

## B-mode and Contrast Enhanced Ultrasound guided biopsy of portal vein thrombosis. Value in the diagnosis of occult hepatocellular carcinoma in liver cirrhosis

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### Abstract

**Aim:** The ultrasonographic (US) detection of hepatocellular carcinoma (HCC) in patients with liver cirrhosis is based on the visualization of focal lesions. However, in some cases HCC cannot be clearly identified at US, the only sign being a portal vein thrombosis (PVT). Contrast enhanced ultrasound (CEUS) is an excellent method to characterize focal lesions and portal thrombosis in patients with liver cirrhosis. The aim of the study was to assess the value of US and CEUS -guided PVT core biopsy in the diagnosis of an occult HCC in patients with cirrhosis. **Material and methods:** Twenty patients with cirrhosis, PVT and no focal lesion on high-resolution US were studied. In 17 cases the thrombus was interpreted as malignant at US. All patients had normal coagulation parameters. The biopsies of an intrahepatic PVT were performed using an 18G Bard needle coupled on "Biopty Gun". US and CEUS guidance was used in 16 respectively 4 patients. In 10 cases with a very inhomogeneous hepatic echostructure near the PVT (coarse echo pattern) a liver biopsy from that area was performed. **Results:** Adequate histological specimens were obtained in all cases, requiring 1 to 2 passes (mean 1.5 per patient). Only 1 patient had severe pain. No major complications were detected. The overall sensitivity of core biopsy in the diagnosis of malignant PVT was 94.4 % (17/18). The sensitivities of US and CEUS guided PVT biopsy were 92.8% (13/14) and 100% (4/4) respectively. In 6 of 10 cases with coarse echo pattern the same type of HCC was found in the surrounding parenchyma. No false positive results were noted. **Conclusions:** US-guided core biopsy of PVT is a safe and useful technique in the diagnosis of occult HCC in cirrhosis and should be performed in all cases with PVT with malignant US features and no evidence of focal lesions. The "coarse echo pattern" found in the vicinity of a malignant thrombus is frequently the expression of an inapparent, occult HCC. CEUS guided PVT biopsy is a new, promising method with excellent results in establishing the nature of a portal thrombus.

**Key words:** liver cirrhosis, portal vein thrombosis, hepatocellular carcinoma, percutaneous core needle biopsy, contrast enhanced ultrasound guided biopsy

### Rezumat

**Scop:** Diagnosticul ecografic (US) al hepatocarcinomului (HCC) la pacienții cu ciroză hepatică este bazat pe vizualizarea leziunilor focale. Totuși în unele cazuri leziunile de HCC nu pot fi vizualizate ecografic, singurul semn de HCC în acest caz la o parte din acești pacienți este tromboza de vena porta (TVP). Ecografia cu substanță de contrast (CEUS) este o metodă imagistică cu ajutorul căreia se pot caracteriza atât leziunile focale precum și trombul portal la pacienții cirofici. Scopul acestui studiu este evaluarea aportului pe care îl are biopsia trombului portal efectuată prin ghidaj US și CEUS în diagnosticul HCC occult la pacienții cu ciroză hepatică. **Material și metodă:** În studiu au fost incluși 20 de pacienți cu ciroză și TVP fără leziuni focale hepatice vizibile ecografic. În 17 cazuri trombul a fost interpretat ca malign la examinarea US. Toți pacienții aveau probele de coagulare în limite acceptabile. S-a efectuat biopsia trombului portal cu un ac Bard 18 G cuplat la "Biopty Gun". Ghidarea US respectiv CEUS a fost folosită la 16 respectiv 4 pacienți. La 10 pacienți, care prezentau o ecostructură foarte inomogena a parenchimul hepatic adiacent venei porte trombozate, s-a efectuat o biopsie hepatică de la acel nivel. **Rezultate:** La toți pacienții fragmentele bioptice recoltate au fost corespunzătoare, necesitând 1-2 paaje (medie 1,5). Un singur pacient a prezentat dureri severe post biopsie. Nu au fost semnalate complicații majore. Sensibilitatea globală, cea prin ghidare US și ghidare CEUS a acestei metode a fost de 94,4% (17/18), 92,8% (13/14) respectiv 100% (4/4). La 6 din 10 cazuri care prezentau o ecostructură foarte inomogenă lângă vena portă trombozată, a fost identificat același tip de HCC în parenchim. Nu a fost semnalate rezultate fals pozitive. **Concluzii:** Biopsia trombului portal prin ghidare US este o metodă sigură și foarte utilă în diagnosticul HCC occult la pacienții cirofici cu TVP cu caractere ecografice de malignitate. Aspectul foarte inomogen al parenchimului hepatic adiacent trombului malign este de cele mai multe ori expresia unui HCC inaparent. Ghidarea CEUS a biopsiei este o metodă nouă, care promite obținerea unor rezultate excelente în stabilirea naturii trombului portal.

**Cuvinte cheie:** ciroză hepatică, tromboză venă portă, carcinom hepatocelular, puncție biopsie percutană cu ac gros, puncție biopsie ghidată prin ecografie armonică cu contrast

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### Introduction

Portal vein thrombosis (PVT) which occurs usually in liver cirrhosis [1–3] may be caused by both malignant and benign conditions. Malignant PVT is a usual complication of hepatocellular carcinoma (HCC) in cirrhosis and signifies an advanced tumoral stage [1]. Because the

prevalence of tumor recurrence is nearly 100%, patients who have HCC and proven neoplastic vascular thrombus are not candidates for any treatment.

In cirrhotic patients with HCC, PVT may have both malignant and benign causes. The presence of a PVT near an HCC usually signifies portal vein invasion; meanwhile, a thrombus remote from a HCC treated by percutaneous ablation techniques such as ethanol injection is in most cases a benign chemical thrombus. In a small percentage of patients, PVT may be the initial sign of an undetected, inapparent HCC which has an intravascular first growth [4].

Benign and malignant thrombi may not be easily distinguishable by conventional imaging studies such as abdominal ultrasound (US), computed tomography (CT) and resonance magnetic imaging so, in many cases a percutaneous fine needle aspiration biopsy is required to establish the diagnosis. In recent years contrast enhanced sonography (CEUS) has emerged as an excellent technique to characterise hepatic tumors and portal thrombosis [5,6]. Moreover, some recent data suggest that CEUS may improve the accuracy of percutaneous US guided biopsies [6-8].

The aim of this study was to investigate the role of percutaneous US and CEUS guided core biopsy in the diagnosis of PVT and to assess the value of this technique in the diagnosis of inapparent, occult HCC.

### Patients and methods

From January 2000 to December 2009 20 patients with liver cirrhosis and portal vein thrombosis, 13 males and 7 females, aged from 41 to 72 years (mean 58.5 years) were enrolled. All, except 2 patients with known HCC nodules treated by percutaneous ethanol injection remote from the present PVT, had no focal lesions on high resolution ultrasonography.

Based on US and color Doppler features of PVT malignant PVT in 17 patients was suspected. None of them had ultrasound recognizable focal lesions. In 10 patients a very inhomogenous echostructure near the thrombus was noted ("coarse echo pattern").

As portal vein invasion precludes curative treatments (surgery, percutaneous ablative techniques) percutaneous biopsy was performed in order to certify the neoplastic nature of the thrombus and to initiate chemotherapy.

### Equipment and procedures

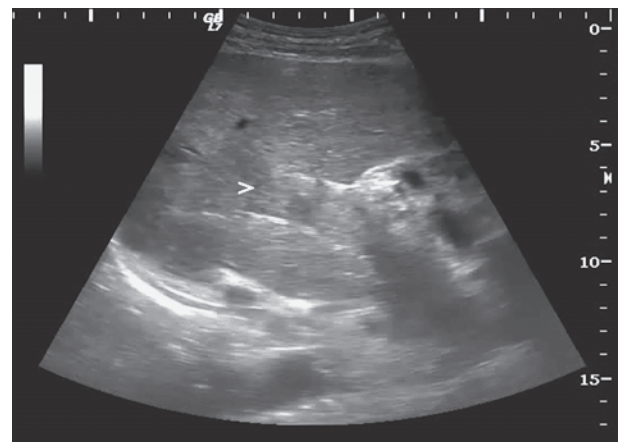
#### *B mode and color/Power Doppler Ultrasound.*

Fifteen patients were examined with an Acuson 128XP machine equipped with a 3.5 MHz transducer. The last five patients were examined with a Logiq 7 machine

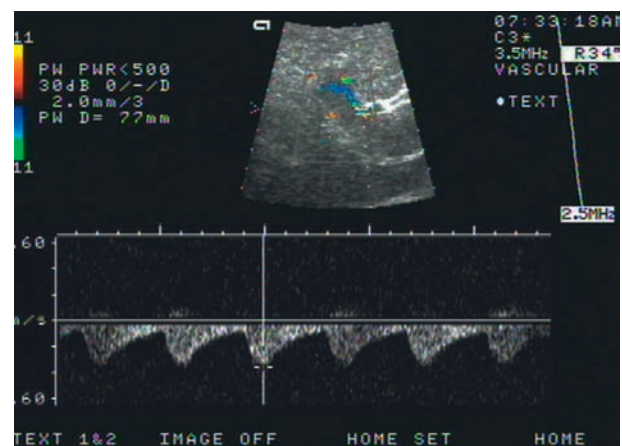
(General Electric, Milwaukee, USA) with real-time contrast specific software and a 3-5 MHz convex array wide band probe. Baseline unenhanced color Doppler sonographic studies were performed using a low pulse repetition frequency (750 to 1200 Hz) to optimize detection of weak signals. The color box was restricted as much as possible to maximize color sensitivity and frame rate.

**PVT** was diagnosed based on the characteristic **B mode ultrasound findings** which include an echogenic thrombus within the lumen of portal vein, lack of visualization of venous flow inside the vein, portal vein collaterals and cavernous transformation [9,10]. Color/Power Doppler sonography was used to demonstrate either the absence of flow or the presence of flow circumventing a clot within the PV [11,12].

Malignant PVT was suspected in the case of expansion of the caliber of vein (fig 1), interruption of the PV wall and the presence of arterial flow inside the PV thrombus at pulsed Doppler sonography (fig 2).



**Fig 1.** Malignant PVT with expansion of the caliber of vein (arrowhead)



**Fig 2.** Malignant PVT. Presence of arterial flow inside the PV thrombus at pulsed Doppler sonography

The localization of PVT was: a) right or/and left PV but no main portal trunk (10 patients); b) main portal trunk and left and/or right PV (10 patients). PVT was complete in 15 patients and incomplete in 5.

#### Contrast enhanced ultrasound

Contrast enhanced imaging was performed according to the protocol used for the Bracco-SonoVue preclinical trial [13]. Examination was performed with low acoustic power (mechanical index under 0.01) after injection of a SonoVue (BR1; Bracco, Milan, Italy). SonoVue consisted of sulfur-hexafluoride (SF<sub>6</sub>) vapor-filled and phospholipid-stabilized microbubbles with a diameter uniformly smaller than 8  $\mu$ m; these microbubbles circulate in the intravascular space crossing pulmonary and systemic capillary circulation. 2.4 mL of contrast-agent were administered for each patient. The low mechanical index technique avoids destruction of bubbles thus allowing to identify the entire vascular phase of contrast agent perfusion, consisting of the arterial phase (15-30 s after injection of agent), the portal phase (30-60 s after injection of agent) and the late parenchymal phase [5].

The diagnosis of PVT was based on the complete or partial absence of enhancement within the vessel lumen in the portal and late phases. A malignant thrombus was certified by the presence of enhancing tissue within the vessel lumen in the arterial phase (fig 3) [14]. Contrast enhanced ultrasonography (CEUS) were performed only in the last 4 patients.

#### Portal vein US guided thrombus biopsy

The biopsy was performed with a 1.2 mm (18G) Bard needle coupled on an automatic device (Biopty Gun). Two sonographic systems (Acuson 128XP and Logiq 7) equipped with a 3.5 MHz sector probe and biopsy guide were used. The use of a probe with color Doppler facilities was useful to avoid the hepatic artery branches and other major vessels.

For thrombi in the left portal vein (6 patients), a subxyphoid approach was used, while for those in the right portal vein (14 patients), an intercostal or right subcostal approach was necessary. The coagulation studies accepted for the PVT biopsy were a platelets count higher than 60000/mm<sup>3</sup> and prothrombin time less than 15 sec.

After localization of an intrahepatic segment of the thrombosed portal vein, with color-Doppler mapping of the adjacent hepatic artery or other major vessels, we chose an appropriate biopsy path avoiding the vascular structures. PVT biopsy was performed with real-time sonographic guidance using 18 G cutting needles (Bard) coupled on a Biopty Gun. The needle has a 1.4 cm long sampling notch. Special care was taken to maintain the

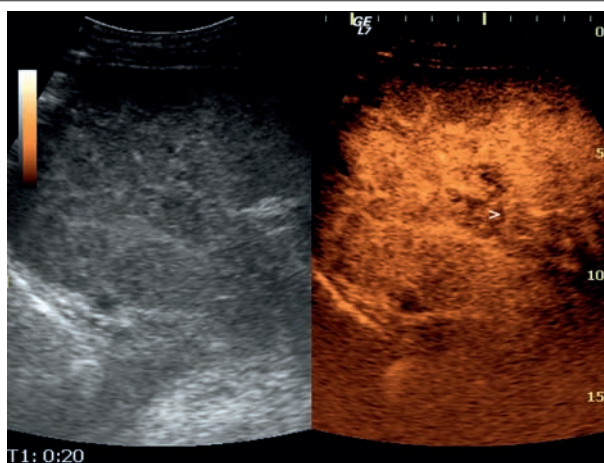


Fig 3. Malignant thrombus. CEUS reveals enhancing tissue within the vessel lumen (arrowhead) in the arterial phase

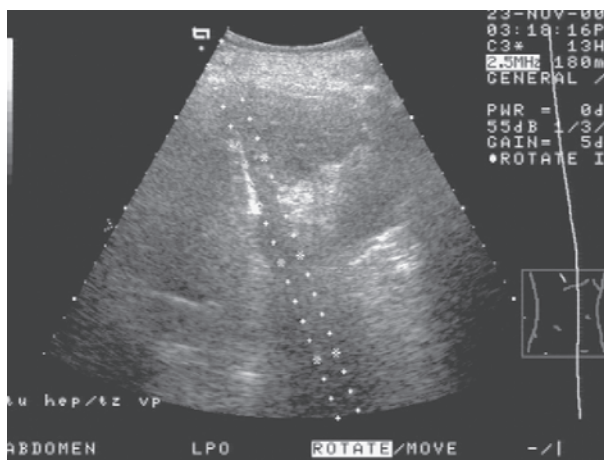


Fig 4. US guided biopsy of a PVT

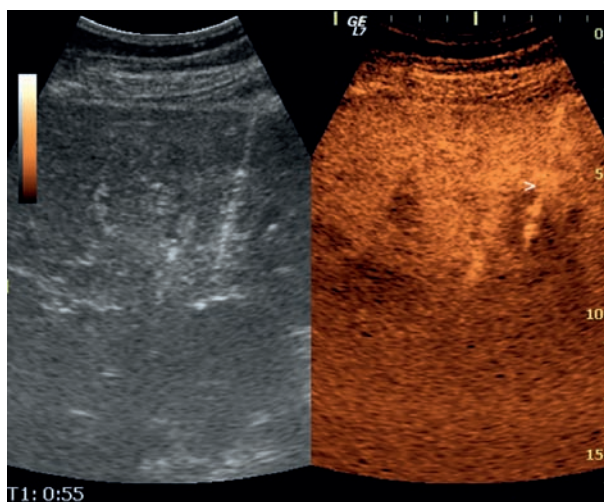


Fig 5. CEUS guided biopsy of an enhancing PVT. Note the presence of the needle inside the enhancing areas of the thrombus

needle within the lumen of PV at all times (fig 4) [15]. The mean diameter of the portal vein where the puncture was performed was 12.1 mm range 10-20 mm).

In 10 cases with a very inhomogeneous hepatic echostructure near the PVT (coarse echo pattern) an additional passage was performed from that area in the same session.

*CEUS guided PVT biopsy* was performed in 4 patients with complete PVT with malignant features, no focal liver lesions and an inhomogenous enhancement of the PVT at CEUS. The puncture of the thrombus was performed in the arterial phase (or in the early portal phase) in an attempt to target the enhancing areas inside the thrombus (fig 5).

The tissue specimens were placed in 10% formaldehyde for histological examination. Pathological diagnosis of HCC was made according to the International Working Party criteria [16]. All patients were observed for 30 minutes after puncture and then sent to the gastroenterological department. They remained in the hospital for the next 24 hours.

**Ethical issues**

All patients enrolled in the study gave their informed consent to participate. The protocol was submitted to and

approved by the Ethical Committee of the 3rd Medical Clinic, Cluj-Napoca.

**Results**

A good histological specimen was sampled in 100% of cases, with a mean 1.5 passages per patients (range 1-3). The mean length of the specimen sampled with US guidance from the thrombus was 1.16 cm (range 0.8-1.3 cm) and from liver parenchyma adjacent to the PVT 1.17 cm (range 0.8-1.4 cm) (difference not significant). With CEUS guidance the specimen had a mean length of 1.13 cm (range 1-1.2 cm).

The overall sensitivity of core biopsy in the diagnosis of malignant PVT was 94.4 % (17/18). US and CEUS guided PVT biopsy have a sensitivity of 92.8% (13/14) and 100% (4/4) respectively. The 2 cases with PVT remote from a treated HCC nodule had benign thrombosis due to the leakage of alcohol into the portal vein (chemical thrombosis). The specificity for both methods was 100%.

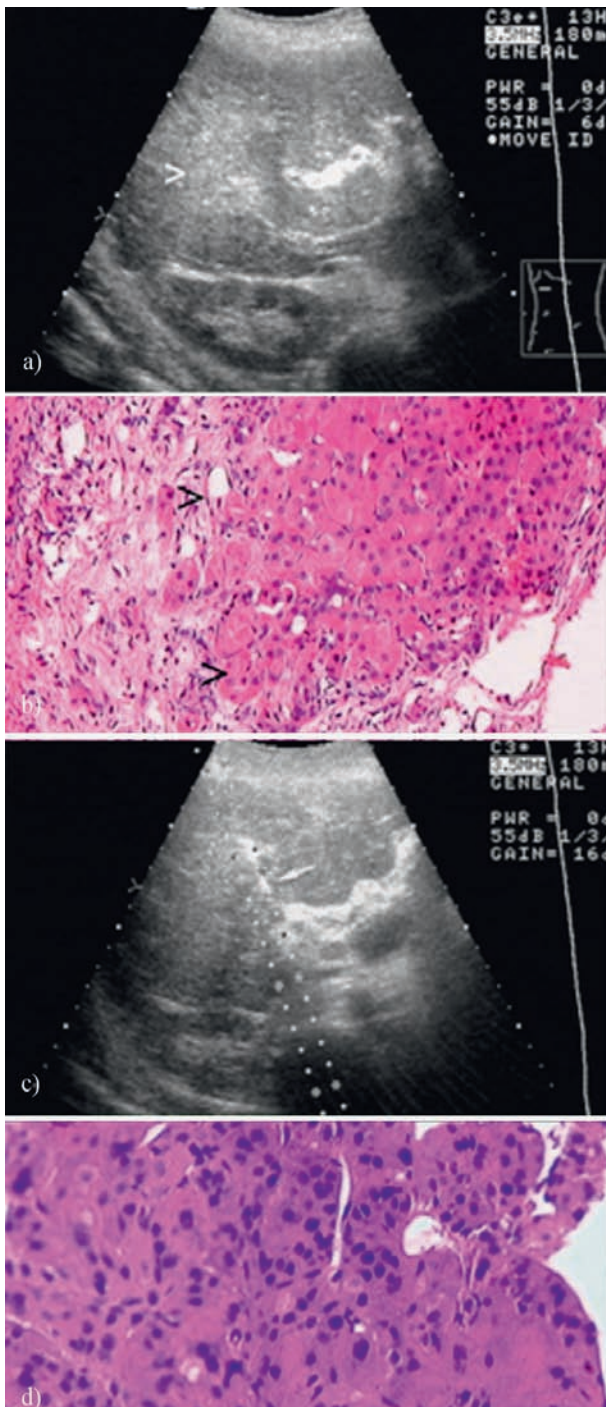
In 6 out of 10 cases with an additional parenchymal biopsy adjacent to the PVT the diagnosis of HCC with a similar pattern was established (table I, fig 6).

There were no major complications. One patient experienced severe pain after a PVT biopsy which ceased after administration of Tramadol.

Table I. Results of PVT and parenchymal biopsy

Nr.	Thrombus biopsy	Adjacent parenchymal biopsy	Observation
1.	HCC medium/poor differentiation	HCC poor differentiation	
2.	HCC medium differentiation	HCC medium differentiation + cirrhosis	
3.	HCC poor dif difer.	HCC poor differentiation	
4.	HCC well/medium differentiation	HCC well/medium differ+ cirrhosis	
5.	HCC well/medium differentiation	HCC well/medium differ+ cirrhosis	
6.	HCC well differentiation	Cirrhosis	
7.	Non neoplastic thrombus	Cirrhosis	Severe PHT
8.	Cholangiocarcinoma	np	Bile ducts invasion
9.	Non neoplastic thrombus	np	Chemical thrombosis
10.	Non neoplastic thrombus	np	Chemical thrombosis
11.	HCC medium differentiation	Cirrhosis	
12.	HCC medium differentiation	Cirrhosis + dysplastic foci	
13.	HCC well differentiation	np	
14.	HCC poor differentiation	np	
15.	HCC medium differentiation	np	
16.	HCC well/medium differ	np	
17.	HCC poor differentiation	np	CEUS guided biopsy
18.	HCC poor differentiation	np	CEUS guided biopsy
19.	HCC medium differentiation	Cirrhosis	CEUS guided biopsy
20.	HCC poor differentiation	np	CEUS guided biopsy

HCC- hepatocellular carcinoma; PHT- portal hypertension, np-not performed



**Fig 6.** Inhomogeneous hepatic echostructure near a malignant PVT: a) PVT biopsy; b) Histology aspect hematoxylin eosin stain 10x enlargement – well differentiated HCC; c) Parenchymal biopsy; d) Histology of the parenchymal (hematoxylin eosin stain 40x enlargement) biopsy confirmed the well differentiated HCC

## Discussion

Patients with liver cirrhosis have a greater risk of developing benign or malignant PVT than the general population [17]. It is a relative rare complication of liver cirrhosis, with 1-5.7% prevalence [2,3] and is caused by benign or malignant processes.

Concerning the **benign causes**, it is difficult to consider cirrhosis per se as a cause of PVT except in terminal cases with severe portal hypertension and venous stasis [3]. PVT occurring in patients without cancer and in good condition is usually associated with a prethrombotic condition [3] and/or local factors such as infections (pancreatitis, cholecystitis, neonatal omphalitis a.o) and injury to the portal venous system such as surgical portocaval shunting and splenectomy. In recent years, an iatrogenic origin of PVT in cirrhosis has also emerged; endoscopic sclerotherapy of esophageal varices and percutaneous ablation therapies (PATs) for HCC may provoke PVT [18-20].

**Malignant PVT** occurs by direct invasion of the portal vein by HCC, a common complication of liver cirrhosis. Based upon autopsy data or imaging techniques, the incidence of PVT in HCC is 20 -70% [21]. In some cases, PVT can be the first echographic or radiologic sign of HCC in absence of any detectable focal lesion [20-22].

Although it seems reasonable to assume that a portal vein thrombus in a patient with HCC is malignant, and in a patient with no evidence of hepatic tumor is benign, in practice benign or malignant portal vein thrombi can occur in either situation. This becomes more evident when a patient with a nodular HCC is treated with percutaneous ablative techniques such as PEI or RFA. In such cases, the presence of a thrombus inside the PV branches located in the vicinity of the tumor could represent either a benign thrombosis as a consequence of the endothelial cell injury caused by the treatment, or an intravascular spread of a residual or a recurrent tumor [20].

The clinical value of recognizing malignant PVT in a patient with cirrhosis and HCC relies on the effect that malignant PVT has on the therapeutic strategy; patients with HCC (even uninodular and <5 cm) and malignant PVT are excluded from surgical treatment or imaging-guided PATs [23].

*Real-time ultrasonography* is a rapid and noninvasive method for evaluating the normal and the pathological portal venous system. The US signs of malignant PVT are the expansion of the caliber of vein, interruption of the PV wall and the presence of an arterial flow inside the PV thrombus at pulsed Doppler sonography.

The sensitivity of the pulsatile flow as a criteria for the diagnosis of malignant PVT vary between 62% and

92% [17,20,24,25]. The sensitivity decreases even to 20% when small thrombi are analysed [4]. Beside size, failures of Doppler imaging to detect pulsatile flow inside a thrombus are encountered in deep located or hypovascular thrombi.

The presence of a pulsatile flow inside a PVT is fairly specific (86-100%) for malignant PVT [17,24,26]. However, there are some cases in which, due to the presence of arterial portal venous shunting, a common phenomenon in cirrhosis, pulsatile flow can be detected inside a benign thrombus, flow similar with that found in the non-thrombosed segment of the PV.

Using contrast-enhanced ultrasonography, the pulsatile flow as a diagnostic criteria of malignant thrombosis yielded a higher sensitivity and specificity (94% and 100% respectively) [27].

Of particular interest is the evaluation of a PVT that appears after a PAT such as PEI for HCC. The development of PVT after PATs may be related to the chemical or thermal injury of the PV with vasculitis and thrombus formation caused directly by PAT or to a venous invasion by a residual or recurrent tumor. The sensitivity and specificity of color Doppler sonography for the diagnosis of tumor thrombosis in such circumstances are 92% and 100%, respectively [20].

#### **PVT as a sign of inapparent, occult HCC**

In HCC, the US patterns generally result in focal echogenic changes which are easily demonstrated, but also in normal features or, in a diffuse nonuniform structure that may be underrated and attributed to diffuse liver disease [22]. Caturelli et al [28] described 4 hepatic parenchymal echo patterns that can be found in liver cirrhosis: (a) normal homogeneous pattern; (b) bright liver pattern; (c) coarse pattern, and (d) coarse nodular pattern. The coarse pattern is represented by the presence of nonhomogeneous, coarse, thick, uneven echo spots without any distinct hypoechoic nodules. The "coarse nodular pattern" has a background displaying the coarse echo pattern and multiple weak hypoechoic nodules (<6 mm in diameter). These 2 patterns were associated with a significantly increased risk for HCC in patients with HBV-, HCV and alcoholic cirrhosis. The "coarse and coarse nodular pattern" was found in the vicinity of PV in 10 of our patients with malignant PVT. Core biopsy from these areas showed HCCs with the same pathological features in 6 of the 10 patients.

Contrast-enhanced helical computed tomography (CT) and contrast-enhanced magnetic resonance (MR) can suggest a malignant origin of the thrombus by visualizing diffuse thrombus enhancement due to neovascularization of the tumor infiltrating the vessel [29]. The sensitivity of CT in the characterisation of PVT in patients with HCC is only 68% [29].

Table II. Indications for portal vein thrombus biopsy

- |    |  |
|----|--|
| 1. | PVT with no imaging evidence of HCC  |
| 2. | PVT remote from a histologically proven HCC                                      |
| 3. | PVT adjacent to a nodule with an equivocal vascular pattern on imaging histology |
| 4. | PVT after a local treatment (PAT) of an HCC                                      |

*Percutaneous biopsy of a portal vein thrombus* can establish the nature of the thrombus, thus making the staging more accurate. It has been proved to be a feasible, accurate, safe and well-tolerated procedure.

Although the indications for PVTB in liver cirrhosis are not well established, in the following circumstances show in table II the PVT biopsy may be indicated [15,30].

The sensitivity of fine needle aspiration in the differential diagnosis of PVT ranges from 76 to 100% [4,15,31]. Needle sampling error can result in both false-positive and false-negative diagnoses for malignant PV thrombi [15,30,31].

As a benign thrombus contains amorphous material, fibrin and blood [21,31] and not hepatocytes, sampling specimens from the periportal hepatic parenchyma could lead to false-positive diagnoses. This could be prevented by a continuous sonographic visualization while the needle is moved inside the thrombus and by choosing a proper needle tract inside the thrombus.

False-negative diagnoses could be produced if the portion of the malignant PVT, which is biopsied, does not contain malignant hepatocytes [15]. Performing the PVT biopsy closest to a hepatic tumor (if present) and choosing the longest possible segment of the PVT can prevent false-negative results.

Possible complications after PVT biopsy are: portal venous or hepatic arterial bleeding, laceration of a bile duct and formation of a vascular-biliary fistula, arteriovenous fistula or pseudoaneurysm. If we use color Doppler guidance in compliant patients with only intrahepatic PV thrombi and normal or corrected coagulations factors, the risk of PVT biopsy is comparable to that of the percutaneous biopsy of HCCs [15,30-32].

The sensitivity of US guided PVT core biopsy found in our study was slightly higher than that found by Yang et al [33] (92.8% vs 87.5%). We obtained only 1 false negative result for malignant thrombi. This may be explained by the sampling from an area which does not contain malignant hepatocytes [34]. In fact the CEUS studies of PVT have shown that frequently these thrombi have an inhomogeneous enhancement in the arterial phase named "mosaic-picture". It was postulated that in these cases a benign thrombosis was superimposed on the initial neoplastic invasion of the portal vein [34].

In our patients' group we had mostly patients with complete PVT, with distended and tumor filled PV. In such cases, if the needle path is safe, a core biopsy should be performed. For incomplete PVT with small thrombi, fine needle aspiration is the method of choice.

It has been shown recently that CEUS has a high sensitivity (88-97.7%), 100% specificity and very good accuracy (92.5-95.5%) in the characterisation of PVT [4,29,34]. The sensitivity of CEUS is higher than of contrast enhanced CT (98 vs 67.6%), especially for non-occlusive thrombi (100% vs 57.1%) [29]. Taking the results of FNA, CEUS and follow up as "gold standard" it has been demonstrated that CEUS is superior even to FNA (sensitivity 100% vs 89.6%) in the diagnosis of PVT in patients with HCC [34]. When confirmation of malignant thrombosis is required, PVT biopsy can be guided on the result of CEUS in order to reduce false-negative results due to blind sampling [34].

CEUS guided percutaneous biopsy is a new technique which has been shown to increase the sensitivity of percutaneous biopsy in tumoral diagnosis, especially in large tumors with frequent necrosis, complex cystic solid masses, less visible or poorly demarcated lesions [6-8,35]. Its superiority over the classic US guided biopsy has been demonstrated for liver [36,37], pulmonary [38], prostatic [39] and soft tissue tumors [40].

Our results showed that CEUS guided PVT biopsy in patient with liver cirrhosis and inapparent HCC is feasible, has a sensitivity of 100% and is safe. Guiding the needle inside the enhancing areas of the thrombus allows the sampling of tumoral cells and not nonmalignant tissue.

An interesting result of our study was to demonstrate that the "coarse and coarse nodular echo pattern" found in the vicinity of a malignant thrombus are frequently the expression of an inapparent HCC. The tumor could have been seen with CEUS which unfortunately was not available in our Center at that time. Contrast enhanced CT performed in 5 of these patients failed to demonstrate the presence of an HCC.

Our study has some strengths and limitations. To our knowledge this is the first study where a very inhomogenous hepatic ecotexture near a PVT was demonstrated to be caused by an HCC.

The low number of patients enrolled in the study represents in fact the small number of patients with cirrhosis and malignant PVT with no evidence of an HCC lesion (inapparent or occult HCC) where pathological diagnosis was necessary in order to commence chemotherapy. Although some case reports have been published, this is the first prospective study to assess the role of core biopsy in malignant PVT and no evidence of an HCC. All other

published studies enrolled patients with detectable HCC where PVT biopsy was performed to stage the disease.

Most of the patients enrolled in the study had no CT studies. It is known that contrast enhanced CT is superior to conventional US in the detection of HCC so, probably some patients from our group would have had an intrahepatic HCC that was missed by conventional US.

The most important result of this study was the excellent sensitivity and safety of the real time CEUS guided puncture of portal vein thrombosis. Although it comprises a very small number of patients the results of this study recommend CEUS guided biopsy as an important diagnostic tool in the diagnosis of PVT.

In conclusion, a sonographically guided percutaneous portal vein thrombosis core biopsy is a safe, accurate and well tolerated procedure in the diagnosis of malignant portal vein thrombosis and no evidence of an HCC lesion. The "coarse and coarse nodular echo pattern" found in the vicinity of a malignant thrombus are frequently the expression of an inapparent HCC. CEUS guided PVT biopsy is a new, promising method with excellent results in establishing the nature of a portal thrombus.

**Conflict of interest:** none

**Acknowledgement**

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