RESEARCH ARTICLE

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Microparticle Suspension Intravenous Applications to Enhance Diagnostic Color Doppler Ultrasonography Signal Intensity in the Differential Diagnosis of Liver Tumors

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Abstract

Objectives: To evaluate the effectiveness of color and power Doppler ultrasonography enhanced with the intravenous microparticle contrast agent Levovist in increasing doppler signal intensity and improving differentiation between malignant and benign liver tumors.

Methods: Between December 1999 and July 2000, 21 patients who were admitted to the Gastroenterology and Gastroenterological Surgery Clinics of the Türkiye High Specialization Hospital were included in the study. Patients referred to the Department of Radiology who underwent thick-needle tru-cut biopsy or pathological examination of the postoperative mass were included in the study. Among these 21 patients (12 males and 9 females; age range 29-77 years; mean age 51.4 years), 18 had hepatocellular carcinoma and 3 had cholangiocarcinoma. A total of 19 patients (12 males, 7 females; age 21-71 years; mean 44.9 years) with 9 hemangiomas, 5 liver metastases, 4 hydatid cysts, and 1 liver abscess were selected as the control group.

Results: During the examination, after the Doppler assessment was completed and the ultrasound contrast agent was administered, the values obtained were compared with previous findings. Similar to the literature, the color flow appearances of the masses were divided into four groups: (a) basket pattern (a view where vessels tightly surround the mass and may branch into it), (b) tumor vascularization (vascularization within the mass), (c) dot pattern (a dot-like appearance within the mass), and (d) tortuous pattern (tortuous vascularization surrounding the mass externally) (sinuous vascularization surrounding the mass externally).

Conclusion: As a non-invasive method, contrast-enhanced color Doppler ultrasonography provides important information for the differential diagnosis in selected cases. We believe that, as color and power Doppler devices are further developed to allow examination of deep-seated and small intraparenchymal tumoral hepatic lesions and to reveal blood flow velocity in very small vascular structures, examinations using contrast agents to increase Doppler signal intensity will provide diagnostically important information.

Keywords: Doppler, liver, ultrasonography, intratumoral vascularization, contrast-enhanced doppler ultrasonography, hepatocellular carcinoma

Introduction

Grey-scale ultrasonography (US), color Doppler ultrasonography (CDUS), and power Doppler ultrasonography are the preferred noninvasive methods in the evaluation of liver masses. However, these methods may not always characterize the lesion. In such cases, triphasic dynamic computed tomography (CT) or magnetic resonance imaging (MRI) is performed for further evaluation. However, the lesion can also be characterized by dynamic contrast US and CDUS with echocontrast agents.

There are two important phases during examination of the liver with echocontrast agents[1,2]: the early vascular phase (arterial and portal phases) and the late parenchymal phase.

In CDUS examinations performed with IV contrast agents, assessment of the accuracy of quantitative perfusion parameters for the effective differential diagnosis of malignant and benign liver lesions is among the most important diagnostic criteria. Some echocontrast agents are retained in cells of the reticuloendothelial system during the late parenchymal phase (Levovist, Sonazoid, among others), and this retention lasts approximately 20 minutes.

Benign lesions show contrast enhancement in both the early vascular phase and the late parenchymal phase. However, a low perfusion defect can be observed in the late phase in some benign lesions. Malignant lesions and metastases usually show contrast enhancement in the early vascular phase, whereas in the late phase they lack enhancement and appear as contrast defects. However, persistent perfusion may be

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observed infrequently in the late phase of malignant lesions. Peripheral contrast uptake may also be present in late-phase examinations of metastases.

In this context, ultrasound contrast agents contribute to the characterization of liver masses and offer an alternative to CT and MRI. Side effects of echocontrast agents are very rare, transient, and mild.[2,3] They do not have specific cerebral, hepatic, or renal toxicities. Therefore, dynamic contrast-enhanced US and Doppler examinations may be preferred in patients with hepatic and renal insufficiency, and in cases where MRI and CT cannot be performed.

SHU 508 A (Levovist), the echocontrast agent used in our study, contains specific microbubbles, galactose, and palmitic acid molecules. Its side effects are nonspecific symptoms, including sensations of heat or cold, injection-site pain, and taste changes. The only contraindication is galactosemia. Its safety profile is considered acceptable.

In this study, the effectiveness of contrast-enhanced and Doppler US in the differential diagnosis of hepatic neoplastic masses and hepatic metastases was investigated, and digital subtraction angiography (DSA) results were compared with vascularization findings.

This research thesis was conducted in the Department of CDUS and in the DSA Unit of the Radiology Clinic at the Türkiye High Specialization Hospital (THIY). The study included 21 patients with primary liver tumors, diagnosed by clinical and pathological examinations, and a control group of 19 patients with intraparenchymal space-occupying lesions in the liver.

In the patient and control groups, color and power Doppler examinations were performed before and after IV administration of Levovist (SHU 508 A), a contrast agent with a molecular structure based on galactose and palmitic acid. Peripheral and intratumoral vascular flow patterns, waveform characteristics, arterial flow velocity, and resistive index (RI) of the mass lesion were examined and recorded.[2-4]

Ultrasound with intravenous contrast agents, including B-mode and Doppler modes, can be performed during the same examination session, providing additional diagnostic information and significantly improving diagnostic performance compared with dynamic CT and MRI with respect to vascularization features and specific contrast-dynamic characteristics.[3,5]

Methods

All procedures involving human participants were conducted in accordance with the ethical standards of the institutional and/or national research committees and with the 1964 Declaration of Helsinki and its later amendments or comparable ethical standards (approval no.: 80576354-050-99/169, date: 29.05.2019). The study was approved by the TYIH Chief Medical Officer Training and Planning Commission and conducted in accordance with the Declaration of Helsinki. Patient consent was obtained.

Between December 1999 and July 2000, 21 patients admitted to the Gastroenterology and Gastroenterological Surgery Clinics of the TYIH were included in the study. Patients who were referred to the Radiology Department and who underwent thick-needle tru-cut core biopsy or who underwent pathological examination of the postoperative mass were selected for inclusion in the study. Of these 21 patients (12 males, 9 females; age range 29-77 years; mean age 51.4 years), 18 had hepatocellular carcinoma (HCC) and 3 had cholangiocarcinoma. A total of 19 patients (12 males, 7 females; age range 21–71 years; mean age 44.9 years) diagnosed with hemangiomas (n=9), liver metastases (n=5), hydatid cysts (n=4), and liver abscess (n=1) were selected as the control group.

All patients included in the study were examined using a LOGIQ 700 MR Doppler US device (GE Medical Systems) with convex and sector probes. Hepatic mass lesions occupying the intraparenchymal space were initially evaluated by B-mode US for size, contour, borders, and echo pattern. Subsequently, a color Doppler examination was performed. In masses showing tumoral vascularization, peripheral and intratumoral color Doppler flow patterns and appearances; waveform; feeding artery; arterial flow velocity; RI; hepatic artery flow velocity; and hepatic perfusion index were evaluated. The US device was adjusted to detect low flows by lowering the color filter and reducing the PRF and wall filter.

During the examination, after completion of the Doppler evaluation, Levovist (galactose palmitic acid-containing granules, 999 mg) was administered intravenously at a concentration of 400 mg/mL in a total volume of 20 mL, at a constant injection rate of 2 mL/sec. This provided a homogeneous increase in the Doppler signal lasting an average of 90 seconds, with maximum effect at 30-60 seconds. Subsequently, the values obtained after administration of the ultrasound contrast agent were compared with the previous findings.[1,4]

The Tanaka et al.[5] classification served as the basis for the study, and color-flow appearances within the masses were divided into four groups. According to this classification,[3,5] the following patterns were investigated: (a) basket pattern (an appearance that tightly surrounds the mass and may give rise to branches into the mass);(b)tumoral vascularization(presence of vascularization within the mass); (c) spot pattern (a punctate appearance within the mass); and (d) detouring pattern (a vascular pattern surrounding the mass in a detouring manner).

Spectra were obtained from colored flow images at Doppler angles between 30° and 60°, and flow velocities and characteristics were determined. Blood flow waveforms were classified into two groups based on their spectral patterns: pulsatile and continuous (Table 1). The mean and median flow velocities within the masses were determined.[5,6]

No significant side effects or adverse events were observed following intravenous administration of Levovist (400 mg/mL), 20 mL, at an injection rate of 2 mL/sec. Only one patient , a 71-year-old, experienced pain and increased temperature at the injection site, followed by nausea; these symptoms resolved within 10 minutes without intervention.[7,8]

Findings on selective celiac and hepatic artery DSA included arterial dilatation and elongation, coarse, dense neovascularization, vascular pooling, and A.V. shunts. Dense neovascularization, staining, contrast enhancement, and tense (stretched) abnormal vascularization may

Table 1. All flow grades and patterns on color doppler ultrasonography

Doppler flow degree	CDUS finding (sign)
0	No current
1	Normal organ blood flow
2	Increased blood flow
3	Patterns of excessive blood supply

CDUS: Color doppler ultrasonography

be observed around areas of necrosis. The lesion may also appear totally hypovascular. DSA alone is sufficient for evaluating vascular invasion and preoperative mapping of the vasculature (e.g., portal vein invasion). CDUS with Levovist can evaluate the feeding artery before chemoembolization. Cholangiocarcinoma appears angiographically similar to anaplastic HCC. It is a highly hypovascular tumor that causes encirclement, occlusion, and displacement of the primary intrahepatic branches of the hepatic artery and the portal venous system.[8,9] Neovascularization is present in approximately 50% of patients, while tumor contrast staining is absent or very weak. The most common locations are the proximal and distal branches of the left and right common hepatic arteries.

Statistical Analysis

The data were analyzed using the Statistical Package for the Social Sciences (SPSS) for Windows, version 20 (SPSS Inc., Chicago, IL, USA). The normality of data distribution was assessed using the Kolmogorov-Smirnov and Shapiro-Wilk tests. Normally distributed numerical variables were presented as mean ± standard deviation, whereas non-normally distributed variables were presented as minimum-maximum values.

The diagnosis of liver lesions in the control group was made clinically and histopathologically, and in some cases was confirmed by laboratory tests and US. For statistical analysis, the Mann-Whitney U test was used because the number of patients in the control group was small. The Student's t-test was used for comparisons between two groups. Friedman's test and Tukey-Kramer multiple-comparison tests were used to compare cases with angiographic findings and those with Power Doppler findings.

Results

The study included 21 patients with a mean age of 51.4 years, of whom 12 were female and 9 were male (Table 2).

When contrast uptake in vascular phases, perfusion properties in late phases, and CDUS and power Doppler characteristics of all hepatic lesions were evaluated, 26 of the 39 cases with color Doppler flow appearance were malignant (96% of all malignant masses), and 13 were benign (13.6% of all benign masses).

The mean maximum blood flow velocities ranged from 7 to 158 cm/s in malignant lesions and from 6 to 39 cm/s in benign lesions. Statistical comparison of mean blood flow velocities revealed statistically significant differences between benign and malignant masses (t: 8.15,

Table 2. CDUS acuity pattern distribution of 21 patients with primary liver tumours and 19 patients in the control group

Cases	Basket pattern	Tumoral Vascularization	Detouring pattern	Spot pattern
HCC (18 patients)	14	4		
Cholangiocarcinoma (3 patients)		2	1	
Liver metastasis (5 patients)		3	2	
Hepatic haemangioma (9 patients)		0	1	7
Liver abscess (1 patient)			1	
Hepatic cyst (4 patients)				

CDUS: Color Doppler ultrasonography

Table 3. Rates of intratumoral vascularisation discovered in the intrahepatic parenchymal lesions examined (number of cases and percentage of vascularization revealed)

Type of intrahepatic nodular lesion	Total lesion	Angiography (WHO)	Conventional colour doppler usg	iv. contrast agent After application (400 mg/mL) Colour doppler usg signal intensity increase
HCC	18 Patients	14* (77)	9 (50)	13* (72)
< 20 mm. HCC	(4)	(2)	(0)	(1)
20-30 mm. HCC	(7)	(5)	(4)	(5)
≥30 mrn. HCC	(7)	(7)	(5)	(7)
Hepatic hemangioma	9 Patients	9 (100)	4 (44.5)	8 (89)
Hepatic metastasis	5 Patients	3 (60)	2 (40)	3 (60)
Cholangiocarcinoma	3 Patients	1 (33)	1 (33)	2 (66)
Total	**35**	**27 (77)**	**16* (46)**	**26* (74)**

WHO: World Health Organization

p<0.001) and between hepatoma and hemangioma (t: 3.38, p<0.001). A significant difference (p<0.05) between HCC and metastatic cases was also observed.

In 13 cases, significant differences in vascularization and Doppler patterns were observed after IV administration of Levovist (galactose + palmitic acid). In these cases, the pre-administration flow grade was 1 (normal organ blood flow), and after administration, a flow grade of 2 (increased blood flow) or 3 (excessive blood flow) was detected (Table 3).

Of the 18 patients diagnosed with HCC, 14 exhibited a basket pattern (77%), and the remaining 4 showed tumoral neovascularization (23%). Tumor sizes measured by US ranged from 23-167 mm (mean, 56 mm). Maximum and minimum flow velocities ranged from 61-158 cm/s (mean 96.35 cm/s) and 0-53 cm/s (mean 32.4 cm/s), respectively. Flow grade ranged from 1 to 3 (mean=2.2). Peak systolic maximum ranged from 1.17-5.2 kHz (mean 3.8 kHz), and peak systolic minimum ranged from 0-3.1 kHz (mean 0.99 kHz).

Discussion

Applications of CDUS were developed by Namekawa et al. and used to investigate major cardiac vessels and intracardiac blood flow.[10] In 1985, Sukigara et al.[11] investigated 11 patients with HCC using CDUS.[12] Although angiography and US provide important diagnostic information for liver tumors, CDUS can provide additional information not revealed by either method.

In CDUS, the color of the blood flow within the mass depends on the flow rate in the vessel and not on vessel diameter or blood volume. Therefore, even thin vessels whose blood flow velocities are not visible on B-mode imaging can be visualized with CDUS, allowing spectral analysis and acquisition of quantitative data.

Our study was based on the Tanaka et al.[5] classification.[9,10] According to this classification, four signs can be identified in liver tumors using CDUS; the basket pattern and tumoral vascularization are characteristic findings of HCC. These two signs were not observed in hemangiomas or metastatic liver tumors. In our study, the sign of tumoral vascularization with a basket-like pattern was found only in cases of HCC, and this result is consistent with the findings of Tanaka et al.[5,9,13,14]

Ueno et al.[9] reported that they could not detect CDUS blood flow in HCC cases smaller than 2 cm,whereas Tanaka et al.[5] detected CDUS blood flow in five cases smaller than 2 cm, attributing this to the greater technological capability and sensitivity of the CDUS device they used. Taylor et al.[10] reported high flow velocity in cases of HCC and attributed this finding to wide pressure gradients across arteriovenous shunts within the tumor. Tanaka et al.[5] reported that the maximum flow velocity in tumor arteries ranged from 70 to 90 cm/s. In our study, although a wider range (61-158 cm/s; mean 96.35 cm/s)was observed, the mean values were comparable.

The direction of flow within the tumor was pulsatile in 13 cases (72%) and continuous in 5 cases (28%). Tanaka et al.[5] reported pulsatile flow in 80% of cases and continuous flow in 20%, indicating that the findings of our study are similar to theirs.[8,11]

The absence of a basket pattern and tumoral vascularization in hemangiomas on CDUS significantly differentiated hemangiomas from HCC; therefore, CDUS can be used in the differential diagnosis between hemangiomas and HCC. In our hemangioma patients, a spot pattern was observed in seven cases and a detouring pattern in one case. In one hemangioma case, no Doppler signal was detected.[7,11]

Among five control-group cases with liver metastases, tumoral neovascularization was observed in three and a detouring pattern in two. Maximum blood flow velocities ranged from 7 to 125 cm/s (mean, 59.12 cm/s). Continuous flow was observed in six hemangioma cases. None of the benign lesions other than hemangiomas (abscesses, hepatic cysts, hydatid cysts, and others) showed Doppler shifts or pathological signals.

Overall, among the 39 cases showing color Doppler flow, 26 were malignant (representing 96% of all malignant masses), and 13 were benign (representing 13.6% of all benign masses). Mean maximum blood flow velocities ranged from 7-158 cm/s in malignant lesions and 6-39 cm/s in benign lesions. Statistical comparison of mean blood flow velocities revealed highly significant differences between benign and malignant masses (t: 8.15, p<0.001) and between hepatomas and hemangiomas (t: 3.38, p<0.001). There was also a significant difference (p<0.05) between hepatomas and metastatic cases.

In the study, 21 patients with primary liver tumors (18 with HCC and 3 with cholangiocarcinoma) received IV Levovist (400 mg/mL, 20 mL) after color Doppler examination; their CDUS evaluations were then repeated. Flow patterns and signal intensity values obtained after IV administration of microparticle suspension (Levovist; galactose + palmitic acid) were compared separately with those obtained by conventional CDUS and Power Doppler US examinations.[6,8,15]

In 13 cases, significant differences were observed in lesion vascularization, Doppler findings, and flow velocities after IV Levovist administration. In these cases, conventional CDUS showed a flow grade of 1 (normal organ blood flow) before administration and grades 2 (increased blood flow) or 3 (excessive blood flow) after administration.

Across all cases, the application of Levovist during conventional CDUS resulted in varying degrees of clarification of the specific and pathognomonic flow patterns of tumor vascularization, particularly at the lesion periphery and within the lesion, manifesting as increased Doppler signal. Compared with the Power Doppler feature, only five cases demonstrated a significant signal increase or other findings that would result in a diagnostic change.[6,8,15]

According to the results of these Doppler examinations, although intravenous administration of microparticle suspensions such as Levovist did not produce a statistically significant difference in advanced CDUS devices with Power Doppler features, evaluation of the five responsive cases suggests that it is more effective, particularly for diagnosing primary liver tumors located deep within the liver and smaller than 3 cm. However, with conventional CDUS devices, IV Levovist increases Doppler signal intensity to varying degrees (p<0.05).

According to our study results and the Tanaka et al.[5] classification, the possibility of HCC should be considered in cases showing a basket pattern and tumoral vascularization, whereas hepatic hemangioma should be considered in cases showing a spot pattern. Color-flow appearance and neovascularization are observed on CDUS in 90-100% of malignant masses. However, the absence of a Doppler signal does not rule out malignancy. When maximum flow velocities are compared statistically, a significant difference is observed between malignant and benign liver masses.[9,11,15]

In conclusion, CDUS examinations provide important information for the differential diagnosis of liver tumors, based on blood-flow velocities and flow-pattern characteristics. However, CDUS may be inadequate for imaging blood flow when tumors are located deep within the liver parenchyma. Therefore, there is a need for CDUS technologies capable of evaluating smaller and deeper tumors, detecting blood flow velocity in very thin vessels, and employing echocontrast agents to significantly increase Doppler signal intensity.

selective celiac and hepatic artery DSA examinations of patients with primary liver tumors (18 HCC and 3 cholangiocarcinoma) revealed arterial enlargement and elongation, coarse neovascularization, vascular ponding, and intratumoral AV shunts in HCC cases. In our study, 14 of the 18 HCC patients exhibited intense neovascularization, pathological staining, contrast enhancement, and stretched abnormal neovascularization around necrotic areas; total hypovascularity was observed in four cases. When these findings were compared with Color- and Power-CDUS results obtained after IV administration of Levovist 400 mg/mL (20 mL), a significant correlation with digital selective angiography findings was observed.[5,8]

Evaluation of vascularity in primary liver lesions by selective celiac and hepatic artery DSA examinations demonstrated a strong correlation and agreement with color and power CDUS findings obtained after administration of Levovist. Fujimoto et al.[12], demonstrated that pulsatile arterial flow and Doppler flow-pattern findings were significantly correlated with arterial angiography results in HCC patients who received IV SH-U-508A contrast agents at three different concentrations (200, 300, and 400 mg/mL).

In that study, administration of the contrast agent SH-U-508A at 400 mg/mL IV increased the prominence of intratumoral arterial flow-pattern features by 83% in HCC patients. Particularly in HCC lesions smaller than 3 cm, the contrast agent significantly enhanced intratumoral flow signals, increasing their intensity.[8,13,16]

In the present study, a basket pattern was observed in the majority of HCC cases, which is consistent with previous reports. Similar vascular patterns and increased peak systolic velocities in malignant liver lesions have been reported in earlier studies. These findings support the concept that malignant tumors tend to exhibit arterial vascularization that is more chaotic and more prominent than that of benign lesions. The significant increase in Doppler signal intensity after contrast administration further emphasizes the role of contrast-enhanced Doppler US in differentiating malignant from benign hepatic tumors.

Digital selective angiography did not reveal intratumoral arterial flow in 15 cases of hypovascular HCC (73%). Focal nodular lesions, particularly those smaller than 2 cm, cannot be reliably distinguished on angiography because of insufficient contrast enhancement. Metastatic lesions can be visualized as hypovascular areas in the parenchymal phase, although intratumoral vascularization may not be detected, they can appear surrounded by relatively enlarged or tortuous arterial structures.

In all cases, intrahepatic blood supply and Doppler signal intensity were enhanced in conventional color Doppler sonographic examinations after IV administration of the SH-U-508A (Levovist®) contrast agent (400 mg/mL).[6,15,17] Color and Power Doppler sonography are now widely used in the differential diagnosis and evaluation of the hemodynamic characteristics of hepatic tumors. As non-invasive methods, they provide important diagnostic information for HCC and other intrahepatic parenchymal lesions and enable the detection of arterial flow characteristics in hypervascular lesions. Wilson SR et al.[17] reported diagnostic accuracies of 85–92% when qualitative CDUS values obtained after IV contrast administration were evaluated using an algorithm-based approach.[16,17]

Beyer et al.[18] differentiated focal benign from malignant hepatic mass lesions by quantifying Doppler blood flow, blood volume, and peak enhancement, reporting receiver operating characteristic (ROC) values of 0.97, 0.96, 0.98, and 0.76 (n = 20).

With further technological improvements in color and power Doppler systems, these Doppler methods may provide information comparable to CTA and digital selective angiography. However, the main limitations of CDUS include the influence of deeply located lesions and background vascular structures on flow signals, which may hinder adequate examination.[9,16,18]

In 1997, Tano et al.[9], investigated the enhancement of Doppler signal intensity using CDUS with a galactose-based contrast agent to differentiate HCCs smaller than 20 mm from hemangiomas and focal fatty areas. Intratumoral color Doppler images were evaluated before and after IV administration of the contrast agent SH-U-508A (Levovist®) (400 mg/mL).[6,13,18] After injection, intratumoral and peripheral vascularization were enhanced in all HCC cases and in two hemangioma cases. They reported that enhancement of Doppler signal intensity using the SH-U-508A contrast agent may be useful in the differential diagnosis of small hyperechogenic HCC lesions from other hyperechogenic parenchymal lesions (mainly hemangiomas and focal fatty areas).[6,16,17]

Recent single-center investigations, including a study by Gatos et al.[19] that proposed a classification algorithm for intrahepatic lesion contrast patterns using computer-assisted evaluations (n=52), have reported diagnostic accuracy rates for Doppler US reaching up to 90.3%.

Furthermore, a clinical study conducted by Goertz et al.[20] (n=33) demonstrated that quantified contrast intensity parameters obtained during the late phases were significantly lower in malignant focal liver lesions than in their benign counterparts.

This phenomenon is attributed to the rapid washout of Doppler contrast from the lesion, which is currently regarded as a well-established qualitative criterion for malignancy.

In a subsequent study (n=148), Wildner et al.[21] quantified late-phase Doppler contrast enhancement patterns across various tumor subgroups—including hepatic focal nodular hyperplasia, HCC, cholangiocellular carcinoma, and hepatic metastases of breast, pancreatic, and colon cancers—revealing statistically significant differences among these cohorts.

Both maximum and minimum flow velocities were significantly higher in malignant lesions than in benign lesions ($p<0.05$). Pulsatile flow patterns were more frequently observed in malignant tumors. Following Levovist administration, Doppler signal intensity increased in benign and malignant lesions, although the increase was statistically significant only in malignant lesions. These findings indicate that contrast-enhanced Doppler US improves the detection and characterization of malignant vascular patterns.

Measurements of flow were obtained at locations that were both central and peripheral in 9 cases, central only in 5 cases, and both inside and outside the tumor in 2 cases.

The enhancement of Doppler signal intensity following intravenous contrast administration may provide additional diagnostic value in cases where baseline Doppler findings are inconclusive. Therefore, contrast-enhanced Doppler US may serve as a useful adjunct in the differential diagnosis of liver tumors, particularly for distinguishing malignant lesions based on vascular characteristics.

Study Limitations

Statistical power could be improved with a larger sample size. Doppler ultrasonographic RI and PI values could also be included. Hepatocyte-specific contrast agents such as Gd-EOB-DTPA could improve correlation between contrast-enhanced dynamic liver MRI and multislice CT imaging.

This study reflects a single-center clinical experience; multicenter studies could broaden the scope.[15,21,22]

Future research involving larger cohorts should evaluate perfusion quantification parameters using intravenous contrast-enhanced Doppler imaging to identify the most effective parameters for differentiating malignant from benign liver lesions.

Additionally, it is imperative to establish statistically significant correlations with standard radiological and diagnostic references, such as histopathological examinations and dynamic liver MRI.

The advent of novel intravenous contrast agents for Doppler US and innovative particulate chemical solutions holds substantial promise to improve diagnostic accuracy in differentiating malignant from benign parenchymal lesions.

Conclusions

With conventional color Doppler sonography, arterial flow and Doppler patterns can be visualized more clearly when contrast agents are used at higher concentrations, and findings can be correlated with selective digital angiography.

As new contrast agents and advanced technologies for IV contrast-enhanced CDUS are developed, and as dynamic CT, MRI, and invasive DSA advance, the differential diagnosis of intrahepatic mass lesions will become clearer, and treatment protocols will be determined more accurately. Technological advancements in Doppler US devices are expected to further contribute to this field.

Ethics

Ethics Committee Approval: The study was approved by the Türkiye High Specialisation Hospital Chief Medical Officer Training and Planning Commission. All procedures involving human participants were conducted in accordance with the ethical standards of the institutional and/or national research committees and with the 1964 Declaration of Helsinki and its later amendments or comparable ethical standards (approval no.: 80576354-050-99/169, date: 29.05.2019).

Informed Consent: Written formal consent for the publication of scientific data and related information has been obtained from all patients included in this scientific study (i.e., the study participants or, where applicable, their first-degree relatives) and has been recorded in the hospital database.

Footnotes

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