

## EVALUATION OF THE IMPORTANCE OF PERCUTANEOUS LIVER BIOPSY IN NEWLY DIAGNOSED DIFFUSE AND FOCAL LIVER LESIONS

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Percutaneous liver biopsy (PLB) is an important diagnostic procedure in routine clinical practice because it allows for a fast pathohistological diagnosis. The aim of this study was to assess the importance of PAB in the diagnosis of newly recognized diffuse and focal liver lesions. This retrospective study included 277 patients who underwent PLB between January 2006 and December 2015. After the initial single dose of midazolam sedation, interventions were conducted using local infiltrative anesthesia (2-8 mL lidocaine 2% with adrenaline) under the guidance of ultrasound or computerized tomography, using the transabdominal or transthoracic approach, depending on the lesion site. Fine 14-20 gauge needles were used. In 52 patients referred with the diagnosis of indeterminate diffuse liver lesions who underwent PLB and histopathological analysis, the following results were obtained: 35 patients had steatosis hepatis (67.3%), 12 patients were with cirrhosis (23.7%), and 5 patients had hepatocellular carcinoma (9%). Of 164 with the diagnosis of primary liver tumors (164), the presence of malignant tumors was confirmed in 140 patients (85.3%), while the remaining 24 patients (14.7%) had benign lesions. From the total of 42 patients with the referral diagnosis of metastatic liver disease, colorectal carcinoma metastases were confirmed in 31 patients (73.8%), while ovarian cancer metastases were diagnosed in 6 patients (14.3%). As a minimally invasive interventional radiology procedure, PLB is an indispensable tool that allows for a fast diagnosis and decision-making in patients with diffuse and focal liver lesions.

*Acta Medica Medianae 2018;57(2):18-23.*

**Key words:** percutaneous liver biopsy, liver lesions, diagnosis

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### Introduction

Significant development of interventional radiology in the past few decades has resulted, among other things, in the introduction of numerous diagnostic and therapeutic procedures for the patients with digestive system diseases. Percutaneous liver biopsy (PLB) is an important diagnostic procedure in routine clinical practice. It allows for a fast non-surgical pathohistological diagnosis and is used in patients with suspected, newly discovered diffuse and focal liver lesions. The main features of this procedure are its minimal invasiveness, low incidence of complications and most commonly uneventful post-procedural reco-

very, which are the reasons why these interventions are usually performed on an outpatient basis, contributing thus to cost-effectiveness as well. The most common complication of these interventions is bleeding. The mortality rate is very low. Due to an increase of routine application of PLB, its importance in the diagnostic algorithm of liver disease should be evaluated.

### The aim of the study

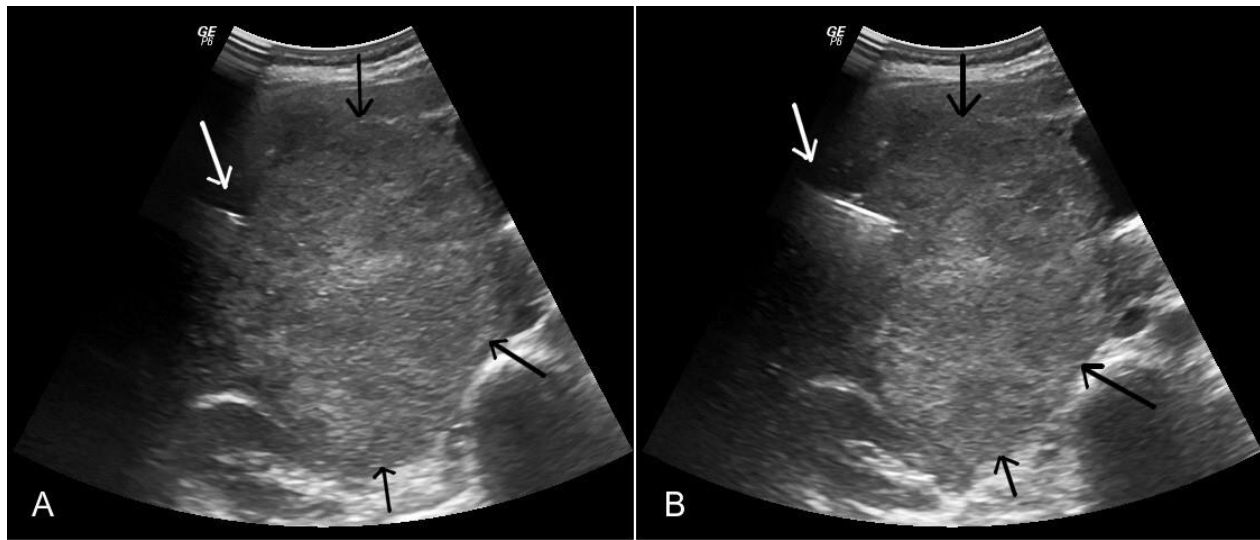
The aim of our study was to assess the role of PAB in the diagnosis of newly recognized diffuse and focal liver lesions.

### Material and methods

This retrospective study included 277 patients who underwent PLB between January 2006 and December 2015. In all the patients, the initial imaging diagnosis of liver tumor(s) was made at the Department of General Surgery, Clinical Center Niš, while the interventional radiological procedures were carried out at the Institute of Radiology, Clinical Center Niš.

There were 162 men (58.4%) and 115 women (42.6%) aged 59 years on the average (range, 19-78 years). After the initial radiological diagnosis, standard preprocedural preparation was carried out, including blood type determination and laboratory tests: complete blood count, blood clotting tests and general serum biochemical analysis - glucose, electrolytes, nitrogenous products, liver function tests, amylase, CRP. The criteria for exclusion were patient non-cooperation, significantly altered coagulation status (platelet count < 60,000/mm<sup>3</sup>, INR > 1.5, hemophilia, recent use of anticoagulants, fibrinolytic and antiplatelet agents), suspected liver hydatid cysts and hemangioma, obesity, infection of the anterior

abdominal wall or right pleural space, unavailability of blood components and derivatives, previous interventions in less than 7 days and small lesions with highly suspected or evident involvement of large perihepatic blood vessels (inferior vena cava, hepatic veins on their origin from inferior vena cava and portal vein). After the initial sedation with a single dose of midazolam, interventions were conducted using local infiltrative anesthesia (2-8 mL 2% lidocaine with adrenaline) under the guidance of ultrasound or computerized tomography, using the transabdominal or transthoracic approach, depending on the position of the lesion. Fine needles of different diameters (14-20 gauge) were used (Figure 1).



\*Bard biopsy system with MAGNUM type of gun and needle for core-biopsy (16 gauge)

**Figure 1.** Two ultrasound images of a large liver tumor percutaneous biopsy (white arrow depicts needle, black arrows depict tumor):  
A – biopsy needle introduced into the liver parenchyma;  
B – needle tip in the tumor during the sample taking

## Results

Initial referral radiological imaging diagnoses indicating PLB in analyzed patients are shown in Table 1.

Of 52 patients referred with the diagnosis of indeterminate diffuse liver lesions after PLB and histopathological analysis, the following results were obtained: 35 patients had liver steatosis (67.3%), 12 patients had cirrhosis (23.7%), and 5 patients had hepatocellular carcinoma (HCC) (9%). The data are shown in Table 2.

After PLB and histopathological analysis in patients with the diagnosis of primary liver tumors (164), the presence of malignant tumors was confirmed in 140 patients (85.3%): hepatocellular carcinoma (HCC) in 101 and cholangiocellular carcinoma (CHC) in 39 patients, while the remaining 24 patients (14.7%) had benign lesions (focal nodular hyperplasia - FNH, adenoma, haemangioma). The results are summarized in Table 3.

From the total of 42 patients with the referral diagnosis of metastatic liver disease, 31 were with suspected metastases of colorectal carcinoma (CRC), and 7 were with suspected ovarian cancer metastasis. In the first subgroup of patients, the diagnosis of CRC metastases was confirmed in 31 patients (73.8%), while in the other subgroup the diagnosis of ovarian cancer metastases was confirmed in 6 patients (14.3%). The remaining five had benign lesions (Table 4).

**Table 1.** Distribution of referral diagnoses.

The referral diagnosis	Primary liver tumor	Metastatic liver tumor	Liver cirrhosis	Wilson's disease	Liver cystadeno-carcinoma	Diffuse liver lesion	Caroli disease
Number/ percentage	164 (59,2%)	42 (15,2%)	10 (3,6%)	2 (0,7%)	6 (2,2%)	52 (18,8%)	1 (0,4%)

**Table 2.** Distribution of patients with the diagnosis of indeterminate diffuse liver lesions after performed PLB

Unknown referral diagnosis	Steatosis hepatis	Cirrhosis hepatis	HCC
Number/ percentage	35 (67,3%)	12 (23,7%)	5 (9%)

**Table 3.** Histopathology results

Primary liver tumors	Benign liver tumors	Malignant liver tumors	
		140 ( 85,3% )	
Number/ percentage	24 ( 14,7% )	HCC	CHC
		101 (72,1%)	39 (27,9%)

**Table 4.** Patients with metastatic liver diseases.

Metastatic liver tumors	Metastases of CRC	Metastases of ovarian cancer	Benign liver lesions
Number/ percentage	31 ( 73,8% )	6 ( 14,3% )	5 ( 11,9% )

There were no lethal outcomes. The incidence of post-interventional syndrome was 11.2% (31 patients) and this included transient symptoms such as pain in the right hypochondrium lasting up to 12 hours and requiring analgesia with metamizol-sodium (4,5 g per patient on the average) and/or nausea which required antiemetic therapy. For 19 of these patients (61,3%), it was necessary to complete the intervention with percutaneous drainage of the Morison's pouch or subhepatic space due to uncertain hemostasis at the biopsy site, but in all of these patients the drain was removed after 24-hour observation, when the possibility of bleeding and other leakage was ruled out.

There was no need for the administration of vitamin K, fresh frozen plasma, platelets or whole blood transfusions in any patient. Two patients required additional second-act percutaneous drainage for post-procedural low productivity (less than 100 ml/24h) biliary fistula from the site of the biopsy which was followed by spontaneous regression after 4 days in both of the patients and subsequent drain

removal. The drains in all the patients were removed after normal follow-up abdominal ultrasound. In our patients there was no significant post-interventional fever which would require treatment. Immediately before the intervention all the patients received single dose prophylactic antibiotics (2 g ceftriaxone).

For all the patients the procedure was performed on an outpatient basis (admission in the morning, release in the evening, after a full-day observation), except in those with post-procedural syndrome (31 patients), who were hospitalized, and released from the clinic after 24 hours because of discomfort and/or drainage, or after 4 days in case of 2 patients with biliary fistulas. Other less common but reported complications were not encountered (such as sepsis, reaction to the anesthetic agent, breaking of the biopsy needle, iatrogenic perforation of neighboring hollow organs with peritonitis, intrahepatic arteriovenous fistula, pneumothorax, hematoma in the abdominal wall at the site of cannulation). None of the patients required operative reintervention (laparotomy).

## Discussion

It is believed that the first aspiration liver biopsy was done by Erlich in 1883, while the first diagnostic PLB was published in 1923 (1). Since then, the technical aspect of the procedure has been, naturally, significantly modified. Therefore, during the last three decades, this intervention has taken a central place in the diagnostic algorithm of liver disease. Due to a very low mortality rate (from 0.01 to 0.17%) and relatively low morbidity, this procedure is now widely used routinely, even in smaller health facilities by interventional radiologists, gastroenterologists and surgeons (2). The progress in the field of medical technology, especially radiological imaging techniques, contributes significantly to the expansion of PLB application, and has caused a significant expansion of the indication areas for this procedure. However, despite the growing experience, there are still significant differences in the basic principles of PLB application, especially in terms of the strategic position of this diagnostic intervention, as evidenced by the lack of standardized protocols in almost all institutions.

Bearing in mind that, although at very low incidence rates, PLB may be accompanied by a variety of complications, even when it is implemented by an experienced physician, according to recommendations, it should be performed only when a pathological finding is necessary for definitive diagnosis and treatment initiation or continuation. In patients with acute hepatitis of unknown etiology, PLB may be indicated for differential diagnosis between viral and other causes of inflammation (e.g., medication damage), while in those with chronic viral hepatitis, the indications for PLB may be different: monitoring of the inflammation activity (e.g., assessment of the so-called Hepatitis Activity Index, a necro-inflammation/necrosis „scoring“-system) (3), monitoring of morphologic response of liver tissue to therapy, or a pathological diagnosis of suspected tumor lesions in the field of viral inflammation (e.g., HCC). Similarly, the primary diagnostic and follow-up diagnostic value of PLB (differential diagnosis and monitoring of the evolution - "staging" of the disease) is undoubtful in patients with other benign liver diseases, such as Wilson's degeneration, Caroli's disease, hepatic steatosis, cirrhosis (alcoholic or primary biliary), primary sclerosing cholangitis, specific infections (e.g., tuberculosis), etc.

The indication for PLB in the patients with focal liver tumefactions largely depends on the clinical circumstances in which radiological diagnosis was made. By far the largest number of patients with both solitary and multifocal tumor lesions of the liver are recruited during the oncological follow-up following surgery for primary CRC. However, unfortunately, metastatic liver disease is an expected and very common form of progression of colorectal malignancy, thus in most of these patients PLB is not necessary, due to high clinical suspicion and assuredness about the metastatic origin of these lesions. The situation is completely the opposite for de novo

discovered tumors of the liver with radiological (US, MSCT or NMR) features of metastases in patients without data on any primary malignant disease. In these patients PLB is a diagnostic method of choice for establishing histopathological diagnosis and therefore detection of primary malignancies. It is similar in patients with primary malignant tumors of the liver with or without jaundice (HCC or CHC), regardless of the possibility of operative treatment. In these patients PLB may have a different diagnostic importance: for histopathological confirmation of the diagnosis to perform curative resection, for the application of neoadjuvant (preoperative) oncological therapy or for the implementation of definitive oncological therapy (for inoperable cases). Mixed cystic-solid malignant lesions (e.g. cystadenocarcinoma) require greater vigilance and skilfulness in performing PLB, considering that a solid component suitable for a biopsy may be a very small part of the lesion, and therefore may not be accessible for percutaneous approach. Caution when indicating PLB in suspected malignant liver lesions is required, because of bleeding risk as well as documented risk of dissemination of tumor cells along the biopsy route (4). Benign liver lesions (e.g. FNH, hemangioma, etc.) are very rare indications for PLB for two reasons: they are mainly characterized by a clear radiological presentation and can be detected with high accuracy using MSCT or NMR, or are commonly associated with complications (e.g., bleeding from hemangioma or due to present amyloidoses).

Both the type and incidence of post-procedural complications in our patients are consistent with the literature data. The pain is by far the most common component of „post-interventional“ syndrome, including our own study (5). Major bleeding is very rare (0,35-0,5%) (6), in contrast to the so-called subclinical bleeding that may occur in up to 23% of patients and does not require treatment (blood supplementation or re-intervention), which was also the case in our patients (7). The reduction of unwanted post-procedural developments is achieved by precise radiological diagnosis, clear indications, good selection and adequate pre-procedural preparation of the patients, as well as by closely observing the technical principles involved in the performance of the procedure (the correct choice of access and equipment used, appropriate needle and analgesia with sedation).

## Conclusion

Rapid development of medical knowledge and related technologies have made PLB an indispensable tool in the diagnosis of many liver diseases. Although it is primarily an interventional radiology procedure, PLB is nowadays used by physicians of numerous other specialties (gastroenterologists, surgeons, oncologists) in their daily routine. However, more research with systematized results is needed to contribute to the strategic standardization of PLB in the diagnostic algorithm.

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Originalni rad

UDC: 616.36-076  
doi:10.5633/amm.2018.0203**PROCENA ZNAČAJA PERKUTANE BIOPSIJE JETRE U  
DIJAGNOSTICI NOVOOTKRIVENIH DIFUZNIH I  
FOKALNIH LEZIJA JETRE***Ilija Golubović<sup>1,2</sup>, Milan Radojković<sup>1,2</sup>, Aleksandar Tasić<sup>3</sup>,  
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Perkutana aspiraciona biopsija (PAB) jetre predstavlja važan dijagnostički postupak u svakodnevnoj kliničkoj praksi, jer omogućava neoperativno postavljanje patohistološke dijagnoze. Cilj rada bio je da se utvrdi značaj PAB jetre u dijagnostici novootkrivenih difuznih i fokalnih lezija jetre. Sprovedena je retrospektivna studija koja je obuhvatila 277 bolesnika kojima je urađena PAB jetre u periodu između januara 2006. godine i decembra 2013. godine. Nakon inicijalne sedacije pojedinačnom dozom midazolama, intervencije su obavljane korišćenjem lokalne infiltrativne anestezije (2-8 mL 2% lidokaina sa adrenalinom) pod vođstvom ultrazvuka ili kompjuterizovane tomografije, transabdominalnim ili transtorakalnim pristupom, u zavisnosti od lokalizacije lezije. Korišćene su punkcione igle različitog promera (14-20 gauge). Od 52 bolesnika sa dijagnozom neidentifikovane difuzne lezije jetre, nakon izvršene PAB jetre i patohistoloških analiza, dobijeni su sledeći rezultati: 35 bolesnika imalo je steatosis hepatis (67,3%), kod 12 je dokazana ciroze jetre (23,7%), a kod 5 bolesnika postojanje hepatocelularnog karcinoma (9%). Od 164 bolesnika sa uputnom dijagnozom primarnih tumora jetre, potvrđeno je prisustvo malignih tumora kod 140 bolesnika (85,3%), dok su preostala 24 (14,7%) dokazano imala benigne lezije. Od ukupno 42 bolesnika sa uputnom dijagnozom metastatske bolesti jetre, metastaze KRK su potvrđene kod 31 bolesnika (73,8%), dok su metastaze karcinoma ovarijuma potvrđene kod 6 bolesnika (14,3%). Iako primarno interventna radiološka procedura, PAB jetre je nezamenjivo oruđe u dijagnostici novootkrivenih difuznih i fokalnih lezija jetre.

*Acta Medica Medianae 2018;57(2):18-23.*

**Ključne reči:** *perkutana biopsija jetre, lezije jetre, dijagnostika*