Abdominal PICTORIAL ESSAY

Contrast enhanced sonographic study of the spleen

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ABSTRACT

The spleen shows a variety of pathological entities. Ultrasound (US) is the first imaging modality performed for its assessment. When it is not conclusive, the addition of intravenous contrast agents improves performance and aids in narrowing the differential diagnosis. Benign entities include cysts, accessory spleen, infarcts, abscess, benign masses and trauma. In most of these cases Contrast Enhanced US (CEUS) can reach a diagnosis. Malignant entities include lymphoma and metastases, where CEUS is also useful with some limitations. The technique is performed easily, fast, with no radiation, even in patients with renal insufficiency. This article reviews CEUS technique, normal and abnormal findings in the spleen, indications and limitations.

KEY WORDS | spleen; ultrasound; contrast agent; CEUS

1. Introduction

Ultrasound (US) is usually the first imaging method used to evaluate the pathology of the spleen. Often baseline US is adequate for setting a diagnosis. In more complex cases, the addition of contrast agents facilitates detection and characterisation of lesions. Even though in computed tomography (CT) and magnetic resonance (MR) imaging the injection of contrast agents has been well-grounded and their use has been assimilated in routine imaging examinations, the same does not apply for Contrast Enhanced US (CEUS), which is still being used in few, specialised centers. CEUS of the spleen is used after baseline, non-enhanced scanning for specific indications. It is easy to perform in everyday clinical practice and answers many different clinical and imaging questions.

2. Anatomy

The spleen measures 10-13 cm (length) x 7 cm (width)

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x 3-4 cm (thickness), weighing 150-200 gr and located under the 9th-12th left ribs, between the gastric fundus and the left hemidiaphragm [1]. It is kept in position by the splenophrenic and the gastrosplenic ligaments. The spleen belongs to the lymphatic system, showing only efferent lymphatic vessels. Blood flow is supplied by the splenic artery, a branch of the coeliac artery. Blood from the spleen drains through the splenic vein, which joins the superior mesenteric vein to form the portal vein.

3. Unenhanced ultrasound vs. CEUS

Splenic echogenicity is normally homogeneous on baseline unenhanced US, with calcifications that can be seen along the splenic artery branches usually of no clinical significance. Focal lesions are less common in the spleen in comparison to other solid organs [2] and benign pathology is more common than malignant [3]. B mode accuracy for the characterisation of focal splenic lesions has been described as low as 50% [4], with Doppler US not adding substantial help. Similarly, the sensitivity of baseline unenhanced US is inferior to that of CT or MR. This sensitivity improves after the injection of US contrast agents [5]. Lesions undetected on baseline US can be seen on CEUS with a sensitivity of 90% and a specificity of 100% in comparison to CT for lymphomatous lesion detection [6]. For the detection of splenic metastases, the addition of US contrast agents has been shown to result in a detection rate increase of 38% [7].

Moreover, CEUS has proved to have higher sensitivity in comparison to CT or FDG PET for detecting Hodgkin lymphoma lesions [8]. However, as in all imaging examinations, knowledge of clinical information is crucial for image interpretation [4]. Readers with access to patient clinical background have proved to perform better in comparison to those with no clinical knowledge on B mode (accuracy 70-74%), as well as on CEUS (accuracy 91-92%), while CEUS sensitivity, specificity, positive and negative predictive values reached 100%, 83.8%, 87.8% and 100% respectively for differentiating between benign and malignant lesions when clinical information were available [4]. These results are comparable to those of 18F-FDG PET/CT [9]. Other studies have also reached high CEUS values of sensitivity, specificity and accuracy (91.1, 95.0 and 92.0% respectively) [10].

The commonest benign entities are cysts. Less common benign lesions include infarcts, haemangiomas, abscesses, pseudotumours, hamartomas, parasitic and tuberculous lesions [2, 11]. The commonest malignancies are lymphoma and metastases.

On baseline US, benign lesions usually appear solitary and hypoechoic. Gas or calcifications may occasionally be seen [3, 12-14]. Simple cysts are anechoic. On the contrary, malignancies are often multiple, with high or mixed echogenicity, ill-defined borders or target-like appearance [3, 15]. These imaging features however are atypical [16]. Normal variants and injuries are also common. Often solitary lesions may appear to belong to the spleen, but are actually extrasplenic, usually lymph nodes next to the organ's hilum.

4. Indications for splenic CEUS

The European Federation of Societies for Ultrasound in Medicine and Biology (EFSUMB) in its 2011 Guidelines for the use of CEUS in non-hepatic indications [17] included the examination of the spleen for:

1. Characterisation of splenic parenchymal inhomogeneity or suspected lesions on conventional US
2. Confirmation of suspected splenic infarction
3. Characterisation of suspected accessory spleens or splenosis
4. Detection of splenic malignant lesions in oncologic patients when CT, MR or PET are contraindicated or inconclusive.

Fine needle biopsy has a considerable risk of complications, especially endoperitoneal haemorrhage. Therefore, a non-interventional diagnostic option like CEUS is of high essence in the case of the spleen. Tumefactive focal lesions, occasionally found in asymptomatic patients, are most often benign. A solitary and hyperechoic lesion is also probably benign, while new multiple and hypoehoic lesions in cancer patients tend to be malignant.

Unfortunately the combination of clinical information and sonographic images is not always sufficient for a safe differentiation between benign and malignant lesions [11]. In addition, CEUS has become a routine method for follow up in patients with haematological malignancies, and physicians have been increasingly requesting CEUS for follow up examination [18].

5. How is CEUS useful

In our experience, we have found that CEUS has proved to be helpful in the following ways:

1. On baseline US, the spleen may appear inhomogene-

ous, but focal lesions cannot be definitely detected: In this scenario, the addition of contrast agents results in clear demarcation of one or more suspected lesions that were not adequately outlined before contrast injection. This has proved helpful in cases of traumatic injuries, lymphoma manifestations, metastases and small infarcts. We have experienced cases of trauma patients where inhomogeneous splenic echogenicity and perisplenic fluid are seen on B-mode US, but no definitive injury is noted. On CEUS, splenic injuries and even extravasation are clearly seen, while fluid collections are better appreciated. In some cases, the patient has been sent straight to the operating room, with no confirming CT performed preoperatively. In this way, CEUS has helped save precious time, as well as reduce CT scanning. In lymphoma and metastases cases, the addition of CEUS has resulted in detection of lesions which would otherwise be missed on baseline US. Usually CT is subsequently performed and in most cases has confirmed CEUS diagnosis. Large infarcts pose no diagnostic problem on baseline US, but smaller ones may be overlooked. On CEUS, even small areas with no perfusion are clearly seen. This is especially useful for the patient, both for initial diagnosis as well as follow up, since infarcts can be complicated by haemorrhage, rupture, pseudocyst formation or infection, resulting in septic infarct and abscess.

2. ***A lesion is detected on unenhanced US, with a probable but not definitive diagnosis:*** In these cases, a lesion can be adequately characterised with CEUS and the patient does not need to undergo a CT scan, thus ionising radiation, time and money are saved. This scenario has proved helpful in haemangiomas, cysts and larger infarcts. Haemangiomas usually appear as echogenic lesions, similar to the well known hepatic appearance. With CEUS, their haemodynamic behaviour can be assessed as in multiple phase CECT or MR with no ionising radiation, less cost and much lower rate of contrast agent adverse reaction. Cysts with echogenic debris can be safely characterised with CEUS with no CT performed. Large infarcts are usually detected on baseline US. CEUS confirms absence of flow in infarcted areas better than colour Doppler and increases the Radiologist's confidence. CEUS can identify areas without contrast uptake in the arterial and venous phases in 100 % of cases [19, 20]. Due to this high diagnostic value of CEUS for infarcts, in our practice no additional CT scan is suggested if CEUS has detected an infarct.

3. One or more incidental lesions have been seen on CT or MR but no diagnosis is set: This is the case especially when CT-MR contrast agents cannot be administered due to allergic history or renal insufficiency. In these cases, CEUS is the only easy way to assess the haemodynamic behaviour of lesions, since US contrast agent(s) are not excreted by the kidneys and do not affect renal function, while their allergic reaction incidence is almost zero.

4. ***Parasplenic lesions:*** A lesion can be seen immediately next to the splenic parenchyma. Differential diagnosis usually includes accessory spleens and lymph nodes. On CEUS the first entity enhances parallel to the rest of the spleen, while the latter shows almost no enhancement. This differentiation is easily made with CEUS, again with no CT being performed.

5. ***Follow up of patients with an initial CT:*** Even if a patient has been subjected to a CT scan for the initial diagnosis, CEUS can be used for follow up, with no additional radiation exposure. We follow this practice in patients with trauma injuries, abscesses and infarcts, in order to evaluate possible reduction in size of lesions.

In all the above scenarios, the patient and the examiner can gain from the added value of CEUS by increase of baseline US diagnostic value, with increased confidence for the Radiologist, and avoiding (completely or its repetition) a CT scan.

6. CEUS examination technique

CEUS of the spleen is performed when baseline examination is inconclusive in order to establish a diagnosis [18]. When a lesion is spotted on B-mode US, CEUS examination is focused on the assessment of its haemodynamic behaviour post injection. In our institution, we use the second generation contrast agent SonoVue (sulfur hexafluoride microbubbles stabilised in a phospholipid cell-Bracco Imaging) at an intravenous dose of 1-2.4 mL [21], followed by a 10 mL normal saline flush. The drug is not excreted by the kidneys, therefore it can be injected in patients with renal insufficiency, while anaphylactoid reaction rate is much lower than the equivalent for CT and practically zero [22]. A simultaneous split screen setting, which is available in all latest technology US machines, allows at the same time imaging with and without the contrast agent, to facilitate the examiner's orientation. The technique is easy to perform and does not prolong the sonographic examination more than 10 min.

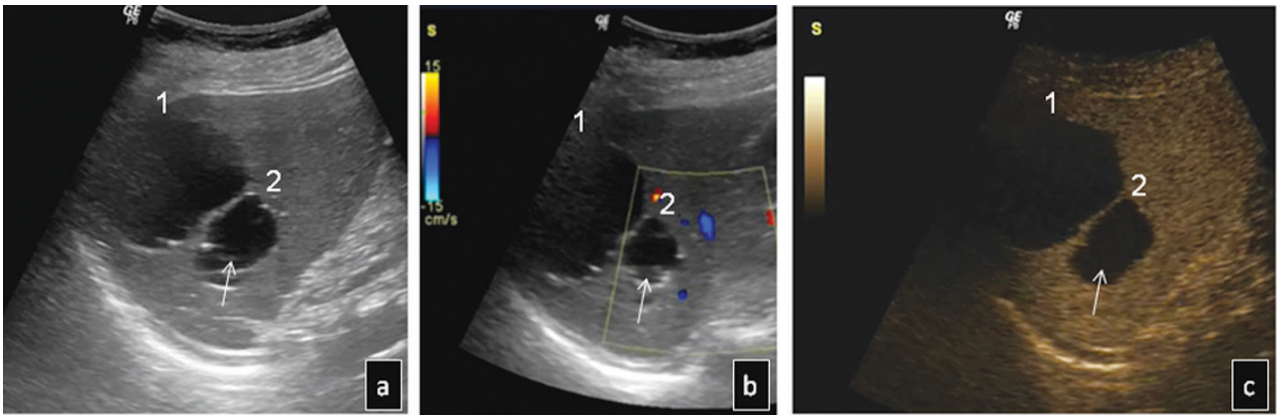


Fig. 1. *Simple splenic cysts: B-mode (a) and colour Doppler US (b) show two anechoic cystic structures of the spleen. Cyst 2 shows an echogenic part (arrows), which cannot be differentiated between debris and perfused tissue on baseline US, therefore contrast agent was added. On CEUS (c) this component shows no enhancement (arrow). Therefore it represents debris. CEUS confirmed the cystic nature of all lesions, which was not evident for cyst 2 before contrast injection*

7. Normal CEUS findings

After the administration of the contrast agent, enhancement begins very fast, around 12 sec post injection. Similarly to the zebra pattern seen on CT, this enhancement is initially inhomogeneous, caused by different uptake from the white and red pulp. Initially, small arteries radiating to the splenic hilum and the periphery of the organ enhance first. Venous enhancement is not rich [18], becoming homogeneous about 50 sec post injection and lasting for 5-7 min. After 2-3 min post injection, the splenic vein tree appears as an enhancing defect, since the spleen acts as a filter for microbubbles [22]. Splenic enhancement is longer than the other abdominal solid organs due to its parenchymal uptake [23]. In comparison to the left kidney, which enhances intensely but for a shorter period, the spleen is hypoechoic in the early phase and hyperechoic in the late phase [18].

Benign enhancement patterns include: **a.** no enhancement (in the case of cysts), or **b.** rapid contrast uptake (wash-in) followed by insisting late phase enhancement (no wash-out) in the case of lesions such as haemangiomas, where there is no need of further imaging for confirming the diagnosis when characteristic findings are observed on CEUS [24]. Malignant CEUS enhancement patterns combine diffuse or peripheral arterial uptake with rapid and intense wash-out, usually seen in metastasis or lymphoma [10]. However, these patterns are only suggestive and benign lesions, such as hamartomas and haemangiomas, can show wash-out and be falsely characterised as malignant.

8. CEUS appearance of common splenic lesions

8.1 Cystic lesions

Cystic splenic lesions include simple cysts, post traumatic, post haemorrhagic and Echinococcal cysts. As in all organs, cysts appear anechoic on baseline US. Simple cysts are easy to characterise on baseline US. Cysts complicated by haemorrhage or infection may pose additional difficulty [25]. In this case, CEUS can be very helpful, since all cysts appear as well defined lesions with no enhancement whatsoever, including haemorrhagic or infectious debris, which is thus differentiated from solid components **(Fig. 1)**. In addition CEUS can help to differentiate simple cysts from necrotic tumours and abscesses, which usually show peripheral uptake [25].

8.2 Accessory spleen

An accessory spleen (*splenunculus*) is a common normal variant. It is in fact the most common perisplenic mass, found in 10-25% of the general population. The diameter of an accessory spleen is usually smaller than 1 cm, but can reach up to 5-6 cm. It is most commonly found around the midline of the spleen, near the hilum or in the lower part of the organ, showing the same echogenicity with the rest of the splenic parenchyma. Differential diagnosis includes parahilar lymph nodes, focal lesions of the adrenals, pancreatic tail mass and metastasis.

Post contrast injection, the enhancement pattern of an accessory spleen is the same as the splenic parenchyma **(Fig. 2)** [26]. In the early phase, the feeding artery which enters the accessory spleen may be seen originating from the splenic hilum towards the periphery [26]. In the late

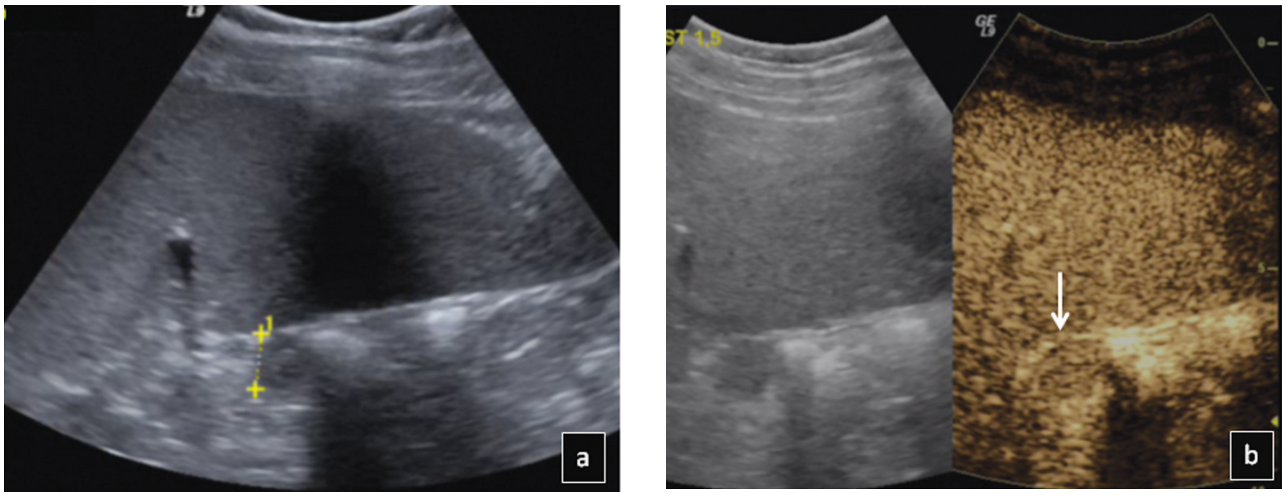


Fig. 2. *Accessory spleen: A solid lesion is located in the splenic hilum on B-mode US (a). Post contrast injection it enhances parallel to the spleen (arrow in b), a finding consistent with an accessory spleen. A lymph node would have a similar appearance on B-mode US, but would not enhance in the same manner on CEUS. Please compare to Fig. 3*

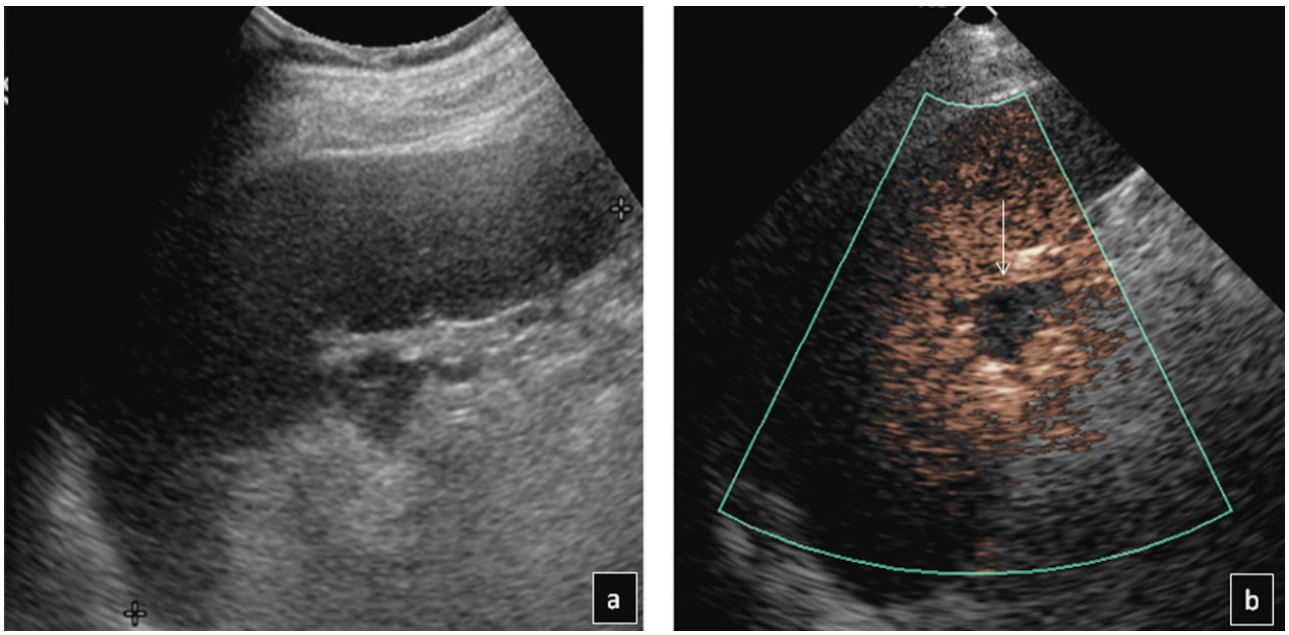


Fig. 3. *Lymph node: A solid lesion is located in the splenic hilum on B-mode US (a). Post contrast injection (b) it does not enhance (arrow). The finding represents a lymph node. An accessory spleen (with similar appearance on B-mode US) would enhance parallel to the splenic parenchyma post contrast injection*

phase, the accessory spleen retains the contrast agent and appears isoechoic to the rest of the organ. In comparison, the rest of the parahilar lesions (lymph nodes or lesions from the adrenals or pancreatic tail) do not present sustained enhancement in the delayed phase. Thus, a splenic hilum lymph node may appear similar to an accessory spleen on B-mode US but on CEUS does not enhance in the same way as the rest of the spleen **(Fig. 3)**. Therefore, CEUS answers this clinical question very easily, with no additional imaging needed for the patient.

The entity of accessory spleen is of special interest when it is located intrapancreatically. Although it is of no clinical significance and no treatment is needed, very often it is misdiagnosed as a tumour and patients are subjected to unnecessary surgery. CEUS has proved to be useful for the diagnosis of intrapancreatic accessory spleen, thus setting the diagnosis and sparing the patient an unnecessary operation [27].

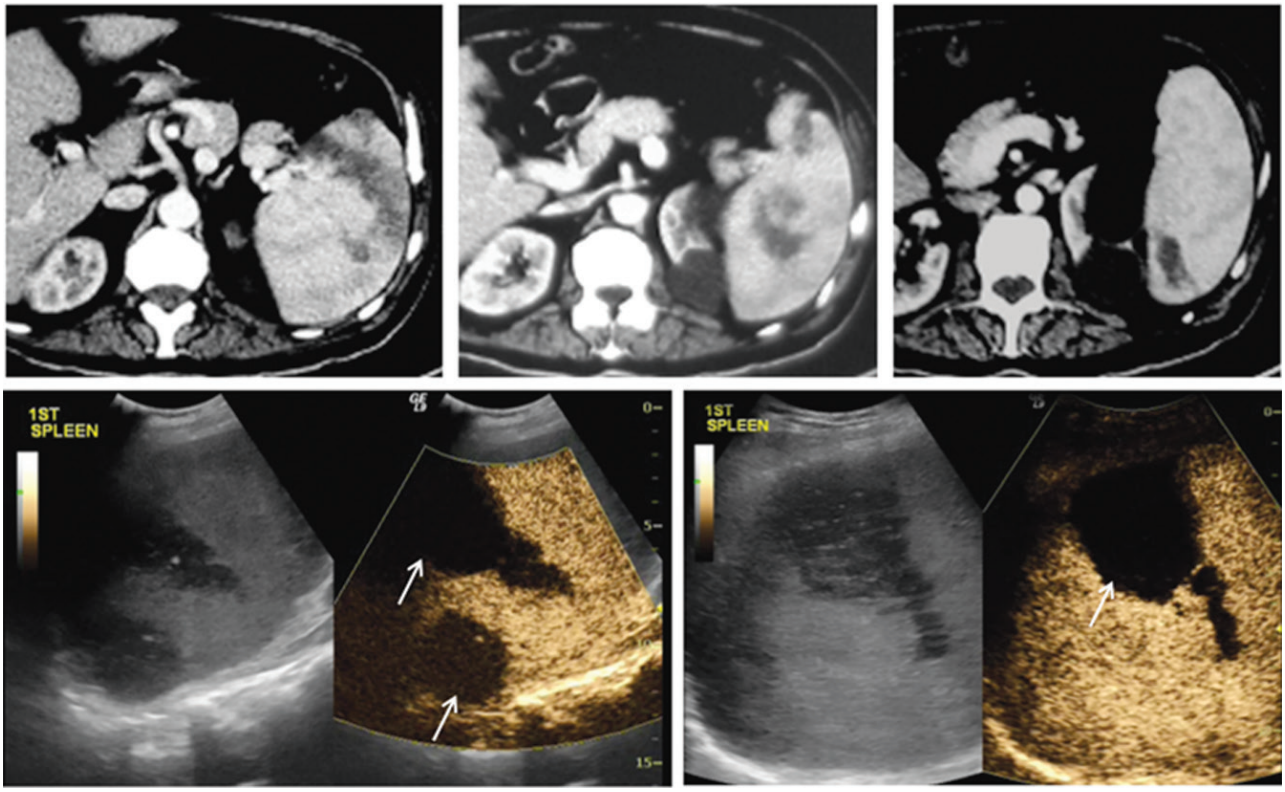


Fig. 4. *CECT shows multiple splenic infarcts. CEUS performed 1.5 month later confirms presence of the infarcts (arrows) with only slight reduction in their size. In this case, follow up was continued to be performed with CEUS and the patient was not subjected to additional CT scans, thus reducing ionising radiation exposure and cost. Note the round appearance of the smaller infarct. This is atypical but not uncommon. The lesion is safely characterised as an infarct on CEUS due to complete lack of enhancement. A malignancy would appear similar on B-mode US but would show some vascularity on CEUS*

8.3 Infarcts

Splenic infarction is one of the most common focal lesions of the spleen. On B mode US infarcts may have variable characteristics. Typically they show low echogenicity and wedge shaped outline [25], with their base directed towards the capsule and their point towards the hilum of the organ [10]. However, infarcts may also appear heterogeneous or mass like. Imaging with CEUS provides a very distinct form of a non-enhancing crescent shaped area on the surface of the spleen, with no enhancement and appearing as a defect throughout the examination [28, 29] **(Fig. 4)**. This is very useful for small infarcts that may be overlooked on baseline US but are safely characterised on CEUS **(Fig. 5)**. A more atypical appearance of an infarction is a nodular, round hypoechoic area. Absence of enhancement after injecting the contrast agent shows the lack of internal vascularity and guides the differential diagnosis towards benign, rather than malignant entities [18]. Occasionally, internal vessels may be seen in an infarcted area. They represent clot lysis with large recanalisation vessel reperfusion. These vessels appear smooth, regular and well demarcated, thus differentiating an infarct from a neoplastic lesion with irregular chaotic vessels [11].

8.4 Abscesses

Splenic abscesses are caused by Gram-negative or Gram-positive bacteria, while fungal abscesses are usually seen in immunosuppressed patients [25]. On B-mode US abscesses are usually hypoechoic with round or ovoid shape. Initially, when no fluid is present, they are ill-defined. When fluid or gas collections evolve, they become more obvious. Although bacterial abscesses are typically hypoechoic, mycotic abscesses in immunocompromised patients show lesions with a target-like or "wheels-within-wheels" characteristics [30].

On CEUS, no enhancement can be seen in the inner parts of the lesions that contain fluid **(Fig. 6)**. Peripheral rim and internal septa however may enhance [18], especially in the late phase. This imaging pattern is very

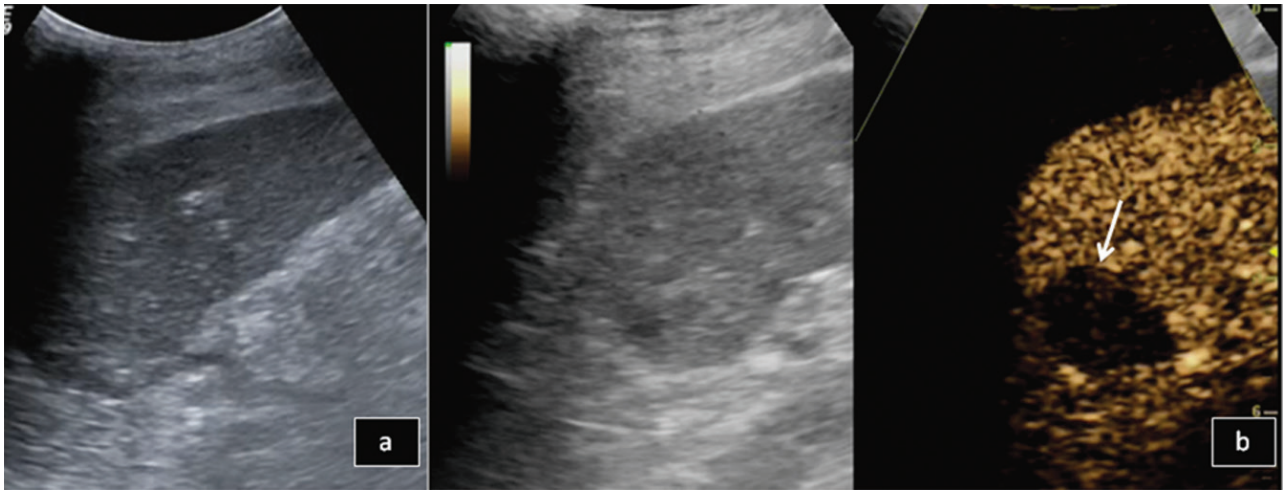


Fig. 5. *On B-mode US (a) no lesion is noted. However, due to left sided patient pain, CEUS was additionally performed. Post contrast injection a small infarct is clearly seen (arrow in b). CEUS obviously improved baseline US performance. The diagnosis of splenic infarct was confirmed by CT*

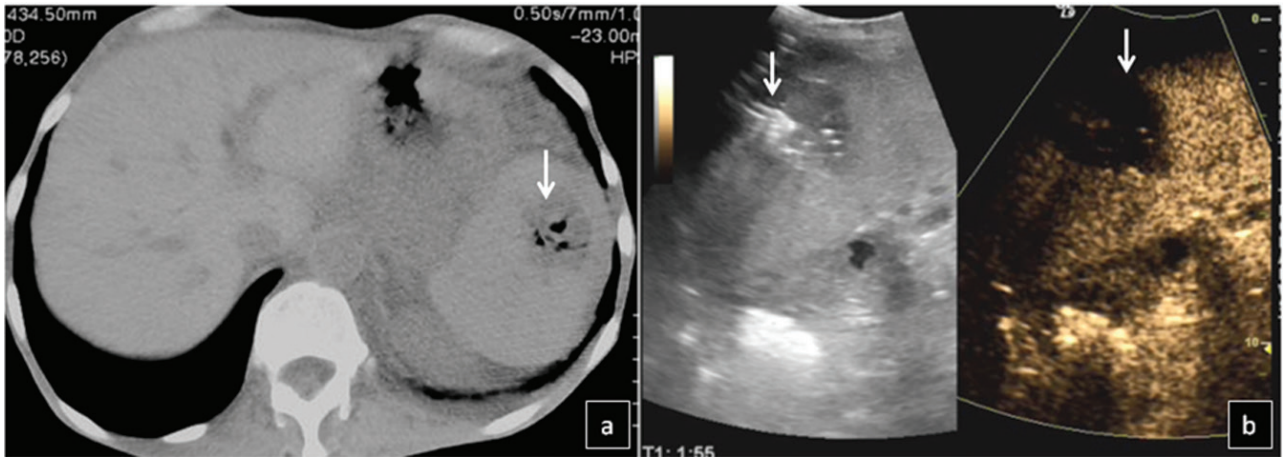


Fig. 6. *CECT shows a gas forming lesion, compatible with a splenic abscess (arrow in a). CEUS performed one week later for patient follow up shows that the abscess is still present: a filling defect is seen on CEUS (arrow in right side of b), while echogenic gas foci are still evident (arrows in left side of b) despite patient's treatment. No additional CT was performed. Follow up was performed only with CEUS*

useful in cancer patients who sometimes present with multiple small abscesses. These small abscesses are very difficult to differentiate from lymphoma or other malignancies, especially in the presence of central necrosis. Clinical correlation, histologic and microbiologic tests and repeat scanning post therapy of an abscess are useful in order to verify resolution and differentiate from neoplastic and inflammatory pathology [31, 32]. In this procedure of follow up, CEUS can be used instead of CT in order to reduce ionising radiation exposure for the patient.

8.5 Benign masses

Haemangiomas are the commonest primary splenic tumour [25]. They are echopoor or echogenic on baseline US. In the latter case, they appear quite similar to hepatic haemangiomas [28, 29]. Post contrast injection, haemangiomas enhance diffusely in the arterial phase [4] and retain contrast enhancement in the late phase, appearing isoechoic to the rest of the spleen, from which they may not be able to differentiate **(Fig. 7)**. If this typical appearance is observed on CEUS, the patient needs no additional imaging with CT [24]. Occasionaly, larger lesions may show arterial peripheral enhancement with centripetal or diffuse filling and dense prolonged enhancement, like in the liver. However this finding is not commonly seen in splenic haeman-

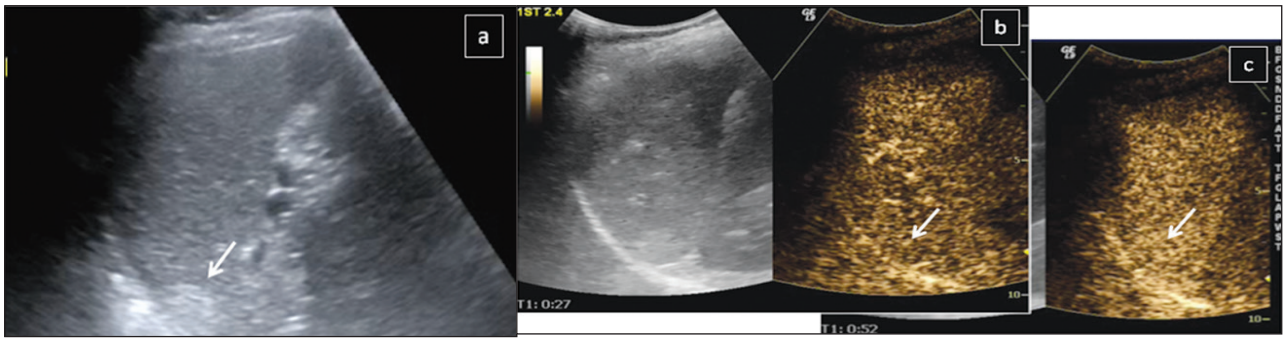


Fig. 7. *Haemangioma: An echogenic lesion is noted in the upper pole of the spleen on B-mode US (arrow in a). On CEUS this lesion enhances parallel to the rest of the splenic parenchyma in all phases (arrows in b: arterial phase and c: late phase). The lesion was characterised as a haemangioma on CEUS, a diagnosis which was not definitive on baseline US. Furthermore, no CT was performed and the patient was spared its ionising radiation exposure*

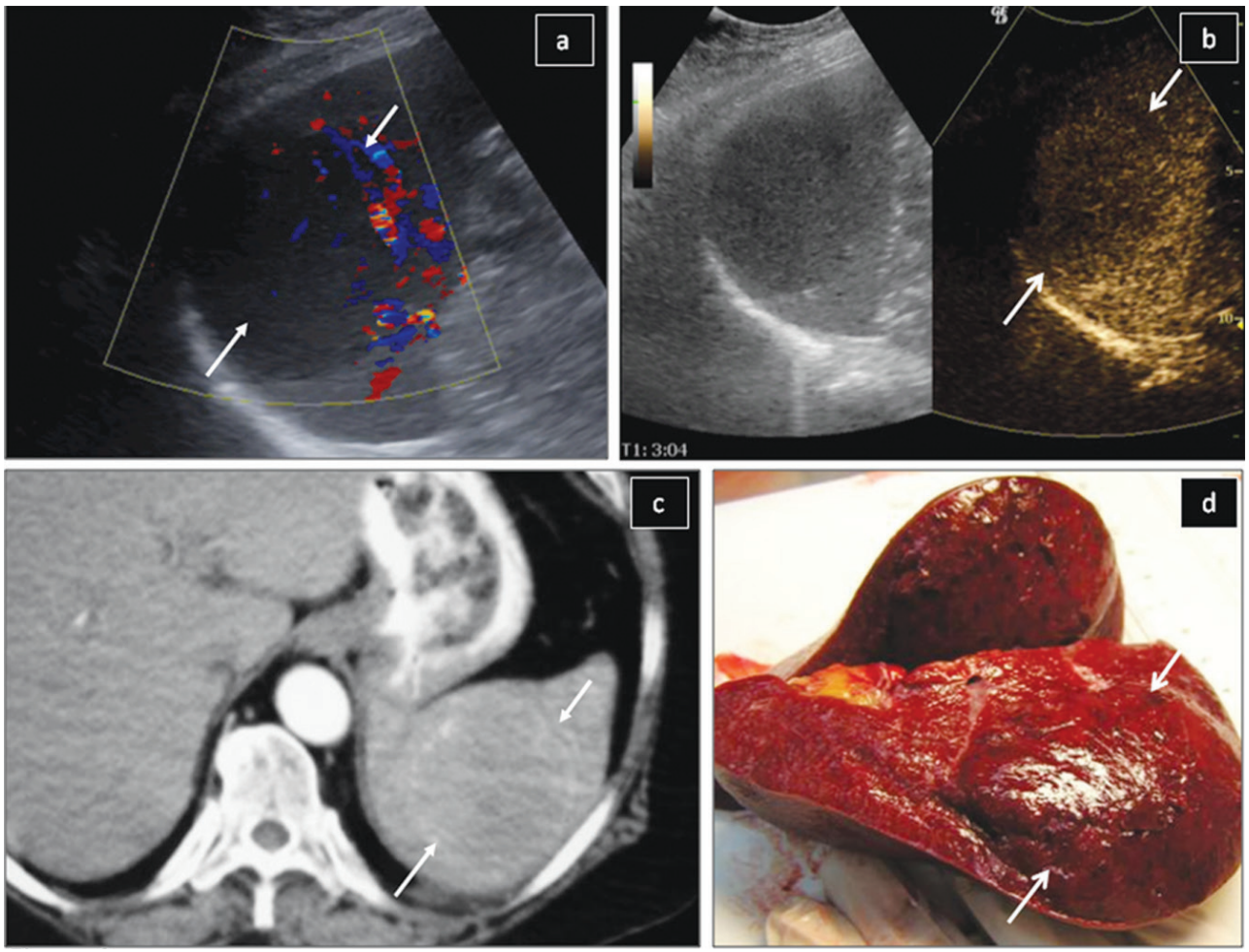


Fig. 8. *On colour Doppler US (a) there is suspicion of a large lesion in the upper part of the spleen (between arrows) with increased peripheral vasculature. Due to this finding CEUS was performed: a lesion is now definitely demarcated (b): there is slightly less internal enhancement compared to the rest of the spleen, with increased peripheral uptake. On CECT performed a day later (c), a lesion with the same features is confirmed. No additional information is offered and no diagnosis can be reached. Diagnosis after surgery was of an inflammatory splenic pseudotumour (arrows in d)*

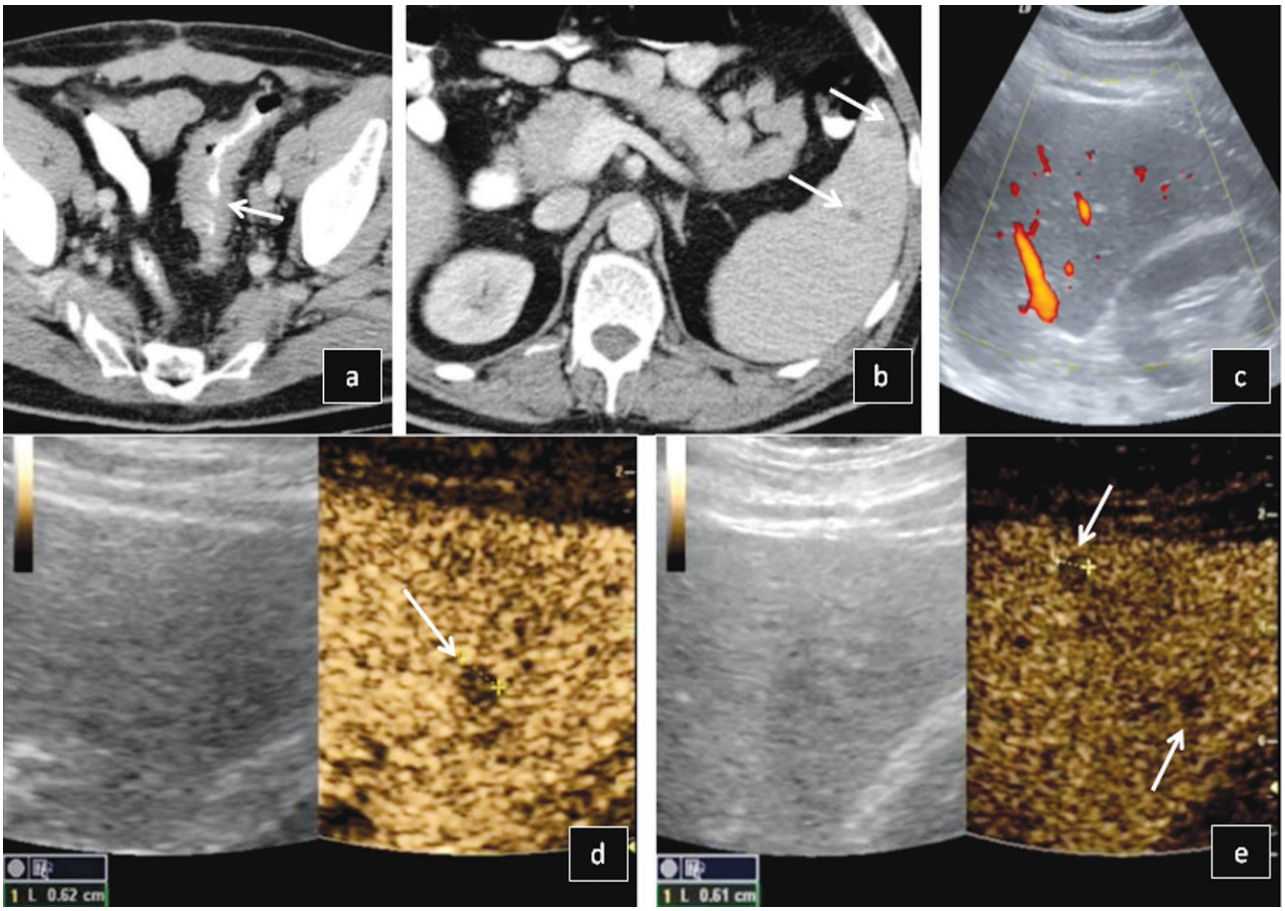


Fig. 9. *Littoral cell angioma: A patient with large bowel cancer (arrow in a) shows hypoattenuating lesions in the spleen on CECT (arrows in b), which were characterised as cysts. However, on Power Doppler US (c) performed on the next day no cystic or other types of lesions are seen and contrast agent was added in order to elucidate. On CEUS (d, e) filling defects (arrows) are noted. They do not show cystic characteristics (completely anechoic content, well defined border, posterior enhancement) on B-mode US and are suspicious of metastases. The spleen was removed and biopsy showed Littoral cell angioma of the spleen, an uncommon entity that cannot be differentiated from metastases preoperatively. In this case, although CEUS did not reach the final diagnosis, it changed the (false) CT characterisation of splenic cysts*

giomas [25]. Extensive, cavernous haemangiomas present with a more intense enhancement, either gradual or rapid, appearing in an either diffuse or afferent way. If they are of a substantial size, a posterior shadow may also be present [18]. Rarely haemangiomas may show late washout. This behaviour appears later than malignant lesion washout.

Inflammatory pseudotumours are uncommon. They can be difficult to detect both on B-mode US, as well as CT. On CEUS, the lesions are better demarcated and may be seen to enhance slightly less than the rest of the spleen in the central part, with increased peripheral enhancement **(Fig. 8)**. Other rare lesions, such as Littoral cell angioma, have atypical findings. They appear hypoechoic on baseline US. On CEUS they present as filling defects and cannot be differentiated from malignancies **(Fig. 9)**. Sarcoidosis of the spleen may appear as splenomegaly, with the addition of mulltiple small parenchymal nodules. These findings can be seen in 15% of patients with sarcoidosis [33]. On CEUS sarcoid lesions do not enhance in any phase [34] **(Fig. 10)**. However, the same appearance is seen in various entities, such as Carney complex tumours **(Fig. 11)**.

Hamartoma is a benign splenic mass originating from the red pulp and composed of an aberrant combination of normal splenic tissue in combination with cystic sinusoidal dilation [35]. It can be found in 0.13% of autopsies and its size is usually less than 3 cm [36]. On baseline US it usually appears hypoechoic, occasionally with cystic areas and hypervascular septa, or with inhomogeneous

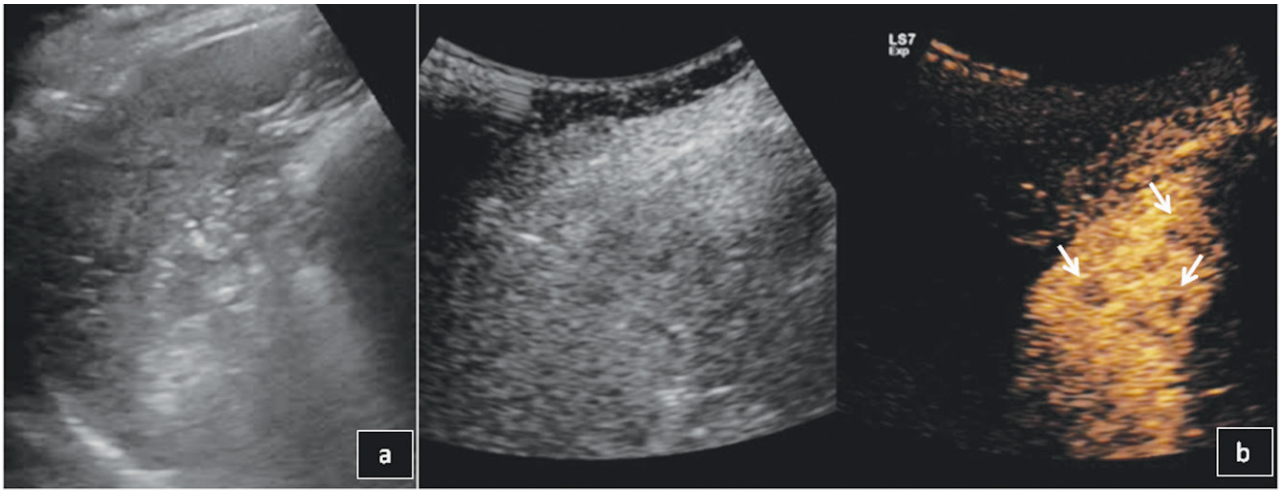


Fig. 10. *Sarcoidosis: B mode US (a) reveals inhomogeneous echogenicity and ill-defined hypoechoic lesions. In order to confirm detection of specific lesions CEUS was performed: these areas are now clearly demarcated (arrows in b), improving detection. However, characterisation of these lesions cannot be achieved only by CEUS image studying alone and studying of patient's relevant clinical and laboratory context is needed*

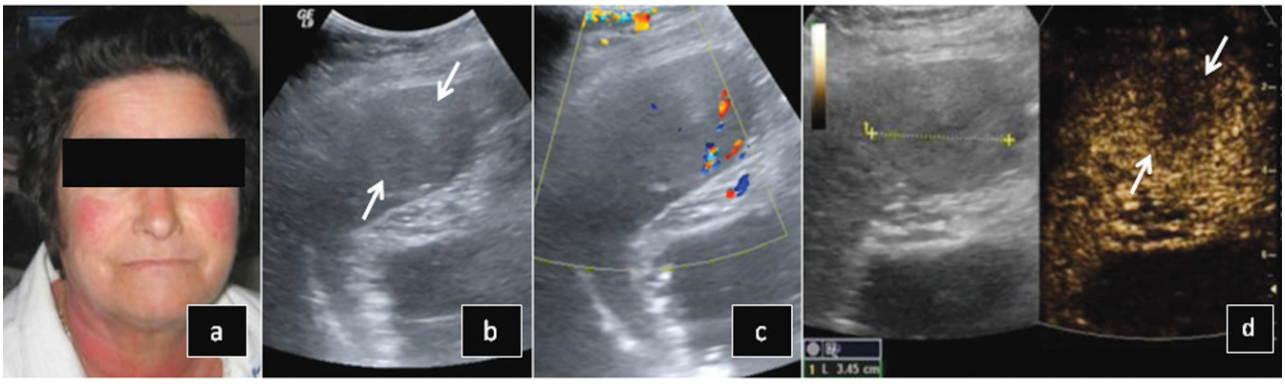


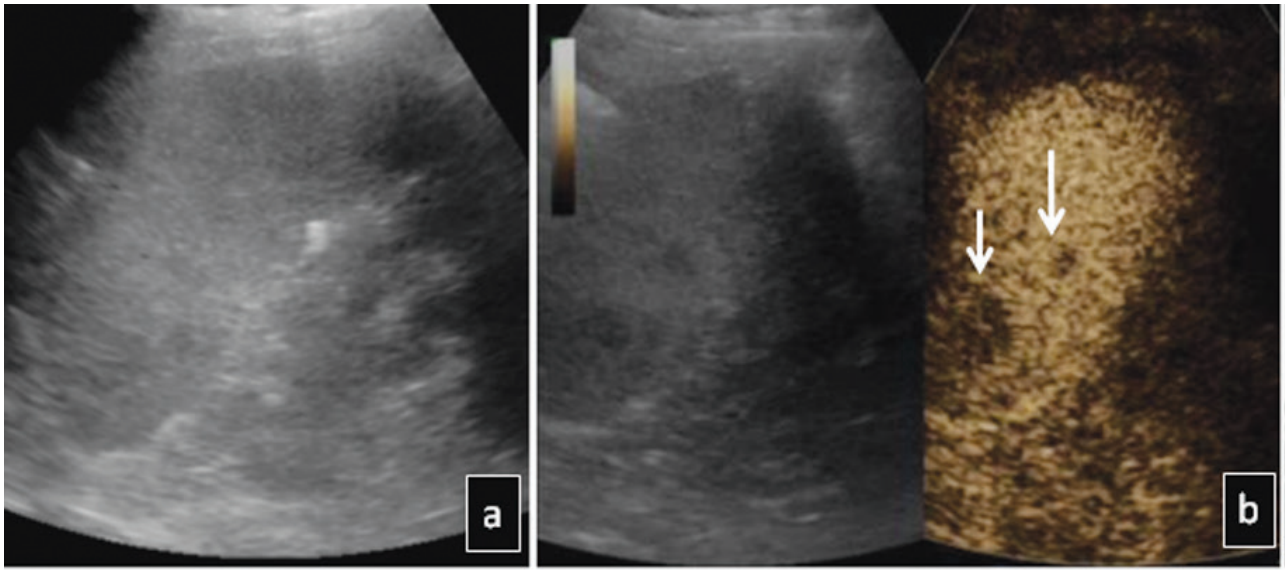
Fig. 11. *Carney complex: This is an autosomal dominant syndrome associated with spotty pigmentation of the skin (a), endocrinopathy, as well as endocrine and nonendocrine tumours. A hypoechoic splenic lesion (arrows) is suspected on B-mode (b) and colour Doppler (c) US. On CEUS (arrows in d) the lesion is better outlined and appears as a filling defect, suggestive of a hamartoma. Findings were confirmed on CT performed elsewhere a year later, where bilateral adrenal adenomas were also noted. Both adrenals were removed surgically due to Cushing syndrome, commonly associated with Carney complex. The patient also showed a frontal lobe brain meningioma, as well as bilateral breast fibroadenomas. Two and a half years after the CEUS examination, she was still being followed up and well in her health*

echogenicity. CEUS confirms the lesion's hypervascular areas, depicting strong homogeneous uptake followed by moderate washout [37]. Differential diagnosis of hamartoma with CEUS, CT and MRI can be difficult from angioma, metastasis, lymphoma and abscess [36]. However, CEUS has proved to improve differentiation between benign vascular and malignant lesions of the spleen, especially when a hypoechoic lesion is not clear on baseline US [38].

In all these benign entities, CEUS improves baseline US imaging by clearly demarcating lesions which were ill defined before contrast agent injection. However, although detection is improved with CEUS, lesion characterisation remains a challenge [18].

8.6 Malignant lesions

These mainly include lymphoma and haematogenous metastases. The spleen is involved in 30-40% of systemic lymphoma cases [25]. On B-mode US, this involvement may appear as small nodular lesions, large masses and infiltrative disease [39], isoechoic or hypoechoic in comparison to the rest of the spleen [28, 29]. On CEUS, lym-



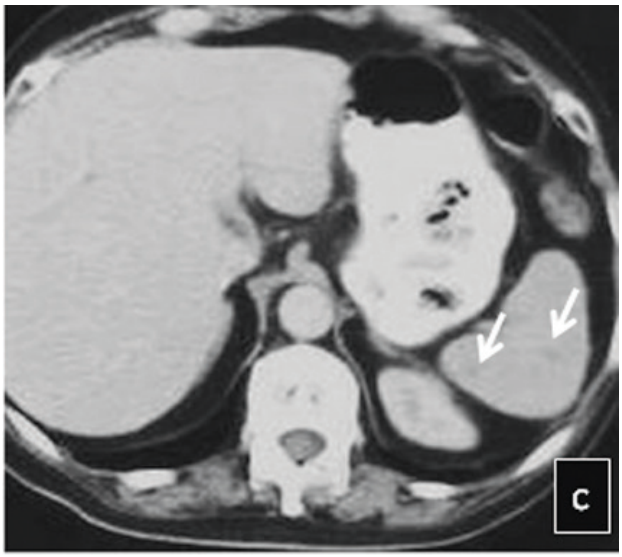


Fig. 12. *Non-Hodgkin lymphoma: On B-mode US (a) the spleen shows inhomogeneous echogenicity, but no definitive lesion, thus CEUS followed, revealing multiple filling defects (arrows in b). CECT performed subsequently confirms the splenic lesions (arrows in c). CEUS improved baseline US performance, by definitively detecting the splenic lesions, which were not evident before the contrast agent injection*

phomatous lesions may appear iso or hypoenhancing compared to the rest of the spleen [40] in the arterial phase. In the late phase, lesions are better demarcated and appear more hypoenahncing [8, 18] **(Fig. 12,13)**. As in benign lesions, lymphoma manifestations may not be well defined on baseline US and are better appreciated after the injection of the contrast agent.

Splenic metastases appear more frequently secondary to lung cancer, breast cancer and melanoma [41]. It can be difficult to differentiate lymphoma from haematogenous metastases on plain US, as well as on CEUS. Post contrast injection, metastases initially enhance slightly less or similar to the rest of the spleen, followed by rapid washout [25]. Enhancement can be observed in a disorderly or homogeneous way. Sometimes the vessels surrounding the lesion can enter from the periphery towards the center [26]. In case of necrotic malignant tissue, there is no enhancement whatsoever in any phase of the enhancement. Post chemotherapy, the lesions may become anechoic with no enhancement in the periphery or the center. Occasionally, it may be difficult to differentiate a necrotic lesion from an abscess, especially since an immunosuppressed patient has high risk of showing either one of these lesions with target appearance. In our experience we have seen cases were inhomogeneous echogenicity on baseline US is followed by clear filling defects on CEUS due to splenic metastases, which would otherwise be missed **(Fig. 14)**. This is important for patients with isolated splenic metastases, where splenectomy is indicated. In addition, when metachronnous metastases are pres-

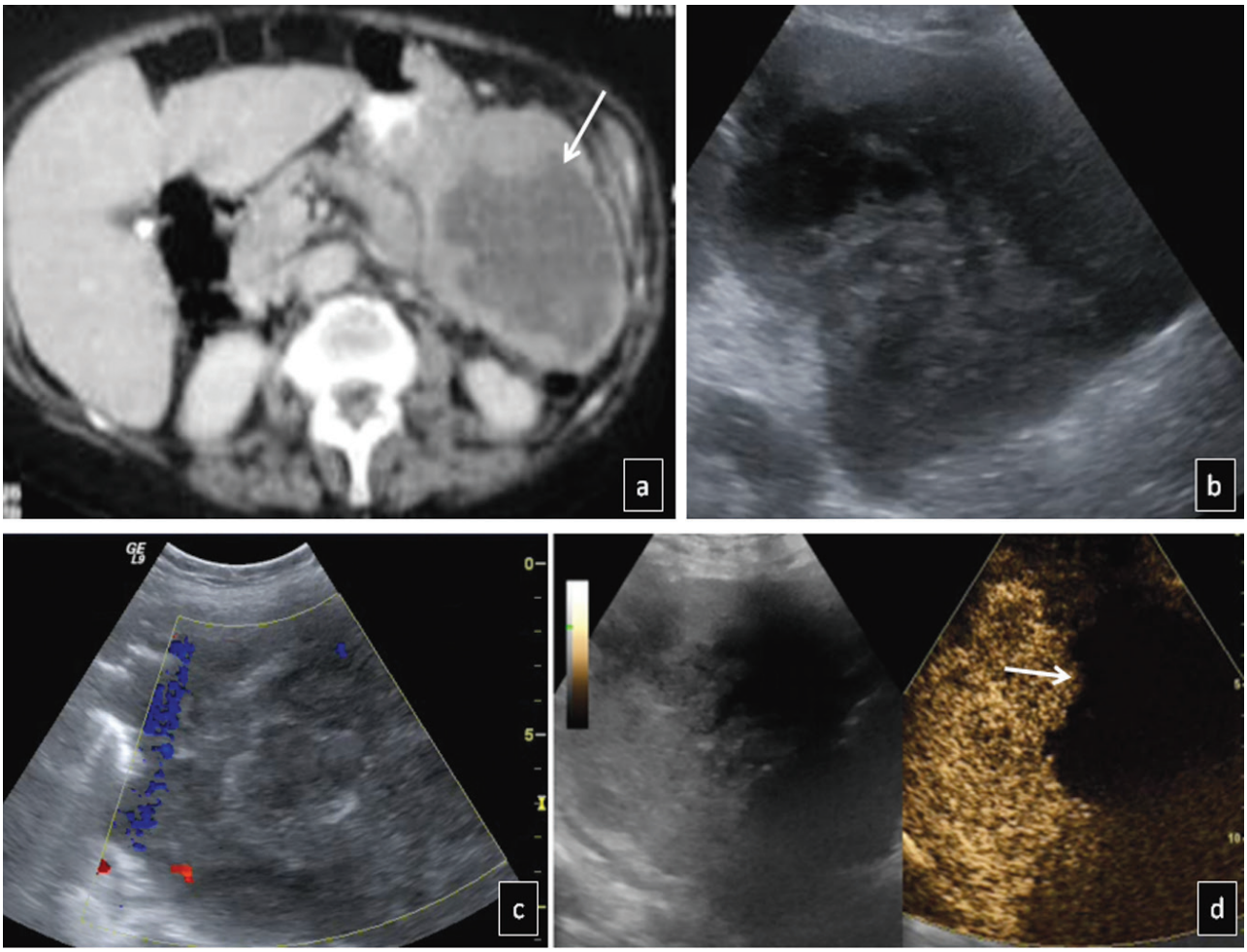


***Fig. 13**. Gastric lymphoma extends towards the spleen on CECT (arrow in a) performed in an outside institution. A week later, a new US examination is requested in order to assess the amount of splenic involvement. The spleen shows inhomogeneous echogenicity on B-mode US (b), while colour Doppler (c) is not helpful for evaluating splenic vasculature and dissemination by the disease. On CEUS (d), about half of the spleen is seen as a filing defect, representing the extent of splenic lymphomatous involvement (arrow), which was not evident before contrast injection*

ent, splenectomy is also appropriate for the removal of all neoplastic tissue and avoiding splenic rupture [42, 43].

8.7 Trauma

The spleen is a common site of abdominal trauma. Perisplenic fluid, subcapsular haematoma and free fluid in any part of the abdomen can suggest splenic contusion, laceration or rupture. Despite these points, splenic injuries can be missed on baseline US, since they are commonly ill-defined and have variable echogenicity, depending on the time of imaging after the patient's trauma. However, the presence of fluid should always raise the question of trauma in a relevant clinical context.

CEUS is invaluable for revealing traumatic lesions which may be overlooked on baseline US. Post contrast injection, traumatic areas show no uptake, especially in the late phase of enhancement. Contusions are ill-defined and hypoechoic, while lacerations are seen as clearly hypoechoic bands, usually perpendicular to the spleen surface [18]. Haematomas become completely anechoic, and therefore pathological areas are clearly delineated. Special care should be taken to differentiate between trauma and the splenic vein tree, appearing hypoechoic in the late phase of enhancement. Fluid collections may be seen around the spleen and are better appreciated on CEUS compared to baseline US. Splenic trauma severity is evaluated according to a CT-based grading system which is based on the American Association for the Surgery of Trauma (AAST) scale [44, 45]. This includes five different injury scales, as follows:

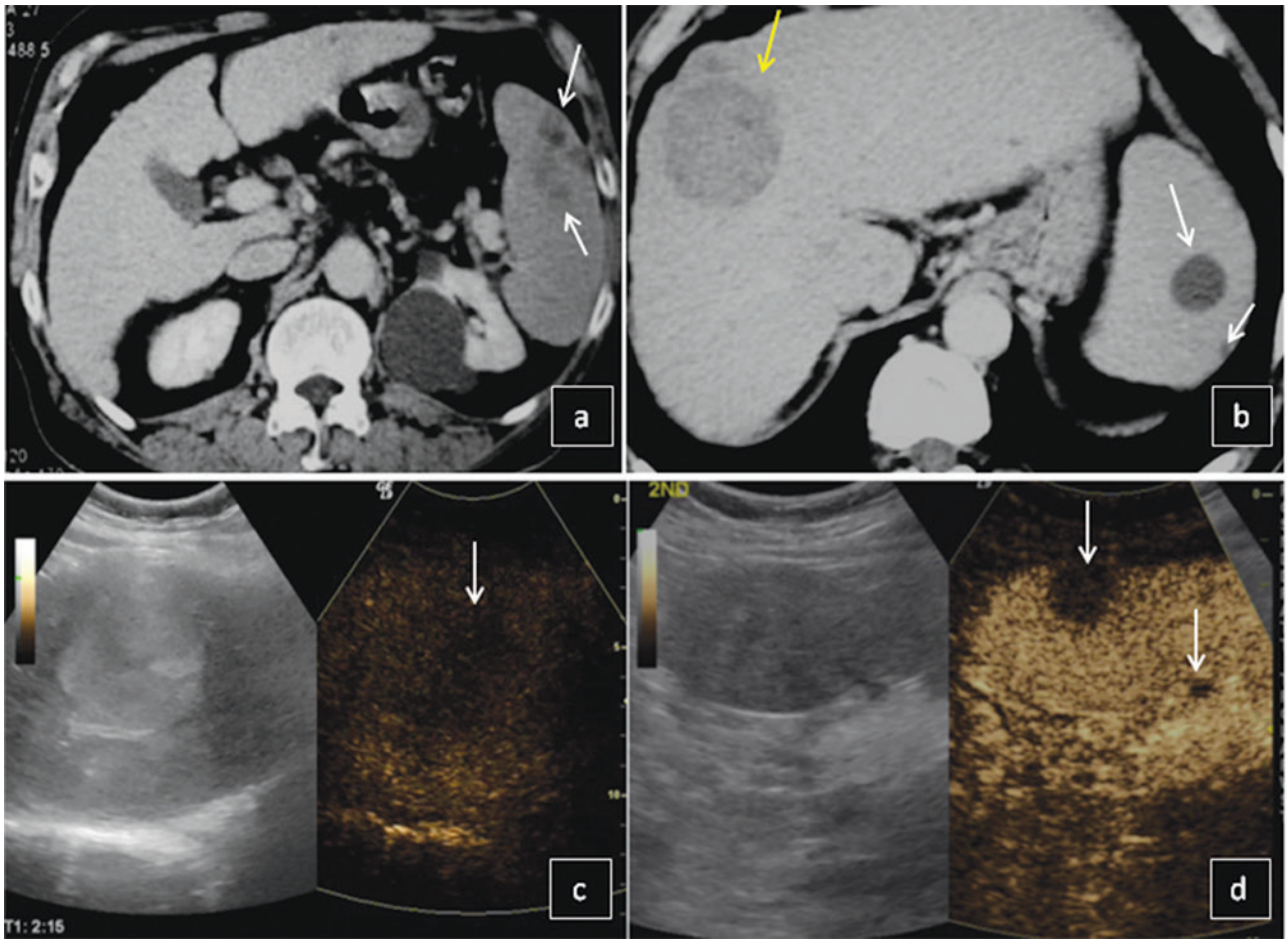


Fig. 14. *Splenic metastases: An outside CECT (a, b) shows multiple uncharacterised splenic lesions (white arrows) and a known hepatocellular carcinoma (HCC-yellow arrow). The patient presents in our Hospital a month later. In order to avoid a second CT scan, CEUS is performed. The diagnosis of HCC is confirmed, showing late phase washout (arrow in c). The splenic lesions present as filling defects on CEUS (arrows in right side of d), which however are not evident on baseline US (left side of d). In this clinical context, the splenic lesions are consistent with metastases. The addition of the US contrast agent enabled sonograhic confirmation of splenic lesions, which were not seen before the injection*

- **Grade I:** Subcapsular haematoma <10% of surface area-capsular laceration <1 cm depth
- **Grade II:** Subcapsular haematoma 10-50% of surface area-intraparenchymal haematoma <5 cm in diameter-laceration 1-3 cm in depth not involving trabecular vessels
- **Grade III:** Subcapsular haematoma >50% of surface area or expanding-intraparenchymal haematoma >5 cm or expanding-laceration >3 cm in depth or involving trabecular vessels-ruptured subcapsular or parenchymal haematoma
- **Grade IV:** Laceration involving segmental or hilar vessels with major devascularisation (>25% of spleen)
- **Grade V:** Shattered spleen-hilar vascular injury with splenic devascularisation.

CEUS has ben reported to have very good concordance with CT for detecting and grading splenic trauma [46]. In our practice, we always perform CEUS for solid abdominal organ injuries when trauma victims show fluid collections. Injuries detected on CEUS have practically always been confirmed on CECT. Furthermore, we have had patients with splenic rupture that were successfully operated upon immediately without waiting for preoperative CT confirmation **(Fig. 15)**. This is extremely helpful for an unstable patient with no time to be spared for CT. Finally, even if the patient undergoes an initial CT, subsequent follow up of small injuries that were treated conservatively can be performed with CEUS, thus minimising ionising radiation exposure. This practice is in accordance with the EFSUMB Guidelines, which recom-

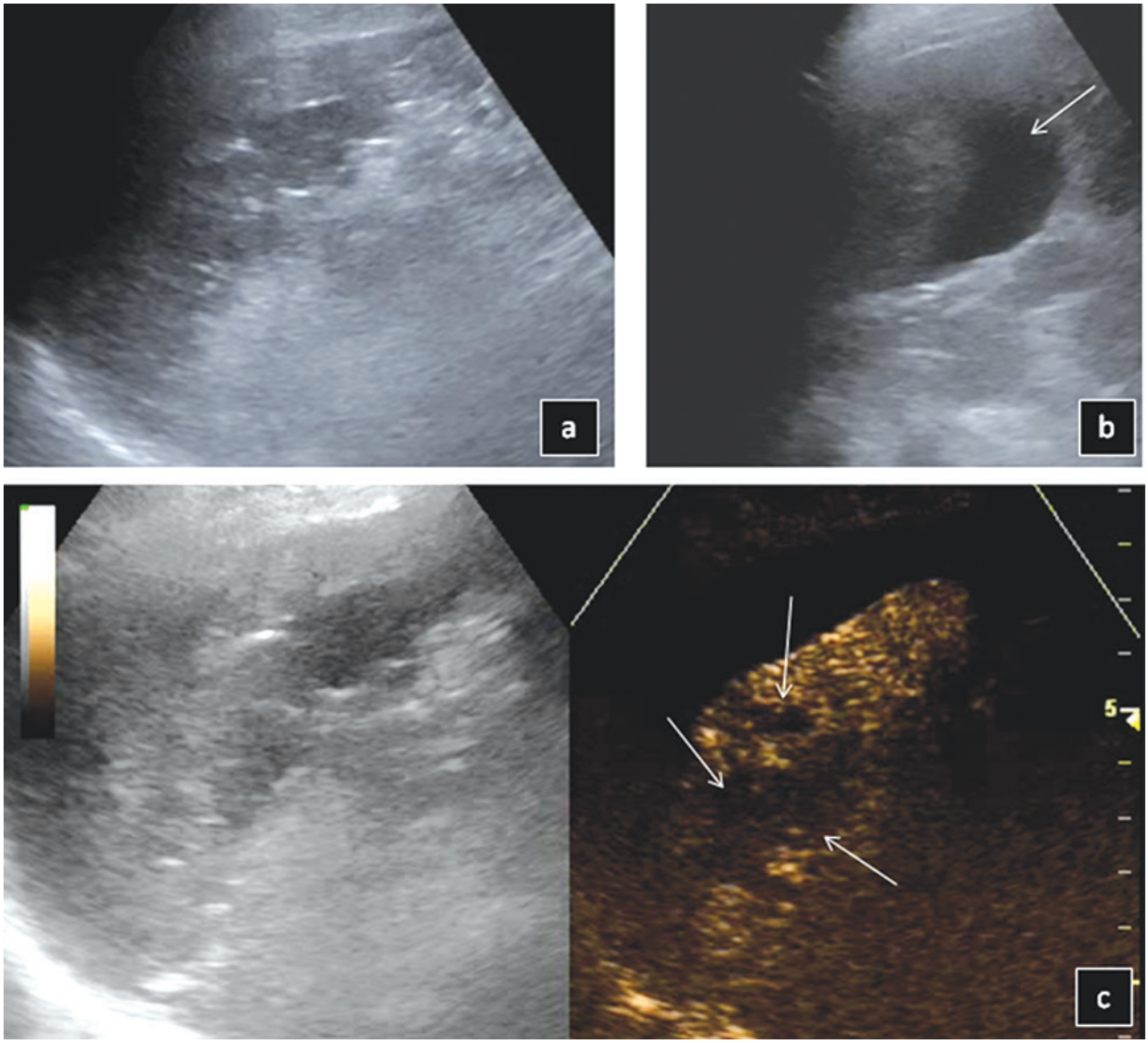


Fig. 15. *Road accident victim with splenic rupture: On baseline US inhomogeneous echogenicity is noted (a) as well as perisplenic fluid collection (arrow in b). Splenic trauma is suspected, therefore CEUS follows. Post contrast injection, enhancement defects are clearly demarcated extending in both sides of the spleen (arrows in c), consistent with splenic rupture (Grade IV injury). The haemodynamically unstable patient was operated upon immediately, without a preoperational CECT. Splenic rupture, a diagnosis which was not definitive on B-mode US, was confirmed in the operating room*

mend CEUS for follow-up of trauma patients with conservative treatment, thus reducing the number of CT scans or increasing confidence in situations where a CT scan is not strictly required [17].

9. CEUS in paediatric imaging

The advantages of CEUS, already established in adults, make this technique even more useful in the paediatric population: Repeatability, good tolerance and safety profile, as well as minimising CT scanning with the related ionising radiation [47], make CEUS an ideal imaging technique for children. Until recently, the role of CEUS for children imaging worldwide has been peculiar, with SonoVue being used in an off-label manner [17]. It was only until very recently that the same drug was approved for adult and paediatric use in the United States (where it is commercially named Lumason) but specifically for the assessment of focal liver lesions only [48]. Therefore, the use of CEUS for splenic pathology in children still remains off-label.

In adults many off-label applications are supported by clinical experience and evidence [48] and the same applies for paediatric CEUS. In this field there is mounting evidence for its usefulness, mainly as an imaging technique that reduces ionising radiation exposure and iodinated contrast medium use and increases the use of a "patient-friendly" modality like ultrasonography [48]. Especially in the early imaging assessment of children undergoing low energy trauma, CEUS is very useful, with sensitivity comparable to CT [49].

Our Institution handles only adult patients and occasionally treats children between 14 and 18 years old. Although we have not performed CEUS in this population so far, an informed consent from the parents after the advantages of CEUS, including reducing CT radiation exposure, have been explained, seems like a logical approach before performing the examination in children.

10. CEUS limitations

Inherent limitations of baseline US, such as decreased ability to image the lower pole and subphrenic parts of the spleen, persist into CEUS. If an area is not adequately visible on unenhanced US, the addition of contrast will not facilitate this problem. Moreover, the majority of splenic lesions are hypovascular and hypoechoic after contrast injection. Although it is not always possible to directly characterise a lesion with CEUS, the resuling increased detectability can facilitate its fine needle aspiration, as the lesion appears better demarcated post contrast injection. Thus, characterisation rate can also be eventually increased.

11. Conclusion

US contrast agents are very useful in every day practice, adding information on lesion nature and demonstrating real time perfusion in a short period with no radiation. The addition of contrast agents improves detection of splenic pathology. Characterisation is also improved, however not in the same degree as in hepatic CEUS. CEUS is very useful for detecting small splenic infarcts, which on plain US may be missed quite easily. It can also differentiate a splenic mass from an infarct, as well as image the benign features of a splenic cyst with unclear borders or inhomogeneous content. On the other hand, differentiating an abscess from necrotic lymphomatoid tissue or metastases is still a challenge for CEUS, as these are all frequent in cancer patients and have similar appearances. In these cases follow up or additional investigation of the patient may be needed. CEUS is very useful for setting a straight forward diagnosis, such as haemangioma, accessory spleen or traumatic contusion, thus reducing CT scanning for the patient. In addition, even if a CT scan is initially performed, the patient can subsequently be followed with CEUS, with no additional CT examinations. **R**

Conflict of interest:
Demosthenes Cokkinos has given an honorary lecture for Bracco Suisse SA

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