

The role of contrast-enhanced ultrasonography with second generation contrast agents in the evaluation of focal splenic lesions

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Abstract

Abdominal ultrasound is the method of choice for first line evaluation of the spleen, allowing not only organ measurement and splenomegaly assessment, but it also detects possible focal lesions. But standard US is not able to answer an important question: whether the focal lesion is benign or malignant.

Contrast enhanced ultrasound (CEUS) with second generation contrast agents (SonoVue) primary allows the characterization of vascular pattern in focal lesions, its first indication being focal liver lesions assessment. The method is studied also for the spleen, in which CEUS allows the description of different focal lesions.

There are 2 main indications for CEUS spleen assessment. First in trauma patients in which standard US was performed and possible spleen lesions or peritoneal liquid were found; or clinical or laboratory signs indicating a possible spleen lesion are present (EFSUMB guidelines). These indications are not discussed in this particular article. The second is for characterization of focal spleen lesions discovered by standard US, as well as for the follow up of patients with malignant hematological disorders.

Available published data confirm that CEUS examination using second generation contrast agents is a promising method also for the characterization of splenic lesions.

Key words: contrast enhanced ultrasound, SonoVue, spleen, focal lesions

Rezumat

Ecografia abdominală este metoda de primă alegere în evaluarea splinei, deoarece permite atât măsurarea organului și aprecierea splenomegaliei, dar și detecția de leziuni splenice focale. Dar ecografia standard nu poate răspunde la o întrebare importantă: dacă leziunea depistată este benignă sau malignă.

Ecografia cu substanțe de contrast de generația a doua (SonoVue) (CEUS) permite caracterizarea patternului vascular al formațiunilor focale, prima indicație fiind evaluarea leziunilor circumscrise hepatice. Metoda este studiată și pentru evaluarea diferitelor leziuni splenice focale.

Exista două indicații principale pentru evaluarea CEUS a splinei. Prima se referă la pacienții care au suferit traumatisme și la care ecografia standard a descris posibile leziuni splenice și lichid intraperitoneal; sau în cazul în care datele clinice și de laborator sugerează o posibilă leziune splenică (EFSUMB guidelines). Aceste indicații nu fac subiectul acestui articol. A doua privește caracterizarea leziunilor circumscrise splenice depistate de ecografia standard precum și pentru urmărirea pacienților cu patologie hematologică malignă.

Datele publicate până în acest moment confirmă CEUS ca o metodă promițătoare de caracterizare a leziunilor focale splenice.

Cuvinte cheie: ecografia cu substanțe de contrast, SonoVue, splina, leziuni focale

Contrast enhanced ultrasound (CEUS), with second generation contrast agents (SonoVue) primary, allows the characterization of vascular pattern in focal lesions, its first indication being focal liver lesions assessment. The method has almost no side effects, and after it was introduced in the routine evaluation of the liver, the number of its applications increased. Some of these are still “off label”, supplementary studies being needed for further validation. This is also the case of spleen, in which CEUS allows the description of diverse focal lesions.

CEUS assessment of the spleen with second generation contrast agents implies, just like for other indications, a low mechanic index [0.06-0.08], using a 2.4-4.8 ml SonoVue. The examination begins with standard ultrasound (US) evaluation, followed by the injection of the contrast agent and the evaluation of the vascular phases using the contrast module.

CEUS evaluation of the spleen is a simple enough method, due to the fact that the spleen is quite superficially located, it has a homogenous structure with good contrast enhancement, not to mention that the method is non-invasive and it has a very good accuracy [2,3].

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- trauma patients in which standard US was performed and possible spleen lesions or peritoneal liquid were found; or clinical or laboratory signs indicating a possible spleen lesion are present [EFSUMB guidelines]. These indications are not discussed in this particular article.

- characterization of focal spleen lesions discovered by standard US, as well as for the follow up of patients with malignant hematological disorders [4].

Normal spleen

The normal vascular pattern of spleen enhancement following contrast must be described in order to be able to evaluate the CEUS utility for focal spleen lesions assessment.

Immediately after contrast agent injection, the arterial enhancement begins, lasting for approximately 12 seconds, followed by an inhomogeneous enhancement of the parenchyma suggesting a “zebra” pattern, similar to that obtained on contrast CT or MRI [5]. In the first minute after injection the small splenic arteries can be visualized, after approximately 50 seconds the parenchyma begins to be homogenous, the enhancement lasting up to 5-7 minutes (fig 1, fig 2).

The parenchymal enhancement of the spleen is longer than the intravascular persistence of contrast, probably due to contrast sequestration in the parenchyma [6]. As

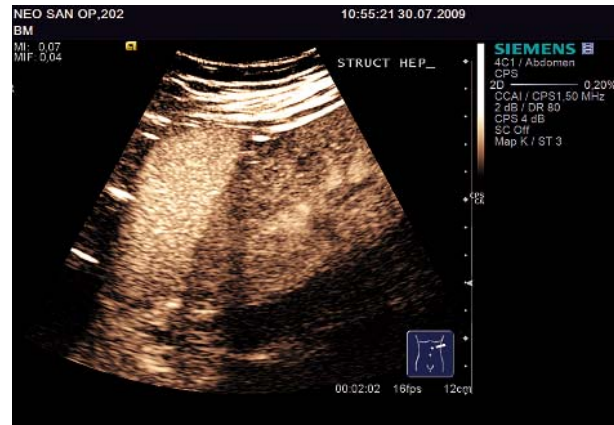


Fig 1. CEUS aspect of the spleen in the late phase as compared to the left kidney – normal aspect

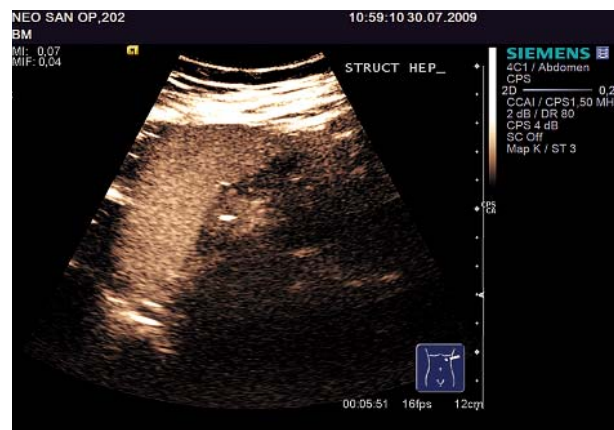


Fig 2. CEUS aspect of the spleen in the late phase – normal aspect

compared to the nearby kidney, the spleen appears as hypoenhancing in the early arterial phase and hyperenhancing in the late phases [4].

There are several focal lesions of the spleen in which CEUS examination might be helpful, such as: splenic infarction, abscesses, tumors and accessory spleens. We will try to describe those lesions.

1. Splenic infarction

In standard US examination, the splenic infarction appears as a hypoechoic area with triangular shape, the base facing the splenic capsule and the tip towards the spleen’s hilum. In standard US, the infarcted area may appear clearly hypoechoic, slightly hypoechoic or isoechoic as compared to the surrounding tissue [4], thus being extremely difficult to diagnose.

As soon as the contrast agent has been injected, the infarcted area becomes clearly hypoechoic as compared to the surrounding tissue, especially in the late phase,

with margins that can be clearly or not so well outlined and with either homogenous or inhomogeneous structure [4]. During the arterial phase, the amputated artery may be seen near the tip of the infarcted area, as well as a peripheral, marginal enhancement area. In atypical shaped infarctions (round or oval), the diagnosis is suggested by the lack of enhancement inside the infarcted area, while in massive infarctions that affect almost the entire spleen, there is a lack of enhancement of the entire organ as compared to the nearby kidney [4,7,8].

2. Abscesses of the spleen

Spleen abscesses usually appear as hypoechoic areas in standard US examination. Following contrast injection, they present a ring-like, round, peripheral enhancement, especially in the late phase, with multiple enhancing septas and a central, non-enhancing area. On CEUS, subcapsular abscesses look like anechoic areas with enhancing margins [4].

3. Splenic tumors

On standard US, splenic hemangiomas appear as hyperechoic masses [7,8]. Following contrast they become isoechoic as compared to the surrounding parenchyma and they remain isoechoic in the late phases. In cavernous angiomas, a centripetal fill-in is present, with intense and prolonged enhancement [4].

4. Lymphomas and splenic metastasis

Lymphomas and splenic metastasis have a similar behavior on CEUS. Usually, in standard US they appear like iso or hypoechoic masses [7,8]. Following contrast they become clearly hypoechoic as compared to surrounding parenchyma (fig 3) [4].

Splenic tumors enhance less than the surrounding normal parenchyma, and, sometimes, in the early phase, vessels can be seen, entering from the periphery to the centre of the lesion [4]. Post effective chemotherapy, lesions may become anechoic with no visible vessels in the periphery or inside the lesion.

In a study performed on 100 consecutive patients diagnosed with Hodgkin lymphoma, Picardi *et al.* [9] demonstrated that harmonic compound US with contrast enhancement for the characterization of possible nodules provides a higher sensitivity than CT or FDG PET does in the detection of splenic involvement by Hodgkin lymphoma.

Rossi *et al.* [10] demonstrated that for the differential diagnosis between benign and malignant lesions of the spleen, the most useful criteria is the hypoechoic aspect during the wash-out phase, associated with the presence of sinuous vessels surrounding the lesion.

5. Accessory spleen

On CEUS accessory spleens have similar behavior to the normal spleen. During the early phase, the nutritive artery entering into the accessory spleen, emerging from the spleen hilum, can be visualized, thus allowing the differential diagnosis with other perisplenic lesions [4,11].

CEUS examination of the spleen has some limitations since most of the splenic lesions are hypovascular, thus hypoechoic, being difficult to differentiate even after contrast injection. Also, subdiaphragmatic lesions are difficult to evaluate, requiring the patient's cooperation for the breathe-in part, lesions from these areas being easy to overlook, as well as those covered by the gas from the splenic angle of the colon.

Having considered all these facts, Görg recommends that CEUS should be used for the differential diagnosis in the following situations [12,13]:

1. Perisplenic tumors - in order to differentiate them from accessory spleens;
2. Small spleen – to diagnose asplenia and functional hyposplenia;
3. Inhomogeneous spleen - to diagnose focal splenic lesions;
4. Splenic tumors accidentally discovered and for the diagnosis of hemangiomas;
5. To confirm or infirm the presence of a possible abscess, hematoma or spleen infarction;
6. In patients with abdominal trauma - to diagnose or exclude a possible splenic lesion.

Standard US is not able to answer an important question: whether the lesion is benign or malignant.

Studies performed on animal models [14] showed that extensive to moderate hypoechogenicity was only seen in malignant lesions during wash-in, at peak enhancement, and during wash-out ($p=0.0001$, odds ratios: 37.9 [95% CI 4.5-316.5], 66.4 [95% CI 8.0-551.1], and 36.9 [95% CI 4.4-308.4]). Also, in another study [10] the most useful criterion associated with malignancy was the hypoechogenicity of the lesion in the wash-out phase combined with the presence of tortuous feeding vessels. On the other hand, a study performed on 35 lesions of the spleen diagnosed by using conventional ultrasound techniques on 35 patients [15] demonstrated typical findings for benign lesions with 2 arrival patterns: no contrast enhancement (neither in the early, nor in the parenchymal phase; $p<0.05$) and the beginning of contrast enhancement in the early phase, followed by contrast enhancement in the parenchymal phase 60 seconds after injection. In contrast, the combination of contrast enhancement in the early phase followed by rapid wash-out and demarcation

Fig 3. Metastases of the spleen



Fig 3. a, b. Standard ultrasound – hypoechoic focal lesion in the middle part of the spleen, around 2 cm, in a patient diagnosed with a right adrenal gland tumor

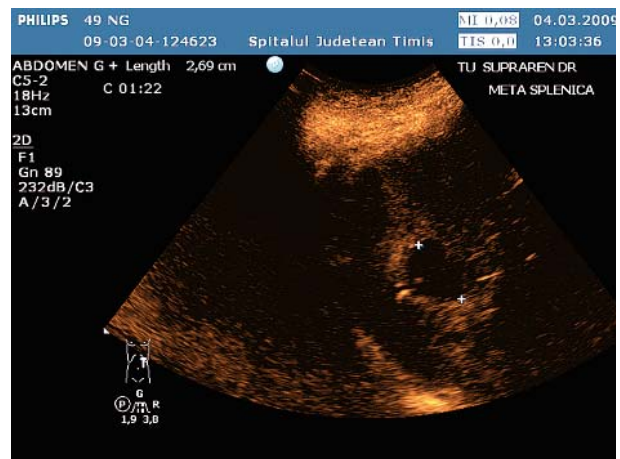


Fig 3. c, d. Portal phase – the splenic lesion has no enhancement in the arterial and portal phase

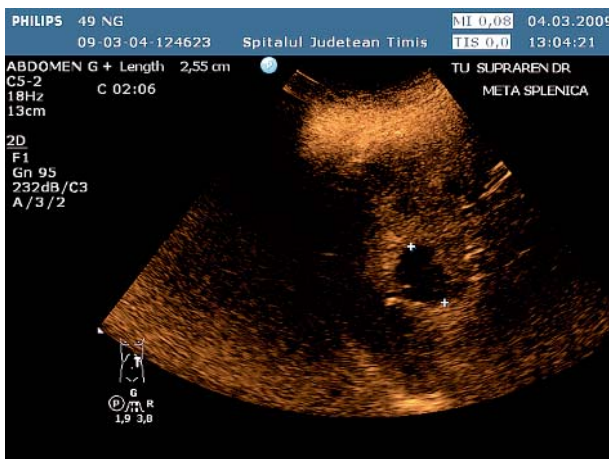


Fig 3. e, f, g. Late phase – the splenic focal lesion has also no enhancement in this phase, and it is well defined in this phase (Fig 3. g → see on page 65)

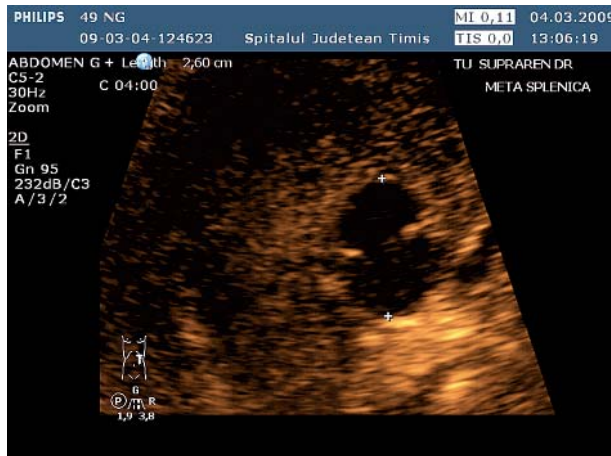


Fig 3. g Late phase

of the lesion without contrast enhancement in the parenchymal phase (60 seconds after injection) was typical for malignant lesions ($p < 0.001$).

In conclusion, available published data confirm that CEUS examination using second generation contrast agents is a promising method also for the characterization of splenic lesions.

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