Original papers

Contrast enhanced ultrasound in the assessment of focal liver lesions

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Abstract:
The aim of this paper was to present our experience regarding an investigation into 100 focal liver lesions consecutively evaluated in the Department of Gastroenterology Timișoara.

Patients and methods: we included 100 consecutive contrast enhanced ultrasonographies (CEUS) performed in patients with focal liver lesions. The arterial phase was considered to be between 10-35 seconds from the IV administration, the venous phase between 35-120 seconds, while the late phase was considered over 120 seconds.

Results: We analyzed 100 lesions from 82 patients. In 64 cases the patients were known to have liver cirrhosis. According to the CEUS description the lesions were classified as follows: 17 hemangiomas, 3 focal nodular hyperplasia, 2 adenomas, 3 fluid collections, 1 case of normal liver, 6 cases of regenerative nodules, 24 hepatocellular carcinomas (HCC), 7 HCCs incompletely treated percutaneously, 16 completely treated HCCs, 10 cases of liver metastases; in 11 cases the lesions could not be classified according to CEUS criteria.

In conclusion: CEUS is a promising method for the evaluation of liver focal lesions, which can replace CT or MRI in many cases. In 11% of the evaluated cases the CEUS pattern was not typical for any specific liver lesion.

Key words: contrast enhanced ultrasound, liver lesions, hepatocellular carcinoma

Introduction

Transabdominal ultrasonography is the easiest imaging technique for liver evaluation. It is a “real time” method, quick, affordable, noninvasive and repeatable, if necessary. On the other hand, it is operator dependent and the discovery of a focal liver lesion usually requires extra investigations. Regardless if the lesion is found randomly, in a healthy patient, or in a patient with a known chronic liver disease or a malignant pathology, the differential diagnosis of focal liver lesions (FLL) can become difficult.

Modern imaging methods like MRI and CT, both using contrast enhancing agents, are useful for diagnosis, being able to characterize the lesions seen on ultrasound and, at the same time, to detect other focal liver lesions. These methods evaluate the lesions only in predetermined moments in time, reported via the injection of the contrast agent (thus obtaining static images of the arteries, veins or parenchyma). They are also expensive and furthermore CT is irradiating.

Contrast enhanced ultrasound (CEUS) is a relatively new imaging method. Its great advantage is that it is a “real-time” imaging technique, just like the standard ultrasound, thus allowing the characterization of the vasculature of the examined lesions, in our case, FLL, allowing their differential diagnosis.

The aim of this paper is to present our experience with CEUS for the evaluation of 100 FLL within the Department of Gastroenterology and Hepatology, Timișoara.

Material and method

We retrieved from our ultrasound database all patients diagnosed with FLL, in whom CEUS was performed between October 2008 and March 2009 (we excluded the patients in whom CEUS was performed for the evaluation of other organ lesions: pancreas, spleen, digestive tube, kidney etc.). We selected 100 CEUS examinations performed for the characterization of FLL.

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All the CEUS examinations were performed by 4 senior operators (1 expert level and 3 level II ultrasonographers, all specialists in gastroenterology) on a Philips HD11 XE ultrasound system. All the investigations were performed according to the following protocol: firstly, standard ultrasound examination and Power Doppler examination (if necessary) were performed; followed by a 2.4 mL i.v. bolus of a second-generation contrast agent, (SonoVue®, Bracco, Milan, Italy), after which a 10 mL bolus of saline solution was injected.

The CEUS examination was then performed by one of the operators, assisted by a second one. All the examinations were documented by capture of loops or still images in order to illustrate the arterial phase, the venous phase and the late phase. The enhancement pattern of the FLL was compared to that of the adjacent normal liver parenchyma. In order to avoid false negative results caused by parvusus injection of SonoVue, we verified the presence of the contrast agent in the vascular system by looking for the aorta enhancement.

It was considered that the arterial phase starts 10-20 seconds after the injection of the contrast agent and lasts another 10-15 seconds from the injection, followed by the venous phase that lasts from the 35 to the 120 second, and, finally by the late phase that starts 120 seconds after the injection. The lesions were characterized according to the enhancement following contrast as: enhancing (hyperechoic), isoenhancing (isoechoic) when the enhancement was similar to that of the adjacent parenchyma, and with no enhancement (hypoechoic). The echogenicity decrease during the investigation was characterized as “wash-out”.

We assessed the CEUS diagnosis, if the lesion appeared on a normal or pathologic liver, and, for lesions also evaluated by means of different imaging methods, we followed up the techniques’ concordance.

**Results**

The 100 FLL which were assessed were discovered in 82 patients, 43 women and 39 men. Some of these patients had more than one lesion. Each of these lesions was characterized by CEUS. In some cases of hepatocellular carcinomas percutaneously treated, the patients were followed up post therapy 30 days and then each 3 months.

In 2 cases the contrast agent was not detectable in the heart and the aorta. This was considered an injection accident (parvusus injection). The injection of contrast agent was repeated in order to perform a new evaluation.

In 33 cases, the FLL were discovered in a normal liver, while in 64 cases the patients had liver cirrhosis and in 3 cases only chronic hepatitis.

According to the CEUS characterization, the FLLs were classified as follows:

- 17 haemangiomas, with typical peripheral, relatively late enhancement, in the late phase the lesion being enhanced as compared to the surrounding hepatic tissue (fig. 1);

**Fig. 1.** BF, 53 year old female, asymptomatic, inactive HBsAg carrier.
A. Standard abdominal ultrasound – in the left liver lobe, inhomogeneous focal lesion 3.5 cm in diameter, with neat contour and slightly hyperechoic border. Diagnosis – possible hemangioma.
B. Arterial phase – Peripheral hyper-enhancement.
C. Portal-venous phase – Complete centripetal filling.
Conclusion – Hemangioma.
Fig. 2. FD, 23 year old female, asymptomatic.
A. Standard abdominal ultrasound – in the left liver lobe, a slightly hyperechoic focal lesion 4 cm in diameter, neatly enough defined.
B. Arterial phase – Complete, rapid hyper-enhancement.
C. Portal-venous phase – Hyper-enhancing lesion.
D. Late phase – Iso-enhancing lesion.
Conclusion – Focal Nodular Hyperplasia

- 3 cases of focal nodular hyperplasia (FNH), with early enhancement in the arterial phase (sometimes with visible central artery), with complete enhancement of the lesion in the venous and late phases (fig 2);
- 2 cases of adenoma, with moderate enhancement in the arterial phase, the lesion continuing to be enhanced in the venous and late phases;
- 3 intrahepatic fluid collections (cysts or abscesses); they had no enhancement in either phase;
- One case, in which standard ultrasound examination revealed a strongly heterogeneous structure, overlapping on a chronic cholestatic liver disease, in which the issue of a possible multicentre HCC was raised, was characterized as normal liver by CEUS;
- 10 cases of liver metastasis (most often hypovascular), with lack of enhancement in all the 3 phases (possibly peripheral enhancement in the arterial phase with rapid “wash-out” in the case of hypervascular metastasis);
- 6 cases of nodules occurring on a cirrhotic liver were diagnosed as regenerative nodules, due to the similar behavior with the surrounding parenchyma after CEUS;
- 24 cases with hepatocellular carcinoma (HCC) (all in patients with liver cirrhosis) with typical behavior: with enhancement in the arterial phase and “wash-out” in the venous phase, the lesion becoming non enhancing in the late phase (Fig.3, 4);
- In 23 cases of HCC, CEUS was used for post-therapy follow-up, after RFA and PEIT. In 16 cases complete treatment was proven by means of CEUS (lack of enhancement), while in 7 cases partial enhancement (enhancement in some areas of the tumor) was an indicator of incomplete therapy, proving the need of further percutaneous procedures;
- In 11 cases the FLL could not be classified due to their atypical behavior following contrast.
Fig. 3. CA, 73 year old female, previously diagnosed with HCV liver cirrhosis.
A. Standard abdominal ultrasound – in the left liver lobe, an inhomogeneous lesion, hypoechogenic with hyperchogenic regions, approximately 4 cm in diameter.
B. Arterial phase – rapid hyper-enhancement.
D. Late phase – Total wash-out.
Conclusion – Hepatocellular carcinoma

Fig. 4. TI, 70 year old male, previously diagnosed with HBV liver cirrhosis.
A. Standard abdominal ultrasound – in the left liver lobe, an inhomogeneous lesion, hypoechogenic, approximately 6.5 cm in diameter, inhomogenous structure of the liver.
B. Arterial phase – rapid hyper-enhancement.
D. Late phase – Total wash-out.
Conclusion – Hepatocellular carcinoma
Discussions

The use of second generation contrast agents in ultrasonography is a method that still requires to be developed and improved, having a wider range of indications [1, 2], not to mention the advantages over other contrast enhancing imaging methods.

The advantages of CEUS are: it is a “real time” examining method, thus allowing a dynamic evaluation of the lesion’s vasculature. It can be performed over and over again, not harming the patient in any way. In addition, the quantity of contrast agent is extremely small, 2.4 ml, with almost no side effects (the rate of allergic reactions quoted in literature is only 0.001% in abdominal applications) [3].

The small quantity of contrast agent can also be considered a disadvantage. If used inappropriately (paravenous injection), due to the small quantity injected, no local signs appear. This is why an ultrasonographic check up should always be performed in order to ascertain that the contrast has reached inside the vascular system, so that the examination can be properly performed.

In our study, the main indications for using CEUS were patients with liver cirrhosis (probably because of the characteristics of our Department – a Gastroenterology and Hepatology one). As a general rule, every newly discovered nodule in a patient with cirrhosis should be considered as a possible HCC until proven otherwise. Still, even a patient diagnosed with liver cirrhosis could have a haemangioma or regenerative nodules. Of course, the treatment is completely different for the two types of pathology.

Currently, in our Department the strategy is to evaluate by means of CEUS, every newly discovered nodule found in the liver in a patient known with liver cirrhosis. If the patient has not been yet diagnosed with cirrhosis, then the first diagnostic method that should be used is liver stiffness measurement by means of transient elastography (FibroScan), a method known to have 90-95% sensitivity for diagnosis of liver cirrhosis.

In our department, the first line of therapy in HCCs smaller than 3-4 cm, without surgical indication, is percutaneous ethanol injection therapy (PEIT). After performing PEIT, CEUS is used again to see if the treated nodules are still enhancing after contrast (sign of incomplete therapy). If needed, the percutaneous therapy could be repeated in the same session. Our rule is to evaluate treated HCCs one month after therapy and then every 3 months, in order to be assured that the nodule is still not enhancing after contrast.

Regarding benign liver lesions, we have the greatest satisfaction when we diagnose a case of FNH that has a typical pattern of enhancement after contrast (rapid enhancement during the arterial phase, usually with the visualization of the nutritive artery, with persistent enhancement even if fading) during the portal phase and even the late phase [4]. That is also the case of hemangiomas with a typical centripetal enhancement that begins during the arterial phase and continues during venous and late phases [5]. The homogeneity of the lesion following contrast depends on the presence or absence of thrombosis that can occur inside the haemangioma.

Regarding patients suspected of having liver metastases, CEUS is useful for detecting these, as well as for evaluating their number and vascular pattern [6]. Metastases, as any other malignant liver lesions, are characterized by the fact that they are hypoenhancing during the portal as well as during the delayed phase [7]. In the arterial phase, metastasis can be either hypoenhancing in the periphery (hypervascular tumors) or hypoenhancing (hypovascular ones) [8, 9].

Large published clinical trials, (the German study - DEGUM and the French study - STIC) [10, 11] which compared the results of CEUS examination either with liver biopsy or with spiral CT or contrast MRI, demonstrated similar results regarding the sensitivity and specificity for the diagnosis of FLL. At least in Germany, this has led to a change of the diagnosis algorithm of FLL. FLL firstly seen by standard ultrasound should be evaluated by means of CEUS. If the lesion could be characterized by using CEUS, then the evaluation was considered complete (the accuracy of CEUS for a correct diagnosis of FLL in the DEGUM study was 90.3%). Regarding more difficult lesions, other more expensive techniques such as CT or MRI should be used.

In order to improve our experience with CEUS, probably a morphological approach (as in the multicenter German study) or an imaging approach (spiral contrast CT or MRI, as in the French study STIC) should be considered, so that accurate diagnosis can be reached. In the future, we could save both money and time if a correct CEUS for FLL could be performed.

Regarding the cost of CEUS evaluation of FLL, the German study concluded that the price for CEUS ranges
between 101 and 186 Euros, with a mean value of 117 Euro, while contrast CT multislice is between 164-223 Euros and MRI between 219-259 Euro. The cost of a liver biopsy was valued at 99 Euros (it was demonstrated that the mean economy/patient investigated through CEUS would be 37-101 Euros).

EFSUMB issued in 2004 guidelines for the good practice of CEUS, updated in 2008 [1, 2]. These guidelines include all the indications for CEUS, instructions on how to use it, the devices that can be used, contraindications as well as possible side effects of SonoVue.

We believe that by introducing CEUS in clinical practice in more Romanian hospitals, a more rapid diagnosis of different FLL would be possible for the majority of patients, together with a reduction in cost and discomfort for both the patient and the medical system.

Conclusions

In our Department, in more than half of the patients, CEUS was used for the evaluation of FLL on a cirrhotic liver, both for primary diagnosis, as well as for the evaluation of percutaneous treatment results. The second indications for CEUS, according to frequency, were benign liver lesions (for example hemangiomas or focal nodular hyperplasia) and the third, the evaluation of patients suspected of having liver metastasis. CEUS evaluation was performed without side effects and allowed a final diagnosis in the majority of cases (only 11% remained without a clear diagnosis because they did not respect any CEUS pattern).

References


