Canadian Association of Gastroenterology²² and more recently the American Association for the Study of Liver Diseases²³ has developed specific guidelines for liver biopsy as an outpatient procedure.

Liver biopsy currently has three major roles: (1) diagnosis; (2) assessment of prognosis (disease staging); (3) assist in making therapeutic management decisions. In several cases, clinical and/or blood tests allows to make suffice in establishing a diagnosis. Typical examples include Hepatitis B Virus (HBV) or HCV infection. However, in selected cases, the biopsy could be

Table III. Prevalence of complications after liver biopsy without and with ultrasound guidance.

Complications	Without ultrasound guidance			With ultrasound guidance		
	Group A OLT (n. 626 biopsies)	Group B non OLT (n. 335 biopsies)	Total (n. 961 biopsies)	Group A OLT (n. 23 biopsies)	Group B non OLT (n. 27 biopsies)	Total (n. 50 biopsies)
Pain	55 (8.8%)	97 (28.9%)	152 (15.9%)	2 (8.7%)	8 (34.6%)	10 (20.0%)
Hypotension	6 (0.9%)	5 (1.5%)	11 (1.1%)	1 (4.3%)	1 (3.8%)	2 (4.0%)
Intrahepatic bleeding	1 (0.2%)	4 (1.2%)	5 (0.5%)	–	2 (7.4%)	2 (4.0%)
Pneumothorax	2 (0.3%)	–	2 (0.2%)	–	–	–
Pancreatitis	1 (0.2%)	–	1 (0.1%)	–	–	–
Hemothorax	1 (0.2%)	–	1 (0.1%)	–	–	–
Total	66 (10.5%)	106 (31.6%)		3 (13.0%)	11 (40.1%)	

crucial in establish the diagnosis in acute and/or chronic liver injury. Although histological assessment alone may be able to make a diagnosis on occasion (i.e. a florid duct lesion in primary biliary cirrhosis), liver histology is typically and most appropriately considered in conjunction with the full gamut of clinical and laboratory data. Acute and chronic hepatitis, cholestatic disorders, fatty liver disease, vascular diseases, infiltrative or storage diseases, some infectious and granulomatous diseases, and other disorders may be associated with characteristic histological abnormalities that are helpful in diagnosis^{24,25}.

A further important use of liver biopsy is in assessing disease severity, notably fibrosis, which, as a precursor to cirrhosis, may predict the emergence of complications of portal hypertension and also liver-related morbidity and mortality. Assessment of liver histology may be particularly beneficial in patients with Human Immunodeficiency Virus (HIV) and HCV who have persistently normal liver function tests, because these patients may have significant fibrosis, which may be of prognostic importance. This allows the clinician to determine the hepatic fibrosis extent and, consequently, to assess suitability for treatment²⁶.

Currently, liver biopsy is used more than ever to develop treatment strategies, evolved thanks to the many new therapies available for patients with a variety of liver diseases.

Assessment of liver histology following OLT is an essential component in the graft managing. It is often important to make a specific diagnosis in the setting of liver test abnormalities early after transplantation to investigate allograft rejection, preservation or reperfusion injury, drug-induced liver injury, viral infection (usually recurrent) or bile duct injury. Liver biopsy is also often helpful in the setting of late allograft dysfunction²⁷ including recurrence of the original disease²⁸. Some liver transplant programs, such in our transplant center, perform a liver biopsy on a protocol basis after transplantation for HCV-related cirrhosis (e.g., annually), even in those patients with normal liver tests, although compelling evidence to support this approach is lacking. In contrast, there is good evidence suggesting that fibrosis progression may be predicted using liver histology in patients following transplantation^{29,30}. In our case load, liver biopsy after OLT was also performed in order to evaluate the feasibility of immunosuppression withdrawal^{31,32} or complete and sustained prophylaxis withdrawal in liver-transplanted patients for HBV-related cirrhosis³³.

The most frequent complication after PLB is the pain. Eisenberg et al³⁴ affirm that the pain during the procedure is present in 84% of patients and can remain in an acute form for 24 hours in 40% of cases. He also argues that there is a correlation between the levels of pre-biopsy anxiety and pain intensity. It is usually located in the intercostal space or in the right shoulder, more common in women. When the pain is not a symptom of other complications (peritoneal irritation or bleeding biliary loss for drilling, etc.) may result from stimulation of skin and hepatic capsule sensory receptors. Shoulder pain can be viscerosomatic type³⁵. Janes et al³⁶ reports a case series of 405 patients of whom 5 (1.2%) required hospitalization for observation after the biopsy. It is interesting to note that the pain is significantly reduced with the use of sedative pre-biopsy, thus confirming the observation of Eisenberg et al³⁴. Gilmore et al³⁷ reported a 30% occurrence of pain and argue that in 40% of patients the pain subsides spontaneously without the use of analgesics. In case of persistence of symptoms is usually sufficient the administration of paracetamol. If pain continues indicates the ketorolac or tramadol administration.

The vasovagal reaction, with transient hypotension, usually resolves spontaneously. For this reason, we have not attributed much importance to this symptom, although in our series was the second for highest frequency.

The intrahepatic bleeding, though less frequent, is the most important complication after liver biopsy. Thampanitchawong and Piratvith³⁸ present their series of 484 PLB with a prevalence of bleeding complications of 4.5% and believe that bleeding was commoner in the patients with raised INR: 3.3% when INR was 1.3-1.5, and increasing to 7.1% above an INR > 1.5. They affirm that the coagulation disorders are the leading cause of bleeding in these patients. Our data do not confirm nor refute this hypothesis because in our study we excluded all patients with severe bleeding disorders.

The trans-thoracic approach determines rare complications described in the literature. Piccinino et al³⁹ conducted a multicenter retrospective study on 68.276 biopsies and reported a 0.35% incidence of pneumothorax and a 0.18% of hemothorax. In the latter case, the accidental injury of a diaphragmatic or intercostal vessel is responsible for the complication. The preventive use of the ultrasound is useless because these vessels are not detectable due to their small size^{40,41}.

The literature describes rare cases of acute pancreatitis after liver biopsy. Most of the Authors consider this event caused by biliary obstruction due to hemobilia following procedure. The risk of hemobilia is less than one per 1000 procedures in the opinion of Jornod et al⁴², while Zhou⁴³ accounts the hemobilia for approximately 3% of all major complications caused by percutaneous ultrasound-guided liver biopsy. Pena et al⁴⁴ describe a case managed with biliary drainage stent. In our case of acute pancreatitis, probably due to hemobilia, the drainage or other procedure were not necessary because the values returned gradually to normal with medical therapy after 5 days, and after 7 days the patient was discharged.

Other complications described in the literature have a much negligible. The literature reported an incidence of less than 0.01% for visceral perforation, biliary fistulas, septic complications and needle breakage^{39,44}.

Another aspect to consider is the size and the possible excessive fragmentation of the small piece of liver parenchyma sample. The extent of fibrotic damage is an important way on the yield of the levy. Therefore, in case of unsatisfactory withdrawal after no more than three consecutive attempts by needle with suction mechanism, it is advisable to repeat the biopsy at another time using a cutting needle type "Tru-cut". In the latter case, since the larger needle increases the risk of complications, it is useful to the use of ultrasound guidance. The majority of pathologists consider suitable scrap of 1.5-2 cm in length taken with needle 16G⁴⁵, which statistically contain at least 10 portal tracts^{6-8,46}.

In the literature, there are no precise results regarding the occurrence of mortality. The few data indicate that mortality post-biopsy varies from 0.01% to 0.1%. However, it is difficult to establish the role of the disease rather than the biopsy^{6,37,41,47}.

The role of the Ultrasound System (US) or Computerized Tomography (CT) in PLB is controversial. It should be stressed that the technique of liver biopsy described by Menghini not contemplate the use of the US^{1,2}. On the other hand, we must distinguish the different indications for biopsy. When the biopsy is performed to obtain a liver parenchyma specimen, the US guidance is unnecessary during the procedure, if anything, can be useful previously to exclude any anatomical anomalies or pathological situations (pres-

ence of angiomas, vascular or biliary duct abnormalities, etc.). Instead, when the biopsy indication is the histological diagnosis of a focal lesion (focal biopsy), the CT or US guidance must be use to allow the targeted localization of the lesion. Also in this case, the sampling could be performed with a cutting needle (Tru-Cut type) of greater size (14G) and with a cutting part, which has a better yield but is more traumatic than Menghini needle, which works with a vacuum mechanism⁴⁷.

The use of US in the prevention of pain is discussed. Al Knawy and Shiffman⁴⁸ affirm that this use reduces the prevalence of pain during and after biopsy, respectively, of 10.9% and 1.8%, but this observation is not confirmed by our series.

Many Authors demonstrated that the use of the US or CT no change the occurrence of bleeding. An audit conducted in England and Wales by the British Society of Gastroenterology and the Royal College of Physicians of London shows there is no difference in the frequency of bleeding between the different techniques (standard vs. image guided)³⁷. Muir and Trotter⁴⁹ report an epidemiological study carried out using a questionnaire sent to 157 members of the Duke University Digestive Epidemiological Studies Consortium (Durham, NC). There are significant data showing that the use of US reduces the incidence of bleeding, but notes that US guidance is recommended only for trainees. In the United States, it is used only in 13% of biopsies. Caldwell and Northup⁵⁰ reported the experience of 10 centers for a total of 2.740 PLB and confirms, according to Stone and Mayberry⁴⁰, that the use of the US does not reduce the incidence of bleeding, arguing that the resolution of this instrument does not allow to avoid the small vessels, generally the most common cause of bleeding².

Menghini, discussing about the clinical applications and problems of biopsy, stressed the importance of speed of execution (not coincidentally the title of this article is "One-second biopsy of the liver"). The US guided biopsy requires longer execution times, and then a more prolonged residence time of the needle into the parenchyma. This would increase the bleeding risk and, therefore, the use of US is justified only in the focal biopsies⁵⁰⁻⁵¹.

The use of imaging driving methods is indicated only in the focal liver biopsy. Lindor et al⁵² analyzed a total of 836 liver biopsies performed in two centers: 489 in Rochester and 347 in

Barcelona. They reported that the use of the US does not alter the prevalence of all complications, but nevertheless reduces hospitalization days. Manolakopoulos et al⁵³ limit the indication of US in obese patients and also focuses on the impact on costs, confirming what was previously stated by Pasha⁵⁴. This is also an indication that emerges in the Guidelines of the British Society of Gastroenterology and the British Association for the Study of the Liver. Therefore, the use of US guidance is not considered the standard of care in all units in the UK⁵⁵.

The trans-thoracic approach can reduce the probability of organs damage, differently, the biopsy performed through subcostal approach exposes the anatomical structures of the liver hilum and the colon. In the absence of other specific indications, the use of US guidance is, therefore, more useful in subcostal approach⁵⁶.

Comparing the results obtained in the groups of patients OLT e non-OLT, we didn't observe statistical significant differences in the major and minor complications neither between patients undergoing PLB without and with US guidance. However, the prevalence of pain and intrahepatic bleeding is lower in Group A. We believe that the denervation of the liver capsule may explain the lower prevalence of pain that we observed in patients with liver transplantation. Regarding the lower prevalence of bleeding in patients in follow-up after OLT, it is possible that the post-operative adhesions in the abdominal wall can contribute to reducing the complication after liver biopsy.

In recent years there have been developed methods surrogates of liver biopsy for the assessment of liver fibrosis. Elastography, or Fibroscan, is a non-invasive method that allows to evaluate the rigidity and elasticity of the liver parenchyma. It uses a probe that is applied to the skin of the chest on the right. The probe transmits a vibration of medium size and low frequency. The propagation velocity is greater in the liver fibrotic than normal^{57,58}. The ARFI (Acoustic Radiation Force Impulse) is an integrated tool in an ultrasound and allows, at the same time US evaluation, the evaluation of the elasticity of the liver by an acoustic pulse ultrasound⁵⁹.

Useful, but based on the evaluation of blood parameters, are also Fibrotest and Actitest^{60,61}. For their performances, these methods can be useful for monitoring of liver diseases, their evolution and response to treatment.

Conclusions

Despite the recent advances in imaging methods (Fibroscan, ARFI) and in laboratory diagnosis (Fibrotest and Actitest), liver biopsy and histological evaluation of liver parenchyma are not replaceable investigations to diagnose several liver diseases and their course and also to monitor the condition of the hepatic parenchyma after transplantation, especially for the evaluation of rejection or recurrence of original disease.

The methods that have been described in the literature for the hepatic biopsy are numerous, and the results are not always concordant. However, the liver biopsy performed according to the standard method of Menghini, with the percutaneous trans costal approach, is preferable because it is less traumatic and with a low prevalence of complications.

The US examination is useful if done in the days or weeks prior to biopsy, in order to know any anatomical liver abnormalities or focal lesions. These conditions may pose a contraindication to the procedure or rather justify the use of an US-guided biopsy. However, the US is not decisive in the prevention of major complications.

Conflict of Interest

The Authors declare that there are no conflicts of interest.

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